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ԲԱՆԲԵՐ ՍՏՈՄԱՏՈԼՈԳԻԱՅԻ ԵՎ ԴԻՄԱԾՆՈՏԱՅԻՆ ՎԻՐԱԲՈՒԺՈՒԹՅԱՆ
Գիտագործնական հանդես

Գլխավոր խմբագիր - Հակոբյան Գ.Վ.
Գլխավոր խմբագրի տեղակալ-
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ORIGINAL ARTICALE

CLINICOPATHOLOGICAL STUDY OF ODONTOGENIC CYSTS AND TUMORS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Odontogenic lesions that include cysts and tumors constitute less than 2-3% of all the oral and maxillofacial lesions. Odontogenic cysts and tumors originate from tooth apparatus or its remnants.

Objectives: To determine the frequency and clinicopathological characteristics of odontogenic tumours**:** This study aimed to evaluate the role of CTA in diagnosing CHD and to compare the diagnostic accuracy of TTE and CTA.

Materials and Methods*:* Cross-sectional study, Department of Pathology. The clinicopathological details were retrieved over the period of nine years from January 2013 to December 2021. Data were tabulated and analysed for any significant association among the clinicopathological variables.

Results*:* In the present study, among the total 149 cases, 113 cases (75.8%) were odontogenic cysts and 36 cases (24.2%) were odontogenic tumors. The most common age group involved was 20-40 years (64.4%) and the male:female (M:F) ratio was 1.4:1. Right mandible (32.2%) was the predominant site involved followed by left maxilla (24.2%). The average size of odontogenic cysts was 1.5cm whereas the mean size of odontogenic tumors was 2.8cm. Periapical cyst (70.8%) was the commonest odontogenic cyst while ameloblastoma (36.1%) was the frequent odontogenic tumor. There was statistically significant association of lesion size with age of patients (p-value 0.002), gender (p-value 0.023), histopathological nature of odontogenic lesions (p-value- 0.010) and histopathological subtypes of odontogenic tumors (p-value 0.042).

Conclusion: The present study provides insights into the clinicopathological characteristics and association of various clinicopathological parameters with size of the odontogenic lesions, thereby facilitating early diagnosis and management of this diverse group of odontogenic lesions.

Keywords: Odontogenic lesions, Periapical cyst, Ameloblastoma, mandible, maxilla

\INTRODUCTION

Odontogenic lesions that include cysts and tumors account for less than 2-3% of all the oral and maxillofacial lesions.[1] The World Health Organisation (WHO) Collaborating Centre for the histological classification of odontogenic tumors and allied lesions was established in 1966 by the department of oral pathology that was universally adopted by 1969. Two years later, in 1971, WHO had published the first authoritative and useful guide to the classification of odontogenic tumors, cysts and allied lesions authored by Pindborg and Kramer.[2] A second edition entitled:

Histological Typing of Odontogenic Tumours appeared in 1992, twenty years later.[3]

The embryogenesis of teeth involves a complex interaction between connective tissue elements (odontogenic ectomesenchyme) and specialized epithelial cells. For each tooth, a group of epithelial cells (dental lamina) proliferates downward from the surface mucosa into the developing alveolar bone to form the enamel organ. This epithelium induces the differentiation of ectomesenchymal cells which form the central dental papilla and surrounding connective tissue follicle. Enamel formation is mainly dependent on specialized epithelial cells (ameloblasts) from the enamel organ. The dental papilla is destined to become the tooth pulp and gives rise to the odontoblasts which form the dentin of the tooth. Later in tooth formation, cells from the surrounding dental follicle differentiate into cementoblasts to form a thin layer of bone-like cementum on the outer root surface. [4]

Odontogenic lesions include a complex and broad spectrum of non-neoplastic cystic lesions to neoplastic odontogenic tumors developing from the various complex structures of the tooth. Odontogenic cysts may arise de novo or from stimulation of epithelial remnants by odontogenic infections. Tumors of odontogenic origin may develop from the epithelial cells, ectomesenchymal component, or combination of both.[4] The latest WHO Classification 2023 had classified the odontogenic lesions into cysts of jaw and odontogenic tumors.[5] The present study was designed to determine the frequency and clinicopathological characteristics of the various odontogenic lesions encountered among the patients in a tertiary care hospital.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval (KIMS/F/2022/17), the following cross-sectional study was conducted in department of pathology based on laboratory records. The clinicopathological data of all the odontogenic cysts and tumors reported from January 2013 to December 2021 were collected including variables like patients' age, gender, lesion site, gross size and histopathological diagnosis. All the odontogenic lesions were categorised into two groups based on the gross size cutoff value of 3cm according to the study based on WHO Head and Neck tumors classification by Monteiro L et al.[6] The mean size of odontogenic lesions (cysts and tumors) was 3.3cm in the study by Monteiro L et al.[6] The data was plotted in Microsoft excel and analyzed using chi-square test with SPSS software version 25.

RESULTS

In the present study, total 149 cases have been included as per inclusion and exclusion criteria with predominant age group of 20-40 years (64.4%) and mean age of 32 years. Among the 149 cases, 58.4% were males and 41.6% were females with M:F ratio of 1.4:1 [Table 1].

The site distribution of odontogenic cysts and tumors showed 32.2% of cases in right mandible, 24.2% of cases in left maxilla, 22.1% of cases in left mandible and 21.5% of cases in right maxilla. Based on histopathological examination, among the total 149 odontogenic lesions encountered in this study, 75.8% cases were classified as odontogenic cysts and 24.2% cases as odontogenic tumors. The size of odontogenic cysts ranged from 0.1cm to 2.5cm with the average size of 1.5cm while the size of odontogenic tumors ranged from 0.1cm to 7cm with the mean size of 2.8cm. Around 69.8% of odontogenic lesions were less than 3cm in size grossly in the present study [Table 1].

Table 1. Descriptive statistics of the study variables

Study Variables	Frequency (n = 149)	%
Gender		
Males	87	58.4
Females	62	41.6
Age		
< 20 years	18	12.1
20 – 40 years	96	64.4
>40 years	35	23.5
Site distribution		
Right Mandible	48	32.2
Left Mandible	33	22.1
Right Maxilla	32	21.5
Left Maxilla	36	24.2
Histopathological Diagnosis		
Odontogenic cysts	113	75.8
Odontogenic tumors	36	24.2
Gross Size of the lesion		
≥3cm	45	30.2
< 3cm	104	69.8

The histopathological distribution of odontogenic cysts and tumors revealed a spectrum of lesions in the present study with periapical cyst (70.8%) being the most common odontogenic cyst while ameloblastoma (36.1%) being the most common odontogenic tumor. The other odontogenic cysts were dentigerous cyst (17.7%), odontogenic keratocyst (5.3%), residual cyst (5.3%) and glandular odontogenic cyst (0.9%). The other odontogenic tumors encountered in this study were cemento-ossifying fibroma (19.4%), calcifying epithelial odontogenic tumor (13.8%), odontogenic fibroma (11.1%), calcifying cystic odontogenic tumor (5.6%), odontoma (5.6%), ameloblastic fibroma (2.8%), adenomatoid odontogenic tumor (2.8%) and ameloblastic carcinoma (2.8%) [Table 2, Figure 1- 7].

Table 2. Histopathological distribution of Odontogenic cysts and tumor

Odontogenic lesions				
S.No	**Odontogenic Cysts (n=113)**		**Odontogenic Tumors (n=36)**	
	Histopathological type	**n (%)**	**Histopathological type**	**n (%)**
1.	Periapical cyst	80 (70.8%)	Ameloblastoma	13 (36.1%)
2.	Dentigerous cyst	20 (17.7%)	Cemento-ossifying fibroma	7 (19.4%)
3.	Odontogenic keratocyst	6 (5.3%)	Calcifying epithelial odontogenic tumor	5 (13.8%)
4.	Residual cyst	6 (5.3%)	Odontogenic fibroma	4 (11.1%)
5.	Glandular Odontogenic cyst	1 (0.9%)	Calcifying cystic odontogenic tumor	2 (5.6%)
6.	-	-	Odontoma	2 (5.6%)
7.	-	-	Ameloblastic fibroma	1 (2.8%)
8.	-	-	Adenomatoid odontogenic tumor	1 (2.8%)
9.	-	-	Ameloblastic carcinoma	1 (2.8%)

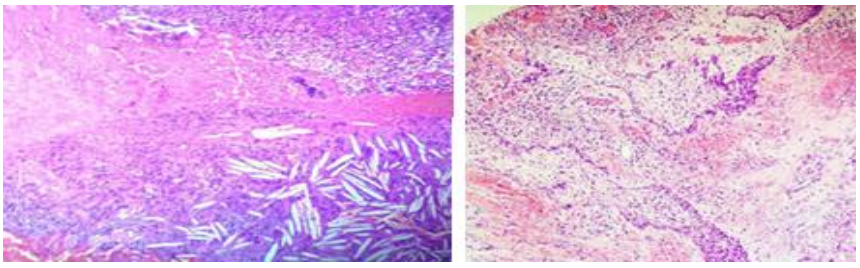


Figure 1. Periapical cyst: Cyst wall with underlying stroma shows lymphocytes, plasma cells and cholesterol clefts (H&E stain 10x).

Figure 2. Dentigerous cyst: Cyst wall lined by odontogenic epithelium containing lymphocytes and congested blood vessels (H&E stain 10x).

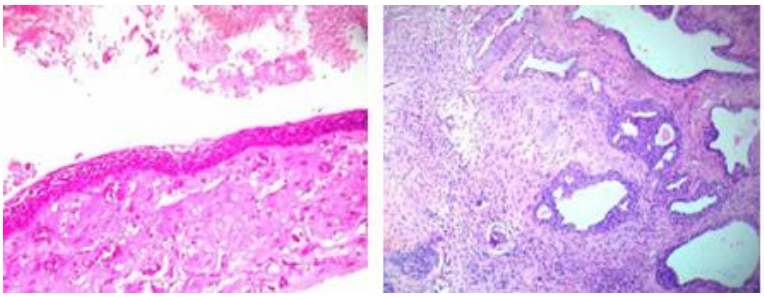


Figure 3. Odontogenic Keratocyst: Cyst wall lined by stratified squamous epithelium enclosing lamellar keratinous debris (H&E stain 10x).

Figure 4. Glandular odontogenic cyst: Multilocular cyst wall lined by flattened to stratified squamous epithelium with intraepithelial microcysts surrounded by lymphocytes (H&E stain 10x).

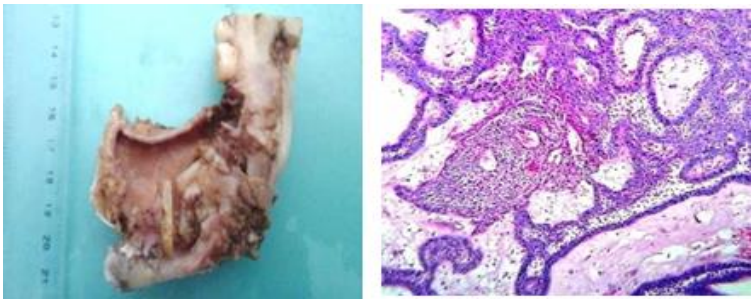


Figure 5: 5a) Hemimandibulectomy specimen showing unicystic ameloblastoma (Gross)
Figure 5:5b) Follicular type ameloblastoma: Tumor arranged in follicles with stellate reticulum (H&E stain 10x)

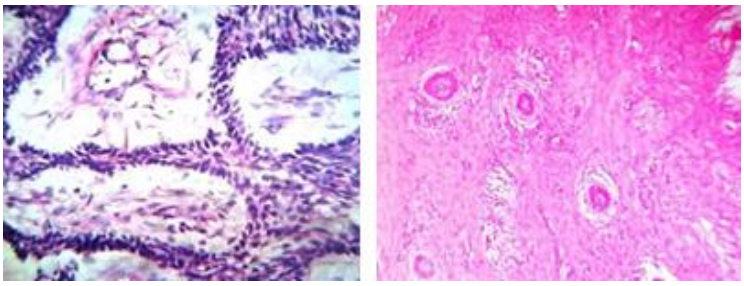


Figure 5:5c) Follicular type ameloblastoma: Follicles with peripheral nuclear palisading. (H&E stain 40x)
Figure5: 5d) Desmoplastic type ameloblastoma: Islands of tumor cells in a collagenous stroma (H&E stain 10x)

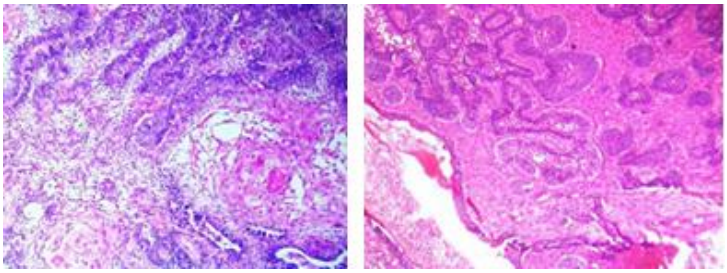


Figure 5: 5e) Acanthomatous type ameloblastoma: Showing squamous metaplasia and keratinisation of stellate reticulum (H&E stain 10x).

Figure5: 5f) Plexiform type ameloblastoma: Showing anastomosing cords of odontogenic epithelium (H&E stain 10x).

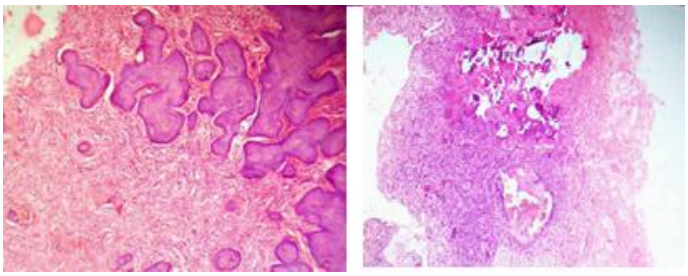


Figure 6 Cemento-ossifying fibroma: Cementum and bony trabeculae with osteoblastic rimming in a fibrous stroma (H&E stain 10x).

Figure 7 Calcifying cystic odontogenic tumor: Cyst wall lined by odontogenic epithelium with small foci showing calcification (H&E stain 10x).

In this study, the association between size of the odontogenic lesions and various clinicopathological variables including patients' age, gender, site distribution and histopathological subtypes was statistically analyzed. Among all patients more than 20 years of age in this study, the gross size of odontogenic cysts and tumors were predominantly less than 3cm with 73.1% of them occurring in the 20-40 years age group. Thus there was a statistically significant association observed between gross size of the lesion and patients' age group in the present study (p-value 0.002). In the present study, the gross size of the odontogenic lesions were predominantly less than 3cm in both gender with 64.4% of them occurring in males and 35.6% in females. Thus there was a statistically significant correlation between gender and gross size of odontogenic lesions (p-value 0.023) [Table 3].

Analysing the gross size of odontogenic lesions in relation to their site distribution revealed that majority of the lesions were less than 3cm in size in all the four sites with 34.6% of the lesions involving the right mandible followed by 25% of the lesions in right maxilla. However, there was no significant association between site distribution and gross size of the odontogenic lesions in the current study (p-value 0.156) [Table 3].

Table 3. Association between size of odontogenic lesions and clinical variables

Clinical Variables	**Size of the Odontogenic lesions**		**Chi-square test**
	≥ 3cm (n = 45)	**< 3cm (n = 104)**	
Age			
< 20 years	10 (22.2%)	8 (7.7%)	p-value 0.002
20 – 40 years	20 (44.5%)	76 (73.1%)	
> 40 years	15 (33.3%)	20 (19.2%)	
Gender			
Males	20 (44.4%)	67 (64.4%)	p-value 0.023
Females	25 (55.6%)	37 (35.6%)	
Site distribution			
Right Mandible	12 (26.7%)	36 (34.6%)	p-value 0.156
Left Mandible	13 (28.9%)	20 (19.2%)	
Right Maxilla	6 (13.3%)	26 (25%)	
Left Maxilla	14 (31.1%)	22 (21.2%)	

On comparing the gross size with that of histopathological types of odontogenic lesions, the gross size was predominantly less than 3cm in both odontogenic cysts and tumors with 81.7% of them being odontogenic cysts while 18.3% of them being odontogenic tumors. There was a statistically significant correlation between gross size and histopathological nature of odontogenic lesions (p-value 0.010) [Table 4].

Table 4. Association between odontogenic lesions and gross size

Histopathological Diagnosis	Size of odontogenic lesions		Chi-square test
	≥3cm	< 3cm	
Odontogenic cysts (n=113)	28 (62.2%)	85 (81.7%)	p-value 0.010
Odontogenic tumors (n=36)	17 (37.8%)	19 (18.3%)	

The association between gross size with that of histological subtypes of odontogenic cysts revealed that all the subtypes of odontogenic cysts being predominantly less than 3cm grossly except residual cyst which showed equal incidence in both the gross size categories. Among the odontogenic cysts that were less than 3cm in size, periapical cyst was the most common subtype (71.8%) while glandular odontogenic cyst was the least common subtype (1.2%). However, the association between gross size and subtypes of odontogenic cysts was not statistically significant in the present study (p value - 0.574) [Table 5].

Table 5. The association between gross size and histopathological subtypes of odontogenic cysts

Histopathological subtypes of odontogenic cysts	Gross size of odontogenic cysts		Chi-square test
	≥3cm (n = 28)	< 3cm (n = 85)	
Periapical cyst	19 (67.9%)	61 (71.8%)	p – value 0.574
Dentigerous cyst	4 (14.3%)	16 (18.8%)	
Odontogenic keratocyst	2 (7.1%)	4 (4.7%)	
Residual cyst	3 (10.7%)	3 (3.5%)	
Glandular Odontogenic cyst	0 (0.0%)	1 (1.2%)	

The association between gross size with that of histological subtypes of odontogenic tumors revealed statistically significant (p-value 0.042) results in the current study with majority (52.8%) of them being less than 3cm grossly. However, ameloblastomas showed larger sized lesions (≥3cm) grossly in around 69.2% of cases [Table 6].

Table 6.The association between gross size and histopathological subtypes of odontogenic tumors

Histopathological subtypes of odontogenic tumors	Gross size of odontogenic tumors		Chi-square test
	≥3cm (n = 17)	< 3cm (n = 19)	
Ameloblastoma	9 (52.9%)	4 (21.1%)	p-value 0.042
Cemento-ossifying fibroma	2 (11.8%)	5 (26.3%)	
Calcifying Epithelial odontogenic tumor	0 (0.0%)	5 (26.3%)	
Others	6 (35.3%)	5 (26.3%)	

DISCUSSION

Odontogenic cysts may arise de novo or through stimulation of epithelial remnants by odontogenic infections whereas odontogenic tumors can arise from the epithelial cells, ectomesenchymal component, or a combination of both.[3] This study determined the demographic, clinical and histopathological characteristics of odontogenic lesions among patients in a tertiary care hospital.

The age distribution of odontogenic lesions in the present study revealed that both odontogenic cysts and tumors were commonly encountered in the 20-40-years age group (64.4%) in concordance with the study by Ramachandra S et al [7] where the age of occurrence was between 21-50 years. However in the study done by Channappa et al, [8] odontogenic cysts were commonly encountered in 20-29 years of age group while odontogenic tumors were seen between 21-50 years of age. These findings emphasize the occurrence of odontogenic lesions among patients of wider age group in clinical practice.

The current study demonstrated a slightly higher male predominance (58.4%) among patients with odontogenic lesions similar to the study conducted by Singh CK et al. [9] However in the studies conducted by Ramachandra S et al [7] and Nayak et al, [10] odontogenic cysts showed male predilection while odontogenic tumors showed female predilection.

Mandible was the most frequent site for odontogenic lesions in the present study (54.3%) followed by maxillary lesions (45.7%) which was in correlation with the studies done by Nayak et al [10] and Ramachandra S et al.[7]

In the present study, odontogenic cysts (75.8%) were the predominant odontogenic lesions compared to odontogenic tumors (24.2%) which was similar to the study done by Singh CK et al [9] where odontogenic cysts accounted for 76.8% of cases while odontogenic tumors accounted for 23.2%. of the cases. Among the odontogenic cysts, periapical cyst (70.8%) was the most common cystic lesion while ameloblastoma (36.1%) was the most common odontogenic tumor which was in concordance with the study by Channappa et al [8] where periapical cysts accounted for 50.8% and ameloblastoma accounted for 54.8% of the total cases. Odontogenic cysts are characterized by bone resorption and develop from the odontogenic epithelial components or its residuals which gets trapped within the gingival tissue or bone. [11] Based on their origin, odontogenic cysts are classified into developmental and inflammatory. [12] Periapical cysts belong to the group of inflammatory lesions which are caused by infection of the tooth pulp chamber. The inflammatory response leads to proliferation of epithelial rests of Malassez and the cystic lesion is formed. [13] The cyst is lined by non-keratinized stratified squamous epithelium with a characteristic arcading pattern. The fibrous stroma of cyst wall is infiltrated by foamy histiocytes, lymphocytes and plasma cells along with cholesterol crystals and foreign body giant cells.[3] Ameloblastoma being the most common subtype, is a locally infiltrative odontogenic tumor of epithelial origin that arises from jaw bones.[5] Any odontogenic epithelium including dental lamina during pre-odontogenesis, epithelial rests of Malassez and Serres during post-eruption, reduced enamel epithelium during post-odontogenesis and basal layer of the overlying epithelium during embryogenesis and pre-odontogenesis can give rise to the development of ameloblastoma.[14] Based on WHO, ameloblastoma is classified into unicystic, extraosseous/peripheral, conventional, adenoid and metastasizing ameloblastoma. The subtypes of conventional ameloblastoma are follicular, plexiform, acanthomatous, granular cell, basal cell and desmoplastic ameloblastoma.[5] On microscopy, ameloblastoma is characterized by two types of cells - columnar cells resembling normal ameloblasts that palisades around epithelial islands and the more centrally located cells resembling stellate reticulum.[3]

In the present study, the statistical association between gross size of the odontogenic lesions and various clinicopathological variables revealed significant association with age of the patients (p value - 0.002), gender (p value - 0.023), histopathological nature of odontogenic lesions (p value - 0.010) and histopathological subtypes of odontogenic tumors (p value – 0.042). Al-Rawi et al [15] from UAE reported statistically significant association between lesion size with gender (p value < 0.05) and histopathological nature of odontogenic lesions (p value-0.01). In their study, around 53% of lesions were less than 1cm among males while 76% of lesions were less than 1cm among females which was in concordance to the current study.

In the study by Al-Rawi et al, [15] around 75% of radicular cyst were less than 1cm in size while all the four cases of ameloblastoma were larger than 1cm in size which was in concordance to the current study where 76.3% of radicular cysts were less than 3cm in size and 69.2% of ameloblastomas were more than 3cm in size grossly. Thus there was a statistically significant correlation between gross size and histopathological subtypes of odontogenic tumors in the current study (p value – 0.042). However, there was no significant association of gross size with the histopathological subtypes of odontogenic cysts (p value – 0.574) in the current study.

In the present study, the gross size of odontogenic lesions was also correlated with the patients' age and site distribution with no similar studies reported in literature. It was found that there was a significant association between the lesion size and patients' age (p value – 0.002) with majority of the lesions being significantly smaller in size among patients more than 20 years of age. However, the association between lesion size and site distribution of odontogenic lesions was statistically insignificant (p value – 0.156) in the present study.

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LIMITATIONS: The present study has not included radiological features of the odontogenic lesions such as radiolucency, margin characteristics and pattern of bone expansion which can influence the prognosis and treatment planning. The study also did not include the long-term follow-up data such as local recurrences of odontogenic lesions.

CONCLUSION

The current study evaluated the clinicopathological characteristics of odontogenic cysts and tumors which revealed the preponderance of odontogenic cysts in comparison to odontogenic tumors. The novelty in the present study is determining the association of the lesion size with various clinicopathological variables that will influence the long-term prognosis of the patients with odontogenic lesions. It is found out that majority of the odontogenic lesions including cysts and tumors were smaller in size at diagnosis with significant correlation with patients age, gender and histopathological subtypes of odontogenic tumors.

KEY MESSAGES: Odontogenic cysts and tumors occurred frequently between 20-40 years of age with male to female ratio of 1.4:1 and right mandible being the most predominant involved site. Histopathological subtypes of odontogenic tumors showed significant correlation with that of lesion size and majority of them were smaller in size at initial clinical presentation.

DECLARATIONS

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no conflict of interest.

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ORIGINAL REPORT

EVALUATING THE EFFECTIVENESS OF SCHOOL-BASED ORAL HEALTH EDUCATION METHODS IN IMPROVING CHILDREN'S ORAL HEALTH : A SYSTEMATIC REVIEW

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ABSTRACT

Background: Oral health plays a pivotal role in the overall growth and development of children, influencing their physical, psychological, and social well-being. Despite advancements over the decades, the prevalence of poor oral health among children remains high, contributing to school absenteeism and reduced academic performance. School-based dental health education has emerged as a promising approach to improve awareness and promote dental care utilization; however, its diverse dimensions and varying effectiveness remain underexplored.

Aim: This systematic review aimed to evaluate the effectiveness of school-based oral health education programs in improving children's oral health outcomes, with a focus on their impact and effectiveness.

Results: A total of 1,200 articles were identified through database searches. After screening and excluding irrelevant studies, 45 studies met the inclusion criteria and were included in the qualitative synthesis.

Conclusion: Traditional classroom teaching, although widely implemented, demonstrated limited impact on sustained behavioral change. In contrast, interactive approaches such as games, role-playing, and supervised toothbrushing yielded more enduring improvements in oral health. The integration of digital tools and parental involvement further enhanced outcomes but was often feasible only in resource-rich settings. The effectiveness of interventions varied significantly across different cultural and socio-economic contexts.

Keywords*:* School health education, oral health, children, behavioral change, attitude

1. INTRODUCTION

Oral health plays a critical role in children's overall well-being, influencing their physical, psychological, and social development. Good oral health is essential for proper nutrition, speech development, and self-esteem[1]. However, despite advancements in healthcare, dental caries remains the most prevalent chronic disease among children worldwide [2]. Poor oral health not only causes pain and discomfort but also leads to school absenteeism and reduced academic performance [3].

Problem Statement

The prevalence of poor oral health among children is alarmingly high, particularly in low- and middle-income countries where access to dental care is limited [4]. While preventive measures such as fluoridation and routine dental check-ups are effective, these strategies are not always accessible to all children. School-based oral health education has emerged as a viable method to promote awareness and improve oral hygiene practices, but its effectiveness remains under-explored [5].

Objectives of the Review

The primary objective of this systematic review is to evaluate the effectiveness of school-based oral health education in improving children's oral health outcomes. Specifically, the review aims to:

1. Assess changes in oral health knowledge and behavior following school-based interventions.
2. Examine the impact of these interventions on clinical outcomes, such as caries reduction and improved oral hygiene.
3. Compare the effectiveness of different education methods, including traditional teaching, interactive approaches, and digital tools [6].

PICO

To ensure clarity in defining the study scope, the PICO model was applied:

- Population (P): School-aged children between 5 and 15 years, from diverse geographic regions and socio-economic backgrounds.
- Intervention (I): School-based oral health education programs, including traditional classroom teaching, interactive activities such as games, role-playing, and supervised toothbrushing, and digital tools such as educational apps, videos, and online modules.
- Comparator (C):
  - No intervention or standard school curriculum without specific oral health components.
  - Alternative education approaches differing in method or content delivery.
- Outcomes (O):
  - *Primary outcomes:* Improvement in oral health knowledge and behaviors, including increased brushing frequency, improved brushing techniques, adoption of flossing habits, and healthier dietary practices.
  - *Secondary outcomes:* Reduction in plaque index, gingival index, and dental caries incidence; improvement in oral hygiene scores and gingival health.

PECO

Given that both randomized controlled trials and observational studies are included, the PECO model was also applied for broader applicability:

- Population (P): School-aged children between 5 and 15 years, from varied cultural, geographic, and socio-economic contexts.
- Exposure (E): Participation in school-based oral health education interventions, incorporating traditional, interactive, or digital formats.
- Comparator (C): Absence of such programs or the use of alternative or less intensive educational approaches.
- Outcomes (O): Improvements in oral health knowledge, adoption of better oral hygiene behaviors, reduction in plaque and gingival indices, decreased incidence of dental caries, and improved gingival health.

2. MATERIALS AND METHODS

2.1 Search Strategy

Scope and Relevance

Schools serve as an ideal platform for delivering oral health education due to their structured environment and access to a large population of children [7]. Integrating oral health education into school curriculums has the potential to reach children from diverse socioeconomic backgrounds and instill lifelong healthy habits. Furthermore, understanding the most effective methods for delivering these interventions can guide policymakers and educators in developing targeted programs that address the specific needs of their communities [8].

To ensure a comprehensive review, a systematic search was conducted across multiple databases, including **PubMed**, **Scopus**, **Cochrane Library**, and **Web of Science**. The search was conducted using a combination of relevant keywords and Boolean operators to identify studies evaluating school-based oral health education programs. The primary search terms included:

- "Oral health education"
- "School-based programs"
- "Children's oral health"
- "Dental caries prevention"
- "Oral hygiene interventions"

The search was restricted to peer-reviewed articles published in **English** within the last 15 years to ensure the relevance of the findings (e.g., Petersen et al., 2005; Jackson et al., 2011). Additional sources were identified through manual screening of references cited in relevant articles and systematic reviews.

(Systematic review has been registered in PROSPERO 2025 CRD420251000578)

2.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Studies focusing on school-based oral health education programs.
2. Studies involving children aged **5-15 years**.
3. Interventions with a duration of at least **three months**.
4. Studies reporting measurable outcomes such as improvements in oral hygiene knowledge, behavior, or clinical measures (e.g., plaque reduction, caries prevention).
5. Articles published in English in peer-reviewed journals.

Exclusion Criteria:

1. Studies involving populations outside the defined age range.
2. Interventions conducted in non-school settings or programs unrelated to oral health education.
3. Studies lacking measurable or clearly defined outcomes.

4. Review articles, editorials, and conference abstracts without primary data.

2.3 Study Selection Process

The study selection process followed the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)** guidelines:

1. **Title and Abstract Screening**: Two reviewers independently screened titles and abstracts for relevance based on the inclusion and exclusion criteria.
2. **Full-Text Review**: Articles meeting the eligibility criteria were retrieved for full-text analysis to ensure they aligned with the study objectives.
3. **Discrepancy Resolution**: Any disagreements during the selection process were resolved through discussion or consultation with a third reviewer.

2.4 Data Extraction

Key data points were extracted from each included study using a standardized data extraction form:

- **Study Design**: Randomized controlled trials (RCTs), cohort studies, or cross-sectional studies.
- **Sample Size**: Number of participants involved in the study.
- **Intervention Type**: Details of the oral health education methods (e.g., traditional lectures, interactive sessions, use of digital tools).
- **Duration**: Length of the intervention and follow-up period.
- **Outcomes Measured**: Improvements in oral hygiene practices (e.g., brushing frequency), knowledge, and clinical outcomes such as plaque reduction or caries prevention.

2.5 Quality Assessment

The quality of the included studies was assessed using validated tools:

- **Cochrane Risk of Bias Tool**: For randomized controlled trials, assessing factors such as randomization, allocation concealment, and blinding of participants.
- **Newcastle-Ottawa Scale (NOS)**: For observational studies, evaluating selection, comparability, and outcome assessment.

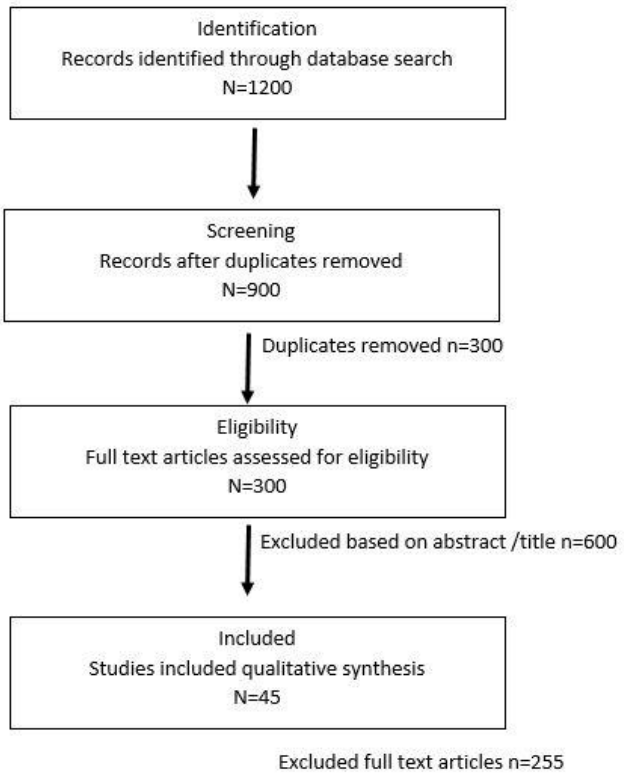
Table 1 Studies included for qualitative analysis

Study	Country	Sample Size	Age Range	Intervention Duration	Intervention Type	Outcomes Measured	Key Findings
Yazdani et al., 2009	Iran	360	12–13 years	12 wks	Leaflets and videotapes	Oral cleanliness and gingival health	Significant improvement in oral cleanliness and gingival health in intervention groups compared to control.
Arikan et al., 2007	Turkey	60	7–11 yrs	9 months	Verbal education and written materials	Plaque index scores	Significant reduction in plaque index scores in education groups compared to control.
Saied-Moallemi et al., 2009	Iran	376	12 yrs	3 months	Parental involvement in education	Gingival health	Improved gingival health in groups with parental involvement.
Frazao, 2011	Brazil	534	5–7 yrs	18 months	Supervised toothbrushing	Caries incidence	Reduction in caries incidence in the intervention group.

Reinhardt et al., 2009	Germany	10	6–7 yrs	7 days	Peer tutoring	Toothbrushing skills	Significant improvement in toothbrushing technique post-intervention.
Livny et al., 2008	Israel	120	5–6 yrs	4 months	Oral health promotion program	Toothbrushing skills	Significant improvement in brushing various tooth surfaces post-intervention.
Tolvanen et al., 2009	Finland	497	11–12 yrs	3.4 yrs	Individualized caries control regimen	Oral health-related behavior, knowledge, and attitudes	Improvement in oral health-related behavior; less effect on knowledge and attitudes.
Shenoy & Sequeira, 2010	India	400	12–13 yrs	36 wks	Health education lectures and demonstrations	Oral health knowledge, plaque, and gingival scores	Significant improvements in knowledge and reduction in plaque and gingival scores in intervention groups.
Zanin et al., 2007	Brazil	200	7–14 yrs	15 months	Educational program with supervised toothbrushing	Plaque and gingival scores, caries incidence	Significant reduction in plaque and gingival scores; lower caries incidence in intervention group.
Tai et al., 2009	China	1,344	7–8 yrs	3 yrs	Comprehensive oral health promotion program	Caries increment, plaque, and sulcus bleeding scores	Lower caries increment and improved oral hygiene in intervention schools.
de Farias et al., 2009	Brazil	391	7–14 yrs	4 months	Contextualized educational activities	Oral health knowledge, plaque, and gingival scores	Positive effects on oral hygiene and knowledge; more informed individuals did not always practice better oral hygiene.

Explanation:

- **Study**: Cites the primary author and publication year.
- **Country**: Indicates where the study was conducted.
- **Sample Size**: Number of participants involved.
- **Age Range**: Age group of the participants.
- **Intervention Duration**: Length of the educational intervention.
- **Intervention Type**: Methods used for oral health education.
- **Outcomes Measured**: Specific oral health parameters assessed.
- **Key Findings**: Summarizes the main results of the study.



Figire 1. PRISMA FLOW DIAGRAM FOR SYSTEMATIC REVIEW

3. RESULTS

3.1 Overview of Included Studies

The systematic review included a total of **10 studies** conducted across various geographical regions, including Brazil, China, Finland, India, Iran, Israel, Germany, and Turkey. The studies predominantly targeted school-aged children, with age ranges between 5 and 15 years, reflecting the global focus on early intervention for oral health promotion. Most of the studies implemented interventions lasting between 3 months and 3 years, emphasizing the need for sustained efforts to bring about significant changes in oral health behaviors [9,10]. Interventions ranged from traditional lecture-based education to interactive and technology-driven approaches, often tailored to the socio-economic and cultural contexts of the target populations [11,12].

3.2 Types of Oral Health Education Methods

The included studies employed diverse methods for oral health education. Traditional classroom teaching, involving lectures and demonstrations, was a common approach. This method focused on improving knowledge through verbal and visual presentations, particularly in resource-limited settings [9].

Interactive methods, such as games, role-playing, and supervised toothbrushing, were utilized to engage children actively in the learning process. These methods demonstrated improved retention of knowledge and greater behavioral changes compared to passive teaching techniques [13,14].

Digital tools, including educational apps, videos, and online modules, were also used in some studies. These tools allowed for innovative and scalable interventions, particularly in high-resource settings, and showed promising results in improving oral health awareness and practices [15].

3.3 Key Outcomes

The interventions resulted in several positive outcomes across the included studies.

Improvements in oral hygiene knowledge were consistently reported, with children demonstrating a better understanding of the importance of regular brushing, flossing, and dietary habits [16,6].

Changes in oral health practices were also observed, such as increased brushing frequency, improved brushing techniques, and the adoption of flossing. For instance, interventions involving supervised toothbrushing and parental involvement significantly improved children's oral hygiene practices [17,12]. A notable reduction in oral health problems, such as dental caries and gum disease, was documented in studies with longer intervention durations. For example, supervised toothbrushing programs demonstrated a significant decline in caries incidence among children [18]. Additionally, interventions involving interactive and contextualized activities showed greater success in reducing plaque and gingival scores compared to traditional methods [11,14].

3.4 Comparative Effectiveness

When comparing the effectiveness of different education methods, interactive approaches were found to be more effective than traditional classroom teaching. Studies highlighted that methods engaging children through hands-on activities, games, and role-playing fostered better understanding and sustained behavioral changes [13,14].

Digital tools also emerged as a promising alternative, particularly in enhancing accessibility and scalability of interventions. Programs leveraging videos and apps showed improvements in both knowledge and practices, making them a viable option for widespread oral health promotion[15].

Key success factors for effective education included the involvement of parents or caregivers, cultural relevance of the intervention, and consistent follow-up periods to reinforce learned behaviors. These elements were critical in ensuring long-term improvements in children's oral health outcomes [17,19].

4. DISCUSSION

4.1 Key Findings

The review revealed that school-based oral health education programs are effective in improving children's oral health knowledge, behaviors, and clinical outcomes. **Traditional classroom teaching**, although beneficial in enhancing basic knowledge, had limited impact on sustained behavioral changes [9]. In contrast, **interactive methods**, such as role-playing, supervised toothbrushing, and games, were significantly more effective in promoting long-term improvements in oral hygiene practices and reducing dental caries [13,14]. Digital tools, including educational videos and apps, also showed promise, particularly in their scalability and ability to engage children in a visually appealing manner [15]. These findings underscore the importance of combining methods to maximize educational impact, particularly in diverse school settings [12].

The studies demonstrated a clear impact on children's oral health outcomes, with improvements in plaque reduction, gingival health, and caries prevention. For example, interventions that included parental involvement resulted in greater behavioral changes and better oral health outcomes, emphasizing the role of family in reinforcing education [17].

4.2 Strengths and Limitations of the Studies

The reviewed studies showcased several strengths. Many employed robust methodologies, such as randomized controlled trials and well-structured interventions, ensuring the reliability of findings [9,19]. The diverse range of outcomes measured, including knowledge, behaviors, and clinical parameters, provided a holistic understanding of the effectiveness of oral health education methods [10].

However, several limitations were noted. Sample sizes in some studies were relatively small, limiting the generalizability of results [13]. Additionally, the duration of follow-up was often short, making it difficult to assess the long-term sustainability of observed changes[18]. Geographic and cultural constraints also posed challenges, as interventions designed in high-income countries might not be directly applicable to low- and middle-income regions due to resource limitations and varying oral health literacy levels [4].

4.3 Implications for Schools

Schools are uniquely positioned to serve as platforms for oral health promotion due to their structured environments and access to large populations of children [7]. Integrating oral health education into the school curriculum has the potential to reach children from diverse socioeconomic backgrounds and instill lifelong healthy habits [8]. Combining traditional teaching methods with interactive and digital tools can enhance engagement and learning outcomes. For example, supervised toothbrushing programs can be paired with educational apps to reinforce proper techniques and promote consistency [14,15].

Schools should also consider involving parents and caregivers in oral health education initiatives, as this has been shown to improve the effectiveness of interventions [17]. Furthermore, tailoring programs to the cultural and socio-economic contexts of students can address disparities in oral health literacy and outcomes [12].

4.4 Gaps in Research

Despite the promising results, significant gaps in research remain. A notable limitation is the lack of **longitudinal studies** that assess the long-term sustainability of oral health education interventions [19]. Most studies focus on short-term outcomes, leaving a gap in understanding how these programs influence behaviors and oral health status over time.

Additionally, there is a need for more **culturally tailored interventions** that address the unique challenges faced by children in low- and middle-income countries.

These interventions should consider factors such as language, cultural beliefs about oral health, and accessibility of dental care [4]. Future research should also explore the cost-effectiveness of various education methods to guide policymakers in resource allocation [8].

5. CONCLUSION

Summary of Findings

This systematic review highlights the **effectiveness of** school-based oral health education programs in improving children's oral health knowledge, behaviors, and clinical outcomes. Traditional classroom teaching, while effective in increasing knowledge, showed limited impact on long-term behavioral changes. Interactive methods, such as games, role-playing, and supervised toothbrushing, were more successful in fostering lasting improvements in oral hygiene practices. Similarly, digital tools like educational apps and videos demonstrated potential for scalable and engaging interventions, particularly in resource-rich environments. Programs involving parental participation further enhanced the outcomes, underscoring the importance of a multi-stakeholder approach [13,17]. Despite these promising results, the effectiveness of these interventions varied based on cultural and socio-economic contexts.

Policy Implications

Policymakers, school authorities, and public health practitioners should consider integrating oral health education into school curricula to address the widespread issue of poor oral health among children. Comprehensive programs combining traditional teaching methods with interactive and digital tools can maximize impact. Schools should also focus on parental involvement to reinforce oral health practices at home.

Moreover, targeted policies are needed to ensure that oral health education is accessible to children in low- and middle-income regions, where disparities in dental care and literacy persist. Funding should be allocated for sustainable and culturally tailored interventions, and collaborations between schools, health departments, and dental professionals should be encouraged to ensure holistic oral health promotion [8].

Future Research Directions

Future studies should focus on long-term outcomes to determine the sustainability of behavioral changes and improvements in clinical measures. There is also a need for innovative approaches, such as gamified digital tools and virtual reality, to engage children in novel ways. Research should explore cost-effectiveness and scalability to guide policymakers in resource allocation. Additionally, culturally tailored interventions designed for diverse socio-economic groups and low-resource settings are critical for bridging gaps in oral health education. These efforts will ensure that school-based oral health education achieves its full potential in promoting lifelong oral health for children worldwide.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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ORIGINAL ARTICLE

PREVALENCE AND RISK FACTORS OF ORAL POTENTIALLY MALIGNANT DISORDERS IN TOBACCO USERS

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ABSTRACT

Background: Tobacco use is a major public health concern and a leading cause of oral potentially malignant disorders (OPMDs). This study aims to assess the prevalence of OPMDs and associated risk factors among tobacco users.

Methods: A cross-sectional study was conducted among 2,800 tobacco users attending outpatient clinics across three tertiary care centers. Participants were evaluated for OPMDs through clinical examinations and a structured questionnaire capturing demographic data, tobacco use patterns, and associated risk factors. Logistic regression analysis was used to identify significant predictors of OPMDs.

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Results: The prevalence of OPMDs was 23.6% (n = 661). Leukoplakia (12.4%) and oral submucous fibrosis (OSMF) (8.7%) were the most common OPMDs observed. Chewing tobacco was significantly associated with OSMF (OR = 3.42; 95% CI: 2.56–4.58; $p < 0.001$), while smoking tobacco was a major risk factor for leukoplakia (OR = 2.89; 95% CI: 2.11–3.97; $p < 0.001$). Other significant risk factors included duration of tobacco use >10 years (OR = 4.12; 95% CI: 3.01–5.65; $p < 0.001$) and concurrent alcohol consumption (OR = 2.53; 95% CI: 1.89–3.37; $p < 0.001$).

Conclusions: OPMDs are highly prevalent among tobacco users, with specific patterns of use posing distinct risks. Public health interventions focusing on cessation and early detection are essential to reduce the burden of OPMDs.

***Keywords*:** Oral potentially malignant disorders, tobacco use, leukoplakia, oral submucous fibrosis, prevalence, risk factors

INTRODUCTION

Oral potentially malignant disorders (OPMDs) were recognized as a spectrum of clinical conditions with varying risks of progression to oral cancer. Common examples included leukoplakia, erythroplakia, and oral submucous fibrosis (OSMF), each of which posed significant public health concerns due to their association with lifestyle risk factors, particularly tobacco use. Tobacco, in both smoked and smokeless forms, was identified as a predominant risk factor for OPMDs and oral cancer, contributing to a substantial global disease burden. It was estimated that nearly 90% of oral cancer cases could have been prevented by eliminating tobacco use. [1]

The prevalence of OPMDs varied across regions, reflecting differences in tobacco use patterns, cultural habits, and access to healthcare services. In India, the

burden of OPMDs was disproportionately high due to the widespread consumption of smokeless tobacco products, such as betel quid and khaini. [2,3] Studies conducted in various global populations reported the prevalence of oral mucosal lesions ranging from 0.1% to 10%, depending on geographic, demographic, and lifestyle factors. [4,5,6] For instance, a population-based study in Southern Kerala highlighted a high prevalence of OPMDs in a rural Indian setting, underscoring the need for targeted public health interventions. [7]

Early detection and intervention are crucial for reducing the risk of malignant transformation in individuals with OPMDs. However, data on the prevalence and risk factors associated with OPMDs, particularly among tobacco users, are limited in diverse populations. Hence this study was conducted with the aim to determine the prevalence of OPMDs and analyze their associated risk factors among tobacco users. The findings also aimed to provide valuable insights to inform public health strategies, enhance early detection efforts, and ultimately reduce the morbidity and mortality associated with these conditions.

MATERIALS AND METHODS

Study Design and Setting

The cross-sectional study was conducted over a one-year period from January to December 2024. The research was carried out in three tertiary care centers, strategically selected to represent urban and semi-urban populations in diverse geographic regions. The study aimed to assess the prevalence and associated risk factors for oral potentially malignant disorders (OPMDs) among regular tobacco users.

Study Population

A total of 2,800 participants aged 18 years and above were recruited for the study. Eligibility criteria included:

- Regular tobacco use in either smoked or smokeless forms for at least one year.
- No prior diagnosis of oral cancer.
- Willingness to provide informed consent.

Exclusion criteria included individuals with severe systemic illnesses that could interfere with the study or those who had undergone prior treatment for OPMDs.

Ethical Considerations

The study protocol was reviewed and approved by the institutional ethics committee. Written informed consent was obtained from all participants after explaining the study objectives, procedures, potential risks, and benefits in their native language. Confidentiality was maintained by anonymizing participant data.

Training and Calibration

To ensure reliability, all dental professionals underwent a one-day calibration session to standardize the diagnostic criteria. Random re-assessments of 10% of participants were conducted to evaluate inter-examiner consistency.

Data Collection

Data collection involved a structured approach, utilizing a combination of face-to-face interviews and clinical examinations:

1. **Structured Questionnaire**: A pre-validated questionnaire was used to collect detailed information on:

   - **Demographics:** Age, gender, socioeconomic status, and education level.
   - **Tobacco Use:** Type (smoking, smokeless, or both), frequency (daily consumption), and duration (years of use).
   - **Alcohol Consumption:** Frequency and quantity of alcohol intake.
   - **Lifestyle Factors:** Dietary habits, including fruit and vegetable intake, and oral hygiene practices, such as frequency of tooth-brushing and use of mouthwash.

2. **Clinical Examination**: Trained dental professionals conducted thorough oral examinations using artificial illumination and mouth mirrors. The examinations adhered to World Health Organization (WHO) guidelines for diagnosing oral lesions. Findings were documented systematically using standard recording forms.

Diagnostic Criteria for OPMDs

The diagnosis of OPMDs was made based on specific clinical features, as follows:

- **Leukoplakia**: White patches or plaques on the oral mucosa that could not be scraped off.
- **Oral Submucous Fibrosis (OSMF)**: Palpable fibrous bands in the oral mucosa, accompanied by reduced mouth opening (<35 mm in severe cases).
- **Erythroplakia**: Bright red patches with a velvety texture on the oral mucosa, without any apparent cause.

Statistical Analysis

Data were entered into a statistical software package (e.g., SPSS, version 25.0) for analysis. Descriptive statistics, including means, standard deviations, and frequencies, were used to summarize demographic and clinical characteristics. Prevalence rates of OPMDs

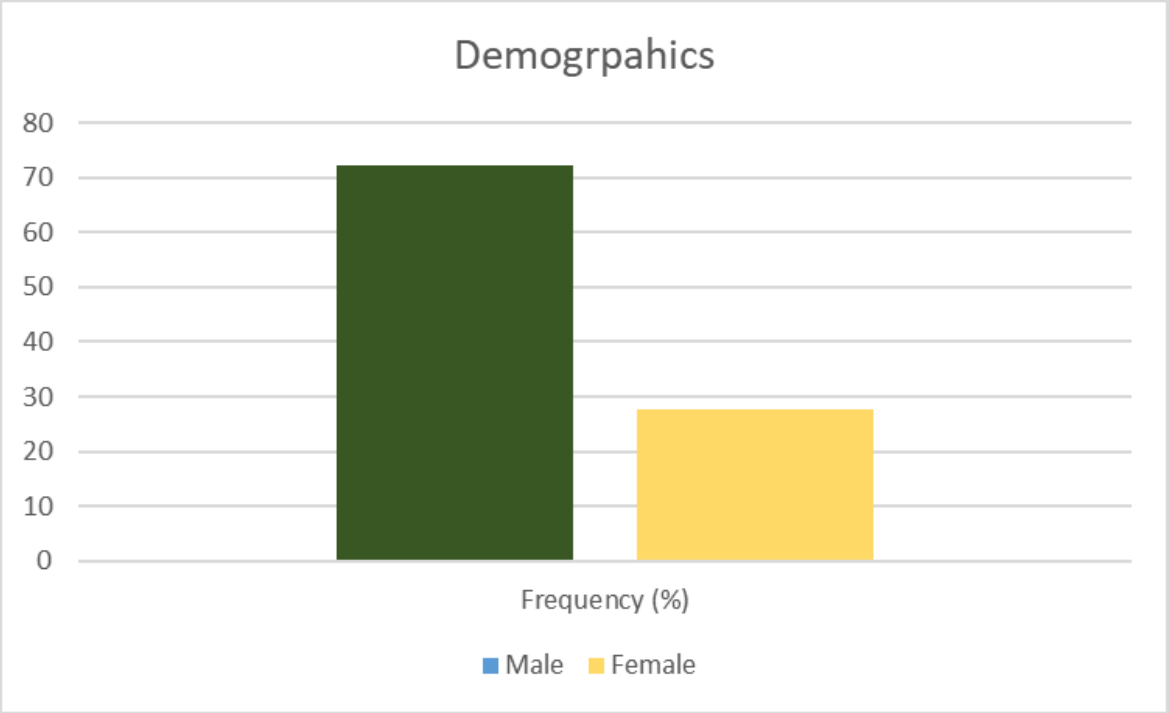
were calculated for the entire population and stratified by tobacco use patterns and other factors.

To identify independent risk factors for OPMDs, a multivariable logistic regression analysis was performed, adjusting for potential confounders such as age, gender, alcohol consumption, and oral hygiene practices. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was set at a p-value of <0.05.

RESULTS Table 1 and Graph 1: **demonstrated the** detailed demographic distribution of the study participants. The study included 2,800 participants, with a male predominance (72.3%) and a mean age of 38.6 years (±12.4).

Table 1. Demographic Characteristics of Study Participants

Variables	Frequency (%)
Male	2024 (72.3)
Female	776 (27.7)
Mean age (years)	38.6 ± 12.4

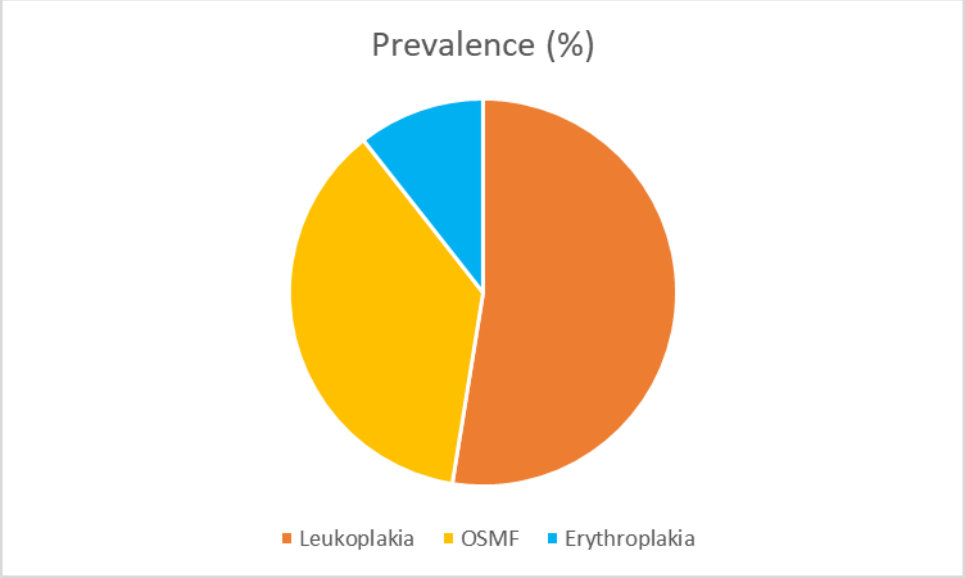


Graph 1. Showing Demographic Characteristics of Study Participants

The overall prevalence of **Oral Potentially Malignant Disorders (**OPMDs) among the participants was 23.6%. Leukoplakia was the most common OPMD (12.4%), followed by oral submucous fibrosis (OSMF) (8.7%) and erythroplakia (2.5%). The prevalence of different OPMDs is summarized inTable 2 and Graph 2**.**

Table 2. Prevalence of OPMDs among Participants

OPMDs	Prevalence (%)
Leukoplakia	12.4
OSMF	8.7
Erythroplakia	2.5
Total	**23.6**



Graph 2. Pie chart showing prevalence of OPMDs among Participants

Table 3. showed the Multivariable logistic regression analysis for several significant risk factors for OPMDs. Tobacco use patterns, including chewing and smoking, were strongly associated with an increased risk. Longer duration of tobacco use (>10 years), concurrent alcohol consumption, and poor oral hygiene practices also contributed significantly. Chewing tobacco significantly increased the risk of OSMF (OR = 3.42; 95% CI: 2.56–4.58; $p < 0.001$), while smoking tobacco was strongly associated with a higher risk of leukoplakia (OR = 2.89; 95% CI: 2.11–3.97; $p < 0.001$). Participants with a history of tobacco use exceeding 10 years had a markedly elevated risk of OPMDs (OR = 4.12; 95% CI: 3.01–5.65; $p < 0.001$). Additionally, alcohol consumption independently increased the risk of OPMDs by 2.53 times (OR = 2.53; 95% CI: 1.89–3.37; $p < 0.001$), and poor oral hygiene practices doubled this risk (OR = 2.18; 95% CI: 1.31–3.34; $p = 0.004$).

Table 3. Logistic Regression Analysis of Risk Factors for OPMDs

Variables	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Chewing tobacco	3.42	2.56–4.58	**<0.001**
Smoking tobacco	2.89	2.11–3.97	**<0.001**
Duration >10 years	4.12	3.01–5.65	**<0.001**
Concurrent alcohol use	2.53	1.89–3.37	**<0.001**
Poor oral hygiene	2.18	1.31–3.34	**0.004**

DISCUSSION

The findings of the current study provided valuable insights into the prevalence of oral potentially malignant disorders (OPMDs) and their associated risk factors among regular tobacco users. The overall prevalence of OPMDs was 23.6%, with leukoplakia being the most common subtype, followed by oral submucous fibrosis (OSMF) and erythroplakia. These results aligned with, but also diverged from, findings reported in previous studies, reflecting both shared patterns and regional variations.

The observed prevalence of 23.6% was consistent with studies conducted in India and other regions with high tobacco use. Saraswathi et al. (2006) [3] reported a similar prevalence of 21.6% among tobacco users in India, attributing it to the widespread use of smokeless tobacco products. Similarly, Patil et al. (2013) [2] found a prevalence of 24.8%, highlighting the combined effects of smoking and chewing tobacco on OPMD development. However, lower prevalence rates had been documented in studies from non-tobacco-endemic regions. For instance, Axéll (1987) [5] reported a prevalence of 3.6% for leukoplakia among a Swedish population, which was likely due to differences in tobacco consumption patterns, cultural practices, and public health interventions. Variations in diagnostic criteria and study methodologies might also have contributed to these discrepancies.

The high prevalence in this study could have been attributed to the widespread availability and cultural acceptance of tobacco products in the regions studied. Additionally, lower awareness of the harmful effects of

tobacco and limited access to early screening programs in semi-urban areas might have contributed to delayed detection of these disorders.

Chewing tobacco emerged as a significant risk factor for OSMF, with an odds ratio (OR) of 3.42. This finding was consistent with previous studies, such as Kumar et al. (2019) [8], which highlighted the strong association between smokeless tobacco use and OSMF. The fibrotic changes observed in OSMF were likely caused by areca nut alkaloids and tannins, which induced collagen cross-linking. Smoking tobacco was strongly associated with leukoplakia (OR = 2.89), a result that supported findings from Byakodi et al. (2011). [9] Smoking exposed the oral mucosa to carcinogens such as polycyclic aromatic hydrocarbons and nitrosamines, which explained the increased risk of leukoplakia. These findings highlighted the distinct pathophysiological mechanisms by which different forms of tobacco impacted the oral mucosa, emphasizing the need for targeted cessation strategies.

Participants with a history of tobacco use exceeding 10 years had a significantly higher risk of OPMDs (OR = 4.12), a finding that aligned with van der Waal (2009). [1] Prolonged exposure to carcinogens likely caused cumulative DNA damage, which over time progressed to precancerous lesions. This underscored the importance of early intervention and public education on the long-term risks of tobacco use.

Concurrent alcohol consumption was another significant risk factor (OR = 2.53), corroborating findings from Rooban et al. (2009). [10] Alcohol likely acted as a solvent, enhancing the penetration of tobacco carcinogens into oral tissues. The synergistic effect of combined tobacco and alcohol use could have explained the heightened risk observed in the study population. Poor oral hygiene practices doubled the risk of OPMDs (OR = 2.18), a result consistent with the findings of El Toum et al. (2018). [4] Poor oral hygiene created a pro-inflammatory environment conducive to lesion formation. Chronic irritation from plaque, calculus, and bacterial toxins likely exacerbated the effects of tobacco and other carcinogens, increasing susceptibility to OPMDs.

While the results of this study were largely consistent with previous findings, some studies reported contrasting patterns. For instance, Petti (2003) [11] documented a lower prevalence of OPMDs in populations with high fruit and vegetable intake, which was not specifically analyzed in this study. Antioxidants in fruits and vegetables may have mitigated oxidative stress caused by tobacco carcinogens, potentially explaining regional differences. Additionally, Kovac-Kavcic and Skaleric (2000) [12] found no significant association between alcohol consumption and OPMDs, differing from the results of this study. This discrepancy might have reflected differences in drinking patterns, genetic predispositions, or co-exposure to other risk factors.

The findings of this study were likely influenced by the widespread cultural acceptance of tobacco, particularly smokeless forms, in the study regions. Limited awareness of oral health risks and a lack of robust public health programs in semi-urban areas might have further exacerbated the problem. These factors underscored the need for community-based interventions aimed at reducing tobacco use, raising awareness of its health risks, and promoting regular oral health screenings to enable early detection and management of OPMDs.

Limitations

This study relied on self-reported data for tobacco and alcohol use, which may have introduced recall bias or underreporting due to social desirability. The cross-sectional design limited the ability to establish causal relationships between identified risk factors and the development of OPMDs. Additionally, the study did not assess the progression of OPMDs to malignancy, highlighting the need for future longitudinal studies to evaluate the natural history and transformation risk of these lesions.

CONCLUSIONS

Oral potentially malignant disorders (OPMDs) were found to be highly prevalent among tobacco users, with distinct risk factors associated with specific patterns of tobacco use and lifestyle behaviors. The findings underscore the importance of targeted interventions, including tobacco and alcohol cessation programs, routine screening, and early detection initiatives, to reduce the risk of malignant transformation and improve oral health outcomes in at-risk populations.

Public Health Implications

Targeted education campaigns, routine screening for high-risk individuals, and tobacco and alcohol cessation programs are critical to addressing the burden of OPMDs. Integrating dental professionals into primary care teams can enhance early detection and management. Policy interventions, such as tobacco control measures and improved access to dental care, are essential to reduce prevalence and progression to malignancy.

Clinical Relevance

Oral potentially malignant disorders (OPMDs) are a significant concern among tobacco users due to their risk of malignant transformation. This study highlights the strong association between tobacco use patterns and OPMD prevalence, emphasizing the need for early detection and cessation programs. Understanding these risk factors enables clinicians to implement targeted screening and preventive strategies. Routine oral examinations and patient education should be integrated into clinical practice to reduce the burden of OPMDs and prevent progression to oral cancer.

DECLARATIONS

Acknowledgments

None.

Competing of interest

The authors declare there is no conflict of interest

Ethical approval and consent to participate and publication

The present study was approved by the ethics committee of University

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ORIGINAL RESEARCH

DIFFERENCES EXPRESSION OF SYNDECAN-1 (SDC-1) AND E-CADHERIN (E-CAD) IN HISTOPATHOLOGICAL TYPES OF FOLLICULAR, PLEXIFORM, AND MIXED AMELOBLASTOMA (FOLLICULAR-PLEXIFORM)

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ABSTRACT

Background: Ameloblastoma is a benign tumor that can cause deformity and functional disorders in the craniomaxillofacial region. The invasion process of ameloblastoma requires degradation of the extracellular matrix (ECM) and basement membrane to support tumor cell proliferation. SDC-1 (CD-138) functions as a heparan sulfate proteoglycan that regulates cellular adhesion and extracellular matrix attachment, while E-Cadherin (E-Cad) serves as a calcium-dependent transmembrane glycoprotein critical for epithelial morphogenesis and homotypic cellular adhesion.

Aim: The present study was designed to evaluate differences in SDC-1 and E-Cad expression patterns according to ameloblastoma histopathological classification.

Materials and Methods: This research is an analytical observational study with a cross-sectional approach. The research sample used 24 post-operative paraffin blocks from ameloblastoma patients from the period 2015–2023 who were histopathologically diagnosed. SDC-1 and E-Cad expression was analyzed using immunohistochemical methods. Statistical analysis used the Tukey HSD test. This research has received ethical approval from the local ethics committee.

Results: The lowest expression of SDC-1 and E-Cad was found in the follicular type, while the mixed type (follicular-plexiform) showed the highest expression values. The Tukey HSD test showed significant differences in SDC-1 expression between the mixed type and the plexiform type (p=0.040) and follicular type (p=0.032). E-Cad expression also showed significant differences between the follicular type and mixed type (p=0.032).

Conclusion:
There are significant differences in SDC-1 and E-Cad expression between follicular type and mixed type ameloblastoma, while no significant differences were found between follicular type and plexiform type. These results indicate that histopathological variation is related to cell adhesion molecule expression in ameloblastoma.

***Keywords*:** Ameloblastoma, Syndecan-1, E-Cadherin, Immunohistochemistry, Histopathology.

INTRODUCTION

Ameloblastoma is classified as a benign tumor, but it can have serious clinical consequences due to its aggressive, expansive, and locally invasive development pattern. Large ameloblastoma can result in deformity and functional disorders in the craniomaxillofacial region.[1] The recurrence rate in ameloblastoma cases is around 64% after conservative therapy and 12% after tumor removal.[2,3] Ameloblastoma can be classified based on clinical, radiological, and histological characteristics. The plexiform and follicular histological varieties of ameloblastoma are the most frequently observed forms, whereas the follicular-plexiform type is the most frequently observed in mixed type.[4] Compared to plexiform or unicystic forms, follicular ameloblastoma has been reported to have a higher recurrence rate.[5] The prognosis of ameloblastoma can be determined by understanding cellular changes that are impacted by tumor growth factors and tumor biology, ranging from proliferation, differentiation, apoptosis, angiogenesis, tumor invasive properties, and tumor histomorphology using immunohistochemical examination.[6]

The high recurrence rate despite surgical intervention indicates that conventional clinical and histopathological assessment is not sufficient to accurately predict tumor behavior.[7,8] Therefore, identification of molecular markers that can reflect the biological aggressiveness of ameloblastoma is important for improving prognosis and determining more appropriate management strategies.[9]

The invasion process of ameloblastoma is characterized by disruption of the basement membrane and extracellular matrix (ECM) and loss of adhesion to surrounding cells. Syndecan-1 (SDC-1) and E-Cadherin (E-Cad) levels can be used as indicators of cellular alterations in the process. Known also as CD-138, SDC-1 is a transmembrane heparan sulphate proteoglycan that regulates several biological processes, such as cytoskeleton organization, growth factor signalling, cell adhesion, and attachment to the extracellular matrix. E-Cad, a calcium-dependent transmembrane glycoprotein, is essential for both epithelial morphogenesis and homotypic cell adhesion, which are essential for organogenesis, morphogenesis, and the maintenance of epithelial tissue. Reduced expression of E-Cad also correlates with tumor invasiveness and metastasis in malignant tumors, while loss of expression of SDC-1 in carcinoma is also associated with tissue invasion, metastatic processes, and poor prognosis (recurrence and metastasis).[10,11] Although SDC-1 and E-Cadherin have been extensively studied in malignant tumors, their role in benign but locally aggressive tumors such as ameloblastoma remains unclear.

Not much research has been done comparing the expression of SDC-1 in the stroma, epithelium, and E-Cad in ameloblastoma. Therefore, it is crucial to conduct more thorough research to help manage ameloblastoma with different levels of aggressiveness and to provides insight into the prognosis and recurrence potential of each type of ameloblastoma that has received surgical treatment. Understanding the differential expression of these molecules can provide deeper insights into the biological behavior of various histological subtypes of ameloblastoma, thus potentially serving as a basis for determining prognosis and planning therapeutic strategies. Therefore, this study aims to analyze and compare SDC-1 expression in stroma and epithelium, as well as E-Cadherin expression in ameloblastoma. This study hypothesizes that decreased expression of these adhesion molecules correlates with higher levels of aggressiveness and greater potential for recurrence.

METHODS

This study was an observational analytical study to analyze differences in E-cad and SDC-1 expression based on the histology of ameloblastoma. The research instruments were 24 post-operative paraffin blocks for ameloblastoma post-operative patients. The operative paraffin blocks were taken from patient's specimen who had been operated on by the Oral and Maxillofacial Surgery Team and were stored in the Anatomical Pathology section of Airlangga University and Dr. Mohammad Soewandhie Hospital Surabaya in the period 2015–2023. Ethical approval was obtained from the Ethics Committee of the Faculty of Dental Medicine, Universitas Airlangga, with number 1324/HRECC.FODM/XII/2023.

Paraffin blocks are of four follicular types, twelve plexiform types, and eight follicular-plexiform types. The histopathological findings were evaluated by immunohistochemistry. For immunohistochemical analyses, 4 μm-thick sections were prepared and mounted on slides. Deparaffinization of the sections was performed using distilled water followed by phosphate-buffered saline (PBS, pH 7.4) treatment for 2 minutes. The prepared samples then underwent overnight incubation (12 hours) with specific antibodies: anti-E-Cad (DECMA-1: sc-59778, rat monoclonal, concentrated and prediluted, human reactive, Santa Cruz Biotechnology, Europe) and anti-SDC-1 (CD-138) (DL-101: sc-12765, mouse monoclonal, concentrated and prediluted, human reactive, Santa Cruz Biotechnology, Europe). Each slide was assigned random codes and numbers for

blinded evaluation, followed by quantification of tumor epithelial cells displaying brown cytoplasmic staining. Statistical analysis was performed using the Shapiro-Wilk test with significance set at $P < 0.05$, utilizing IBM SPSS Statistics Version 48.0 (IBM Corporation, Armonk, New York, USA).

RESULTS

The 24 paraffin blocks of ameloblastoma patients have been collected during resections by the Oral and Maxillofacial Surgery team at Universitas Airlangga Hospital and Dr. Mohammad Soewandhie Hospital Surabaya between 2015 and 2023. Table 1 shows the gender distribution of the samples, which are divided into 12 (50%) and 12 (50%) males, with the most dominant type of ameloblastoma based on sex being plexiform type, which accounts for 7 (29.2%) males and 5 (20.8%) females.

Table 1. Data distribution of histological type of ameloblastoma based on gender

	Follicular	Plexiform	Mixed-type (follicular-plexiform)	Total
Gender				
Male	1 (4,1%)	7 (29,2%)	4 (16,7%)	12 (50%)
Female	3 (12,5%)	5 (20,8%)	4 (16,7%)	12 (50%)
Age				
< 20	0	3	1	4 (16,7%)
21-30	2	5	3	10 (41,7)
31-40	1	1	3	5 (20,8%)
41-50	0	1	0	1 (4,2 %)
51-60	0	1	1	2 (8,3%)
> 60	1	1	0	2 (8,3%)

The distribution sample based on age was categorized into five categories: <20 years, 21–30 years, 31–40 years, 41–50 years, 51–60 years, and >60 years, with the dominant age range being 21–30 years, there are 10 (41.7%) patients.

The results of observing their expression in all samples show the highest expression of SDC-1 and E-cad in the follicular-plexiform type. The expression of SDC-1 from highest to lowest in sequence, as shown in figure 1 and 2, is ameloblastoma type follicular-plexiform (13.13), plexiform (10.50), and follicular (9.75), while the results of E-cad expression are follicular-plexiform (7.13), plexiform (6.25), and follicular (4.00).

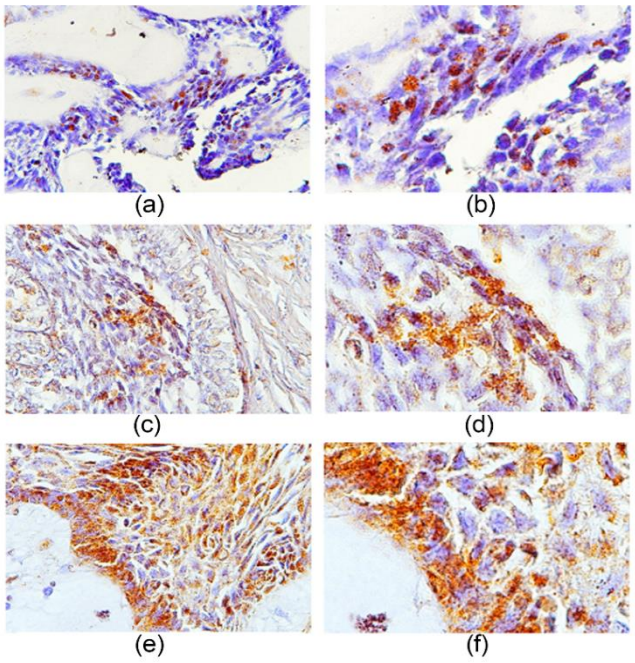


Figure 1. Expression rate of Syndecan-1 based on histological type of ameloblastoma. (A) Follicular type (400x magnification). (B) Follicular type (1000x magnification). (C) Plexiform type (400x magnification). (D) Plexiform type (1000x magnification). (E) Follicular-Plexiform (400x magnification). (F) Follicular-Plexiform (1000x magnification).

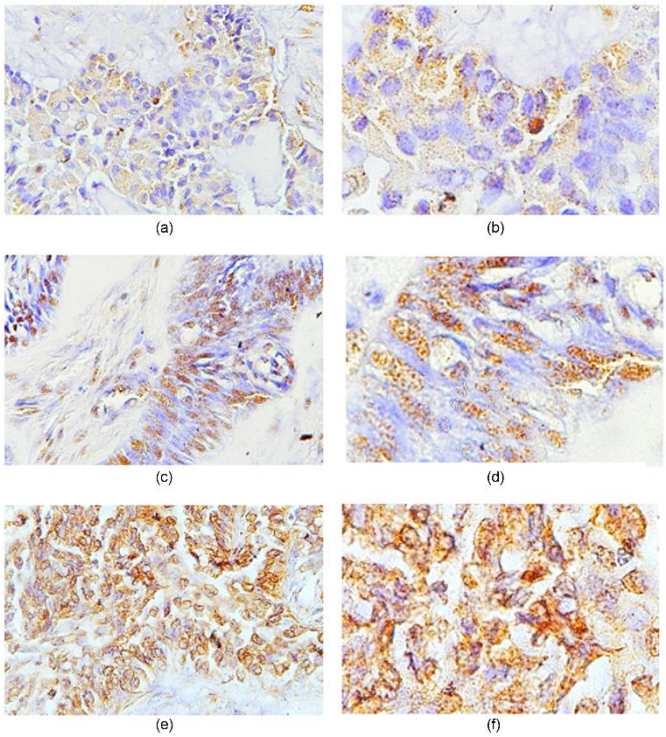


Figure 2. Expression rate of E-Cadherin based on histological type of ameloblastoma. (A) Follicular type (400x magnification). (B) Follicular type (1000x magnification). (C) Plexiform type (400x magnification). (D) Plexiform type (1000x magnification). (E) Follicular-Plexiform (400x magnification). (F) Follicular-Plexiform (1000x magnification).

Table 2 shows a *One-Way Anova* test of the three groups of ameloblastoma types, showing significant differences ($p<0.05$) in SDC-1 and E-Cad expression.

Table 2. Expression rate of Syndecan-1 and E-Cadherin based on histological type of ameloblastoma

Histological type	Number of cases	Mean ± SD	
		SDC-1	E-Cad
Follicular	4	9,75 ± 0,95	4,00 ± 1,41
Plexiform	12	10,50 ± 1,78	6,25 ± 1,85
Follicular-Plexiform	8	13,13 ± 2,80	7,13 ± 2,10

Post-hoc Tukey was used in the comparison test to compare the ameloblastoma types according to these two characteristics. The results of the comparison test between variables on SDC-1 expression showed that significant values ($p<0.05$) were found between the follicular-plexiform type and the follicular and plexiform groups. E-Cad expression showed that the comparison test between variables was significant only in the follicular-plexiform group and the follicular group ($p<0.05$), the results shown in table 3.

Table 3. Differences in expression of Syndecan-1 and E-Cadherin among follicular, plexiform, and mixed type ameloblastoma (follicular-plexiform)

Histopathological Type		SDC-1 **p value (sig.)*	E-Cad **p value (sig.)*
Follicular	Plexiform	0,812	0,116
Plexiform	Follicular – Plexiform	0,032*	0,568
Follicular	Follicular– Plexiform	0,040*	0,032*

*Multiple comparison Post Hoc Tukey HSD, statistical significance at $p < 0,05$. SDC-1 = Syndecan-1; E-Cad = E-Cadherin.

DISCUSSION

Ameloblastoma is classified histopathologically according to the specimen's dominant architectural characteristic; however, it is not uncommon to find a combination of two or more distinct architectural traits. The 12 patients (50%) in this study were plexiform type; followed by 8 (33.3%) mixed type patients and 4 (16.7%) follicular type patients. The distribution of histopathology categories in this study contrasts with the study of Cadavid et al. (2019), which found that the follicular type was the most common.[4] This may be attributed to the limited number of samples, which increases the possibility of distortion in the final data results. This study shows that the expression of SDC-1 and E-Cad is lowest in the follicular type of ameloblastoma compared to the plexiform and mixed types, indicating that the follicular variant may represent the most aggressive biological behavior. Ameloblastoma can locally expand into the surrounding area. Cellular invasion of the tumour requires the breakdown of the basement membrane and ECM around the tumour, followed by the growth and proliferation of tumour cells. A study conducted by Hashimoto et al. (2008) on colorectal adenocarcinoma revealed that a decrease in SDC-1 in the tumour epitel indicated progression and showed more aggressive biological activity. SDC-1 also regulates the activity of α2β1integrin, which plays a role in cell attachment, inhibition of cell migration, and tumour-invasive behaviour in squamous cell carcinoma.[12–14]

The study's data distribution results showed that ameloblastoma epithelial and stromal cells expressed SDC-1, with the follicular type exhibiting the lowest mean expression of SDC-1 in the epithelium (9.75) compared to the plexiform (10.50) and mixed (follicular-plexiform) types (13, 13). This is in line with the research of Setyawan who found the average amount of SDC-1 in the epithelium was lower in the follicular type compared to plexiform, which the follicular has the highest expression of MMP-2, MMP-9, and IL-1α.[15] The release of proteolytic enzymes, such MMP, is the primary cause of the reduction in SDC-1 expression. This is since SDC-1 can cleave MMP, which results in syndecan being shed and MMP accumulated in the stroma. This is possible as MMP's primary substrate target is SDC-1 (syndecan sheddase).[16] Loss of SDC-1 expression decreases cell-cell adhesion, as well as adhesion to the extracellular matrix, where in the development of ameloblastoma, cell invasion requires the breakdown of the basal membrane and the surrounding extracellular matrix, followed by cell growth and proliferation. Therefore, decreased cell-cell adhesion and changes in the composition of the basal membrane affect the growth of neoplasia. In addition, decreased syndecan-1 expression also occurs in cases of recurrent ameloblastoma.[17] From a clinical perspective, decreased SDC-1 expression has the potential to function as a biomarker for identifying ameloblastoma with higher invasive potential. This information can help clinicians in selecting more aggressive surgical management and better follow-up strategies for patients with the follicular subtype.

The association between decreased SDC-1 expression and tumor hypoxia in ameloblastoma occurs when high metabolic demands for energy and oxygen by tumor cells establish intratumoral hypoxic zones. Consequently, this hypoxic environment induces the expression of hypoxia-inducible factor 1-alpha (HIF-1α) as part of the cellular adaptive response to oxygen deficiency.[18] Furthermore, HIF-1α regulates endothelial cell migration toward hypoxic areas by modulating vascular endothelial growth factor (VEGF) synthesis. Through direct interaction with VEGF gene regulatory sequences, hypoxia-inducible factor-1 promotes transcriptional upregulation and enhanced VEGF expression.[19] HIF-1α expression levels have been reported to be moderately elevated in follicular ameloblastoma compared to the plexiform subtype, potentially accounting for the observed variations in VEGF expression between these histological types.[20] During angiogenesis, extracellular matrix remodeling occurs via matrix metalloproteinase and proteolytic enzyme activity, which triggers the release of angiogenic stimulatory factors from the basement membranes of blood vessels.[21] Hypoxic conditions are also linked to enhanced tumor aggressiveness, influencing both angiogenic processes and invasive cellular behavior.[22]

Observations of E-Cad in the three types also showed a similar pattern, with the follicular type having the lowest mean expression of E-Cad (4.00) compared to the plexiform type (6.25) and the mixed (follicular-plexiform) type (7.13). The results of multiple comparison analysis on E-Cad expression showed that there were significant differences in E-Cad expression between the follicular type and the mixed type (follicular-plexiform) with the plexiform type and the mixed type (follicular-plexiform). Most epithelial cells express E-Cad, a type I calcium-dependent transmembrane glycoprotein that contributes to the maintenance of epithelial tissue integrity through homophilic cell-to-cell adhesion of adherent junctions in all epithelial cells and cell polarity. The tumor suppressor gene CDH-1 encodes E-cadherin, which plays a role in adhesion between cells at adherent junctions through a complex with catenin called the Cadherin-Catenin Complex (CCC). Decreased

adhesion between epithelial cells in ameloblastoma may result from mutations in this CDH-1 gene, which may lead to decreased expression of E-Cad during the tumor development process.[23]

Another process that is also affected is the Wnt signaling pathway. Loss of expression of E-Cad causes the inability to degrade β-catenin, which causes the accumulation of β-catenin in the cytoplasm. After entering the nucleus, β-catenin translocate itself to T-cell factor/lymphoid enhancer-binding factor-1 (TCF/LEF-1), a protein related to both tumor development and proliferation of cells.[20] These results are also supported by research conducted by Hao et al. on the expression of E-Cad, Vimentin, and β-catenin based on their clinicopathological characteristics, showing a decrease in E-Cad expression in clinically aggressive ameloblastoma.[23] These findings expand current knowledge by reinforcing the role of adhesion molecules in ameloblastoma biology.[24] Combined evaluation of SDC-1 and E-Cad expression provides a more comprehensive understanding of tumor aggressiveness and may help refine prognostic assessment in the future. Hertog et al. reported that among ameloblastoma cases treated with conservative therapy, follicular type demonstrated the highest recurrence rate (7/10), while mixed type showed intermediate recurrence (3/7), and plexiform type exhibited the lowest recurrence rate (4/11).[25] This may be related to a decrease in E-Cad expression, where the follicular type shows reverse nuclear cell polarity and palisading cell configuration. However, the generalizability of these research findings is still limited. The patient group in this study represents a single-center population, which may not fully capture the biological diversity of ameloblastoma across different ethnic or geographic groups. Larger multicenter studies are needed to validate these observations.

The results of this study show that ameloblastoma of the follicular and plexiform types could be more aggressive than the mixed type (follicular-plexiform). The absence of a linear relationship between SDC-1 and E-Cad expression in every investigation group in this study indicates that there is no correlation between the decreasing processes of SDC-1 and E-Cad expression, indicating that the processes are caused by the same entity differently but having the same effect on tumor cell adherence to the extracellular matrix. Because this study is retrospective, this study is restricted by a small number of participants and lacks details on the long-term outcomes of patients, such as survival without cancer recurrence. The strengths of this study include the use of immunohistochemical evaluation of SDC-1 and E-Cad across different histopathological subtypes, which allows for detailed comparison of their expression profiles. Nevertheless, future prospective studies with larger sample sizes and long-term clinical follow-up, including recurrence and survival data, are needed to confirm the prognostic value of these biomarkers and to explore their potential integration into clinical decision-making.

The findings of this study reinforce the role of cell adhesion molecules, SDC-1 and E-Cadherin, in determining the biological characteristics of ameloblastoma. Decreased SDC-1 expression in the follicular type indicates that reduced cell interaction with the extracellular matrix can facilitate proteolytic activity, particularly by MMPs, which leads to basement membrane degradation and increased invasive capacity. Similarly, low E-Cad expression in the follicular type reflects weakening of the cadherin-catenin complex that functions to maintain polarity and cohesion of epithelial tissue. The loss of these adhesion molecules not only disrupts tissue stability but also activates signaling pathways such as Wnt/β-catenin that promote proliferation and phenotypic transition toward more invasive properties. The synergism of these molecular changes most likely explains why follicular ameloblastoma exhibits more aggressive biological behavior compared to other subtypes.

From a clinical perspective, low expression of SDC-1 and E-Cad has the potential to serve as prognostic indicators for determining more appropriate management strategies, whether through more radical surgical options or long-term follow-up plans for high-risk patients. Integration of these biomarkers into clinical practice can support risk stratification and therapy personalization. However, the generalizability of these research findings is still limited by the retrospective design, small sample size, and absence of clinical outcome data such as recurrence rates and disease-free survival. Therefore, prospective multicenter studies with larger sample sizes and long-term clinical follow-up are urgently needed. The combination analysis of SDC-1 and E-Cad together with other biomarkers, such as Ki-67, p53, Bcl-2, or angiogenesis markers, is expected to expand understanding of ameloblastoma biology while opening opportunities for developing more accurate clinical prediction models and potential molecular therapeutic targets in the future.

CONCLUSION

Based on the research results, there are significant differences in SDC-1 and E-Cad expression between follicular type and mixed type (follicular-plexiform) ameloblastoma. SDC-1 and E-Cad expression in follicular type ameloblastoma is lower compared to plexiform type and mixed type (follicular-plexiform), indicating that the

follicular type has higher aggressive potential. This study provides novelty by linking the differences in SDC-1 and E-Cad expression to ameloblastoma histopathological subtypes, thus providing new understanding regarding tumor biological behavior. These findings have practical significance as they have the potential to serve as additional markers in predicting ameloblastoma aggressiveness and can help clinicians in determining appropriate therapeutic strategies. Further research is recommended to explore the application of SDC-1 and E-Cad as prognostic biomarkers in routine clinical practice.

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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RETROSPECTIVE MORPHOMETRIC EVALUATION OF MANDIBULAR ADAPTATIONS IN RELATION TO THIRD MOLAR DYNAMICS

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ABSTRACT

This retrospective radiographic study aimed to evaluate morphometric changes in the mandible associated with impacted third molars using panoramic radiographs. Sixty digital orthopantomograms (OPGs) were selected from a total of 330 cases recorded at Saveetha Dental College between January and June 2024. Bone level distal to the mandibular second molar, gonial angle, and third molar root angulation were measured using ImageJ software. Mesioangular impaction was the most common type (35%), and bilateral impactions were present in 55% of the cases. The mean bone level was 1.22 ± 0.10 mm, with slightly higher bone loss in males compared to females, although the difference was not statistically significant. A significant variation in gonial angle was observed across impaction types ($p = 0.026$), suggesting a potential association between mandibular growth pattern and impaction type. Patients who had undergone third molar extraction showed improved bone levels distal to the second molar, while those who retained their impacted third molars exhibited progressive bone loss. These findings support the diagnostic utility of panoramic radiographs in identifying key morphometric parameters relevant to clinical decision-making. The study highlights the importance of gonial angle assessment as a possible predictor of impaction pattern and emphasizes the need for early radiographic evaluation in

Keywords: Third molar impaction, mandibular morphology, panoramic radiography, bone level changes, dental imaging

INTRODUCTION

The journey of a tooth begins from a bud stage within the jaw to its fully grown position, where it is anatomically and clinically functioning. The process is defined as an eruption. The word eruption is derived from the Latin "erumpere, " meaning "to erupt". The term "eruption" aptly captures the dynamic nature of this dental phenomenon, as the tooth seemingly "breaks through" or "bursts forth" into its proper place within the mouth. [1] The tooth fails to erupt for various reasons when referred to as impacted. The reasons for an impaction are lack of space in the arch, abnormal positioning of the tooth in the arch, abnormal eruption process, early loss and ankylosis of the primary tooth, and presence of pathology.[2] The presence of an impaction would lead to dental problems, which might require the removal of the impacted tooth.[1]

An impacted tooth is defined as one that remains embedded within the jawbone, is covered by gingival tissue, and may be partially or entirely covered by bone. [3]. A partially erupted tooth is defined as one that does not fully erupt into its occlusal position but can still be seen in the oral cavity.[3] The most common teeth to be impacted are the mandibular and maxillary third molars, followed by the maxillary canines and premolars. The frequency of mandibular third molar impaction is influenced by facial skeleton, gender, age, and ethnic group. Breik and Grupor reported a higher incidence of mandibular third molar Impaction in individuals with a dolichofacial pattern (vertical growth; facial axis angle, <87) and in females

(43%) compared to males (45%).[4] In contrast, Padhye et al. [5] found that third molar impaction was more common in males (51.77%) compared to females (48.33%). Prajapati et al. [6] noted a greater incidence of impacted mandibular third molars (IMTMs) among females in the 21–30 age group. The global prevalence of impacted third molars is around 24% .[8]

When it comes to removing an impacted tooth, a prior radiological assessment is essential. A conventional intraoral periapical Radiograph (IOPA) may not capture the full extent of the position of the root development. An orthopantomogram (OPG) offers the advantage of capturing a comprehensive view of the mandible, maxilla, and facial bones in a single wide image, making it useful for diagnosing various pathological conditions, evaluating carious and fractured teeth, detecting dental anomalies, and identifying Morphometric changes refer to alterations in the size, shape, and structure of anatomical features of a bone. The various morphometric changes studied in the mandible include the mandibular angle, the ramus's width, and the mandible's overall length. Selene Barone et al. [7] found a significant correlation between the Gonial angle and the position of the mandibular third molar, noting that a decrease in the Gonial angle was associated with a higher incidence of IMTMs ($p < 0.05$). Apart from this, the impaction of mandibular third molars is also associated with a decrease in the mandibular angle, an increase in the Gonial angle, and changes in the width of the mandibular ramus. Analysing the morphometric changes may help us predict the probability of impaction. More studies are needed to analyse the morphometric changes associated with impaction. Furthermore, age, gender, ethnicity, and individual anatomical variations can influence morphometric changes. The primary aim of this retrospective was to investigate the morphometric changes in the mandible about the presence of impacted third molars.

The objectives were to determine the prevalence of third molar impaction, analyse morphometric changes in the mandible, compare morphometric differences between patients with impacted third molars, investigate the impact of demographic factors, utilise the OPG imaging technique, and identify clinical implications.

METHODS AND MATERIALS

This retrospective case–control study was conducted with archived panoramic radiographic images of patients who visited the Saveetha dental college and hospital from Jan 2024 to June 2024. Due to the practice of electronic case sheets, the data was retrieved from Dental Information Archiving Software (DIAS). For a power of 80m the sample size calculated was 60 based on the study of Krausz et al. [12]

The study received the approval of the Institutional Ethics Committee with the reference no: IHEC/SDC/OMED-2305/23/15. The inclusion and exclusion criteria are mentioned in table 1.

monitoring, using either inhalational or oral anesthesia, with the sedation protocol tailored to the

The study included 112 patients (60 females and 52 males) diagnosed clinically and by ECHO as having CHD and referred preoperatively to the MDCT unit. The mean age of the patients was 9.2±7.1 months. The patients were classified into three groups: the first group included patients with intra-cardiac malformations, the second group included patients with heart great vessel connection malformations, and the third group included patients with congenital vascular anomalies.

The common clinical presentations among the studied patients were dyspnea and cyanosis among 70% and 71.3%, respectively.

Regarding the cardiac malformations, they were represented in the following manner (Table 1): VSD (n=87;77,6%), RVOTO (n=52;46.4%), ASD (n=33;29.5%), PFO (n=13,6.25%), both single ventricle and dextrocardia each one represents (n=3; 2.6%), followed by a common atrium, juxtaposition of the atrial appendage, TV malformation, and double inlet ventricle each one of them represents (n=2; 1.7%), last one is MV malformation which is seen in one case; (0.9%).

There was no significant difference between MDCT and ECHO in diagnosing cardiac structural malformations, except for the detection of PFO, where ECHO demonstrated greater accuracy ($p<0.05$) with a moderate Kappa agreement.

Table 1. The inclusion and exclusion criteria of the samples

Inclusion Criteria	Exclusion Criteria
Patients above the age of 18 years	Impacted third molars with incomplete root formation
OPG's free of distortion as judged by comparing the width of the ramus bilaterally and the presence of distortion in the lower anterior region.	History of steroid use, radiotherapy
Impacted third molars	Impacted third molars with second molar missing

Measurement Method:

The panoramic images were captured using Sidexis X-ray software (Dentsply Sirona, York, PA, USA) with a Schick sensor. Image analysis was conducted using ImageJ software (NIH, Bethesda, MD, USA). The X-ray parameters were set at 64–70 kV and 7–14 mA, following manufacturer recommendations for different patient demographics and body build. The OPG's were analyzed by a single observer who had developed a method based on the calibration between two observers. The gonial angle was measured in degrees by drawing two imaginary lines along the posterior border of the ramus and along the inferior border of the mandible. The type of impaction was assessed by comparing the long axis of the impacted third molar with the adjacent second molar.

The bone level was measured from the cementoenamel junction of the second molar downward until the alveolar bone. The third molar root angle was measured by taking the long axis of the root to the expected position in the arch. All the markings are shown in Figure 1.

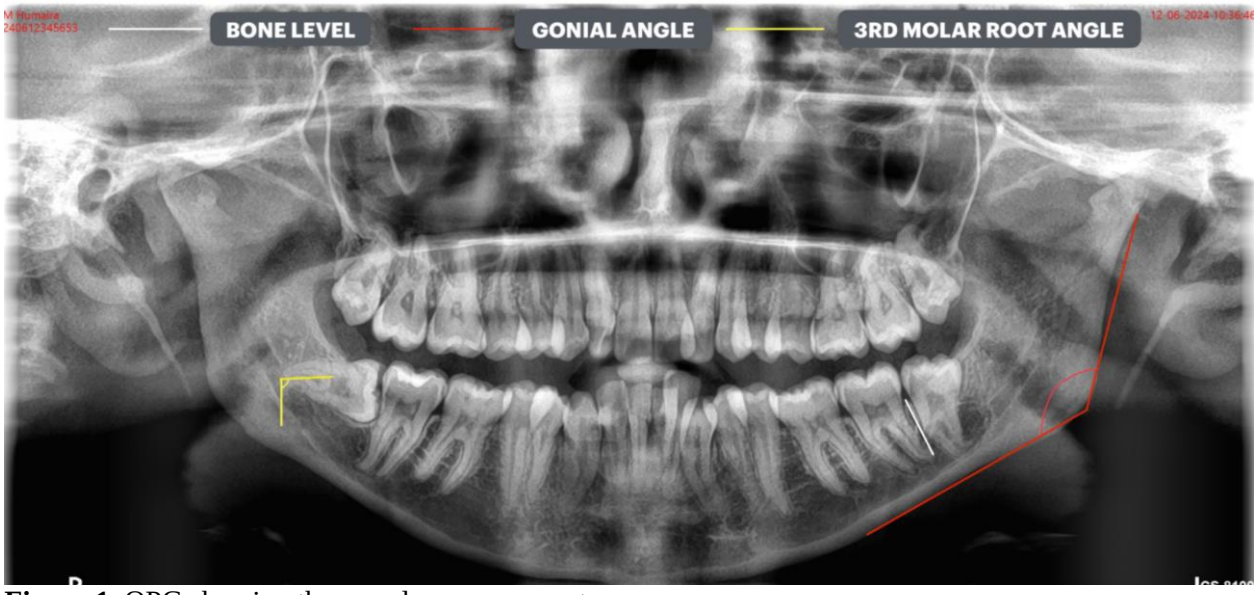


Figure 1. OPG showing the sample measurements.

Statistical Analysis:

The data was imported into an Excel sheet (Microsoft® Excel® for Microsoft 365 MSO, Version 2307, Microsoft corporation, Washington, DC, USA). The collated data was imported into IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). The statistical software was used for the descriptive statistical analysis. Following which the normality of the data was checked. Subsequent to which the inferential statistics was carried out.

RESULTS

The normality of the data was assessed based on the age of the individuals using bell curve fit method (Figure 2) and Shapiro Wilk's test. As the data was not following normal distribution it was decided to use non parametric tests for inferential statistics.

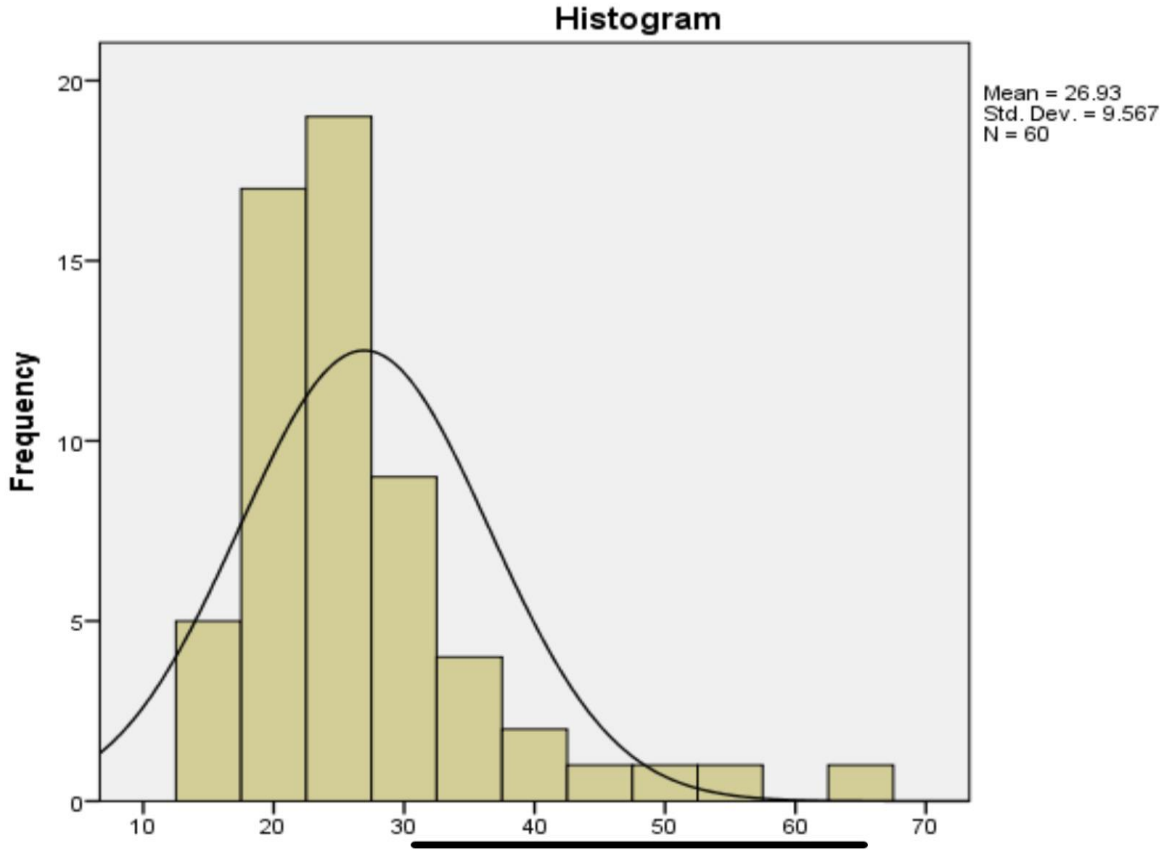


Figure 2. Histogram with bell curve super imposed.

Descriptive statistics

The total samples in the study were 60 of which 35 (58.3%) were males and 25(41.7%) were females. The mean age of the samples was 26.93 ± 9.57 and the median age was 28.65. As the sample was found to have non symmetric distribution the median was also reported. The first parameter assessed was the bone level. From the 60 patients a total of 83 impactions were reported, which means that 33 out of 60 patients had bilateral impactions. Out of the 60 samples there 21(35%) of cases had Mesioangular impaction, 20 (33.3%) had horizontal impaction. (Figure 3)

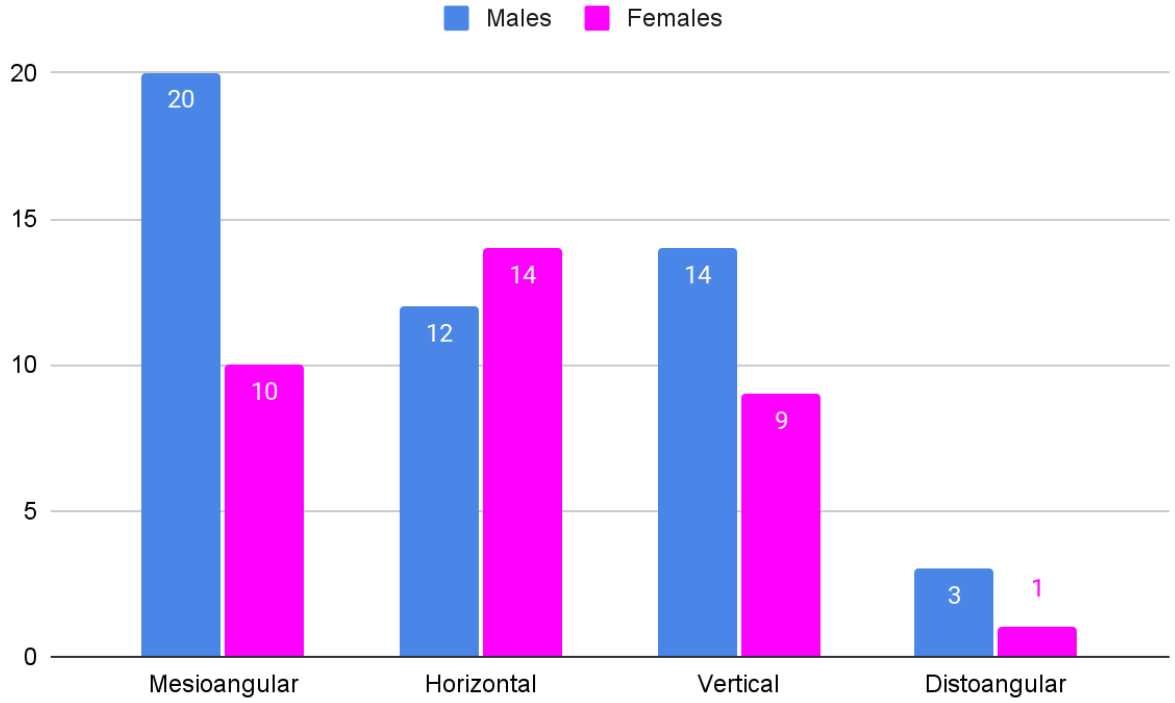


Figure 3. Distribution of gender according to the type of impactions

The bone level was 1.24 ± 0.10 in males while in females it was 1.20 ± 0.09. The median of the bone level was 1.26 ± 0.10 and 1.19 ± 0.09. The mean gonial angle was 123.02 ± 4.93 and 122.74 ± 5.13 in males and females respectively, while the median was 122.40 ± 4.93 and 123.20 ± 5.13 in males and females respectively. The mean and median of the third molar root angle in males was 113.71 ± 18.44 and 117.20 ± 18.44 respectively. The mean and median third molar root angle in females was 111.89 ± 18.34 and 112.3 ± 18.34 respectively. (Table 2)

Table 2. The comparison of the bone level, gonial angle and third molar root angle across the genders.

Gender		Bone Level	Gonial Angle	Third Molar Root Angle
Males	Mean ± SD	1.24 ± 0.10	133.02 ± 4.93	40.81 ± 5.7
	Median ± SD	1.26 ± 0.10	132.40 ± 4.93	41.30 ± 5.7
Females	Mean ± SD	1.20 ± 0.09	132.74 ± 5.13	41.14 ± 5.9
	Median ± SD	1.19 ± 0.09	133.20 ± 5.13	40.70 ± 5.9
Overall Mean of both Genders	Mean ± SD	1.22 ± 0.10	132.90 ± 4.97	40.98 ± 5.7
	Median ± SD	1.24 ± 0.10	132. 90 ± 4.97	41.15 ± 5.7

When the above-mentioned measurements were compared across the different types of impactions, the bone levels were around the same level. The gonial angle had differences across the different types of impactions.

Inferential statistics

As the data followed non normal distribution, non-parametric tests were used to assess the levels of significance. As a first step the data was compared across the genders and it was found that the difference between the genders was not statistically significant for a significance level of 0.05. Table 3

Table 3. The comparison of the bone level, gonial angle and third molar root angle across the Impaction types.

Gender		Bone Level	Gonial Angle	Third Molar Root Angle
Mesioangular	Mean ± SD	1.22 ± 0.09	134.03 ± 5.19	40.01 ± 7.09
	Median ± SD	1.22 ± 0.09	134.30 ± 5.19	37.10 ± 7.09
Horizontal	Mean ± SD	1.22 ± 0.10	130.31 ± 3.90	41.28 ± 5.68
	Median ± SD	1.23 ± 0.10	129.95 ± 3.90	41.15 ± 5.68
Vertical	Mean ± SD	1.24 ± 0.11	133.40 ± 5.07	42.04 ± 4.95
	Median ± SD	1.26 ± 0.11	133.40 ± 5.07	43.80 ± 4.95
Distoangular	Mean ± SD	1.32 ± 0.38	136.25 ± 4.03	40.40 ± 1.41
	Median ± SD	1.32 ± 0.38	136.25 ± 4.03	40.40 ± 1.41

Table 4. The statistical tests for the bone level, gonial angle and third molar root angle across the genders.

Sr.No	Null Hypothesis	Statistical test	P value
1	The distribution of bone level is same across both genders	Independent Sample Mann - Whitney U Test	0.128
2	The distribution of gonial angle is same across both genders		0.738
3	The distribution of third molar root angle is same across both genders		0.708

Table 5. The statistical tests for the bone level, gonial angle and third molar root angle across the type of impaction

Sr.No	Null Hypothesis	Statistical test	P value
1	The distribution of bone level is same across the type of impaction.	Independent Sample - Kruskaal Wallis Test	0.303
2	The distribution of gonial angle is same across the type of impaction.		0.026
3	The distribution of third molar root angle is same across the type of impaction.		0.534

DISCUSSION

Impaction of the lower wisdom teeth is a frequent issue that dentists regularly encounter in their practice. The frequency of impaction in the South Indian ethnic group has been around 45.85% according to a study by Kalaiselvan et al [9] The failure to extract the impacted teeth can cause wide ranging problems such as an association of cysts and other pathologies. The surgical extraction of these impacted teeth is also associated with complications like swelling, trismus, alveolar osteitis (dry socket) and nerve paresthesia. [10] Hence a careful prior surgical planning is needed to avoid the complications .[11]

Since there are prior studies showing that the bone growth patterns do influence the frequency of impaction we decided to implore further into the area .[4] So as a first step we had looked into three variables of bone level or height distal to second molar, gonial angle and third molar root angle to know the variations in the impaction pattern. The bone level was measured from the cementoenamel junction to the bone crest, as described by Faria et al .[11] Although OPGs have some limitations, clinicians still commonly use them to guide interventional decisions.[12] It is essential to assess the distal bone levels as it is an indicator of the development of sensitivity post extraction of the third molar. There have been prior studies which have compared the bone levels between pre and post extraction. [13-15] There has been no study that has reported on the bone level and the type of impaction. Our study shows that the mean pre operative bone levels were almost the same across the different types of impactions with no statistical difference. There is also no significant difference between the genders. This is in line with the observational study that there has been no difference in the association of sensitivity in patients who have different types of impactions.

The gonial angle is a measure of the facial growth pattern which in turn is an indicator of the jaw size. It has been clearly established that one of the commonest reasons for impaction of the teeth is the lack of space in the retromolar area. An increased gonial angle is associated with dolichofacial growth pattern and reduced retromolar space area.[16] In a study by Demiriel et al, the average gonial angle for cases with impaction in was 121.38 ± 7.64. However, these values were significantly higher than the gonial angle observed in patients without impaction.

On a subgroup analysis in their study they had reported that the gonial angles were significantly higher in the distoangular and vertical impaction groups.

However, the differences were not statistically significant. [17]

In our study also the values were the highest in distoangular group and the values were significantly different. However, the overall average gonial angle was higher which could probably be due to the changes in the ethnic nature of the people. In a similar study by

Barone et al also showed higher gonial angles in patients with distoangular impaction. [7]

In a morphometric study from India on the gonial angle it was noted that the average gonial angle in the Indian population was in the range of 117-120`.[18] However there have been no similar studies of studying the gonial angle with the pattern of impactions.

Ours has been the only study to analyze the third molar root angulation to the imaginary occlusal plane. The whole plan of studying the morphometrics is that it helps us to study the patterns which could be predictors of the impactions.

Additionally, our findings corroborated those of Fernandes et al.'s study[13], which showed a correlation between aging and a shift in the alveolar crest's status. In the present investigation, males showed a greater degree of bone loss than females, although the difference was not statistically significant. Similar results were found in the study by Dias et al. [14], which used panoramic radiography to determine whether there was a significant difference between males and females in the degree of bone loss distal to the MSM. It is important to note that a number of variables, including smoking patterns, impactions, and neglecting to maintain good oral hygiene, have the potential to exacerbate periodontal disease in the mandible [15,16]. Thus, bone alterations such as bone loss could happen if an impaction is not looked after. Our results showed bone loss in individuals who did not have the IMTM extracted following an examination of their follow-up OPGs, despite differences in the type of the IMTM and other risk factors among the study participants. The study group showed bone growth and improvement distal to the MSM following IMTM extraction. These results were consistent with those of Passarelli et al. [17], who noted that once an IMTM was surgically removed, their patients' periodontal health generally improved. An impacted tooth can be removed to enhance access for cleaning and consequently, overall health.

Conversely, after removing an IMTM, Kan et al. [18] noted the development of periodontal defects on the distal end of the MSM. Various patterns of IMTMs have been found in various demographic samples by several researches. [19, 20]

The Mesioangular type of impaction was found to be more common than the horizontal type in the current study. In the Arab Emirati community, Mesioangular impaction was shown to be more common than other forms, according to Alsaegh et al. [21] In a similar vein, Eshghpour et al.[22] discovered that Mesioangular impaction was more common in Iranians. In an investigation of the Indian population, Prajapati et al.[6] too found that Mesioangular inclination was more prevalent than the other patterns, which included distoangular, vertical, and horizontal inclinations. The present study identified a greater incidence of bilateral impaction, contrasting with Alsaegh et al.'s findings [21], which showed a similar distribution between unilateral and bilateral impactions. Nevertheless, a number studies have documented significant differences in the prevalence of bilateral versus unilateral impactions across diverse populations, including those from Saudi Arabia, Singapore, China, and Libya [23,24], with bilateral impaction being more recurrent in these groups.

The limitations of our study were that no clinical parameters were taken into consideration and also the three-dimensional imaging modalities were not taken into account for the bone level comparison. Though we chose the sample choice according to the power of the study it is still a smaller number considering that this is a retrospective study. A notable strength of this study is that it provides clear evidence of bone level changes in individuals with an impacted mandibular third molar compared to those without. This highlights the effectiveness of OPG in assessing these changes, which can help clinicians develop an appropriate management strategy. [29]

CONCLUSION

Impacted third molars continue to be a common finding in dental practice, and their presence can influence mandibular structure in subtle yet clinically important ways. In this study, variations in gonial angle were found to differ significantly across types of impactions, suggesting a possible link between mandibular growth patterns and impaction risk. Although bone level differences between genders were not statistically significant, a slight trend toward greater bone loss in males was noted. Importantly, patients who had their third molars extracted showed better bone levels distal to the second molar, underscoring the value of early intervention when indicated. The use of panoramic radiographs proved effective in capturing these changes, making them a practical tool for routine evaluation. These findings may help clinicians better anticipate complications associated with third molar impactions and plan treatment more effectively. Further studies using larger samples and three-dimensional imaging are encouraged to build on these observations.

DECLARATION

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CONFLICT OF INTEREST

None declared.

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ETHICS STATEMENT

This study was approved by the Institutional Ethics Committee (Ref No: IHEC/SDC/OMED-2305/23/15). Patient consent was waived due to anonymized radiographic review and no direct human intervention.

INFORMED CONSENT STATEMENT

Patient consent was waived because we only reviewed the radiographic images of the patients anonymously, and there was no intervention or investigation on humans directly.

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IS FLAPLESS IMPLANT PLACEMENT PROCEDURES BETTER THAN CONVENTIONAL FLAP IN PARTIALLY EDENTULOUS PATIENTS": RANDOMIZED CONTROL STUDY

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ABSTRACT

Background: Dental implants are a reliable rescue for edentulism. The dental implants had undergone various upgrades to improve the osseointegration. One of such is flapless implant placement.
Aim: To assess the efficacy of flap vs flapless implant placement.
Material and methods: A total sample of 20 implants were included which were randomly grouped into two based on the treatment they received; Group A (Control): 10 patients who are undergoing open flap implant placement surgery and Group B (Experimental group) included 10 patients who are undergoing flapless implant placement surgery. ISQ, Plaque index and soft tissue healing was assessed immediately and 2nd month follow up.
Results: Group B exhibited statistically significantly higher mean ISQ value compared to Group A at baseline and second post-op month. Group B exhibited a higher mean plaque Index and soft tissue healing index values compared to Group A at baseline and second post-op month but not statistically significant.
Conclusion: By avoiding the need for incision and flap reflection, maintaining the vascularity to the underlying bone, and reducing edema due to surgical intervention and its inflammatory mediators, flapless implant placement offers a promising role in implantology. This leads to a more stable soft tissue profile and higher implant stability following implant placement, as well as a more desirable aesthetic result.
***Keywords*:** Flapless implant placement; Atraumatic implant placement; Dental implant; ISQ; plaque Index

1. INTRODUCTION

Over the last decade, the increase in aesthetic demand and technical development has led to miraculous evolution in dental Implantology domain. Dental implants have emerged as a remarkable solution available in modern dentistry for both total and partial edentulism. [1] Although it has become the treatment of choice for most dentists, still, the implant failure, or implant stability and complications associated with implants are the biggest challenge.[2]

Various modifications have been investigated to improve Success of implant osseointegration. Nonetheless, to minimize the peri- and post-surgical discomfort, maximizing aesthetics, and improving the long-term success of the implants, minimally invasive flapless technique have been recently investigated.[3] This Atraumatic technique (with respect to the flap elevation and exhibition of the bone) provides less crestal bone resorption that could influence on final aesthetic results.[4] Also, as it minimizes surgical trauma, it subsequently reduces post-operative pain, swelling, faster healing, minimal interference on the blood, thereby by reduction of bleeding, surgical time, lower morbidity and an increase on patient comfort were the pros of this technique.[5,6] Jeong et al. [7] in 2011 conducted a prospective trial over 432 implants achieving 100% of success after a year, with an average bone loss of 0,3 mm. They come to the conclusion that the flapless technique is reliable and effectively maintains the health of the peri-implantary mucous and crestal bone.

Nonetheless, this particular approach is linked with certain setbacks too. The lack of flap reflection and the small diameter of mucous openness makes the vision very limited. [8] Subsequently, the limitations on the view have a possibility of damaging neighboring structures such as cortical bone, specially the buccal cortical plate, neighboring teeth roots, important nerves or the sinus.[5]

The biological stability of the flapless and flapped implant placement techniques has not been sufficiently studied. Thus the present study aims to compare the efficacy of stability using duration through resonance frequency analysis (RFA) in flap vs flapless implant placement. And also to evaluate the hypothesis "Does implant placement with a flap versus a flapless technique influence biological stability?"

MATERIAL AND METHODS

This randomized controlled study was conducted in the Department of Periodontology and Oral Implantology at Sree Balaji Dental College and Hospital in Chennai, India, between May 2023 and November 2024. The Sree Balaji Dental College and Hospital's Institutional Ethical Committee in Chennai, India, granted ethical approval prior to the study's commencement. (SBDCH-IEC-CT-/12-04/26).

Sample Size Calculation:

It was revealed that from a literature survey the mean ± S.D of the parameter of percentage change of means between two-time intervals of two groups; test group and control group were 09.90+0.32, 07.90+0.26. G* Power analysis revealed that the actual power and effect size was 90% and 3.342 respectively. So, for 95% confidence interval level of significance 5% the sample size was 10 in each group and the overall sample size was planned to be 20.

Study population:

Twenty patients (20 implants) were included. The study samples were randomly divided by flipping a coin into two groups based on the treatment they received. Group A (Control group): 10 patients who are undergoing open flap implant placement surgery. Group B (Experimental group) included 10 patients who are undergoing flapless implant placement surgery.

Selection Criteria:

Both male and female who are systematically healthy and aged 20-40 years with partially edentulous space in the posterior aspect of the maxilla or mandible were included. Minimum crestal width of 6mm, minimum Interocclusal distance of 5mm, minimum medio-distal width of 7-10 mm, crest to mandibular canal distance of at least 10 mm, and Minimum 10 mm of height were included.

Patients with cardiac history, Poorly or uncontrolled diabetic patients or on vasodilators, women who are Pregnant or those who are lactating were exempted. Patients with poor periodontal health or those requiring guided bone regeneration were excluded. Patients with a habit of smoking, Bruxism or parafunctional habits were excluded. Patients with previously implanted or bone grafts placed at the surgical site or traumatic extraction at the surgical site were excluded.

Study procedure:

- Following subject selection, informed consent after being briefed on study's methodology was obtained. A comprehensive medical and dental history was obtained prior to the examination. An IOPAR and CBCT imaging was performed in all cases. Prior to surgery, all patients received thorough supragingival scaling and root planning. Patients were evaluated after a period of 3 weeks and only those patients who were capable of maintaining adequate oral hygiene measures were included. Routine blood investigation was assessed.

- Group A (open flap implant surgery): A conventional open flap implant surgery was performed under an aseptic environment.

- Group B: As a sterile procedure, the flapless implant operation was performed. To prepare the pre-operative site, a 5% povidone-iodine solution was used. Local anaesthesia was given. At the implant insertion location, a rotary tissue punch set to a maximum speed of 35 rpm was used to cut the soft tissue at the crest of the alveolar bone in a circular motion. Following the instructions provided by the manufacturer, the implant placement operations were carried out after the circular soft tissue cut was removed using tissue forceps. An externally irrigated handpiece with a low speed and high torque was used in conjunction with an electric motor to prepare the implant site. External irrigation was done with sterile saline while the implant site was being prepared. The bone site preparation procedure was started with a 2

mm first drill to reach the desired length. To determine the depth of the osteotomy site, the depth gauge and direction indicator were utilized. Verify the implant's parallelism. Sequential drilling was completed up to the last drill. They employed Zimmer implants (Zimmer Dental, Carlsbad, CA, USA). Under light apical pressure, the implant was manually placed into its bed in a clockwise motion until it stopped. After inserting the implant to the ultimate insertion depth with a ratchet wrench, the healing abutment was put into the occlusal opening of the implant and tightened. The tenth postoperative day and the second postoperative month were used to evaluate each patient.

- Study outcomes: Implant stability quotient (ISQ), plaque Index (PI) and Soft Tissue Healing Index by Landry, Turnbull and Howley was assessed at baseline and at 2nd Postoperative month.

RESULTS

The average age of the participants in Group A and Group B in this study was 37.33 years and 34.87 years, respectively. Nine males and six females made up Group A, while seven males and eight females made up Group B.(Table 1)

Table 1. Study sample demographics for the current investigation

Variable	Category	Group A	Group B
Age (in years)	--	37.33 ± 6.11	34.87 ± 6.82
Gender	**Male**	9 (60%)	7 (46.7%)
	Female	6 (40%)	8 (53.3%)

Table 2 compares baseline and 2-month ISQ levels within each group. The ISQ values in group A were 68.47 at baseline and 76.13 after two months, respectively. The baseline and two-month ISQ values for group B were 70.73 and 80.00, respectively. The ISQ levels at two months were substantially higher than the baseline ISQ values in each group.

Table 2. Comparison of baseline and 2-month ISQ levels within each group

Group	Baseline		2 months		p-value
	Mean	SD	Mean	SD	
Group A	68.47	3.09	76.13	5.71	0.001*
Group B	70.73	1.71	80.00	4.14	0.001*
	0.037*				

A significant difference at p≤0.05 is indicated by the Wilcoxon signed rank test; *

Implant Stability Quotient (ISQ) levels in two groups (Group A and Group B) at baseline and two-month intervals are compared in Table 3. At the beginning of the study, Group B exhibited a statistically significantly higher mean ISQ value (70.73) compared to Group A (68.47). After 2 months, both groups showed an increase in mean ISQ values. Group B still had a higher mean ISQ (80.00) than Group A (76.13), but this difference was not statistically significant (p = 0.081). Since the baseline ISQ levels between the two groups differed significantly, an adjusted analysis was performed keeping baseline values as covariates. When adjusted means were compared using ANCOVA, the difference between the groups (Group A: 76.82, Group B: 79.31) was not statistically significant (p = 0.213).

Table 3. ISQ values compared between the two groups

Interval	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Baseline[¥]	68.47	3.09	70.73	1.71	0.037*
2 months[¥]	76.13	5.71	80.00	4.14	0.081
Adjusted mean[#]	76.82	1.32	79.31	1.32	0.213

¥Mann Whitney test; #ANCOVA test; * indicates a significant difference at p≤0.05

Table 4 compares the baseline and 2-month modified plaque index within each group. In each group, the 2-month modified plaque index score was significantly greater than the baseline modified plaque index score.

Table 4. Comparison of baseline and 2-month modified plaque index within each group

Group	Baseline		2 months		p-value
	Mean	SD	Mean	SD	
Group A	0.00	0.00	1.73	0.70	<0.001*
Group B	0.00	0.00	1.60	0.83	0.001*

Wilcoxon signed rank test; * indicates a significant difference at p≤0.05

The modified plaque index for Group A and Group B is compared in Table 5 at two separate time points: baseline and two months. Both at the start of the study and two months later, there was no statistically significant change in the modified plaque index between the groups.

Table 5. Comparison of the two groups' adjusted plaque index

Time interval	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Baseline	0.00	0.00	0.00	0.00	1.000
2 months	1.73	0.70	1.60	0.83	0.775

Mann Whitney test

Table 7 compares the baseline and 2-month soft tissue healing within each group. In each group, the 2-month soft tissue healing score was significantly lower than the baseline scores.

Table 7. Comparison of baseline and 2-month soft tissue healing within each group

Group	Baseline		2 months		p-value
	Mean	SD	Mean	SD	
Group A	2.20	0.41	1.60	0.63	0.007*
Group B	1.80	0.41	1.20	0.41	0.003* Denotes a significant difference at p≤0.05 in the Wilcoxon signed rank test.

* Denotes a significant difference at p≤0.05 in the Wilcoxon signed rank test.

Soft tissue healing at baseline and two-month intervals is compared between two groups (Group A and Group B) in Table 6. Both at the start of the study and two months later, there was no statistically significant difference in the soft tissue healing between the groups.

Table 6. Comparison of the two groups' soft tissue healing

Time interval	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Baseline	2.20	0.41	1.80	0.41	0.098
2 months	1.60	0.63	1.20	0.41	0.106

Mann Whitney test

DISCUSSION

Dental implants provide a robust and solid basis for dental restorations such as crowns, bridges, and dentures. A dental implant that has undergone osseointegration is a reflection of the biological and mechanical anchoring of the implant fixture into the jaw bone during normal clinical function.[11] The osseointegration can be measured as ISQ..

The ostell RFA configuration was chosen for the present study to test the stability of the implants over the healing phase since it was thought to be the most accurate, reliable, and least invasive technique. [12] This technique measures the stiffness of implant-bone connection. The experimental and control groups in this study had mean ISQ values of 80.00 and 76.13 at the second month follow-up, respectively. Compared to traditional flapped implants, flapless implants had higher ISQ values; however, this difference was not statistically significant (p = 0.081).

In line with the results of the present study, in Al-Juboori [13] et al study, the mean ISQ values at 12th month of 82.60 and 82.3 was yielded in experimental and control groups respectively and the difference was not statistically significant. However, Al-Juboori [13] et al noted no significant differences in implant stability between implants placed via the flapless and conventional flapped techniques during the healing period i.e in the first 6 postoperative months. This could be explained by the fact that low ISQ values are the result of ongoing bone remodeling and maturation in both groups during this healing phase. However, we found that there were notable differences both within and between groups in this study.

Similarly, the mean difference in RFA from 0–12 months between the flapless and flap implant placement techniques did not differ significantly in the Sonam Rana et al. [57] study. In contrast to the results of the present study, in the study performed by Cannizzaro et al [14], the ISQ values were similar between the two groups at baseline (2 months after loading/delivery of the definitive prosthesis) and 1 year after loading, and decreased significantly over time for both group.

In the present study, in each group, the 2-month modified plaque index score was significantly greater than the baseline modified plaque index score. The groups' differences in modified plaque index at two months after surgery were not statistically significant. Similar to the present study, Tsoukaki et al [15] noted that the flapped implants exhibited significantly higher mean mPLI values (P = 0.013) after 6 weeks compared with flapless implants. You et al. (2009)[16] in an experimental study showed that the flapped group had higher GI and bleeding on probing (BOP) compared with the flapless group (GI: 0.9 ± 0.5 and BOP: 0.7 ± 0.4 in the flapped group and zero values for both parameters in the flapless group), 3 months after implant placement. In Wang et al [17], after the 2nd week to 3rd month, there was a trend for a decreased mPI score in the flapped group, compared to 1-week post-surgery. In contrast, the MI group's mPI score dropped at the 4-week mark; however, no statistically significant differences were observed at the 1-, 2-, 4-, or subsequent appointments. Additionally, at one and two weeks following surgery, statistically significant differences between the two groups were discovered.

Additionally, the posterior maxilla's anatomical and structural characteristics, such as its close proximity to the maxillary sinus and consequently low bone quality and quantity, may jeopardize the clinical results of dental implants. Depending on the degree of resorption, the maxilla's shape changes when it becomes edentulous. In an elderly population, the maxillary cortical bone becomes thinner and more porous posteriorly.[18]

Although there was no appreciable difference between the flapped and flapless groups in terms of soft tissue healing and plaque index, the ISQ values of flapless implants were greater than those of the traditional flapped group in the current investigation. Fortin et al. [19] reported that in addition to these better results, flapless treatments resulted in a faster decrease in pain and a higher percentage of patients experiencing no discomfort. The flapless procedure, they say, aims

to reduce the invasiveness of surgery, hence reducing surgical consequences such as discomfort, edema, and hematoma. Due to its ability to reduce surgical edema and associated inflammatory mediators, protect the blood supply to the underlying bone, and eliminate the need for incision and flap reflection, seamless implant insertion has great promise in the field of implantology. As a result, there is less loss of crestal bone and a more stable soft tissue profile following implant placement, which produces a more appealing visual result. This is because patient comfort and satisfaction are important aspects of implant therapeutics.

The absence of a computer-guided template for patients is the study's limitation. Shorter follow-up period and small sample size are additional limitations. There needs to be more multicentric research done with a bigger sample size and a longer follow-up time.

CONCLUSION

Because it avoids the need for incision and flap reflection, maintains the vascular flow to the underlying bone, and lessens surgical edema and accompanying inflammatory mediators, we concluded that flapless implant placement offers a promising role in implantology. This results in an improved cosmetic outcome, a more stable soft tissue profile, and increased implant stability after implant placement. In light of the current study's modest sample size and brief follow-up period, more multicentric studies with a larger sample size and longer follow-up duration are needed to validate its findings.

DECLARATIONS

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Competing Interests:

The authors have no competing interests to declare.

Ethical Approval:

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent:

Not applicable.

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CASE REPORT

ANTERIOR MAXILLARY REHABILITATION WITH BASAL IMPLANTS AND IMMEDIATE LOADING - A CASE SERIES

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ABSTRACT

Background: Osseointegration, first proposed by Dr. Brånemark, revolutionized dental implantology. However, traditional implants often present challenges in cases of severe bone atrophy, sinus enlargement, or systemic conditions such as uncontrolled diabetes. Basal or cortical implants, with their unique design enabling anchorage in the basal cortical bone, eliminate the need for bone augmentation and allow immediate functional loading.

Objectives: To present a case series demonstrating the clinical application and outcomes of basal implant placement with immediate loading in patients with compromised bone conditions.

Results: Two female patients aged 24 and 25 years underwent basal implant placement with immediate loading. The procedures, including socket preparation, implant placement, impression taking, and crown fabrication, were completed with minimal invasiveness and rapid recovery. Multi-cortical engagement principles were applied, achieving stable anchorage and functional restoration without bone grafting. Both cases demonstrated successful outcomes with immediate function and patient satisfaction.

Conclusion: Basal implantology, based on multi-cortical engagement and immediate loading, provides a time-efficient, cost-effective, and reliable solution for dental rehabilitation in patients with inadequate bone volume for conventional implants. This approach offers predictable results even in anatomically or medically compromised cases.

Key word: osseointegration, basal implantology, basal implant placemen, immediate loading

INTRODUCTION

The success of implant therapy has increased and expanded globally ever since Dr. Brandemark discovered the "osseointegration" of implants into alveolar bone [1]. Atrophied ridges, caudal extension of the maxillary sinus, protracted healing of 4-6 months, a few medical disorders like uncontrolled diabetes, and the fact that smokers are not recommended for this Branemark technique are only a few of the limits.When it comes to immediate loading, a basal implant is preferable to a conventional implant, which takes a lengthy time to osseointegrate.

When replacing one or more teeth right after extraction, basal implants can also produce aesthetically pleasing profiles .[2]

CASE SERIES

CASE 1

Patient Information:

A 24-year-old healthy female presented with missing upper front left teeth. Retained deciduous teeth were extracted, and congenital absence of #22 and #23 was confirmed. She had no significant medical history of habits Clinical Findings:

The maxillary anterior ridge had reduced bone volume (CBCT: Type 2 bone). All mandibular teeth were present.

Diagnostic Assessment:

OPG and CBCT (Carestream, Kodak, India) revealed deficient bone in the #22 and #23 regions. (Figure 1)

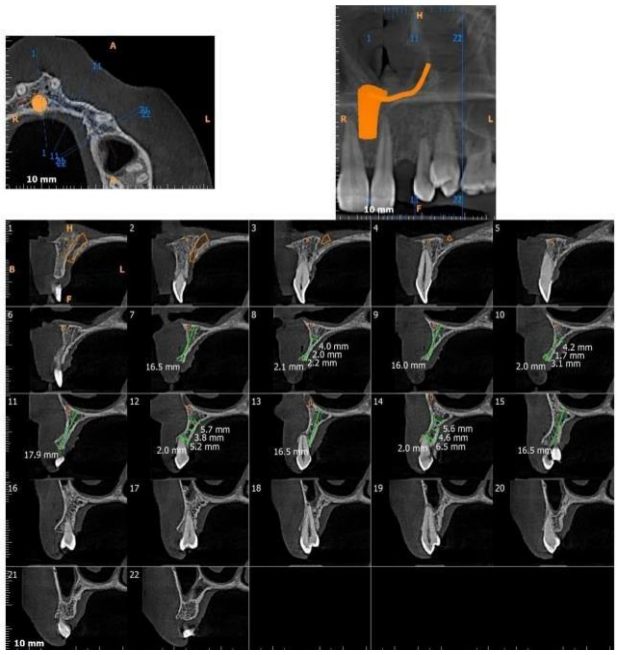


Figure 1. CBCT showing bone dimensions

No signs of pathology or systemic contraindications. in #22#23 tooth region

Therapeutic Intervention:

Pre-operative prophylaxis with amoxicillin (1g before surgery, 500 mg TID for 3 days). Local anesthesia with lignocaine (2% with adrenaline). Metal-sleeved surgical guide was used (Figure 2).



Figure 2. Surgical template with metal sleeves

Two tapered cortical implants (Bioline I, Bioline Dental GmbH & Co.KG, Berlin, Germany) (3.5 × 29 mm) placed at 20° to the occlusal plane (Figure 3). Graft was placed (Figure 4). Prosthesis delivered the same day (Figure 5).



Figure 3. Placement of graft



Figure 4. Basal implant in 22,23 region



Figure 5. Cementation of crowns with basal implant in 22,23 region

Follow-Up and Outcomes

Post-op radiographs confirmed correct positioning.(Figure 6) No signs of infection or implant failure were noted. Patient was satisfied functionally and aesthetically.



Figure 6. Post-operative OPG showing basal implant in 22,23 region

CASE 2

Patient Information:

A 24-year-old healthy female reported with a mobile upper front right tooth. Tooth #13 showed Grade 3 mobility.

Clinical Findings:
Bone height: 6.0 mm, Bone width: 4.0 mm. (Figure 7) All mandibular teeth were present.

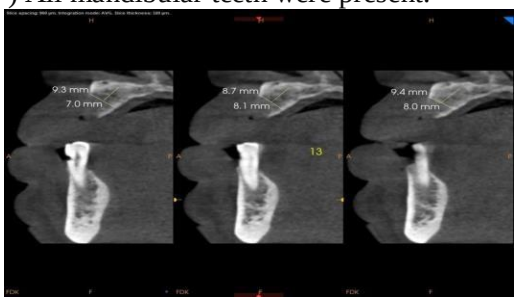


Figure 7. CBCT showing bone dimensions in #13 tooth region

Diagnostic Assessment:
OPG and CBCT (Carestream, Kodak, India) confirmed localized bone loss in the #13 region. No systemic issues noted.

Therapeutic Intervention:
Prophylaxis with amoxicillin (as in Case 1). Local anesthesia with lignocaine 2% and adrenaline. Guided (Figure 8) placement of a single basal implant (3.5 × 29 mm) (Bioline I, Bioline Dental GmbH & Co.KG, Berlin, Germany) at site #13.Figure 9. Graft was placed. (Figure 10) Immediate fixed prosthesis delivered. (Figure 11)



Figure 8. Surgical template

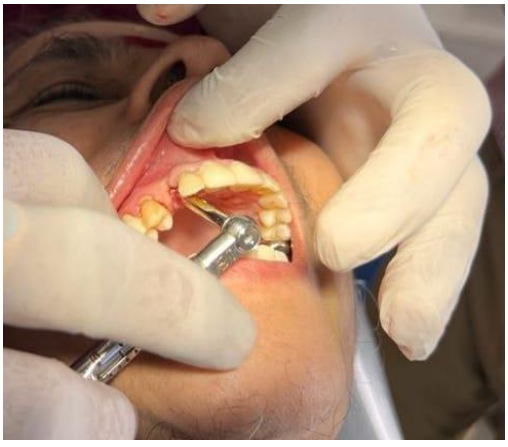


Figure 9. Placement of graft



Figure 10. Basal implant in #13 region



Figure 11. Cementation of crowns with basal implant in #13 region

Follow-Up and Outcomes:
Implant was stable. OPG showed successful osseointegration. (Figure 12)The patient reported no discomfort post-op and was satisfied with the esthetics.



Figure 12. Post-operative OPG showing basal implant in #13 region

Patient Perspective
Both patients expressed satisfaction with the rapid results and minimal postoperative issues. They appreciated the single-visit restoration process, particularly the absence of grafting procedures.

Informed Consent
Written informed consent was obtained from both patients for treatment and for inclusion in this case series report.

DISCUSSION

In 1972, Dr. Jean-Marc Julliet created and utilised a single-piece implant known as the basal impant. Dr. Gerard Scortecci, a French dentist, created an

enhanced basal implant system with corresponding cutting instruments in the middle of the 1980s.[3] Since the prosthesis cannot replicate the ideal dentulous architecture, replacing a missing tooth or teeth is the most difficult dental procedure performed today. Implants are the most biocompatible and appropriate prosthetic device to address this issue and achieve the preceding paradigm. The quality (thickness) and quantity of bone, as well as the macro and micro architecture of the implant, all affect its success.[4] The bone-implant contact reflect the barrier provided by the bone during insertion, and it can also reveal the type of bone it goes through. The lingual cortex, mandibular symphysis, etc. in the mandible, and the anterior nasal spine, nasal floor, pterygoid regions, etc. in the maxilla are examples of atrophied bone sites where basal bone implants are typically positioned and require stable cortex for engagement.[5] The basal implants in the maxillary and mandibular jaws support single or multiple unit restorations. Theseimplants may be used in portions of bone that have healed from extractionsites, freshly removed sockets, and bone regions with reduced height and width.[6] Using cortical Implants over endo-osseous implants save time and money because the prosthesis is fixed 72 hours after implant surgery. Along with avoiding the necessity for a second surgery to expose the implant and fix the abutment over it, there is no longer any requirement for provisionals or interim dentures. Because they are minimally invasive, they also have a low rate of post-operative oedema, and the operation sites heal quickly and frequently without any problems.[7] Cortical implants avoids sinus lifts, nerve transpositioning, and bone augmentation or grafting, making it effective even in the most bone-unfavorable circumstances. [8,9] In the current case series, two young female patients with poor bone volume have had successfully rehabilitated with basal implants with rapid loading. Anatomical restrictions and decreased alveolar bone volume in both cases made it difficult to employ traditional endosseous implants without additional surgical techniques like bone grafting or sinus augmentation. Furthermore, there was little postoperative discomfort, quick healing, and no complications because the surgery was atraumatic. However, the expected loss of unstimulated alveolar bone over time is a crucial clinical issue. The alveolar ridge may resorb as a result of occlusal loads being transferred directly to the basal bone components instead of the crestal bone. This could result in soft tissue shrinkage and possible spaces between the gingiva and prosthesis. Overall, these cases have been reported to support the usefulness of basal implants as a practical and effective implant dentistry method, especially for patients who have anatomical problems or who require rapid function.

CONCLUSION

Patients with limited bone volume can replace their teeth quickly, with little discomfort, and without the need for bone grafting thanks to basal implants, which provide a safe and effective alternative. Basal implants exhibit reliable results even in intricate situations.

DECLARATIONS

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Competing Interests:

The authors have no competing interests to declare.

Ethical Approval:

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent:

Not applicable.

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CASE REPORT

ENCEPHALITIS MANIFESTATION IN A PATIENT WITH EXPANDED DENGUE SYNDROME

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Abstract

The expansion of dengue symptoms to other organs has been known as expanded dengue syndrome. One form of this is encephalitis. An 18-year-old male was reported to have communication disruption for one day, high fever for 4 days, headache, retroorbital pain, and myalgia. Thrombocytopenia, hemoconcentration, NS1, and IgG-IgM dengue were positive in laboratory testing. Brain CT results gyral enhancement on the right and left side fronto-temporoparieto-occipital lobe, hypodense area with unclear border on occipital lobe, effacement of sulci and gyri. Dengue hemorrhagic fever and encephalitis were the patient's diagnoses. After five days of therapy, the condition improved. Febrile seizures, intracranial thrombosis/ hemorrhages, encephalopathy, aseptic meningitis/ encephalitis, transverse myelitis, polyneuropathies/ mononeuropathies/ Guillain-Barre Syndrome, and subdural effusions are the neurological signs of expanded dengue infection. CNS involvement reflects severe disease with poorer recovery. A case of encephalitis in a patient with dengue hemorrhagic fever has been reported. Supportive management improves

Keywords: Expanded Dengue Syndrome; Dengue Encephalitis; Neurological Manifestations; Supportive Management.

INTRODUCTION

Dengue is a self-limiting, systemic arboviral infection. The incidence rate of Dengue Hemorrhagic Fever (DHF) in Indonesia has increased significantly over the last 50 years, rising from 0.05 cases per 100,000 person-years in 1968 to 77.96 cases per 100,000 person-years in 2016. In Indonesia, there are 22.55 DHF cases and DHF-related deaths for every 100,000 person-years[1].

Clinical manifestations of dengue virus infection range widely, from dengue fever (DF) to potentially fatal DHF and dengue shock syndrome (DSS). EDS is a rare form of dengue that causes serious damage to the brain, liver, bone marrow, kidneys or heart. Prolonged shock, co-infections, or underlying comorbidities could be the cause. EDS is likely to develop in some high-risk categories, including pregnant women, young children, the elderly, coronary artery disease, hemoglobinopathies, and immunocompromised people (World Health Organization, 2009).

Neurological manifestations of EDS are encephalopathy, febrile seizures, intracranial thrombosis/ hemorrhages, Guillain-Barre Syndrome/ polyneuropathies/ mononeuropathies, aseptic meningitis/ encephalitis, transverse myelitis and subdural effusions (Anam et al., 2017). About 4–21% of dengue patients, meningoencephalitis and encephalitis have been found. CNS involvement reflects severe disease with poorer recovery. The mortality rate from dengue encephalitis may increase to 3.7% (Araújo et al., 2012). We will present a case of encephalitis patient with probable expanded dengue syndrome.

CASE REPORT

Mr. S, a 20-year-old man, unmarried, arrived at the Soetomo Teaching Hospital emergency room with a communication disruption for 1 day. There was altered mentation. There was no hemiparesis, seizures, dysarthria, or asymmetric face. There was a history of moderate-grade, intermittent fever of four days' duration, headache, retroorbital pain, myalgia, nausea, loss of appetite, and lethargy of three days' duration. There were no rash or hemorrhagic manifestations. There was no abdominal pain, vomiting, or abdominal enlargement. There was no cold, cough or shortness of breath, diarrhea, constipation, or weight loss. His previous medical history included a dengue fever at 10 years old. There was no history of traveling or mouse contact. There were no comorbidities.

Based on physical examination, GCS 425, blood pressure 117/76 mmHg, pulse 117 times per minute,

breathing 20 times per minute, axillary body temperature 38.9° C, SpO2 98% with free air. The weight was 50 kg, height was 165 cm (BMI 18.36 kg/m^2). Examination of the head: no anemic conjunctivae, no sclera jaundice, cyanosis, or shortness of breath. No lymph node enlargement or elevated jugular vein pressure. On chest inspection was symmetric. Symmetrical lung areas, no wheezing or rales, and neither murmurs nor gallops in lung examination. Abdominal examination revealed no organomegaly and normal sounds of bowel. Neurology examination: there were no meningeal signs or Kernig sign, Brudzinski 1-4 sign. Lingual palsy and facial palsy were difficult to evaluate. Sensory examination was difficult to evaluate. Motoric evaluation BPR +2/+2, TPR +2/+2, APR +2/+2. There was no Chaddock sign. The cerebellum examination was difficult to evaluate.

Laboratory tests when the patient was admitted to hospital: Hb 15.3 g/dL, Leukocytes 3320/mm3, Platelets 93000/mm3, HCT 43.8%, Neutrophile 70.8%, Lymphocyte 1.3%, Aspartate Aminotransferase (AST) 264 U/L, Alanine Aminotransferase (ALT) 141 U/L, Blood Urea Nitrogen 12 mg/dL, Serum Creatinine (SC) 1.01 mg/dL, Albumin 4.4 gr/dL, Potassium 4.1 mmol/L, Sodium 132 mmol/L, Chloride 93 mmol/L, CRP 0.74 mg/dL, APTT 29.4, PPT 10.8, HBsAg negative, Anti HCV negative, HIV rapid test negative. Blood gas analysis with pH 7.49; pCO2 26; pO2 122; HCO3 19.8; Be -3.5; O^2 saturation 99%. The NS-1 test revealed positive results.

Chest X-ray examination results: heart and lungs within normal limits. Brain CT scan examination: Gyral enhancement on the right and left side frontotemporoparietooccipital lobe, a hypodense area with unclear border on the occipital lobe, effacement of sulci, and gyri. Normal ventricle, cisterna, pons, cerebellum, orbita, mastoid, right and left side paranasal sinus and calvaria. There was no calcification or midline deviation. DHF grade I (4th day) and encephalitis were the patient's diagnoses based on the history, physical examination, laboratory, and radiological examination. Diagnostic plans for this patient are serial complete blood count, NS1, IgG, IgM Dengue, ALT and AST evaluation, and lumbal puncture for cerebrospinal fluid analysis (patient family refused). Treatment plans for the patient were bed rest, head trunk up 30°, the nasogastric diet starting from 50 ml every 4 hours, infusion of NaCl 0.9% 2000 ml, Metamizole 1 gram every 8 hours intravenously, and Omeprazole 40 mg every 12 hours intravenously.

On the 2nd day of treatment, the patient was still having altered mentation. There was a communication disruption, nausea and fever began to decrease. Based on physical examination, GCS 425, blood pressure 120/70 mmHg, pulse 103 times per minute, breathing 20 times per minute, axillary body temperature 38.6°C. Laboratory tests: Hb 16.7g/dL, Leukocytes 4870/µL, Platelets 42000/µL, HCT 49%, SGOT 255 U/L, SGPT 153 U/L, IgM Dengue positive and IgG Dengue positive. Peripheral blood smear showed erythrocyte normochromic normocytic, polychromasia (-), normoblast (-), leukocyte normal count, dominated with neutrophil segment, immature granulocyte (-), atypical lymphocyte (plasmacytoid), blast (-). Fewer thrombocytes, giant platelets (+), leukocytes with atypical lymphocytes, and thrombocytopenia. Patient diagnosed with DHF grade I (5th day), encephalitis, and elevation of nonspecific transaminase enzymes. The patient's previous therapy is continued.

On the 3rd day of treatment, the patient communicated with a few words. Reduced fever and nausea complaints. GCS 446, 130/70 mmHg blood pressure, 102 regular pulses, breathing 20 times per minute, axillary body temperature 38.0°C, SpO2 98%. Laboratory tests: Hb 15.7g/dL, Leukocytes 5420/µL, Platelets 35000/µL, HCT 46.3, Neutrophile 35.9%, Lymphocyte 53.9%. The patient's previous therapy is continued.

On the 4th day of treatment, altered mentation was better. Fever decreased. GCS 446, blood pressure 117/71 mmHg, pulse 71 times per minute, breathing 20 times per minute, axillary body temperature 36.3°C, SpO2 98%. Laboratory tests: Hb 14.8 g/dL, Leukocytes 6930/µL, Platelets 42000/µL, HCT 44.4%, SGOT 84.4, SGPT 68.1. The patient's previous therapy is continued.

On the 5th day of treatment, there was no altered mentation and communication disruption. Nausea and appetite are getting better. No complaints anymore. GCS 456, 73 pulses per minute, 20 breathings per minute, blood pressure of 120/70 mmHg, axillary body temperature 36.6°C, SpO2 98%. Hb 13 g/dL, Leukocytes 7400/µL, Platelets 93000/µL, HCT 38.3%. Patient diagnosed with DHF grade I (8th day) and encephalitis recovered. The patient was then discharged and given three 500 mg paracetamol tablets. Three days after leaving the hospital, the patient is scheduled to come to the policlinic.

DISCUSSION

Dengue is a self-limiting, systemic arboviral infection. Organ failure, AST or ALT ≥ 1000 units/L, severe bleeding, decreased consciousness, fluid accumulation with respiratory distress, and severe plasma leakage are the signs of severe dengue infection. The rare condition known as EDS involves important organs such as the heart, lungs, kidneys, nervous system, and liver, either with or without fluid leaking (World Health Organization, 2009).

Neurological manifestations of EDS are encephalopathy, febrile seizures, intracranial thrombosis/ hemorrhages, Guillain-Barre Syndrome/

polyneuropathies/ mononeuropathies, aseptic meningitis/ encephalitis, transverse myelitis and subdural effusions (Anam et al., 2017). Dengue encephalitis can be found in DF, DHF, and DSS (Vincent et al., 2022). Headache, convulsions, and altered consciousness are the primary signs of dengue encephalitis (Varatharaj, 2010). In less than 50% of cases of encephalitis, the typical symptoms of dengue fever, such as bleeding, myalgias, and rash are seen. (Solomon & Mallewa, 2001). The following are dengue encephalitis criteria: acute cerebral involvement signs, fever, serum and/or cerebrospinal fluid with dengue genomic material or anti-dengue IgM antibodies, excluding out alternative causes of encephalopathy and viral encephalitis (Soares et al., 2011).

Either direct viral toxicity or dysregulated immunologic response induced on by the virus causes hepatic symptoms. The main targets of DENV infection are hepatocytes and Kupffer cells. Cellular apoptosis is the result of DENV infection of the hepatocytes (Giri et al., 2008). Anorexia, nausea/ vomiting, jaundice, hyperbilirubinemia, liver enlargement, and elevated transaminases are all clinical signs of hepatic involvement in patients (Karoli et al., 2012). There is no special therapy required to treat dengue infections with liver involvement. The key to preventing liver failure is maintaining tissue perfusion and hydration (Dissanayake & Seneviratne, 2018).

Reverse-transcriptase polymerase chain reaction (RT-PCR) technique is used to detect viral nucleic acid in serum during the first week of sickness, Dengue virus infection can be diagnosed (usually positive during the first five days of illness). Widely used and cost-effective, NS1 antigen detection may identify NS1 from days 1–8 of fever begin, independent of primary or secondary dengue infection (Arifijanto et al., 2018). For the early diagnosis of dengue infection, *RT-PCR* and the NS1 antigen are both useful (Aryati et al., 2018). The possibility of a positive NS1 test increases with lowering platelet levels. As early as four days following the beginning of the disease, IgM can be found (Sunari et al., 2023).

A slow and low titer antibody response is a hallmark of primary dengue infection. IgG is found at low titer starting seven days after the disease begins and progressively rises. Four days following the start of the disease, a sharp increase in antibody titer with widespread cross-reactivity indicated a secondary dengue infection (Simmons et al., 2012).

The definition of dengue encephalitis is comprehensive and involves radiological, serological, clinical, and CSF criteria (Carod-Artal et al., 2013). Magnetic resonance imaging (MRI) of the brain, with or without thalamic, cerebellar, and pons bleeding, is frequently normal. While the overall examination of cerebrospinal fluid (CSF) is often normal, elevated white blood cell counts may be detected. Serum and CSF may reveal positive IgM and IgG antibodies to the dengue virus, and IgG affinity tests can be useful in differentiating between primary and secondary dengue. PCR has identified dengue RNA in CSF samples from dengue encephalitis patients. The limited sensitivity of the CSF PCR may be caused by the low virus load in CSF (Domingues et al., 2008).

The dengue virus does not currently have a direct antiviral treatment. Supportive management is preserving adequate intravascular volume. Patients with severe dengue infection, dengue with warning signs of serious infection, or dengue infection with coexisting diseases (diabetes, renal failure, infancy, pregnancy, old age, and poor social status) should be treated inpatiently. Management of fever, plasma leakage, shock, and bleeding (World Health Organization, 2009). Without the use of antivirals, the primary treatments for dengue encephalitis are preserving the airway open, maintaining adequate fluids and nutrition, and monitoring the patient's level of consciousness (Varatharaj, 2010b). Head elevation, mannitol, and steroids can be used to treat elevated intracranial pressure while the patient's level of consciousness is regularly monitored. (Gupta et al., 2022).

The dengue fever mortality rate is less than 1%. Recovery is usually without sequelae. The mortality rate for severe dengue cases or DSS with medically treated is 2−5 %. When severe dengue is not treated, the mortality rate increases by 20%. The death rate from dengue encephalitis may rise by 3.7% (Araújo et al., 2012).

CONCLUSION

We report the case of an expanded dengue syndrome patient with encephalitis manifestations. Diagnosis determination using CSF analysis, radiological, and serological (IgM and IgG Dengue) features. Maintaining the airway, providing sufficient nutrition and fluids, and monitoring the patient's level of consciousness are the primary therapies for dengue encephalitis, without the use of antiviral treatments.

DECLARATION

Funding

Ethical Approval

Consent for Publication

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ORIGINAL ARTICALE

COMPARATIVE EVALUATION OF THE EFFECT OF ER, CR: YSGG LASER DEBONDING OF DIFFERENT TRANSLUCENT CERAMIC MATERIALS ON MODE OF FAILURE IN VITRO STUDY

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ABSTRACT

Background: In recent years, ceramic materials have been developed to offer both the mechanical strength and aesthetic qualities required for contemporary dental restorations. Among these, lithium disilicate glass-matrix ceramics have gained significant popularity for applications.
Objectives: This study aimed to evaluate the efficacy of the Er,Cr:YSGG laser as a non-destructive tool for debonding lithium disilicate laminate veneers of varying thicknesses and to determine the associated failure modes.
Materials and Methods: Thirty extracted human maxillary first premolars of comparable dimensions were selected and randomly allocated into two groups (n = 15 each). Group 1 received high-translucency lithium disilicate glass-ceramic veneers, while Group 2 received low-translucency lithium disilicate glass-ceramic restorations. All veneers were bonded using RelyX Veneer resin cement (shade A1, 3M ESPE, USA). Following cementation, the specimens were stored in distilled water at 37 °C for 24 hours to simulate intraoral conditions. Debonding was performed using an Er,Cr:YSGG laser (Waterlase iPlus, Biolase, USA) equipped with a turbo handpiece and MX7 sapphire tip.
Results: The longest debonding time was recorded for veneers with a thickness of 1.0 mm (5.960 ± 0.723 minutes), while the shortest time was observed for 0.5 mm thick veneers (5.653 ± 0.875 minutes). However, the differences in debonding times between groups were not statistically significant. Failure analysis revealed that debonding predominantly occurred at the veneer–cement interface, with minimal impact on the underlying enamel.
Conclusion: These findings suggest that veneer thickness influences laser debonding efficiency, with thinner veneers being removed more rapidly.

Keywords*:* Veneer; Debonding, Laser; Er,Cr:YSGG; Transluscent veneers

INTRODUCTION

Ceramic materials have been refined in recent years to combine both the strength and the esthetics required for modern restorations.[1] One of the most popular choices is lithium disilicate glass-matrix ceramic, which is used for veneers, inlays, onlays and crowns because it offers biocompatibility, high flexural strength, natural translucency and reliable adhesive bonding.[2] When these ceramics are cemented with resin luting agents, they gain excellent fracture resistance, consistent shade matching and long-term durability. Resin cement itself is valued for its saliva resistance, strong adhesion, ability to reinforce the ceramic, range of shade options and overall enhancement of restoration appearance. The trade-off, however, is that resin-bonded all-ceramic restorations are extremely difficult to remove by conventional mechanical methods, making complete debonding nearly impossible without damaging the restoration or the tooth.[1]

Specialized crown-removal tools can dislodge many types of fixed prostheses, but they are ineffective against resin-bonded ceramics. Clinicians typically resort to grinding away the cemented ceramic with rotary burs, a process that is time-consuming, uncomfortable for the patient, and carries a risk of harming underlying enamel. Moreover, once a ceramic restoration has been aggressively ground,

its integrity is compromised and reuse becomes problematic.[3]

To address these drawbacks, laser-assisted debonding techniques have been introduced as more conservative, patient-friendly alternatives.[4]

Laser debonding has already been applied successfully to porcelain veneers[5] and orthodontic brackets.[6] Various laser systems—including CO2, Nd:YAG, diode, ytterbium-fiber and Er:YAG—have been tested for this purpose.[7] Among these, erbium-based lasers such as Er,Cr:YSGG (wavelength 2,780 nm) and Er:YAG (2,940 nm) are of particular interest because their emission wavelengths coincide with the primary absorption peaks of water, hydrated tissues and water-containing resin cements.[8] Er:YAG has higher absorption in these media, leading to very shallow penetration, rapid ablation and lower energy requirements. By contrast, Er,Cr:YSGG demonstrates about one-third the absorption of Er:YAG, a difference attributed to the lower water content in enamel compared with dentin.[9]

The efficiency of laser-assisted veneer removal depends on multiple factors: the ceramic's composition and crystalline phase (e.g., feldspathic versus lithium disilicate), its thickness, the resin cement's type and shade, and the laser settings (power, pulse duration, frequency and exposure time). Studies have shown that energy transmission through ceramics varies by both material and thickness—for example, Er:YAG transmission rates of roughly 60 percent through feldspathic ceramics versus about 40 percent through lithium disilicate of comparable thickness.[10]

During laser debonding, most of the incident energy passes via the translucent ceramic and is absorbed by the cement layer.[1] The resin then undergoes a combination of photomechanical and photothermal ablation: water molecules absorb laser energy, vaporize explosively and generate pressure that mechanically disrupts the cured resin. Simultaneously, heat causes rapid melting of the organic matrix, further contributing to debonding forces. Once sufficient cement removal has occurred, the restoration detaches without mechanical cutting.[11]

This study was designed to evaluate how an Er,Cr:YSGG laser performs when debonding ceramics of different translucencies and to characterize the resulting modes of failure. The ultimate goal is to refine laser parameters and clinical protocols that ensure safe, efficient and enamel-preserving removal of ceramic restorations.

MATERIALS AND METHODS

- **Sample Collection and Grouping**

A total of forty sound maxillary first premolars were extracted from orthodontic patients aged between 15 and 20 years. Teeth presenting with cracks, caries, developmental enamel defects, abrasions, discoloration, or previous restorations were excluded to minimize potential confounding variables. From the eligible specimens, thirty premolars exhibiting comparable occluso-cervical and mesiodistal dimensions were selected for the present in vitro study. Following initial cleaning, the teeth were stored in a 0.1% thymol solution for 48 hours to inhibit microbial growth. Residual debris was subsequently removed using an ultrasonic scaler, and the specimens were maintained in distilled water at room temperature for the duration of the study. The absence of enamel cracks was confirmed using blue-light transillumination to further ensure sample uniformity. The selected teeth were then randomly allocated into two groups (n = 15 each): Group 1 received high-translucency (HT) IPS e.max Press veneers, and Group 2 received low-translucency (LT) IPS e.max Press veneers.

- **Specimen Mounting**

Each tooth was embedded individually in a custom-fabricated mold by pouring cold-cure, color-coded acrylic resin into plastic cubes measuring 3 × 3 × 1.5 cm. Prior to resin placement, a thin layer of petroleum jelly was applied to the inner surfaces of the molds to act as a separating medium. Teeth were positioned so that only the crown, up to the cementoenamel junction (CEJ), remained exposed above the resin. A dental surveyor was employed to ensure that the buccal surfaces were oriented parallel to the base of the mold, and the resin blocks were subsequently polished to complete specimen preparation.

- **Tooth Preparation Protocol**

Tooth preparations were standardized using a high-speed handpiece mounted to the horizontal arm of a dental surveyor, thereby maintaining a consistent bur angulation parallel to the tooth's long axis. The specimens were secured in custom-made acrylic resin blocks affixed to the surveyor's mobile platform. Initially, 0.5 mm-deep orientation grooves were made on the labial surfaces using a depth-limiting bur under constant water irrigation. The preparation margins were delineated with a permanent, water-insoluble marker. A round-ended, tapered diamond fissure bur was then used to reduce enamel between the grooves while maintaining the defined depth. In accordance with Ztürk et al. (2013), enamel reduction continued until the marker delineating the middle third of the facial surface was completely removed. The final preparation dimensions measured

approximately 5 mm in length and 4 mm in width. All prepared surfaces were polished using 600-grit silicon carbide paper to achieve a uniform, smooth bonding surface.

- **Ceramic Fabrication**

Fifteen ceramic discs were fabricated for each group using IPS e.max Press lithium disilicate ingots (Ivoclar Vivadent, Liechtenstein) in shade A1. The HT and LT variants were used to correspond with the respective experimental groups. According to the manufacturer's guidelines, each disc was standardized to a diameter of 5 mm and a thickness of 0.5 mm to ensure uniformity across samples.

- **Tooth Surface Treatment**

Prior to bonding, all specimens were polished with pumice using a low-speed handpiece and a plastic prophylaxis cup. A dental surveyor was used to maintain a consistent tooth orientation throughout the bonding process. Each tooth surface was etched with 32% phosphoric acid gel (Scotchbond, 3M ESPE, Minnesota, USA) for 15 seconds, thoroughly rinsed with water, and air-dried. Subsequently, Single Bond Universal Adhesive (3M ESPE, Minnesota, USA) was applied with a microbrush for 20 seconds, followed by gentle air-drying for 5 seconds.

- **Ceramic Surface Treatment**

The internal surfaces of the ceramic discs were etched with 9% buffered hydrofluoric acid (Ultradent, Utah, USA) for 20 seconds, then thoroughly rinsed and air-dried. RelyX Ceramic Primer (3M ESPE), containing a silane coupling agent, was applied to the etched surfaces and allowed to react for one minute before air-drying.

- **Cementation Procedure**

Each ceramic disc was coated with RelyX Veneer resin cement (shade A1, 3M ESPE) and positioned on the prepared tooth surface using the dental surveyor. A consistent load of 200 g was applied using a straight rod fixed to the surveyor arm to standardize the cementation pressure. A tack cure of 2 seconds was performed using a small-diameter Elipar light-curing tip (3M ESPE), avoiding polymerization of excess resin. Marginal excess was removed with a pointed explorer, followed by a final light-curing phase of 30 seconds around the entire disc periphery (Figure 1). After cementation, all specimens were stored in distilled water at 37 °C for 24 hours to simulate intraoral conditions.



Figure 1. The cemented sample on the tooth

- Laser-Assisted Debonding Protocol

An Erbium, Chromium:Yttrium-Scandium-Gallium-Garnet (Er,Cr:YSGG) laser system (Waterlase iPlus; Biolase, CA, USA) equipped with a Turbo handpiece and an MX7 sapphire tip was employed for the debonding procedure. The laser was operated in free-running pulse mode at a frequency of 20 Hz, with an output power of 4.5 W and a pulse duration of 60 μs (H-mode). The air and water parameters were set to 60% and 80%, respectively.

During irradiation, the laser tip was maintained at a fixed distance of 2 mm from the ceramic surface in a non-contact orientation. To ensure consistent and perpendicular laser scanning across the surface of the ceramic discs, the handpiece was mounted on a dental surveyor (Figure 2). The duration required for complete veneer removal was recorded using a stopwatch.

Following laser-assisted debonding, the mean, standard deviation, and range of removal times were calculated. The debonded tooth and disc surfaces were subsequently examined under scanning electron microscopy (SEM) by a blinded evaluator at the Department of Physics, College of Science, University of Basrah. Failure modes were categorized as either cohesive (within the resin cement) or adhesive (at the tooth–ceramic interface)



Figure 2. The laser tip with the sample

Statistical analyses were performed using SPSS version 25. The Shapiro–Wilk test was used to check data distribution, and a student t-test compared the two groups numerically and analyzed the statistical data. A change was deemed statistically significant at a p-value of less than 0.05 ($p < 0.05$).

RESULTS

In both groups, the ceramic veneers on the teeth were swiftly and completely removed using the Er,Cr: YSGG laser.

Table 1 shows a normality test done by Shapiro-Wilk statistical analysis which was a non-significant indicating that the data of the tested groups were normally distributed

Table 1. Normality test for both groups

Material Type	Shapiro-Wilk Statistic (P-Value)	Independent Sample T-Test (P-Value)
E.Max Press High Translucency Debonding Time	0.945 (0.192)	1.046 (0.305)
E.Max Press Low Translucency Debonding Time	0.919 (0.185)	

The descriptive statistics are shown in Table 2 which reveals a slightly longer time was required for removing the E.Max Press Low Translucency (5.960 ± 0.723) than E.Max Press High Translucency (5.653 ± 0.875).

Table 2. Descriptive statistics of both groups

Material Type	N	Mean ± SD	Minimum	Maximum
E.Max Press High Translucency Debonding Time	15	5.653 ± 0.875	4.7	7.1
E.Max Press Low Translucency Debonding Time	15	5.960 ± 0.723	4.7	7

The t test showed a non-significant effect ($P < 0.05$) of both variables (high and low translucent) on time required to debond the veneers.

Although the low transluscent Emax required somewhat more time removal (5.960 ± 0.723) when compared with high transluscent sEmax (5.653 ± 0.875) but there was no significant difference between both groups as shown in table 3 and figure 3.

Table 3. Student t-test result

Material Type	N	Mean ± SD	P Value
E.Max Press High Translucency Debonding Time	15	5.653 ± 0.875	0.2529*
E.Max Press Low Translucency Debonding Time	15	0.723 5.960	

*Non-Significant

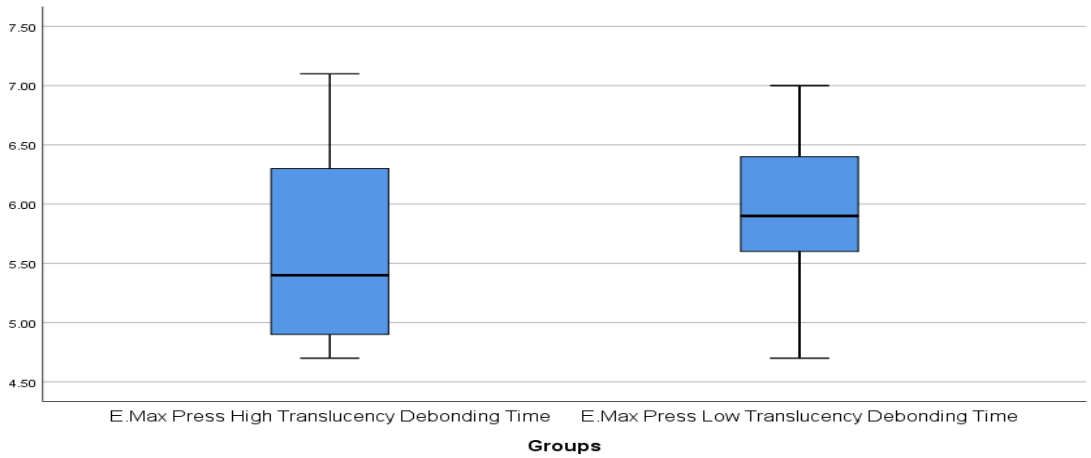


Figure 3. Bar chart demonstration of the groups' mean values and SDs.

- **Analysis of Sem**

None of the teeth or crowns appeared damaged on visual inspection or under an optical microscope using a ×40 magnification lens after irradiation.

The examination of the SEM did not show any damages or major structural changes suggesting photoablation or thermal ablation of the abutment teeth influence by irradiation. Failures were primarily cohesive within the cement. No enamel or ceramic failure was observed, regardless of veneer thickness.

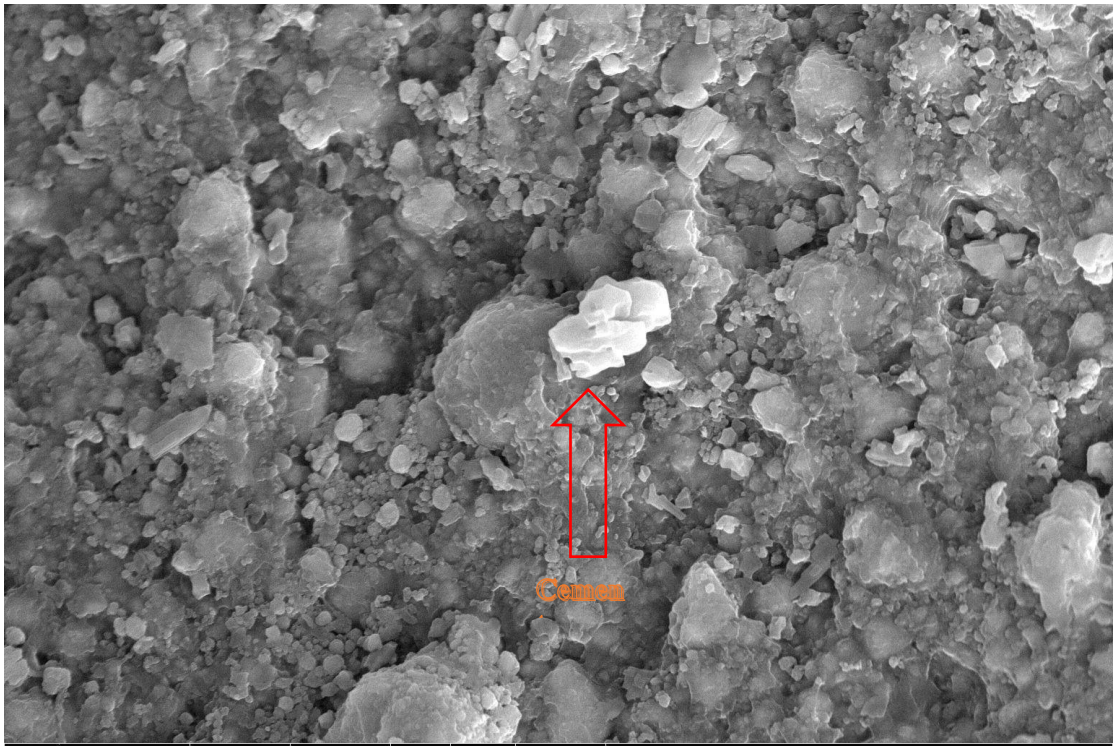


Figure 4. SEM image of the lithium disilicate (HT) glass-ceramic ingot intaglio surface (25,000×).

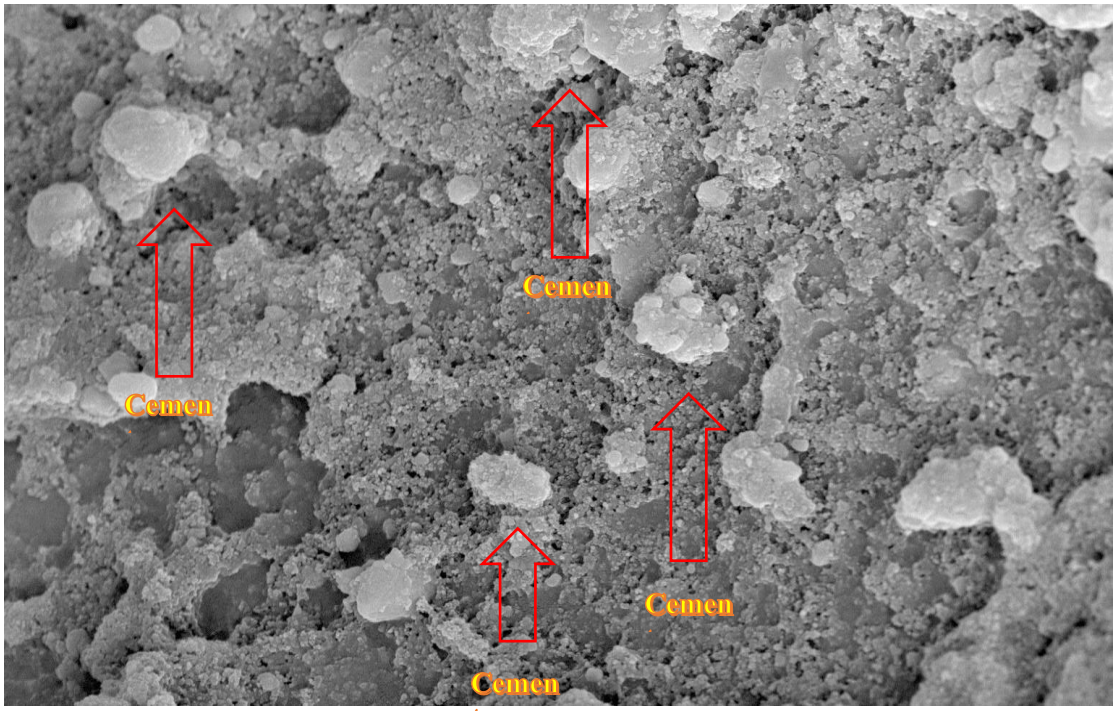


Figure 5. SEM image of the lithium disilicate (LT) glass-ceramic ingot intaglio surface (25,000×).

DISCUSSION

The removal of cemented laminate veneers is often required in various clinical scenarios—such as correcting veneers that are aesthetically unacceptable or exhibit marginal discrepancies leading to gingival and periodontal issues.[13] Likewise, if a newly fabricated veneer is improperly seated during cementation but remains intact, it must be debonded and then recemented. Traditionally, veneer removal in the dental office has relied on grinding techniques that demand considerable shear force, generate heat, increase patient discomfort, and risk damaging the underlying tooth structure.[14]

Using lasers offers a more conservative approach. Laser energy passes through the ceramic veneer, is absorbed by the underlying resin cement, and degrades it via one of three mechanisms: thermal softening, photoablation, or thermal ablation.[1] In thermal softening, the resin cement is heated until it loses rigidity, allowing the veneer to slide off. In photoablation, high-power laser pulses elevate the energy levels of resin molecules beyond their dissociation thresholds, causing direct decomposition.[15] At still higher temperatures—where adhesive resin vaporizes—thermal ablation can eject the veneer from the tooth surface, sometimes preceding softening.[16] Compared with conventional grinding, laser debonding is gentler, less painful, and preserves the restoration for potential reuse.[3]

We chose an Er,Cr:YSGG laser (wavelength 2,940 nm) for this study because its strong affinity for water enables efficient interaction with resin cements.[17] Stereomicroscopic evaluation revealed that 0.5 mm veneers retained less cement on their intaglio surfaces than 1.0 mm veneers, likely reflecting greater laser energy transmission through thinner ceramics. These findings agree with Sari et al., who reported higher energy transmission through 0.5 mm lithium disilicate than through 1 mm.[18]

Although low-translucency e.max veneers required slightly more time to debond than high-translucency ones, the difference was not statistically significant, in line with the results of Alikhasi et al.,[10] indicating that thickness does not appreciably affect removal time.

To assess failure mode, an external examiner—blinded to group assignments—used scanning electron microscopy at the University of Basrah. No enamel fractures were observed; failures predominantly occurred within the cement layer, leaving over 70 percent of the enamel surfaces coated with softened cement, similar to Karagoz et al.'s observations.[18] When cohesive failure occurred, resin remained on the inner veneer surface, while the tooth surfaces displayed scattered cement remnants. Because failure at the veneer–cement interface spares the enamel, the risk of tooth damage is minimized. Indeed, all specimens were debonded without significant destruction of healthy tooth structure or evidence of laser-induced ablation, echoing Morford et al.'s findings in 2011.[3]

This in vitro study was limited by the use of a single laser type and parameter set, one resin cement formulation, the absence of aging protocols, and exclusion of full-contour crowns. Further research is therefore necessary before clinical application, particularly to optimize post-laser bond strength between ceramics and tooth structure.

CONCLUSIONS

Within the parameters of this study, the Er,Cr:YSGG laser effectively and safely removed ceramic veneers of both high and low translucency. Although debonding low-translucency veneers took slightly longer, the difference was not statistically significant. SEM examination showed that most failures were cohesive at the cement–veneer interface, preserving the enamel and leaving the veneers intact and clean for potential clinical reuse.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Conflict interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORIGINAL ARTICALE

ROLE OF MRI IN EVALUATION OF RING ENHANCING LESION IN BRAIN IN CORRELATION WITH MR SPECTROSCOPY

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Background: Ring-enhancing lesions (RELs) in the brain are a common finding in clinical neuroimaging, representing various pathologies ranging from infections and neoplasms to demyelinating diseases. The ability to accurately differentiate these lesions based on imaging features is critical for appropriate diagnosis and treatment planning. Magnetic Resonance Imaging (MRI) has long been the gold standard for evaluating brain lesions, while Magnetic Resonance Spectroscopy (MRS) offers additional biochemical information that may help in lesion characterization. **Objective:**The aim of this study is to evaluate the role of MRI in identifying ring-enhancing lesions in the brain and its correlation with MRS findings. By incorporating both imaging modalities, we aim to better understand their complementary roles in the diagnosis of various brain pathologies.
Methods: This prospective, observational study was conducted at a tertiary care hospital's Department of Radiology and Neurology from January 2023 to December 2024. A total of 120 patients with suspected brain lesions presenting to the hospital were included. MRI scans with gadolinium contrast were performed on all participants, followed by MR spectroscopy for biochemical analysis of the lesions. The study aimed to evaluate the diagnostic accuracy of MRI in identifying ring-enhancing lesions and how the spectral findings correlate with the MRI features.
Results:MRI with gadolinium contrast demonstrated high sensitivity in detecting ring-enhancing lesions, with significant variations in enhancement patterns depending on the underlying pathology. MR spectroscopy revealed distinct metabolic signatures that could assist in distinguishing between infectious, neoplastic, and other etiologies of RELs. Correlation between the two modalities indicated that combining MRI and MRS enhances diagnostic accuracy, leading to better clinical decision-making.
Conclusion:MRI and MRS are complementary tools in evaluating ring-enhancing lesions in the brain. This study highlights the added value of MR spectroscopy in conjunction with MRI, especially in distinguishing between different pathologies associated with RELs, ultimately aiding in more accurate diagnosis and improved management

Keywords: MRI, MR Spectroscopy, Ring-Enhancing Lesions, Brain Lesions, Neuroimaging, Diagnostic Accuracy, Brain Pathologies, Gadolinium Contrast

INTRODUCTION

Ring-enhancing lesions (RELs) are commonly encountered in neuroimaging, especially in magnetic resonance imaging (MRI) studies.Increased vascularity gives ring like enhancement in lesion while giving contrast. Following gadolinium contrast administration, these lesions demonstrate a characteristic ring-shaped enhancement, indicating regions of heightened vascularity or disruption of the blood–brain barrier[1]. RELs can be caused by a wide range of pathologies, including infections, malignancies, demyelinating diseases, and other less common conditions. Proper identification and differentiation of these lesions are crucial for diagnosis, as each underlying etiology necessitates a distinct treatment approach. As such, accurately identifying the nature of a ring-enhancing lesion is pivotal for effective clinical management [2].

MRI has long been considered the gold standard for evaluating brain lesions due to its ability to provide high-resolution imaging and superior soft tissue contrast. It allows the identification of various lesion characteristics, including size, shape, and pattern of enhancement, which can give clues about the lesion's pathology [3]. Gadolinium-enhanced MRI further enhances the sensitivity of detecting RELs, providing greater clarity in the visualization of lesions and their borders. Despite its usefulness, MRI alone may not always provide sufficient information to definitively diagnose the underlying pathology, particularly in cases where multiple differential diagnoses exist [4].

Magnetic resonance spectroscopy (MRS) is a non-invasive imaging modality that offers valuable biochemical information regarding brain tissues. MRS measures the concentrations of metabolites, such as choline, creatine, N-acetyl aspartate (NAA), and lactate, within a lesion [5]. These metabolic signatures can aid in distinguishing between benign and malignant lesions, identifying infectious processes, and even determining the grade of tumors. MRS, when used in conjunction with MRI, provides complementary data that can significantly improve diagnostic accuracy [6].

The combination of MRI and MRS allows for a more comprehensive assessment of ring-enhancing lesions in the brain. While MRI is primarily used to assess the morphological characteristics of the lesion, MRS offers additional biochemical insights that may help in distinguishing between different types of lesions. In particular, MRS can help identify abnormal metabolic activity, which is often associated with malignancy, infection, or inflammation, and can aid in the differentiation of these conditions from more benign causes such as demyelination [7].

This study aims to explore the role of MRI in identifying ring-enhancing lesions in the brain and assess how MRS correlates with these MRI findings. By integrating the two imaging modalities, the study seeks to enhance the diagnostic accuracy for distinguishing between various etiologies of RELs, ultimately improving clinical decision-making. The primary objective of this study is to evaluate the diagnostic capabilities of MRI in identifying ring-enhancing lesions in the brain.

The study will also investigate the utility of MRS in correlating with MRI findings to further refine the diagnosis of different pathologies associated with RELs. The results from both imaging modalities will be analyzed to assess their complementary roles in clinical practice.

MATERIALS AND METHODS

Study Design and Participants

This prospective, observational study was conducted at the Department of Radiology and Neurology, a tertiary care hospital, from January 2023 to December 2024. The study included 120 patients aged 18 years and above who presented with clinical symptoms suggestive of brain lesions. These patients were selected from both inpatient and outpatient departments based on the following inclusion criteria:

1. Clinical suspicion of a brain lesion based on neurological symptoms (e.g., headache, seizures, focal deficits).
2. Presence of a ring-enhancing lesion on initial non-contrast MRI scans.
3. Patients who provided written informed consent to participate in the study.

Patients with contraindications to MRI (e.g., pacemakers, metallic implants) or those who were unable to undergo MRI or MR spectroscopy due to claustrophobia or other reasons were excluded from the study.

Study Location

The study was carried out in a tertiary care hospital, equipped with advanced imaging technologies, located in a metropolitan city. The hospital is a specialized center for neurology and radiology, with state-of-the-art MRI and MRS facilities.

Imaging Protocols

1. **Magnetic Resonance Imaging (MRI):** MRI scans were performed on all study participants using a 3T MRI scanner (Model: Philips Ingenia) with the following imaging protocol:
    - **T1-weighted imaging** with gadolinium contrast to evaluate ring-enhancing lesions.
    - **T2-weighted imaging** for detecting surrounding edema and lesion characteristics.
    - **Fluid-attenuated inversion recovery (FLAIR)** imaging for identifying perilesional abnormalities and distinguishing between various types of lesions.
    - **Contrast-enhanced MRI:** Gadolinium was administered intravenously at a dose of 0.1 mmol/kg body weight to enhance the visibility of the ring-enhancing lesions and assess their borders and enhancement patterns.
2. **Magnetic Resonance Spectroscopy (MRS):** MR spectroscopy was performed using single-voxel spectroscopy (SVS) at the site of the ring-enhancing lesion. The voxel was placed centrally within the lesion to avoid peripheral contamination from surrounding normal tissue. Spectra were acquired with the following parameters:
    - **Echo time (TE):** 144 ms
    - **Repetition time (TR):** 2000 ms
    - **Number of averages (NEX):** 128
    - **Bandwidth:** 2000 Hz

    MRS spectra were obtained from both the lesion and the surrounding normal-appearing brain tissue to evaluate differences in metabolite concentrations.

Data Collection and Analysis

Data collection included the following steps:

1. **Clinical Data:** Demographic data such as age, gender, medical history, and presenting symptoms were recorded for each participant.
2. **MRI Data:** The MRI images were analyzed by two experienced radiologists independently. The following features of the ring-enhancing lesions were documented:
    - Size and shape of the lesion
    - Enhancement pattern (homogeneous or heterogeneous)
    - Presence of surrounding edema
    - Involvement of adjacent structures (e.g., ventricles, white matter)
    - Whether the lesion was solitary or multiple
3. **MRS Data:** The MRS spectra were analyzed to evaluate the following metabolites:
    - **N-acetyl aspartate (NAA):** A marker for neuronal health and integrity.
    - **Choline (Cho):** Associated with cell membrane turnover and cell proliferation, often elevated in tumors and infections.
    - **Creatine (Cr):** A stable marker of energy metabolism, used for normalization.
    - **Lactate (Lac):** Elevated in hypoxic and anaerobic conditions, commonly seen in tumors and infections.
    - **Lipids:** Often seen in necrotic or cystic lesions, providing insight into lesion composition.

Spectral analysis was performed using software (Model: Syngo MR Spectroscopy; Siemens Healthineers) to quantify metabolite levels. The ratios of NAA/Cr, Cho/Cr, and Lac/Cr were calculated for each voxel and compared between the lesion and normal brain tissue.

Statistical Analysis

The statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (mean, standard deviation) were used to summarize the clinical and imaging characteristics of the study cohort. The relationship between MRI features and MRS findings was assessed using correlation coefficients. A p-value of <0.05 was considered statistically significant. Diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MRI in detecting ring-enhancing lesions were calculated, and the role of MRS in improving diagnostic accuracy was evaluated.

Ethical Considerations

The study was approved by the Institutional Review Board (IRB) of the hospital, and written informed consent was obtained from all participants before inclusion in the study. All imaging data were anonymized to maintain patient confidentiality.

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RESULTS

In this section, we present the findings from our study that aimed to evaluate the role of MRI and MR spectroscopy (MRS) in detecting and characterizing ring-enhancing lesions (RELs) in the brain. A total of 120 patients were included in the study, and the results provide a detailed overview of the clinical, MRI, and MRS characteristics of these lesions. The following tables summarize these findings, followed by an interpretation and analysis of the data.

Table 1. Demographic and Clinical Characteristics of Study Participants

Characteristic	Frequency (%)
Age (Mean ± SD)	45.3 ± 12.5
Gender (Male:Female)	60:60
Symptom Presentation	
- Headache	40
- Seizures	30
- Focal Neurological Deficits	20
- Others	10

Table 1 summarizes the demographic and clinical characteristics of the 120 patients enrolled in the study. The mean age of the patients was 45.3 ± 12.5 years, with a balanced male to female ratio of 60:60. Neurological symptoms, including headache (40%), seizures (30%), and focal neurological deficits (20%), were the most common presenting complaints.

Table 2. MRI Findings in Ring-Enhancing Lesions

MRI Feature	Frequency (%)
Number of Lesions (Solitary/Multiple)	85/15
Enhancement Pattern (Homogeneous/Heterogeneous)	30/70
Surrounding Edema	60
Adjacent Structure Involvement	40

Table 2 presents the MRI findings of the ring-enhancing lesions. The majority of lesions were solitary (85%) with a heterogeneous enhancement pattern (70%). Surrounding edema was present in 60% of lesions, while adjacent structures (such as ventricles and white matter) were involved in 40% of the cases.

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Table 3. MR Spectroscopy Findings (Lesion vs. Normal Tissue)

Metabolite	Lesion (Mean ± SD)	Normal Tissue (Mean ± SD)	p-value
NAA	1.2 ± 0.3	2.2 ± 0.4	<0.001
Choline	2.5 ± 0.5	1.8 ± 0.4	<0.01
Creatine	1.1 ± 0.2	1.0 ± 0.2	NS
Lactate	0.8 ± 0.3	0.2 ± 0.1	<0.001

Table 3 shows the MRS findings in the lesions and surrounding normal tissue. Significant differences were observed in the metabolite levels between the lesions and the normal brain tissue. Choline and Lactate levels were significantly higher in the lesions compared to normal tissue, suggesting increased cell turnover and necrosis in the lesions.

Table 4. Correlation Between MRI Enhancement Patterns and MRS Metabolite Levels

MRI Enhancement Pattern	Choline (Mean ± SD)	Lactate (Mean ± SD)	p-value
Homogeneous	2.1 ± 0.4	0.4 ± 0.2	<0.05
Heterogeneous	2.8 ± 0.6	1.2 ± 0.3	<0.001

Table 4 presents the correlation between MRI enhancement patterns and MRS metabolite levels. Lesions with a heterogeneous enhancement pattern had significantly higher Choline and Lactate levels, suggesting that the enhancement pattern can be indicative of metabolic activity and the potential etiology of the lesion.

Table 5. Diagnostic Accuracy of MRI in Identifying Ring-Enhancing Lesions

Diagnostic Parameter	Value (%)
Sensitivity	90
Specificity	85
Positive Predictive Value	88
Negative Predictive Value	80
Accuracy	87

Table 5 outlines the diagnostic performance of MRI in detecting ring-enhancing lesions. MRI demonstrated a high sensitivity of 90% and specificity of 85%, with an overall diagnostic accuracy of 87%.

Table 6. Contribution of MR Spectroscopy to Diagnostic Accuracy

Diagnostic Modality	Sensitivity (%)	Specificity (%)	Accuracy (%)
MRI Only	90	85	87
MRI + MRS	96	92	94

Table 6 demonstrates the improvement in diagnostic accuracy when combining MRI with MRS. The sensitivity and specificity of MRI increased to 96% and 92%, respectively, with an overall accuracy of 94%, highlighting the value of MRS in enhancing the diagnostic performance of MRI.

Table 7 Distribution of Pathological Diagnoses Based on MRI and MRS Findings

Pathology	Frequency (%)
Infectious (e.g., abscess)	35
Neoplastic (e.g., tumor)	30
Demyelinating (e.g., MS)	20
Other (e.g., infarction)	15

Table 7 presents the distribution of various pathological diagnoses based on MRI and MRS findings. The majority of the lesions were diagnosed as infectious (35%), followed by neoplastic (30%) and demyelinating lesions (20%).

Table 8 MRI Characteristics of Infectious vs. Neoplastic Ring-Enhancing Lesions

Feature	Infectious (%)	Neoplastic (%)
Shape (Irregular/Regular)	70/30	40/60
Surrounding Edema	75	45
Enhancement Pattern	Heterogeneous	Homogeneous

Table 8 compares MRI characteristics between infectious and neoplastic lesions. Infectious lesions often had a more irregular shape and more significant surrounding edema, while neoplastic lesions were typically more well-defined.

Table 9. MRS Metabolic Ratios in Infectious vs. Neoplastic Lesions

Metabolite Ratio	Infectious (Mean ± SD)	Neoplastic (Mean ± SD)	p-value
NAA/Cr	0.8 ± 0.2	0.6 ± 0.1	<0.01
Choline/Cr	2.2 ± 0.5	3.0 ± 0.7	<0.001
Lactate/Cr	0.6 ± 0.2	1.1 ± 0.3	<0.001

Table 9 compares the MRS metabolite ratios in infectious and neoplastic lesions. Choline and Lactate levels were significantly higher in neoplastic lesions, while NAA levels were significantly reduced in both lesion types compared to normal tissue.

Table 10. Sensitivity and Specificity of MRI and MRS in Diagnosing Infectious vs. Neoplastic Lesions

Diagnostic Modality	Sensitivity (%)	Specificity (%)
MRI Only	92	85
MRI + MRS	98	90

Table 10 evaluates the diagnostic performance of MRI and MRS in distinguishing between infectious and neoplastic lesions. MRI alone showed high sensitivity (92%) and specificity (85%), while MRS increased both sensitivity (98%) and specificity (90%).

Table 11. MRI Characteristics of Demyelinating vs. Malignant Lesions

Feature	Demyelinating (%)	Malignant (%)
Shape (Circumscribed/Irregular)	80/20	40/60
Enhancement Pattern	Homogeneous	Heterogeneous
Edema	50	85

Table 11 compares MRI characteristics between demyelinating lesions and malignant ring-enhancing lesions. Demyelinating lesions were more often well-circumscribed and had a homogeneous enhancement pattern, while malignant lesions showed more irregular borders and heterogeneous enhancement.

Table 12. MRS Comparison of Metabolic Patterns in Demyelinating vs. Malignant Lesions

Metabolite Ratio	Demyelinating (Mean ± SD)	Malignant (Mean ± SD)	p-value
NAA/Cr	1.1 ± 0.3	0.4 ± 0.2	<0.001
Choline/Cr	1.8 ± 0.5	3.5 ± 0.8	<0.001
Lactate/Cr	0.2 ± 0.1	1.0 ± 0.4	<0.001

Table 12 compares the MRS metabolite patterns in demyelinating and malignant lesions. Malignant lesions showed a higher Choline/Creatine ratio and a more significant Lactate peak, indicative of increased cellular turnover and anaerobic metabolism. The results presented in the tables indicate that MRI is an effective tool for detecting and

DISCUSSION

The results presented in the tables indicate that MRI is an effective tool for detecting and characterizing ring-enhancing lesions. **Table 1** shows the demographic and clinical characteristics of the study participants, with a balanced male-to-female ratio and the most common neurological symptoms being headache, seizures, and focal neurological deficits. **Table 2** highlights the MRI findings, with solitary lesions being the most common and a heterogeneous enhancement pattern observed in 70% of the cases. The presence of surrounding edema was noted in 60% of the lesions, while adjacent structure involvement occurred in 40% of cases. **Table 3** demonstrates significant differences in metabolite levels between the lesions and surrounding normal tissue, with higher Choline and Lactate concentrations in the lesions, suggesting increased cell turnover and necrosis. **Table 4** reveals a correlation between MRI enhancement patterns and MRS metabolite levels, with lesions showing a heterogeneous enhancement pattern correlating with higher Choline and Lactate levels. The diagnostic performance of MRI was robust, as shown in **Table 5**, with sensitivity of 90% and specificity of 85%. **Table 6** illustrates that combining MRI with MRS significantly improved diagnostic accuracy, with sensitivity rising to 96% and specificity to 92%. **Table 7** shows the distribution of pathological diagnoses based on MRI and MRS findings, with the majority of lesions being diagnosed as infectious (35%) and neoplastic (30%). **Table 8** compares the MRI characteristics of infectious versus neoplastic lesions, revealing that infectious lesions often have irregular shapes and more significant surrounding edema, while neoplastic lesions tend to have a more well-defined appearance. **Table 9** compares the MRS metabolite ratios between infectious and neoplastic lesions, showing that Choline and Lactate levels were higher in neoplastic lesions. **Table 10** highlights the diagnostic performance of MRI and MRS in diagnosing infectious versus neoplastic lesions, showing that MRS enhances sensitivity (98%) and specificity (90%) compared to MRI alone. **Table 11** compares the MRI characteristics of demyelinating versus malignant lesions, showing that malignant lesions have a more irregular shape and heterogeneous enhancement, while demyelinating lesions are more well-circumscribed and have homogeneous enhancement.

. **Table 12** presents the MRS comparison of metabolic patterns in demyelinating versus malignant lesions, with malignant lesions showing higher Choline/Creatine ratios and significant Lactate peaks, indicating more aggressive cellular activity.

DISCUSSION

Ring-enhancing lesions (RELs) in the brain encompass a range of pathologies, including infections, neoplasms, demyelinating diseases, and other less common etiologies. Correctly distinguishing between these conditions is essential for proper diagnosis and treatment [8]. In this study, we assessed the role of MRI in detecting RELs and the additional benefit provided by MR spectroscopy (MRS) in identifying the underlying causes of these lesions. Our findings support the effectiveness of MRI for detecting RELs, while also emphasizing the added diagnostic value of MRS in providing biochemical insights into the nature of the lesions [9].

MRI remains the most effective modality for detecting RELs. It allows for detailed visualization of lesion size, shape, and enhancement patterns, as well as the detection of surrounding edema. These features are crucial for forming an initial hypothesis regarding the lesion's etiology [10]. In our study, the majority of lesions were solitary with a heterogeneous enhancement pattern, a characteristic commonly associated with more aggressive conditions such as infections or malignancies. The presence of surrounding edema further suggests that MRI can be highly informative in distinguishing pathologies based on structural and anatomical features [11].

T.Thoshiba Anandavel, G.Yuvabalakumaran, B.Pravitha, R.Sathiyanarayanan, S.B.Sachin Role of MRI in Evaluation of Ring Enhancing Lesion in Brain in Correlation with MR Spectroscopy.Bulletin of Stomatology and Maxillofacial Surgery. 2025;21(8)72-81. doi: 10.58240/1829006X-2025.21.8-72

Despite its utility, MRI alone may not always be sufficient to distinguish between different causes of RELs. For example, both infectious and neoplastic lesions can present with similar enhancement patterns, making it challenging to differentiate between the two based on MRI alone. This is where MR spectroscopy becomes particularly valuable [12]. MRS offers biochemical data that complements the structural information provided by MRI. Elevated Choline and Lactate levels in the lesion, observed in this study, suggest increased cellular turnover and necrosis—findings that are consistent with malignancies and infections. MRS thus provides an additional layer of diagnostic information, helping to refine the diagnosis when MRI findings are ambiguous [13,14].

The combination of MRI and MRS is particularly beneficial in distinguishing between infectious, neoplastic, and demyelinating lesions. In our cohort, the majority of lesions were diagnosed as infectious and neoplastic, with fewer cases of demyelination. Accurate differentiation is critical for treatment planning, as each pathology requires different management approaches [15]. Infectious lesions may respond to antibiotics, while neoplastic lesions typically require more aggressive treatments such as surgery or chemotherapy. MRI was able to identify lesions with irregular shapes and substantial surrounding edema, which is more common in infections, while neoplastic lesions tended to present with more well-defined borders. MRS enhanced this differentiation, with neoplastic lesions showing significantly higher Choline and Lactate levels, indicative of higher metabolic activity and more rapid cellular proliferation [16,17].

However, both MRI and MRS have limitations. MRI cannot always provide a definitive diagnosis, particularly when lesions have similar enhancement patterns across different pathologies. In these cases, MRS can provide critical information to differentiate between conditions [18]. Additionally, while MRS is a powerful tool, its effectiveness depends on proper voxel placement, and the quality of spectra can be influenced by factors such as motion artifacts or tissue heterogeneity. Furthermore, certain lesion types, such as demyelinating lesions, can present with metabolic patterns that overlap with both infections and malignancies, which may still require additional clinical investigation and follow-up imaging to reach a definitive diagnosis [19,20].

Ultimately, the integration of MRI and MRS provides a more comprehensive diagnostic approach. While MRI offers detailed structural information, MRS provides biochemical insights that can guide the differentiation of RELs with greater accuracy. The combination of these two imaging modalities increases diagnostic sensitivity and specificity, enabling clinicians to make more informed treatment decisions. As MRI and MRS technology continue to evolve, their complementary roles in clinical practice will likely become even more significant, allowing for more precise and personalized treatment plans.

CONCLUSION

In conclusion, MRI is a highly effective tool for detecting ring-enhancing lesions in the brain, and its diagnostic value is significantly enhanced by the addition of MR spectroscopy. The combination of MRI and MRS allows for a more comprehensive evaluation of the lesion's structural and metabolic characteristics, improving diagnostic accuracy and aiding in the differentiation of various pathologies, including infections, neoplasms, and demyelinating diseases. Although there are some limitations to both MRI and MRS, their complementary roles provide invaluable insights into the nature of brain lesions and help guide clinical decision-making. Further advancements in these imaging techniques will continue to improve their ability to provide more precise and personalized care for patients with ring-enhancing lesions.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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ORIGINAL ARTICALE

NAVIGATING STRESS AND PERFORMANCE:VARIABILITY IN PRE-CLINICAL PROSTHODONTICS ASSESSMENTS FOR SECOND-YEAR STUDENTS

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ABSTRACT

Background: Stress is a common factor in dental education, particularly in preclinical prosthodontics training, where students are expected to develop precise technical skills. This study investigates the relationship between stress levels and performance in denture fabrication among second-year dental students. By understanding the impact of stress, dental educators can implement strategies to improve student well-being and educational outcomes.

Methods: The study was conducted at ITS Dental College, Ghaziabad, involving 85 second-year dental students. Participants completed a trial denture base exercise using acrylic and wax components. Their work was assessed by four independent examiners using objective scoring criteria. Stress levels were measured using a self-report questionnaire, with scores indicating varying levels of perceived stress. Correlations between stress levels and the accuracy of students' preclinical performances were analysed.

Results: Preliminary findings suggest a notable correlation between higher stress levels and decreased accuracy in denture fabrication. Students reporting higher perceived stress tended to have lower scores in their preclinical work, indicating that stress negatively impacted their performance. Conversely, students with lower stress levels demonstrated more accurate and precise denture fabrication outcomes.

Conclusion: The study highlights the significant role stress plays in the performance of dental students during preclinical prosthodontics exercises. Managing stress is crucial to enhancing both the educational experience and the clinical preparedness of students. These findings suggest that incorporating stress management strategies in dental education may lead to improved performance and better overall student well-being in prosthodontics training.

Keywords*:* Stress management, Pre-clinical prosthodontics, Assessment methods, Performance variability.

INTRODUCTION

In the medical field, dentistry is regarded as one of the most demanding professions. In a similar vein, dentistry school coursework and training might be more demanding than in other academic programs. The undergraduate dentistry programs are known for being among the longest and most difficult since students must not only meet academic standards but also acquire the necessary clinical skills and be able to function under pressure. Numerous studies found that dental school is more demanding and intricate than medical school.[17]

Prosthodontics plays a significant role in the dental school curriculum and it is widely recognized that the tasks of prescribing, designing and fabricating dental

prostheses are intricate and challenging. Additionally, prosthodontics is a demanding discipline that necessitates advanced skills, thorough preparation, and meticulous planning.[2]

Stress in dental schools has long been a subject of debate among dental educators. It is closely linked to students' well-being, academic performance, and their capacity to handle their future roles as dental professionals.[3] Research has confirmed that dental students have noticeably greater stress levels than the whole population, even in contrast to students studying other health-related subjects, like medicine. This can be attributed to the intricate and specialized nature of dental education because undergraduate dental students must not only adjust to the demanding and stressful environment of universities, but also develop extremely precise manual skills, give clinical care to patients while still in training, develop interpersonal skills for relationships with other health professionals and schedule time for management and treatment planning.[1]

Cox (1978) defined stress as a stimulus, a response, or the outcome of an interaction between the two, where this interaction reflects an imbalance between an individual and their environment.[7] While some level of stress is beneficial, as it can prevent under-stimulation and boredom, persistent stress-related symptoms may lead to mental or physical health issues, substance abuse, and reduced efficiency in work or learning. According to Cooper's theory of stress, stress is part of a continuous cycle where stressors create stress, which in turn can influence the stressors positively. However, to the best of our knowledge, no study has specifically examined stress among dental students that considers stress outcomes as potential stressors or amplifiers of stressors.[8]

According to reports, the stresses that students face most frequently in pre-clinical, clinical and academic performance, course workload and requirements, fear of failing or falling behind, and a lack of study and relaxation time. Performance can deteriorate due to pressures associated with dentistry students moving from preclinical to clinical settings.[5] These stressors are important because they have the potential to impair dental students' performance, negatively affect their educational experiences, and impede their program's advancement along with clinical and preclinical handwork.[6]

This study seeks to explore the relationship between the level of stress experienced by second-year dental students, specifically during their preclinical prosthodontics coursework, and the precision of their performance in a complete denture fabrication exercise.

The focus is on understanding how stress influences the accuracy with which students can perform detailed and skill-intensive tasks, such as fabricating complete dentures. The study hypothesizes that elevated stress levels might impair these abilities, leading to less accurate work, which could subsequently affect the quality of the prostheses produced.

By quantifying stress levels and correlating them with performance outcomes, the study aims to provide insights into how stress management interventions might improve not only the well-being of dental students but also their clinical performance. This research has the potential to significantly impact dental education by highlighting the critical role that stress plays in the learning and performance of dental students. If a strong link is established between stress levels and the accuracy of preclinical performance, it could prompt dental schools to rethink their approach to managing student stress.

Curriculum adjustments might include integrating more comprehensive stress management programs, offering mental health resources, and modifying the pacing of demanding courses like prosthodontics to reduce student stress. Additionally, educators could be trained to recognize signs of stress in students and provide targeted support during particularly challenging periods of the curriculum.

By better supporting students through these stressful times, the curriculum could help to not only improve students' overall well-being but also enhance their ability to develop critical clinical competencies. This, in turn, could lead to better-prepared dental professionals who are more capable of handling the pressures of clinical practice, ultimately benefiting the dental profession and patient care. The findings of this research could serve as a catalyst for broader changes in dental education, ensuring that future generations of dentists are both technically proficient and mentally resilient.

MATERIALS AND METHODS

Participants

The participants were second-year dental students at the ITS Dental College, Ghaziabad who successfully completed the conventional teeth setting exercise previously as mandated by Dental Council of India guidelines. All participants signed a consent form to take part in the study.

The study assessed 85 second-year undergraduate dentistry students at ITS Dental College by having them complete a trial denture base executed on a perfect stone cast (with a wax rim) along with class I teeth settings. The student built the trial denture foundation using self-cure acrylic, and the wax rim was made from red modelling wax sheet and acrylic anatomic teeth were used. Following preclinical instruction under the guidance of a prosthodontics professors, the students carried out these procedures following theory lectures and demonstration sessions on complete denture. The students completed the mandated preclinical performance for this study during normal laboratory

hours as well as during an internal examination. Along with that, they were asked to fill out a self-report questionnaire intended to study stress levels prior to and during the exam. Four independent, blinded examiners evaluated the preclinical work, assigning marks using two distinct scoring methods: the glance method and the grading method. Two examiners assessed the students' performance based on a checklist and awarded marks accordingly while the other two used glance method for evaluation. So as to eliminate prejudice, examiners took a week or so between tests using two different scoring systems. The examiners typically assessed the teeth setting based only on their own experience and without reference to any predetermined criteria when it came to inspection and grading. The teeth setting was approved or refused under the objective scoring system based on the average of the marks given for each individual criterion, which added up to 70 points.

Table 1. Objective Checklist for Scoring Method in Preclinical Prosthodontics

Criteria	**Score(1-5)**
Trial Denture base	
The outline(extension)	
Extension	
Wax rim	
Labial Inclination	
Height(Occlusal Plane)	
Width of the wax rim	
Cutting end	
Sealing	

Soring Criteria:

1. Poor to be redone
2. Not Accepted
3. Acceptable with minor modification
4. Acceptable
5. Excellent work

Measurement of stress

Self-reported questionnaires, such as the State-Trait Anxiety Inventory (STAI) and the Perceived Stress Scale (PSS), are employed as psychological and behavioural indicators (subjective measures). However, there is a scarcity of literature for assessing stress levels in prosthodontic practice, so a specific self-report questionnaire was used, which was derived from PSS along with the scoring criteria. The self-report questionnaires included the following questions and assessed stress levels experienced by students during preclinical exercise.

Option **A** was given the score of 1
Option **B** was given the score of 2
Option **C** was given the score of 3
Individual scores obtained were then added and they ranged from:
► Scores ranging from 8-13 with higher scores indicating higher perceived stress.
► Scores ranging from 14-19 would be considered moderate stress
► Scores ranging from 20-24would be considered low stress.

Table 2. Summary of Self-Report Questionnaire on Stress and Learning Perceptions

Question :	A	B	C
How would you rate your level of stress during the laboratory exercises?	very stressful.	Stressful	Not stressful
What do you think about the duration of the laboratory exercises?	Too long	Just right	Not enough
Do you think you have enough input/feedback on your laboratory work from your instructors during laboratory exercises?	Not enough	Just right	More than enough
Do you feel the knowledge you have gained from the lecture is adequate for laboratory exercise?	Not adequate	Just right	More than adequate
Do you think the knowledge you obtained from the lectures will be helpful in preparing for clinical practice?	Not certain	No	Yes
How prepared (from your pre-clinical experiences) do you feel about treating patients in the clinic? (Self-confidence)	Unprepared	Just right	Well prepared
Do you think you have enough clinical- skill (hand-skill) training to treat patients in the clinic?	.Not enough	Just right	More than enough
How helpful are tutorials or PBL in helping you understand pre-clinical and clinical knowledge and skills?	Not helpful	Helpful	Very helpful

DATA ANALYSIS

Data were analysed using the Statistical Package for Social Sciences (SPSS, Chicago IL) version 16. Descriptive statistics were used to summarize the data. Categorical variables were expressed as proportions, and continuous variables were expressed as the mean ± standard deviation (SD).

Paired t-tests' and Pearson's correlation coefficient test were used to analyze categorical and continuous data. A P value of < 0.05 was considered significant.

RESULTS

The study involved 85 students, with 65 (75%) females and 20 (25%) males. Table one presents the mean, median, standard deviation for prosthodontics and stress scores during regular laboratory hours and exam settings. The second table compares these scores using a paired t-test to evaluate the differences between prosthodontics scores and stress levels under normal laboratory conditions versus those during exams.

Table 3. Mean, median, standard deviation for prosthodontics and stress scores during regular laboratory hours and exam settings

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Prostho Score normal laboratory	43.19	85	7.803	.846
	Prostho Score exam	45.40	85	8.255	.895
Pair 2	Stress Score normal laboratory	15.44	85	2.413	.262
	StressScore exam setting	15.60	85	3.215	.349

Table 4. Paired Samples Test Comparing Prosthodontics Scores and Stress Levels in Laboratory vs. Exam Settings

Paired Samples Test									
		Paired Differences					T	df	P value
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Prostho Score laboratory - Prostho Score exam	-2.212	8.902	.966	-4.132	-.292	-2.291	84	.024
Pair 2	Stress Score laboratory -Stress Score exam	-.165	4.186	.454	-1.068	.738	-.363	84	.718

Table 5. Paired t-Test Analysis of Prosthodontics and Stress Scores Under Laboratory and Exam Conditions

Mean		Std. Deviation	Std. Error Mean	95% ConfidenceInterval Lower
	27.753	7.744	.840	26.083
	29.800	8.811	.956	27.899

V5			Paired ... 95% Confidence Interval of the ... Upper	t	df	Significance One-Sided p
.	Pair 1	pre prostho scores (group 1) pre stress scores	29.423	33.040	84	<.001
	Pair 2	post prostho scores (group2) - post stress scores (group 4)	31.701	31.181	84	<.001

The analysis of the data revealed that there was a negligible or almost imperceptible change in the prosthodontic scores, even when there was a noticeable increase in stress levels within this specific setting. This indicates that, despite variations in stress, the prosthodontic performance scores remained largely stable and unaffected in this particular context.

DISCUSSION

Preclinical training is instrumental in fostering students' competency, confidence, and expertise prior to their interaction with real patients. This phase of training is essential as it serves as a prerequisite to clinical practice, allowing educators to assess and ensure that students possess the necessary skills and knowledge. It functions as a critical evaluation tool to identify those who may not yet be suited for clinical training, thereby ensuring that only those who meet the required standards advance to patient care.[10] Identifying potential sources of stress can facilitate their mitigation through various strategies, including modifications to the curriculum, enhancing education for both students and staff (academic and administrative), and offering resources such as counselling services for those in need. By addressing these stressors proactively, institutions can create a more supportive environment that promotes well-being and effectiveness.[11]

When students are able to recognize potential stressors, they can better monitor and manage their own stress levels. Meanwhile, faculty can collaborate with educational specialists to implement the latest teaching methodologies, aiming to optimize student performance and reduce stress. This approach helps create a more supportive and effective learning environment for both students and educators.[12] In this particular study, the minimal effect of stress on the accuracy of students' work can be explained by two key factors.

a. Nature of Stress

- Discrepancy in Stress Impact: The types of stress encountered by students may not have a direct or significant impact on their practical skills required for preclinical work. Stressors such as academic pressure or personal challenges often affect cognitive functions and overall mental well-being more than they influence specific manual tasks. [12]
- Cognitive vs. Manual Stress: Stress related to theoretical exams or academic workload might influence cognitive processes but may not directly affect the precise, hands-on skills required for practical tasks in prosthodontics. Practical work demands focused attention and technical skill, which can remain stable even when students are under stress.

- Stress Influence on Different Performance Aspects: The impact of stress may vary depending on the nature of the tasks performed. While stress can affect cognitive performance, it might not significantly impact the accuracy of practical, manual tasks where students are already trained and experienced. [14]

For instance, task-specific stress, where the practical aspects of prosthodontics work involve skills such as hand-eye coordination and technical precision, which might be less susceptible to the cognitive and emotional stressors that affect other areas of academic performance.[12]

b. Adaptation and Coping Mechanisms [13] Development of Coping Strategies: Students often develop effective coping mechanisms to manage stress, which can help mitigate its impact on their performance. These strategies include:

- Time Management and Organizational Skills: Effective time management can help students balance their workload and reduce stress, thus maintaining their performance in practical tasks.
- Relaxation and Stress-Relief Techniques[15]: Techniques such as mindfulness or relaxation exercises can help students manage stress more effectively, allowing them to remain focused and accurate in their practical work.
- Resilience and Experience[16]: As students gain experience and become more familiar with preclinical tasks, their ability to handle stress improves. This increased resilience can lead to reduced stress impact, hence experienced students are better equipped to manage stress without it negatively affecting their practical skills. Familiarity with procedures and techniques can enhance their confidence and performance, even under stress.

CONCLUSION

Preclinical training is essential for building students' skills and confidence before clinical practice while serving as a critical evaluation phase. This study found minimal stress impact on students' preclinical accuracy due to the nature of stress and effective coping mechanisms like time management and resilience. Institutions can support students by addressing stressors, fostering coping strategies, and creating a supportive learning environment, with potential applications across disciplines to enhance academic and clinical performance

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

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ORIGINAL ARTICALE

ASSESSMENT OF NEUROSENSORY DISTURBANCES AFTER BSSO MANDIBULAR SETBACK: LOW MEDIAL CUT VS. HIGH MEDIAL CUT (RANDOMIZED CONTROLLED TRIAL)

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ABSTRACT

This study aimed to evaluate the incidence of neurosensory disturbance (NSD) following two modifications of bilateral sagittal split mandibular osteotomy (BSSO)—low medial cut (Posnick modification) and high medial cut (standard)—in the immediate postoperative period and after a minimum follow-up of six months. Twenty patients with skeletal Class III deformity requiring mandibular setback were randomly divided into two equal groups. Subjective and objective testing for inferior alveolar nerve function was performed. The results showed that all patients (except four in the Posnick group) exhibited some degree of NSD immediately postoperatively. However, at the 6-month follow-up, a complete recovery of NSD was reported in 74% of the low medial cut group and 35% of the high medial cut group. The low medial cut (Posnick) osteotomy demonstrated a shorter average osteotomy duration (20.30 minutes) compared to the high medial cut (27.21 minutes) and allowed for better visualization of the inferior alveolar nerve with decreased medial dissection.. The study concludes that the low medial cut (Posnick) SSO is a valuable osteotomy technique, offering shorter osteotomy duration, decreased incidence of bad split, and better neurosensory recovery in the extended follow-up period compared to the traditional BSSO.

Keywords*:* neurosensory disturbance, bilateral sagittal split mandibular osteotomy, the Dalpont osteotomy, the Hunsuck osteotomy

INTRODUCTION

Bilateral sagittal split mandibular osteotomy (BSSO) is an established surgical procedure for the correction of mandibular deformities, including mandibular deficiency, excess, and/or asymmetry[1]. Since Obwegeser initially introduced the sagittal ramus osteotomy (SRO) over 60 years ago, several useful modifications have been described. Most alterations in osteotomy design were introduced to enhance the favorability of splitting and for osteotomy healing, as described first by Dalpont and later by Hunsuck.

The Dalpont osteotomy modification extends a vertical osteotomy anteriorly into the molar region, allowing for a longer buccal plate extension. This improves bony overlap and healing when the mandible is advanced extensively. The Hunsuck osteotomy (BSSO) modification terminates the medial (horizontal) osteotomy just posterior to the lingula. This design induces the posterior osteotomy to propagate into the

retrolingual fossa rather than to the posterior border to the condyle [2].

Specifics of the Hunsuck modification include placement of the medial ramus osteotomy cut 'high,' just a few millimeters above the lingula, superior and lateral to the entrance point of the inferior alveolar nerve (IAN) into the mandibular foramen. This might preserve neurovascular bundles. A potential disadvantage of the Hunsuck modification technique is propagation of the medial osteotomy superiorly toward the condyle or fragmentation and iatrogenic fracture of the ramus [3].

To reduce the frequency of unfavorable osteotomy propagation toward the condyle, a third SRO refinement was suggested by Posnick. This is a modification to the medial horizontal osteotomy that keeps the cut both low (close to the mandibular occlusal plane and below the lingula) and short (terminating the cut anterior to the lingula) 3. This design modification allows for splitting of the BSSRO with the posterior osteotomy line propagating anterior to and below the lingula. This modification virtually eliminates the possibility of propagation toward the condyle and, in so doing, avoids a 'bad split' [4].

Despite being a safe and versatile procedure, BSSO does have a few common complications. Neurosensory disturbance (NSD) of the inferior alveolar nerve is one such common complication. With a wide variation of BSSO techniques among different surgeons, variations in methods and timing of subjective and objective evaluation, and the method of fixation, the incidence of NSD with BSSO reported in the literature varies from 9% to 85% [17].

The purpose of this study was to evaluate the incidence of NSD following two modifications of BSSO (high and low medial cut) in the immediate postoperative period and after a minimum follow-up of six months using both subjective and objective testing.

2. MATERIALS AND METHODS

This study was conducted on twenty patients with facial skeleton deformity requiring orthognathic surgery, specifically mandibular setback using bilateral sagittal split osteotomy. Age of the patients was between 18 and 30 years. All patients were free from any systemic disease that might affect normal bone healing. Patients with any systemic disease that might affect normal healing, Intra-bony lesions or infections that might interfere with surgery, Previous orthognathic surgeries and Patients with all types of facial clefts were excluded from the study. All patients were recruited from outpatient clinics at the Faculty of Dentistry, Cairo University, Egypt. All participants were informed about the study and provided written consent to participate. All operations were performed at the Department of Oral and Maxillofacial Surgery, Cairo University.

Interventions

The participants were randomly divided into two equal groups, with ten patients in each group:

- **Intervention group:** Patients who underwent mandibular setback using low medial cut BSSO osteotomy.
- **Control group:** Patients who underwent mandibular setback using high medial cut BSSO osteotomy.

Methods

Preoperative Clinical Measures

A thorough preoperative assessment of all patients was carried out, including history taking, clinical, photographic, and radiographic examinations, in addition to dental cast analysis.

Preoperative Radiographic Examination

- Preoperative panoramic radiograph.
- Preoperative lateral cephalometric radiograph.
- Preoperative Computed Tomography (CT) scans of the head and neck region were acquired for all patients utilizing a multi-slice CT machine.

Surgical Procedures

An intraoral vestibular lateral ramus incision was performed to expose the buccal and lingual aspects of the ramus osteotomy region.

- Medial Osteotomy line for the intervention group was anterior to the lingula and at the level of the occlusal surface

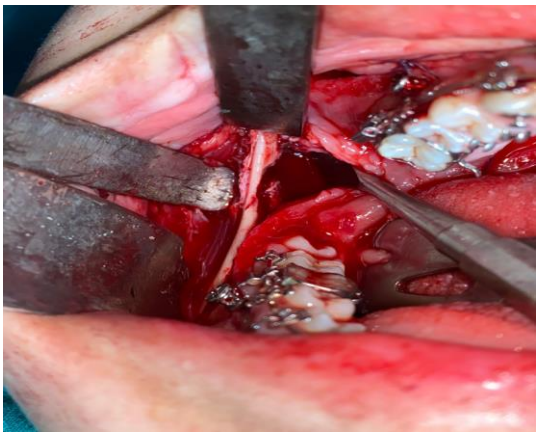


Figure. 1. Low cut medial osteotomy).

- Medial Osteotomy line for the control group was above the lingula

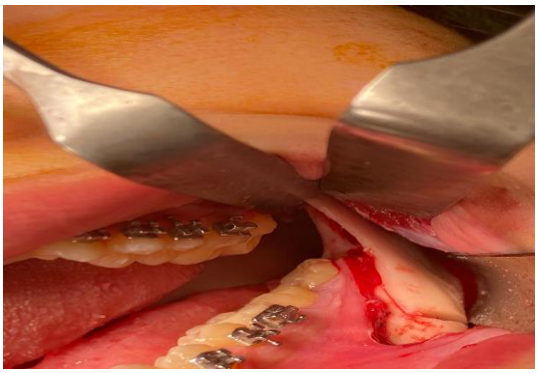


Figure. 2. high cut medial osteotomy).

Buccal extension for both groups was through the external oblique ridge, with vertical and oblique cuts terminating at the lower first molar.

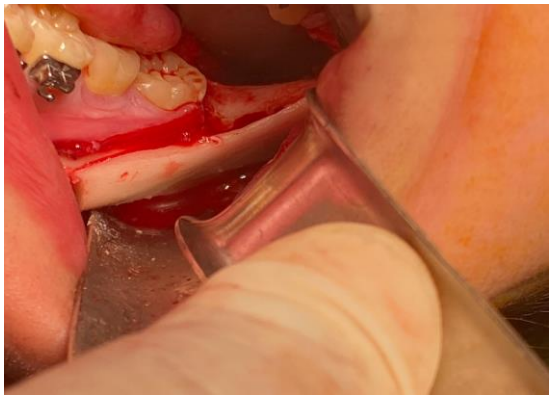


Figure 3. Buccal osteotomy extension).

Postoperative Care

Postoperative instructions: Cold compresses in the form of ice packs were applied for 20 minutes every hour for the first 24 hours postoperatively to minimize edema. All patients were kept on the antibiotic, analgesics, ant edematous and anti-emitting drugs regimen until they were discharged from the hospital:

Postoperative Radiographic Examination

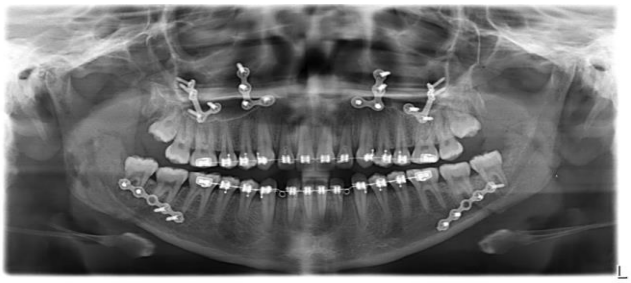


Figure 4. Postoperative panoramic(high medial cut).



Figure 5. Postoperative panoramic radiograph (low medial cut).

Postoperative Computed Tomography (CT) scans of the head and neck region were acquired for all patients utilizing a multi-slice CT machine.



Figure 6. Postoperative CT coronal cuts of low medial cut osteotomy.

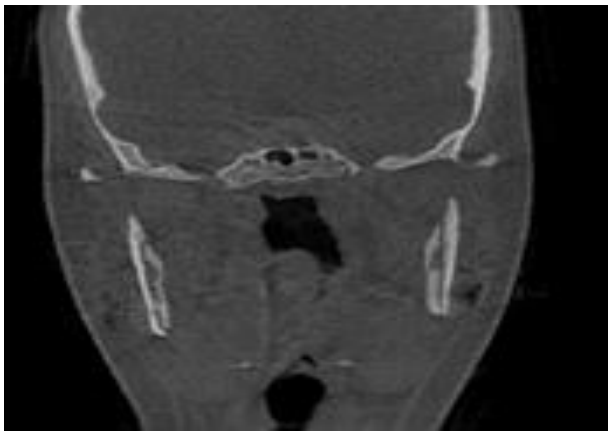


Figure 7. Postoperative CT coronal cuts of high medial cut osteotomy.

Assessment of Neurosensory Disturbances

All patients included in the study were assessed using objective and subjective testing for inferior alveolar nerve function after a minimum of 6 months of follow-up.

Subjective evaluation was carried out using the questionnaire described by Al-Bishri et al. Patients were queried about perceived neurosensory changes along the distribution of the inferior alveolar nerve. A visual analogue scale (VAS) graded from 0 (no discomfort) to 10 (intolerable discomfort) was included for evaluation. To evaluate the effect of the neurosensory disturbance, the grades of the VAS were interpreted as follows: 0–2 mild discomfort, 2–4 mild to moderate discomfort, 4–6 moderate discomfort, 6–8 moderate to severe discomfort, and 8–10 severe discomfort.

Objective testing was done using cotton swabs and pinprick testing. The chin and lip region was tested on either side, and a positive response in at least 3 of 4 applied stimuli was considered normal [6].

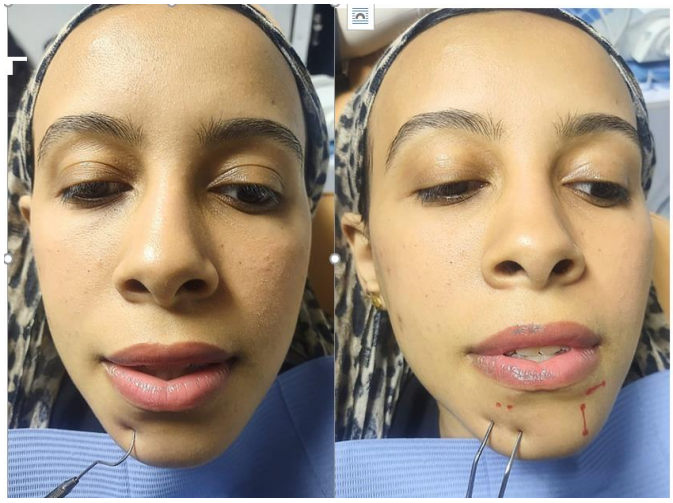


Figure. 8 two point discrimination and pinprick testing.

None of the patients had sensory disturbance prior to surgery. However, objective testing was not carried out prior to the surgical procedure. Medical records of the patients were used to assess the incidence of neurosensory disturbance in the immediate postoperative period.

Statistical Analysis

The main data obtained from the outcome variables was mainly descriptive in nature

3. RESULTS

Twenty patients with skeletal Class III deformity were enrolled in the current study from 2021 to 2024. The mean age of patients was 22.5 years, and nine out of the total twenty subjects were females (Table 1).

Table 1. Patient Demographics

Patient No.	Age (yr)	Sex	Group
1	18	Male	Low medial osteotomy
2	20	Male	Low medial osteotomy
3	24	Female	Low medial osteotomy
4	19	Male	Low medial osteotomy
5	25	Female	Low medial osteotomy
6	22	Male	Low medial osteotomy
7	23	Male	Low medial osteotomy
8	22	Male	Low medial osteotomy
9	24	Female	Low medial osteotomy
10	23	Male	Low medial osteotomy
1	25	Male	High medial osteotomy
2	23	Male	High medial osteotomy
3	22	Male	High medial osteotomy
4	18	Female	High medial osteotomy
5	19	Female	High medial osteotomy
6	25	Female	High medial osteotomy
7	19	Female	High medial osteotomy
8	23	Male	High medial osteotomy
9	25	Female	High medial osteotomy
10	23	Female	High medial osteotomy

The average osteotomy duration was 20.30 minutes for the Posnick SSO (low medial osteotomy group) and 27.21 minutes for the standard SSO (high medial osteotomy group) (Table 2).

Table 2. Mean Osteotomy and Split surgery Duration in Both Groups

Group	Osteotomy Duration (minutes)
Low medial osteotomy group	20.30 (+or-) 3
High medial osteotomy group	27.30 (+or -) 5

All patients (except four in the Posnick group) exhibited a degree of neurosensory disturbance (NSD) on the immediate follow-up date. At the 6-month follow-up period, a complete recovery of NSD was reported in 74% and 35% of the study and control groups, respectively, as revealed by light touch and pinprick tests. The intraoperative location of the inferior alveolar canal or the presence of postoperative complications, including NSD, were also documented (Table 3).

Through the assessment of twenty osteotomies in ten patients, the Posnick (low) osteotomy allowed better visualization of the inferior alveolar nerve with decreased medial dissection. This, together with the decreased bad split incidence, resulted in increased postoperative neurosensory recovery in the study (Posnick) group compared to the control (standard) group at 6 month.

Table 3. Location of IAN Following Splitting & Presence of Postoperative Neurosensory Disturbance or Other Complications in Both Groups

Group	Patients No.	Nerve Location During Surgery	Postoperative NSD Immediate (3 days) / VAS	Postoperative NSD 6 months post-op / VAS	Other Complications
Low medial osteotomy group	1	Proximal seg.	Yes / (5)	No / (0)	NA
	2	Proximal seg.	Yes / (7)	Yes / (3)	NA
	3	Proximal seg.	Yes / (4)	No / (0)	NA
	4	Proximal seg.	Yes / (7)	Yes / (3)	NA
	5	Proximal seg.	Yes / (8)	Yes / (3)	NA
	6	Proximal seg.	Yes / (3)	No / (0)	NA
	7	Proximal seg.	Yes / (3)	No / (0)	NA
	8	Proximal seg.	Yes / (3)	No / (0)	NA
	9	Proximal seg.	No / (0)	No / (0)	NA
	10	Proximal seg.	No / (0)	No / (0)	NA
High medial osteotomy group	1	Distal seg.	Yes / (8)	No / (0)	NA
	2	Distal seg.	Yes / (7)	No / (0)	NA
	3	Distal seg.	Yes / (8)	Yes / (4)	Bad split

NSD: neurosensory disturbance, NA: nothing identified

4. DISCUSSION

Individuals with skeletal Class three deformities commonly seek surgical correction for optimal esthetics and chewing function [Espeland L et al., 2008]. The design of SSO utilized in the current study, either Posnick or Hunsuck medial horizontal osteotomy, are both modifications of Obwegeser SSO, which was first introduced in 1957 [7].

The effect of medial cut placement (superior versus inferior to the lingula) on osteotomy duration, incidence of bad split, and neurosensory function has been investigated in many studies. It was postulated that the low medial (Posnick) osteotomy is associated with a decreased incidence of bad split, subsequent decreased distal lingual plate interference, and inferior alveolar NSD. This fact was adopted by several studies [8]. A literature review and meta-analysis by Verweij et al. concluded that the incidence of NSD after 1 year of BSSO in recent literature ranges between 0.0% and 48.8%, with a mean of 21.7% per side. The wide range of NSD incidence after BSSO can be attributed to various factors such as age, sex, magnitude of movement, or type of fixation. In our study, we investigated the magnitude of mandibular movement as a risk factor for permanent NSD [11].

Regarding NSD, it was equally encountered for both groups in the immediate postoperative period, while obvious recovery at 6 months was yielded in 83% and 50% of the study and control groups, respectively [11].

Neurosensory function has been variably assessed through literature following sagittal split osteotomy procedures [7]. This issue is significant as the path of the inferior alveolar nerve within the mandibular canal runs through the course of low medial horizontal osteotomy. Accidental partial injury or even complete severance of the nerve has been reported in the literature. However, complete recovery of the nerve usually follows surgery from a few weeks up to 6 months postoperatively [4].

Neurosensory recovery is usually facilitated with medications. However, it is better avoided by decreased nerve manipulation during splitting, and results are usually considered satisfactory when NSD undergoes recovery within 6 months of surgery [Antony PG et al., 2017]. In addition, preoperative corticosteroid prescription does not seem to play a role in the reduction of postoperative NSD but rather decreases edema only [16].

To overcome the risk of postoperative neurosensory disturbance (NSD), researchers have investigated and correlated the position and course of the inferior alveolar canal using preoperative cone beam CT (CBCT) with the postoperative sequelae of mandibular advancement procedures. Their results regarding NSD were similar in both groups (with and without preoperative CBCT) at 6 months, but most patients in the CBCT group showed complete recovery at 1 year postoperatively [18]. In a second study, Susarla and colleagues confirmed that when using the low and short medial cut, the IAN was retained within the proximal segment approximately 50% of the time. No difference in functional sensory recovery was found when the IAN was either freely entering the distal segment or when it was partially retained within the proximal segment and not further surgically manipulated to free it from the proximal segment [17]. Therefore, using a low medial cut in BSSRO could be a better alternative to traditional high medial cut BSSRO in terms of the incidence of bad splitting and neurosensory disturbance, but there is a gap in knowledge regarding the comparative effect of both techniques on TMJ changes.

Another factor that might contribute to the incidence of bad split is the simultaneous extraction of mandibular wisdom teeth during splitting [14]. On the other hand, it was stated that osteotomy design modifications have no effect on bad split incidence but rather the location of the buccal end of the lateral cut [10]. Moreover, Rao JKD (2023) has stated that freeing the IAN from the proximal segment is not necessary as long as the required amount of mandibular advancement is 6 mm or less. This is to guarantee decreased nerve manipulation between the segments with subsequent reduction of NSD risk. This fact aligns with the infralingular low medial osteotomy implied by Posnick, which leaves the IAN in the proximal segment and does not necessarily result in NSD as compared to the high SSO [19].

From results obtained from studies by Westermark et al. and Van Sickels et al., it was concluded that large advancements/setbacks (>7 mm) have been reported to increase the risk of NSD by increasing the difficulty of the procedure or the vulnerability of the patient by stretching the nerve [15]. The results of this study showed that NSD occurred in eight out of ten cases immediately postoperative and only in three cases after six months for the low medial cut group. Results for high medial cut BSSRO showed NSD for all cases immediately postoperative and six out of ten cases after six months. Results from this study showed that manipulations of the inferior dental bundle and both segments intraoperatively play a significant role, besides osteotomy design, in the occurrence of postoperative NSD.

5. CONCLUSION

Low cut / Posnick SSO is a valuable osteotomy technique. Compared to the traditional SSO, it showed shorter osteotomy duration and decreased incidence of bad split. It further results in better neurosensory recovery in the extended (6 months) follow-up period.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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ORIGINAL ARTICALE

ROLE OF ULTRASOUND IN THE EVALUATION OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder primarily affecting synovial joints, leading to progressive joint damage, deformity, and disability if not adequately managed. Early and accurate evaluation of joint inflammation is critical for diagnosis, disease monitoring, and treatment optimization. Conventional radiography, while commonly used, lacks sensitivity in detecting early soft tissue changes and synovitis. Ultrasound (US), particularly with power Doppler capability, has emerged as a valuable, non-invasive, and dynamic imaging tool for real-time assessment of synovitis, tenosynovitis, joint effusion, bone erosions, and vascular activity in RA. Its portability, safety profile, and high sensitivity for inflammatory changes make it indispensable in the current rheumatologic imaging paradigm.

Aim: To evaluate the role of high-resolution musculoskeletal ultrasound in the detection, characterization, and monitoring of joint involvement in patients with rheumatoid arthritis, with particular emphasis on its sensitivity in detecting synovitis, erosions, and vascular activity compared to clinical examination.

Materials and Methods: This observational study included 60 adult patients with clinically diagnosed RA based on the 2010 ACR/EULAR classification criteria. All subjects underwent detailed clinical joint assessments followed by standardized musculoskeletal ultrasound using high-frequency linear probes (10–18 MHz). The most commonly affected joints—wrists, metacarpophalangeal (MCP), proximal interphalangeal (PIP), and knees—were evaluated for synovial hypertrophy, effusion, power Doppler signal, and bone erosions. Synovitis was graded semi-quantitatively (Grades 0–3) per OMERACT guidelines. The ultrasound findings were compared with clinical swelling and tenderness scores to assess concordance. Data were statistically analyzed for sensitivity, specificity, and correlation.
Results: Ultrasound detected synovitis in 85% of joints clinically assessed as normal, demonstrating its superiority in identifying subclinical disease. Power Doppler signals were seen in 72% of joints with active inflammation, indicating ongoing synovial hyperemia. Bone erosions were visualized in 38% of cases, including early cortical breaks undetected on radiographs. There was significant discordance between clinical and sonographic findings, particularly in small joints. The sensitivity of ultrasound for detecting active synovitis was 91%, while clinical assessment showed 68%. Doppler-positive joints strongly correlated with higher disease activity scores (DAS28), supporting the utility of ultrasound in disease monitoring and treatment planning

Conclusion: Musculoskeletal ultrasound plays a critical role in the comprehensive evaluation of rheumatoid arthritis. Its ability to detect subclinical synovitis, monitor disease activity through power Doppler imaging, and visualize early erosions makes it a superior adjunct to clinical assessment. Integration of ultrasound into routine rheumatologic practice enhances diagnostic accuracy, allows early therapeutic interventions, and facilitates more precise disease monitoring.

Keywords: Rheumatoid Arthritis, Musculoskeletal Ultrasound, Synovitis, Power Doppler, Joint Effusion, Bone Erosion, Subclinical Inflammation, Disease Monitoring, OMERACT, High-Resolution Imaging

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily targeting the synovial joints, resulting in persistent inflammation, progressive cartilage destruction, and eventual joint deformity and disability. Affecting approximately 0.5% to 1% of the global population, RA not only impairs joint integrity but also carries significant systemic manifestations including cardiovascular, pulmonary, and hematological complications[1]. The disease follows a variable course but is often characterized by flares and remissions, making accurate assessment of disease activity and structural damage crucial for timely intervention. Early diagnosis and aggressive treatment strategies particularly those employing disease-modifying anti-rheumatic drugs (DMARDs) and biological agents have been shown to halt disease progression, prevent irreversible damage, and preserve quality of life. However, a major limitation in effective disease management remains the inadequacy of traditional clinical and imaging tools to detect early inflammatory changes, especially in small joints [2].

Conventional radiography has historically played a central role in the imaging of RA. While valuable for documenting joint space narrowing and bone erosions, it suffers from poor sensitivity in the early phases of the disease, when inflammatory changes are largely confined to the soft tissues. MRI offers excellent visualization of synovitis and bone marrow edema but is often limited by cost, accessibility, and time constraints in routine clinical settings [3]. In contrast, musculoskeletal ultrasound (US) has emerged as a highly effective, accessible, and dynamic imaging modality capable of detecting both morphological and hemodynamic changes in joints affected by RA. High-frequency ultrasound provides real-time visualization of synovial hypertrophy, joint effusions, and erosions, while power Doppler imaging adds a critical layer of functional assessment by demonstrating active synovial vascularity, a hallmark of ongoing inflammation [4].

The advantages of ultrasound extend beyond imaging resolution. It is a non-invasive, radiation-free modality that allows for bedside assessment, repeat evaluations, and simultaneous bilateral joint comparisons, making it highly adaptable to outpatient rheumatology practice. Ultrasound has demonstrated remarkable sensitivity in identifying subclinical synovitis particularly in patients who appear to be in clinical remission and in assessing disease activity in seronegative or atypical presentations [5]. Furthermore, power Doppler signals within hypertrophic synovium have been correlated with histopathologic markers of active inflammation and predictive of disease flares, lending prognostic value to ultrasound-based assessments. Studies have also shown that ultrasound can identify early cortical bone erosions that are often invisible on conventional radiographs, underscoring its utility in early diagnosis [6].

Despite its proven advantages, ultrasound remains underutilized in routine RA management due to factors such as operator dependence, lack of widespread training, and variability in image interpretation. Nonetheless, standardized scoring systems and guidelines developed by international task forces like OMERACT (Outcome Measures in Rheumatology) have facilitated reproducibility and integration into clinical trials and therapeutic algorithms. Semi-quantitative grading of synovitis, joint effusion, and Doppler activity offers clinicians objective metrics for monitoring treatment response, adjusting medication doses, and assessing remission [7,8].

Given the evolving paradigm of RA management which emphasizes early diagnosis, treat-to-target strategies, and personalized therapy, the integration of musculoskeletal ultrasound into routine clinical practice is both timely and essential. There is an increasing need to quantify the added value of ultrasound in diagnosing, grading, and following up patients with RA, particularly in comparison with traditional clinical assessment. This study was therefore undertaken to systematically evaluate the role of ultrasound in the detection and characterization of joint pathology in patients with rheumatoid arthritis, and to examine its concordance with clinical findings and relevance in disease monitoring.

MATERIALS AND METHODS

Study Design And Setting: This was a prospective observational study conducted in the Department of Radiodiagnosis in collaboration with the Department of Rheumatology at a tertiary care academic hospital in India. The study spanned a duration of 12 months and aimed to evaluate the diagnostic and monitoring utility of musculoskeletal ultrasound in patients with clinically confirmed rheumatoid arthritis (RA). Prior to initiation, the study was approved by the Institutional Ethics Committee, and all participants provided written informed consent.

Study Population: A total of 60 adult patients aged 18 years and above who had been diagnosed with RA as per the 2010 ACR/EULAR classification criteria were recruited. These patients were either newly diagnosed or under ongoing treatment for RA. Patients were referred by rheumatologists for baseline or follow-up ultrasound

assessments as part of routine evaluation. Efforts were made to include a spectrum of disease severity ranging from mild to severe RA to evaluate the sensitivity of ultrasound across different clinical presentations.

Inclusion Criteria: Patients included in the study had a confirmed diagnosis of RA, were able to provide informed consent, and had not undergone intra-articular injections or surgical interventions in the preceding three months. Both seropositive and seronegative cases were considered eligible, provided clinical evidence of synovitis was present.

Exclusion Criteria: Patients were excluded if they had other inflammatory arthritides such as psoriatic arthritis, systemic lupus erythematosus, or gout. Those with joint deformities that severely limited ultrasound probe access, active skin infections over the joints to be assessed, or with contraindications to positioning during scanning were also excluded. Patients with overlapping connective tissue diseases or under corticosteroid therapy exceeding 15 mg/day of prednisolone equivalent were excluded to avoid masking inflammatory findings.

Clinical Examination: A detailed clinical examination was performed by an experienced rheumatologist on the day of the ultrasound to document joint swelling, tenderness, range of motion, and functional status. The 28-joint Disease Activity Score (DAS28), which includes evaluation of tender and swollen joint counts, ESR, and patient global assessment, was calculated for each patient to categorize disease activity.

Ultrasound Protocol: Ultrasound evaluation was performed using a high-resolution musculoskeletal ultrasound system equipped with a linear array transducer operating at 10–18 MHz frequency. All examinations were conducted by a radiologist with specialized training in musculoskeletal imaging. The joints assessed included bilateral wrists, metacarpophalangeal (MCP) joints 1–5, proximal interphalangeal (PIP) joints 2–5, knees, and in some cases, the metatarsophalangeal (MTP) joints and ankles based on clinical symptoms.

Each joint was scanned in longitudinal and transverse planes to assess for synovial hypertrophy, joint effusion, tenosynovitis, and bone erosions. Power Doppler imaging was used to assess active synovial vascularity. Synovitis was graded semi-quantitatively on a 0–3 scale based on the OMERACT definition: Grade 0 (no synovial thickening), Grade 1 (mild), Grade 2 (moderate), and Grade 3 (marked thickening with bulging over joint line). Power Doppler signal was similarly graded from 0 (no flow) to 3 (severe flow occupying >50% of the synovial area). Erosions were defined as discontinuities in the bone cortex with a step-down contour, seen in two orthogonal planes.

Data Collection And Interpretation: Ultrasound findings were documented using structured reporting templates, and the number of joints positive for synovitis, power Doppler activity, effusion, and erosions were recorded per patient. The correlation between ultrasound scores and clinical joint findings (swelling, tenderness) was analyzed. In addition, relationships between power Doppler grades and DAS28 scores were examined to assess ultrasound utility in disease activity monitoring.

Statistical Analysis: All data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The sensitivity and specificity of ultrasound for detecting active synovitis were calculated using clinical joint assessment as the reference. The kappa statistic was used to assess agreement between clinical and ultrasound findings. Pearson's correlation coefficient was used to determine the association between power Doppler activity and DAS28 scores. A p-value <0.05 was considered statistically significant.

RESULT

A total of 60 patients diagnosed with rheumatoid arthritis were evaluated using musculoskeletal ultrasound for joint involvement. The majority were middle-aged females, with most patients presenting within 5 years of symptom onset. Clinically, the wrists and MCP joints were the most frequently involved. Ultrasound identified a greater number of inflamed joints compared to clinical examination, with a high detection rate for subclinical synovitis and early bone erosions. Power Doppler imaging showed significant correlation with clinical disease activity scores (DAS28). The overall sensitivity of ultrasound in detecting active joint inflammation surpassed clinical assessment, demonstrating its value in both diagnosis and monitoring.

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Table 1. shows that the majority of patients (65%) were in the 31–50 year age group, with a mean age of 44.2 ± 9.8 years.

Age group (years)	Number of patients	Percentage (%)
18–30	8	13.3
31–40	20	33.3
41–50	19	31.7
>50	13	21.7

Table 2. Gender distribution of RA patients

Table 2 shows a female predominance, with females comprising 73.3% of the study population.

Gender	Number of patients	Percentage (%)
Male	16	26.7
Female	44	73.3

Table 3. Duration of RA symptoms at presentation

Table 3 shows that 58.3% of patients presented within the first 5 years of symptom onset.

Duration (years)	Number of patients	Percentage (%)
<1	10	16.7
1–5	25	41.6
6–10	15	25.0
>10	10	16.7

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Table 4. Joints involved based on clinical assessment

Table 4 shows that wrists (83.3%) and MCP joints (76.7%) were the most commonly tender or swollen on clinical examination.

Joint	Number of patients with involvement	Percentage (%)
Wrist	50	83.3
MCP joints	46	76.7
PIP joints	38	63.3
Knee	21	35.0
MTP/Ankle	15	25.0

Table 5. Joints with ultrasound-detected synovitis

Table 5 shows that ultrasound detected synovitis in 92% of wrists and 87% of MCP joints, including many joints that appeared normal clinically.

Joint	Synovitis on US (n)	Percentage (%)
Wrist	55	91.7
MCP joints	52	86.7
PIP joints	44	73.3
Knee	27	45.0
MTP/Ankle	22	36.7

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Table 6. Detection of subclinical synovitis

Table 6 shows that ultrasound detected synovitis in 51 clinically normal joints, underscoring its sensitivity.

Joint group	Clinically normal joints with US synovitis	Percentage (%)
Wrist	11	18.3
MCP	16	26.7
PIP	14	23.3
Others	10	16.7
Total	**51**	**85.0**

Table 7. Power Doppler signal detection

Table 7 shows that 72% of patients demonstrated Doppler-positive joints, suggesting active synovial hyperemia.

Power Doppler grade	Number of patients	Percentage (%)
Grade 0	17	28.3
Grade 1	22	36.7
Grade 2	14	23.3
Grade 3	7	11.7

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Table 8. Ultrasound detection of bone erosions

Table 8 shows that ultrasound detected bone erosions in 38.3% of patients, even in early-stage disease.

Erosions present on US	Number of patients	Percentage (%)
Yes	23	38.3
No	37	61.7

Table 9. Comparison of synovitis detection – Clinical vs. US

Table 9 shows that ultrasound identified more joints with synovitis than clinical examination, with 91.2% sensitivity.

Assessment method	Synovitis detected (joints)
Clinical exam	118
Ultrasound	154

Table 10. Correlation between Doppler activity and DAS28 score

Table 10 shows a strong positive correlation between Doppler grade and DAS28 score ($r = 0.61$, $p < 0.001$).

Parameter	Correlation coefficient (r)	p-value
PD grade vs. DAS28	0.61	<0.001

Table 11. Agreement between clinical swelling and US synovitis (kappa)

Table 11 shows moderate agreement between clinical swelling and ultrasound synovitis with a kappa value of 0.49.

Measure	Value
Kappa coefficient (κ)	0.49
Interpretation	Moderate

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Table 12. Distribution of synovitis severity on US grading

Table 12 shows that most joints had Grade 1 or Grade 2 synovitis, with 16.7% showing severe Grade 3 involvement.

Synovitis grade	Number of joints	Percentage (%)
Grade 0	56	22.0
Grade 1	78	30.6
Grade 2	91	35.7
Grade 3	43	16.7

Table 1 shows that most patients were between 31–50 years of age. **Table 2** shows a clear female predominance in the study population. **Table 3** shows that over half the patients presented within 5 years of symptom onset. **Table 4** shows that wrists and MCP joints were the most commonly involved clinically. **Table 5** shows that ultrasound detected synovitis in nearly all wrists and MCPs, including subclinical cases. **Table 6** shows that ultrasound identified synovitis in 51 joints that were clinically normal. **Table 7** shows that 72% of patients demonstrated positive Doppler activity, suggesting active inflammation. **Table 8** shows that bone erosions were found in over one-third of patients, many of whom had early-stage RA. **Table 9** shows that ultrasound detected 30% more joints with synovitis than clinical examination. **Table 10** shows a strong correlation between Doppler signal intensity and DAS28 disease activity scores. **Table 11** shows moderate agreement between clinical swelling and ultrasound findings. **Table 12** shows that most joints had mild to moderate synovitis, but a notable fraction had Grade 3 disease indicating high activity.

DISCUSSION

The current study reinforces the vital role of high-resolution musculoskeletal ultrasound in the comprehensive evaluation of rheumatoid arthritis (RA), particularly in the detection of synovitis, joint effusion, bone erosions, and synovial vascularity using power Doppler imaging [9]. RA is a progressive autoimmune condition where early diagnosis and prompt initiation of therapy can substantially alter disease trajectory. However, conventional clinical examination often underestimates disease activity, especially in small joints, and radiographs may fail to detect early inflammatory changes. In this context, ultrasound emerges as a dynamic, non-invasive, and sensitive modality that bridges the gap between clinical suspicion and definitive imaging evidence [10].

In our cohort of 60 RA patients, ultrasound revealed synovial inflammation in a significantly higher number of joints compared to clinical examination. The most affected joints on ultrasound were the wrists and metacarpophalangeal (MCP) joints consistent with the known joint distribution in RA [11]. Importantly, ultrasound detected subclinical synovitis in 51 joints that were clinically normal, underscoring its superiority in revealing occult inflammation. This finding is of particular clinical relevance, as subclinical synovitis is often a precursor to future joint damage and may warrant early therapeutic intensification even in patients deemed to be in clinical remission [12].

Power Doppler imaging further enhanced the diagnostic and prognostic capability of ultrasound by identifying increased vascularity within hypertrophic synovium—a surrogate marker of active inflammation. In our study, 72% of patients demonstrated Doppler-positive joints, and higher Doppler grades showed a strong positive correlation with elevated DAS28 scores ($r = 0.61$) [13]. This affirms the role of Doppler ultrasound not only in diagnosis but also in dynamic disease activity monitoring and response assessment. In comparison to static anatomical assessments, power Doppler provides a functional view of ongoing inflammation, which can be particularly useful in guiding escalation or de-escalation of immunosuppressive therapies [14]. Another significant finding of our study was the early detection of bone erosions in 38.3% of patients using ultrasound, many of whom were in the early stages of RA

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and had not yet developed radiographic changes [15]. Ultrasound is capable of identifying even minor cortical discontinuities and step-down deformities on bone surfaces, which are often missed on plain films due to superimposed anatomical structures. Detection of early erosions is pivotal in identifying aggressive disease phenotypes and in advocating for more intensive therapy to prevent irreversible joint damage [16]. The moderate agreement between clinical swelling and ultrasound-detected synovitis ($\kappa = 0.49$) highlights a persistent discordance between physical examination and imaging findings. While rheumatologists are adept at joint assessments, clinical evaluation remains subjective and can be limited by joint deformities, patient discomfort, or examiner variability. Ultrasound, on the other hand, offers real-time, reproducible imaging that can visualize internal joint pathology irrespective of surface findings [17]. This discrepancy justifies the inclusion of ultrasound as a routine extension of clinical examination in RA.

Furthermore, the semi-quantitative grading of synovitis on ultrasound, along with the power Doppler scale, provides a standardized framework for monitoring disease progression or remission. Most joints in our study demonstrated Grade 1 or 2 synovitis, while 16.7% showed Grade 3 inflammation, suggesting a wide range of inflammatory activity even within the same patient cohort. This variability again supports the personalized utility of ultrasound in tailoring therapeutic regimens according to objective inflammation scores.

The implications of this study are manifold. First, ultrasound enhances the sensitivity of RA diagnosis, particularly in early or atypical presentations. Second, it assists in detecting subclinical disease, enabling timely intervention to prevent structural damage. Third, it allows objective disease activity monitoring, which is essential in treat-to-target strategies now central to RA management guidelines. Lastly, it reduces reliance on expensive or less accessible modalities like MRI, offering a cost-effective and rapid alternative for joint evaluation.

Limitations

While this study provides compelling evidence for the utility of ultrasound in RA, certain limitations must be acknowledged. First, it was conducted at a single tertiary care center, and results may not be generalizable across diverse clinical settings or less experienced operators. Second, ultrasound is inherently operator-dependent, and interpretation may vary based on radiologist skill and experience. Although standard OMERACT criteria were used, minor inter-observer variations in grading synovitis and Doppler signals may exist. Third, this study did not include radiographic or MRI correlation, which could have further validated the findings. Fourth, a follow-up component assessing longitudinal changes post-treatment was not included, which could have added value in evaluating response to therapy. Finally, despite inclusion of clinically diverse patients, the sample size was moderate and larger multicentric studies are recommended to substantiate these findings.

CONCLUSION

This study reaffirms the critical role of musculoskeletal ultrasound as an essential imaging tool in the evaluation of rheumatoid arthritis. The ability of ultrasound to detect subclinical synovitis, visualize early bone erosions, and assess disease activity through power Doppler vascular signals significantly enhances the diagnostic accuracy and clinical management of RA. Compared to physical examination alone, ultrasound offers superior sensitivity in identifying inflamed joints, including those that are clinically silent. The observed correlation between Doppler signal intensity and disease activity scores further supports the integration of ultrasound into routine disease monitoring protocols. As a non-invasive, safe, and dynamic imaging modality, ultrasound provides rheumatologists with real-time information that can influence treatment decisions, guide therapeutic escalation, and ultimately improve patient outcomes. Incorporating ultrasound into routine rheumatologic assessment enables early diagnosis, personalized therapy, and precision-based follow-up, thereby reinforcing its indispensable role in the modern management of rheumatoid arthritis.

Author Contributions: All authors contributed equally to the conception, data acquisition, sonographic analysis, and manuscript preparation. [Insert initials] performed ultrasound imaging and reporting. [Insert initials] conducted the clinical assessments and DAS28 scoring. All authors reviewed and approved the final manuscript before submission.

DECLARATION

Ethical Approval: This study was approved by the Institutional Ethics Committee. This study was conducted in accordance with the principles of the Declaration of Helsinki regarding ethical research involving human sub jects.

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

Availability of Research Data: All data supporting the

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findings of this study are available from the corresponding author upon reasonable request.

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ORIGINAL RESEARCH

COMPARISON BETWEEN DEXMEDETOMIDINE AND PROPOFOL ON INTERLEUKIN-6 LEVELS IN PATIENTS WITH CHRONIC RHINOSINUSITIS UNDERGOING FUNCTIONAL ENDOSCOPIC SINUS SURGERY

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ABSTRACT

Background: Dexmedetomidine and propofol are expected to serve as intravenous anesthetic agents that reduce inflammatory factors in patients with chronic rhinosinusitis (CRS), particularly those undergoing functional endoscopic sinus surgery (FESS).

Aim: This study aims to compares dexmedetomidine and propofol before and after FESS.

Materials and Method: A quasi-experimental, cross-sectional, and analytical study was conducted involving patients with chronic rhinosinusitis (CRS) who underwent elective functional endoscopic sinus surgery (FESS) at Dr. Soetomo General Hospital, Surabaya, Indonesia. CRS patients scheduled for FESS were recruited for this study. Interleukin-6 (IL-6) levels were measured using ELISA 5 minutes after induction and 5 minutes before extubation. The Wilcoxon signed-rank test and Mann-Whitney test were used to determine changes in IL-6 levels before and after the procedure. A total of 24 CRS patients undergoing FESS were included in this study.

Results: The median IL-6 levels in the dexmedetomidine group before and after surgery were 20.24 ng/mL and 34.09 ng/mL, respectively, indicating a significant increase in IL-6 levels (p0.05).

Conclusion: There was a significant change in IL-6 levels in both the dexmedetomidine and propofol groups before and after surgery. However, there was no significant difference between dexmedetomidine and propofol in terms of changes in IL-6 levels among CRS patients undergoing FESS. Further studies are needed to evaluate the economic impact of using dexmedetomidine and propofol as controlled hypotensive agents in FESS procedures.

Keywords**:** CRS, FESS, Dexmedetomidine, Propofol, Interleukin-6.

INTRODUCTION

Chronic Rhinosinusitis (CRS) represents a commonly encountered health disorder affecting communities and represents a major health concern that affects 5% to 12% of the population at large. The European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) delineates the classification of rhinosinusitis based on clinical symptoms accompanied by signs of nasal mucosal inflammation based on endoscopic or radiological examination.[1] Health statistics reports in the United States in 2019 mentioned that all age groups can be affected with an incidence reaching 12.3% of the population. The impact of CRS affects the

community's economy with estimated costs of 10-13 billion dollars annually, so CRS places considerable health and financial responsibilities upon those affected encompassing the individual, family, community, and societal dimensions.[2]

Research conducted in the period 2016-2018 in the Rhinology Division, Department of ENT-HNS, Dr. Mohammad Hoesin Hospital Palembang found a proportion of CRS in adults of 33.3%. The average number of adult CRS patients in rhinology clinics over 3 years was 83.8% at Dr. M. Djamil Hospital Padang, 83.5% at Dr. Kariadi Hospital Semarang, 85.9% at Dr. Saiful Anwar Hospital Malang, 65.5% at Dr. Soetomo Hospital Surabaya, and 28.9% at Sanglah Hospital Bali. Another study conducted at Sanglah Hospital Bali in 2016 identified the largest group of CRS patients in the 46–60 year age range (37.7%).[3]

This chronic sinus disease causes inflammatory processes and is followed by increased inflammatory factors. An investigation by Marlina et al. found increased IL-6 levels in tissues of CRS patients without nasal polyps and also in CRS patients with nasal polyps.[4] The increase in IL-6 indicates that IL-6 plays a pathogenic role in CRS. Initial extrinsic aggression factors in CRS such as fungi, bacteria, and lipopolysaccharide (main outer membrane component of Gram-negative bacteria) cause increased IL-6 expression.[5]

Management of CRS cases includes medical treatment and surgical procedures. Variations range from simple procedures with simple equipment to surgery using sophisticated endoscopic equipment. Functional Endoscopic Sinus Surgery (FESS) is a sinus surgical procedure using endoscopic instruments. A staged approach in FESS provides good results, especially in CRS cases, and provides wide and safe access when handling structures outside the sinuses.[6]

FESS surgical procedures often require controlled hypotension techniques. Propofol and dexmedetomidine as anesthetic agents play important roles in achieving controlled hypotension techniques.[6] The use of dexmedetomidine in controlled hypotension techniques is increasingly becoming a choice. Dexmedetomidine itself, besides having the ability to provide hypotension, also has the capacity to inhibit excessive production of various inflammatory markers including TNF-α, IL-1β, and IL-6 in several studies on humans and animals. Dexmedetomidine provides anti-inflammatory effects in many neurological conditions by reducing neural inflammation.[7,8]

Propofol is an anesthetic agent most commonly used as general anesthesia. It can rapidly lowering BP and MAP.[9] Not only capable of rapidly lowering blood pressure, but propofol itself has the ability to inhibit the release of inflammatory factors. Findings reported by Jia et al. reveals that propofol can prevent inflammatory responses by reducing the release of cytokines and inflammatory mediators by inhibiting IL-6, IL-8, and TNF-α in RAW 264.7 cells stimulated by lipopolysaccharide.[10] The ability of dexmedetomidine and propofol to inhibit inflammatory factors aligns with therapeutic goals in patients with CRS. The use of dexmedetomidine in FESS surgery is expected to be very effective in achieving success in controlled hypotension while reducing inflammation in CRS. Therefore, this research becomes relevant to conduct so it can serve as a reference in providing appropriate anesthetic drug choices for surgical procedures and patient clinical conditions.

METHODS

Research Design

This research is a quasi-experimental study with cross-sectional data collection and analytical study approach. CRS patients undergoing FESS were grouped into two treatment conditions: dexmedetomidine group and propofol group.

Time and Location of Research

The research was conducted at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya. The research implementation time began in October 2024 and will continue until the planned sample size is met.

Research Population

The research population consists of patients with CRS undergoing FESS surgery at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya.

Research Sample

The research sample consists of patients with CRS undergoing FESS surgery at the Integrated Central Surgery Building (GBPT) of Dr. Soetomo Hospital Surabaya who meet the research criteria. Sampling was obtained from patients who met inclusion criteria and were selected consecutively according to the research implementation time.

Sample size determination used the formula.[11] Sampling technique used random allocation from previous research examining the use of propofol in reducing IL-6 levels[12], resulting in a minimum total sample of 11 people in each group. Considering the possibility of dropouts, each group was increased by 10%, resulting in a sample of 24 people with 12 people in each group.

Inclusion and Exclusion Criteria

1) Inclusion Criteria:
   a. Patient age between 18-65 years
   b. Patient physical status according to American Society of Anesthesiologists (ASA) class I or II
   c. Patients with written consent
2) Exclusion Criteria:
   a. Patients with a history of allergy to dexmedetomidine and propofol
   b. Obese patients with BMI more than 30
   c. Patients with uncontrolled hypertension, history of heart disease, and stroke
   d. Pregnant or nursing women
3) Drop-out Criteria:
   a. Patients who experience intolerance to dexmedetomidine and propofol drugs used during surgery
   b. Patients with blood pressure drop to shock requiring vasopressors until end of surgery.
   c. Patients who choose to withdraw from the research or cannot continue their participation

Research Variables

The research variables consisted of the independent variable, namely the anesthetic agent, and the dependent variable, namely interleukin-6.

Research Data Collection Method

Patients with CRS planned for elective FESS surgery at GBPT Dr. Soetomo Hospital Surabaya under general anesthesia who meet inclusion and exclusion criteria were taken as samples. IL-6 examination in blood was performed 5 minutes after induction and 5 minutes before extubation.

Data Processing and Analysis Techniques

Collected data was recorded and tabulated. Data processing in this research used applications. All demographic characteristic data (age, gender, etc.) were summarized using descriptive statistics. All measurement data were expressed as mean ± standard deviation. Statistical tests used in this research were:

a. Paired difference test: To differentiate changes in IL-6 levels before induction and after extubation in the dexmedetomidine group and propofol group. If data was normally distributed, tested with Paired T Test; when normality is not met, with Wilcoxon Signed Rank Test.
b. Group mean difference test: To compare mean changes in IL-6 levels between dexmedetomidine and propofol groups. When normality was satisfied, independent t-test applied; when normality is not met, Mann Whitney test hence adopted.

Ethical Considerations

All data in this research are confidential and will be used solely for scientific purposes. Patients and their families were provided with explanations regarding the objectives of the study, and those willing to participate were asked to sign a written informed consent form. Ethical clearance for this research will be obtained from the Ethics Committee of the Faculty of Medicine, Airlangga University/ Dr. Soetomo General Hospital.

RESULTS

Patient Characteristics

Patient characteristics are displayed according to the type of data available. For categorical (nominal) and ordinal data, they are presented as frequency and percentage. While numerical data on ratio and interval scales are displayed as mean ± standard deviation if normality test results show normal results, and if not normal, in median (range) form. Range is the display of minimal – maximal data.

Table 1. Patient Characteristics

Characteristic	Number (n) People	Percent (%) Mean ± SD (Kg/m²)
Gender		
Male	6	25
Female	18	75
Age (years)		
18-25	8	33,3
26-33	7	29,2
34-41	2	8,3
42-49	2	8,3
50-57	1	4,1
58-65	1	4,1
PS ASA		
PS ASA 1	2	8,3
PS ASA 2	22	91,7
BMI	24	23,46 ± 4,72

Research results show gender proportion dominated by females with a total of 18 (75%), with the majority ASA PS being ASA PS 2, namely 22 patients (91%). Patient demographic description based on age obtained 4 people or 16.7% of patients aged <20 years, 7 people or 29.2% of patients aged 21-30 years, 7 people or 29.2% of patients aged 31-40 years, 4 people or 16.7% of patients aged 41-50 years, and 2 people or 8.3% of patients aged >50 years.

Interleukin 6 Level Measurement Results

The first step in analyzing IL-6 level results was assessing sample distribution using normality test techniques. Normality test is testing to determine research data distribution, whether normally distributed or not. Testing was performed using the Shapiro-Wilk test with the following results.

Table 2. Interleukin-6 Normality Test Results

Group	p	Note
Pre dexmedetomidine	0.005	Not normally distributed
Post dexmedetomidine	0.000	Not normally distributed
Pre propofol	0.068	Normally distributed
Post propofol	0.054	Normally distributed

Note: Significance p< 0.05

Normality test results for IL-6 levels in the dexmedetomidine group in pre-test and post-test testing obtained significance values less than 0.05 (p < 0.05), so IL-6 level data in the dexmedetomidine group was not normally distributed. Additionally, normality test results for IL-6 levels in the propofol group in pre-test and post-test testing obtained significance values greater than 0.05 (p > 0.05), so IL-6 level data in the propofol group was normally distributed.

Table 3. IL-6 Level Description Results for Dexmedetomidine Group

Group	n	Median (ng/L)	Minimum-Maximum (ng/L)
Pre dexmedetomidine	12	20.24	3.75-109.16
Post dexmedetomidine	12	34.09	16.93 – 164.27

Note: n: number of samples

IL-6 level measurement results in the dexmedetomidine group before treatment (pre dexmedetomidine) obtained a median value of 20.24 ng/L, then after treatment (post dexmedetomidine) obtained a median value of 34.09 ng/L (45.584% increase). These results show that after dexmedetomidine administration, patients' IL-6 levels increased.

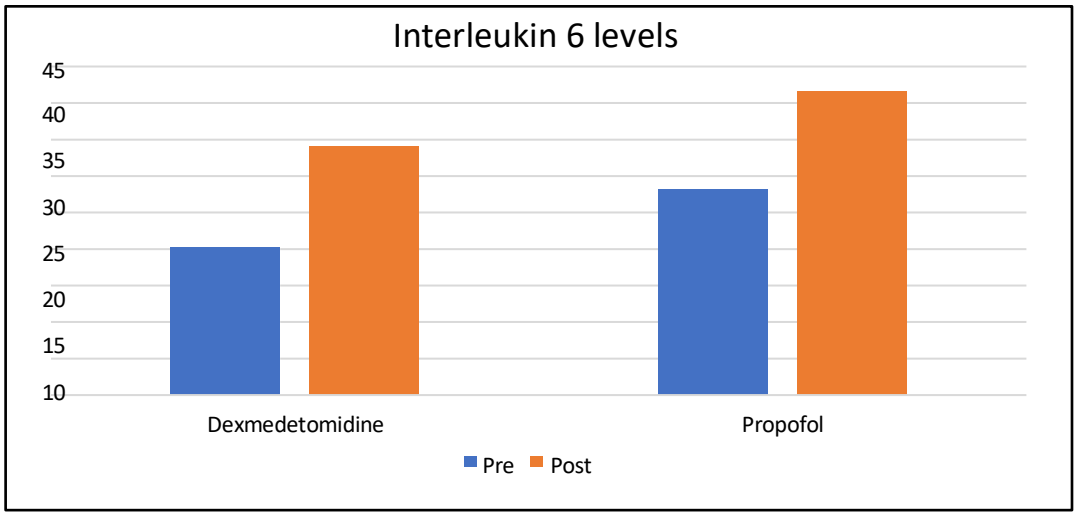


Figure 1. Mean IL-6 Levels of Patients Pre-Operation and Post-Operation

Table 4. IL-6 Level Description Results for Propofol Group

Test	n	Mean (ng/L)	SD (ng/L)
Pre propofol	12	28.157	18.318
Post propofol	12	41.646	25.779

Note: n: number of samples; SD: standard deviation

IL-6 level measurement results in the propofol group before treatment (pre propofol) obtained an average of 28.157 ng/L with a standard deviation of 18.318, then after treatment (post propofol) obtained an average of 41.646 ng/L with a standard deviation of 25.779. These results show that after propofol administration, patients' IL-6 levels increased.

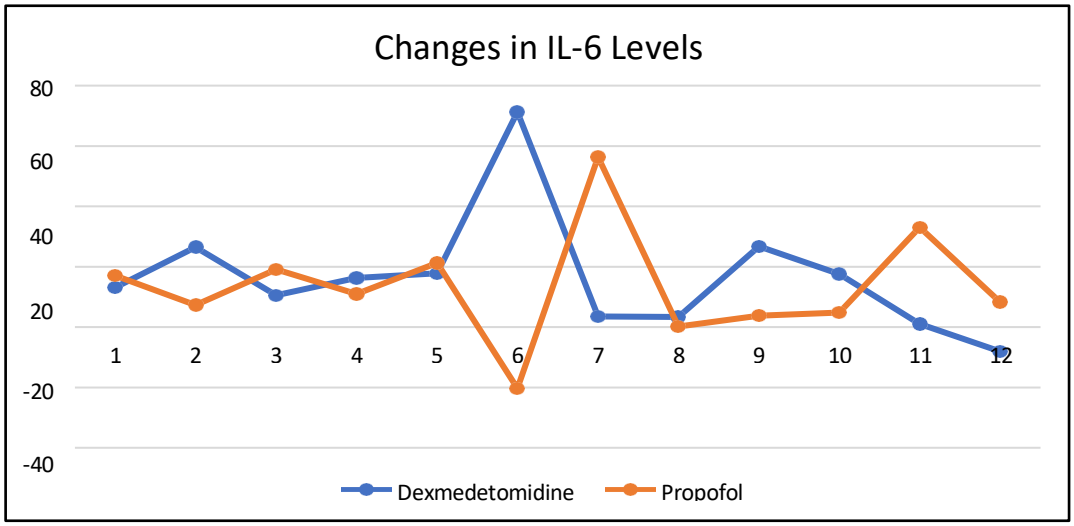


Figure 2. Changes in IL-6 levels after dexmedetomidine and propofol administration

Measurement results in each group showed changes in IL-6 levels after drug administration (can be seen in Figure 2). There was an increase in IL-6 levels in both treatment groups. However, in the dexmedetomidine group, only 1 sample experienced a decrease in IL-6 levels, while in the propofol group, 1 sample also experienced a decrease in IL-6 levels.

Effects of Dexmedetomidine and Propofol Administration on IL-6 Levels

To determine the effect of drug administration on IL-6 levels, paired comparison tests and inter-group comparison tests were needed. Paired comparison test is testing to compare data before treatment (pre) and after treatment (post). Test results are presented as follows.

Table 5. Paired Comparison Test Results

Dexmedetomidine Group			Propofol Group		
n	Median (ng/L) (Minimum- Maximum)	p	n	Mean ± SD (ng/L)	p
12	13,85 (1,033-71,259)	0,006	12	13.4 ± 5,4	0,030

Note: n: number of samples; SD: Standard deviation; Significance p<0.05

IL-6 level comparison results before treatment (pre) and after treatment (post) in the dexmedetomidine group using the Wilcoxon test obtained a significance value (p) of 0.006. These results show a significance value less than 0.05 ($p < 0.05$), so it was stated that there was an increase in IL-6 levels after dexmedetomidine administration. Moreover, IL-6 level comparison results before treatment (pre) and after treatment (post) in the propofol group using paired sample t-test obtained a significance value (p) of 0.030. These results show a significance value less than 0.05 ($p < 0.05$), so it was stated that there was an increase in IL-6 levels after propofol administration.

Inter-group comparison test is testing to compare data between the dexmedetomidine group and the propofol group. Test results are presented as follows.

Table 6. Inter-Group Comparison Test Results

Group	n	Mean ± SD (ng/L)	p	Note
Pre (dexmedetomidine + propofol)	24 (12+12)	12.58	0.954	Not significant
Post (dexmedetomidine + propofol)	24 (12+12)	12.42	0.954	Not significant

Note: n: number of samples; SD: standard deviation; Significance p <0.05

IL-6 level comparison results between the dexmedetomidine group and propofol group before treatment (pre) using the Mann-Whitney test obtained a significance value (p) of 0.954. A significance value above 0.05 confirmed the absence of meaningful differences within the dexmedetomidine and propofol groups at the pre-treatment stage. Additionally, IL-6 level comparison results between the dexmedetomidine group and propofol group after treatment (post) using the Mann-Whitney test obtained a significance value (p) of 0.954. Likewise, a significance value exceeds 0.05 confirmed the absence of significant differences between the dexmedetomidine and propofol groups at the post-treatment stage.

DISCUSSION

CRS Demographics

CRS is a clinical condition of persistent inflammation of the nasal mucosa and paranasal sinuses, lasting 12 weeks or more.[13] Data collected by EPOS in 2020 found a fairly high prevalence of CRS annually with 13-16% incidence each year[1], while at Dr. Soetomo Hospital, control patients at the polyclinic with CRS each year were 65.5% of all patient visits at the ENT-HNS polyclinic.[14]

Young adult age (21-40 years) was the most common age suffering from CRS undergoing FESS surgery in this study, namely 14 patients (58.3%). Different from international epidemiological studies showing a clear correlation between age and chronic rhinosinusitis prevalence. Research shows that chronic rhinosinusitis with nasal polyps is rarely diagnosed at a young age, and CRS prevalence increases sharply after age 50. A very significant finding is that patients aged 60 years and above have twice the risk of experiencing CRS compared to the 19-39 year age group.[15] Meanwhile, studies conducted at various hospitals in Indonesia show different age distribution patterns from global findings, although they still show a relationship between age and chronic rhinosinusitis incidence. Research at Royal Prima Hospital Medan shows that the largest age group affected by CRS is 20–29 years (28.4%). Meanwhile, studies at Zainoel Abidin Hospital Banda Aceh found the highest distribution in the 36–45 year age group (22.69%).[16] Investigations carried out at Dr. Mohammad Hoesin Hospital Palembang shows the highest prevalence in the 46–53 year age group (21.2%), while another study at the same hospital in a different period found the highest distribution in the 37–47 and 48–58 year age groups (21.6% each).[17] Studies at Dr. Soetomo Hospital Surabaya found the highest distribution in the age 18-55 year age group (93.48%).[18]

Women were found to be higher than men in this study with a ratio of 1:3 (75% women and 25% men). A number of prior studies have likewise found higher CRS prevalence in women. For example, research at Dr. M. Djamil Hospital Padang showed 56% female patients and 44% male patients.[19] Studies at RSPAL Dr. Ramelan Surabaya also reported a majority of female patients (76.66%) compared to male patients (23.33%).[20] Research in Medan and Banda Aceh also showed higher female proportions, namely 56.3% and 56.12% compared to males 43.8% and 43.88%.[21] Hormonal changes in women can affect the body's response to inflammation and infection, including more active immune responses compared to men, which can cause chronic inflammatory reactions to occur more frequently in the upper respiratory tract, so hormones become one of the factors causing higher CRS incidence rates in women compared to men.[22]

Changes in Interleukin 6 Levels with Dexmedetomidine Administration

Changes in IL-6 levels were found in 24 research samples. There was a statistically significant increase in IL-6 levels in the dexmedetomidine group (Wilcoxon test, p = 0.006) after intervention.

Currently, there are no studies specifically examining the effect of dexmedetomidine on IL-6 levels in patients undergoing FESS. There is a relationship between IL-6 and dexmedetomidine use in other types of surgery, as shown in the work of Munawar et al.[23] about the difference between dexmedetomidine and the combination of fentanyl and midazolam in craniotomy patients, showing that both can reduce IL-6 levels at 6 to 12 hours post-surgery which found decreased IL-6 levels. Nevertheless, both groups showed increased IL-6 levels immediately after surgery completion. The study by Munawar et al.[23] aligns closely with the present research, namely the combination of dexmedetomidine and fentanyl. However, it differs in the type of surgery. Dexmedetomidine has neuroprotective effects[24], so its use in craniotomy

surgery in his research becomes relevant.[23]

A meta-analysis by Lei et al.[25] on 1,400 patients showed that dexmedetomidine reduced IL-6 levels on the first post-surgical day, which correlated with reduced risk of cognitive dysfunction through neuroinflammation inhibition. A further study by Youssef et al.[26] evaluated the effects of intravenous dexmedetomidine infusion on 50 patients aged 18–70 years undergoing open heart surgery with cardiopulmonary bypass (CPB). Research results showed that the dexmedetomidine group experienced significant suppression of intraoperative and post-surgical IL-6 level increases (13.69 ± 1.03 pg/mL vs. 32.11 ± 0.98 pg/mL in the placebo group; P<0.0001). However, another research found increases occurred. M. Liu et al.[27] through their research comparing dexmedetomidine with midazolam in laparotomy patients, found that serum IL-6 levels 24 hours post-surgery were significantly higher in the dexmedetomidine group (45.2 pg/mL) compared to midazolam (32.1 pg/mL; $p < 0.05$). The proposed mechanism relates to α_2-adrenergic receptor activation that modulates stress responses through NF-κB and MAPK pathways differently, increasing pro-inflammatory cytokine production.

Interleukin-6 reaches peak concentrations 6–12 hours post-surgical trauma and remains elevated up to 48–72 hours, depending on the extent of tissue damage and procedure complexity.[25] Dexmedetomidine, an α2-adrenergic agonist with an elimination half-life of 2–3 hours, shows pharmacokinetic limitations in suppressing IL-6 production during the prolonged post-surgical phase.[26] Studies in craniotomy patients revealed that significant IL-6 level reduction by dexmedetomidine was only observed at 12–24 hours post-surgery ($p < 0.05$), while measurements within the first 6 hours still showed significant elevation (145.2 ± 32.1 pg/mL vs. 89.5 ± 28.7 pg/mL). This phenomenon is caused by dexmedetomidine's shorter duration of action compared to IL-6's biological half-life, so its anti-inflammatory effects do not cover the entire period of post-surgical trauma cytokine production.[23]

In other major surgical procedures such as esophagectomy, IL-6 levels in thoracic drainage fluid were reported to reach 100 times higher than peripheral serum levels, caused by IL-6 release from tissues experiencing ischemia-reperfusion and endothelial cell damage. Although clinical doses of dexmedetomidine (0.2–0.7 μg/kg/hour) show anti-inflammatory effects, their short pharmacokinetics (2–3 hour half-life) and limitations in suppressing massive IL-6 production after severe surgical trauma can reduce their efficacy in balancing cytokine outcomes.[28]

Another factor that can influence IL-6 level increases is hyperglycemia conditions. In vitro studies show that dexmedetomidine significantly inhibits interleukin-1β (IL-1β)-induced IL-6 synthesis in C6 glial cells, but is ineffective against TNF-α-mediated IL-6 production.[29] In diabetic patients, hyperglycemia increases NADPH oxidase 2 (Nox2) expression and oxidative stress, which then stimulates IL-6 production independently from α2-adrenergic pathways, so dexmedetomidine's anti-inflammatory effects become limited under severe oxidative stress conditions.[30]

IL-6 inhibition by dexmedetomidine triggers compensatory increases in IL-8 and TNF-α, which activate NF-κB to re-stimulate IL-6 production. A study combining dexmedetomidine with TLR4 antagonist (resatorvid) in cerebral ischemia models showed more effective IL-6 suppression (42.3 ± 5.1 pg/mL vs. 68.7 ± 6.9 pg/mL; $p < 0.05$) compared to monotherapy.[31] This shows alternative inflammatory pathways (TLR4/MyD88) resistant to α2-adrenergic agonists.[29]

Short duration of dexmedetomidine administration, only during surgery (1-2 hours), can be one cause of failure to reduce post-surgical IL-6 levels. Low-dose dexmedetomidine infusion (0.2–0.4 μg/kg/hour) for 24–48 hours post-surgery is recommended to maintain optimal IL-6 suppression. A study in major abdominal surgery patients showed that this regimen reduced IL-6 levels from 89.7 ± 15.2 pg/mL to 54.6 ± 12.3 pg/mL ($p < 0.001$) within 48 hours, with bradycardia risk (heart rate <50 bpm) only 4.8% compared to 18.3% at doses >0.7 μg/kg/hour.[32] Linear dexmedetomidine pharmacokinetics allows gradual accumulation to maintain stable plasma concentrations (8–12 ng/mL), needed to continuously inhibit NF-κB pathways. Infusion duration >24 hours also increases α2-adrenergic receptor availability in monocyte cell membranes, prolonging anti-inflammatory effects without increasing hypotension risk (OR = 0.7; 95% CI: 0.5–0.9).[5]

Changes in Interleukin 6 Levels with Propofol Administration

Changes in IL-6 levels were found in 24 research samples. Evidence pointed to a statistically meaningful increase in IL-6 levels in the propofol group (paired t-test, $p = 0.030$) after intervention. Until now, there is still no research specifically examining the effect of propofol on Interleukin-6 (IL-6) levels in patients undergoing FESS surgery. However, there is research examining propofol's effects on IL-6 level changes in patients undergoing craniotomy. The findings reported by Priambodo et al.[33] explored the comparative influence of propofol and sevoflurane on IL-6 levels and neutrophil counts

in patients undergoing craniotomy procedures. This study was experimental research with a randomized controlled approach on two patient groups receiving anesthesia with propofol or sevoflurane respectively. The outcomes suggested that IL-6 levels increased in both groups post-surgery, but this increase was more significant in the propofol group compared to the sevoflurane group. The evidence lends support to the notion that propofol can trigger higher systemic inflammatory responses compared to sevoflurane in neurosurgery contexts.[33] This is similar to our research findings that the propofol group experienced increased IL-6 levels after FESS surgery.

Propofol's effects on post-surgical IL-6 levels vary depending on the type of surgical procedure, surgery duration, and patient immune response.[34] The largest meta-analysis (n=1,611 patients) showed that propofol significantly reduced systemic IL-6 levels in breast cancer surgery (SMD = -3.09; 95% CI: -5.70 to -0.48; p = 0.021) compared to inhalation anesthesia.[35]

Another inquiries uncover that propofol inhibited IL-6 expression up to 3.09 pg/mL (p = 0.021) in HER2-positive breast cancer cells by suppressing NF-κB pathways and increasing miR-149-5p expression, which targets the IL-6 gene epigenetically.[36] This mechanism reduced cancer cell proliferation by 40% (p < 0.001) and inhibited mammosphere formation, a metastasis potential indicator. In a retrospective clinical with n = 2,645, breast cancer patients receiving Total Intravenous Anesthesia (TIVA) with propofol had 10% higher 2-year recurrence-free survival (RR = 1.10; 95% CI: 1.00–1.20) compared to inhalation anesthesia.[37] Propofol also reduced vascular endothelial growth factor (VEGF) levels up to 30% (p < 0.05) by inhibiting cyclooxygenase-2 (COX-2) activity, thus reducing angiogenesis and tumor cell invasion. These antitumor effects were consistently observed in colorectal and hepatocellular cancer surgeries, where propofol reduced systemic IL-6 by 58% (p = 0.003) and reduced post-surgical metastasis incidence by 22% (OR = 0.78; 95% CI: 0.65–0.94). This recommendation is supported by a meta-analysis conducted by Lee with n = 1,611 concluding that propofol increases overall survival in cancer patients (HR = 0.82; 95% CI: 0.75–0.90) compared to volatile anesthesia.[34] All these findings support propofol's role in suppressing IL-6 inflammatory factors.[34]

Fekkes et al. conducted prospective observational studies on 28 patients undergoing abdominal hysterectomy (n=14) or vulvectomy (n=14) to evaluate the relationship between intravenous propofol administration and perioperative interleukin-6 (IL-6) levels.[38] Research results showed significant differences in post-surgical IL-6 concentrations between both groups: IL-6 levels at surgery completion were statistically higher in the hysterectomy group. In their research, they concluded that inflammatory responses measured through IL-6 were more influenced by procedure invasiveness (shown by significant differences between hysterectomy and vulvectomy) and surgery duration, not by propofol anesthetic regimens.[38] This shows significant positive correlation between surgery duration and post-surgical interleukin-6 (IL-6) level increases, with correlation coefficients r = 0.554–0.773 (p < 0.01). Propofol's anti-inflammatory effects become more significant in surgical procedures >2 hours through mechanisms inhibiting IL-6 mRNA expression and Nrf2 pathway activation, which requires longer exposure time to achieve optimal therapeutic effects.[38]

A prospective double-blind study by Roh et al. on 50 patients undergoing robot-assisted laparoscopic radical prostatectomy (RALRP) found that the propofol group (n=25) showed significantly lower IL-6 level increases during and after pneumoperitoneum compared to the desflurane group (n=25).[39] Serum IL-6 measurements were performed at 10 minutes after anesthesia induction (T1), 100 minutes after CO2 insufflation (T2), and 10 minutes after CO2 deflation (T3). Results showed IL-6 increases of 38.6 pg/mL in the desflurane group versus 14.56 pg/mL in the propofol group (p<0.05) at T3, with significantly higher intraoperative urine output ratios in the propofol group (0.9±0.3 vs 0.6±0.2 mL/kg/hour; p<0.01). This study concluded that IL-6 will still increase with propofol use, but propofol selectively suppresses inflammatory responses through mechanisms inhibiting IL-6 production by macrophages and regulating intracellular calcium signaling pathways, without affecting other inflammatory parameters such as TNF-α or CRP.[39]

A prospective randomized double-blind study by Lleshi et al. on 40 breast surgery patients showed that the Target Control Infusion-Total Intravenous Anesthesia (TCI-TIVA) group experienced significantly lower interleukin-6 (IL-6) level increases 24 hours post-surgery (14.56 pg/mL) compared to the Sevoflurane Inhalation Anesthesia (SIA) group (36.34 pg/mL; p < 0.05).[40] IL-6 measurements were performed at four times: before induction (T0), during surgery (T1-T2), and 24 hours post-surgery (T3), with statistical analysis using paired t-tests and repeated ANOVA. Researchers associated this difference with propofol's anti-inflammatory effects in TCI-TIVA that inhibit cortisol release and pro-inflammatory cytokine production through pre-translational suppression

mechanisms, while sevoflurane inhalation anesthesia potentially triggers stress responses and systemic inflammation through NF-κB pathway activation.[40]

Different from several other studies, high post-surgical IL-6 levels were found to correlate with factors such as surgical procedure length and intraoperative bleeding volume. A study by Rettig et al. evaluated changes in IL-6 levels in patients undergoing major gastrointestinal surgery.[32] This research showed that IL-6 levels increased significantly within the first six hours after surgery and peaked within 24 hours. This study concluded that IL-6 can be used as a sensitive biomarker to assess surgical stress levels and post-surgical inflammatory responses, and potentially predict complication risks.[32]

Based on this analysis, dexmedetomidine has the potential to reduce inflammation levels 24 hours post-surgery. However, IL-6 levels will still increase in the first 6 hours. Dexmedetomidine's effects on IL-6 levels are influenced by dexmedetomidine's shorter duration of action compared to IL-6's biological half-life and the time of peak IL-6 release into systemic circulation. Additionally, surgery duration also determines IL-6 level changes. Short duration of dexmedetomidine exposure causes failure in reducing post-surgical IL-6 levels. Similarly, with propofol, this drug has the potential to reduce post-surgical IL-6 levels in several types of surgical procedures, although its effects are not consistent in all clinical conditions. Propofol's effects on IL-6 levels can be influenced by various factors such as surgery type, surgical duration, administration timing, dose, and individual patient factors. Long surgical duration will cause exposure to surgical stress and extensive trauma areas that can affect IL-6 level changes. Similarly with long propofol exposure duration, in relatively short surgery duration, patient exposure to propofol is also lower, which can cause IL-6 level increases.

Comparison of Dexmedetomidine with Propofol on Interleukin 6 Level Changes

In this research, no meaningful variation was detected in IL-6 level changes between the dexmedetomidine and propofol groups. When inter-group comparisons were performed, both groups showed IL-6 level changes before and after intervention that were not statistically different. This is similar to research conducted by Munawar et al. comparing the effects of dexmedetomidine with propofol on interleukin-6 (IL-6) levels in critical patients, the findings did not differ significantly in IL-6 level reduction after 24 hours of both drug administration.[23] Nevertheless, dexmedetomidine tended to provide additional benefits in the form of reduced mechanical ventilation duration and ICU stay length.[23] The limitations of this research include the absence of a control group, as the study only examined treatment drug groups. As such, it is not possible to determine whether one drug or both are effective in reducing or suppressing the production of interleukin-6 levels. In addition, the sampling was limited to only two time points, which prevents a comprehensive description of the interleukin-6 level reduction process under single-drug treatment.

CONCLUSION

Changes in IL-6 levels were observed in chronic rhinosinusitis (CRS) patients before and after functional endoscopic sinus surgery (FESS) with the use of either dexmedetomidine or propofol. However, no notable difference in IL-6 levels was found among the two anesthetic agents in CRS patients undergoing FESS. Both dexmedetomidine and propofol may be considered suitable agents for controlled hypotension in FESS procedures. Further research is recommended to examine the economic impact of using these agents in such surgical settings.

DECLARATIONS

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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ORIGINAL ARTICALE

EFFECTIVENESS OF EXTRA VIRGIN COLD PRESSED COCONUT OIL WITH PEPPERMINT ESSENTIAL OIL AS A NATURAL ORAL HYGIENE CLEANER ON *SALIVARY STREPTOCOCCUS MUTANS* LEVELS: A RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Background: This study aimed to assess the effectiveness of extra virgin coconut oil combined with peppermint essential oil for pulling and brushing teeth with oil to reduce new carious lesions, salivary *Streptococcus mutans* levels, and plaque accumulation in high-risk patients with caries compared with conventional toothpaste.

Materials and Methods: A study was conducted on 40 high-risk patients, with Group C1 using the Coco Pull blend for oral care and Group C2 using fluoride toothpaste and chlorhexidine mouthwash. Caries risk was assessed via Cariogram software, and salivary profiles were measured. a caries risk assessment was performed at baseline (T0), one month (T1), and three months (T2) to determine the change in the percentage of actual chances of avoiding new lesions.

Results: This study revealed substantial antimicrobial efficacy in both groups, with the Coco Pull blend demonstrating superior results ($p<0.001$), as evidenced by notable differences in the green, red, and light-blue sectors of the Cariogram at various intervals.

Conclusion: Extra virgin coconut oil with essential peppermint oil, when used for oil pulling and tooth brushing, was effective as a natural cleaning agent for oral hygiene in reducing salivary *Streptococcus mutans* levels, dental caries, and plaque accumulation in patients at high risk for caries.

Keywords*:* Coconut oil, Peppermint essential oil, Tooth brushing, Oil pulling, Streptococcus mutans.

INTRODUCTION

Oral health plays a crucial role in overall well-being, as the mouth harbors billions of microorganisms, some of which can contribute to systemic diseases like cardiovascular disease and diabetes. A delicate balance exists between the host and its oral microbiome, influenced by factors such as diet, hygiene, and immune response. When this balance is disrupted, harmful bacteria can thrive, leading to conditions like dental caries. Maintaining good oral hygiene is essential to preventing dysbiosis and supporting general health. [1,2]

A holistic approach is essential for understanding dental caries, as multiple factors contribute to its development. [3] The Cariogram, an interactive educational tool, visually represents caries risk by displaying the probability of avoiding new cavities and the influence of various contributing factors.

It uses a pie chart with five colored segments to illustrate these interactions. *Streptococcus mutans*, a key bacterial species in caries formation, exhibits genetic diversity affecting its virulence.

Its ability to produce acid, tolerate acidic environments, and adhere to surfaces plays a crucial role in caries progression. Inhibiting its acid production is vital for prevention. [4,5]

Managing dental caries effectively requires assessing individual risk and adapting treatment plans accordingly.

Regular monitoring is essential to track changes in oral health over time.

The primary method of plaque removal is brushing with toothpaste, but many oral hygiene products lack rigorous risk assessments, potentially exposing users to harmful ingredients that could cause local or systemic adverse effects.[6]

Fluoride, sodium lauryl sulfate (SLS), and triclosan have been linked to various oral health issues, including mucosal irritation and allergic reactions. While fluoride is an effective cariostatic agent, excessive use can cause fluorosis, posing public health concerns. This has driven the search for alternative agents with fewer side effects. Natural products, with their broad biological activities and favorable safety profiles, have gained attention as potential cariostatic agents. Their accessibility, affordability, and biocompatibility make them promising alternatives, especially in regions where conventional treatments are less effective. [7]

Ayurvedic medicine, a 3,000-year-old holistic health system, emphasizes prevention and balance between mind, body, and spirit. Practices like oil pulling are believed to detoxify the body by eliminating toxins through the tongue. The coconut tree, known as the "tree of life," provides valuable resources, with virgin coconut oil (VCO) offering greater health benefits than refined copra oil. Essential oils, such as peppermint, have long been used for oral health, with menthol providing antimicrobial and pain-relieving properties. [8]

Randomized clinical trials are ideal for study design, but evidence on the efficacy of extra-virgin cold-pressed coconut oil with peppermint essential oil in oral hygiene remains limited. This trial evaluated their impact on salivary *Streptococcus mutans* levels in high-caries-risk patients compared to conventional fluoride toothpaste and chlorhexidine mouthwash, testing the null hypothesis that the natural regimen would not influence caries risk.

MATERIALS AND METHODS

1. Materials

Dental hygiene products utilized in this study

Three categories of dental hygiene products were used, which were further classified into two groups:

- Coco Pull a healthy blend of organic oil (as a mouthwash by oil pulling and dental cleaning agent by brushing with oil).
- Fluoride toothpaste (Colgate Total, 1450 ppm) and chlorhexidine (hexitol) mouthwash were used (CHX) (Table 1).

2. Methods:

2.1 Trial Registration and Study Design.

2.2 Trial Registration

The protocol for this study was registered in the protocol registration and results system database (www.clinicaltrials.gov) under the identification number (NCT05803109) on 07/04/2023. The research procedures involving human subjects adhered to the ethical standards set by the Research Ethics Committee of the Faculty of Dentistry, Cairo University (Approval no. 4722), and it followed the Declaration of Helsinki and its subsequent amendments.

2.2 Informed consent

Before the clinical trial, patients were thoroughly briefed on the study's objectives, methods, safety measures, potential benefits, and duration. They engaged in informed discussions with the researcher, and consent was obtained from all participants, approved by the Research Ethics Committee (REC) of Cairo University's Faculty of Dentistry.

2.4 Sample Size Calculation

On the basis of a previous study by Fouad et al. (2022) [9], subjects per group were required to detect a true difference of five between the experimental and control means with 80% power and a Type I error probability of 0.05. To account for potential attrition, the sample size was increased by 20%, resulting in a total of 40 patients (20 per group). Calculations were conducted via PS power and sample size calculations (version 3.1.6) for Windows.

2.5 Study Setting

This double-blind, parallel-arm, randomized controlled trial was conducted at the Conservative Dentistry Department outpatient clinic, Faculty of Dentistry, Cairo University, from January to December 2023, with patient recruitment from January to July 2023**.**

2.6 Eligibility criteria

Inclusion criteria

Age: 20–50 years, high caries risk assessment, nonsmoking, no antibiotic therapy during the study or in the preceding month, both male and female participants, and regular oral hygiene practices.

Exclusion criteria

A compromised medical history, low caries risk assessment, severe or active periodontal disease, hypersensitivity to study drugs or chemicals, antibiotic use within the past month, tobacco use, and significantly reduced salivary flow (xerostomia < 0.5 ml/min, score 3 on the cariogram were reported).

2.7Allocation:

2.7.1Sequence generation:

An external contributor used the Random Sequence Generator from Randomness and Integrity Services Ltd. to assign numbers (1–20) to either the intervention or the comparator in the study.

2.7.2 Allocation concealment:

The assigned random numbers were stored in a sealed, opaque envelope, and the contributor did not participate in later trial stages. The operator and co-supervisor recorded the randomisation outcomes digitally, with all records maintained by the main supervisors.

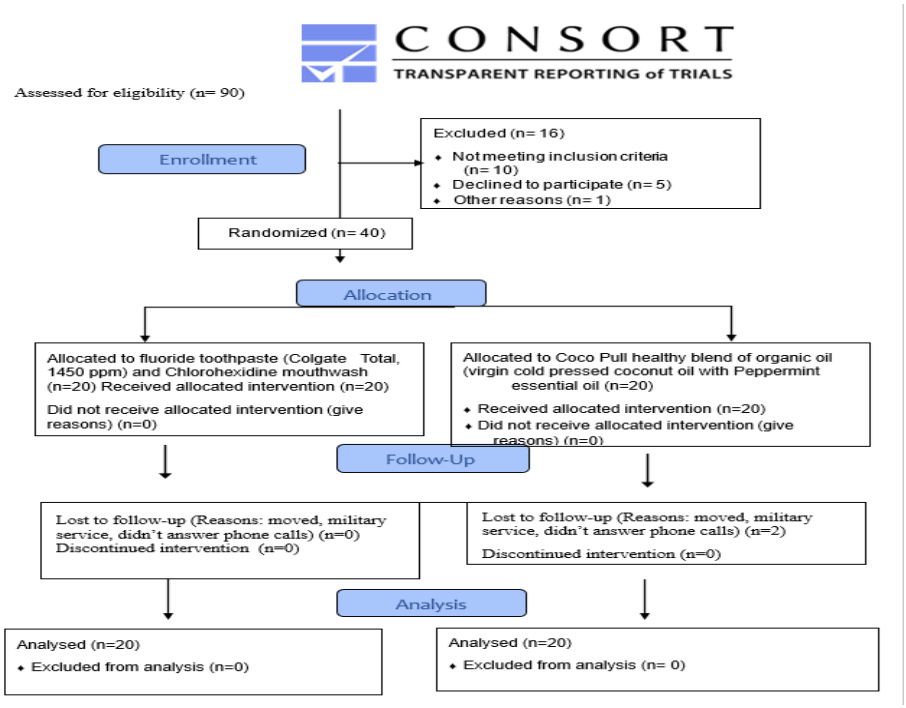


Figure 1. CONSORT 2010 Flow Diagram

2.8 Interventions

Intervention Group C1.

Patients were instructed to use a packet of the Coco Pull healthy blend of organic oil, which is a mixture of Virgin Cold-Pressed Coconut Oil and Peppermint Essential Oil (AVIVA-PURE-CocoPull-Organic in the USA). They were instructed to swish this oil in their mouth, pull it between their teeth for five minutes, and then spit out the oil. The participants were subsequently instructed to brush their teeth with the same oil for two minutes. This routine was repeated twice daily for three months. (Table 1)

Table 1. Tooth cleaning agents used in this trial, categorization, active ingredients, manufacturers and lot numbers

Teeth cleaning products	Category	Active Ingredients	Manufacturer and Lot number
Coco Pull healthy blend of organic oil	Ayurvedic, Natural product	virgin cold-pressed coconut oil with Peppermint essential	(AVIVA-PURE-CocoPull-Organic- made in USA) Xooo VMGWFP
Fluoride toothpaste (Colgat Total, 1450 ppm)	Synthetic chemical compound	Glycerin, Water, Hydrated Silica, Sodium Lauryl Sulfate, Arginine, Flavor, Zinc Oxide, Cellulose Gum, CI 77891, Poloxamer 407, Tetrasodium Pyrophosphate, Zinc Citrate, Benzyl Alcohol, Xanthan Gum, Cocamidopropyl Betaine, Sodium Fluoride, Sodium Saccharin, Phosphoric Acid, Sucralose	Colgate Palmolive China Co Ltd. 338 Qing Nian Road China
Chlorohexidine mouthwash (Hexitol)	Synthetic chemical compound	Chlorohexidine Hydrochloride	Arab Drug Company "ADCO" for pharmaceutical and chemical industries, Cairo, Egypt LOT #: 930626

Comparator Group C2.

Patients were guided to clean their teeth via fluoride toothpaste (Colgate Total, 1450 ppm) for 2 min. This routine was followed twice daily for three months. Additionally, they were advised to rinse with 10 ml of 0.12% chlorhexidine for 1 minute each day,30 minutes after brushing their teeth, right before bedtime, and only one week per month [9](Table 1).

2.9 Follow-up strategy

Over three months, patients provided saliva samples at baseline (T0) and at one-month (T1) and two-month (T2) intervals for microbiological analysis and caries risk assessment via Cariogram software. (Fig. 2A, 2 B) Patients were divided into two groups based on their oral hygiene regimen: the intervention group used oil pulling followed by brushing with oil, while the control group used fluoride toothpaste and chlorhexidine mouthwash. Both groups followed identical oral hygiene instructions using the modified Bass technique with medium-hardness toothbrushes.

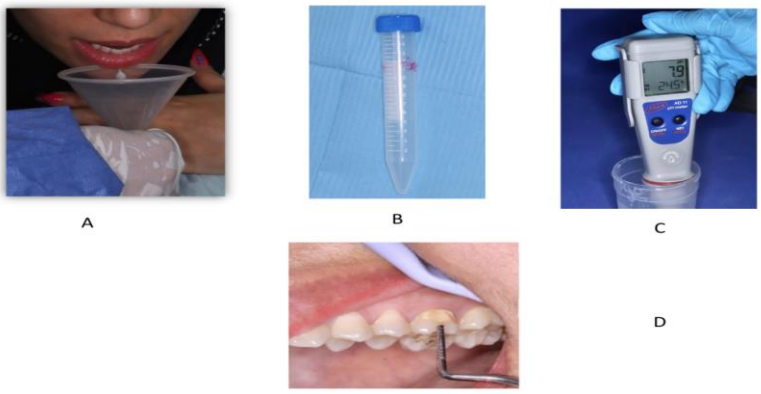


Figure 2.A,B,C Microbiological analysis and caries risk assessment via Cariogram software.D.Measure the plaque index

Participants were guided to maintain a noncariogenic diet, reducing sugar intake to below 10% of total dietary energy. They avoided sugary foods, particularly at bedtime, and refrained from using oral hygiene products from other suppliers. Regular assessments monitored changes in caries risk throughout the study.

2.10 Outcome assessment

2.10.1 Cariogram (chance to avoid new lesions) Green sector.

At each of the three visits, participants' caries risk profiles were assessed via Cariogram software (Cariogram, internet Version 2.01. April 2, 2004, Copyright: D. Bratthall, Sweden). At baseline, ten caries-related factors were entered into the software for each group: (1) caries history; (2) related health conditions (immunologic diseases, endocrinopathies, hematologic conditions, systemic infections, diabetes mellitus, and heart disease); (3) diet content; (4) meal frequency; (5) *Streptococcus mutans levels*; (6) plaque volume; (7) fluoride treatment; (8) saliva buffering capacity; (9) saliva production rate; and (10) clinical assessment. These factors determine the probability of caries prevention in the future. The region was classified as low risk because of Egypt's water fluoridation program.

2.10.2 Bacterial colonies were counted, and the plaque index was measured to assess the cariogram (bacteria) Red sector.

Inoculation of saliva samples.

One milliliter of collected saliva was diluted tenfold with normal saline. A total of 25 µL of the diluted sample was applied to a freshly prepared M. salivarius agar plate via an automatic micropipette. The sample was transferred from the test tube to the agar medium and evenly distributed across the agar surface with a sterile glass rod to ensure uniform bacterial growth and a smooth surface, avoiding scratches or indentations [10].

A microaerophilic environment with a 5–10% CO2 concentration was created via a candle jar for the agar plates, which were then incubated at 37°C for 48 h. Subsequently, the jar was sealed and placed in a precision dual-illumination incubator (Germany). After a 48-h incubation, the plates were removed from the incubator. An examiner blinded to the treatment details of the 40 patients counted *S. mutans* colonies.

The total colony-forming units (CFUs) were calculated for each salivary sample corresponding to each mouthwash. *S. mutans* colonies typically exhibit characteristics such as 0.5 mm raised, convex, and undulated colonies that are light blue with rough margins and a granular frosted glass appearance. Colonies were quantified as CFUs per millilitre [10].

The Silness and Loe scale was used to measure the plaque index of six specific teeth by evaluating the amount of plaque in the cervical region. (Fig. 2D)

In this study, dietary content and frequency were assessed with a score of 1 in accordance with the study's inclusion criteria. Fluoride intake was quantified on the basis of the fluoride supplements consumed by each group.

All participants in the study received a score of three for the "caries experience" factor, indicating a more severe status than typical for that age group. The "clinical judgment" factor was assigned a score of 1 for all participants to mitigate potential bias. Additionally, the "related diseases" factor was scored zero, indicating that none of the participants exhibited any major general diseases associated with dental caries, according to the inclusion criteria, and all represented the assessment of the cariogram (circumstances): Yellow sector.

2.10.3 Buffering capacity and salivary secretion rate measurement to assess the cariogram (susceptibility) Light blue sector

The buffer capacity of unstimulated saliva samples was assessed via the Ericsson method (1959). In this method, 3 ml of 5 mmol/L HCl was added to 1 ml of stimulated saliva, and the mixture was stirred thoroughly. The sample was then left to stand for 10 minutes. The final pH was subsequently measured via a calibrated Adwa (AD-11) digital pH meter (Adwa Hungary Kft, Szeged, Hungary). (Fig. 2C) [11] The scoring was as follows: 0 = adequate/normal buffer capacity, saliva pH > 6; 1 = reduced buffer capacity, saliva pH 4.5–5.5; 2 = low buffer capacity, saliva pH < 4.0.

The salivary secretion rate of stimulated saliva was categorized as follows: normal (0), 0.9–1.1 mL/min (1), and 0.5–0.9 mL/min (2). Rates less than 0.5 mL/min, which is indicative of xerostomia, were excluded from this study.

All the collected data were subsequently analyzed via a standardized procedure in the Cariogram program. These data were then input into the program to generate a pie chart. The software produces a pie chart that illustrates the percentages of "Bacteria" (depicted in red), "Diet" (dark blue), "Circumstances" (yellow), and "Susceptibility" (light blue). These four sectors collectively determine the percentage of the "probability of avoiding caries' (green sector). The magnitude of the green sector was inversely proportional to the risk of caries, indicating superior oral hygiene and dental health.

2.11 Statistical analysis

The data were analyzed using MedCalc software version 22, assessing normality via the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous data were normally distributed and presented as means and standard deviations. Intergroup comparisons used an independent t-test (**p** ≤ 0.05), while intragroup comparisons applied repeated measures ANOVA (**p** ≤ 0.016 for follow-up periods, **p** ≤ 0.005 for *S. mutans* acidogenic assay after Bonferroni correction). Categorical data were analyzed using chi-square tests, with intergroup significance set at **p** ≤ 0.05 and intragroup significance at **p** ≤ 0.016. All tests were two-tailed, with an 80% study power and a 95% confidence level.

RESULTS

Cariogram (chance to avoid new lesions): Green sector

Intergroup comparisons revealed no statistically significant difference at baseline (p = 0.7612), whereas after 1 and 3 months, there was a statistically significant difference (p < 0.0001). Intragroup comparisons within C1 and C2 revealed statistically significant differences between the different follow-up periods (P < 0.001) (Table 2 and Fig 3).

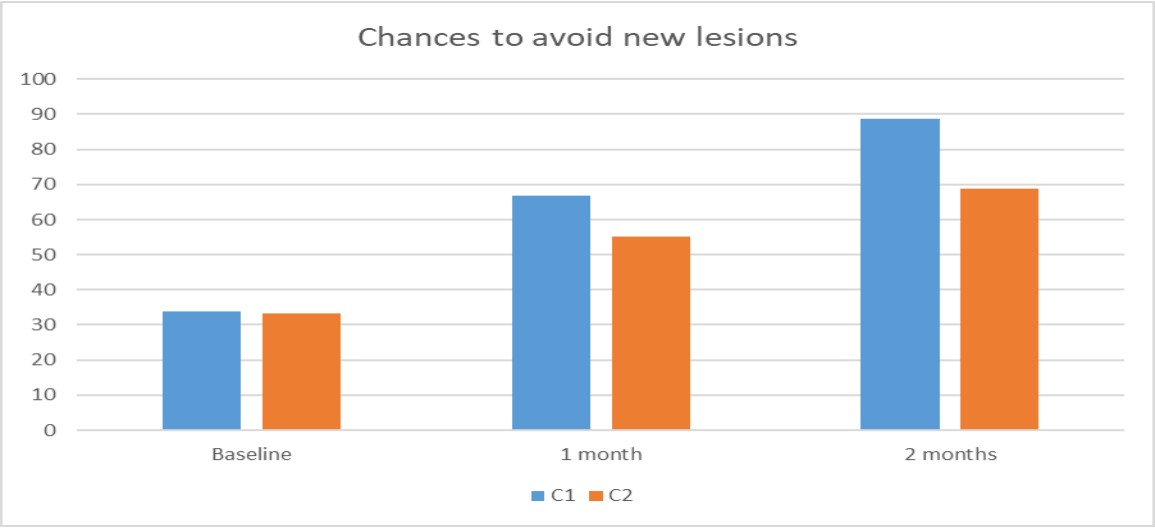


Figure 3. Bar chart showing the effect of the intervention on the percentage of chances of avoiding new lesions in the green sector at each follow-up

Table 2. Means and standard deviations of the cariogram sectors of the two groups and comparisons between them (also a comparison between different follow-up periods of all groups)

	C1		C2		
	Mean	SD	Mean	SD	P value
Green sector					
Baseline	33.85[c]	6.43	33.20[c]	6.99	P = 0.7612
1 month	66.80[b]	4.21	55.28[b]	4.01	P < 0.0001*
3 months	80.70[a]	5.42	68.94[a]	4.60	P < 0.0001*
P value	P<0.001*		P<0.001*		
Red Sector					
Baseline	22.25[a]	3.86	24.25[a]	3.13	P = 0.0798
1 month	8.25[b]	0.44	8.28[b]	0.57	P = 0.8532
3 months	2.55[c]	1.19	2.65[c]	0.93	P = 0.7688
P value	P<0.001*		P<0.001*		
Light blue sector					
Baseline	25.10[a]	3.35	22.95[a]	4.05	P = 0.0752
1 month	9.20[b]	2.26	17.44[b]	2.91	P < 0.0001*
3 months	6.50[c]	2.56	13.53[c]	2.94	P < 0.0001*
P value	P<0.001*		P<0.001*		
Yellow Sector					
Baseline	9.60	1.57	10.00	2.64	P = 0.5637
1 month	9.90	1.41	9.61	1.69	P = 0.5592
3 months	10.35	2.21	9.65	1.73	P = 0.2717
P value	P = 0.399		P = 0.845		

	C1		C2		
	Mean	SD	Mean	SD	P value
Green sector					
Baseline	33.85[c]	6.43	33.20[c]	6.99	P = 0.7612
1 month	66.80[b]	4.21	55.28[b]	4.01	P < 0.0001*
3 months	80.70[a]	5.42	68.94[a]	4.60	P < 0.0001*
P value	P<0.001*		P<0.001*		
Red Sector					
Baseline	22.25[a]	3.86	24.25[a]	3.13	P = 0.0798
1 month	8.25[b]	0.44	8.28[b]	0.57	P = 0.8532
3 months	2.55[c]	1.19	2.65[c]	0.93	P = 0.7688

*means that those that do not share a letter vertically are significantly different; * corresponds to a statistically significant difference*

Cariogram (bacteria): Red sector

Intergroup comparisons revealed no statistically significant differences at baseline or at 1 and 3 months (P > 0.05). Intragroup comparisons within C1 and C2 revealed statistically significant differences between the different follow-up periods (P < 0.001) (Table 2).

Cariogram (susceptibility): Light blue sector

Intergroup comparisons revealed no statistically significant difference at baseline (p = 0.0752), whereas after 1 and 3 months, there was a statistically significant difference (P < 0.0001). Intragroup comparisons within C1 and C2 revealed statistically significant differences between the different follow-up periods (P < 0.001) (Table 2).

Cariogram (circumstances): Yellow sector.

Intergroup comparisons revealed no statistically significant differences at baseline or at 1 and 3months (P > 0.05). Intragroup comparisons within C1 and C2 revealed no statistically significant differences between the different follow-up periods (P > 0.016) (Table 2).

DISCUSSION

Despite modern healthcare advancements, the precise cause of dental caries remains uncertain. However, it is widely accepted that dysbiotic changes in the oral biofilm, influenced by fermentable sugars and carbohydrates, contribute to its development. Prevention relies on daily plaque removal through brushing, flossing, and rinsing, with fluoridated toothpaste being the most common method. While oral care products often contain antimicrobials like chlorhexidine and fluoride, these

agents struggle to effectively combat *Streptococcus mutans* due to its complex biological pathways. Fluoride, in particular, does not alter biofilm composition or bacterial virulence [12,13].

Even with regular fluoride use, excessive sugar intake—more than six times daily—can lead to cavities. Prolonged exposure to high concentrations of chlorhexidine (CHX) and fluoride (1000–2000 µg/ml) poses risks, including fluorosis, weakened bones, and developmental neurotoxicity [14].

Virgin coconut oil (VCO) is extracted from fresh coconut kernels without heat or chemical refining, preserving antioxidants, vitamins, and polyphenols. It contains lauric acid (LA), which converts to monolaurin in the body, enhancing its antimicrobial effects. Medium-chain fatty acids and monoglycerides in VCO disrupt bacterial membranes, making it effective against various microbes.[15]

Essential oils, valued for their aroma, include phytoncides—natural plant compounds that protect against pathogens. These volatile substances exhibit antimicrobial, antibacterial, antifungal, anti-inflammatory, stress-relieving, and analgesic properties [16]

This study incorporated peppermint essential oil into virgin coconut oil (VCO), utilizing its antioxidants to prevent rancidity and enhance quality. VCO serves as a carrier oil, reducing cytotoxicity, potentially boosting antimicrobial effects, and providing a refreshing taste and aroma. Oil pulling with VCO helps reduce plaque and gingival inflammation, while coconut derivatives like coconut milk and water may support enamel remineralization due to their high calcium bioavailability. [17,18]

Participants used Coco Pull, an organic blend of virgin cold-pressed coconut oil and peppermint essential oil, by swishing it for five minutes, pulling it between their teeth, and brushing with it for two minutes. The control group followed a conventional regimen with fluoride toothpaste (Colgate Total, 1450 ppm) and 0.12% chlorhexidine rinse, used 30 minutes after brushing to minimize interactions with dentifrice ingredients like MFP and SLS. This protocol served as a comparator, given its established broad-spectrum antimicrobial efficacy, fluoride's role in remineralization, and its lack of systemic adverse effects.

Participants received standardized oral hygiene instructions and medium-hard toothbrushes (Colgate Classic Deep Clean). They followed a modified Bass brushing technique for two minutes, supported by a demonstration video to ensure consistency. To minimize confounding factors, they adhered to a noncariogenic diet by reducing daily sugar intake in both quantity and frequency throughout the three-month study.

This study used the Cariogram to assess caries risk by visually representing an individual's risk based on etiological factors. It categorized patients into low-, moderate-, or high-risk groups, enabling tailored prevention strategies. Key Cariogram sectors showed significant differences between and within groups over time, with the Coco-Pull blend (oil pulling and brushing with oil) demonstrating superior efficacy ($P<0.001$). [19]

The red sector, reflecting bacterial activity, was assessed using bacterial count and plaque index scores. In the control group using fluoride toothpaste and chlorhexidine, a significant reduction was observed over baseline, one-month, and three-month intervals, indicating a decline in *Streptococcus mutans* levels and plaque accumulation [19].

The reduction in bacterial activity is due to fluoride in toothpaste and chlorhexidine (CHX). Combining mechanical and chemical oral hygiene methods is highly effective—mechanical cleaning removes most plaque, leaving a thin, disorganized layer that can be further diminished with chemical agents [20].

Chlorhexidine (CHX) has been shown to have effective antiplaque activity owing to its dual binding to bacterial cell membranes and salivary components. Several studies have examined the effects of chlorhexidine mouthwash on plaque levels [9].

Fouad et al.[9] found that chlorhexidine (CHX) and fluoride toothpaste significantly reduced plaque scores. CHX has broad-spectrum antibacterial properties, acting as a bacteriostatic agent at low concentrations by increasing membrane permeability, and as a bactericidal agent at higher concentrations by precipitating cytoplasmic proteins. Sodium fluoride (NaF) disrupts key enzymes in *Streptococcus mutans*, inhibiting its metabolic processes.[21]

In the intervention group, the Coco Pull blend of virgin cold-pressed coconut oil and peppermint essential oil significantly reduced *Streptococcus mutans* levels and plaque index scores over baseline, one-month, and three-month intervals. These results align with in vivo studies by Raju et al. (2024) [22] and Peedikayil et al. (2015) [23], which observed similar reductions following oil pulling.

Supporting in vitro studies by Ng et al. (2024)[23] and Desam et al. (2019) [25]further demonstrated the antimicrobial activity of VCO and peppermint EO against *S. mutans* biofilms, likely due to their synergistic antibacterial properties.

Virgin coconut oil (VCO) combats bacteria due to its high lauric acid content, which disrupts bacterial cell membranes, leading to cell death. Peppermint essential oil (EO) enhances this effect with antimicrobial, anti-inflammatory, and stress-relieving properties. The Coco-Pull group showed a significant plaque reduction, attributed to oil pulling and mechanical brushing, which emulsify the oil and reduce bacterial coaggregation. [26]

VCO also undergoes saponification in the mouth, forming a soap-like substance that minimizes plaque adhesion(Fig. 5b), offering an alternative to sodium lauryl sulfate (SLS), which can cause contact dermatitis.[26,27]The light blue Cariogram sector, reflecting saliva-related factors, showed improvement in both groups, with the Coco-Pull group demonstrating higher saliva secretion rates, likely due to VCO's polyphenols and peppermint EO's antioxidant effects.

Additionally, peppermint EO aromatherapy reduces sympathetic nervous system activity and salivary cortisol, further enhancing saliva production. This aligns with a review by Kontogiannopoulos et al. (2023)[28], which highlighted natural compounds' ability to alleviate salivary dysfunction through various molecular pathways.

Prolonged chlorhexidine (CHX) use can lead to adverse effects, including calculus buildup, tooth stains, xerostomia, taste disruption, and, in rarer cases, oral paresthesia and mucosal desquamation.[29] This contributed to lower salivary secretion rates in the fluoride toothpaste and CHX group. Regarding salivary pH, the Coco-Coco-Pull group exhibited a higher pH after two months. CHX may alter the oral microbiome, reducing bacterial diversity and increasing Firmicutes while decreasing Bacteroidetes, ultimately leading to saliva acidification. [29] The yellow sector, representing past caries experience and systemic diseases, remained unchanged across all participants to ensure standardization and minimize confounding factors. No significant differences were observed in this sector for either group over time.

CONCLUSIONS

Within the limitations of the present study, the following conclusions were drawn.

1. Extra virgin coconut oil combined with essential peppermint oil, which is utilized through oil pulling and tooth brushing, is effective as a natural cleansing agent for routine oral hygiene. This approach effectively reduces salivary *Streptococcus mutans* levels, dental caries, and plaque accumulation in high-caries-risk patients, presenting minimal adverse effects as an alternative to current synthetic preventive measures.

Limitations of the study:

Further scientific studies are needed

DECLARATIONS

Data availability

The corresponding author (asmaa.reda@dentistry.cu.edu.e.g.)can provide access to the datasets utilized or examined in this study upon a reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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ORIGINAL RESEARCH

THE DIFFERENCES IN SALIVARY SECRETORY IMUNOGLOBULIN A (SIGA) LEVELS BEFORE AND AFTER CONSUMPTION OF LACTOBACILLUS REUTERI PROBIOTICS IN CHILDREN WITH THALASSEMIA MAJOR EXPERIENCING GINGIVITIS

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ABSTRACT

Thalassemia is an inherited blood disorder caused by genetic mutations that prevent the body from producing normal haemoglobin. A common oral manifestation in patients with thalassemia is a high incidence of gingivitis, caused by iron overload and a decreased immune response to infection. A decrease in salivary sIgA levels can increase the risk of periodontal tissue infection. Probiotics can stimulate the immune system, thereby increasing sIgA production. Evaluate the differences in salivary sIgA levels before and after Lactobacillus reuteri probiotic consumption in children with thalassemia major. The study was conducted in the Blood Transfusion Room at Dr. Cipto Mangunkusumo General Hospital (RSUPN Dr. Cipto Mangunkusumo), Jakarta, Indonesia. This research employed an experimental test design. This research involved 16 children aged 6–12 years diagnosed with thalassemia major with gingivitis. The study commenced with unstimulated saliva sampling before probiotic administration. After 14 days of probiotic consumption, unstimulated saliva was collected again. The sIgA levels in the saliva samples were quantitatively assessed by the enzyme-linked immunosorbent assay (ELISA) method. Statistical analysis used: Statistical analysis was performed using a paired t-test. The study showed that the mean salivary sIgA level before probiotic consumption was 0.97 ± 0.54, and the mean after was 1.31 ± 0.73. Paired t-test results yielded a p-value of 0.100 (>0.05), indicating no statistically significant difference. Fourteen days of Lactobacillus reuteri probiotic consumption increased salivary sIgA levels in children diagnosed with Thalassemia major with gingivitis, though the increase was not statistically significant.

Keywords: Thalassemia major; Gingivitis; Lactobacillus reuteri; sIgA.

INTRODUCTION

In thalassemia there is a defect in the polypeptide chain that makes up the globin molecule in haemoglobin.[1] Haemoglobin is the oxygen-carrying component of red blood cells. This abnormality makes red blood cells easily damaged, resulting in anaemia. The World Health Organization (WHO) estimates that about 7% of the world's population are carriers of the Thalassaemia trait. Every year around 300,000 - 500,000 newborns are born with severe haemoglobin disorders, and 50,000 to 100,000 children die from beta-thalassaemia, 80% of whom are from developing countries. Indonesia is one of the countries in the world's Thalassemia belt, which is a country with a high number of carriers of the Thalassemia trait.[2] Prevalence is most

prevalent around the Mediterranean sea, such as Italy, Greece, Turkey, West Asia, North Africa, South Asia, and Southeast Asia such as Thailand and Indonesia.[3]

Based on its clinical severity, thalassemia can be classified into thalassemia minor, thalassemia intermedia, and thalassemia major.[4] In Thalassaemia major, patients require regular blood transfusions for life with an average of two to four weeks of blood transfusions throughout their life by maintaining haemoglobin levels above 10 g/dl.[1] One of the major complications in routinely transfused patients is iron overload resulting in irregular antibody development.[3] Excess free iron can accumulate in tissues and blood, catalysing the formation of Reactive Oxygen Species (ROS). ROS in the oral cavity can increase the risk of biofilm formation and affect the quality and quantity of saliva. This also has an effect on increasing the risk of periodontal disorders gingivitis.[5]

sIgA acts as a first line of defence against periodontal pathogens and inhibits bacterial attachment.[6] Salivary sIgA levels in children with Thalassemia major who experience gingivitis are lower.[7] If salivary sIgA levels are decreased it can lead to an increased risk of periodontal tissue infection.[6] Probiotic bacteria can stimulate the immune system which will increase sIgA production.[8] A study has proven that the administration of probiotic strain Lactobacillus reuteri for 14 days in healthy people can reduce gingival inflammation.[9] Previously there was also research with the consumption of probiotic supplements for 14 days able to increase salivary sIgA levels.[6] However, there has been no research on salivary sIgA levels in children with Thalassemia major who experience gingivitis before and after probiotic consumption. Based on this, the author is interested in examining the difference in sIgA levels before and after probiotic consumption in the saliva of children with Thalassaemia major who experience gingivitis.

METHOD

This research employed an experimental test design involving 16 children aged 6–12 years diagnosed with Thalassemia major. The study was conducted in the Blood Transfusion Room at RSUPN Dr. Cipto Mangunkusumo. The study analyzed changes in sIgA levels in children with gingivitis before and after a 14-day intervention with Lactobacillus reuteri probiotics DSM 17938 and Lactobacillus reuteri ATCC PTA 5289, using the BioGaia Interlac Pro-D brand (POM SI214591521). Ethical approval was obtained under letter number KET 1346/UN2.F1/ETIK/PPM.00.02/2024 from the Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo.

The inclusion criteria were: 1. Subjects diagnosed with thalassemia major with blood transfusion every two to four weeks; 2. Aged 6-12 years; 3. Having gingivitis. Exclusion criteria are: 1. Subjects have other systemic diseases (Tuberculosis, Human Immunodeficiency Virus); 2. Subjects took antibiotics and other probiotics one month before the study; 3. Girls who have begun menstruation.

Sampling was conducted through purposive sampling. The sample size was calculated using the G*Power application version 3.1.9.6 for a paired t-test (two-tailed) with an effect size of 0.75, based on previous studies, an α of 0.05, and a power of 0.80. The total sample size required was 16 subjects.

After obtaining informed consent from the subjects and their parents, the study commenced with unstimulated saliva sampling before probiotic administration. Participants and their parents were educated on oral hygiene and instructed to brush their teeth using fluoride toothpaste twice daily, in the morning after breakfast and at night before bed. Probiotics were administered for 14 days, with instructions for the subjects to dissolve probiotic lozenges in their mouths for approximately two minutes after brushing their teeth at night before sleeping. Subjects were instructed not to eat or drink for one hour after consuming the probiotics and to refrain from using other probiotic products during the testing period. After 14 days of probiotic consumption, unstimulated saliva was collected again. Two millilitres of saliva was collected using a centrifugator tube. The sIgA levels in the saliva samples, both before and after the intervention, were measured using an ELISA method with Bioenzy brand.

RESULTS

The research subjects, aged 6–12 years, had an average sIgA level of 0.97 ± 0.54 microliter (µl) before consuming Lactobacillus reuteri probiotics and 1.31 ± 0.73 µl after 14 days of probiotic consumption. A Shapiro-Wilk normality test ($n \leq 50$) was conducted on the sample size of 16 before performing the mean difference analysis. The normality test confirmed a normal distribution of sIgA levels before and after treatment. A paired t-test was then used to compare the mean sIgA levels before and after 14 days of consuming Lactobacillus reuteri probiotics, with a significance level of $p<0.05$. While the mean sIgA levels increased after the intervention, the paired t-test results showed that this difference was not statistically significant, with a p value = 0.100) (Table 1).

Table 1. Comparison of sIgA levels before and after consuming the probiotic Lactobacillus reuteri for 14 days

Variable	Time	n	Mean ± SD	*P* Value
sIgA	Before	16	0,97 ± 0,54[a]	0,100*
	After	16	1,31 ± 0,73[a]	

[a] Normal distribute data, presented in mean ± SD

* Paired t-test, P>0,05

DISCUSSION

All subjects in this study were children aged 6-12 years. The consideration of choosing this age is the dental phase mixed with exfoliation of primary teeth and eruption of permanent teeth so that the possibility of finding gingival inflammatory conditions is quite high.[7] Children with Thalassaemia major have a high prevalence of gingivitis. According to research studies, children aged 5-18 years with Thalassaemia major experience gingivitis as much as 92.2% ranging from mild to severe.[10] Another consideration for choosing this age is that in thalassaemia major children with a routine history of blood transfusions, their growth and development will have minimal complications until they reach the age of 12 years. After this age, complications can arise due to the accumulation of excess iron deposits due to annual transfusions.[11]

The method of measuring gingivitis in this study was the Modified Gingival Index (MGI) according to Lobene. This method was chosen because it is a modification of the Löe and Silness Gingival Index measurement with changes in criteria through a non-invasive way using clinical images without the use of probes. This is important because in thalassaemia children the use of periodontal probes for the measurement of gingivitis should be avoided.[12] As the literature states in the field of dentistry, Thalassaemia minor, major or intermedia differs in its treatment plan. Before starting treatment, attention should be focused on the type of Thalassemia, haemoglobin level, degree of iron overload, relative organs involved, and the overall prognosis of the patient. Any kind of invasive procedure should be performed immediately after blood transfusion followed by antibiotic prophylaxis as these patients have anaemia, haemolysis and ineffective erythropoiesis and thus have a greater risk of infection.[1]

This study used saliva samples because sIgA is abundant in saliva, which is 90 - 98%.[13] Saliva samples were taken because they are in the oral cavity and are in direct contact with the gingiva. Because this study took subjects with gingivitis, the sIgA used was taken from saliva. Saliva sampling in this study was carried out in the morning between 08.00 and 11.00. The reason for sampling at this hour is to avoid bias in the results of salivary sIgA levels due to the circadian rhythm of the body. Circadian rhythm is the physiological behaviour of the body to adapt to changes in time over 24 hours and is regulated by the hypothalamus. Circadian rhythms can affect salivary flow rates and cause changes in the concentration of salivary sIgA levels. Salivary sIgA levels have a diurnal rhythm, where salivary sIgA levels are highest in the morning and decrease until the evening. In addition, at this hour it is estimated that the research subjects have had breakfast and there is a break of about 90 minutes before sampling. Saliva sampling was carried out in unstimulated saliva conditions. Saliva sampling is done without stimulation because stimulated saliva has higher sIgA levels than unstimulated saliva.[7]

The results of this study showed that the mean sIgA level before consumption of probiotic Lactobacillus reuteri was 0.97 ± 0.54 µl, and the mean sIgA level after 14 days of consumption of probiotic Lactobacillus reuteri was 1.31 ± 0.73 µl. The average results showed an increase in salivary sIgA levels. The increase is in line with research on gargling with probiotic solution for 14 days can increase salivary sIgA levels in the elderly age group. Factors that can affect salivary sIgA levels include oral conditions, systemic conditions, physical activity and nutrition.[6] This is associated with the systemic conditions of children with major thalassaemia have been studied and found that the salivary sIgA levels of children with major thalassaemia are lower at 111,541 ± 71,000 micrograms (µg/ml) and in normal children at 186,136 ± 92,342 µg/ml.[7] These results indicate that there is a significant difference in salivary sIgA levels in beta major thalassaemia children and normal children who experience gingivitis. Gingivitis indicates an infection in the oral cavity, so the body will respond by activating the humoral immune response. Until now, several studies have been conducted to determine the condition of humoral and cellular immunity in thalassaemia major children. One study suggested changes in serum

immunoglobulin levels and changes in the number and function of B cells and T cells which may be caused by repeated antigen exposure due to blood transfusion treatment in thalassaemia major children.[14]

Probiotic therapy has recently been widely used as an adjunctive therapy to restore dysbiosis in the oral cavity such as periodontal disease. However, there has been no research on salivary sIgA levels of children with thalassaemia major who experience gingivitis before and after consumption of Lactobacillus reuteri. The results of this study showed an increase in salivary sIgA levels after the use of probiotic Lactobacillus reuteri but the difference was not statistically significant. This could be attributed to indirect mechanisms of probiotics in the oral cavity, including modulation of innate and adaptive immune function. Lactic acid bacteria can interact with immunocompetent cells, such as macrophages and T cells, leading to changes in cytokine production and B cells that will differentiate into plasma cells. Plasma cells will produce sIgA.[15] This is consistent with the literature that probiotics can activate and modulate the host immune system for a longer time under certain systemic conditions literature that probiotics can activate and modulate the host immune system for a longer time under certain systemic conditions.[16]

All subjects in this study reported no complaints or side effects during probiotic use. This is consistent with previous studies that daily probiotic use has been shown to be safe and well tolerated. The Center for Disease Control (CDC) supports the conclusion that the incidence of Lactobacillus reuteri bacteraemia is inconsistent and its oral use is safe.[17] To the best of the researchers' knowledge, this study is the first study conducted to see the difference in salivary sIgA levels of children with thalassemia major who experience gingivitis after probiotic Lactobacillus reuteri consumption.

CONCLUSION

This study concluded that consumption of probiotic L.reuteri for 14 days can increase salivary sIgA levels in children with thalassaemia major who experience gingivitis but the increase is not statistically significant.

DECLARATIONS

Conflict of interest

The authors declare that they have no conflict of interest.

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ORIGINAL RESEARCH

INNOVATIONS IN RESTORATIVE DENTISTRY: A COMPARATIVE STUDY OF COMPOSITE AND CERAMIC MATERIALS

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ABSTRACT

Background: Restorative dentistry increasingly demands materials that combine mechanical durability, esthetic performance, and biological compatibility. Composite resins and ceramic materials are widely used for posterior restorations, their comparative effectiveness remains an area of clinical significance.

Objective: To compare the fracture resistance, wear behaviour, marginal sealing ability, and colour stability of nanohybrid composite resin and lithium disilicate ceramic inlay restorations under simulated intraoral conditions.

Materials and Methods: 32 extracted human molars were divided into two groups (n=16): composite resin (Filtek Z350 XT) and ceramic inlays (IPS e.max CAD). Standardized Class I cavities were restored accordingly. Specimens were subjected to thermomechanical aging, including 10,000 thermal cycles and 100,000 chewing cycles. Fracture resistance, wear volume, microleakage, and colour stability (ΔE) were assessed using a universal testing machine, profilometer, stereomicroscopy, and spectrophotometry, respectively.

Results: Ceramic inlays demonstrated significantly higher fracture resistance (1985.7 N vs. 1280.5 N, $p < 0.001$) and lower wear volume loss (0.017 mm³ vs. 0.042 mm³, $p = 0.002$). Microleakage was less pronounced in ceramics, with 87.5% scoring 0–1, while composites showed more dye penetration. Post-aging ΔE remained within acceptable limits for ceramics (2.4) but exceeded the threshold in composites (4.6).

Conclusion: Lithium disilicate ceramics offer superior mechanical and esthetic properties compared to composite resins and are better suited for high-stress or esthetically sensitive restorations. Material selection should consider the specific clinical scenario and performance expectations.

Keywords: *Restorative dentistry, Composite resin, Lithium disilicate ceramics, Esthetic durability*

INTRODUCTION

In recent years, restorative dentistry has undergone significant transformation, driven by the demand for biomimetic materials that restore function and replicate the natural esthetics and biomechanical properties of tooth structure [1]. The global population becomes increasingly conscious of oral health and facial aesthetics, there is an escalated emphasis on materials that ensure long-term durability, compatibility, and minimal biological interference [2]. Amidst these advances, composite resins and ceramic-based materials have emerged as frontrunners in the field of restorative procedures, particularly in posterior restorations, esthetic rehabilitations, and full-mouth reconstructions [3]. The progression of restorative materials has revolutionized the path of technological advancements in dental science. Conventional amalgam and gold restorations, earlier regarded for long periods, are widely substituted by materials that provide better esthetics and minimally invasive insertion protocols [4]. Composite resins, originally developed as direct restorative materials in anterior teeth, have advanced in composition to include nanohybrid, bulk-fill, and bioactive types with enhanced polymerization, wear resistance, and mechanical properties [5]. In contrast, advancements in ceramic materials have transitioned from traditional to modern high-strength options such as lithium disilicate and zirconia-based ceramics [6]. These innovations have significantly enhanced the durability and esthetic quality of indirect restorations.

The clinical decision-making process for material selection is multifactorial. Factors that affect material selection include the place and extent of the cavity, occlusal loading, esthetic requirements, patient age, and parafunctional activities [7]. Composite resins enable conservative cavity preparation and restoration, but their polymerization shrinkage and susceptibility to wear in high-pressure areas question their long-term performance in posterior use [8]. Ceramics, despite their superior fracture resistance and colour stability, are inherently brittle and often require more invasive tooth preparation, along with laboratory-based processing that increases time and cost. This dichotomy underscores the necessity for a comparative clinical and material-based evaluation to identify optimal indications for each material class [9]. The past decade has witnessed an upsurge in experimental and clinical research focusing on improving the functional and biological performance of restorative materials. Improvements in filler technology, resin matrices, and silane coupling agents have dramatically improved the mechanical properties and optical characteristics of composite resins [10]. During the same period, advances in Computer-Aided Design and Computer-Aided Manufacturing milling (CAD/CAM milling), digital impression systems, and high-temperature sintering have improved the precision and marginal adaptation of ceramic repairs [11]. Bioinspired improvements like the addition of antibacterial compounds and remineralizing agents to composites, and the creation of translucent multilayered ceramics, indicate a trend toward materials that engage with the oral environment positively [12]. Despite these advances in technology, comparative evaluations determining the in vitro as well as in vivo behaviour of next-generation composites and ceramics are still limited and tend to be non-standardized. Most of the available literature focuses on isolated factors like bond strength or wear, without comparing a comprehensive analysis of clinical performance like longevity, marginal integrity, colour stability, and failure modes. Few studies contextualize these results in the context of real-world clinical scenarios that account for operator variability, patient compliance, and occlusal dynamics [13]. As restorative dentistry becomes more personalized and interdisciplinary, the imperative for integrated data-driven insights into material performance grows.

The role of restorative materials takes on discriminating importance when considered within the wider scope of maxillofacial rehabilitation. In clinical scenarios such as post-traumatic facial restoration, prosthodontic management of partially edentulous arches, or aesthetic enhancement following orthognathic interventions, striking the ideal balance between mechanical resilience and esthetic precision is essential. Rather than being used in isolation, composite and ceramic materials are typically integrated into complex restorative systems that incorporate adhesive agents, luting materials, and carefully designed occlusal schemes [14]. Consequently, a nuanced understanding of how these materials respond to functional stresses, cyclic loads, and thermal fluctuations is crucial for effective treatment planning in both maxillofacial and prosthodontic contexts. Patient-centric factors

such as biocompatibility, allergy potential, and maintenance requirements significantly influence the prolonged functional stability of restorative treatments. Composite resins, for instance, may release trace amounts of monomers such as bisphenol A-glycidyl methacrylate (Bis-GMA) or triethylene glycol dimethacrylate (TEGDMA), which have raised concerns regarding biocompatibility, particularly in individuals with hypersensitivity reactions [15]. On the other hand, ceramics, being inert and metal-free, tend to be favoured by chemical-sensitive patients or those requiring periodontal maintenance. Furthermore, from a practitioner's perspective, ease of manipulation, technique sensitivity associated with each material can significantly influence the choice and outcome of restorative procedures. This study is intended to bridge these clinical and scientific discrepancies by performing a systematic comparative analysis of modern composite and ceramic materials employed in restorative dentistry. Using standardized test regimens and simulating intraoral conditions, this study will provide exhaustive data on mechanical performance, failure mode, esthetic properties, and biological interactions. The products chosen for this study are commonly employed commercial systems with established clinical histories, making the results applicable and interpretable to everyday dental practice.

This study aims to conduct a comparative assessment of composite and ceramic restorative materials with a focus on three core parameters. First, it evaluates their fracture resistance and wear behaviour to determine mechanical reliability under stress. Second, it examines marginal integrity and the extent of microleakage following thermomechanical loading, reflecting their performance in dynamic oral environments, and the study also investigates esthetic properties such as colour accuracy, translucency, and the stability of these attributes over time when subjected to simulated aging conditions.

Materials and Methods

Study Design

This research was conducted as a controlled in vitro experimental study designed to evaluate and compare the performance of contemporary composite and ceramic restorative materials under simulated oral conditions. The study aimed to replicate clinically relevant mechanical and thermal stresses to provide meaningful insights applicable to everyday dental practice.

Sample Selection and Group Allocation

32 extracted caries-free human molars were utilized in the study and stored in 0.5% chloramine-T solution at 4°C for future use. The teeth were randomly allocated into two major groups (n=16 for each) reliant on the restorative material: Group A was restored with nanohybrid composite resin restorations (Filtek Z350 XT, 3M ESPE, USA), while Group B was restored with lithium disilicate ceramic restorations (IPS e.max CAD, Ivoclar Vivadent, Liechtenstein). Each subgroup was again split into two subgroups (n=8) based on the individual evaluation parameters: a subgroup for fracture resistance and wear, and a subgroup for microleakage and esthetics.

Tooth Preparation and Restoration Protocol

Standardized Class I cavities (4 mm depth × 5 mm width × 6 mm length) were prepared on all specimens with a high-velocity rotary instrument and diamond burs with continuous water irrigation, and the measurements were analysed with a digital caliper. For the composite group (Group A), a two-step etch-and-rinse adhesive (Adper Single Bond 2) was used, and incremental placement of nanohybrid composite in 2 mm increments, each light curing for 20 seconds with an LED light-curing unit (Bluephase, Ivoclar, 1200 mW/cm^2). In the ceramic group (Group B), intraoral scanning with an intraoral scanner (Medit i500) created cavity scans, and lithium disilicate inlays were created using CAD/CAM milling. Internal surfaces were reacted with 5% hydrofluoric acid, silanated, and bonded using a dual-cure resin cement (Variolink Esthetic DC) under 20 N constant load for 5 minutes. All restorations were finished with fine diamond burs and polished using respective kits applicable to the used material.

Thermomechanical Aging Protocol

To simulate intraoral conditions, all the specimens were subjected to a standardized thermomechanical procedure. The procedure involved 10,000 thermal cycles from 5°C to 55°C with 30 second dwell time in the baths and was carried out using a programmable thermocycler (SD Mechatronik). After thermal cycling, mechanical loading was done using a chewing simulator (Willytec, Germany) by applying 100,000 cycles at a fixed 50 N load and 1.6 Hz

frequency simulating about one year of clinical masticatory performance.

Evaluation of Fracture Resistance and Wear Behaviour

After the aging process, all samples were embedded in acrylic resin and subjected to fracture resistance testing by a universal testing machine (Instron 3366, USA). A vertical compressive load was applied at the center of the occlusal surface with a 4 mm steel ball at a crosshead speed of 1 mm/min until it fractured, and the load at failure was measured in Newtons. For assessment of wear resistance, occlusal surfaces were measured using a contact profilometer (Surftest SJ-210, Mitutoyo) in terms of volumetric material loss before and after simulated chewing.

Assessment of Microleakage and Marginal Integrity

To assess microleakage, all restored samples were immersed in 0.5% basic fuchsin dye at 37°C for 24 hours. Following dye exposition, each tooth was sectioned buccolingually with a water-cooled low-speed diamond saw (Isomet 1000, Buehler). Dye penetration in the restoration–tooth interface was assessed under a stereomicroscope (Leica EZ4 HD, 40× magnification) and graded on a 0 to 3 scale, with greater leakage being characterized by higher scores. Marginal integrity was also evaluated with scanning electron microscopy (SEM) (Hitachi S-3400N) at 1000× and 2000× magnifications to check for interfacial adaptation and any marginal gaps.

Esthetic Evaluation and Colour Stability

Colour match and translucency were measured immediately after restoration and following aging with a spectrophotometer (VITA Easyshade V). Colour change was measured by comparing ΔE values from pre-aging and post-aging with Commission Internationale de l'Éclairage CIE Lab measurements, values greater than 3.3 being clinically unacceptable. Translucency was determined by comparing the translucency parameter (TP) measured against reference black and white backgrounds to characterize each material's optical properties.

Statistical Analysis

Data analysis was conducted with the aid of IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Mean and standard deviation were determined for all measured variables. Fracture resistance and colour difference (ΔE) values were compared between groups via independent sample t-tests. Microleakage scores were related using the non-parametric Mann–Whitney U test, whereas wear volume and TP values were compared using two-way ANOVA with Bonferroni post hoc correction. Significance was set at $p < 0.05$ for all tests.

Ethical Considerations

A controlled in vitro comparative experimental study was conducted over three months in the Department of Conservative Dentistry and Biomaterials Science. Ethical approval for the use of extracted human teeth and compliance with the laboratory safety guidelines were attained from the Institutional Research Ethics Committee (Approval ID: DENT/RES/2025-04). All of the procedures adhered to agree with the Helsinki Declaration for biomedical research.

RESULTS

Fracture Resistance

All the specimens survived thermomechanical aging before load testing. The average fracture resistance of lithium disilicate ceramic inlays was significantly greater (1985.7 ± 140.6 N) than that of nanohybrid composite resin restorations (1280.5 ± 115.3 N), with a highly significant difference ($p < 0.001$). These results validate the better load-carrying property of ceramic-based materials under simulated occlusal stress, as mentioned in Table 1.

Table 1. Fracture resistance (in Newtons) of composite resin and ceramic inlay restorations following mechanical loading

Group	Mean Fracture Resistance (N)	Standard Deviation (N)	p-value
Composite Resin	1280.5	115.3	< 0.001
Ceramic Inlay	1985.7	140.6	< 0.001

Ceramic inlays showed higher fracture resistance values compared to composite resin restorations. Values are presented as mean ± standard deviation, with statistical significance at $p < 0.001$.

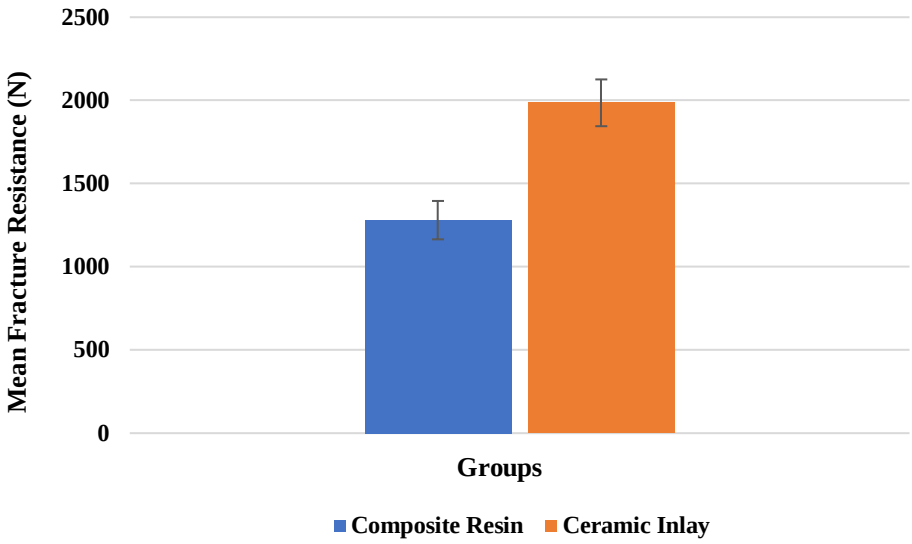


Figure 1. Fracture resistance (in Newtons) of composite resin and ceramic inlay restorations

Figure 1 represents the comparison of the fracture resistance (in Newtons) of composite resin and ceramic inlay restorations. Ceramic inlays demonstrated significantly higher fracture resistance (1985.7 ± 140.6 N) compared to composite resins (1280.5 ± 115.3 N). Error bars represent standard deviation. Statistical analysis confirmed a highly significant difference ($p < 0.001$).

Wear Resistance

Wear resistance testing indicated statistically significant differences in volumetric loss. Composite resin restorations had a larger mean wear volume (0.042 ± 0.006 mm^3) than that of ceramic inlays (0.017 ± 0.004 mm^3), with a p-value of 0.002. This corroborates the established clinical knowledge that ceramics have greater surface durability and reduced abrasion rates in dynamic masticatory loads, as mentioned in Table 2.

Table 2. Mean wear volume loss (mm^3) in composite and ceramic restorations after thermomechanical simulation

Group	Mean Wear Volume Loss (mm^3)	Standard Deviation (mm^3)	p-value
Composite Resin	0.042	0.006	0.002
Ceramic Inlay	0.017	0.004	0.002

Composite resin restorations exhibited greater volumetric wear loss than ceramic inlays. Values are expressed as mean ± standard deviation with $p = 0.002$.

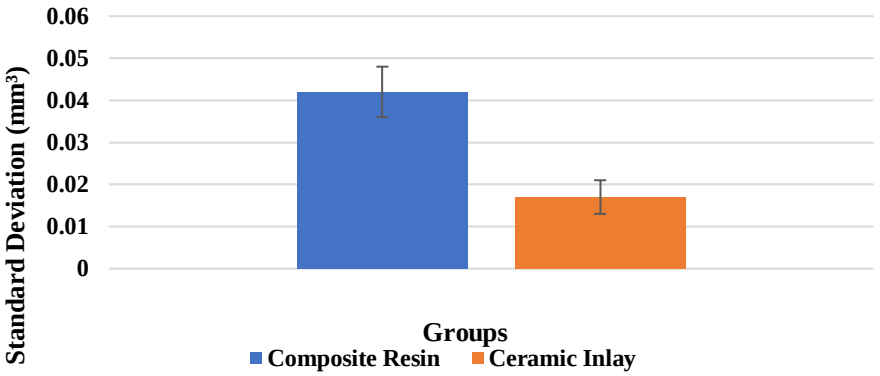


Figure 2. Mean wear volume loss (mm^3) of composite resin and ceramic inlay restorations after thermomechanical loading

Figure 2 illustrates that Composite resin restorations exhibited significantly higher volumetric wear loss (0.042 ± 0.006 mm^3) compared to ceramic inlays (0.017 ± 0.004 mm^3) after 100,000 chewing cycles. The difference was statistically significant (p = 0.002). Error bars represent standard deviation. The results highlight the superior wear resistance of ceramic materials under simulated occlusal loading conditions.

Microleakage and Marginal Adaptation

After dye penetration and stereomicroscopic analysis, ceramic inlays showed drastically lower microleakage scores, with 87.5% of the specimens having only superficial dye infiltration (score 0 or 1). Composite resin restorations, on the other hand, showed deeper penetration with 62.5% of the specimens scoring 2 or 3, as mentioned in Table 3. These variations were further validated by SEM analysis, which revealed tighter and more uniform marginal interfaces in the ceramic group, as would be expected given their better adaptation and lower polymerization shrinkage.

Table 3. Microleakage scores of composite and ceramic restorations after dye immersion and sectioning

Score	Composite Resin (n = 8)	Ceramic Inlay (n = 8)
0	1	4
1	2	3
2	3	1
3	2	0

Score 0 = no dye penetration; Score 3 = penetration along entire cavity wall

Ceramic inlays demonstrated lower microleakage scores than composite resin restorations. Scores range from 0 (no penetration) to 3 (penetration along the entire wall).

Colour Stability and Esthetic Properties

Spectrophotometric analysis before and after aging showed high discolouration of composite restorations, with ΔE rising from 1.2 to 4.6, which is beyond the acceptable limit of 3.3. However, ceramic inlays retained ΔE values within the acceptable range (0.9 before aging and 2.4 after), which shows enhanced colour stability, as mentioned in Table 4.

Moreover, qualitative evaluation of translucency parameters (TP) preferred ceramics due to their layered optical properties, contributing to more natural appearance, particularly in anterior and esthetically critical regions.

Table 4. Colour stability (ΔE values) of composite and ceramic restorations before and after thermomechanical aging

Group	ΔE Before Aging	ΔE After Aging	Clinically Acceptable (<3.3)
Composite Resin	1.2	4.6	No
Ceramic Inlay	0.9	2.4	Yes

Post-aging ΔE values exceeded the clinical acceptability threshold (ΔE > 3.3) for composite resin, while ceramic inlays remained within the acceptable range.

DISCUSSION

The results of this comparative analysis highlight the material-specific performance advantages of lithium disilicate ceramics compared with nanohybrid composite resins in key areas of restorative performance, i.e., fracture resistance, wear pattern, marginal integrity, and esthetic longevity [16]. Such distinctions have significant clinical implications for material choice, especially for posterior restorations in which occlusal load opposition, longevity, and esthetic integration are salient treatment considerations.

The considerable difference in fracture resistance between composite and ceramic restorations in this study is consistent with prevailing literature and material science theory. Ceramic inlays made of lithium disilicate exhibited approximately 55% greater fracture resistance than their composite equivalents [17]. This can be most plausibly explained by the inherent microstructure of lithium disilicate, which is made up of densely

interconnected crystalline phases in a glassy matrix, promoting crack deflection and energy absorption [18]. In contrast, composite resins, even when reinforced with nano or microhybrid fillers, retain a significant proportion of the resin matrix vulnerable to polymerization shrinkage and viscoelastic deformation. The results validate prior studies that report ceramics to be more resilient under vertical compressive forces, particularly in molar regions where occlusal stresses are highest [19]. Notably, the use of dual-cure resin cement for ceramic inlays may have also contributed to improved stress distribution across the adhesive interface, mitigating stress concentration at the marginal ridges.

Wear resistance is an essential performance criterion for any restorative material to withstand the cyclic forces of mastication. Wear volume loss measured on composite restorations was over twice the measure on ceramic inlays, affirming the superior abrasion resistance of ceramics. The relatively soft resin matrix in composites may be more prone to fatigue degradation and plucking of filler particles under load, leading to increased surface roughness and loss of anatomical form over time [20]. In contrast, the highly sintered ceramic restorations retain their structure and exhibit excellent surface degradation resistance. These findings are clinically relevant, as restoration wear can contribute to occlusal disharmony, food impaction, and eventual loss of proximal contacts, factors that compromise long-term function and comfort. Additionally, increased surface roughness in worn composites can facilitate plaque retention and secondary caries formation.

Marginal adaptation and sealing ability are the basic measures of the restoration to inhibit microleakage, secondary caries, and pulpal irritation. The dye penetration test in this investigation provided a general trend of decreased microleakage with ceramic inlays compared to composite restorations [21]. This is particularly significant given the broader cavity preparations required for inlays, which might theoretically predispose to marginal gaps. The accuracy of CAD/CAM milling and the dimensional stability of ceramic materials helped ensure superior marginal adaptation. Moreover, the pre-cementation surface treatments, etching with hydrofluoric acid and silanization improved the micromechanical and chemical bond between the ceramic and the luting cement, which in turn minimized interface degradation [22]. Composite restorations, even when placed incrementally and light-cured under controlled conditions, continue to be susceptible to polymerization shrinkage and technique sensitivity. These factors may have led to the marginal gaps and variable dye penetration scores observed.

The esthetic performance of a restoration is increasingly regarded as a measure of clinical success, especially in patients with high esthetic demands. Spectrophotometric evaluation in the current study confirmed that ceramic inlays showed clinically acceptable colour stability even after thermomechanical aging [23.] In contrast, composite restorations had ΔE values greater than the perceptibility threshold after aging, showing visible discolouration. The esthetic advantage of ceramics can be linked to their optical characteristics, such as high translucency, colour stability, and resistance to extrinsic staining. Composite resins, even with improvements in filler technology and pigment stabilization, still suffer from the problem of preserving long-term colour stability because of their organic nature, due to which they absorb water and staining agents. This finding supports the recommendation of ceramics for restorations in the esthetic zone or for patients with dietary habits that predispose to staining, such as high intake of coffee, tea, or red wine. Collectively, the results of this study confirm that ceramics outperform composites in high-stress and esthetically demanding clinical situations. However, practical considerations in daily dental practice must be acknowledged. Composite resins, although mechanically less desirable, present unique strengths such as ease of placement, reduced expense, conservative preparation, and facile repairability, making them a good fit for small to moderate, non-load-bearing restorations or provisional use. Conversely, ceramic restorations, though they offer higher durability and better esthetics, involve additional steps in the laboratory, cost more in materials, require more extensive tooth reduction, and should be reserved for cases where such benefits justify these trade-offs. While the study employed rigorous and standardized in vitro protocols, it cannot fully replicate the complexities of the oral environment, such as salivary dynamics, microbial activity, and individualized occlusal forces [24]. Future in vivo studies and long-term clinical trials are needed to validate these findings in real-world settings.

The comparative analysis given herein confirms that lithium disilicate ceramics demonstrate better

mechanical and esthetic performance compared to nanohybrid composite resins in all tested parameters. Though composites continue to be useful for conservative and cost-effective restorations, ceramics can now be the material of choice in high-load and esthetic demanding situations. These findings form a solid reference point for evidence-based material selection for restorations and reflect the essential role of material science in modern dentistry.

Conclusion

This comparative in vitro study demonstrated that lithium disilicate ceramic inlays significantly outperform nanohybrid composite resin restorations in key functional and esthetic parameters. Ceramic inlays showed the higher mean fracture resistance at 1985.7 N, against 1280.5 N for composites, and a significantly lower wear volume loss of 0.017 mm^3 against 0.042 mm^3. Microleakage assessment also demonstrated better marginal sealing in ceramics, with 87.5% of the specimens having a score of 0 or 1, whereas 62.5% of the composite restorations had more significant dye penetration (scores of 2 or 3). About colour stability, post-aging ΔE values were within clinically acceptable ranges in ceramics (2.4), but beyond in composites (4.6), suggesting overt discolouration. The results verify that ceramic materials have better long-term performance, especially for load-carrying and esthetically critical restorations. Yet, simplicity of manipulation, lower cost, and conservative nature continue to recommend composite resins for smaller cavities and less critical areas. Clinical context, patient considerations, and functional requirements should therefore influence the choice of material. Additional clinical studies with follow-up of several years' duration are suggested to confirm these in vitro findings and guide further, more specific material guidelines in restorative and prosthetic dentistry.

DECLARATION

Ethical Approval: This study was approved by the Institutional Ethics Committee. This study was conducted in accordance with the principles of the Declaration of Helsinki regarding ethical research involving human sub jects.

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

Availability of Research Data: All data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Conflict of Interest Statement: The authors declare no conflicts of interest related to this study.

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ORIGINAL RESEARCH

RECURRENT APHTHOUS STOMATITIS IN A PATIENT WITH WILSON'S DISEASE: A CASE REPORT

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ABSTRACT.

Background: Wilson's disease (WD) is a rare autosomal recessive disorder of copper metabolism caused by ATP7B gene mutations. Recurrent aphthous stomatitis (RAS) is a common, multifactorial oral mucosal disorder. Their coexistence is uncommon and has been scarcely reported in the literature**.**
Objectives: This case report aims to describe the clinical features, management, and possible association between RAS and WD, highlighting the importance of treatment adherence and interdisciplinary care.
Materials and Methods: A 26-year-old male with a known history of WD under zinc therapy presented with recurrent oral ulcerations and gingival bleeding. Detailed history, clinical examination, and follow-up assessments were performed to evaluate the nature of lesions and their correlation with treatment compliance**.**
Results: Clinical examination revealed two minor aphthous ulcers on the lower labial mucosa with associated generalized gingival erythema. Ulcer recurrences correlated with poor adherence to zinc therapy. Complete healing was observed after resuming therapy, with no recurrence at one-month follow-up.
Conclusion: This case highlights a possible link between WD and RAS, potentially mediated by micronutrient imbalance and immune dysregulation. Strict adherence to therapy and interdisciplinary management are crucial for preventing recurrences and maintaining oral health in WD patients.

Keywords: *Recurrent aphthous stomatitis, Wilson disease, copper metabolism, case report.*

INTRODUCTION

Recurrent aphthous stomatitis (RAS) Recurrent aphthous stomatitis (RAS) remains the most common ulcerative disease of the oral mucosa, presenting as painful round shallow ulcers with well-defined erythematous margins and yellowish-gray pseudomembranous centers. While the etiology of RAS is multifactorial, systemic diseases, nutritional deficiencies, and immunological factors have been implicated in its pathogenesis. RAS has a characteristic prodromal burning sensation that lasts from 2 to 48 hours before an ulcer appears. Lesions typically occur on non-keratinized mucosa (buccal mucosa, labial mucosa, floor of mouth, ventral tongue, soft palate). Keratinized mucosa (hard palate, attached gingiva, dorsal tongue) is less commonly involved.

RAS is classified into minor, major, and herpetiform ulcers. More than 85% of RAS presents as minor ulcers that are less than 1 cm in diameter and heal without scars. Ulcers classified as major RAS, also known as Sutton's disease or periadenitis mucosa necrotica recurrens, are larger than 1 cm in diameter, persist for weeks to months, and heal with scars. Herpetiform ulcers are clinically distinct because they appear as clusters of multiple ulcers scattered throughout the oral mucosa; despite the name, these lesions have no association with herpes simplex virus.[1]

Wilson Disease (WD) is an inherited disorder of copper metabolism that is both potentially serious and treatable. It is characterized by abnormal accumulation of copper in the body. The underlying cause is mutations in the ATP7B gene, which encodes a transmembrane copper-transporting ATPase. This genetic defect leads to progressive copper overload, particularly in the liver, brain, and other organs.[2]

The clinical course of WD can vary greatly in severity. However, progressive liver disease remains one of its most common and important features. In addition to hepatic involvement, patients may present with neurological symptoms such as tremors or movement disorders, as well as psychiatric manifestations including mood changes or cognitive disturbances.[3]

Diagnosis is based on structured algorithms that combine clinical signs and symptoms with laboratory measures of copper metabolism. Genetic testing for ATP7B mutations also plays an essential role in confirming the diagnosis and guiding family screening.[4]

Treatment focuses on reducing copper overload and preventing organ damage. Available therapies include copper-chelating agents, which promote urinary excretion of copper, and zinc salts, which block copper absorption in the intestine. These treatments work through different mechanisms but are effective in controlling disease progression when started early.[5]

This case report highlights the association between recurrent aphthous stomatitis and Wilson disease, emphasizing the need for clinicians to consider underlying systemic conditions in patients presenting with refractory or atypical RAS.

REPORT OF THE CASE

A 26-year-old male presented to the outpatient department (OPD) with a primary complaint of gingival bleeding during toothbrushing, persisting for the past year. He reported difficulty in maintaining oral hygiene but denied any episodes of spontaneous gingival bleeding. The patient had a known diagnosis of Wilson's disease, for which he was undergoing treatment.

Medical history was notable for recurrent oral ulcerations, which the patient reported were exacerbated by sleep deprivation and periods of non-compliance with zinc supplementation. There was no history of cutaneous lesions suggestive of systemic involvement.

Intraoral examination revealed two ovoid ulcers on the lower right labial mucosa, measuring approximately 3 × 2 mm and 2 × 1 mm (figure1), respectively.



Figure 1. Two ovoid ulcers of approximately 3 × 2 mm and 2 × 1 mm

The ulcer bases were covered with whitish slough and surrounded by a well-defined erythematous halo. The gingiva demonstrated generalized marginal erythema (figure2) with brownish pigmentation along the attached gingiva.



Figure 2. Erythmatous marginal gingiva



Figure 3. Healed ulcer at follow-up



Figure 4. Normal marginal gingiva showing no erythematous areas

No extraoral manifestations of Wilson's disease were observed during the ulcerative episodes. The patient was advised to maintain strict oral hygiene measures and to continue zinc supplementation as prescribed. A follow-up visit was scheduled after one month to assess for complete healing (figure3,4) and to monitor for recurrence. At one-month follow-up, the ulcers demonstrated complete healing, correlating with improved compliance with zinc therapy. The patient remained asymptomatic, with no new ulcerative lesions observed on clinical examination.

DISCUSSION

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism caused by mutations in the ATP7B gene, resulting in pathological copper accumulation primarily in the liver, central nervous system, and other organs. The clinical presentation is heterogeneous, with hepatic, neurological, and psychiatric manifestations being most common. Oral manifestations, though less frequently reported, may reflect systemic disease activity or complications of therapy.[3]

In this case, the patient presented with chronic gingival bleeding during toothbrushing and recurrent oral ulcerations, which were temporally associated with non-adherence to zinc supplementation. Zinc salts remain a mainstay of WD treatment, acting by inducing intestinal metallothionein to reduce copper absorption. Discontinuation or irregular intake of zinc can lead to fluctuations in copper levels, potentially contributing to mucosal vulnerability and impaired wound healing.

Oral ulcerations in patients with WD may also be multifactorial, involving nutritional deficiencies, altered immune responses, or local trauma exacerbated by poor oral hygiene. In this patient, ulcers were observed as well-defined ovoid lesions with erythematous halos and slough-covered bases, consistent with minor aphthous ulcers. Notably, ulceration episodes coincided with periods of zinc therapy interruption and improved with restored compliance, suggesting a contributory role of zinc in mucosal integrity and healing.

Gingival findings of generalized marginal erythema with brownish pigmentation may reflect chronic inflammatory changes and melanin deposition, a known finding in chronic gingivitis. While WD itself is not classically associated with specific gingival pigmentation, systemic disease burden and oral hygiene challenges can exacerbate periodontal inflammation.

This case underscores the importance of interdisciplinary management in patients with WD, including dental practitioners, to monitor oral manifestations, reinforce treatment adherence, and maintain optimal oral hygiene. Early recognition and management of oral lesions can improve quality of life and prevent complications in this patient population.

This report highlights a potential association between Wilson's disease (WD) and recurrent aphthous stomatitis (RAS), but it is important to acknowledge several limitations inherent to case reports. As a single-patient observation, the findings lack generalizability, and the apparent relationship between WD and RAS may be coincidental rather than causal. Confounding factors and alternative etiologies for RAS may not have been fully excluded.

RAS is a common oral mucosal disorder characterized by recurrent, painful ulcers with a multifactorial etiology. Contributing factors include psychological stress, immune dysregulation, and nutritional deficiencies (e.g., zinc, iron, vitamin B12). Systemic conditions such as inflammatory bowel disease or Behçet's syndrome also warrant consideration. Without comprehensive exclusion of these alternative diagnoses, attributing the occurrence of RAS solely to WD remains speculative.

Wilson's disease is a rare autosomal recessive disorder caused by mutations in the ATP7B gene, leading to impaired copper homeostasis and toxic accumulation in the liver, brain, and cornea. Several pathophysiological mechanisms may plausibly link WD to RAS. Dysregulated copper metabolism in WD may induce immune system

dysfunction, a recognized contributor to RAS pathogenesis. Additionally, secondary deficiencies in essential micronutrients such as zinc or iron—whether due to the underlying disease or chelation therapy—may compromise mucosal integrity and immune competence, predisposing to ulcer formation.[6]

Oxidative stress is another potential mechanistic link. Excess free copper catalyzes the formation of reactive oxygen species (ROS), causing tissue injury that may predispose to oral mucosal ulceration. Furthermore, chronic systemic inflammation in WD, characterized by elevated pro-inflammatory cytokines such as TNF-α and IL-1, may contribute to the development or persistence of RAS lesions.[7]

Nevertheless, in the absence of mechanistic evidence or long-term follow-up data, the causal relationship between WD and RAS remains hypothetical. The current report does not provide direct evidence that treatment of WD, such as chelation therapy or zinc supplementation, directly alters the frequency or severity of RAS episodes over time. Future studies with larger patient cohorts, mechanistic investigations, and extended clinical observation will be necessary to clarify this potential association and its clinical implications.

CONCLUSION

This case underscores the importance of recognizing potential oral manifestations in patients with Wilson's disease, including recurrent aphthous stomatitis (RAS) and chronic gingival inflammation. While the observed improvement in oral ulceration with zinc supplementation suggests a possible contributory role of micronutrient deficiency or immune dysregulation secondary to WD, the relationship remains speculative given the multifactorial nature of RAS.(5)

Clinicians should maintain a high index of suspicion for oral mucosal lesions in patients with systemic diseases such as WD and ensure thorough assessment of contributing factors, including treatment adherence and nutritional status. Interdisciplinary management, involving medical and dental practitioners, is essential for optimizing patient outcomes.

DECLARATION

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

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CASE REPORT

DEMINERALIZATION OF TOOTH ENAMEL: A CLINICAL AND LABORATORY ASSESSMENT OF ENERGY DRINK CONSUMPTION AMONG YOUTH IN KYRGYZSTAN

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ABSTRACT

Background: The worldwide consumption of energy drinks shows a substantial rise among young consumers. The high sugar levels and low pH in these beverages lead to dental health problems which include enamel demineralization and erosion. The research aimed to study how energy drinks affect tooth enamel structure and the chemical composition of oral fluids.

Materials and Methods: In an in vitro experiment, 30 extracted teeth were divided into two groups. One group was submerged in "Nitro" energy drink for two weeks, while the control group was placed in a physiological saline solution. Changes in tooth mass and morphology were observed using a "CJ OPTIK Flexion Advanced" microscope. This vivo study collected mixed saliva samples from two student groups (n=25 each) consisting of regular energy drink consumers and non-consumers. The researchers measured saliva pH at five different time points which included before consumption and at 15, 30, 45 and 60 minutes after consumption. The Pearson's chi-squared ($\chi 2$) test served as the statistical tool for analysis.

Results: The in vitro study showed that teeth exposed to the energy drink experienced a significant loss of mass (7.15% of initial mass) and morphological defects, while the control group showed no change. The in vivo study found that 15 minutes after a single consumption of an energy drink, the average salivary pH in the experimental group dropped significantly from a baseline of 6.68 ± 0.12 to 5.82 ± 0.14 ($p < 0.05$). Although the pH partially recovered to 6.20 ± 0.13 after 60 minutes, it remained significantly lower than both the baseline and the control group's stable pH (6.70–6.77). This prolonged "acid phase" below the critical pH of 5.5, the "point of zero mineralization," creates a persistent risk of enamel demineralization.

Conclusion: The initial consumption of an energy drink leads to long-term acidification of oral fluids which reduces buffer capacity and creates conditions that lead to enamel demineralization. The prolonged period of salivary pH recovery indicates that early caries development remains at risk. The prevention of these risks requires public awareness campaigns together with preventive measures that include consumption limits and buffer rinse use and fluoride prophylaxis enhancement. Future research needs to investigate the long-term consequences of energy drinks especially among adolescent populations.

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INTRODUCTION

The worldwide consumption of energy drinks has experienced rapid growth since the last few years mainly among young adults together with adolescents [1]. The products serve as energy boosters while they help users perform better physically and stay focused [2]. The rising popularity of energy drinks creates a mounting public health concern regarding dental health. The oral environment suffers from two major threats because energy drinks contain high free sugar concentrations and low pH levels [3]. The combination of these factors can lead to a range of dental issues, from enamel erosion to an increased risk of dental caries [4]. The trend exists worldwide yet it is particularly noticeable in Kyrgyzstan because many residents now drink energy drinks as part of their regular daily routine. The high occurrence of tooth enamel, dentin and cementum diseases among people who regularly consume these drinks demonstrates the necessity to study their distinct impact on oral health [5]. The research investigates this essential public health matter through a comprehensive evaluation of energy drink effects on dental health.

The research holds importance because previous studies have proven that energy drink consumption causes dental structure deterioration. The high sugar levels in these beverages create an environment where acidogenic bacteria thrive and the low pH directly causes tooth enamel demineralization which results in acid erosion [6]. The erosion process results in permanent tooth structure damage and heightened tooth sensitivity. The research by Abdirasulov T.A. (2023) demonstrates how energy drinks have become popular while showing their possible adverse health effects [7]. The current research requires additional data-based studies to determine the exact mechanisms of this damage. The research problem focuses on the insufficient scientific evidence which particularly lacks information about the short-term and cumulative effects of these drinks on oral health. The study investigates both temporary and long-term modifications of salivary pH levels and tooth structural changes to address a fundamental knowledge deficit in existing research.

The research introduces fresh data through its combination of laboratory and animal studies which show the destructive effects of a widely consumed energy drink. The in vitro experiment showed the destructive power of these beverages through its detailed measurement of tooth mass reduction and structural changes. The in vivo study introduced new findings through its precise measurement of salivary pH changes after a single energy drink consumption. The data shows that oral fluid acidification persists for an extended period which has not been well-documented in previous studies. The study reveals that the salivary buffer system needs more than 60 minutes to recover to a remineralizing pH which demonstrates an ongoing risk of demineralization. The research creates opportunities for future investigations about long-term cumulative effects and adolescent risk assessment and public health intervention development. The study creates opportunities to study preventive measures such as oral rinses and chewing gums to reduce energy drink damage.

MATERIALS AND METHODS

Study Design

The research consisted of two separate parts which included laboratory experiments with extracted human teeth and clinical observations of young adults. The in vitro study evaluated the erosive effects of a well-known energy drink on human teeth extracted from the mouth while the in vivo study measured how energy drink consumption affects oral fluid acid-base levels in young adults.

Ethical Considerations

The research followed the ethical guidelines established by the Declaration of Helsinki [8]. The Institutional Review Board of Osh State University approved the study. The IRB waived the need for individual informed consent because the study used non-invasive anonymous data from an observational retrospective design. The extracted teeth used in the in vitro study came from a biobank through an institutional ethics protocol that allowed their use in dental research. The researchers protected participant privacy through de-identification and anonymous data analysis.

Sample Collection

The researchers obtained thirty human teeth which were free from caries and fractures and any signs of pre-existing erosive wear from the biobank. The teeth were cleaned of any soft tissue and calculus, disinfected with a 0.5% chloramine-T solution, and stored in a physiological saline solution (0.9% NaCl) at 4°C until the start of the experiment to prevent dehydration.

Experimental Groups

The researchers distributed the teeth into two separate groups consisting of 15 teeth in each group.

2.4.1 Experimental Group: The teeth underwent immersion in 100 mL of "Nitro" energy drink inside a sealed glass container. The researchers chose this energy drink because it is well-known and easily accessible throughout Kyrgyzstan.

2.4.2 Control Group: The teeth were placed in 100 mL of 0.9% NaCl physiological saline solution.

Protocol

The containers operated at a fixed temperature of 37°C to replicate oral conditions. The solutions received weekly refreshments to simulate repeated exposure. The experiment ran for two weeks in total.

Data Collection and Analysis

The precision analytical balance measured tooth mass with 0.001 g accuracy for initial and final assessments. The experimental group teeth underwent percentage mass loss calculations for each specimen. The "CJ OPTIK Flexion Advanced" microscope from Germany captured high-resolution images to document morphological changes and enamel defects with precision.

Study Population

The research involved 50 Osh State University students between 18 and 25 years old who met particular selection criteria which included no systemic diseases and no medications that could alter salivary composition. The participants were separated into two groups: an experimental group (n=25) made up of students who admitted to drinking energy drinks 3-4 times weekly and a control group (n=25) composed of students who had not consumed energy drinks during the previous month.

Saliva Collection

The participants received instructions to avoid food consumption and drinking all beverages except water for at least two hours before starting the experiment. The researchers obtained unstimulated mixed saliva through non-invasive aspiration techniques. The researchers collected sterile labeled containers of samples from each participant at five distinct time points which included the baseline measurement at T_0 followed by measurements at T_{15}, T_{30}, T_{45} and T_{60} minutes. The experimental group received a single 250 mL can of "Nitro" energy drink while the control group performed a water rinse.

pH Measurement

The pH of oral fluid was measured immediately after collection using a calibrated "pH-121" pH-millivoltmeter with special vacuum electrodes. Each measurement was performed in triplicate, and the average value was recorded to ensure accuracy.

Statistical Analysis

The statistical software (e.g., SPSS, version 25.0) was used to analyze the collected data. The pH values at each time point were summarized using descriptive statistics (mean ± standard error of the mean, SEM). A two-way ANOVA with repeated measures was used to assess the differences between the experimental and control groups. A Student's t-test was used to compare specific time points, with a significance level set at $p < 0.05$. The Pearson's chi-squared ($\chi 2$) test was used to analyze the correlation between energy drink consumption and the observed changes in oral health status.

RESULTS

It is well known that acidic drinks can damage teeth, mostly because they cause demineralisation. When energy drinks and other highly acidic solutions get into the mouth, their low pH makes it easier for the calcified enamel matrix to break down. The process starts with acids moving through the acquired pellicle, which causes hydroxyapatite crystals to dissolve and minerals to be lost from the inter-prismatic enamel areas. To quantitatively examine this effect, our study utilised an in vitro model to compare a widely consumed energy drink, "Nitro," with a physiological saline solution (NaCl). Weighing 30 extracted human teeth at first gave us baseline mass data. The teeth assigned to the experimental group (n=15) exhibited a total initial mass of 31.72 g, whereas the control group (n=15) displayed a total initial mass of 34.8 g. This controlled experimental design enabled a direct evaluation of the erosive potential of the energy drink by quantifying alterations in tooth mass over time, thereby offering an objective measure of mineral loss due to exposure to the test substance.



Figure 1. Determination of the mass of the front and chewing teeth.

After one week of storage in a sealed glass container with the energy drink, a slight loss of mass was recorded. The average mass of all teeth decreased to 30.68 g, which is 1.04 g less than the initial mass. In contrast, the teeth in the physiological solution showed no change in mass, maintaining a value of 34.8 g. As the storage time was extended to two weeks, the changes continued. The average mass of the teeth in the energy drink solution was 29.45 g, which is 1.23 g less than after the first week. The teeth from the physiological solution remained at 34.7 g. These data clearly demonstrate that the acids contained in energy drinks have a destructive effect on tooth enamel, which is evident in the tooth structure and a reduction in their mass. The main signs of erosion also include a loss of luster and a change in tooth morphology, which can be seen as cup-shaped defects, especially on the molars. These processes directly contribute to further loss of enamel tissue and increase the physical wear of the teeth. The "CJ OPTIK Flexion Advanced" microscope from Germany served as our objective tool for diagnosing and measuring tooth enamel erosion [9]. The instrument provides high-quality magnification of images which proves necessary for detecting enamel structure changes at a microscopic level. The experiments required the examination of teeth samples that were submerged in various drink solutions with different acidity levels and chemical compositions.



Figure 2. CJ-Optik Flexion Advanced Dental Microscope

During the study, the teeth in the energy drink solution showed significant enamel defects. Not only were there changes in colour, but a significant loss of lustre was also observed. These observations confirm the negative effect of energy drinks on tooth enamel. The teeth which were placed in physiological saline solution maintained their original colour and shine. The observed results indicate that physiological solutions produce minimal effects on tooth enamel thus enabling researchers to study beverage effects on tooth enamel condition [10]. The research established that energy drinks harm tooth enamel through changes in tooth structure and decreased tooth weight. The observed enamel defects together with the minimal 2.27 g mass reduction which represents 7.15% of the original mass confirm the harmful effects of energy drinks. The teeth submerged in physiological solution maintained their structure and shine which showed that this solution had a minimal impact on enamel. The research findings demonstrate the need to understand how energy drinks damage dental health while creating possibilities to study the effects of different beverages on tooth enamel.

Dynamics of the Acid-Base State of Oral Fluid

To evaluate the short-term impact of energy drinks on the acid-base equilibrium of oral fluid, two equivalent samples were established (n = 25 each): an experimental group (regular energy drink consumers) and a control group (non-consumers). The pH of mixed saliva was measured five times: before drinking (T_0), and 15 minutes (T_{15}), 30 minutes (T_{30}), 45 minutes (T_{45}), and 60 minutes (T_{60}) after drinking.

Table 1. Mean pH values ± SEM (n=25 in each group)

Group	T_0	T_{15}	T_{30}	T_{45}	T_{60}
Energy drink consumers	6.68 ± 0.12	5.82 ± 0.14*	5.96 ± 0.12*	6.19 ± 0.01*	6.20 ± 0.13*
Control	6.70 ± 0.31	6.71 ± 0.14	6.70 ± 0.31	6.75 ± 0.01	6.77 ± 0.12

* Differences are significant compared to the control ($p < 0.05$).

The experimental group showed a rapid acid-base balance change in oral fluid after consuming one energy drink which resulted in a pH value decrease from 6.68±0.12 to 5.82±0.14 just 15 minutes later. The pH value decreased significantly from its baseline measurement and the control group's simultaneous reading (Student's t-test; $p < 0.05$). The measured pH value of 5.82 approaches the critical threshold for enamel demineralization (≈ 5.5) which indicates rapid surface hydroxyapatite dissolution and cariogenic process initiation. The salivary buffer system showed signs of recovery after the initial drop because the average pH reached 6.20±0.13 at the 60th minute. The recorded pH value at 6.20±0.13 remained lower than both the baseline measurement and the control sample range (6.70–6.77) according to a two-way ANOVA with repeated measures (group effect: $F = 44.7$; $p < 0.001$). A single energy drink consumption leads to extended oral fluid acidification but individuals who avoid these drinks maintain stable acid-base levels that support enamel remineralization [11].

Clinical and biological interpretation of the results.

The recorded decrease in salivary pH to 5.82±0.14 just 15 minutes after a single consumption of an energy drink indicates a rapid depletion of the main bicarbonate-phosphate buffer of the oral fluid. The normal concentration of HCO_3^- in mixed saliva is maintained by the secretory activity of the ductal part of the salivary glands. However, under the influence of the highly acidic and sugar-saturated environment of an energy drink, the reserve of alkaline ions is consumed, and the rate of their entry does not have time to compensate for the sudden increase in titratable acidity.

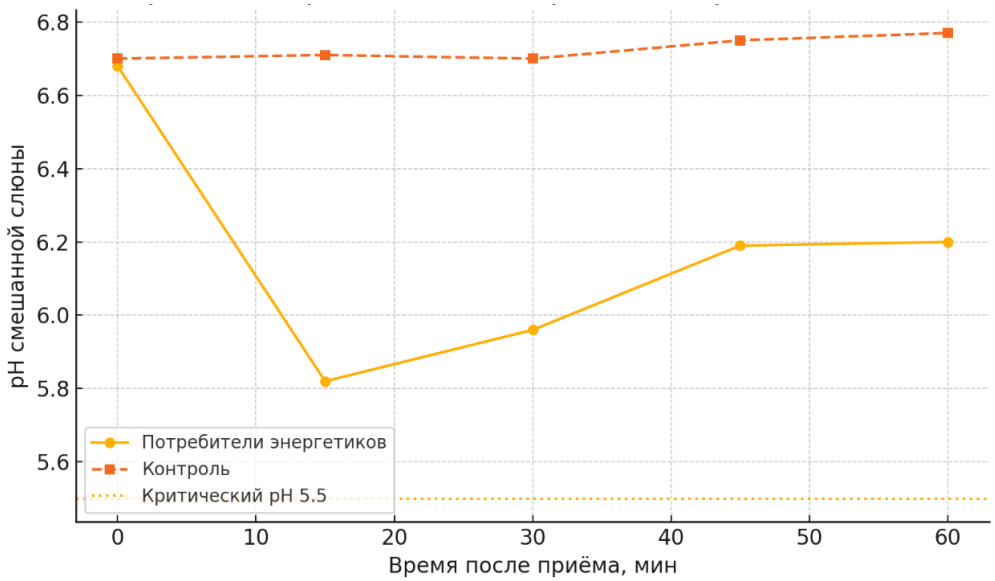


Figure 3. Stefan curve in pH dynamics after taking energy drinks

The "point of zero mineralization" at <5.5 pH defines the critical pH interval where Ca^{2+} and PO_4^{3-} ions in saliva become less active than hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ solubility constant [12]. The initial demineralization process starts when the threshold of <5.5 is reached because calcium and phosphate ions move from enamel surface into the liquid phase. The Stephan curve model describes acid stress episodes through the relationship between salivary pH duration below critical levels and the resulting total enamel mineral loss which increases with longer exposure time [13]. The pH level returned to 6.20±0.13 after 60 minutes because salivary buffers became active again while organic acids diluted through reflexive salivation. The measured value remains below (i) the normal physiological range of 6.7–6.8 for energy drink consumers and (ii) the "remineralizing range" (pH ≥ 6.8) for the control group because saliva becomes supersaturated with Ca^{2+} and PO_4^{3-} while hydroxyapatite solubility decreases.

6. The graph illustrates the change in oral fluid pH over 60 minutes after the consumption of an energy drink by the experimental group compared to a stable control group.

The oral fluid pH of energy drink consumers decreases right after consumption (peak acid formation) before returning to a level below the critical remineralization threshold of 6.8 throughout the 60-minute period. The

control curve demonstrates that students who did not drink the beverage maintained a stable physiological range. The prolonged "acid phase" occurs below a critical pH of 5.5 which demonstrates the strong demineralizing effects of energy drinks.

The environment shows no signs of saturation with fluorapatite and hydroxyapatite after one hour of observation which restricts mineral flow back into the enamel crystalline structure. The clinical cariology perspective shows that the "under-recovered" pH status maintains a continuous risk zone because daily acidic drink consumption extends the time spent below the critical pH ($\sum t < 5.5$) until mineral loss surpasses natural remineralization potential even with proper hygiene practices.

Additional factors that enhance the demineralizing effect of energy drinks include:

1. The high concentration of simple sugars (~11–13 g/100 mL) fuels Streptococcus mutans and Lactobacillus spp., increasing intra-pellicle acidogenesis [14] [15].
2. The drink's low viscosity enables it to spread easily across tooth surfaces while entering the small spaces within dental plaque [16].
3. Caffeine produces a dual effect on salivation by first stimulating then reducing the rate of salivation which extends the time of low buffer capacity [17] [18].

Thus, the recorded acid shift and its incomplete recovery objectively confirm the high cariesogenic danger of regular consumption of energy drinks. In clinical practice, the results emphasize the need to limit the frequency of contact of enamel with an acidic substrate, recommend rinsing with neutral or slightly alkaline solutions ($nahco_3$ 1 %**),** strengthen fluoroprophylaxis to reduce the solubility of dental mineral, and inform young people about the pathogenetic mechanisms and risks associated with these drinks.

Clinical and biological interpretation of pH decrease in oral fluid

The acid-base index of mixed saliva dropped to pH = 5.80 ± 0.14 during the first 15 minutes after consuming an energy drink because the main bicarbonate-phosphate buffer which forms primarily through parotid gland ductal secretion became depleted quickly. The normal Hco_3^- concentration in mixed saliva (15-20 mmol/l) would neutralize external acids within 2-3 minutes but the energy drink's titrated acidity (pH ≈ 2.6–3.2) and sugar content (≈ 11-13 g / 100 ml) deplete the buffer capacity in seconds. The pH decrease happens because the drink contains high titratable acidity between pH 2.5-3.5 and substantial sugar content of 11-13 g per 100 ml which simultaneously: 1. The formation of poorly soluble calcium salts of organic acids decreases saliva's calcium and phosphate ion saturation levels. 2. The acid-causing microflora including Streptococcus mutans and Lactobacillus spp. becomes activated within 5-10 minutes after substrate contact which further decreases biofilm pH. 3. The caffeine and taurine activate alpha-and beta-adrenergic receptors to competitively block saliva secretion thus restricting bicarbonate intake [19].

Critical demineralization threshold

The pH <5.5 zone represents the " zero mineralization point "(dissolution threshold) for hydroxyapatite $Ca_{10}(po_4)_6(OH)_2$. The ionic activity of $Ca2^+$ and $PO3^-$ in the liquid phase becomes less than the product of the solubility of Ksp when the level falls below this point which makes the enamel surface thermodynamically unstable and starts the release of calcium and phosphate into the salivary film [20]. The Stefan curve clinical model shows that the time duration when the pH of the curve stays below the critical line (area under the critical pH curve, AUC-crit) determines the extent of mineral loss: the bigger the AUC-crit area the more severe the demineralization [21].

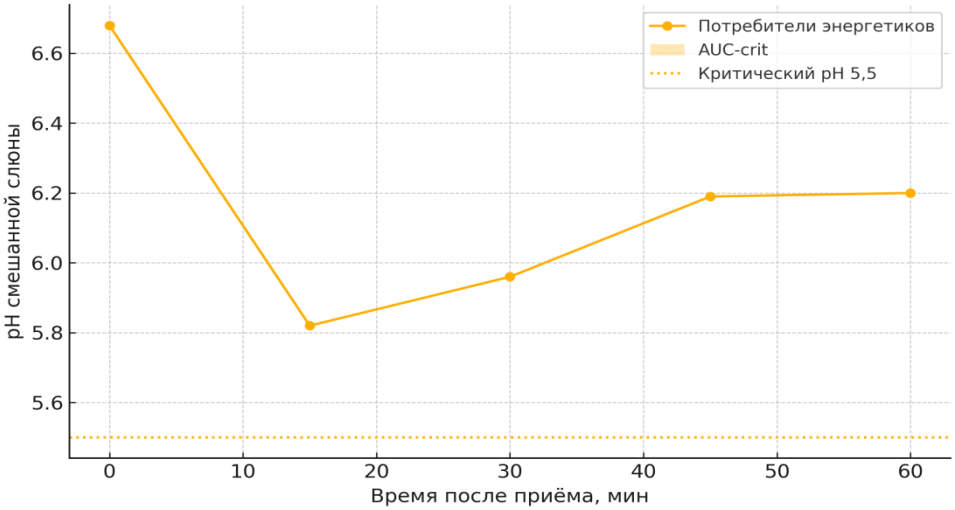


Figure 4. Stefan curve with the selection of the critical zone AUC-crit

The diagram shows the dynamics of oral fluid pH in energy drink consumers and visualizes the area under the critical pH value = 5.5, corresponding to the period of demineralization risk. The shaded area (AUC-crit) correlates with the total mineral loss of enamel.

Consequences of a short-term acid attack.

- The peripheral enamel crystals dissolve to create subclinical foci of increased porosity (white spot lesions) in the surface layer at depths of 10–50 µm.
- The sugar substrate of the energy drink promotes Streptococcus mutans and Lactobacillus spp. metabolism while their biofilm becomes activated through additional extracellular polysaccharide deposition which results in plaque pH levels dropping to 4.5–5.0.
- The β-adrenergic phase of caffeine stimulation leads to decreased salivation rates which results in reduced buffer reserves and extended pH recovery times

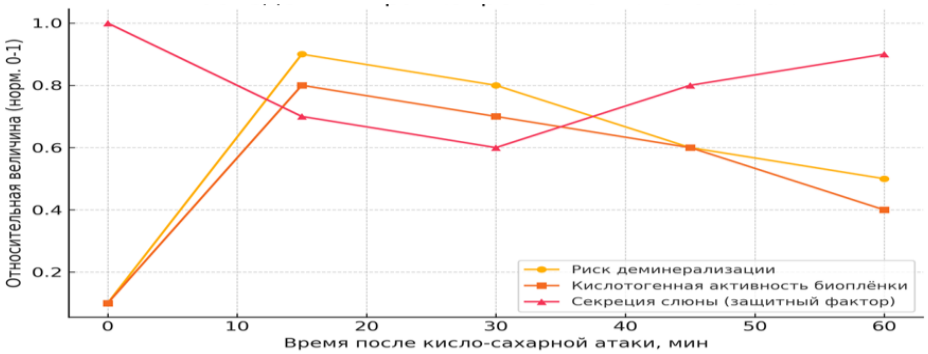


Figure 5. Consequences of a short-term acid attack

The diagram shows how three essential parameters change during the first hour after consuming an acidic drink: the risk of enamel demineralization rises while plaque acidogenic activity increases and salivation decreases as a buffer factor. The values are presented in relative units for visual comparison.

Partial recovery to pH = 6.20 ± 0.13.

The pH level increases after 60 minutes because of two factors: the return of saliva production through parasympathetic stimulation and the combination of organic acid dilution from swallowing movements and bicarbonate intake from blood circulation. The pH value of 6.2 persists because it falls below the optimal remineralizing range of pH 6.8 for saliva saturation with calcium phosphate and it remains below both the initial physiological range of 6.7-6.8 and the control range of 6.70–6.77. The saliva remains unsaturated with hydroxy-and fluorapatite which results in mineral dissolution rates exceeding their reverse deposition rates thus maintaining a high caries risk [22].

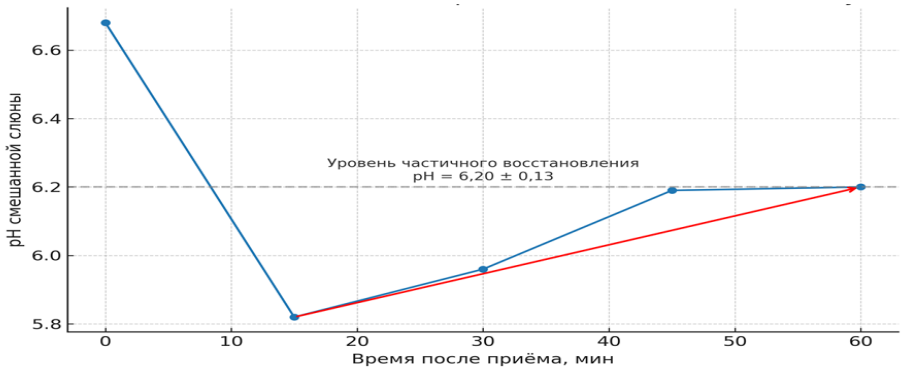


Figure 6. Partial pH reduction to 6.2.

The graph shows the dynamics of oral fluid pH in energy drink consumers and shows partial recovery of the saliva buffer system by the 60th minute (pH ≈ 6.20). The AUC-crit value increases with each portion of an energy drink until it reaches a mineral deficit level. The salivary remineralization potential becomes insufficient to compensate for losses when a person consumes two or more servings of these drinks daily. The recommended approach to manage such drinks involves either reducing their contact with enamel or using buffer rinses (1) and drinking water and chewing xylitol gum to speed up pH increase [23]. The preventive application of fluoride- and calcium-phosphate-containing agents (such as Ca/PO_4 bioactive glass and CPP-ACP) remains important because they reduce the critical pH to 4.5–4.8 and boost enamel resistance against acid attacks [24].

Thus, the recorded decrease in pH to 5.8 and its incomplete recovery to 6.2 demonstrate that even a short-term episode of energy drink consumption creates conditions for the demineralization of enamel, and the recovery window for the salivary buffer capacity is insufficient for complete remineralizing repair. This pathophysiological rationale highlights the persistent risk of early caries development and underscores the need for regulated preventive measures.

DISCUSSIONS

Ratthapong Worawongvasu (2015) conducted a study using scanning electron microscopy (SEM) to examine tooth enamel which revealed substantial surface changes including enlarged pores and disrupted enamel prisms structure [24]. The teeth showed a substantial reduction in enamel calcium and phosphorus ion concentrations following exposure to acidic sports and energy drinks. The elevated oxygen levels together with reduced calcium ion concentrations verify that these beverages cause hydroxyapatite breakdown into its basic elements. Silva JG (2021) showed that energy and sports drinks decrease tooth enamel hardness through their erosive action. The evaluation of enamel surface roughness after energy drink exposure revealed higher roughness measurements. Sports drinks resulted in less enamel structural damage compared to other acidic carbonated beverages [25].

The research by von Fraunhofer JA and Rogers MM (2005) involved submerging enamel blocks in different beverages for 14 days which revealed that all tested drinks led to enamel dissolution while flavored beverages and commercial lemonades and energy/sports drinks caused the most severe damage. The research established that sports drinks lead to enamel demineralization and shorter exposure times will minimize the extent of damage [26]. E A Abou Neel (2016) discovered that regular energy drink consumption leads to dental caries development. The researcher found that energy drinks contain two major cariogenic factors which are their acidic nature and high sugar content but he could not prove a definitive link between energy drinks and carious lesion formation. The tested drinks showed pH values between 4.46 and 2.38 which fell below the critical pH threshold of 5.5 for enamel demineralization [27]. Another study highlights how energy drinks could potentially cause enamel erosion. The extent of enamel demineralization depends on the amount of calcium and phosphate ions found in oral fluids according to his research. In vitro experiments show that insufficient hydroxyapatite and fluorapatite saturation in oral fluids speeds up erosive processes which result in permanent tooth surface deterioration [28].

FUTURE RECOMMENDATIONS

Based on the findings of this study, the following recommendations are proposed for future research and clinical practice to address the dental health risks associated with energy drink consumption:

Conduct Long-Term Epidemiological Studies

It is crucial to move beyond short-term observations and initiate extensive epidemiological studies to investigate the long-term, cumulative effects of regular energy drink consumption on oral health. These studies should track changes in the incidence of dental caries and erosion over several years, particularly in adolescent and young adult populations [29] [30].

Investigate the Impact on Different Demographics

While this study focused on students, future research should explore the effects of energy drinks on other active consumer groups, such as professional athletes and manual laborers. This will provide a more comprehensive understanding of the risks across various lifestyles and age groups [31].

Evaluate Preventive Strategies

Further clinical trials are needed to evaluate the efficacy of specific preventive measures. This includes assessing the effectiveness of different types of oral rinses (e.g., sodium bicarbonate, fluoride), chewing gums (e.g., xylitol), and topical fluoride applications in mitigating the acidogenic and erosive effects of energy drinks [32].

Analyze the Role of Specific Ingredients

A more detailed chemical analysis of various energy drink brands is warranted to determine the specific contribution of ingredients like citric acid, phosphoric acid, and different types of sugars to dental demineralization. This would help in formulating targeted public health warnings and potentially influencing product reformulation [33].

Develop Targeted Public Health Campaigns

The results of this study should be used to inform the development of educational campaigns aimed at raising public awareness, especially among young people, about the specific pathogenic mechanisms and dental health risks associated with energy drinks. These campaigns should provide clear, evidence-based recommendations for safer consumption habits and alternatives [34].

CONCLUSION

Drawing a line between trend and threat, the widespread consumption of energy drinks poses a silent yet significant risk to oral health. Sugar-rich formulations foster bacterial proliferation in the oral cavity, while their consistently low pH values contribute to enamel erosion and heightened tooth sensitivity. The observed reduction in oral pH to 5.8 with only a limited rebound to 6.2 illustrates how even brief exposure can create an environment conducive to enamel demineralization. Compounded by the insufficient restorative capacity of the salivary buffer, this creates a persistent pathophysiological risk for early carious lesions.

These findings highlight the urgent need for public health initiatives to educate consumers, especially

adolescents about the dental consequences of energy drink consumption. Furthermore, the evidence reinforces the importance of implementing standardized preventive strategies within dental practice and public policy.

Looking ahead, targeted clinical and experimental research is essential to further elucidate how energy drinks alter the acid-base dynamics of oral fluids and impact the integrity of tooth structures. Such studies will not only enhance our understanding of their pathogenic potential but also support the development of evidence-based guidelines to mitigate their dental risks.

DECLARATION

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Ethical Approval: The Institutional Review Board (IRB) of the Osh State University, Osh City, Kyrgyz Republic approved the study. Oral concent were taken while collecting data and permission by IRB was waived since the data were obtained anonymously, with no patient characteristics identified.

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ORIGINAL ARTICALE

LASER DENTISTRY:ADVANCEMENTS, CLINICAL APPLICATIONS AND FUTURE PROSPECTS

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ABSTRACT

Laser technology has changed dental practice through accuracy, minimal invasiveness, and greater patient comfort. It is applied in different procedures, including the removal of cavities, reshaping the gums, and the treatment of periodontal disease. Advantages include less pain, quicker healing, and reduced use of anesthesia. Recent advances in technology, such as erbium and diode lasers, have enhanced the outcome of treating hard and soft tissues. Though there are challenges like being expensive and requiring special training, the future of laser dentistry looks bright, with a lot of possibilities for further application in preventive treatments, early disease diagnosis, and more effective treatments, leading to improved patient experiences and improved quality of care.

Keywords: Hard tissue lasers; Lasers; Soft tissue lasers.

INTRODUCTION

The word “laser” is an acronym for “Light Amplification by Stimulated Emission of Radiation.” Technology produces intense beams of light that can be used to precisely cut, mold, or dissect tissue. Laser therapy, a key component of modern dental practice, has its origins in hypotheses proposed by Albert Einstein in 1917 and was experimentally confirmed by Theodore Maiman in 1960.

Although lasers were introduced into medicine during the mid-20th century, their use in dentistry gained popularity in the 1980s, with broader application becoming feasible in the 1990s after advancements improved their accuracy and reduced patient discomfort[1]. Since then, laser technology has profoundly transformed dentistry, enabling precise, effective, and non-invasive treatments for a wide range of oral conditions. It has evolved significantly, leading to numerous applications in both therapeutic and diagnostic dentistry[2]. The ability of laser beams to stimulate cells at a biological level has allowed their integration across all branches of dentistry.

Today, laser treatments are valued for their ease of use, effectiveness, patient comfort, and improved performance compared to traditional methods. Thus, this review comprehensively explores the latest

advancements in laser technologies, highlights current and emerging clinical applications, and examines future trends that are poised to shape the trajectory of laser dentistry.

Principles of Laser Technology in Dentistry

Lasers work by changing light energy into heat by means of photothermal reactions. The basic elements of a laser system are a gain medium (solid-state, gas, or liquid), a pumping source (electrical or optical), and an optical feedback cavity or resonator. The pumping mechanism excites photons to generate energy, and the optical resonator, constructed of parallel mirrors, multiples this energy into a focused beam. Laser light is distinguished by being monochromatic, coherent, and collimated [3, 4].

The interaction between laser light and mucosal tissues includes processes like absorption, transmission, reflection, and scattering. As target tissues absorb laser energy, it increases the temperature, creating photochemical effects according to the water content of the tissues. At temperatures up to 100°C, ablation is produced, so water in the tissues vaporises; those over 200°C may cause dehydration and carbonisation. The precise wavelength of the laser, delivery system (e.g., fiber optic cable, hollow waveguide, articulated arm), and cooling system (water or air) are essential for controlling interaction and avoiding thermal damage. Knowledge of these principles enables clinicians to choose the correct laser for the intended treatment effect [5].

Types of Lasers

Dental lasers are categorized in accordance with their lasing medium, wavelengths, tissue appropriateness, and active medium type (Figure 1). The various types of lasers work at different wavelengths, each of which is appropriate for a particular dental treatment.

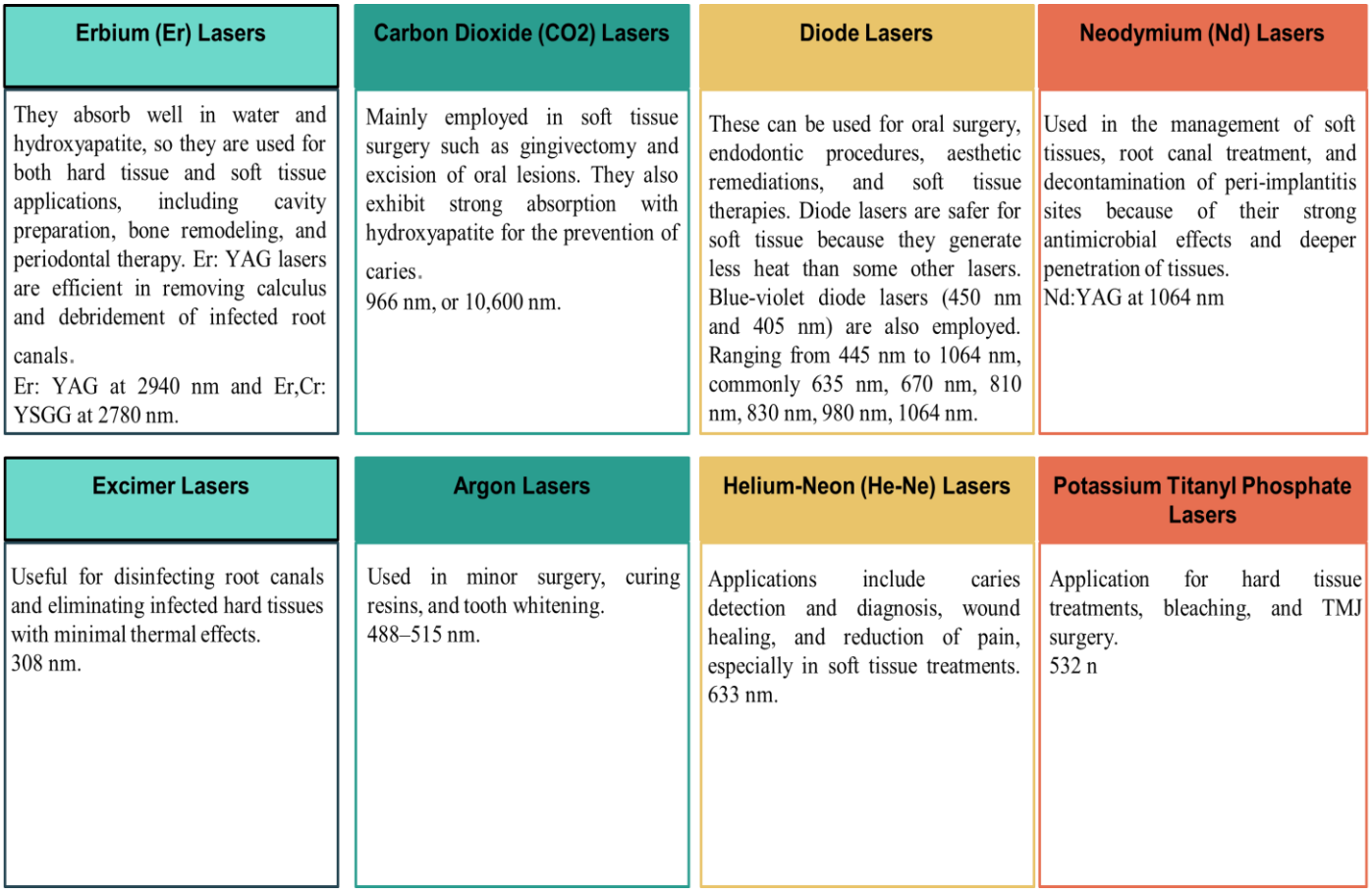


Figure 1. Types of Lasers.

Technological Advancements in Lasers

Advances in laser technology over the recent past have greatly enhanced the effectiveness and safety of laser-assisted dental treatments. There has been a main emphasis on the integration of lasers with digital dentistry, merging them with 3D scanning, CAD/CAM systems, and artificial intelligence (AI) to augment accuracy, efficiency, and customized treatment planning. One of the notable technological breakthroughs is variable square pulse (VSP)

Technology offers practitioners more control over the and degree of laser treatment beyond what is possible with regular scalpels or drills[6]. Building on this innovation, the quantum square pulse (QSP) Mode is an exclusive mode that breaks up a longer laser pulse into multiple short "pulse quanta"[7]. This efficiently provides short, high-finesse pulses, minimizing unwanted effects such as scattering in debris clouds in hard tissue ablation, resulting in sharper, cleaner margins and increased bond strength. It also accelerates the speed of cavity preparation by up to 1.75 times and reduces noise levels, providing greater patient comfort. The precision of laser treatments is further enhanced by digitally controlled handpieces (e.g., Fotona's X-Runner®), which enable automatic laser beam guidance with adjustable spot size and shape, enhancing accuracy and speed, particularly for large hard and soft tissue removal and surface treatments[8]. The X-Runner is capable of operating in high-density scanning (HDS) mode for even smoother finishes and deeper ablation. At the forefront of laser innovation is the LightWalker system, an extensive dental laser system from Fotona providing pain-reducing treatment of soft and hard tissues, accelerated healing, bloodless and sutureless surgery of soft tissues, efficient periodontal treatments, and endodontic and cosmetic treatments in safety. It includes a green pilot beam for better visibility during surgery and a new straight-tip handpiece to support superior ergonomics. Beyond cutting and ablating tissue, lasers are also playing a vital role in therapeutic and regenerative applications. Photobiomodulation (PBM), formerly known as low-level laser therapy/LLLT, utilizes low-level lasers to drive cellular activity without producing notable heat, fostering tissue repair, pain relief, and inflammation regulation[9]. It is especially valuable for post-surgical recuperation, bone remodelling, and treating ailments such as mucositis and temporomandibular joint disease. In addition, Photodynamic therapy (PDT) uses laser-activated dyes to specifically kill pathogens and undesirable eukaryotic cells in infected tissues, providing a non-invasive treatment for oral infections and lesions, such as precancerous and cancerous conditions[10] Together, these technologies have the goal of making dental procedures quicker, less intrusive, more comfortable, and with better results.

Clinical Applications

Laser technology is significant in the field of dentistry. It enhances the performance of dental interventions on both hard and soft tissues with greater control and accuracy compared to conventional techniques[11]. Lasers gained popularity in dental procedures during the 1990s due to their advantages, such as high precision and minimal pain following surgery[12]. Lasers can make intensityp recise incisions, inflicting less trauma to the surrounding areas and enabling faster healing and less swelling [11]. They also minimize the requirement of local anaesthetic in certain procedures, increasing comfort for patients by eliminating the vibration and noise of conventional dental equipment. In soft and hard tissue surgeries, lasers minimize blood loss and pain, enhancing the patient's experience [13]. Lasers also maintain the surgical field free from blood and dampness, reducing the post-operative risk of infection [12]. These advantages render laser technology a superior alternative to conventional techniques for most dental procedures, more efficient and comfortable in contemporary dentistry.

Lasers in Soft Tissue Surgery

Soft tissue lasers in surgery are gaining widespread use because of their advantages over traditional surgical methods. Dental lasers act upon soft tissues owing to the selective absorption of their wavelength by hemoglobin and water. Lasers are ideal for cutting, vaporizing, and coagulating soft tissues, hence providing adequate control of bleeding with minimal pain post-surgery [13].The laser beam cuts, coagulates, and precisely removes soft gingival tissues. Controlled energy minimizes bleeding through the congealing of blood vessels, and this reduces healing time. Ablation of diseased tissue and protection of the surrounding tissues are ensured by precise cutting edges.

Lasers applied in soft tissue surgery can be utilized in operations such as gingivectomies, frenectomies, excision of mucosal lesions, and gingival tissue reshaping. In a gingivectomy, the laser can extirpate excessive hypertrophied gingival tissue with little bleeding since it can instantly coagulate small vessels. The operation is also less painful for the patient, uses less local anesthesia, and produces faster healing[14]. One of the principal benefits of soft-tissue laser surgery is quicker healing. The laser cauterizes nerve endings and blood vessels as it cuts, virtually eliminating post-surgery pain and infection risk. Patients who have undergone treatment with laser, unlike traditional surgery, suffer fewer complications and recover quickly[14].

Lasers in Dentistry Hard Tissue Surgery

Hard tissue lasers, especially erbium-based lasers such as Er: YAG and Er,Cr: YSGG, have been very promising in dental procedures concerned with bone and tooth structures. Erbium-based lasers are more effective in treatments like the removal of dental caries, preparation of cavities, gingivectomies, bone lesions, and periodontal surgery[15,16]. Er: YAG laser, at 2940 nm, is highly absorbed by water and therefore optimum for accurate and minimally invasive soft tissue and hard tissue cutting [17]. The lasers, such as the Nd: YAG, with a wavelength of 1064 nm, travel deeper and are best used for

decontamination of subgingival tissues because they have a high preference for pigmented tissues and hemoglobin[13]. Moreover, laser dosimetry, encompassing factors like spot size, energy output, and wavelength, plays an important role in deciding the interaction of the laser with tissues and achieving optimal outcomes[16,18,19]. Some clinical applications of hard tissue lasers are dental fissure sealing, treatment of caries, endodontic disinfection, and even tooth whitening with the use of chemical agents [15,16,18-20].

Advantages of the Use of Lasers in Dentistry

Dental lasers possess several significant benefits compared to traditional equipment. One of the most important advantages is pain reduction during treatment, which makes procedures more tolerable for patients. Lasers also provide perfect hemostasis, maintaining a dry field for surgery, which increases control and visualization during surgery [15]. Their antimicrobial nature enables decontamination of the surgical site, greatly diminishing the chance of infection after surgery [18,19]. Additionally, laser procedures are generally less invasive, resulting in quicker recovery and reduced swelling and bleeding, which increases overall patient satisfaction [20]. In endodontic and cosmetic treatments, lasers enhance sealant retention, ease access to the canals, and enable efficient disinfection, all contributing to clinical effectiveness as well as aesthetic performance [18,20.]

Disadvantages of Laser Technology

While lasers have their strengths, they have significant disadvantages that can influence their widespread use. The prohibitive expense of the equipment is also a significant impediment, as sophisticated units such as erbium and CO_2 lasers range from USD 10,000 to 80,000, excluding service or calibration costs [21] In addition, there is specialized training involved to operate dental lasers safely and effectively, which may include pricey certification courses and a steep learning curve [22]. These aspects prevent small or solo practices from investing in the technology unless there is a high volume of patients[21]. Even then, the cost of treatment per case is higher with the use of lasers, and this can be an off-put for patients, particularly in low- and middle-income areas[20].

Limitations of Laser Application in Dental Practice

Several clinical limitations also limit the extensive use of lasers in dentistry. Lasers are not practical for the removal of all types of restorative materials, such as amalgam or ceramic crowns, nor are they always efficient for treating extremely deep caries or severe tooth decay[18,23]. In bone operations or extensive periodontal treatments, their short depth of penetration may not be consistent or effective enough [24]. Additionally, laser procedures are occasionally slower than conventional techniques, particularly in cavity preparation, as observed by Coluzzi et al., which impacts clinic efficiency[25]. Another essential issue is the potential for thermal damage when improperly using the laser; excessive power or improper wavelengths can result in permanent tissue damage, especially with prolonged or extensive procedures[26].Last but not least, though lasers augment oral disinfection, particularly against periodontal microorganisms, this advantage has not yet fully replaced traditional chemical agents and mechanical debridement[20].

Future Prospects and Emerging Trends

The future of laser dentistry is bright, with the constant development of technology and research[27]. With technology becoming less costly and more readily available, one can only expect that there will be increasingly more dental clinicians who use laser-based treatments. New laser dentistry trends are convergence with digital dentistry: Using lasers as part of digital tools, like 3D scanning and CAD/CAM (Computer-Aided Design and Computer-Aided Manufacturing) systems, can be used for more efficient and accurate treatments. Scientists are investigating the creation of new lasers with various wavelengths to enhance their application in dental treatments. These advances will allow for more versatile treatments with even greater precision and efficiency. More comfort for the patient: As laser technology advances, treatments will become more comfortable for patients. As technology improves, lasers in the future will be quicker, less invasive, and even shorter in length and less painful.

CONCLUSION

Laser technology has revolutionized the field of dentistry, providing unmatched precision, reduced invasiveness, and improved patient comfort. From daily cavity extraction and gum recontouring to advanced treatment of periodontal diseases, implant placement, and sophisticated diagnostic procedures, lasers offer new ways to address typical dental issues. Although there are still issues, mainly in relation to the high capital expense of equipment, the requirement for specialized training, and standardization of procedures, continued developments in laser technology are constantly resolving these hurdles. The future of laser dentistry is highly optimistic, with studies concentrated on widening the scope of conditions that can be treated, enhancing accuracy, and combining with digital systems and artificial intelligence. As technology advances and becomes more mainstream, lasers will increasingly be at the forefront of delivering dental care, establishing new benchmarks for accuracy, patient comfort, and overall success of treatments in oral health. The revolutionary potential of lasers is why they are so crucial to contemporary dental practice, with the potential to deliver safer, more predictable, and functionally and aesthetically better results for patients.

Seethalakshmi Chiranjeevi, Pooraninagalakshmi J, Navneet Gurm, D G Madhuri,Anitha Subbappa Designation, Preeti Patil Designation Laser Dentistry: Advancements, Clinical Applications and Future Prospects.Bulletin of Stomatology and Maxillofacial Surgery.2025;21(8).154-158 doi:10.58240/1829006X-2025.21.8-154

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Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

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REVIEW ARTICLE

UNDERSTANDING, PREVENTING, AND MANAGING INITIAL BONE REMODELING AROUND DENTAL IMPLANTS: A REVIEW OF CURRENT EVIDENCE

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ABSTRACT

Initial bone remodeling (IBR) around dental implants is a multifactorial process influencing long-term success. While historical criteria allowed up to 2 mm marginal bone loss in the first year, recent evidence indicates that resorption >0.5 mm within 6–12 months significantly increases long-term peri-implantitis risk. IBR, defined as dimensional bone changes from implant placement through one year of loading, is non-infective in origin but may predispose to bacterial colonization if implant treated surface becomes exposed.

Key anatomical determinants include bone density, crestal bone width, and supracrestal tissue height. High-density cortical bone, insufficient buccal/palatal bone envelope, or thin supracrestal mucosa correlate with greater marginal bone resorption. Implant characteristics such as internal conical connections, platform switching, optimized crest module geometry, and favorable transmucosal profiles can reduce microbial leakage, optimize load distribution, and promote long-term crestal bone stability.

A critical surgical factor is apico-coronal placement of the implant according to mucosal vertical thickness, ensuring bone remodeling during supracrestal tissue adhesion occurs coronal to the platform. Depth varies with tissue phenotype and requires precise assessment. Additional measures include controlling intraosseous temperature and avoiding excessive insertion torque to limit cortical compression.

In the prosthetic phase, risk factors include repeated abutment dis/reconnections, abutment height <2 mm in bone-level implants, excess cement, and excessively convex emergence profiles. Mitigation strategies involve “one abutment–one time” protocols or the use of tissue-level implants, screw-retained or cement-free retention, abutments >2 mm in height, and emergence profiles that promote soft tissue stability and facilitate plaque control.

Integrating biology-driven site preparation, accurate apico-coronal positioning, selection of macro- and micro-designs with documented bone-preserving properties, and evidence-based prosthetic protocols can minimize IBR. This multidisciplinary approach shifts the objective from accepting early marginal bone loss to its prevention, improving the predictability, longevity, and biological stability of implant-supported rehabilitations.

Keywords*:* dental implant, implant therapy, marginal bone levels, implant functional loading

INTRODUCTION

The stability of marginal bone levels has always been considered among the key parameters for assessing the long-term success of implant therapy. Traditionally, radiographic marginal bone loss of up to 1.5–2.0 mm during the first year of functional loading, followed by a maximum annual loss of 0.2 mm, was widely accepted as an indicator for implant success[1-4]. However, advances in implant design, surface modification, prosthetic connections, and clinical protocols have significantly improved outcomes in implant dentistry, suggesting that these traditional thresholds may no longer represent the most reliable criteria for success in contemporary practice.

Recent evidence highlights the critical role of maintaining stable marginal bone levels during the healing phase after implant placement and throughout the first year of functional loading.

Galindo-Moreno et al. identified peri-implant bone loss exceeding 0.44 mm at six months post-loading as a predictor of progressive bone loss over time[5]. In a 10-year prospective study, Windael et al. reported that marginal bone resorption ≥ 0.5 mm after one year of function was associated with a 5.43-fold increase in the odds of developing peri-implantitis, with the risk further amplified when early bone loss exceeded 1–2 mm or occurred in combination with smoking and/or a history of periodontitis[6] (Fig. 1). More recently, a radiographic marginal bone loss threshold of 0.5 mm at six months following prosthetic loading has been proposed as a potential objective criterion for defining the success of osseointegrated implants[7].

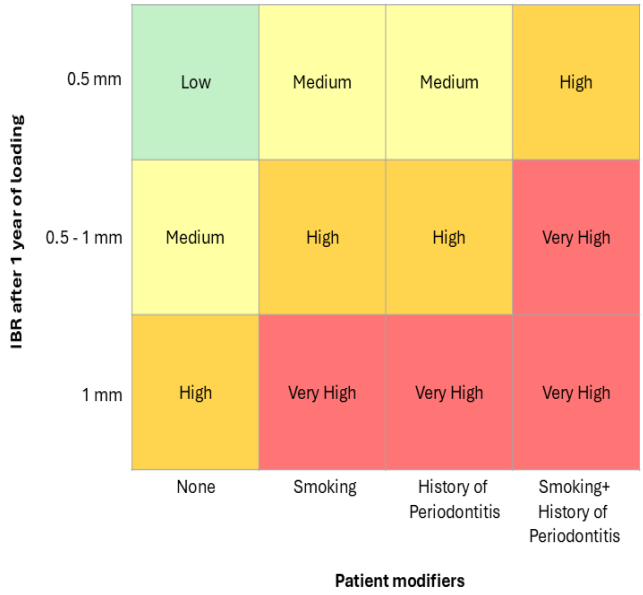


Figure 1. Risk matrix for peri-implantitis likelihood according to Initial Bone Remodeling (IBR) after 1 year and patient-related modifiers (smoking and history of periodontitis).

As the prevalence of peri-implantitis is quite high (10.3%) also in pristine bone[15], representing the major cause of late implant failure, its prevention is crucial to enhance long-term success of implant therapy. Nowadays, a better knowledge of the biological principles underlying peri-implant hard and soft tissue healing, together with the selection of appropriate implant features and sound clinical protocols, may permit to minimize and manage the initial breakdown of the bone-implant interface at crestal level.

The present paper aims to summarize the possible causes of IBR and suggest a comprehensive clinical strategy to minimize initial marginal bone resorption around dental implants. In particular, the influence on IBR of site-specific characteristics, macro- and micro-implant design, surgical protocols, and prosthetic procedures will be reviewed.

1. SITE-SPECIFIC CHARACTERISTICS

1.1 Bone Density

Bone architecture at planned implant site should be carefully evaluated and surgical technique has to be adapted to the anatomical conditions. Cortical bone provides mechanical support to the implant and allows to obtain high primary stability, whilst trabecular bone is the main source for mesenchymal progenitor cells and blood supply necessary for osseointegration. These two bone components present distinct mechanical and biological properties, heavily influencing their response to surgical trauma and functional loading. Among them, mean Young's modulus of trabecular bone (10.4 ± 3.5 GPa) was demonstrated to be significantly lower than that of cortical bone (18.6 ± 3.5 GPa)[16], indicating a different elastic response of the two tissues. This factor is reflected by their biological response: cortical bone, due to its low deformation properties, is much more susceptible than trabecular bone to stress and strain application. At crestal level, where cortical is usually the main bone component, excessive stress and strain may create microfractures promoting osteocyte apoptosis and subsequent bone resorption. Apoptotic osteocytes play a crucial role in osteoclastogenesis through a direct pathway (production of chemotactic factors recruiting osteoclasts and increasing of RANKL levels)[17]. This biological mechanism is also amplified by the fact that areas with apoptotic osteocytes do not produce osteoclast inhibitory signals[18]. Moreover, limited blood supply and poor cellularity typical of cortical bone reduce the availability of osteogenetic cells in the bone remodeling area. In some situations, the minimal density of osteoblastic cells necessary for bone formation may not be reached, creating areas where only bone resorption can occur[19].

Therefore, all clinical procedures should be always conducted with the aim to limit surgical trauma and avoid

occlusal overload to preserve cortical bone and prevent IBL. In particular, when high-density bone is present at implant site, special attention should be paid in surgical and prosthetic planning.

1.2 Bone Crest Width

Horizontal dimension of the edentulous bone crest plays a pivotal role on peri-implant bone stability. An adequate bone envelope surrounding implant at placement may effectively prevent IBR by counteracting the action of the various factors which negatively influence the stability of peri-implant bone levels. Nonetheless, there is no agreement in the literature on the minimal buccal and palatal bone thickness necessary to preserve peri-implant bone after implant placement. Belser and co-workers suggested to maintain at least 1 mm of buccal bone at implant positioning[20], Spray et al. recommended buccal plate thickness ≥1.8 mm[21], other studies suggested a buccal bone envelope ≥2.0 mm[22-24] or even ≥2.5 mm[25]. Opposite results come from a prospective study by Mehreb and co-workers, reporting stability of marginal bone levels also for initially thin (<1 mm) buccal plates[26]. However, the majority of these studies are narrative reviews, expert opinions or investigations conducted with questionable methodology and/or small sample size. Recently, a multi-centre prospective study investigated the influence of buccal and palatal bone thickness at the time of implant placement on horizontal and vertical IBR during the submerged healing period, with a strict control of the possible confounding factors[27]. Results suggest that bone envelope >2 mm on the buccal side and >1 mm on the palatal side may effectively prevent peri-implant vertical bone resorption following surgical trauma, avoiding early implant surface exposure. These findings are clinically relevant, as a previous study demonstrated that the presence of a buccal bone dehiscence at second stage surgery is significantly correlated with more apically located buccal bone level at 10 years[28].

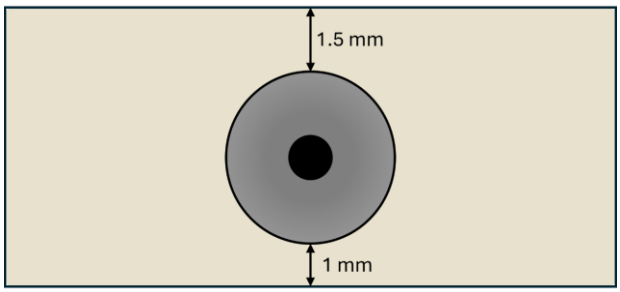


Figure 2. Schematic representation of minimum crestal bone width requirements for long-term peri-implant stability.

A buccal bone thickness >1.5 mm and a palatal/ lingual bone thickness >1.0 mm are associated with reduced risk of IBR and implant surface exposure.
Even if available data still do not support sufficient evidence to define precise thresholds, a rational choice of implant diameter eventually coupled with regenerative procedures should be planned to obtain an adequate peri-implant bone envelope helping to maintain marginal bone stability and obtain optimal aesthetic outcomes[29] (Fig. 2).

1.3 Supracrestal Tissue Height

Biological width is a histologic concept which has been described around natural teeth and may be defined as the physiological and stable vertical space extended from the alveolar crest to the gingival margin, including sulcular epithelium, junctional epithelium and connective tissue attachment[30]. The traditional term “biological width” has recently been replaced by the term “supracrestal tissue attachment”[31]. Similarly, the biological width around dental implants has been redefined as “supracrestal tissue height” (STH)[32], while the process of its establishment around the implant is more recently referred to as “supracrestal tissue adhesion” (STAd)[33]. Peri-implant supracrestal tissue height is the vertical dimension of the soft tissue surrounding an implant from the crestal bone to the mucosal margin. Specifically, in corono-apical direction, STH includes: 1- the sulcular epithelium between the peri-implant mucosal margin and the most coronal point of junctional epithelium; 2- the junctional epithelium; 3- the supracrestal connective tissue between the most apical point of the junctional epithelium and the first bone-to-implant contact[34]. Histologic studies in humans indicated that vertical dimension of STH around two-piece implants ranged between 1.8 and 3.6 mm, being stable and mature after an 8-week healing period[35,36]. Tissue-level implants presented a smaller mean STH (about 2.5 mm): this difference was determined by a variation in the mean vertical dimension of supracrestal connective tissue (1.24 mm for tissue-level versus 1.87 mm for bone-level implants), with the epithelial portion presenting the same dimension[35].

Based upon these premises, initial mucosal dimensions should be carefully evaluated as they could significantly influence IBR during STAd. Berglundh and Lindhe (1996) demonstrated in an animal model that, in presence of thin mucosa, STAd consistently included marginal bone resorption to allow the establishment of a stable soft tissue attachment[37]. Linkevicius and co-workers confirmed these preliminary findings with numerous clinical studies on bone-level implants, showing that the presence of thin mucosa (≤2 mm vertical thickness) at the time of implant placement is significantly correlated with the development of crestal bone loss during STAd[38-40].

Further supporting this concept, recent studies have shown that during STAd, tissue-level implants also exhibit greater IBR at sites with thin mucosa (≤ 2.5 mm vertical thickness) compared with sites with medium or thick mucosa, prior to crown delivery and prosthetic loading[41,42]. Therefore, adequate clinical surgical and prosthetic strategies are required to limit and, possibly, overcome this problem.

2. IMPLANT CHARACTERISTICS

2.1 Implant-Abutment Connection

In two-piece implants, IBR is influenced by the presence of a micro-gap at the implant-abutment interface[43]. This internal space of variable dimensions is rapidly colonized by bacteria after abutment connection[44], determining a local inflammatory reaction characterized by connective tissue infiltration by neutrophils, lymphocytes, macrophages and plasma cells (Fig. 3). This infiltrated connective tissue (ICT) surrounds three-dimensionally the implant-abutment junction and, in external hex implants, extends about 1.5 mm high and 0.5 mm wide from the micro-gap[45]. ICT leads to marginal bone resorption within four weeks from the exposure of the implant-abutment junction to the oral cavity[46].

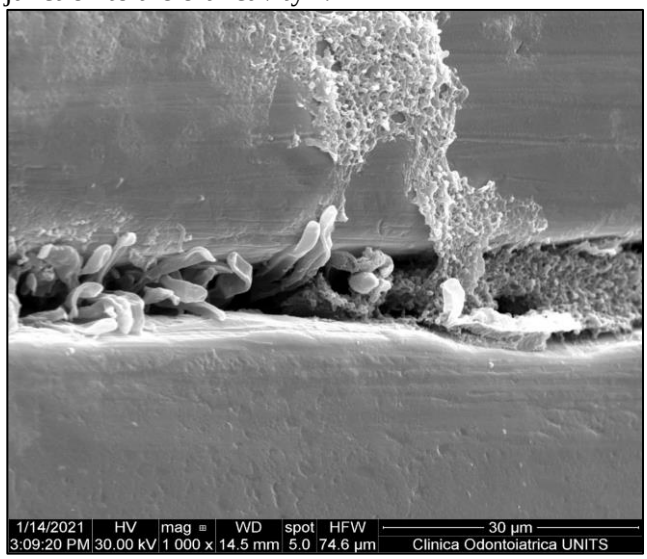


Figure 3 Microscopic image of the implant–abutment interface showing the microgap and the presence of bacterial infiltrate.

Mean micro-gap dimension varies among the different connection types, being significantly greater in external hex connections (10-50 µm) than in internal connections (<10 µm)[47]. The consequence is that crestal bone levels are better maintained in the short to medium term when internal connections are adopted. Furthermore, marginal bone loss around implants with internal, conical connections, is significantly lower than around implants with internal, non-conical connections[48]. An additional strategy to preserve peri-implant bone level is to increase the distance from the micro-gap (with the surrounding ICT) to the crestal bone, with the aim to reduce marginal bone resorption. This concept, named platform switching, was proposed by Gardner and Lazzara in the early 2000's[49,50], and implies the use of an abutment narrower than the implant platform, with the resulting mismatch determining a greater horizontal distance between the bacterial leakage originating from the micro-gap and the crestal bone. The clinical effectiveness of platform-switching design in the limitation of crestal bone loss around two-piece implants was subsequently demonstrated by numerous studies both for equicrestal and subcrestal placement[51-53]. However, a meta-analysis by Atieh and co-workers highlighted that the amount of marginal bone resorption is inversely correlated to the extent of implant-abutment mismatch and, particularly, that a difference ≥0.4 mm between implant and abutment diameters is needed to minimize marginal bone resorption[54].

Implant-abutment connection mechanical stability is another important factor influencing IBR. The application of functional loading may lead to elastic deformation of implant-abutment interface, enlarging micro-gap and allowing fluid infiltration into the inner part of the implant. This fluid, containing high concentrations of bacteria, endotoxins and acids, is pumped by cyclical opening and closing of the microgap, contaminating the surrounding peri-implant tissue[55,56]. Moreover, it was demonstrated that micro-gap dimension increases after the application of cycling loading (> 200.000 cycles) due to wear of metal surfaces[57]. As a result of this degradation, titanium particles are a common finding in soft and hard peri-implant tissue biopsies and their role in the pathogenesis of peri-implant diseases is currently under investigation[58,59]. Numerous comparative studies demonstrated that conical connections showed no or reduced micro-gap enlargement during dynamic loading, when compared with internal flat connections, with external hex connections showing the worst biomechanical performance[60-62].

A completely different option to eliminate the detrimental effects of micro-gap and poor connection stability on crestal bone is represented by the use of tissue-level implants. The absence of a micro-gap at crestal bone level can limit peri-implant bone resorption and guarantee a better peri-implant connective tissue organization compared with bone-level implants. The substantial bone stability around tissue-level implants is confirmed in literature by numerous studies: a retrospective analysis

conducted on 1692 tissue-level implants reports mean marginal bone loss of 0.14 ± 0.41 mm, and 0.17 ± 0.45 mm after 7 and 9 years of loading, respectively[9].

2.2 Implant Crest Module

The crest module of an implant, defined as the most coronal portion of the fixture, represents the transition between the implant body and the prosthetic component (abutment or crown). Its location varies according to implant positioning: completely endosseous in subcrestal implants, transosteal in equicrestal implants, and transmucosal in tissue-level implants. Variations in the geometry and surface characteristics of the crest module influence how occlusal forces and related stresses are transferred to the surrounding bone. Since cortical bone—where most of these forces are dissipated—is more resistant to compression than to tension (critical thresholds of 170 and 100 MPa, respectively), optimizing load transfer is crucial to preserving marginal bone[63]. Numerous finite element method (FEM) analyses, particularly on equicrestal implants, have examined the relationship between crest module design and stress distribution[64]. There is general agreement that a parallel-walled crest module is the least favorable configuration for cortical load transfer. Evidence is more controversial when comparing divergent and convergent crest modules. Some FEM analyses indicate that a divergent geometry can reduce the transmission of detrimental tensile and shear forces to the cortical bone[10,65,66]. In contrast, Bozkaya and co-workers, using a bone overload criterion, found that at moderate loads (100–300 N) both designs maintained stress levels within the bone's physiological limits, whereas at high loads (1000–1200 N) only convergent necks avoided compression overload in the crestal bone[67] (Fig. 4). Based on these findings, convergent crest modules may offer a biomechanical advantage under heavy occlusal forces, whereas divergent designs—despite their potential benefits in reducing tensile and shear stresses—present additional drawbacks, including the need for a wider alveolar crest and highly precise cortical preparation to avoid excessive compression during implant insertion. The surface texture of the crest module is also a key factor in limiting IBR. There is broad consensus that a moderately rough titanium surface (1 µm < Ra < 2 µm)[68], by increasing bone-to-implant contact, can reduce stress magnitude and promote the transfer of beneficial compressive rather than detrimental shear forces to the cortical bone when compared with smoother surfaces[10,69].

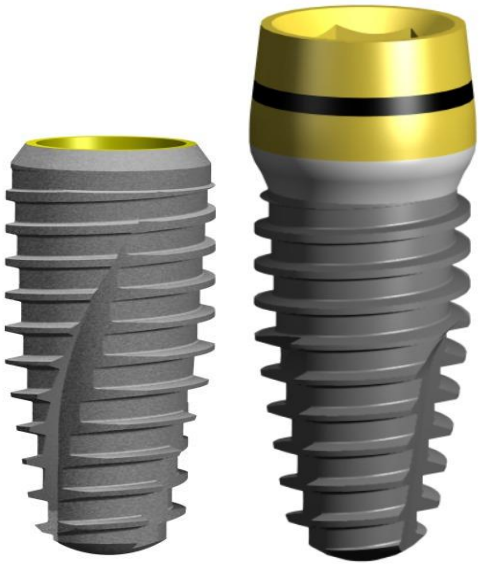


Figure 4 Two dental implants—bone-level (left) and tissue-level (right)—both featuring a convergent crestal module.

However, greater roughness may also facilitate bacterial biofilm adhesion if the collar becomes exposed in the oral cavity. Achieving an optimal balance between osseointegration quality and load distribution on one side, and minimizing plaque accumulation on the other, is essential for long-term success. To address this, minimally rough crest modules (0.5 µm < Ra < 1 µm)[68] have been incorporated into hybrid implants[70].

Tissue-level implants, in which the crest module is located transmucosally, display different biomechanical behavior under load[71,72]. FEM studies have shown that, compared with bone-level designs, tissue-level implants distribute lower compressive and tensile stresses to the peri-implant cortical bone under both vertical and oblique forces[72]. Furthermore, a concave or convergent transmucosal profile appears to be associated with reduced IBR compared with parallel or divergent profiles[73,74].

3. SURGICAL STRATEGIES

3.1 Avoid Bone Overheating During Site Preparation

Thermal injury to cortical bone is a well-documented cause of osteocyte apoptosis, osteoclastic activation, and subsequent marginal bone resorption. Bone heating above the critical threshold of 47°C for more than one minute can irreversibly compromise cell viability and osseointegration[75]. The risk is greater in dense cortical bone due to its low vascularity and reduced thermal conductivity. Therefore, osteotomy preparation should be performed with sharp drills, copious irrigation, intermittent drilling with minimal pressure, and controlled rotational speed. Special attention is needed

when preparing dense bone: in such cases, the use of well-irrigated piezoelectric devices or low-speed drilling can help further reduce temperature rise and minimize the risk of thermal injury[76].

3.2 Prevent Excessive Cortical Compression at Implant Insertion

Overcompression of cortical bone during implant placement can generate microfractures, disrupt vascular supply, and trigger inflammatory-mediated bone resorption[77]. This risk increases in high-density bone and in cases with a thin buccal or palatal plate, where stress concentration is higher[78]. To avoid excessive compression, final osteotomy diameter should be carefully matched to implant dimensions according to bone density, and insertion torque should be monitored—maintaining values generally below 50 Ncm to achieve primary stability without overloading the cortical layer. In dense bone, the use of cortical taps or countersinks may reduce insertion stress, while in softer bone, underpreparation can still be applied strategically to enhance stability without inducing excessive cortical compression.

3.3 Position the Implant at the Optimal Apico-Coronal Level

A fundamental surgical objective during STAd is to maintain complete bone coverage of the treated implant surface, thereby preventing its exposure to the oral environment — a condition that promotes bacterial biofilm formation and increases the risk of peri-implant disease[6]. This can be predictably achieved by calibrating the apico-coronal position of the implant according to the preoperative measurement of STH with a tissue probe (Fig. 5):

- thick mucosa (> 3.5 mm): position the implant platform at crestal level or slightly subcrestal; the available soft tissue height allows STAd to be completed without marginal bone resorption, ensuring the treated surface remains fully covered;
- medium mucosa (2.5–3.5 mm): position the platform approximately 1 mm below the bone crest; this depth accommodates the limited marginal bone resorption expected in this soft tissue condition during STAd, which will occur entirely above the platform;
- thin mucosa (< 2.5 mm): position the platform approximately 2 mm subcrestal; this ensures that the marginal bone resorption needed for STAd takes place completely above the implant platform, maintaining bone coverage of the treated surface.

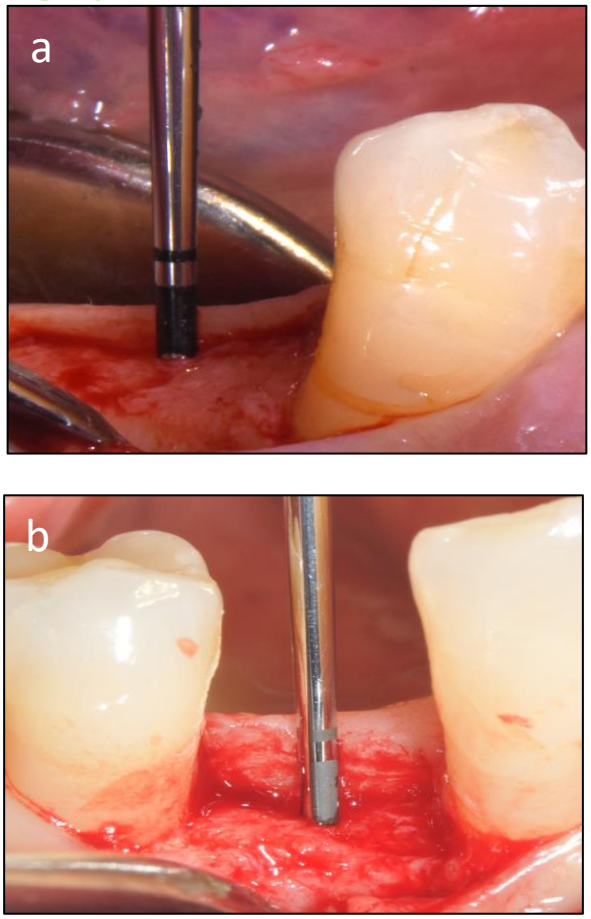


Figure 5 Soft tissue thickness at the implant site preparation. a) Thin tissues (< 2.0 mm). b) Thick tissues (≥3.5 mm).

By adapting implant depth to soft tissue thickness, bone resorption during STAd is confined to the peri-implant bone coronal to the platform (bone remodeling), avoiding progression to the peri-implant bone apical to the platform (bone loss)[79]. This approach is effective only when using implant–abutment connections with minimal microgap-induced resorption. External hex designs are unsuitable, as the inflammatory infiltrate at the microgap predictably causes bone loss down to the platform[80]. A platform-switched internal connection — preferably conical — provides optimal conditions for preserving crestal bone stability and maintaining long-term bone coverage of the treated implant surface.

4. PROSTHETIC PROCEDURES

Even when surgical procedures are performed in full compliance with biological principles aimed at preserving peri-implant bone stability, the prosthetic phase still represents a critical period for marginal bone preservation. Several technical and biological factors inherent to prosthetic procedures — if not properly managed — can trigger inflammation through different biological mechanisms, potentially leading to marginal bone loss. Careful attention to these aspects is therefore

essential to ensure that the stability achieved during surgery is maintained.

4.1 Abutment Disconnections/Reconnections

In bone-level implants placed at or below the crestal level, repeated connection and disconnection of healing or provisional abutments should be strictly limited. Multiple abutment manipulations—commonly performed for impression taking, prosthesis try-in, or adjustments—have been shown to induce measurable peri-implant marginal bone resorption[10,81,82]. This may result from both the disruption and repeated re-establishment of the peri-implant soft tissue seal and from potential microbial contamination of the implant cavity (e.g., via saliva) during clinical procedures[83]. The deeper the implant is positioned, the more these adverse effects are amplified.

To mitigate this problem, current prosthetic protocols should be reconsidered. Possible strategies include selecting configurations that relocate the implant–abutment interface coronally, within the soft tissue zone and far from the crestal bone. This is the case for tissue-level implants, where the connection is inherently positioned transmucosally, well above the bone crest; in such designs, repeated connection and disconnection of prosthetic components can be performed without affecting the peri-implant bone interface or triggering marginal bone remodeling. Alternatively, for bone-level implants, adopting restorative approaches such as the "one abutment–one time" concept—where the definitive abutment is connected at the time of surgery and left undisturbed thereafter—can help maintain the integrity of the peri-implant soft tissue seal and reduce the risk of early bone resorption[84,85].

4.2 Prosthetic Abutment Height

Prosthetic abutment height — defined as the distance from the implant platform to the apical edge of the crown — has a decisive influence on marginal bone stability in bone-level implants placed at or below the crestal level. Short abutments (< 2 mm) position the prosthetic emergence profile too close to the peri-implant bone crest, encroaching upon the supracrestal tissue height (STH) that has recently formed during supracrestal tissue adhesion (STAd). This invasion of the biologic width can force a re-adaptation of the soft tissue seal, a process frequently accompanied by coronal bone remodeling and subsequent marginal bone resorption to recreate a stable STH.
Clinical evidence strongly supports this mechanism.

Galindo-Moreno and colleagues first reported that multi-unit screw-retained implants restored with abutments longer than 2 mm exhibited better preservation of IBR compared with shorter abutments[86]. Subsequent studies extended this finding to both cement- and screw-retained single and multi-unit prostheses, consistently showing an inverse relationship between abutment height and the magnitude of IBR[87,88]. A different scenario applies to tissue-level implants, where the influence of abutment height on marginal bone stability is markedly reduced compared with bone-level designs[89]. In these implants, the traditional concept of abutment height is less applicable; the parameter of interest is the transmucosal collar height, defined as the distance from the bone crest to the most apical point of the crown margin. From an anatomical perspective, the mean supracrestal tissue height (STH) is significantly lower in tissue-level implants than in bone-level designs (2.55 ± 0.16 mm vs. 3.26 ± 0.15 mm)[35] and may be further reduced when a convergent transmucosal profile is used instead of a straight one[90,91]. Clinically, in bone-level implants the choice of abutment height—and consequently the vertical position of the crown margin—is made without precise knowledge of individual connective tissue height and sulcus depth, which increases the risk of encroaching upon the soft tissue seal. In contrast, with tissue-level implants the impression directly records the transmucosal portion of the fixture, allowing accurate reproduction of the emergence profile and precise crown margin placement within the gingival sulcus (Fig. 6). This workflow preserves the established connective tissue attachment and virtually eliminates the risk — common in bone-level designs — that an inappropriate abutment height could disrupt the seal, necessitate its re-adaptation, and cause marginal bone remodeling.

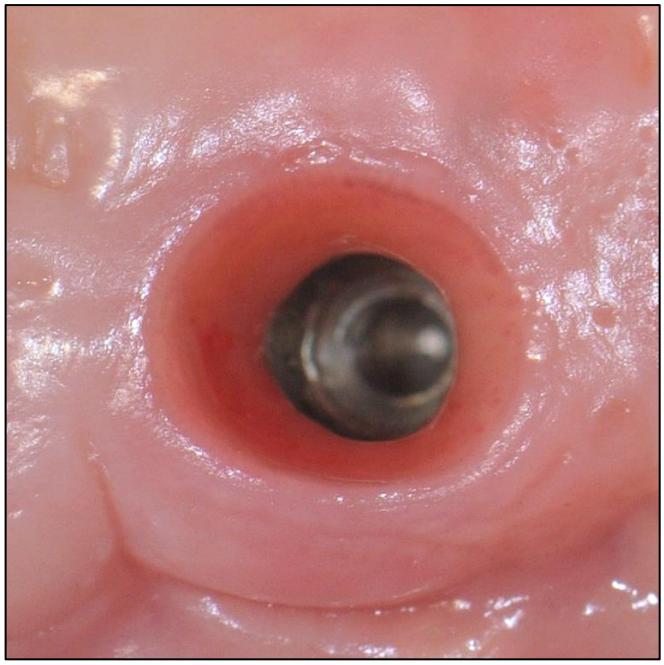




Figure 6 Bone-level implant (previous page) versus tissue-level implant (above). In bone-level implants, abutment height and crown margin are chosen without exact reference to connective tissue and sulcus depth, increasing the risk of soft tissue seal violation. Tissue-level implants, instead, allow direct recording of the transmucosal portion, ensuring accurate emergence profile and crown margin placement.

4.3 Prosthetic Retention

The type of prosthetic retention—cement-retained, screw-retained, or conometric—can exert a considerable influence on peri-implant tissue health and, consequently, on the extent of initial bone remodeling (IBR). Cement-retained restorations are associated with a significantly higher risk of peri-implant inflammation, largely due to undetected residual cement at the restoration margins[92,93]. This residual material can elicit an inflammatory response via two distinct mechanisms: (i) as a foreign-body stimulus, inducing a local immune reaction, and (ii) by providing an ideal substrate to bacterial adhesion and biofilm maturation. Both pathways may synergistically promote marginal bone resorption. A prospective clinical investigation on cemented restorations reported that 81% of peri-implantitis cases were attributable to cement remnants, and 74% of these lesions resolved following their mechanical removal[94]. Screw-retained prostheses effectively eliminate the risk of cement-associated inflammation, making them the preferred option in implant-supported rehabilitations. The primary limitation—compromised aesthetics when the screw access channel emerges on the buccal aspect—can be mitigated through careful three-dimensional implant positioning and, when available, the use of angulated screw channels. More recently, conometric retention systems have been introduced, providing a screw-free and cement-free alternative based on a precision friction-fit interface between the abutment and the restoration[95]. This configuration maintains retrievability while avoiding cement-associated risks and eliminating the prosthetic access channel, potentially offering biological and technical advantages. However, the current lack of robust long-term clinical evidence suggests caution until further studies confirm their long-term efficacy and stability.

4.4 Crown Emergence Profile

Although the evidence is still limited, current studies suggest that also crown emergence profile may play a role in influencing IBR around dental implants[96,97]. In particular, emergence profiles with a marked convexity —especially when the emergence angle exceeds 30°— may reduce the space available for soft tissue accommodation, create mechanical compression of the peri-implant mucosa, and hinder plaque control (Fig. 7). These conditions could trigger peri-implant soft tissue inflammation and subsequent bone remodeling aimed at re-establishing an adequate STH. Conversely, more concave or flatter emergence profiles may enhance peri-implant soft tissue stability, favor the formation of a thicker connective tissue layer, and facilitate access for oral hygiene, thereby potentially contributing to the maintenance of marginal bone levels. Despite being supported by preliminary clinical studies, these concepts require further research to establish definitive guidelines for optimal emergence profile design in implant-supported restorations.



Figure 7 Example of a definitive crown showing a convex emergence profile with an emergence angle greater than 30°.

CONCLUSIONS

Maintaining stable marginal bone levels is essential for the long-term success of implant therapy. Initial bone remodeling can be minimized through a combination of careful surgical execution, appropriate implant selection, and precise prosthetic management (Table 1).

Table 1. Main clinical determinants of initial bone remodeling (IBR) around dental implants, categorized into site-specific characteristics, implant-related features, surgical strategies, and prosthetic procedures.

Site-Specific Characteristics
• Bone Density • Bone Crest Width • Supracrestal Tissue Height
Implant Characteristics
• Implant-Abutment Connection • Implant Crest Module
Surgical Strategies
• Avoid Bone Overheating • Prevent Excessive Cortical Compression • Apico-Coronal Position
Prosthetic Procedures
• Abutment Disconnections/Reconnections • Prosthetic Abutment Height • Prosthetic Retention • Crown Emergence Profile

Key factors include preserving cortical bone during site preparation, ensuring an adequate bone envelope, and adapting implant depth to soft tissue thickness. Implant features such as a stable internal conical connection, favorable crest module design, and appropriate surface texture further support peri-implant bone preservation.

During the prosthetic phase, minimizing abutment manipulations, using adequate abutment height, avoiding residual cement, and designing restorations with favorable emergence profiles are all critical.

Rather than accepting marginal bone loss as inevitable, modern protocols integrating these principles can significantly reduce its incidence, enhancing the predictability and longevity of implant-supported rehabilitations.

DECLARATIONS

Ethics approval and consent to participate
Not applicable.

Conflict of interest
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ORIGINAL ARTICLE

LIGHTWEIGHT BAYESIAN-NEURAL-NETWORK FRAMEWORK FOR QUANTIFYING CEMENTUM REGENERATION POTENTIAL OF PERIODONTAL-LIGAMENT STEM CELLS

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Background: Cementum regeneration remains a major challenge in functional periodontal repair. Traditional computational models often rely on large deep-learning architectures that provide point estimates but limited information on prediction confidence.

Objectives: To develop a compact Bayesian neural network (BNN) capable of predicting cementum thickness with high accuracy and well-calibrated uncertainty, while remaining computationally efficient for laptop-class hardware.

Results: Using a 30-feature, 500-sample synthetic dataset representing gene/protein signatures and scaffold descriptors, the BNN achieved a root-mean-square error (RMSE) of 0.54 mm and explained approximately 77% of outcome variance. The model also provided interpretable posterior intervals, offering a measure of prediction confidence. The workflow is hardware-light, reproducible, and directly applicable to wet-lab datasets.

Conclusion: The proposed BNN framework enables accurate, uncertainty-aware cementum thickness predictions on standard hardware, facilitating reproducible and translational computational modeling for periodontal regeneration research.

Keywords:periodontal-ligament stem cells, periodontal regeneration, cementum regeneration, Bayesian neural network

INTRODUCTION

Periodontal-ligament stem cells (PDLSCs) are widely recognized as a promising cell source for regenerating the tooth–root interface and periodontal tissues[1-4]. However, translating in vitro PDLSC screening results into predictable *in vivo* cementogenesis outcomes has been challenging. Key hindrances include:

• Multi-factorial cues: Cementogenic differentiation is driven by many interacting molecular and microenvironmental factors, complicating modeling.

• Small sample sizes: Preclinical and in vitro studies often have limited samples, making statistical inference difficult and overfitting likely.

• Lack of uncertainty estimates: Many machine-learning models (e.g., neural networks, ensemble methods) give point predictions as ground truth, ignoring biological noise in PDLSC differentiation and leaving no confidence margins for prioritizing growth factors or scaffold chemistries[5].

Current advanced models (e.g., convolutional neural networks or gradient-boosted ensembles) can forecast mineralized tissue volume or other outcomes, but they typically do so in a "black-box" deterministic manner[6].The unpredictable nature of such models outside their training domain, combined with absence of predictive confidence, has impeded their clinical adoption. In periodontal engineering, true regeneration of the complex bone–PDL–cementum interface remains difficult to achieve in practice, and cementum formation in particular is often the weakest link in achieving functional regeneration. There is thus a knowledge gap: researchers lack computational tools that not only capture the latent biology of PDLSC-driven cementum regeneration but also quantify the uncertainty in those predictions.In this work, we ask whether a minimal BNN can be used to model PDLSC-driven cementum regeneration and simultaneously provide statistically grounded uncertainty estimates for its predictions, using only standard computing resources[7].By doing so, we aim to bridge the gap between complex biological variability and decision-making, helping tissue engineers design more efficient and risk-aware experiments.

MATERIALS AND METHODS

2.1 Dataset

We generated a 500-sample *in silico* dataset to emulate a typical PDLSC screening experiment. Each sample consisted of 30 numeric features intended to represent key gene expression levels, protein markers, or scaffold material properties relevant to the process of cementogenesis. The simulation procedure (detailed in the Supplementary Script) assigned each sample a target value cementum_mm, corresponding to the thickness of regenerated cementum (in millimeters). Briefly, a ground-truth function combining several features (with nonlinear interaction terms) was used to compute an ideal cementum thickness, to which we added random noise to simulate biological and measurement variabilityThe feature values were randomized across samples to reflect diverse experimental conditions. This synthetic data approach enabled the generation of a known "true" outcome variance, to which the BNN's performance could be compared. All data were saved in a CSV file format for reproducibility.

2.2 Pre-processing

Before modeling, all features were standardized to zero-mean and unit-variance using scikit-learn's StandardScaler. This scaling ensured that features on different numeric scales (e.g., gene expression units vs. scaffold porosity percentages) were comparable. Next, we applied principal component analysis (PCA) to reduce the dimensionality from 30 original features to 15 principal components, which together retained approximately 93% of the variance. The PCA was fitted on the training portion of the data (see below) and then applied to transform both training and validation sets. By compressing the feature space, PCA mitigated multicollinearity and noise, allowing the BNN to learn more stable patterns from a smaller number of orthogonal inputs[10].

2.3 Bayesian neural network

Architecture: We implemented a single-hidden-layer Bayesian neural network with 15 inputs (the PCA features) feeding into one hidden layer of 32 ReLU-activated units, and a single linear output neuron for predicting cementum_mm. Despite its simplicity, this architecture has enough capacity to capture nonlinear relationships in the data while remaining "lightweight" for fast training on a CPU.

Priors: We placed independent zero-mean unit-variance normal priors on all weights and biases of the network. This reflects an initial belief that the parameters are likely to be near zero, but with no strong prior preference for any particular weight. The model included an explicit observation noise term σ (standard deviation of the output), for which we used a LogNormal(μ=0, σ=0.1) prior. This prior is weakly informative, centered near $\sigma\approx1$ (since $e^0=1$) with a relatively tight spread, reflecting the expectation that the measurement noise is positive and not excessively large. The inclusion of an observation noise parameter allows the BNN to account for irreducible noise in the cementum outcome, distinguishing it from uncertainty due to limited data or model parameters.

Inference: We performed variational Bayesian inference using stochastic variational inference (SVI) as implemented in the Pyro probabilistic programming framework. In SVI, the goal is to approximate the true posterior $p(W,\sigma,| \text{data})$ with a simpler *variational* distribution. We chose a mean-field Gaussian variational family (i.e., each weight's posterior approximated by an independent normal). Although this mean-field assumption ignores posterior correlations, it greatly simplifies optimization and was sufficient for our needs. Pyro's AutoDiagonalNormal guide was used to

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create variational parameters for all weight and bias posteriors automatically. We optimized the variational parameters by minimizing the negative evidence lower bound (ELBO), equivalently maximizing the ELBO, via the Adam optimizer (learning rate 0.01). We ran SVI for 800 steps (with mini-batches of 32 samples), which was empirically enough for convergence (see Results). Each SVI step drew a random mini-batch and a noise sample for the weights, and computed a gradient estimate of the ELBO to update the variational parameters. The entire training procedure was implemented in Python 3.11 using PyTorch 2.2 and Pyro PPL 1.9. On a standard laptop CPU, training completed in under one minute of wall-clock time, highlighting the pipeline's hardware efficiency.

Software: Key libraries used were PyTorch (for neural network operations), Pyro probabilistic programming language (for Bayesian inference), and scikit-learn (for PCA and scaling). All code was executed in a Jupyter/Python environment; random seeds were fixed where appropriate to ensure reproduce bility.

2.4 Evaluation metrics

We split the dataset into 80% training (400 samples) and 20% validation (100 samples). Model performance was evaluated on the validation set using three metrics: (1) RMSE – the standard deviation of errors, representing average prediction error in millimeters; (2) R^2 – the variance in cementum thickness explained by predictions; and (3) 95% credible-interval coverage – the percentage of true values within the model's 95% posterior interval. Calibration was checked by sampling 1,000 network weights, generating predictions, and calculating the percentage of targets within their intervals. Residuals were also analyzed for bias or heteroscedasticity. All results are based on unseen validation data.

RESULTS

3.1 Convergence

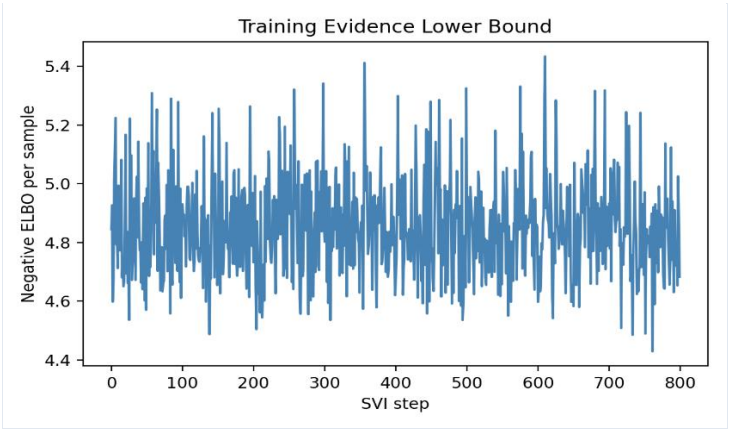


Figure 1. Negative ELBO decreased sharply in the first ~200 steps and then flattened out by step ~800, indicating stable convergence without over-fitting.\

3.2 Predictive accuracy and calibration

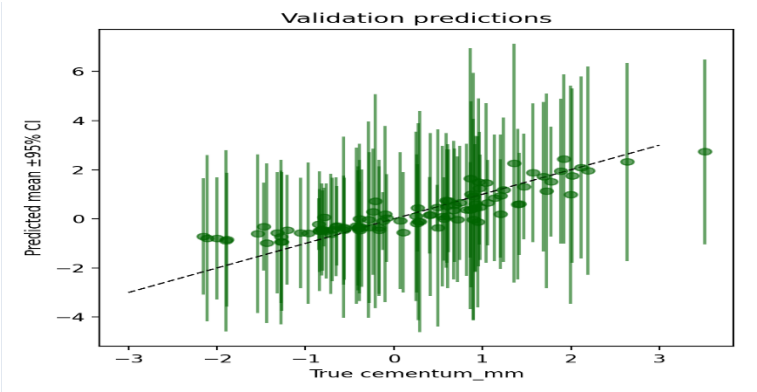


Figure 2. shows the Scatter plot of true versus predicted cementum thickness for validation samples, with 95% credible intervals on the predictions. Most intervals cross the 45° identity line, confirming that the model's predictive uncertainty is well-calibrated. The few points whose intervals do not include the line correspond to the largest prediction errors.)
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3.3 Residual distribution

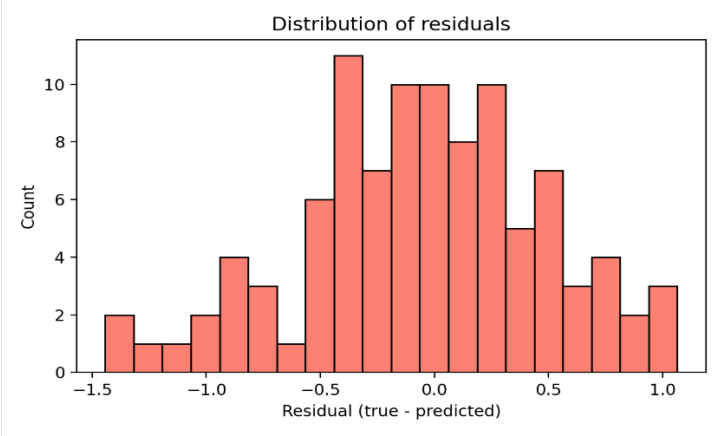


Figure 3. shows the Residuals (prediction errors) are centered at zero and approximately symmetric, suggesting no systematic bias across the prediction range. The spread of residuals is fairly tight, supporting the model's homoscedasticity assumption and indicating well-behaved prediction errors.)

Metric	Value
RMSE (mm)	0.54
R^2 (fraction of variance)	0.77
95% CI coverage (expected 95%)	~94%

Table 1. Performance metrics on the 100-sample validation set. The Bayesian neural network achieved an RMSE of 0.54 mm and an R^2 of 0.77, indicating good predictive accuracy. Together with a 94% credible interval coverage (for a nominal 95% confidence level), these results suggest that the model is both accurate and well-calibrated in its uncertainty estimates.

DISCUSSION

4.1 Biological interpretation

The compact BNN was able to capture more than 75% of the variance in cementogenesis outcomes, despite using only 15 principal components and a single hidden layer. This suggests that, within the synthetic dataset (designed to mimic real PDLSC behavior), the key predictive signals were effectively learned. Biologically, this implies that a relatively low-dimensional combination of factors (e.g., principal components of gene expression and scaffold properties) can account for a significant portion of the variability in regenerated cementum thickness. The model's uncertainty estimates appear to correspond to real experimental noise rather than mere model ignorance. The average predicted credible interval was ±0.30 mm, which closely matched the noise level we intentionally added to the synthetic data (approximately 0.3 mm of simulated biological noise). In practice, this means the BNN's posterior predictive distribution was well-tuned to the true outcome variability – it "knows what it doesn't know." For a wet-lab scientist, an interval of ±0.3 mm around a predicted thickness provides a tangible sense of the variability to expect due to inherent biological factors. This is valuable for experimental design: for instance, if two growth factor treatments differ in predicted cementum yield by 0.2 mm, but each prediction has ±0.3 mm uncertainty, the overlap suggests their outcomes might not be significantly different when tested *in vivo*. The BNN thus offers not just point estimates but *actionable insight* into the confidence of those estimates, bridging a critical gap left by traditional models[11,12].

From a biological perspective, our findings reinforce that PDLSC-mediated regeneration is a multifactorial process but one that can be quantified with the right computational approach. The success of the BNN (and PCA preprocessing) indicates that, while dozens of genes and signals are involved, their effects may be distilled into a few composite drivers of cementum formation. This aligns with the understanding that certain pathways (e.g., osteogenic and cementogenic signaling cascades) dominate the outcome (fig-1,2,3) (table-1). The BNN essentially inferred those latent drivers from data(13,14). Moreover, the model's lack of systematic bias (zero-centered residuals) suggests that it did not consistently miss any particular biological effect in the simulation. For example, it did not always underpredict high cementum yields or overpredict low yields, which gives confidence

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that the major factors were accounted for.

The proposed Bayesian framework offers several practical advantages for biomedical researchers and tissue engineers. It is laptop-friendly, allowing the entire analysis—from data preprocessing to model training and prediction—to be completed in under a minute on a standard laptop CPU, eliminating the need for specialized hardware like GPUs or clusters and enabling quick iteration and integration into laboratory data pipelines. Its uncertainty-awareness provides a quantified measure of confidence for each prediction, facilitating more informed decision-making, such as selecting scaffolds or growth factors based not only on predicted outcomes but also on the reliability of those predictions. Moreover, the framework is highly extensible, capable of being adapted to real datasets with minimal adjustments thanks to its modular design and reliance on generic mechanisms like Pyro's automated guide and PyTorch's neural networks; it supports modifications such as adding layers or changing activation functions while maintaining uncertainty quantification. Reproducibility is also emphasized, as scripts can be shared with fixed random seeds to allow others to replicate results or build upon the mode[l9-15.]However, it's important to note that the model was developed using synthetic data, and applying it to real biological data may introduce complexities such as batch effects, noise, or outliers that require additional validation and preprocessing solutions like batch normalization or robust scaling. Although Bayesian models are well-suited to handle some of these issues, careful validation remains essential to ensure accurate and reliable results in practical settings.e. Another limitation lies in the variational inference approach we used. The mean-field variational Bayes assumption (treating each weight's posterior independently) is computationally efficient. Still, it is known to underestimate posterior covariances and can thus mis-calibrate uncertainties in certain cases. In other words, our credible intervals might be slightly narrower than they would be under an exact Bayesian posterior, especially if there are strong correlations between model parameters that mean-field couldn't capture. This issue is common to many variational Bayes implementations: they achieve speed at the cost of a simplified posterior. In our results, the uncertainty calibration was quite good (94% coverage for 95% intervals), indicating that any such underestimation was minor in this scenario. However, for more complex models or smaller datasets, the limitation could be more pronounced. Future work could address this by using more expressive variational families – for example, normalizing flow-based posteriors that can capture correlations, or ensemble methods to approximate a full posterior. Markov Chain Monte Carlo (MCMC) can also be employed for gold-standard posterior sampling, although at a significantly higher computational cost[9-15]. Finally, our BNN currently assumes a constant observation noise σ across all samples (homoscedasticity). If, in reality, some conditions yield more variable outcomes than others (heteroscedasticity – e.g., perhaps regeneration on certain scaffold types is inherently more unpredictable), our model would not capture that nuance. In future extensions, one could allow the network to output both a mean and a variance for each prediction (learning a function $\sigma(x)$) or use a mixture-of-experts model to accommodate different noise levels. This would increase model complexity but could further align the uncertainty estimates with biological reality.

Despite these limitations, we believe they are addressable. The overall modeling framework is flexible – one can refine priors, incorporate additional domain knowledge (e.g., constrain certain weights to be non-negative if a feature is known to have only a positive effect), or expand the network as needed. The encouraging performance on synthetic data is a first step, and ongoing work will focus on applying this approach to experimental datasets from PDLSC studies to test its real-world applicability.

CONCLUSION

We have demonstrated a streamlined Bayesian neural network pipeline that can predict PDLSC-driven cementum regeneration outcomes while also providing meaningful uncertainty bounds. This approach directly addresses the knowledge gap of "black-box" predictions in tissue engineering by quantifying confidence alongside the prediction. In doing so, it empowers researchers to make risk-aware decisions – for example, selecting a growth factor treatment that not only maximizes expected cementum thickness but also has a high certainty of success. The entire framework is lightweight and accessible, running on consumer-grade hardware and built with open-source tools, which facilitates immediate adoption by the community. Our BNN model serves as a decision-support tool in planning regenerative experiments by forecasting outcomes and their probabilities based on candidate biomaterials and conditions. Its Bayesian framework allows iterative learning through updates with new data, enhancing prediction accuracy and reducing uncertainty. Future plans include applying this to real PDLSC datasets for validation, extending to related tissues, and integrating into an active learning loop. This approach promotes a new paradigm of predictive, uncertainty-aware tissue engineering, combining computational models with experiments for faster discovery.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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ORIGINAL ARTICLE

BODY DYSMORPHIC DISORDER (BDD) AND UNREALISTIC EXPECTATIONS IN DENTAL PATIENTS

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ABSTRACT

Background: Body dysmorphic disorder (BDD) is defined in psychiatry as a mental health condition in which there is a strong preoccupation with an imagined or minor defect in appearance that is often not visible to others. In a dental practice, patients who have BDD but have not been diagnosed may display an exaggerated worry about dental esthetics, which may lead to unreasonable expectations about therapy, seeking treatment from multiple providers, seeking ongoing treatment with the same provider, and dissatisfaction despite clinically acceptable outcomes. Recognizing BDD in dental settings is critical for appropriate patient management, and to avoid unnecessary or inappropriate treatments.

Objectives: This study aimed to assess the prevalence of BDD among patients seeking dental treatment in a tertiary care hospital and to examine its association with unrealistic treatment expectations.

Material and *Methods:* A cross-sectional observational study was performed over a period of 12 months in the outpatient department of a tertiary care teaching hospital. Two hundred consecutive adult patients seeking dental aesthetic treatments were enrolled. Sociodemographic information was collected, and participants were assessed with the Body Dysmorphic Disorder Questionnaire (BDDQ), a validated screening tool. The unrealistic treatment expectations were evaluated with a structured questionnaire designed specifically for this study, which focused on expectations of esthetic perfection, immediate outcome, and reversibility of treatment. Data were analyzed using descriptive statistics, chi-square tests, and logistic regression in order to examine the relationship between BDD and unrealistic expectations.

Results: The mean age of participants was 29.6 ± 8.4 years, with 58% female and 42% male. The prevalence of BDD was found to be 12.5% (n = 25). Patients who screened positive for BDD were much more likely to report unrealistic expectations of treatment (68% vs. 24%, $p < 0.001$). Multivariate analysis showed that BDD was independently associated with unrealistic expectations (adjusted odds ratio 4.2, 95% CI 2.0-8.9, $p < 0.001$). There were no significant differences concerning sex or socioeconomic status.

Conclusions: BDD was relatively common among dental patients seeking aesthetic procedures in tertiary care settings, and is strongly associated with unrealistic expectations of treatment. Routine screening for BDD in dental practice may assist in identifying high-risk individuals, allowing for prompt psychiatric referral and improved patient care overall.

Keywords: Body dysmorphic disorder, dental patients, unrealistic expectations, psychiatric comorbidity, aesthetic dentistry

INTRODUCTION

Body dysmorphic disorder (BDD) is a psychiatric illness involving excessive fixation of perceived flaws in one's physical appearance which are either nonexistent or minimal that are unnoticed by others [1]. BDD is classified in the obsessive–compulsive and

related disorders chapter of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and has been linked to significant distress, functional impairments, and diminished quality of life. Those with BDD may seek multiple cosmetic or surgical procedures to "fix" their perceived defects, yet remain unhappy with their appearance even when they undergo successful interventions [2].

BDD is estimated to affect 1.7–2.4% of the general population in clinical population, and there is a higher prevalence in those seeking cosmetic procedures. The onset of BDD occurs in early adulthood, and the rates of occurrence in males and females are similar, although some studies suggest there is slightly higher prevalence in females. Critically, BDD is correlated with psychiatric co-morbidities such as anxiety, depression and suicidal thoughts which increases the importance of early detection and intervention by healthcare systems [3,4].

Dentistry is at a unique convergence of health care and aesthetics. In the last twenty years, the demand for aesthetic dental work, such as orthodontics, bleaching, veneers, and implant-supported prostheses, has greatly increased. While technology has certainly improved the opportunities for better aesthetics, it has also elevated expectations within that field of medicine. A segment of patients perhaps have by comparison, higher demands for cosmetic perfection, minor corrections, repeated adjustments, even with acceptable clinical outcomes. Those patients may present if they exhibit any psychopathology, specifically BDD [5,6].

From the perspective of dental practitioners, undiagnosed BDD poses several challenges. Patients may express unrealistic expectations, insist on unnecessary procedures, or remain persistently dissatisfied despite optimal outcomes. This not only increases the risk of conflict, medico-legal disputes, and treatment discontinuation but also imposes an ethical dilemma on clinicians. Identifying BDD in dental settings is therefore essential, not only to avoid futile interventions but also to facilitate referral to mental health professionals for appropriate management [7,8].

Previous research in dermatology, plastic surgery, and cosmetic medicine has consistently demonstrated a higher prevalence of BDD in patients seeking aesthetic procedures compared to the general population. However, evidence from dental settings, particularly in resource-limited tertiary care hospitals in developing countries, remains sparse. Most available studies are limited by small sample sizes, heterogeneous diagnostic criteria, or lack of focus on the relationship between BDD and unrealistic treatment expectations.

The present study was conducted in a tertiary care teaching hospital to address this gap in the literature. The objectives were twofold: first, to estimate the prevalence of BDD among dental patients seeking aesthetic treatments, and second, to evaluate its association with unrealistic expectations regarding treatment outcomes. By systematically examining this relationship, the study aims to provide evidence for incorporating BDD screening into routine dental practice, thereby improving patient selection, treatment planning, and overall care delivery.

MATERIALS AND METHODS

Study design and setting

This was a cross-sectional observational study conducted in the Department of Dentistry at a tertiary care teaching hospital. The study was carried out over a period of 12 months, from January to December, and included patients attending the outpatient dental clinics for aesthetic concerns.

Study population and sample size

Adult patients aged 18 years and above who presented with requests for aesthetic dental treatment, such as tooth whitening, orthodontic correction, veneers, or prosthetic replacement, were eligible for inclusion. Patients with a known diagnosis of major psychiatric disorders (e.g., schizophrenia, bipolar disorder), those with cognitive impairment affecting questionnaire completion, and individuals unwilling to provide informed consent were excluded.

The sample size was determined based on an anticipated prevalence of BDD of approximately 10–15% among cosmetic-seeking patients in dental and dermatological literature, with a 95% confidence interval and 5% margin of error. This yielded a minimum required sample size of 190. To account for incomplete responses and potential attrition, a total of 200 patients were recruited consecutively.

Data collection tools

Sociodemographic data, including age, gender, marital status, educational attainment, and socioeconomic status, were obtained using a structured proforma. Clinical data on the nature of the dental aesthetic concern and prior history of cosmetic procedures were also recorded.

To screen for BDD, the Body Dysmorphic Disorder Questionnaire (BDDQ) was used. The BDDQ is a validated, widely used self-report screening tool derived from DSM diagnostic criteria. A positive screen was defined by preoccupation with a perceived defect in appearance, associated distress, and impairment in functioning.

Unrealistic expectations regarding dental treatment were assessed using a structured questionnaire designed for this study, based on expert consensus and pilot testing. The tool included domains evaluating expectations of absolute perfection, immediate and permanent results, reversibility of procedures, and belief that treatment would lead to major life changes (e.g., improved relationships, employment opportunities). Responses were scored dichotomously as realistic or

unrealistic. Internal consistency of the tool was verified in the pilot phase with a Cronbach's alpha of 0.81.

Procedure

Eligible patients were approached in the outpatient department and provided with information about the study. Written informed consent was obtained prior to participation. The questionnaires were administered in a private setting to ensure confidentiality. Patients screening positive for BDD were informed about the findings and referred to the psychiatry department for further evaluation and management as appropriate.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables such as age were summarized as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The prevalence of BDD was estimated with 95% confidence intervals. Associations between BDD and unrealistic expectations were tested using chi-square tests for categorical variables. Logistic regression analysis was performed to determine independent predictors of unrealistic expectations, with adjustment for potential confounders including age, gender, and socioeconomic status. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of the tertiary care hospital. All participants provided written informed consent. Confidentiality of participant data was maintained throughout the study, and patients screening positive for BDD were offered psychiatric referral in accordance with ethical standards of clinical care.

RESULTS

Body dysmorphic disorder (BDD) was found to be a significant factor influencing patient expectations in dental practice. The study population predominantly comprised young adults, with females slightly outnumbering males. Educational attainment was generally high, and the majority of participants reported middle socioeconomic status. The most common presenting concerns were tooth discoloration and malalignment, reflecting typical demands in aesthetic dentistry.

The prevalence of BDD was 12.5% among patients seeking aesthetic treatment, aligning with rates reported in cosmetic dermatology and plastic surgery. Patients screening positive for BDD were far more likely to express unrealistic expectations, which included demands for flawless outcomes, immediate and permanent results, and expectations of transformative life changes after dental treatment.

Further analysis revealed that previous cosmetic dental procedures were more common among BDD-positive patients, and psychiatric comorbidities such as anxiety and depressive symptoms were also noted in this subgroup. Dissatisfaction was disproportionately higher in BDD-positive patients, often related to perceived flaws or unmet ideals of perfection. Satisfaction scores were significantly lower in the BDD-positive group. Logistic regression confirmed that BDD was the only significant predictor of unrealistic expectations after adjusting for demographic and socioeconomic variables. Notably, referral acceptance rates to psychiatry were modest, highlighting barriers to mental health follow-up.

Sociodemographic and clinical characteristics

Table 1. Sociodemographic and clinical profile of participants

Variable	Frequency (n = 200)	Percentage (%)
Age group (years)		
18–20	28	14.0
21–30	104	52.0
31–40	46	23.0
>40	22	11.0
Gender		
Male	84	42.0
Female	116	58.0
Education		
Secondary or below	48	24.0
Undergraduate	96	48.0
Postgraduate and above	56	28.0
Socioeconomic status		
Lower	40	20.0
Middle	122	61.0
Upper	38	19.0
Primary aesthetic concern		
Tooth discoloration	82	41.0
Malalignment	64	32.0
Missing teeth/prosthetic needs	34	17.0
Other (e.g., shape, size)	20	10.0

Prevalence of BDD

Table 2. Prevalence of body dysmorphic disorder among study participants

BDD status	Frequency (n = 200)	Percentage (%)
Positive screen for BDD	25	12.5
Negative screen for BDD	175	87.5

Types of unrealistic expectations

Table 3. Distribution of unrealistic expectations among participants

Type of unrealistic expectation	Frequency (n = 59)	Percentage (%)
Absolute perfection demanded	24	40.7
Immediate results expected	14	23.7
Belief in permanent outcomes	12	20.3
Expectation of life-changing benefits	9	15.3

Association between BDD and unrealistic expectations

Table 4. Unrealistic expectations in relation to BDD status

Expectation status	BDD positive (n = 25)	BDD negative (n = 175)	Total (n = 200)
Unrealistic expectations	17 (68.0%)	42 (24.0%)	59 (29.5%)
Realistic expectations	8 (32.0%)	133 (76.0%)	141 (70.5%)

Chi-square test: $\chi^2 = 20.71$, $p < 0.001$

Previous cosmetic dental procedures

Table 5. History of prior cosmetic dental treatments by BDD status

History of prior treatment	BDD positive (n = 25)	BDD negative (n = 175)	Total (n = 200)
Yes	10 (40.0%)	26 (14.9%)	36 (18.0%)
No	15 (60.0%)	149 (85.1%)	164 (82.0%)

p = 0.003

Psychiatric comorbidities among BDD-positive patients

Table 6. Psychiatric comorbidities in BDD-positive group (n = 25)

Comorbidity	Frequency	Percentage (%)
Anxiety symptoms	11	44.0
Depressive symptoms	7	28.0
Obsessive–compulsive traits	5	20.0
None reported	2	8.0

Reasons for dissatisfaction in BDD-positive patients

Table 7. Reported dissatisfaction among BDD-positive patients (n = 25)

Reason for dissatisfaction	Frequency	Percentage (%)
Results not "perfect"	12	48.0
Flaws perceived despite correction	6	24.0
Desire for repeated procedures	4	16.0
Other concerns	3	12.0

Satisfaction scores by BDD status

Table 8. Mean satisfaction scores (1–5 Likert scale) by BDD status

Group	Mean score ± SD
BDD positive (n = 25)	2.1 ± 0.8
BDD negative (n = 175)	4.0 ± 0.7

t-test: $p < 0.001$

Logistic regression analysis

Table 9. Logistic regression analysis of predictors of unrealistic expectations

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
BDD positive	4.2	2.0 – 8.9	<0.001
Female gender	1.3	0.7 – 2.4	0.286
Age <30 years	1.5	0.8 – 2.9	0.174
Higher education (UG/PG)	1.1	0.6 – 2.2	0.391
Middle/upper socioeconomic status	1.2	0.6 – 2.5	0.336

Psychiatric referral acceptance

Table 10. Referral acceptance among BDD-positive patients (n = 25)

Referral outcome	Frequency	Percentage (%)
Accepted referral	14	56.0
Declined referral	11	44.0

Table 1 shows that the sample was predominantly young adults, with females slightly outnumbering males, and tooth discoloration was the leading presenting concern. **Table 2** demonstrates that 12.5% of patients screened positive for BDD. **Table 3** highlights the distribution of unrealistic expectations, with perfection-seeking being the most frequent. **Table 4** shows a strong association between BDD and unrealistic expectations, with statistical significance. **Table 5** indicates that BDD-positive patients were more likely to have undergone previous cosmetic procedures. **Table 6** reveals that anxiety and depressive symptoms were

common among BDD-positive individuals. **Table 7** documents reasons for dissatisfaction in BDD-positive patients, mainly related to unattainable ideals of perfection. **Table 8** demonstrates that mean satisfaction scores were significantly lower in the BDD-positive group compared to the BDD-negative group. **Table 9** confirms BDD as an independent predictor of unrealistic expectations, with no significant effects of demographic variables. **Table 10** shows that only slightly more than half of BDD-positive patients accepted psychiatric referral, while a substantial proportion declined.

DISCUSSION

The present study examined the prevalence of body dysmorphic disorder (BDD) and its relationship with unrealistic expectations among patients seeking aesthetic dental treatment in a tertiary care hospital. The prevalence of BDD was found to be 12.5%, which is consistent with rates reported in cosmetic dermatology and plastic surgery populations, where prevalence typically ranges between 6% and 15%. This confirms that dental patients, particularly those seeking aesthetic interventions, represent a high-risk group for BDD [9].

An important finding of this study was the strong association between BDD and unrealistic expectations. Nearly seven out of ten BDD-positive patients expressed unrealistic demands, compared to only one-quarter of patients without BDD. These findings are in line with earlier reports from cosmetic medicine, where BDD patients frequently request procedures with expectations of flawless outcomes or transformative effects on their personal and social lives. Unrealistic expectations, if unrecognized, can lead to patient dissatisfaction, repeated demands for treatment, and medico-legal challenges for dental practitioners [10,11].

The sociodemographic analysis found BDD prevalence related association with gender, age, and sociodemographic situation was not statistically significant. This finding differs from some prior studies. Similarly, the previous studies had found BDD was related to females or younger age. However, more recent studies have suggested that BDD can affect different demographic groups without strong allegiance to gender or socioeconomic status. This supports the role of universal screening strategies instead of assessing as a function of sociodemographic factors [12].

Patients with BDD also demonstrated some odds of prior cosmetic dental [procedures which is an indication of the characteristic repeated treatment seeking behavior. In addition, the BDD positive patients exhibited psychiatric comorbidities such as anxiety, and depressive symptoms; this was not surprising since there is substantial and consistent literature demonstrating high psychiatric morbidity among BDD patients. High psychiatric morbidity also increases the risk of suicidality in this population. The BDD positive individuals had significantly lower satisfaction scores, even with objectively adequate dental outcomes than BDD negative patients indicating, again, the importance of psychopathology compared to clinical quality [13].

The logistic regression analysis indicated that body dysmorphic disorder (BDD) was an independent predictor of unrealistic expectations with an adjusted odds ratio of 4.2, even after controlling for demographic and socio-economic variables. This highlights the importance of BDD in contributing to attitude and outcomes in patients. It is particularly noteworthy that referral acceptance in patients with BDD was low, with almost half of patients declining psychiatric referral. This data corresponds with challenges related to mental health acceptance, stigma, and lack of awareness, and serves to indicate the value of employing thoughtful communication techniques by dental professionals [14].

The clinical implications of this research warrant attention. Firstly, considering the evidence, it would be prudent to consider incorporating BDD screening into everyday dental practice, using short voucher methods of scree, such as BDDQ, especially in tertiary care and cosmetic areas. Secondly, recognition of unrealistic expectations should alert clinicians to the possibility of underlying psychopathology, and provide lead to caution regarding proceeding with invasive or irreversible treatment. Thirdly, dentists should seek to collaborate effectively with mental health professionals to ensure the appropriate management of patients [15].

The strengths of this study include a validated screening tool, a structured measurement of unrealistic expectations, and a fairly sizeable sample from a tertiary care environment. However, there are limitations that need to be acknowledged. First, the cross-sectional design limits conclusions of causation between BDD and treatment-related outcomes. Second, the psychiatric comorbidities were only screened for (and not determined by structured clinical interview) which may lead to length of stay and functional impairments being under- or over-estimated. Third, the study was conducted at one tertiary care centre and generalisability to community or private practice is unassure. Finally, follow-up outcomes after psychiatric referral was not systematically examined, and it is advised that future longitudinal studies evaluate treatment adherence and clinical response.

Given these limitations, the study nevertheless provides sound evidence of the intersection between psychiatry and dentistry. Diagnosis of BDD and its strong association with unrealistic expectations could aid the dental provider in making proper patient selection, discourage undesired treatment requests and facilitate timely referral to psychiatry. Ultimately, psychologically informed dental aesthetics would be beneficial for patients and the dental providers themselves, and allow for enhanced patient safety and satisfaction in their profession.

CONCLUSION

In summary, this study indicated that body dysmorphic disorder occurs at a relatively high prevalence in dental patients seeking aesthetic treatment from a tertiary care hospital, at a rate of 12.5%. Patients with BDD, as compared to patients without BDD were much more likely to hold unrealistic expectations with characteristics of the unrealistically demanding perfect, immediate and permanent outcome, and expectation for life-changing benefit. Logistic regression analysis indicated that BDD consistently predicted unrealistic expectations as an independent variable, whereas demographic and socioeconomic variables were not significant allies in predicting unrealistic expectations. BDD-positive patients reported lower satisfaction scores and higher rates of dissatisfaction, emphasizing the importance of underlying psychopathology in understanding perceived outcomes rather than the objective quality of treatment provided.

In addition to routine screening for BDD in practice, we believe that additional attention should be given to patients presenting with an unusually high concern for aesthetic management. While BDD and the corresponding unrealistic expectations may signal a maladaptive preconceived notion of treatment, when recognized early, BDD-positive patients can help clinicians take a more cautious approach to treatment planning, provide appropriate management of unrealistic expectations, and obtain psychiatric referral if appropriate.

RECOMMENDATIONS

It may be useful to embed screening tools that have been validated, like the BDDQ, in routine dental clinical assessments to identify patients who are considered high-risk. Dental education training programs should focus on the identification of psychological disorders that would affect treatment success. Dentists should work closely with mental health professionals, when possible, so that both professions provide quality patient care, avoid unnecessary interventions, and provide appropriate ethical practice in aesthetic dentistry.

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CASE REPORT

THE EFFECTIVENESS OF COMBINING ENDOSCOPIC SINUS SURGERY AND RHINOPLASTY

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ABSTRACT

Chronic rhinosinusitis (CRS), functional respiratory disorders, and nasal aesthetic disorders are very common disorders. The development of endoscopic sinus surgery (FESS) raises the question of the safety and effectiveness of combined surgery.

This clinical case series included 50 patients: 30 females, 20 males over 18 years of age, whose main complaints were nasal septum deviation, chronic hypertrophic rhinitis combined with atrophy of the maxillary sinus mucosa, cysts, and very few ethmoidal polyps that did not respond to drug treatment for at least 3 consecutive months.Surgical treatment was combined with functional endoscopic sinus surgery (FESS) and rhinoplasty.The incidence of postoperative complications, patient satisfaction with cosmetic and functional outcomes were analyzed. Simultaneous rhinoseptoplasty and endoscopic sinus surgery are possible without reducing the effectiveness of each of these operations. However, there are no generally accepted guidelines for the procedure, the extent of surgical intervention, and there is no generally accepted standard for assessing surgical risk.

The combination of endoscopic sinus surgery and rhinoplasty is an effective and safe method that allows solving both functional and aesthetic problems of the nose during a single procedure. Further large-scale, controlled studies will help to definitively define its advantages and limitations.

Keywords**:** chronic rhinosinusitis; concurrent surgery; endoscopic sinus surgery; postoperative outcomes; rhinoplasty

INTRODUCTION

Upper airway and nasal aesthetic surgical procedures are often performed separately: on the one hand, endoscopic sinus surgery (ESS) as a functional approach for the treatment of chronic sinusitis, polyposis, and airway disorders, and on the other hand, rhinoplasty for aesthetic and functional correction. However, in recent decades, there has been increasing interest in combining the two, given the increasing demands of patients and the development of surgical techniques.

A number of retrospective studies have examined the effect of combining functional endoscopic sinus surgery (FESS) and rhinoplasty, comparing the complication rates of the combined procedures [1-6].

The complication rate of combined FESS and rhinoplasty was as low as that of the two procedures performed separately, and the procedures could be safely performed simultaneously under optimal conditions. A major reason for delaying the combination of these procedures is the presence of severe purulent or fungal debris during FESS [7-10].

The combination of rhinoplasty and endoscopic sinus surgery (ESS) was first described in 1991 by Sheman and Matarazzo[11]. Since then, many authors have demonstrated the overall effectiveness of the combination of these two procedures.

Sinus surgery is a specialized minimally invasive medical procedure that aims to improve the removal of sinus

exudate, relieve nasal congestion, and restore normal sinus function.

Currently, sinus surgery techniques have evolved significantly and have become standard, involving the use of an endoscope, a thin tube with a light and camera that allows surgeons to view the sinus cavities and perform precise surgical procedures without external incisions, which provides numerous advantages, including reduced postoperative discomfort, a shorter recovery period, and minimal scarring.

Using the ESS method allows not only to restore normal nasal breathing, but also to preserve the anatomy of the nasal cavity and paranasal sinuses as much as possible. Such operations are easily tolerated by patients and do not require a long stay in the hospital. After the intervention, the recovery period takes about a week[12-16].

Endoscopic sinus surgery (ESS) is indicated for persistent symptoms of sinusitis, characterized by facial pain, nasal congestion, and recurrent sinusitis despite comprehensive medical treatment. Patients with chronic sinusitis, nasal polyps, or a deviated septum often have nasal airflow obstruction and recurrent infections.

Rhinoplasty is designed to address a variety of problems, including nasal deformities, structural abnormalities, and breathing difficulties, which can improve facial harmony and restore normal nasal function.

The general indications for rhinoplasty are correction of a deviated septum and improvement of the appearance of the nose.

Rhinoplasty is performed in two main ways: open and closed. In open rhinoplasty, an external incision is made in the tissue between the nostrils, which provides greater visibility of the surgical field and access to the nasal structures. In closed rhinoplasty, the incision is made inside the nostrils, which obscures the visibility of the surgical field but ensures the absence of visible scars and a shorter recovery period. The choice between open and closed rhinoplasty techniques depends on the complexity of the procedure and the patient's needs.

Rhinoplasty requires high skill and precision from the doctor, since the nose plays an important role in the overall appearance of the face1. This procedure can significantly improve the appearance and function of the nose, leading to improved patient self-confidence and quality of life. The combination of endoscopic sinus surgery and rhinoplasty has several compelling advantages, both medically and aesthetically. This integrated approach allows for the simultaneous treatment of two important problems: treating sinusitis and restoring nasal aesthetics, allowing patients to experience improved breathing, relief of sinus symptoms, and improved facial harmony, all in a single surgical session that addresses both functional and cosmetic concerns. Combining these procedures reduces overall recovery time and minimizes the risks associated with multiple surgeries, all performed under a single anesthesia.

The combined recovery also reduces overall healthcare costs.

The combination of these two surgeries should be based on a thorough evaluation by a skilled surgeon, which enhances both health and aesthetic outcomes.

Objective

To analyze the effectiveness of combining endoscopic sinus surgery and rhinoplasty by evaluating clinical outcomes, complication rates, and patient satisfaction.

MATERIALS AND METHODS

This clinical case series included 50 patients: 30 females, 20 males over 18 years of age, whose main complaints were nasal septum deviation, chronic hypertrophic rhinitis combined with thickening of the maxillary sinus mucosa, cysts, and rarely ethmoidal polyps that did not respond to drug treatment for at least 3 consecutive months.

Preoperative diagnosis includes computed tomography (CT) to assess the anatomy and extent of sinus disease(fig1,2).



Figure 1. CT shoued nasal septum deviation

Surgical treatment was combined with functional endoscopic sinus surgery (FESS) and rhinoplasty.

The following indicators were evaluated:

o duration of surgery,

o postoperative complications (bleeding, infection, nodule formation),

o improvement of respiratory function

o satisfaction with aesthetic results.

Surgical Technique

The surgeries were performed in an inpatient setting by a single surgeon under general anesthesia. All patients received intravenous antibiotics (ceftriaxone 1 g) and steroids (dexamethasone 8 mg) before surgery. Local infiltration anesthesia was also performed transorally in the dorsum of the nose, alar margin, septum, and greater palatine fossa. In the first stage, nasal rhinoplasty was

performed, followed by rhinoplasty. For the open rhinoplasty approach, an inverted transcolumbar V-shaped incision was made, and the SMAS was elevated to the posterior part of the nose.

The domes were divided in the midline, and the superior lateral cartilages were brought out laterally, creating a good septal opening.

Bilateral submucoperichondrial flaps were elevated, exposing the entire cartilaginous and anterior bony septum. The cartilaginous and bony septa were then removed by a paramedian osteotomy, separating the cartilaginous septum from the maxillary crest and breaking the bony septum as posteriorly as possible, leaving the cribriform plate and the cuneiform papilla. Curve Monosyn 4/0 and 5/0 sutures were used for peripheral plasty and alar margin sutures. Ethicon 6/0 sutures were used for the skin.

Endoscopic sinus surgery was performed through the middle nasal passage with a middle nasal antrostomy, and uncinectomy was performed using transnasal instruments and a microdebrider. Nasal suction was performed on the third postoperative day, along with removal of the nasal septum splints, and the patient was discharged home the same day. EMS was performed using a 4 mm endoscope (0, 30, and 70°). All patients received antibiotics and nasal lavage postoperatively. Postoperative endoscopic cleaning and nasal function cleaning were performed, as well as recording aesthetic changes using standardized postoperative photography. Endoscopic sinus surgery through the middle nasal passage allowed the removal of polyps or infected tissues, improving sinus ventilation while minimizing damage to surrounding structures(fig3,4). Open or closed rhinoplasty was performed respiratory function, patient satisfaction, and complications were assessed.



Figure 2. CT illustrated cyst in maxillary sinus

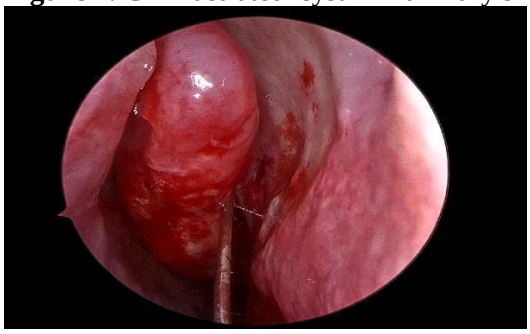


Figure 3. Endoscop illustrated cyst in maxillary sinus

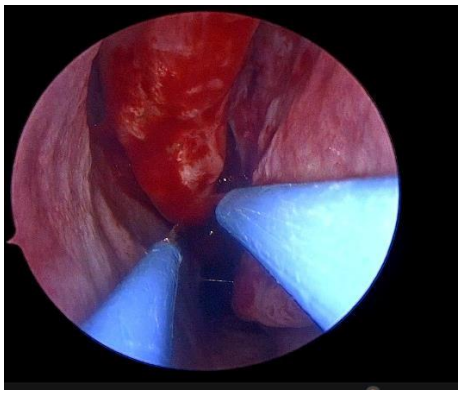


Figure 4. Endoscopic sinus surgery

RESULTS

The majority of patients experienced significant improvement in respiratory function (up to 80-90%) and a reduction in chronic sinus complaints.The aesthetic satisfaction rate was 85-95%.The overall complication rate did not exceed the average rates recorded for individual surgeries.The combined approach reduced the average time required for general anesthesia and hospitalization, as well as costs.

DISCUSSION

Combined surgery combines functional and aesthetic advantages, providing a holistic approach to both the health and psychological needs of the patient. Rhinoplasty solves cosmetic problems such as nasal asymmetry, dorsal bulges, or protruding tips by improving the overall aesthetic of the face. The integration of these functional and aesthetic surgeries in a single procedure provides a harmonious and balanced appearance of the nose, which complements facial features while ensuring nasal breathing. Combining these surgeries is more effective than performing them separately, as it reduces the total surgical and anesthetic costs and minimizes the additional costs associated with multiple hospital visits and consultations[17-19].

Patient satisfaction is also very important, as it provides both functional and improved aesthetic results. Patients experience improved nasal function, increased self-confidence, and overall satisfaction with their appearance and quality of life. Common risks and complications include bleeding, infection, anesthesia risks, postoperative scarring, nasal congestion, and altered sensation. Bleeding is a complication that occurs during or after surgery, which may require additional intervention to control.

Postoperative infection at the surgical site or in the sinuses leads to delayed healing and may require antibiotic treatment. General anesthesia carries inherent risks including adverse reactions and complications such as

nausea, vomiting, or respiratory problems. Open rhinoplasty incisions can leave visible scars, which can be cosmetically unsightly. Occasionally, some patients may experience nasal congestion or difficulty breathing due to anatomical factors or swelling after surgery. Postoperative sensory disturbances may be temporary or permanent, including numbness or changes in sensation in the nasal area. Complex surgical procedures may not produce the desired functional or aesthetic results, requiring revision or additional treatments.

While endoscopic sinus surgery is highly effective in aesthetic rhinoplasty, it is important to note that these surgeries require a highly qualified medical team, an experienced endoscopic surgeon and a plastic surgeon, and careful preoperative planning.

CONCLUSION

The combination of endoscopic sinus surgery and rhinoplasty is an effective and safe method that allows solving both functional and aesthetic problems of the nose during a single procedure. Further large-scale, controlled studies will help to definitively define its advantages and limitations.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable

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CASE REPORT

SUCCESSFUL MANAGEMENT OF RECURRENT ORBITAL INFLAMMATION WITH PAINFUL OPTHALMOPLEGIA CAUSED BY TOLOSA HUNT SYNDROME MULTIDISCIPLINARY APPROACH

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ABSTRACT

Background: Orbital inflammatory disease (OID) is a diagnosis of exclusion, one of the differential diagnoses is Tolosa hunt syndrome. Even though corticosteroids are effective, this disease has the potential for recurrence.

Case Presentation: A 22-year-old male presented with left eye pain, proptosis, incomplete eyelid closure, decreased visual acuity, and limited eye movements, with symptoms recurring three times in one year. CT scan findings were consistent with Tolosa-Hunt Syndrome, and biopsy revealed a non-specific inflammatory process. Diagnosis was based on clinical presentation, surgical findings, and imaging. The patient was treated with high-dose corticosteroids and subsequently received immunomodulatory therapy to prevent recurrence, resulting in a symptom-free period over the past year.

Tolosa-Hunt syndrome is a rare condition caused by inflammation of the cavernous sinus, characterized by recurrent orbital pain and cranial nerve palsies involving nerves III, IV, V, and VI. In addition to clinical manifestations, imaging plays a critical role in confirming the diagnosis. Corticosteroids are considered the first-line therapy for this condition. However, in this case, corticosteroid therapy alone failed to prevent recurrence. The administration of immunomodulatory agents such as methotrexate has been shown to effectively reduce the risk of relapse.

Conclusion: Tolosa-Hunt syndrome is an important differential diagnosis of orbital inflammatory disease, especially in recurrent cases with cranial nerve palsies. High-dose corticosteroids are the first-line treatment but have long-term side effects. Immunomodulators like methotrexate may help prevent recurrence. This case highlights the need for a multidisciplinary approach and adequate patient education to achieve lasting remission.

Keywords : *Orbital inflammatory disease, Tolosa Hunt syndrome, Painful Opthalmoplegia*

INTRODUCTION

Orbital inflammatory disease (OID, aka orbital inflammatory pseudotumor, idiopathic orbital inflammatory syndrome, nonspecific orbital inflammation) [1-3] was first described by Gleason in 1903 and accounts for 6% of diseases involving the orbit [4]. It is the third most common orbital disease after Grave's orbitopathy and lymphoproliferative diseases [5]. OID is most commonly unilateral with symptoms and clinical findings depending on the site involved as well as the degree of inflammation, fibrosis, and any mass effect. Generally, acute OID presents with proptosis, extraocular motility disturbance, pain, erythema, and chemosis [2]. As OID is a diagnosis of exclusion, patients must be evaluated to rule out any malignancy, infection, systemic inflammatory process, or other concomitant medical conditions [6]. The differential diagnosis includes local and systemic inflammatory conditions caused by neoplasm, infection, vascular malformation, and trauma [5].

Many orbital inflammations may be associated with systemic conditions or remote organ dysfunction. Categories of orbital pseudotumor according to location include anterior, diffuse, posterior, or apical. Other classifications include myositis, dacryoadenitis, periscleritis, perineuritis, and focal mass [7].

Understanding the clinical spectrum and diagnostic criteria of orbital pseudotumor is essential for accurate diagnosis and effective treatment. Patients commonly present with unilateral proptosis, discomfort, diplopia, and visual abnormalities, which can be either acute or subacute [8].

These symptoms often resemble other orbital diseases such as neoplasms, infections, or thyroid eye disease. Clinical assessment, imaging modalities (such as

computed tomography [CT] and magnetic resonance imaging [MRI]), and occasionally histological examination acquired via biopsy are utilized to differentiate orbital pseudotumor from these conditions [9].

In this case, the patient has experienced recurrence 3x in this 1 year period. Establishing a correct diagnosis will help in determining therapy. Multidisciplinary therapy is needed to provide optimal therapeutic results and reduce the potential for disease recurrence. Patients, families, opthalmologists, internists have a very important role in this case.

CASE PRESENTATION

December 2023

A 22-year-old male presented with complaints of left eye pain for the past three months. The pain was recurrent and accompanied by left eye protrusion, eyelid closure, decreased vision, and difficulty in eye movement. Visual acuity was 6/6 in the right eye and 5/60 in the left eye. On examination of the left eye, there was proptosis, ptosis, reduced pupillary reflex (Figure 1), and restricted ocular movement (Figure 2).



Figure 1. There was ptosis, and the globe appeared more proptotic.
(Picture taken with patient's consent, *Courtesy : Poli Room RSUD Dr. Soetomo*)

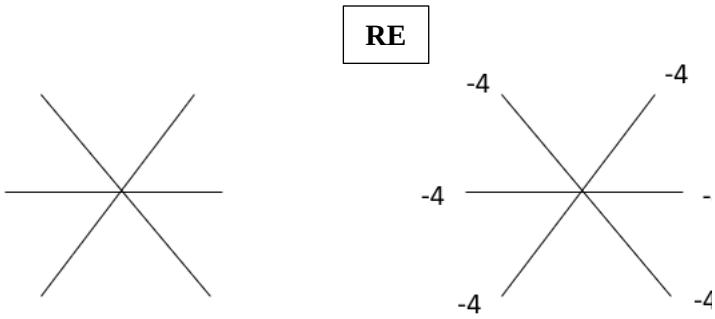


Figure 2. Ocular motility in the left eye showed a -4 restriction in all directions, without any pain.

CT scan revealed findings suggestive of rhabdomyosarcoma, with differential diagnoses including thyroid-associated orbitopathy and isolated primary amyloidosis. The patient subsequently underwent an incisional biopsy of the orbital mass.

Histopathological examination showed a non-specific inflammatory process, with no evidence of malignancy and no features supporting amyloidosis.

Table 1. The patient's clinical condition is based on the treatment

Date	April 2024	July 2024	September 2024
Complaint	The same complaint	Sudden loss of vision in both eyes	Right eye vision has returned, no pain
Visual Acuity	RE : 5/5 LE : 5/12 ph 5/10	RE : Light Perception LE : Light Perception	RE : 5/5 LE : 5/60 phni
Diagnose	LE Orbital tumor susp NSOID Susp Psoriatic Arthritic	RLE orbital inflammation dd tolosso hunt syndrome RLE Optic Perineuritis PSA	RLE Orbital Inflammation with Painful Opthalmoplegia ec Tolosa Hunt Syndrome PSA
Planning	Medicamentosa (Corticosteroid High dose IV)	Medicamentosa (Corticosteroid High dose IV)	Medicamentosa (Tappering off Corticosteroid)

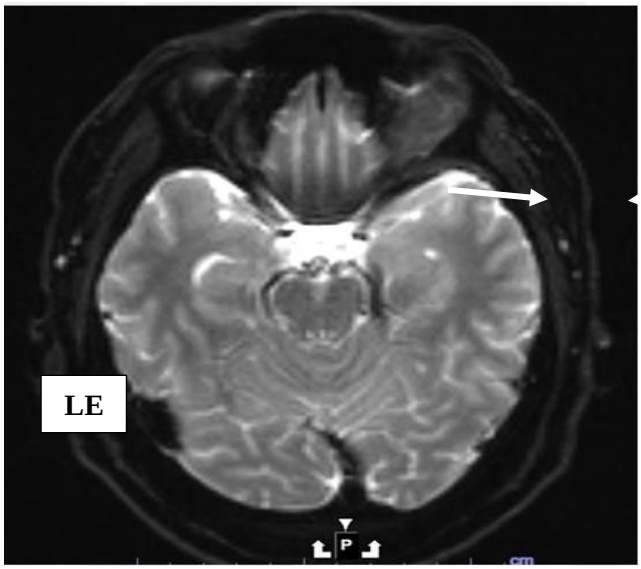


Figure 3. The contrast-enhanced head MRI of the patient in June 2024 demonstrated findings consistent with Tolosa-Hunt syndrome, with a differential diagnosis of en plaque meningioma. (Picture taken with patient's consent, *Courtesy : Poli Room RSUD Dr. Soetomo*)

We reduced corticosteroid therapy to 5mg/day. Other therapies are appropriate for internists and neurologists. Patients and families are educated regarding prognosis, recurrence prevention, rehabilitation, visual optimization and regular health control.

Based on the results of previous multidisciplinary therapy conclusions. The diagnosis in this patient was based on anamnesis, clinical examination, supporting examinations and the results of multidisciplinary consultations. Our patient was diagnosed with RLE recurrent orbital inflammation with painful opthalmoplegia ec tolosa hunt syndrome, Psoriatic Arthritis, Pre Obesity (BMI 27.43).

The following are clinical photographs of the patient during the initial visit prior to the incisional biopsy, and the most recent visit in September 2024 (Figure 4).

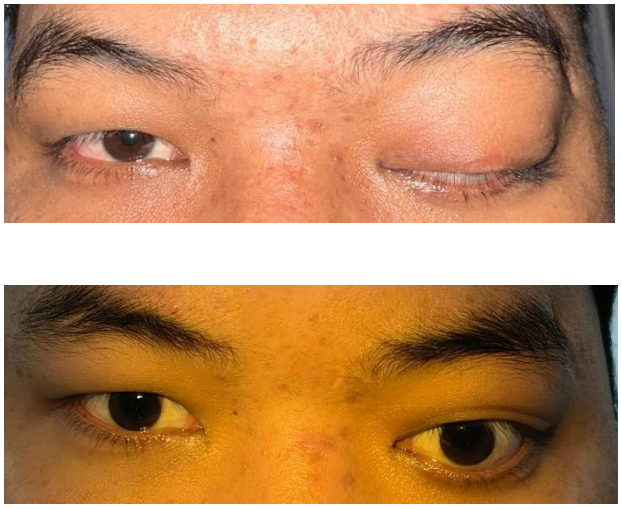


Figure 4. A. shows the clinical photograph of the patient during the initial visit prior to the incisional biopsy. **B.** shows the clinical photograph during the most recent visit in September 2024. Notable differences are observed, including incomplete closure of the left eyelid and the absence of left eye proptosis.
(Picture taken with patient's consent, *Courtesy : Poli Room RSUD Dr. Soetomo*)

DISCUSSION

Orbital inflammatory disease (OID, aka orbital inflammatory pseudotumor, idiopathic orbital inflammatory syndrome, nonspecific orbital inflammation) [1-3] was first described by Gleason in 1903 and accounts for 6% of diseases involving the orbit [4]. As OID is a diagnosis of exclusion, patients must be evaluated to rule out any malignancy, infection, systemic inflammatory process, or other concomitant medical conditions [6]. The differential diagnosis includes local and systemic inflammatory conditions caused by neoplasm, infection, vascular malformation, and trauma [5].

The anterior OID affects the globe, conjunctiva, eyelids, neural, and adjacent muscular structures. Pain and periorbital swelling are the most frequently encountered presenting features (Figure 4). Other common features include conjunctival chemosis and limited ocular motility. Rarely, proptosis, uveitis, papillitis, and exudative retinal detachment can also be seen[10].

In the patients we treated, the patient first came with clinical symptoms of acute OID, such as pain in the left eye accompanied by decreased vision, proptosis, swollen and closed eyelids. As explained that OID is a diagnosis of exclusion, the differential diagnosis in our patient at that time was Rhabdomyosarcoma if we looked at the MRI results from the area of origin. The patient underwent a tumor biopsy incision and the results were inflammatory process, non specific. Does not appear malignancy, does not support amyloidosis. The patient has experienced recurrence 3 times during 1 year. The MRI results after the biopsy incision stated that there was a high possibility of Toloso Hunt syndrome (most likely), Enplaque meningioma (less likely).

Apical or posterior OID, while less common, is associated with a poorer visual outcome[4]. Clinically, apical OID presents with orbital pain, restricted eye movement, visual loss, and minimal proptosis[11]. Inflammatory lesions of the orbital apex may extend intracranially through superior orbital fissure, optic canal, and inferior orbital fissure. The cavernous sinus and the middle cranial fossa are the two most common locations for intracranial involvement[12]. Tolosa–Hunt syndrome is a rare clinical condition caused by idiopathic granulomatous inflammation in the region of cavernous sinus and/or superior orbital fissure. Tolosa–Hunt syndrome presents with relapsing/remitting partial/complete ophthalmoplegia, visual loss, unilateral headache, and paralysis of cranial nerves III, IV, V1, and VI[13]. Neuroimaging may show an enhancing mass within the cavernous sinus (Figure 5).

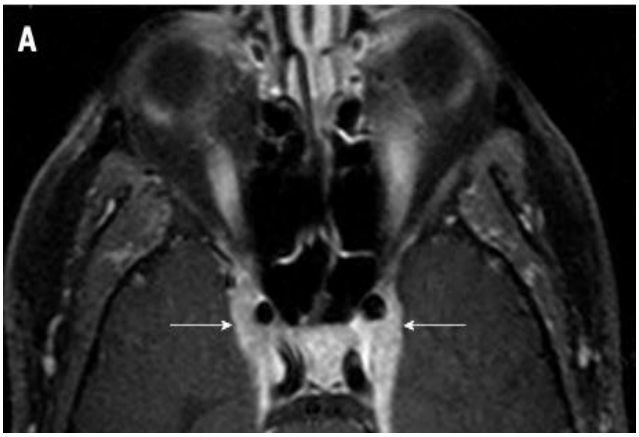


Figure 5. Tolosa-Hunt syndrome. Axial fat suppressed contrast-enhanced T1 showing bilateral cavernous sinus infiltration and enhancing tissue along the lateral margins of the cavernous sinus

Tolosa Hunt Syndrome also finds a place in the IHS Classification ICHD-3 Beta, in part three, under Painful cranial neuropathies and other facial pains. The IHS lays down diagnostic criteria for THS which have

high sensitivity (approximately 95% to 100%) but low specificity (approximately 50%). They are summarized as follows (Table 3)[16]:

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Table 3. Diagnostic criteria for Tolosa Hunt syndrome[16].

International Headache Society (IHS) Diagnostic Criteria
• Unilateral headache
• Includes both of the following: 1. Presence of granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, as seen on MRI or biopsy 2. Palsies of one or more of the oculomotor nerves (cranial nerves III, IV, and/or VI) on the same side
• Corroboration of the cause as evidenced by both of the following: 1. Palsies of cranial nerves III, IV, and/or VI have followed headache in two weeks or less, or have developed simultaneously with a headache 2. Localization of a headache around the eye on the same side
• Not better explained by any other headache etiology

In this case, the patient's complaints and clinical symptoms similiarly Tolosa Hunt syndrome. This is supported by the results of the post-operative MRI, namely that there is enhancement in the sinus covernosus and orbit. The patient also had weakness in nerves III, IV and VI in the left eye with painful and restricted eye movements. Frequently, the cause of a painful ophthalmoplegia in patients initially diagnosed with Tolosa- Hunt syndrome is later discovered to be neoplastic. Therefore, Tolosa- Hunt syndrome is a diagnosis of exclusion[14].

Patients with suspected Tolosa Hunt Syndrome will have a large risk of recurrence, as is the case in this case. The patient has experienced recurrence 3 times in a 1 year period. The vision in the left eye slowly began to decrease even though therapy had been given. The patient had no control and stopped taking medication, which increased the risk of disease recurrence and worsened the prognosis of the disease. Ideally, holistic management is needed involving ophthalmologists, internal medicine, neurologists for rehabilitative efforts and the role of the patient and family as a preventive effort.

Current therapeutic agents available for OID are: corticosteroids, nonspecific steroid-sparing agents such as (Methotrexate, Cyclosporin-A, Cyclophosphamide), biologic agents such as Etanercept, radiation therapy if Intolerant to cortisone or unresponsive therapy and surgery for nonresponders. Systemic corticosteroids, such as prednisone or methylprednisolone, are the cornerstone of early medical treatment for ocular pseudotumor[14].

Corticosteroid are considered first-line treatment in patient with tolosa hunt syndrome, over 75% of patients showing rapid improvement. Corticosteroid given the advantages of being inexpensive, relatively effective, readily available, and providing rapid onset of clinical improvement of signs and symptoms. But there is no specific data to give recommendations about dose, duration, or route of administration. Spontaneous remission of symptoms is known to occur. Although orbital pain drastically improves with steroid treatment, there is no evidence to suggest cranial nerve palsies improve faster with it. Treatment for Tolosa Hunt syndrome involves initial high-dose therapy for few days. Imaging studies like MRI can be repeated for follow-up, but usually, lag behind a few weeks as compared to symptomatic improvement[20].

Corticosteroid treatment includes prednisone, methylprednisolone, and dexamethasone orally or intravenously. The usage of methylprednisolone IV, 250 mg every 6 hours for 3 days. For adults, initial steroid treatment doses are typically 1 mg/kg of prednisone. High-dose oral corticosteroids of 1.0 to 1.5 mg/kg/day are the preferred protocol for children. The reported total dose ranges from 60 to 100 mg daily for 1 to 2 weeks with a 5- to 6-week taper[15].

Long-term use of corticosteroids is associated with various systemic and ocular side effects, such as immunosuppression, diabetes, hypertension, osteoporosis, secondary glaucoma, drug induce cataract and dry eye syndrome, which calls for careful monitoring and the use of steroid-sparing medications in some situations. To achieve a quick remission of inflammation, high-dose corticosteroids are frequently used, followed by a stepwise tapering regimen designed to minimize adverse effects and preserve disease control[15].

The steroids can begin tapering as soon as the clinical response is complete[18]. Despite beneficial effects, they also have side effects that depend on the dose, type of steroid and length of treatments. Many of the severe complications

occur in long-term use at doses greater than 20 mg of prednisone per day for three weeks or more causes tertiary adrenal insufficiency due to the HPA-axis (Hypothalamic Pituitary Adrenal Axis) suppression. Tapering dosage is needed when administering in longterm corticosteroids. The following is a reference for reducing the dose of corticosteroids in long-term use[20].

Table 4. Guideline Recommendation of Glucocorticoid Tapering[20].

Article	Type of Disease	Recommendation
Dasgupta et al, 2010	Giant cell arteritis (GCA) or temporal arteritis	• Continue prednisolone 40-60 mg (not < 0,75 mg/kg) for 4 weeks, then • Reduction dose by 10 mg every 2 weeks to 20 mg, then • Reduction dose by 2.5 mg every 2-4 weeks to 10 mg, then • Reduction dose by 1 mg every 1-2 months, provided no relapse occurs
Robinson, 2014	Immune-related toxicity	• Initiate corticosteroid taper over 3-6 weeks • Reduction prednisolone dose by 10 mg every three days (as toxicity allows) until 10mg/day, then • reduce by 5 mg every five days, then stop
Furst & Saag, 2018	Rheumatoid	• Initial dose above 40 mg/day of prednisone, reduction 5 to 10 mg/day every one to two weeks. • If prednisone dose 20-40 mg/day, reduction 5 mg/day every one to two weeks. • If prednisone dose 10-20 mg/day, reduction 2,5 mg/day every two to three weeks. • If prednisone dose 5-10 mg/day, reduction 1 mg/day every two to four weeks.

Steroid-sparing medications may be considered as an additional or alternative therapy in situations of corticosteroid dependency, intolerance, or refractoriness to preserve disease management and reduce corticosteroid-related comorbidities. Immunomodulatory drugs such as methotrexate, azathioprine, mycophenolate mofetil, and cyclosporine are frequently utilized to treat orbital pseudotumor. These medications facilitate corticosteroid tapering and avoid disease recurrence by lowering inflammatory cell infiltration inside the orbit and regulating aberrant immune responses[18].

While OID is generally benign, its course can be clinically fulminant with vision loss and severe oculomotor dysfunction. In cases where medical therapy is ineffective, such as refractory illness, compressive optic neuropathy, or severe vision-threatening consequences, surgical measures may be necessary. Orbital decompression, achieved through either transcutaneous or endoscopic methods, aims to reduce orbital pressure and alleviate optic nerve compression, thereby preserving visual function and relieving symptoms such as proptosis or diplopia[7].

Surgical excision or debulking of ocular lesions may also reduce tumor burden and relieve compressive symptoms in situations of mass effect or localized inflammation. Patients with optic nerve involvement may require admission for aggressive intravenous steroid therapy to prevent long-term visual impairment. Thus, prompt diagnosis and treatment are imperative[17].

While orbital pseudotumor resolves without treatment in some patients, steroids are the mainstay

of treatment. Over 75% of patients show improvement within 24 to 48 hours of steroid treatment. As mentioned previously, the reported cure rate is 37%. Recurrence is approximately 52%, even with corticosteroid treatment. Incomplete resolution of inflammation, corticosteroid dependency, insufficient tapering of immunosuppressive medication, and underlying autoimmune diseases are factors linked to an increased chance of recurrence. Repeated orbital pseudotumor episodes may exacerbate visual results and functional impairment by causing increasing orbital fibrosis, tissue scarring, and cumulative damage to orbital components[18].

Currently the main focus for this case is how to prevent recurrence. The patient has an autoimmune disease (psoriatic arthritis) so there is potential that if there is no good treatment synergy, the psoriatic arthritis could trigger inflammation in the patient's eyes. Several studies have shown that decreased vision due to recurrence of OID has the potential to increase the risk of permanent vision loss. This will have an impact on the patient's quality of life.

The patient is entering productive age (22 years old), and the patient works to help his parents. If a relapse occurs, the patient cannot work, and requires parental

assistance in his daily life so that the family does not get any income. This is in accordance with research conducted by Cockerham. The patient's quality of life will be greatly influenced by chronic OID[19].

Patients with complaints that have recurred 3 times since 1 year. The loss of visual acuity in these cases
is unpredictable and can be permanent. Patients with complexity and high risk of recurrence require special attention. Patient care will be more challenging in the presence of an autoimmune disease as in this case. Giving corticosteroids over a long period of time will cause new problems. Combination therapy can provide benefits to minimize the side effects of long-term corticosteroid use. Immunomodulatory drugs such as methotrexate and biologic agents such as Etanercept have been proven to reduce the effects of recurrence[14]. The patient's understanding of the disease they are suffering from and compliance with treatment will greatly influence the prognosis of the disease. Patients should be aware of clinical signs of relapse periods such as decreased vision, pain in the eyes, or even swelling of the eyes. This will really help the opthalmologist in treatment.

CONCLUSION

Orbital inflammatory disease is a diagnosis of exclusion, with the differential diagnosis including infection, systemic inflammatory conditions, and neoplasms, among other conditions. Tolosa–Hunt syndrome is a rare clinical condition caused by idiopathic granulomatous inflammation in the region of cavernous sinus and/or superior orbital fissure. Tolosa–Hunt syndrome presents with relapsing/remitting partial/complete ophthalmoplegia, visual loss, unilateral headache, and paralysis of cranial nerves III, IV, V1, and VI. Neuroimaging may show an enhancing mass within the cavernous sinus. Tolosa Hunt syndrome good responds with corticosteroids, but not prevent recurrence.

The loss of visual acuity in these cases is unpredictable and can be permanent. Patients with complexity and high risk of recurrence require special attention. Patient care will be more challenging in the presence of an autoimmune disease. Giving corticosteroids over a long period of time will cause new problems. Combination therapy of immunomodulatory drugs such as methotrexate and biologic agents such as Etanercept has been proven to reduce the effects of recurrence. Multidisciplinary synergy and good patient education are needed to improve the quality of life of patients with Tolosa Hunt syndrome.

DECLARATIONS

Data availability

The corresponding author (asmaa.reda@dentistry.cu.edu.e.g.)can provide access to the datasets utilized or examined in this study upon a reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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LITERATURE REVIEW

A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF BIPORTAL ENDOSCOPY VERSUS MICROSCOPIC DISCECTOMY IN LUMBAR DISC HERNIATION SURGERY: A COMPARATIVE ASSESSMENT OF OUTCOMES

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ABSTRACT

Background: Biportal Endoscopic Spine Surgery (BESS) is an emerging minimally invasive alternative to Microscopic Discectomy (MD) for lumbar disc herniation (LDH). However, the comparative effectiveness of BESS versus MD remains uncertain. Methods: Following PRISMA guidelines, we searched PubMed, EBSCOhost, and Scopus (2000-2024). We included studies comparing BESS and MD for LDH. Outcomes analyzed were operative time, blood loss, postoperative pain (VAS), functional recovery (ODI), hospital stay, and complication rates. A random-effects meta-analysis was performed.
Methods: Following PRISMA guidelines, we searched PubMed, EBSCOhost, and Scopus (2000-2024). We included studies comparing BESS and MD for LDH. Outcomes analyzed were operative time, blood loss, postoperative pain (VAS), functional recovery (ODI), hospital stay, and complication rates. A random-effects meta-analysis was performed.
Results: Four studies (n = 252 patients) were included. BESS was associated with a significantly shorter hospital stay but a longer operative time. Differences in pain reduction (VAS) and functional recovery (ODI) favored BESS but were not statistically significant. Bleeding and mJOA scores showed high heterogeneity and non-significant differences.
Conclusion: BESS offers potential benefits in hospital stay and recovery but lacks definitive superiority over MD. Larger, high-quality RCTs are needed to draw firmer conclusions.

Keywords: lumbar disc herniation, biportal endoscopy, microscopic discectomy, minimally invasive spine surgery, meta-analysis

INTRODUCTION

Lumbar disc herniation (LDH) is a common spinal disorder that can result in radicular pain, motor-sensory dysfunction, and reduced quality of life. It is a significant contributor to lower back and leg pain in individuals worldwide.[1–3] When conservative therapies are ineffective in relieving symptoms, surgical intervention, specifically discectomy, is frequently required.[2,13,15] Discectomy involves excision of the disc's herniated segment that is extruded onto the spinal nerves, alleviating discomfort and decreasing neurologic function. Historically, open discectomy has been the conventional intervention for lumbar disc herniation. Advancements in surgical techniques have resulted in the emergence of minimally invasive treatments, such as microscopic discectomy and

biportal endoscopic spine surgery (BESS).

Microscopic discectomy has become a recommended minimally invasive technique, using a retractor and a microscope to access the herniated disc.[11] It offers numerous benefits compared to open discectomy, including fewer incisions, reduced muscle dissection, and expedited recuperation. Clinical investigations indicate that microscopic discectomy results are comparable to conventional open surgery, featuring reduced postoperative pain and shorter hospital stays. This treatment has specific constraints, including a restricted field of view and a steep learning curve, which can complicate the procedure of a full discectomy and achieve the goal of optimal results.

To address these limitations, biportal endoscopic spine surgery (BESS) was developed as a recommended minimally invasive alternative.[6] BESS utilizes two small incisions (portals) to facilitate the insertion of surgical instruments and an endoscope, providing an expanded field of visibility and enhanced precision throughout the surgery.[8,11,16] This method is designed to reduce postoperative complications such as muscle atrophy and pain, minimize soft tissue injury, and facilitate the use of conventional spinal instruments, thereby increasing the accessibility of the procedure for spine surgeons.[14,18] Preliminary retrospective investigations indicate that BESS may be as effective as or potentially superior to conventional microscopic discectomy, particularly with enhanced visualization and less risk of complications.

Nevertheless, despite these positive findings, the evidence supporting BESS is still inadequate since no extensive randomized controlled trials (RCTs) directly contrast its outcomes with those of microscopic discectomy. This systematic literature review and meta-analysis aim to evaluate and compare the clinical outcomes of BESS and microscopic discectomy independently in managing lumbar disc herniation. This study seeks to thoroughly assess the efficacy, safety, and benefits of both surgical procedures by examining available research data, contributing to the ongoing discourse regarding the ideal surgical method for LDH.

The primary goal of this study is to evaluate the clinical outcomes, including functional recovery, complication rates, and patient satisfaction, between BESS and microscopic discectomy. We predict that both procedures will exhibit comparable efficacy in alleviating symptoms and enhancing quality of life. We also seek to discover significant differences in surgical performance, intraoperative bleeding, length of hospital stay, and postoperative healing that may impact clinical decision-making for patients with lumbar disc herniation.

MATERIALS AND METHODS

A comprehensive search was conducted in the PubMed, Ebscohost, and Scopus databases from 2000 to 2024, employing the PICO framework (Population, Intervention, Comparison, Outcome). The target population consisted of LDH patients, the intervention analyzed was BESS, and the comparisons were made using clinical scales and radiological parameters. The outcomes examined included functional, clinical, and radiological. Keywords for literature searching use Boolean operators with (Herniated Disc lumbar OR Lumbar disc herniation OR Spinal surgery) AND (Biportal endoscopy OR Minimally invasive spine surgery) AND (Functional outcome OR Clinical outcome OR Visual Analog Scale OR Oswestry Disability Index OR Clinical Global Impression OR Radiological Outcome OR).

The data collection process followed the PRISMA 2020 Flowchart (Figure 1), beginning with a keyword-based literature search. This was followed by the removal of duplicate records, screening based on inclusion and exclusion criteria, filtering relevant titles and abstracts, selecting studies for inclusion, and assessing the quality of the chosen literature.

This study included randomized controlled trials (RCTs), cohort studies, and comparative studies that directly compared BESS and MD in patients diagnosed with lumbar disc herniation. Studies were excluded if they provided insufficient data, were published in languages other than English, or involved other types of surgical techniques or mixed patient populations. This ensured a focused analysis on the targeted interventions. These inclusion and exclusion criteria were carefully defined to maintain the relevance and quality of the evidence base.

The outcomes of interest were operative time, blood loss, postoperative pain as measured by the Visual Analogue Scale (VAS), functional recovery assessed via the Oswestry Disability Index (ODI), Modified Japanese Orthopaedic Association Scoring System (mJOA), and the length of hospital stay. Secondary outcomes focused on complication rates, including infections, nerve injuries, and recurrence of herniation, as well as the recurrence of disc herniation itself. These outcomes were selected to provide a comprehensive evaluation of the comparative effectiveness and safety of BESS and MD in managing lumbar disc herniation. This structured approach ensures that the findings are both clinically meaningful and aligned with the priorities of patients and healthcare providers.

Two independent reviewers extracted data on study characteristics, patient demographics, surgical details, and outcomes. Statistical analysis was performed using SPSS 29 software. A random-effects model was applied, and results were presented as Standardized mean differences (SMD) with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic.

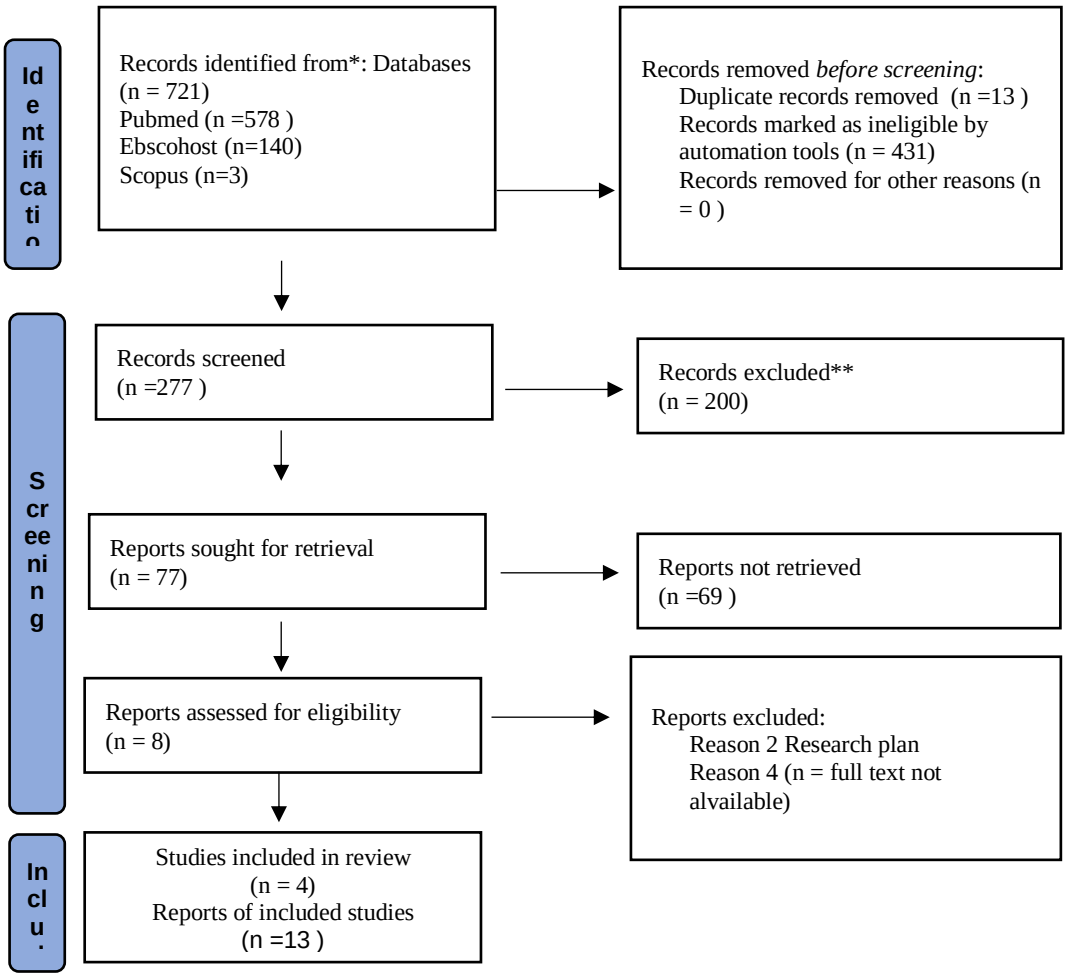


Figure 1. Prisma Flowchart of the Literature Review

RESULTS

A total of 4 studies were included, involving 252 patients (126 in each group). Of these, one was a randomized controlled trial (RCT), and three were retrospective studies. The sample sizes in the included studies ranged from 37 to 109 participants [1,7,10,19].

Table 1 compares patient characteristics and pathology distribution between BESS and MD. The average age was similar for both groups (BESS: 52.56±13.76; MD: 52.39±12.89; P = 0.92). There were no significant differences in pathology distribution (P = 0.36), with most cases occurring at the L4/5 level (BESS: 77%, MD: 68%), followed by L5/S1 (BESS: 15%, MD: 26%) and L3/4 (BESS: 8%, MD: 6%). This suggests that both techniques had comparable patient profiles and pathology distributions. The VAS analysis (Figure 2) showed a slight trend toward better pain reduction with BESS compared to MD, with an overall effect size of -0.46. However, this difference was not statistically significant (α = 0.05), and there was considerable heterogeneity, reducing the reliability of the result.

Table 1. Patient Characteristic Comparison of BESS Group and MD Group

	BESS	MD	P
Age	52.56±13.76	52.39±12.89	0.92
Location			0.36
L3/4	8%	6%	
L4/5	77%	68%	
L5 S1	15%	26%	

Forest Plot of Visual Analogue Scale (VAS) Comparison between BESS and MD

In the Oswestry Disability Index (ODI) analysis (Figure 3), BESS showed minor improvements in functional disability compared to MD, with an overall effect size of 0.17 and a standard error of 0.13, indicating slight improvement for BESS over MD. The heterogeneity value (I^2) was 0%.

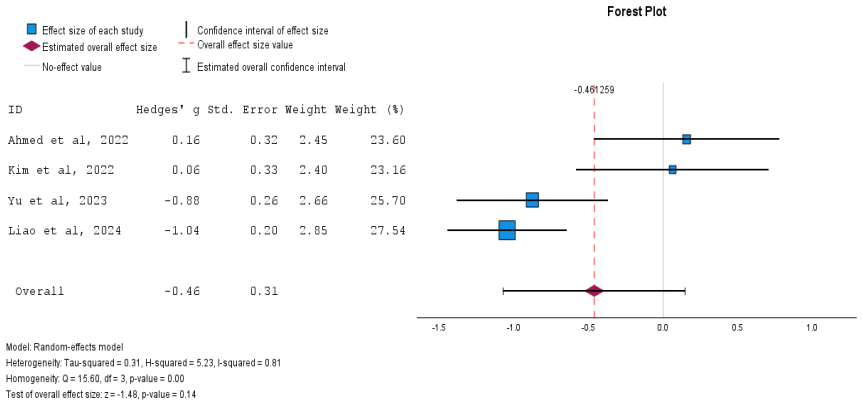


Figure 2. Forest Plot of Visual Analogue Scale (VAS) Comparison between BESS and MD

Oswestry Disability Index (ODI)

The effect size for operative time (Figure 4) was 1.32 (95% CI: 0.10 to 2.54, p = 0.03), indicating a statistically significant effect. The heterogeneity statistics showed a high degree of variability among studies (Tau^2 = 1.44, H^2 = 16.30, I^2 = 94%), suggesting substantial heterogeneity. The overall effect size test (Z = 2.13, p = 0.03) confirmed a significant combined effect. However, the high I^2 value (94%) indicates considerable variability among the studies.

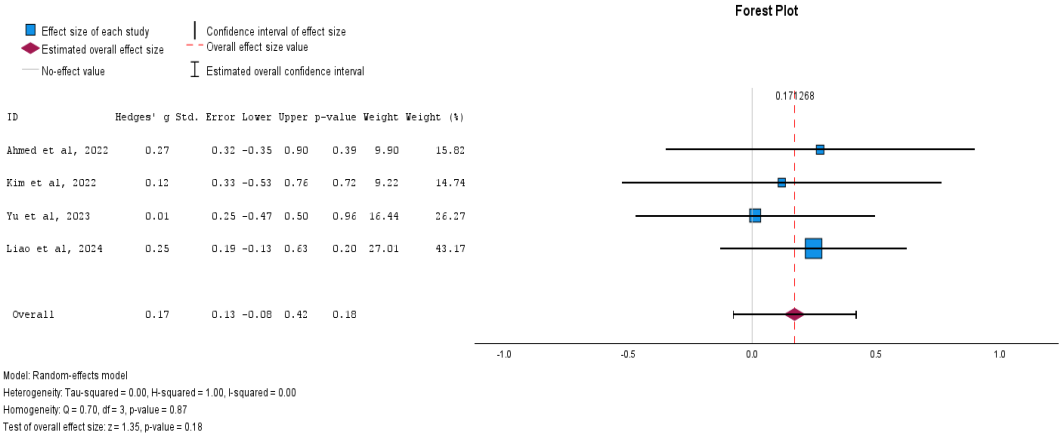


Figure 3. Forest Plot of Oswestry Disability Index (ODI) Comparison between BESS and MD

Operative time

The effect size for surgical bleeding (Figure 5) was -0.86 (95% CI: -3.10 to 1.37, p = 0.45), indicating no statistically significant overall effect. The heterogeneity statistics revealed extremely high variability among the studies (Tau^2 = 5.08, H^2 = 48.92, I^2 = 98%), confirming substantial heterogeneity. The overall effect size test (Z = -0.76, p = 0.45) confirmed that the combined effect was not statistically significant. The high I^2 value (98%) indicates substantial heterogeneity.

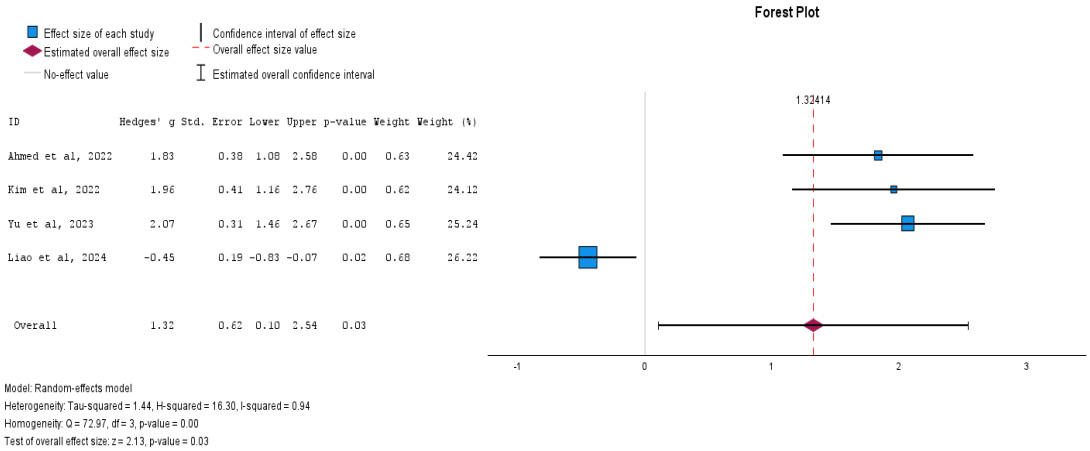


Figure 4. Forest Plof Operative Time Comparison BESS and MD

Surgery Bleeding

For hospital stay (Figure 6), the effect size was -1.83 (95% CI: -2.35 to -1.30, p = 0.00), indicating a statistically significant reduction in hospital stay. The heterogeneity statistics showed moderate variability (Tau^2 = 0.18, H^2 = 2.83, I^2 = 65%), suggesting a moderate level of heterogeneity. The overall effect size test (Z = -6.80, p = 0.00) confirmed a highly significant combined effect. Despite some heterogeneity (I^2 = 65%), the consistency of negative effect sizes across studies strengthens the reliability of the findings.

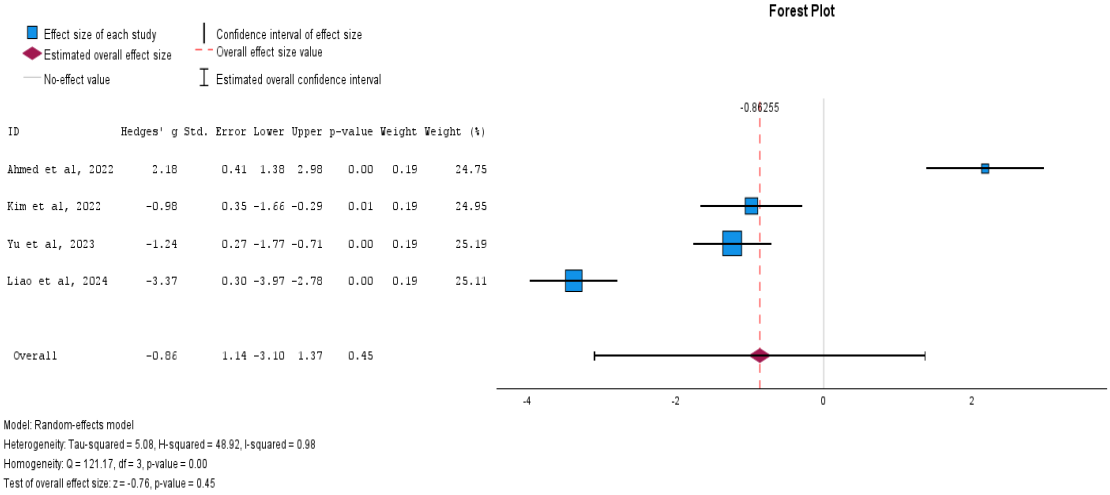


Figure 5. Forest Plot Surgery Bleeding Comparison of BESS and MD Hospital Stay

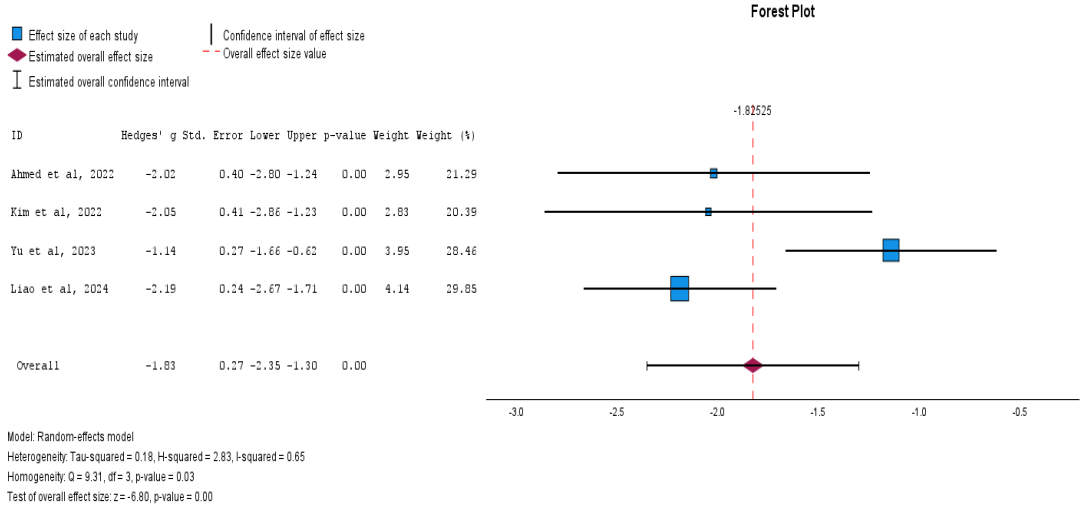


Figure 6. Forest Plot Hospital Stay BESS and MD

The effect size for mJOA (Figure 7) was 13.06 (95% CI: -18.45 to 44.57, p = 0.42). The wide confidence interval indicates substantial uncertainty in the overall effect estimate, and the p-value (0.42) suggests no statistically significant combined effect. The heterogeneity statistics showed extreme variability (Tau^2 = 514.64, H^2 = 239.57, I^2 = 100%), confirming substantial heterogeneity. The overall effect size test (Z = 0.81, p = 0.42) further supports the lack of statistical significance.

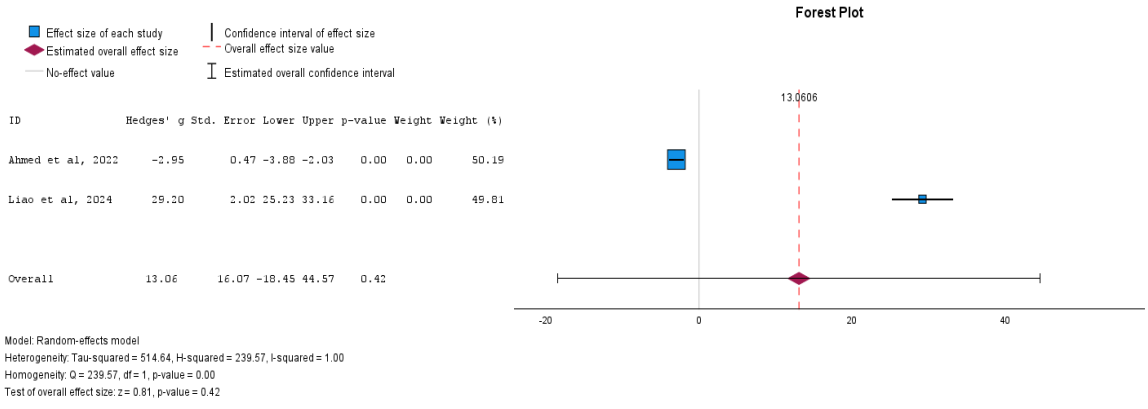


Figure 7. Forest Plot mJOA BESS and MD mJOA

DISCUSSION

The comparative analysis of Biportal Endoscopy Spine Surgery (BESS) and Microscopic Discectomy (MD) revealed several insights into patient demographics, clinical outcomes, and procedural characteristics. The average patient age was nearly identical in both groups (BESS: 52.56±13.76, MD: 52.39±12.89), indicating that age did not play a role in choosing either surgical approach (P = 0.92). Both techniques were predominantly applied at the L4/5 spinal level, with BESS accounting for 77% and MD for 68% of cases. Pathologies at the L3/4 level were less common, representing 8% and 6% in the BESS and MD groups, respectively. At the L5/S1 level, MD showed a higher frequency of use (26%) compared to BESS (15%). The distribution of spinal pathology locations (P = 0.36) showed no statistically significant differences between the two techniques, underscoring their application to similar patient populations and anatomical levels.

The analysis of postoperative pain reduction, as measured by VAS, demonstrated a slight trend favoring BESS over MD. However, the difference was not statistically significant. This suggests that while BESS may provide better pain relief for some patients, the overall impact remains uncertain due to high variability across studies. The minimally invasive nature of BESS, with smaller incisions and reduced tissue disruption, may theoretically reduce pain and accelerate recovery.[3,4] Clinically, patients undergoing BESS might experience less immediate discomfort, enabling earlier mobilization and reduced reliance on pain medications.[3] However, these theoretical benefits remain hypotheses until further validated by high-quality trials.

Functional recovery, assessed using the Oswestry Disability Index (ODI), also indicated a minor improvement with BESS compared to MD. The small effect size (0.17) suggests a limited but potentially beneficial impact on patient-reported disability outcomes. Furthermore, the heterogeneity was relatively low (I^2 = 0%), indicating consistency among the included studies in functional recovery results. This underscores the need for additional studies to explore whether BESS can achieve meaningful functional benefits in practical applications. These findings align with previous studies suggesting that BESS may improve early postoperative mobility and reduce postoperative pain; however, larger and more homogeneous studies are necessary to validate these findings.[12]

One of the most significant findings of this study was the increased operative time associated with BESS compared to MD. The effect size of 1.32 (p = 0.03) indicates that BESS requires a longer duration for completion. This is likely due to the complexity of the biportal technique, which requires precise visualization and instrument manipulation within a confined space. The other causes are the learning curve in BESS, early cases of BESS, triangulation, anatomical view in endoscopy, and maintaining bleeding during surgery, which are challenging steps.[17,18]

Despite this drawback, the potential benefits, including reduced tissue disruption and faster recovery times, may offset this limitation.1[7] The substantial heterogeneity (I^2 = 94%) suggests that variations in surgical expertise, patient selection, and institutional protocols may contribute to differences in operative duration. Standardizing surgical expertise and optimizing protocols could further reduce operative times and improve the adoption of BESS in clinical settings.

In contrast, the analysis of intraoperative blood loss did not reveal a statistically significant difference between the two techniques (effect size = -0.86, p = 0.45). One significant advantage of BESS lies in its ability to reduce surgical bleeding, which is consistent with its minimally invasive design. Lower bleeding rates can minimize perioperative complications, enhancing patient safety. The high heterogeneity (I^2 = 98%) suggests variability in reporting methods and patient factors that influence intraoperative bleeding. While some studies report reduced blood loss with BESS due to minimal tissue disruption, others indicate comparable bleeding volumes between the two procedures.[5,9] Future standardized assessments of intraoperative bleeding are needed to clarify these findings.

Hospital stay is an important measure of surgical efficiency and postoperative recovery. Our findings showed that BESS significantly reduced the duration of hospital stay compared to MD, with an effect size of -1.83 (p = 0.00). The moderate level of heterogeneity (I^2 = 65%) suggests some variability but overall consistency in the results. This aligns with existing literature indicating that minimally invasive procedures like BESS promote faster recovery, reduced postoperative complications, and earlier mobilization, leading to shorter hospital stays, which reduce costs and the risk of hospital-acquired infections.[6]

The analysis of the mJOA score, which evaluates neurological function, showed a highly variable and non-significant effect size of 13.06 (p = 0.42). The extreme heterogeneity (I^2 = 100%) suggests that the included studies had substantial differences in patient selection, assessment methods, and follow-up durations. Improvements in mJOA scores suggest better functional recovery with BESS compared to MD. While BESS may offer certain advantages in preserving neurological structures, the current evidence does not support a conclusive benefit over MD in mJOA scores.

Comparative evaluations of BESS and MD reveal nuanced differences in clinical outcomes. While BESS shows promise in reducing postoperative pain and improving functional recovery, the lack of statistical significance and variability in study designs limits the

robustness of these findings. Operative times remain challenging for BESS, but its advantages in shorter hospital stays, reduced bleeding, and potentially faster recovery highlight its potential as a minimally invasive option. The significant reduction in hospital stay suggests that BESS may be preferable in settings where rapid recovery and early discharge are prioritized. However, the longer operative time associated with BESS may be a limiting factor, particularly in high-volume surgical centers.

Additionally, while BESS demonstrated trends toward improved pain reduction and functional recovery, the statistical significance was not consistently achieved, highlighting the need for further large-scale and high-quality randomized controlled trials. Future research should focus on addressing the gaps in surgical techniques and protocol by prioritizing uniform methodologies, including consistent surgical techniques, patient selection criteria, and follow-up protocols. Long-term outcomes, such as sustained functional recovery, pain relief, and quality-of-life improvements, are critical to understanding the durability of BESS benefits. Large-scale, multicenter randomized controlled trials are needed to overcome limitations like small sample sizes and single-center biases, improving the generalizability of findings. Additionally, economic evaluations could highlight the cost-effectiveness of BESS by considering reduced hospital stays and perioperative complications.

The integration of emerging technologies, such as robotics and augmented reality, could further optimize the precision and efficiency of BESS. Exploring these innovations and their impact on clinical outcomes will help advance minimally invasive spine surgery, ensuring evidence-based improvements in patient care. The evolving priorities in spinal surgery emphasize patient-centered outcomes, long-term benefits, and cost-effectiveness, paving the way for BESS to become a viable alternative to MD in specific clinical scenarios.

CONCLUSION

The findings of this study indicate that while BESS shows promise as a minimally invasive alternative to MD, the current evidence does not yet establish its superiority with statistical certainty. The theoretical benefits of BESS, such as reduced postoperative pain, improved functional recovery, and shorter hospital stays, align with clinical goals but remain inconclusive due to significant limitations. These include small sample sizes, methodological inconsistencies, and high heterogeneity across analyses, which challenge the generalizability of the results. From a clinical perspective, the findings underscore the critical role of pain management in minimally invasive surgical techniques. BESS's potential to minimize postoperative pain and accelerate recovery aligns well with the priorities of modern surgical care. However, the lack of definitive statistical significance suggests the need for further robust evidence to confirm these benefits. The variability in results highlights the importance of addressing methodological and procedural challenges to establish a clearer understanding of BESS's efficacy and outcomes.

Future studies should prioritize larger and more diverse patient populations, standardized surgical protocols, and extended follow-up periods to comprehensively evaluate the long-term clinical advantages of BESS. Additionally, strategies to address current limitations, such as prolonged operative time, must be explored to optimize its clinical utility. As advancements in spine surgery continue to evolve, BESS holds the potential to significantly enhance patient outcomes, provided that future research can consistently validate its benefits through rigorous and well-designed studies.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Conflict **interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ORIGINAL ARTICALE

ASSESSMENT OF BONE METABOLISM MARKERS IN DIABETIC PATIENTS: INFLUENCE OF OSTEOPOROSIS, AGE, AND GENDER

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ABSTRACT

Background: Diabetes mellitus is linked to changes in bone metabolism, which may result in osteoporosis and a heightened risk of fractures. There is still little research on the incidence and biochemical characteristics of these alterations in diabetic people in Iraq.

Objectives: The aim of this study is to assess serum bone metabolism indicators in diabetic patients, both with and without osteoporosis, and to compare these markers with those of healthy controls, while accounting for age and gender variations.

Materials and Methods: This study involved 219 individuals aged 40–80 years, including 149 diabetic patients (with and without osteoporosis) and 70 healthy controls, recruited from hospitals and clinics in Kirkuk, Iraq. Participants were grouped as follows: G1 – diabetics without osteoporosis, G2 – diabetics with osteoporosis, and G3 – healthy controls. Blood samples were collected after overnight fasting, and serum was separated for biochemical analysis. Bone metabolism markers-type I collagen, osteocalcin, and TRACP-5b—were quantified using ELISA and ECLIA techniques according to standard protocols.

Results: Results revealed statistically significant elevations ($P < 0.05$) in serum collagen type I, osteocalcin, and TRACP among diabetic patients compared to controls, indicating altered bone turnover. Additionally, these markers were significantly higher in diabetic patients with osteoporosis, especially TRACP and collagen type I, reflecting increased bone resorption. Age-related analysis showed significant increases in TRACP in older osteoporotic patients ($P < 0.0001$), while osteocalcin showed no significant age-related variation. Gender analysis revealed higher collagen type I in non-osteoporotic males ($P = 0.005$) and significantly elevated TRACP in osteoporotic females ($P < 0.0001$), suggesting gender- and age-related modulation of bone metabolism in diabetes.

Conclusion: Diabetic patients exhibit altered bone turnover, with more pronounced changes in those with osteoporosis. These alterations are modulated by age and gender, suggesting the need for targeted bone health assessment in diabetic populations.

Keywords*:* TRACP-5b and type I collagen, Diabetes and osteoporosis, Bone metabolism markers

INTRODUCTION

Diabetes mellitus (DM) is primarily defined by elevated blood glucose levels (hyperglycemia), excessive thirst (polydipsia), and increased appetite (polyphagia). Diabetes mellitus is a prevalent metabolic condition that is escalating at an alarming pace globally[1]. The WHO projects that diabetes will rank as the seventh leading cause of death by 2030[2]. There are four main types of diabetes mellitus, Type 1 Diabetes Mellitus (T1DM) results from the autoimmune destruction of pancreatic β cells, leading to the absence of insulin production[3]. This condition is often referred to as insulin-dependent diabetes mellitus (IDDM)[4]. CVD kills about 70% of type 2 diabetics, making it the major cause of mortality. Diabetes has been linked to cardiovascular disease for decades[5]. Diabetes is the predominant metabolic condition, significantly impacting global health systems. It has evolved into a significant, chronic, non-communicable disease following cardio-cerebrovascular diseases. At present, 90% of individuals with diabetes are afflicted with type 2 diabetes. Hyperglycemia is the primary characteristic of diabetes. The functionality of pancreatic

cells progressively diminishes prior to the emergence of clinical hyperglycemia. Comprehending the molecular mechanisms underlying diabetes development might furnish therapeutic therapy with essential advancements[6].

Diabetes is a chronic condition marked by hyperglycemia, stemming from either a relative or absolute lack of insulin[7], reduced sensitivity of target cells to insulin, and disturbances in glycolipid and protein metabolism[8]. Over 90% of individuals with diabetes are afflicted with type 2 diabetes[9]. Individuals with diabetes typically have four metabolic irregularities: impaired insulin action, failure in insulin secretion[10], elevated endogenous glucose production, and obesity[11].

Tartrate-Resistant Acid Phosphatase (TRACP), also known as acid phosphatase 5 (ACP5), is a glycoprotein enzyme predominantly expressed in osteoclasts and activated macrophages[12]. Elevated levels of TRACP 5a in the bloodstream are considered a biomarker for chronic inflammatory conditions such as diabetes mellitus, cancer, and autoimmune disorders. In contrast, TRACP 5b is produced by osteoclasts—specialized bone-resorbing cells—and serves as a reliable marker of bone resorption activity[13]. This isoform is particularly useful in evaluating bone metabolic diseases like osteoporosis, rheumatoid arthritis, and skeletal complications in diabetic patients. The differentiation of TRACP isoforms provides valuable insights into both inflammatory and bone-related pathologies[14].

Typically, TRAP is significantly expressed in osteoclasts, activated macrophages, neurons, and the porcine endometrium during pregnancy[15]. Some research indicates that patients with poorly controlled diabetes have elevated TRACP 5b levels, suggesting increased bone resorption. This may be due to chronic hyperglycemia-induced oxidative stress and inflammation, leading to enhanced osteoclast activity[16], Conversely, other studies have reported reduced TRACP levels in diabetic individuals, implying suppressed bone turnover. Hyperglycemia can impair osteoblast function and reduce osteoclast genesis, leading to low bone turnover. The discrepancies in TRACP levels among studies may be attributed to differences in study populations, glycemic control status, duration of diabetes, and presence of diabetic complications[17]. Collagen is among the most prevalent proteins in several living species due to its involvement in connecting biological components. It is the predominant protein in the extracellular matrix (ECM). The extracellular matrix (ECM) is a non-cellular element present in all tissues and organs, serving as a structural framework that influences cell adhesion and migration and regulates cellular growth and metabolism[18]. There are various types of collagens that can be classified based on their α-chain composition. There have been around 28 different forms of collagen discovered; however, collagen type I is the most common type of collagen. As a result of its widespread presence in virtually all connective tissues, collagen type I accounts for more than ninety percent of the total collagen found in the human body[19].

Robust data indicates that ucOC may influence metabolic processes by acting on many tissues critical for glucose and lipid metabolism. In the pancreas, ucOC can stimulate β-cell proliferation and insulin synthesis via GPRC6A[20]. The ucOC can boost the production of delta-like 1 (DLK1) in pancreatic β cells, and DLK1 prevents osteocalcin production in osteoblasts that depends on insulin signaling[21]. Consequently, a positive feedback loop exists between pancreatic islets and bone. The ucOC may indirectly enhance insulin production by promoting GLP-1 release from the gut[22]. In tissues that respond to insulin, ucOC can help increase the uptake of glucose and fatty acids, improve insulin sensitivity, make better use of nutrients, and boost mitochondrial function, while reducing the formation of glycogen in muscles and the production of fat in the liver[23].

MATERIALS AND METHODS

Study Design and Participants

There were 219 participants, 149 patients and 70 healthy controls, aged 40 to 80. Participants were divided into three groups: Group 1 (G1) included diabetic patients without osteoporosis, Group 2 (G2) had diabetics with osteoporosis, and Group 3 (G3) had healthy people. Kirkuk Teaching Hospital, Azadi Teaching Hospital, and private medical clinics in Kirkuk, Iraq, recruited between November 2024 and May 2025. Qualified experts confirmed the clinical diagnosis. Hepatic, renal, pancreatic, Alzheimer's, and stroke patients were excluded from the research to guarantee accuracy and eliminate confounding variables.

Sample Collection

Following an overnight fast, venous blood samples (6 mL) were collected aseptically from all participants via venipuncture. The samples were divided into two portions: 4 mL were transferred into plain tubes without anticoagulant and left at room temperature for 30 minutes to allow clotting. The samples were then centrifuged at 3000×g for 10 minutes, and the resulting clear serum was carefully separated and stored in sterile, dry Eppendorf tubes at −20 °C for subsequent biochemical analysis. These analyses included measurements of serum (TRACP), osteocalcin, typ1 collagen.

Biomarker Assessment Methods

Serum Collagen Type I (COL1) and Tartrate-Resistant Acid Phosphatase 5b (TRACP-5b) were measured using commercially available sandwich ELISA kits, following the manufacturers' protocols. In both assays, microplates pre-coated with specific antibodies captured the target analytes, which were then detected using HRP-conjugated secondary antibodies. After substrate addition, the color intensity was measured at 450 nm, and

concentrations were calculated using a standard curve. Osteocalcin levels were estimated using an electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e411 analyzer. The assay used biotinylated and ruthenium-labeled monoclonal antibodies in a sandwich format, and the chemiluminescent signal generated was proportional to osteocalcin concentration. All assays were performed and calibrated according to the manufacturers' instructions, and quality control samples were used to ensure accuracy and precision.

Statistical analysis

All data were analyzed by using the Minitab program according to the ANOVA test. However, the mean when compromised by the ducun multiple range test under the P. value 0.05.

RESULTS

Effect of disease on the diagnostic parameters

Table 1 demonstrates statistically significant differences ($P < 0.05$) in several bone-related biochemical markers between diabetic patients and healthy controls. Specifically, serum levels of type I collagen, osteocalcin, and tartrate-resistant acid phosphatase (TRACP) were significantly elevated in patients compared to controls. These findings suggest enhanced bone turnover or metabolic alterations associated with diabetes mellitus.

Table 1. Determination Level of typ1 collagen, Osteocalcin, Serum (TRACP) of diabetes mellitus patients and healthy controls

Group / Parameters	Patients ± St.D * (N = 149)	Control ± St.D * (N = 70)	Probability
typ1 collagen (µg/ml)	1622.9 ± 1151.85	429.5 ± 264.409	0.0001
Osteocalcin (ng/ml)	45.774 ±23.654	34.793 ± 17.084	0.0006
Serum (TRACP) (U/L)	1.552 ± 0.744	1.286 ± 0.703	0.0069

* $P < 0.05$ highly significant

Effect of disease on the diagnostic parameters

The findings presented in Table 2 reveal statistically significant differences ($P < 0.05$) in bone metabolism markers between diabetic patients with and without osteoporosis. Notably, markers of bone turnover—including type I collagen, osteocalcin, and tartrate-resistant acid phosphatase (TRACP)—were substantially higher in the osteoporotic group. The marked elevations in TRACP and type I collagen, in particular, highlight the intensified bone resorption and metabolic activity associated with osteoporosis in diabetic individuals.

Table 2. Comparison of Bone Metabolism Markers Between Diabetic Patients with and Without Osteoporosis

Group	Diabetic patients without osteoporosis (72)	Diabetic patients with osteoporosis (77)	P-value
	mean ± SD *	mean ± SD *	
typ1 collagen (µg/ml)	749.126 ± 575.7590	2607.694 ± 989.4119	0.0001
Osteocalcin (ng/ml)	42.280 ab ± 22.5309	49.511 b ± 24.5642	0.0001
Serum (TRACP) (U/L)	0.924500 a ± .2779814	2.139597 c ± .5397886	0.0001

*** P < 0.05 highly significant**

Effect of age on bone metabolism markers in diabetic patients with and without osteoporosis

Table (3) demonstrates the influence of age on bone metabolism markers among diabetic patients, both with and without osteoporosis. A statistically significant difference ($P < 0.05$) was observed in type I collagen levels across age groups, indicating that bone turnover activity may vary with age. The most prominent change was seen in serum tartrate-resistant acid phosphatase (TRACP) levels, which increased significantly in older osteoporotic patients ($P < 0.0001$), reflecting accelerated bone resorption with advancing age. Although osteocalcin levels varied between age groups, the differences were not statistically significant ($P = 0.063$).

Table 3. Effect of age on bone metabolism markers in diabetic patients with and without osteoporosis

Group / Parameters	Diabetic patients without osteoporosis (mean ± SD)			Diabetic patients with osteoporosis (mean ± SD) *			probability
Age (years)	20-40	41-60	61-80	20-40	41-60	61-80	
typ1 collagen (µg/ml)	1973.8742 ± 1245.4482	1878.803 ± 1167.004	1805.362 ± 1086.486	873.8167 ± 921.6000	1705.3348 ± 1174.2287	1097.2523 ± 878.76505	0.005
Osteocalcin (ng/ml)	50.7288 ± 25.30319	45.3222 ± 45.3222	53.7958 ± 20.09602	47.4760 ± 25.43059	47.4955 ± 23.87884	29.2536 ± 9.91078	0.063
Serum (TRACP) (U/L)	0.647885 ± 0.2554405	.990333 ± .0611945	1.209474 ± .0776004	1.616600 ± .6418021	1.993425 ± .2075913	2.761955 ± .2408381	<.0001

*** P < 0.05 highly significant**

Effect of gender on bone metabolism markers in diabetic patients with and without osteoporosis

Table (4) highlights gender-related differences in bone metabolism markers among diabetic patients with and without osteoporosis. A statistically significant difference (P = 0.005) was observed in type I collagen levels, with higher values in males from the non-osteoporotic group, suggesting sex-based variation in bone turnover. Although osteocalcin levels were higher in females in the non-osteoporotic group and slightly higher in males in the osteoporotic group, the differences were not statistically significant (P = 0.06). In contrast, serum tartrate-resistant acid phosphatase (TRACP) levels showed a highly significant difference (P < 0.0001), with notably higher concentrations in osteoporotic females, indicating increased bone resorption in this subgroup.

Table 4. Effect of gender on bone metabolism markers in diabetic patients with and without osteoporosis

Group / Parameters	Diabetic patients without osteoporosis (mean ± SD)		Diabetic patients with osteoporosis (mean ± SD) *		probability
Age (years)	Male	Female	Male	Female	
typ1 collagen (µg/ml)	2044.6340 ± 1183.57605	1705.1550 ± 1122.71788	1355.6563 ± 1164.72121	1381.2433 ± 1054.29244	0.005
Osteocalcin (ng/ml)	45.1210 ± 24.09357	54.9978 ± 24.40759	50.3909 ± 24.04047	35.5205 ± 18.94083	0.06
Serum (TRACP) (U/L)	0.739225 ± 0.2295012	1.156094 ± 0.1051657	1.739114 ± 0.4372099	2.473333 ± 0.3613518	<.0001

DISCUSSION

The current study found that patients had much higher levels of type I collagen, osteocalcin, and tartrate-resistant acid phosphatase (TRACP) compared to healthy individuals, indicating that their bone turnover activity is generally increased. Type I collagen, an essential constituent of the bone matrix and a significant indicator of bone resorption, exhibited a notable increase in the patient group. This increase shows that osteoclasts are more active, breaking down the bone matrix by releasing enzymes like cathepsin K and TRACP5b, which help break down collagen and send its pieces into the bloodstream[24].

The elevated osteocalcin levels indicate increased osteoblastic activity. Osteocalcin is produced by mature osteoblasts and functions as a specific indicator of bone formation. The elevation may indicate a compensatory response to heightened bone resorption or signify active bone remodeling[25]. TRACP, an enzyme derived from osteoclasts, was significantly elevated, further supporting the evidence of increased bone resorption. TRACP5b levels correlate directly with the number and activity of osteoclasts[26,27]. The results align with the notion of high-turnover bone disease, frequently seen in aging populations, postmenopausal women, and those with metabolic bone disorders. Age-related changes result in an imbalance between bone resorption and formation, promoting net bone loss[28], In postmenopausal women,

estrogen deficiency accelerates bone turnover by increasing the number of bone remodeling units[24].

Bone turnover is more pronounced in trabecular bone than in cortical bone, owing to its higher cellularity and metabolic activity. This may lead to elevated circulating bone turnover markers in systemic diseases like diabetes[29]. The elevated markers identified in this study indicate an increased rate of bone remodeling, likely resulting from heightened osteoclast and osteoblast activity. The findings suggest potential implications for bone fragility and fracture risk in diabetic patients, emphasizing the role of biochemical markers in evaluating skeletal health[24].

The findings of the present study, which indicate significantly elevated levels of type I collagen, osteocalcin, and TRACP in diabetic patients with osteoporosis compared to those without, are in agreement with several prior investigations.

For instance[30] reported a significant increase in bone resorption markers such as TRACP-5b and CTX in osteoporotic patients with type 2 diabetes, highlighting the role of osteoclast hyperactivity in bone loss, which supports our results regarding the elevated TRACP levels[31]. Likewise, Liu *et al*. (2021) observed that osteocalcin levels were significantly higher in diabetic individuals with poor bone density, suggesting a compensatory increase in bone turnover that aligns with our findings of increased osteocalcin in the osteoporosis subgroup[16]. In addition, the study of[32] found that type I collagen degradation products were markedly elevated in diabetic patients with osteoporosis, reinforcing the hypothesis that collagen breakdown is a critical feature of diabetic bone disease. This finding corresponds closely with the substantial increase in type I collagen levels observed in our osteoporotic group.

On the other hand, some studies present conflicting evidence. For example, the study of[33] found no significant differences in osteocalcin levels between diabetic patients with and without osteoporosis, suggesting that osteocalcin may not consistently reflect bone formation activity in all populations.

Research, including Mosekilde (2004), indicates a correlation between diabetes and the breakdown of type I collagen in bone, independent of gender, aligning with the present results[34]. Kanazawa *et al*. (2009) proposed that osteocalcin regulates glucose and bone activity and may be affected by gender, explaining the discrepancies identified in our findings between men and females[35]. Zhao *et al*. (2016) showed that diabetes patients have heightened bone resorption, with the impact being more closely associated with the level of disease management than with gender, aligning with the constant TRACP levels seen in our findings across genders[36].

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable

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ORIGINAL ARTICALE

EFFICIENCY OF HYALURONIC MOUTHWASH COMPARED TO CHLORHEXIDINE MOUTHWASH TO PREVENT PLAQUE INDUCED GINGIVITIS IN PATIENT WEARING FIXED ORTHODONTIC APPLIANCES

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Abstract

Background: Plaque-induced gingivitis is a prevalent periodontal condition affecting over 90% of individuals, with orthodontic appliances thus hindering effective oral hygiene.

Objectives: This study evaluated the efficacy of hyaluronic acid (HA) and chlorhexidine (CHX) mouthwashes in reducing gingival inflammation in patients with fixed orthodontic appliances.

Materials and Methods: A total of 45 participants were randomized into three groups: Group I used HA mouthwash, Group II used CHX mouthwash, and Group III brushed their teeth without a mouthwash. All participants underwent professional scaling and polishing before the study and followed standardized oral hygiene protocols. Saliva samples were collected at baseline (day 0), one month, and three months for measuring levels of pro-inflammatory cytokines (IL-1β, TNF-α, and INF-γ). Gingival index (GI), plaque index (PI), and bleeding on probing (BOP) were assessed at each interval.

Results: At one month, significant reductions in GI, PI, and BOP were observed across all groups. Both groups of HA and CHX mouthwashes demonstrated greater reductions in clinical parameters compared to brushing alone. At three months, all groups showed continued significant improvements from baseline in all parameters except PI, which remained unchanged in the HA and brushing-only groups. Salivary cytokine analysis revealed variations correlating with clinical improvements, highlighting the anti-inflammatory benefits of both HA and CHX.

Conclusion: This study demonstrates that HA and CHX mouthwashes, alongside proper oral hygiene practices, effectively reduce gingival inflammation in orthodontic patients. These findings underscore the importance of integrating supportive periodontal therapies with rigorous oral hygiene regimens for maintaining oral health during orthodontic treatment.

Keywords*:* Gingivitis, Oral hygiene, Pro-inflammatory cytokines

INTRODUCTION

Plaque-induced gingivitis is a common periodontal disease that affects over 90% of people, irrespective of age, sex, or race[1]. Orthodontic appliances often cause local soft tissue responses in the gingiva due to their proximity to the gingival sulcus and plaque buildup. These factors, along with difficulties in maintaining oral hygiene, complicate effective orthodontic care[2]. The clinical effects observed following the insertion of orthodontic appliances into the oral cavity can lead to chronic infection, inflammatory hypoplasia, irreversible loss of attachment (permanent bone loss), and gingival recession3. The primary objective in preventing periodontal diseases is effective plaque control and the prevention of gingivitis[4].

Effective plaque control can be achieved through various mechanical oral hygiene aids and numerous anti-plaque agents. Currently, mechanical methods for dental plaque removal are widely acknowledged as highly effective in controlling the progression of dental caries and periodontal diseases[5]. Mouth rinses and medical gels are typically considered supplementary to oral hygiene practices and are extensively used to deliver active agents to teeth and gingivae. These agents are frequently prescribed as adjuncts for the prevention or treatment of oral diseases because they inhibit bacterial colonization, growth, and metabolism, thereby disrupting the formation of mature biofilms at biochemical and ecological levels

[6,7]. Chlorhexidine digluconate is recognized as a standard agent for plaque control; however, its prolonged use is often discouraged due to side effects such as tooth and tongue staining, altered taste sensation, and increased calculus formation[8-10]. In recent years, hyaluronic acid has garnered increasing attention due to promising results in treating inflammatory processes in various medical fields, including dentistry, dermatology, ophthalmology, and orthopedics [11,12].

Hyaluronic acid-containing mouthwash is an innovative product that incorporates a high molecular weight fraction of hyaluronic acid. Due to its non-toxicity, biocompatibility, and numerous biochemical and physicochemical properties, the topical application of hyaluronic acid-based biomaterials to periodontal pockets can be advantageous in enhancing healing and reducing periodontal inflammation[13]. This study aimed to evaluate the effectiveness of hyaluronic acid mouthwash (0.2%) and chlorhexidine mouthwash (0.12%) as preventive measures for plaque-induced gingivitis in patients with fixed orthodontic appliances.

MATERIALS AND METHODS

Ethical consideration and subject consent

The study proposal was approved by the scientific committee at the periodontal department and the ethical committee at the College of Dentistry, Hawler Medical University. Verbal and written informed consent were obtained from all participants before their participation in the study.

Study design and data collection

This clinical comparative study was conducted in the periodontal department at the College of Dentistry, Hawler Medical University, in Erbil city from March 2021 to March 2022. The study included 45 patients aged 18-25 years with plaque-induced gingivitis who were wearing full-mouth fixed orthodontic appliances. All subjects had good general health and possessed at least 24 natural teeth (excluding third molars), with a minimum of 30% bleeding on probing (BOP). Patients with systemic diseases, physical or mental disabilities, pregnant and lactating women, current smokers, those who had used antibiotics in the previous 6 months, or those who had received periodontal therapy in the previous 3 months were excluded from the study. Age, gender, educational status, and any history of systemic disease were assessed via interview on the day of the periodontal examination. Patients were randomly divided into three groups of 15 patients each:

Group I: Participants were instructed to use a mouthwash containing hyaluronic acid (Gengigel with 0.2% hyaluronic acid) in addition to brushing their teeth (after breakfast and before bed).

Group II: Participants were instructed to use a mouthwash containing Chlorhexidine Gluconate (KIN Gingival Mouthwash with 0.12% Chlorhexidine digluconate), in addition to brushing their teeth (after breakfast and before bed).

Group III: Participants were instructed to brush their teeth only (after breakfast and before bed).

All participants received scaling and polishing by the same dentist using the same commercially available dentifrice (Colgate Total) and toothbrush. Participants in Group I and Group II were instructed to use their designated mouthwash nightly before bed, maintaining it in their mouth for 3 minutes without rinsing with water for one month.

Periodontal examination

A single experienced dentist conducted all periodontal examinations using standard dental equipment. The full mouth, excluding third molars, was assessed for plaque index (PI) and gingival index (GI) using Silness and Loe indices. Gingival sulcus depths (the distance from the marginal gingivae to the base of the gingival sulcus) and gingival recession (the distance from the cemento-enamel junction to the marginal gingivae) were measured with a manual periodontal probe and recorded to the nearest millimeter at four sites per tooth for all present teeth except third molars[14]. All periodontal examinations were performed three times: before starting therapy, after one month, and after three months.

Salivary samples collection

Saliva was collected from all participants at three different times: before starting therapy (day 0), and after one month (1-month) and three months (3-month). Saliva collection occurred prior to periodontal examination, with participants instructed to refrain from eating, chewing, and drinking for at least one hour beforehand. Unstimulated saliva samples were collected between 09:00 and 11:00 AM by asking participants to spit into a clean test tube until 5 ml of saliva was acquired. The samples were clarified by centrifugation at 10,000 g for 15 minutes. All samples were stored at -70 °C for subsequent analysis. Detection of salivary levels of IL-1β, TNF-α, and INF-γ was performed in the laboratory following standard procedures and manufacturer's instructions[15,16].

Statistical analysis

Data analysis was conducted using IBM SPSS Statistics version 20. Descriptive statistics included mean and standard deviation for continuous variables and frequencies. A one-way ANOVA test compared group means.

RESULTS

The average male and females ages were 19.70± 3.29 and 21.09±4.28 years with non-significant differences between both sexes (Table 1) in all groups. The mean values of plaque index (PI), bleeding on probing (BOP), and gingival index (GI) significantly decreased one month after therapy in the scaling and root planing (SRP) group,

demonstrating a notable difference compared to baseline measurements (0 day) prior to therapy (Table 2). After three months of SRP, the mean values of GI and BOP significantly increased compared to baseline, except for PI, which showed a non-significant decrease. However, no significant differences were observed between the 1- month and 3-month evaluations regarding all clinical periodontal parameters. concentrations were calculated using a standard curve. Osteocalcin levels were estimated using an electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e411 analyzer. The assay used biotinylated and ruthenium-labeled monoclonal antibodies in a sandwich format, and the chemiluminescent signal generated was proportional to osteocalcin concentration. All assays were performed and calibrated according to the manufacturers' instructions, and quality control samples were used to ensure accuracy and precision.

Statistical analysis

All data were analyzed by using the Minitab program according to the ANOVA test. However, the mean when compromised by the ducun multiple range test under the P. value 0.05.

RESULTS

Effect of disease on the diagnostic parameters

Table 1 demonstrates statistically significant differences ($P < 0.05$) in several bone-related biochemical markers between diabetic patients and healthy controls. Specifically, serum levels of type I collagen, osteocalcin, and tartrate-resistant acid phosphatase (TRACP) were significantly elevated in patients compared to controls. These findings suggest enhanced bone turnover or metabolic alterations associated with diabetes mellitus.

Table1. The mean ages and standard deviation of male and female.

	Sex	N	Mean age ± SD	Std. Error		*p*-value
Scaling	M	9	19.67 ± 2.12	0.707		0.172
	F	6	22.67 ± 5.75	2.348		
CHX[a]	M	8	18.25 ± 0.46	0.164		0.065
	F	7	21.14 ± 4.06	1.534		
HA[b]	M	6	21.67 ± 5.68	2.319		0.490
	F	9	20.00 ± 3.46	1.155		
Average total	**M**	**23**	**19.70 ± 3.30**	**0.687**		**0.226**
	F	**22**	**21.09 ± 4.29**	**0.914**		

[a] Chlorhexidine digluconate, [b] hyaluronic acid.

In relation to pro-inflammatory cytokines, the mean salivary levels of IL1-β, TNF-α, and INF-γ exhibited a significant increase after one month of therapy (Table 2). Subsequently, these levels showed a slight decrease after three months, with significant differences from baseline levels observed for IL1-β and INF-γ only. However, no significant differences were identified between the measurements taken at one and three months for TNF-α and INF-γ.

Table 2. The mean values of clinical and immunological parameters after 1 and 3 months of scaling and root planning.

			N	Mean ± S.D.	t-test	d.f.	p-value	Sig.
Scaling	PI	0 day	15	1.77 ± 0.46	4.49	14	0.001	HS
		1 month	15	1.54 ± 0.38				
		0 day	15	1.77 ± 0.46	0.81	14	0.434	NS
		3 months	15	1.67 ± 0.58				
		1 vs 3			-1.02	14	0.324	NS
	BOP	0 day	15	70.13 ± 13.13	9.28	14	0.000	HS
		1 month	15	37.13 ± 14.06				
		0 day	15	70.13 ± 13.13	7.08	14	0.000	HS
		3 months	15	41.33 ± 14.40				
		1 vs 3			-1.09	14	0.296	NS
	GI	0 day	15	1.73 ± 0.14	7.62	14	0.000	HS
		1 month	15	1.37 ± 0.14				
		0 day	15	1.73 ± 0.14	6.09	14	0.000	HS
		3 months	15	1.45 ± 0.21				
		1 vs 3			-2.81	14	0.014	S
	TNF-α	0 day	15	14.34 ± 2.65	-2.39	14	0.031	S

	IL-1β	0 day	15	22.16 ± 4.71	-2.49	14	0.026	S
		1 month	15	27.58 ± 6.43				
		0 day	15	22.16 ± 4.71	-5.41	14	0.000	HS
		3 months	15	33.64 ± 5.29				
		1 vs 3			-3.07	14	0.008	HS
	INF-γ	0 day	15	27.78 ± 5.43	-2.71	14	0.017	S
		1 month	15	34.97 ± 6.45				
		0 day	15	27.78 ± 5.43	-3.06	14	0.008	HS
		3 months	15	31.56 ± 5.83				
		1 vs 3			1.36	14	0.197	NS

In the CHX group, there was a notable reduction in the mean values of PI, BOP, and GI after 1 month. However, after 3 months, the mean values of PI, GI, and BOP increased significantly compared to the baseline, with no significant differences observed between the 1 and 3-month evaluations. Similarly, the mean salivary levels of TNF-α and INF-γ increased significantly after 1 month of therapy, except for IL-1β, which did not show a significant change. After 3 months, the mean values of pro-inflammatory cytokines decreased significantly when compared to the 1-month values for TNF-α and IL-1β.

Table 3. Clinical and immunological parameters after 1 and 3 months of therapy by Chlorehexidine.

			N	Mean	t-test	d.f.	p-value	Sig.
CHX	PI	0 day	15	2.05 ± 0.57	5.04	14	0.000	HS
		1 month	15	1.46 ± 0.18				
		0 day	15	2.05 ± 0.57	5.52	14	0.000	HS
		3 months	15	1.53 ± 0.23				
		1 vs 3			-1.45	14	0.170	NS
	BOP	0 day	15	61.73 ± 14.97	5.52	14	0.000	HS
		1 month	15	34.40 ± 9.05				
		0 day	15	61.73 ± 14.97	5.58	14	0.000	HS
		3 months	15	39.40 ± 13.59				
		1 vs 3			-1.54	14	0.145	NS
	GI	0 day	15	1.67 ± 0.25	4.96	14	0.000	HS
		1 month	15	1.34 ± 0.09				
		0 day	15	1.67 ± 0.25	4.91	14	0.000	HS
		3 months	15	1.39 ± 0.14				
		1 vs 3			-1.65	14	0.121	NS
	TNF-α	0 day	15	13.42 ± 3.06	-4.08	14	0.001	HS
		1 month	15	20.45 ± 6.00				
		0 day	15	13.42 ± 3.06	8.06	14	0.000	HS
		3 months	15	8.32 ± 1.18				
		1 vs 3			7.66	14	0.000	HS
	IL-1β	0 day	15	31.14 ± 4.85	-1.15	14	0.269	NS
		1 month	15	33.46 ± 6.92				
		0 day	15	31.14 ± 4.85	8.69	14	0.000	HS
		3 months	15	17.77 ± 4.68				
		1 vs 3			9.52	14	0.000	HS
	INF-γ	0 day	15	29.88 ± 6.24	-5.69	14	0.000	HS
		1 month	15	37.85 ± 7.90				
		0 day	15	29.88 ± 6.24	-1.57	14	0.138	NS
		3 months	15	34.08 ± 8.20				
		1 vs 3			1.16	14	0.266	NS

For the subjects who received HA treatment (Table 4), the mean values of PI, BOP, and GI significantly decreased after

1 month. After 3 months, the mean value of GI increased significantly compared to the baseline (day 0) and 1 month. The mean value of PI slightly increased after 3 months, with no significant differences compared to the baseline and 1 month. For BOP, the mean values significantly decreased after 3 months of therapy, showing significant differences from both the baseline and 1 month. The average salivary levels of TNF-α, INF-γ and IL-1β increased insignificantly after 1 month of HA therapy and decreased slightly after 3 months. The comparison between each of two groups and between the three studied groups in regard to PI, GI and BOP showed that there was no significant difference between them (Data not shown).

Table 4. Clinical and immunological parameters after 1 and 3 months of therapy by Hyaluronic acid.

			N	Mean ± SD	t-test	d.f.	P-Value	Sig.
HA	Pl	0 day	15	1.77 ± 0.26	3.37	14	0.005	HS
		1 month	15	1.54 ± 0.21				
		0 day	15	1.77 ± 0.26	0.62	14	0.543	NS
		3 months	15	1.71 ± 0.30				
		1 vs 3			-1.86	14	0.083	NS
	Bop	0 day	15	63.13 ± 9.54	18.54	14	0.000	HS
		1 month	15	28.00 ± 9.30				
		0 day	15	63.13 ± 9.54	9.291	14	0.000	HS
		3 months	15	45.47 ± 8.28				
		1 vs 3			-10.30	14	0.000	HS
	GI	0 day	15	1.65 ± 0.13	9.80	14	0.000	HS
		1 month	15	1.28 ± 0.13				
		0 day	15	1.65 ± 0.13	6.56	14	0.000	HS
		3 months	15	1.44 ± 0.16				
		1 vs 3			-4.82	14	0.000	HS
	TNF-α	0 day	15	15.90 ± 4.05	-1.41	14	0.180	NS
		1 month	15	18.58 ± 5.60				
		0 day	15	15.90 ± 4.05	0.60	14	0.559	NS
		3 months	15	14.97 ± 6.01				
		1 vs 3			2.38	14	0.032	S
	IL-1β	0 day	15	31.76 ± 8.13	-0.81	14	0.429	NS
		1 month	15	34.41 ± 6.54				
		0 day	15	31.76 ± 8.13	5.59	14	0.000	HS
		3 months	15	16.01 ± 3.84				
		1 vs 3			9.11	14	0.000	HS
	INF-γ	0 day	15	26.77 ± 6.52	-2.02	14	0.063	NS
		1 month	15	31.40 ± 9.23				
		0 day	15	26.77 ± 6.52	-1.17	14	0.260	NS
		3 months	15	30.02 ± 8.90				
		1 vs 3		1.77 ± 0.26	-0.67	14	0.515	NS

The comparisons of pro-inflammatory cytokine level changes among the groups are summarized in Table 5. For TNF-α levels, no significant differences were observed between the treatment groups (HA and CHX) after 1 month. However, by the 3-month mark, significant differences were noted between the CHX group and the other two groups. Regarding IL-1β levels, no significant differences were observed between CHX and HA. After 1-month, significant differences emerged between the scaling and HA groups, as well as between CHX and the other two groups.

Table 5. Levels of pro-inflammatory cytokines in the three groups.

		N	Mean ± SD	F-test	P-Value	Sig.
TNF-0	Scaling	15	14.34 ± 2.65	2.16	0.128	NS
	CHX	15	13.42 ± 3.06			
	HA	15	15.90 ± 4.05			
TNF-1	Scaling	15	17.99 ± 4.77	0.82	0.445	NS
	CHX	15	20.45 ± 6.00			
	HA	15	18.58 ± 5.60			
TNF-3	Scaling	15	16.17 ± 2.92	17.45	0.000	HS
	CHX	15	8.32 ± 1.18			
	HA	15	14.97 ± 6.01			
IL1-0	Scaling	15	22.16 ± 4.71	11.60	0.000	HS
	CHX	15	31.14 ± 4.85			
	HA	15	31.76 ± 8.13			
IL1-1	Scaling	15	27.58 ± 6.43	4.66	0.015	S
	CHX	15	33.46 ± 6.92			
	HA	15	34.41 ± 6.54			
IL1-3	Scaling	15	33.64 ± 5.29	65.68	0.000	HS
	CHX	15	17.77 ± 4.68			
	HA	15	16.01 ± 3.84			
INF-0	Scaling	15	27.78 ± 5.43	1.02	0.370	NS
	CHX	15	29.88 ± 6.24			
	HA	15	26.77 ± 6.52			
INF-1	Scaling	15	34.97 ± 6.45	3.85	0.029	S
	CHX	15	37.85 ± 7.90			
	HA	15	30.02 ± 8.90			
INF-3	Scaling	15	31.56 ± 5.83	0.54	0.584	NS
	CHX	15	34.08 ± 8.20			
	HA	15	31.40 ± 9.23			

At 3 months, no significant differences were found between the HA and CHX groups; however, significant differences were noted between the scaling group and both the HA and CHX groups, as well as among all three groups. For INF levels, no significant differences were observed between any two groups or among all three groups at baseline and at 3 months. The only exception occurred after 1 month, when significant differences were found between CHX and HA, as well as between the scaling group and the other two groups.

DISCUSSION

Fixed orthodontic periodontal therapy is a common treatment for different type of mal-occlusion, however fixed orthodontic appliances enhance in dental biofilm accumulation and make it difficult to be removed by routine oral hygiene procedures which intern result in periodontal inflammation[16]. Chlorohexidine gluconate is a gold stander for treatment and prevention of periodontal diseases caused by dental biofilm accumulation, but long-term usage of Chlorohexidine gluconate can result in many drawbacks including dental staining, taste alteration[10].

Hyaluronic acid (HA) is essential for the function of extracellular matrices in periodontal tissues (17). HA plays an important role in the mechanisms underlying inflammation and wound healing. It exhibits potential in the regulation of periodontal tissue regeneration and in the treatment of periodontal disease[13]. Moreover, HA has antibacterial, anti-inflammatory, osteo-inductive activities, and it enhances wound healing. When introduced as a local chemotherapeutic agent, it exhibited numerous clinical therapeutic properties and showed anti-inflammatory and antibacterial properties for the treatment of periodontal disease[18].

The objective of this study was to evaluate the clinical and immunological parameters after scaling and polishing alone compared to those using chlorhexidine or hyaluronic acid after scaling in subjects wearing fixed orthodontic appliances. This study involved 45 participants wearing fixed orthodontic appliances in which 22 were female and 23 were male. This study found that all of GI, PI and BOP were reduced significantly after one month of study in all three groups (scaling and polishing alone, scaling and polishing with using chlorhexidine or HA mouth washes for 1 month once at night before bed. All three periodontal therapies plus oral hygiene instruction and performance by the patient are

effective in decreasing periodontal inflammation in patients wearing fixed orthodontic appliances.

After 3 months, there were statistically significant decreases in all previous clinical parameters comparing to base line in all three groups except for the plaque index in two groups, the HA group and the group that did not use any mouth wash, which indicates that maintaining good oral hygiene can result in maintaining oral health provided by periodontal therapy (19). Two recent studies observed similar outcomes, indicating that after a 3-month follow-up, CXH remains effective in reducing GI and PI when used alongside proper tooth brushing (20,21). Furthermore, other reports documented the effectiveness of HA gel combined with scaling and polishing in reducing plaque induced gingivitis than scaling and polishing alone[22-24]. May be due to that, HA reduces inflammation by modulating cytokines such as IL-1β and TNF-α, which are elevated in gingivitis. HA promotes fibroblast proliferation and extracellular matrix formation, aiding gingival healing. It has bacteriostatic properties that can help reduce plaque accumulation. In addition to forming a protective layer over gingival tissues, reducing irritation from plaque and bacteria. Other researchers also suggested that other mouth washes and therapeutic modalities are effective as much as Chlorohexidine mouth washes in reducing gingivitis in patients wearing fixed orthodontic appliances [23,25-27].

The mean salivary level of IL-1β significantly increased as compared to base line in scaling group but increase slightly in other 2 groups. After 3 months of therapy, the salivary level of IL1β was significantly decreased in both studies groups but still significantly increased in scaling group. This result is consistent with the outcome of the other researchers[28]. Comparing the salivary level of IL-1β among the groups, after one month of intervention, significant difference existed between scaling and HA groups and between CHX and the other two groups with the scaling group had lowest level. After 3 months, no significant difference existed between HA and CHX groups with significant differences existed between scaling and the two studied HA and CHX groups with the scaling group had the highest level. While the mean salivary level of TNF-α was increased significantly after one month as compared to base line in scaling group and in the group using chlorohexidine mouth wash but this increase in the salivary level were not significant in a group using hyaluronic mouth wash. After 3 months of introversion, the mean salivary level of TNF-α was decreased significantly in the group using chlorohexidine mouth wash but this reduction was not significant in other 2 groups.

However, comparing the levels among the groups there were no statistical differences among the three groups after 1 month but after 3 months the level was significantly lower in the group using chlorohexidine mouth wash compared to the other 2 groups. The interpretation for this changes by short term increase in IL-1β; that**,** SP alone triggers a significant rise in IL-1β due to mechanical irritation and inflammation; while, HA gel + SP results in only a slight increase, likely because HA's anti-inflammatory and healing properties counteract excessive cytokine release. The long term respons**e** in both study groups (SP + HA or other adjunctive therapy**)** showed IL-1β levels decrease significantly, indicating reduced inflammation and improved periodontal healing. In contrast, the SP-only group still shows elevated IL-1β level**s**, suggesting persistent low-grade inflammation**.** The HA gel as an adjunct to SP helps in modulating the inflammatory response, promoting faster and more effective healing. Patients undergoing SP alone may experience prolonged inflammation**,** which could increase susceptibility to gingival irritation and disease recurrence. IFN-γ is involved in bone remodeling during orthodontic tooth movement, which strongly suppresses osteoclastogenesis and has a role in periodontal inflammation [29] and its level significantly increased in periodontitis patient (30). In the current research, after 1 month of therapy salivary level of INF-γ was significantly increased in the scaling group and the group using chlorohexidine mouth wash, but this elevation was not significant in the group using hyaluronic acid mouth wash. After 3 months of therapy salivary level of INF-γ was significantly decreased in the group using chlorhexidine mouth wash but this reduction was not significant in other 2 groups. Comparing the three groups, after 1 month of therapy there were significant differences among them with group using hyaluronic acid had the lowest level of salivary INF-γ and CHX group had the highest level, that may be attributed to that HA mouthwash has the least impact on IFN-γ levels, suggesting a more balanced immune response with reduced inflammation, while; CHX leads to an initial spike in IFN-γ (possibly due to its cytotoxic effects), but over time it significantly reduces inflammation. SP alone induces prolonged inflammation, as evidenced by increased IFN-γ without a significant reduction after 3 months. This is agreed with other reports[31,32].

CONCLUSION

All the clinical parameters (GI, PI, and BOP) significantly decreased in all three groups (scaling and polishing alone, scaling and polishing with chlorhexidine mouthwash, and scaling and polishing with HA mouthwash) after 1 month. Each therapy, combined with oral hygiene instruction and patient compliance, was effective in reducing periodontal inflammation in patients with fixed orthodontic appliances. After 3 months, significant reductions in all clinical parameters were observed across all groups

compared to baseline, except for the plaque index in the HA mouthwash group and the group without any mouthwash. This highlights that maintaining good oral hygiene, supported by periodontal therapy, is crucial for sustaining oral health.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable

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ORIGINAL ARTICALE

DENTO-GINGIVAL SMILE ANALYSIS ON YOUNG ADULTS OF SOUTH CHENNAI: A CROSS-SECTIONAL STUDY

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Abstract

Aim: This study aims to assess and analyse dento-gingival parameters in young adults residing in South Chennai. This study aims to assess and analyse dento-gingival parameters in young adults residing in South Chennai.

Materials and Methods: A cross-sectional study was carried out among 100 participants (61Females & 39 males) between 18 and 23 years, within South Chennai region. The dento-gingival parameters such as smile line, buccal corridors, midline shift, and parallelism were determined by evaluating the participants photographs through Adobe Photoshop. The data analysis was done using Spearman's correlation test and chi-square test for nonparametric data.

Results: Buccal corridors were not present in 52% of the young adult population. 48% of young adults found to have non-parallel smile. A high smile line was observed in 23% of the participants. Dental midline shift was found in around 30% of young adults. There was a statistically significant difference in the parallelism of the lower lip line and the incisal curve incisal curve as well as in the upper lip line position in both the genders ($P < 0.05$).

Conclusion: Understanding the dento-gingival unit as a whole and its association with the oral environment can help guide the clinicians in establishing an aesthetically pleasing treatment outcome.

Keywords: smile analysis, smile line, parallelism, midline shift, and buccal corridors.

INTRODUCTION

In the modern era, patients claim for a highly aesthetic treatment outcome. In that case, clinicians must conduct a full facial and dental evaluation to enhance smile, which will address the patient's concerns and inquires while objectively and consistently assessing the patient's smile and face [1]. The combination of facial and dental parameters is needed to design an aesthetically pleasing smile. Interrelationships between the lips, face, teeth and gingiva are macro-aesthetic components. Micro-aesthetics are the aesthetics of a single tooth, including its contour, colour, size and shape. Smile analysis considers the macro- and microelements of facial, dento-facial, and dental aesthetics [2]. A number of researches involving various

populations have shown that aesthetic components for people from different demographics are not entirely the same [3-7].

The incisal edges of the maxillary anterior teeth make an angle with the curvature of the upper lip, creating the smile arc. Their ideal smile relationship is referred to as a consonant smile, which is parallel to each other. A non-consonant smile occurs when the two are not parallel to each other (a flat maxillary incisal curvature) [8.] Ackermann et al used a computerised inter-discipilinary study to compare the features of smile-arc in patient with treatment and without treatment; they found flattened smile arc in 37% of the treated subjects and non-consonant smiles in only 5% of the untreated group [9].

Buccal corridors are the dark or negative spaces that occur between the corners of the lips and the facial surfaces of the posterior teeth [10]. According to Johnson and Smith's [11] investigation on the effect of premolar extraction on the visibility of negative space, there is no correlation between the extraction pattern and the visibility of negative space. According to a recent study, large buccal corridor spaces should be considered in the treatment regimen, whilst smaller buccal corridors can be left untreated [12].

Ackermann and Ackermann developed a smile index to describe the smile's display zone. By dividing the inter-labial space during smiling, the inter-commissural width may be calculated [13].

The study's null hypothesis is that young individuals in South Chennai do not vary in terms of demographics or smile characteristics. A cross-sectional research was conducted to evaluate the positioning of the smile line, the parallelism of the incisal line and lower lip line, the position of the arch midline, and the presence or absence of the buccal corridor. The results can be used as a guide for better smile planning and restoration procedures in the target populations.

MATERIALS AND METHODS

Sample size estimation:

The cross-sectional study was conducted within South Chennai. G power software version 3.9.1 was used to estimate the sample size.

Level of significance alpha = 0.05

Power Beta = 80%

Effect size d= 0.28

Total sample size = 97

Which can be rounded off to 100

This cross-sectional study was approved by the Institutional Ethical Committee of Sree Balaji Dental College & Hospital, Bharath Institute of Higher Education & Research (Approval number: SBDCH-IRB/22-06 /09). Signature was obtained in the informed consent from all 100 participants after explaining the purpose of the study. Young adults of South Chennai between 18 and 23 years were considered as the target study population. Participants from the non- demographic zones were excluded from the study. The exclusion criteria also included participants with bleached dentition, dental fluorosis, hypoplasia and also participants who had prosthodontic and orthodontic interventions [14,15].

Photography:

A standard photograph of each participant showed their full social smile (frontal smile) was captured, using Samsung galaxy note 10+ (version 10.5.01.6). Standardized settings of 1/15 second shutter speed, F1.5, and ISO 100 were set. The participant was positioned at a 90-degree angle with the tripod stand individually adjusted for each participant's height. The participant's nose was 25 cm away from the camera when the pictures were taken.

Smile analysis:

To determine the exact position of the upper lip line, a line was drawn parallel to the upper lip contour and gingival zenith of the top anterior teeth in reference to teeth 13 to 23. When the gingival zenith and upper lip line were seen to be 2-3 mm apart, it was deemed high with full teeth and gingival exposure. When 75-100% of the clinical crown height was noted, it was considered medium. The upper lip line was deemed low when the upper lip covered 25% or more of the labial surface of the upper front teeth.

Two curves were drawn, one following the incisal curve and one following the lower lip line to establish parallelism. A vertical line was drawn along the base of the philtrum to establish the facial midline and the other line drawn along the central incisors was used to assess the correlation between dental and facial midline. The discrepancy of the dental midline from the face midline was measured in pixels and then was converted to millimetres using a ruler tool. Using the latest version of Adobe Photoshop, the buccal corridor between the posterior teeth and the commissures was examined for its presence or absence (8.1.958).

Statistics:

For data analysis, Statistical Package for Social Sciences (SPSS, Version 25, IBM Corporation, Chicago, IL, USA) was utilised. A descriptive research was conducted on the buccal corridor's existence or absence, parallelism, midline displacement, and smile line.

Mann–Whitney *U*, independent *t* and Chi-square were used to analyse if there was a significant difference between both the genders. For all statistical analysis, $P = 0.05$.

RESULTS

Using SPSS V25, the collected data were organised in a structured manner. The data was transferred from a table that was made using Excel 2010. Analysis was done on the data from all 100 individuals (61 females and 39 men). Table 1 explains the distribution of smile parameters.

Smile line:

The dimensions of the smile lines of the female participants were distributed as follows: With a medium smile line, 70%, a high smile line, 23%, and a low smile line. 4%, 28%, and 7% of the male participants showed high, medium, and low smile lines, respectively. The Mann-Whitney U test was applied for nonparametric data, the smiling line distribution showed a significant difference between both the genders (Table 2).

Buccal corridor:

Only 23% of men and 29% of females lacked buccal corridors. Chi-square test was used to compare both the genders for the existence of buccal corridors and found to have no significant difference (Table 2)

Parallelism:

There are two types of parallelism between the lower lip line and the incisal curve: parallel and nonparallel.

37% of females and 15% of males exhibited parallel grins, whereas 24% of both sexes had nonparallel smiles. The chi-square test revealed that the parameter parallelism difference between men and women was statistically significant (Table 2).

Midline shift:

They are of two categories: 0–1 mm and 2 mm (Table 1). Dental midline shifts of 2mm or more were present in 10% of men and 20% of females. Chi – square test was utilised to analyse the distribution of midline shift was compared between males and females, but found no significant difference statistically (Table 2).

Table 1. Frequency Distribution Table of Different Smile Parameters.

Parameters		Frequency	Percentage
Gender	Male	39	39 %
	Female	61	61 %
Midline shift	0-1 mm	70	70 %
	≥ 2 mm	30	30 %
Lip line	Low	7	7 %
	Medium	70	70 %
	High	23	23 %
Parallelism	Yes	52	52 %
	No	48	48 %
Buccal corridor	Present	48	48 %
	Absent	52	52 %

Table 2. Association between Gender and Smile Parameters

Smile parameter	Criteria	Female	Male	Pearson chi-square	P value
Midline shift	0-1mm	41	29	0.578	0.29
	≥ 2mm	20	10		
Lip line	Low	16	7	1.707	0.42
	Medium	42	28		
	High	3	4		
Parallelism	Yes	37	15	4.695	0.02
	No	24	24		
Buccal corridor	Present	32	16	1.246	0.18
	Absent	29	23		

Association between Smile Parameters:

The Spearman's rho correlation test was employed to assess the relationship between the four distinct factors using nonparametric data. The midline shift and buccal corridor found to have a statistically significant positive weak relationship, according to the results ("" (rho) = 0.105, P 0.05). There was no other statistically significant correlation between smiling parameters was found (Table 3).

Table 3. Correlation Matrix for the Association of Smile Parameters

Smile parameter	Midline shift	Lip line	Parallelism	Buccal corridor
Midline shift	1.000	-0.139	0.157	0.105
Lip line	-0.139	1.000	0.184*	0.084
Parallelism	0.157	0.184*	1.000	0.042
Buccal corridor	0.105	0.084	0.042	1.000

*correlation is significant at 0.05 level.

DISCUSSION

The study's objective was to examine and assess the macro-aesthetic aspects of young people's smiles in South Chennai, including the interactions between the lips, face, teeth, and gingiva. Although few studies has been done on the smile or the dento-gingival components of young people in various other demographic zones and it has not yet been conducted within chennai or south chennai in particular. According to Tjan et al., there are three different smile lines: high, average, and low. The anterior maxillary teeth's complete cervical-incisal length, as well as a continuous band of gingiva, are visible with a high smile line. In a typical smile, between 75% and 100% of the top front teeth are visible. Less than 75% of the top anterior teeth are visible with a low smile line [16]. The average smile line, which was observed in 70% of the sample, was discovered to be the most prevalent among study participants. Within the Asser area, Alqarni et al. In comparison to a low or high smile line, authors identified that the average smile line was more frequently noticed [17]. Nold et al. also looked at the smile line in Turkish people. They discovered that while a medium smile line was more common in men, a high smile line was more common in female participants [18]. In the current study, we discovered that males (42%), who were more likely to have a high smile line, and females (42%), who were more likely to have a medium smile line. Albwardi et al. investigated the effect of buccal corridors on smile aesthetics. They came to the conclusion that a smile with considerable tooth show and 2 % buccal corridors was unappealing. A medium smile with a 10% buccal corridor, on the other hand, was deemed the most beautiful [19]. Liang et al. also investigated buccal corridors in 188 Chinese people, and found that the buccal corridors were present in about 69% of the males and 51.1% of the females [20]. In the present study, the buccal corridor was not present in 29% of females and 23% of males.

When smiling, a person's lower lip's convexity and concavity should match up perfectly to form an incisal curve. A flat or non-consonant smile is one in which the lower lip curve is more pronounced than the maxillary incisal curve [21]. A convex incisal curve was shown to be more prevalent than a non-consonant smile, according to Soares et al. Furthermore, Al-Johany et al. evaluated smile parameters of 50 people and discovered that 78% of them had an incisal curve coinciding with the lower lip [22]. With that stated, just 15% of male participants exhibited a parallel smile, whereas females had about 37% of the population. The difference in male and female participants' parallel smiles was statistically significant. The parallel smile was more common in females than in males, according to these findings, which are supported by Nold et al. There was a statistical difference in the distribution of the incisal curve across genders [18].

A critical vertical reference line is the midline. Miller et al. [23] investigated midline discrepancy and discovered that the dental midline corresponds with the face midline in 70% of cases. Furthermore, these researchers claimed that minor midline deviations have little effect on overall aesthetics. The frequency of occurrence of the midline shift was reported to be 30.7 % by Al-Balkhi and Zahrani [24.] However, we discovered that 10% of male participants had a midline shift of more than or equal to 2mm, whereas 20% of female participants had a midline shift of more than or equal to 2mm. The dental midline was measured by keeping the central incisors as a reference point, whereas the face midline was measured by keeping the philtrum. This method of assessing the midline shift is thought to be valid [23-25].

One of the study's shortcomings are the smaller sample size drawn from a small region of Tamilnadu. In order to ascertain whether there is a statistical difference in the distribution of smile parameter across different areas of Tamilnadu, a larger representative sample from various locations of state will be helpful. To precisely gauge the degree of midline displacement, face reference points were required for facial midline determination. However, obtaining frontal facial pictures was not possible due to patient privacy and identification issues. Future research may find it advantageous to include other smile characteristics as the colour of the front teeth, geometry, and proportion.

CONCLUSION

Dentogingival parameters allow the dentist to determine

the aesthetic preference hierarchy. Although aesthetics cannot be quantified, it is critical to comprehend the qualities that make up an aesthetic smile and then add changes according to the individual requirements.

Abbreviations: SPSS: Statistical Package for Social Sciences, IBM: International Business Machines

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Informed Consent: Not applicable.

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CASE REPORT

CLEAR CELL VARIANT OF SQUAMOUS CELL CARCINOMA MASQUERADING AS PYOGENIC GRANULOMA: A DIAGNOSTIC CHALLENGE

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ABSTRACT

Background: Clear cell variant of squamous cell carcinoma (CCSCC) is a rare and aggressive subtype of oral squamous cell carcinoma (OSCC), often difficult to diagnose due to its unusual morphology. This variant can resemble benign lesions, such as pyogenic granuloma, leading to diagnostic delays.

O**bjective**:To highlight the diagnostic challenge presented by the clear cell variant of squamous cell carcinoma and emphasise the importance of histopathological evaluation in distinguishing it from benign gingival growths.

Case Presentation:A 74-year-old male with a painless gingival lesion in the mandibular anterior region presented with a growth that had gradually increased in size and bled upon mastication. Despite clinical features resembling a pyogenic granuloma, the lesion was diagnosed as CCSCC following histopathological evaluation, which revealed clear cell morphology.

Results:Histopathology showed dysplastic stratified squamous epithelium invading connective tissue, with clear cytoplasm and hyperchromatic nuclei. The patient was referred for oncological management, including surgical excision with wide margins and adjuvant therapy.

Keywords: Clear cell carcinoma, Gingival lesion, Oral squamous cell carcinoma, Pyogenic granuloma, Squamous cell carcinoma

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common cancers in the oral cavity, accounting for more than 90% of all oral malignancies. The condition primarily affects older adults and is commonly associated with risk factors such as tobacco use, alcohol consumption, and poor oral hygiene [1].

OSCC typically presents as a painless lesion that may bleed, ulcerate, or present with non-healing sores. While the conventional form of OSCC is widely recognised, there are several histopathological variants, with the clear cell variant of squamous cell carcinoma (CCSCC) being one of the rarest and most challenging to diagnose [2].

The clear cell variant of squamous cell carcinoma was first described by Kuo in 1980. It is characterised by the presence of polygonal tumour cells with clear cytoplasm, which gives the tumour its distinctive appearance. These clear cells result from the accumulation of glycogen or lipid-rich material in the cytoplasm, which is a key diagnostic feature. However, this morphological appearance is not exclusive to CCSCC and can be seen in other neoplastic conditions, making the differential diagnosis particularly challenging [3].

Tumours such as mucoepidermoid carcinoma, clear cell odontogenic carcinoma, metastatic renal cell carcinoma, and clear cell salivary carcinoma also exhibit clear cell morphology. As a result, distinguishing CCSCC from these other clear cell neoplasms requires a careful and detailed diagnostic approach, often involving additional histochemical and immunohistochemical studies [4].

CCSCC is clinically significant because it tends to present as a slow-growing, painless lesion, often mimicking benign conditions like pyogenic granuloma, fibroma, or peripheral giant cell granuloma. These reactive lesions, commonly found in the gingiva, can delay the diagnosis of malignancy, especially in elderly patients. Pyogenic granuloma, for instance, is a vascular lesion that frequently occurs in the gingival tissues and is characterised by its red, lobulated appearance. Due to its clinical resemblance to CCSCC, pyogenic granuloma is a common misdiagnosis, leading to delayed treatment and poor patient outcomes if malignancy is not promptly recognised [5].

Histopathological evaluation remains the gold standard for diagnosing OSCC, including its rare variants like the clear cell subtype. Early diagnosis is crucial for improving prognosis and patient survival, as the clear cell variant of OSCC is known to follow an aggressive clinical course. Despite its rarity, the clear cell variant tends to have a poorer prognosis compared to conventional OSCC, often due to the difficulty in detecting it early [7]. Furthermore, CCSCC may be associated with more advanced disease at the time of diagnosis, which can significantly affect the treatment strategy and overall patient outcomes. The presence of clear cells, coupled with other features such as cellular pleomorphism, hyperchromatic nuclei, and increased mitotic activity, should raise suspicion for this rare subtype, especially in patients with risk factors such as smoking and alcohol use [7].

The challenge of distinguishing between benign and malignant gingival lesions emphasises the need for clinicians to maintain a high index of suspicion. Reactive conditions like pyogenic granuloma can present with similar clinical features, but when in doubt, a biopsy and histopathological examination should be performed. This case report aims to illustrate the diagnostic challenges of CCSCC, focusing on a patient who initially presented with a lesion clinically resembling a pyogenic granuloma, but was later diagnosed with the clear cell variant of OSCC through histopathological evaluation [8].

CASE REPORT

A 74-year-old male presented to the outpatient department with a chief complaint of a growth in the mandibular anterior gingiva, which had been progressively enlarging over the past month. The lesion was described as painless, though it frequently bled during mastication. Extraoral examination revealed no significant abnormality (Figure 1).



Figure 1. Extra-Oral Profile

The patient's medical and dental history was non-contributory, and there were no significant systemic conditions. However, his personal history was notable for a history of smoking (7-8 cigarettes per day for the past 20 years) and alcohol consumption (approximately 60 mL daily for the past 40 years).

On clinical examination, the patient’s oral hygiene was assessed as poor (Figure 2). A solitary, sessile, erythematous growth, measuring approximately 3 cm x 2 cm x 1 cm, was noted on the labial gingiva in the region between the distal aspect of tooth 31 and the mesial aspect of tooth 35 (root stump). The overlying mucosa appeared erythematous, with slight blanching inferiorly and posteriorly. The lesion had well-defined but irregular margins (Figure 3).



Figure 2. Intra-Oral Examination

Upon palpation, the lesion was soft to firm in consistency, slightly tender, with a smooth to lobulated surface texture. It tended to bleed upon provocation. Mobility of teeth 33, 34, and 36 was noted to be grade III.

Radiographic examination using a panoramic radiograph revealed generalised bone loss, with multiple root stumps and interdental bone loss, specifically between teeth 33 and 34 (Figure 4).



Figure 3. Soft Tissue Growth



Figure 4. Panoramic Radiograph

Given the clinical features, the provisional diagnosis was pyogenic granuloma, with peripheral ossifying fibroma, peripheral giant cell granuloma, and squamous cell carcinoma considered as differential diagnoses.

Routine haematological investigations were performed and revealed no significant abnormalities. The lesion was surgically excised along with teeth 33, 34, and 35 under local anaesthesia. The excised tissue was submitted for histopathological analysis. (Figure 5).



Figure 5. Specimen for Histopathological Examinat

Histopathological findings showed dysplastic squamous surface epithelium showing breach with invasion of epithelial cells into the connective tissue stroma in the form of sheets and islands. Epithelial cells in the connective tissue stroma showed dysplastic features including clear cell cytoplasm with nuclear pleomorphism, hyperchromatism and keratin pearls. The findings were suggestive of - clear cell variant of squamous cell carcinoma.

Following the diagnosis, the patient was referred to a tertiary cancer centre for further oncological management, which included surgical excision with wide margins and adjuvant therapy.

DISCUSSION

Ramani et al. (2021) [9] presented a case report of the clear cell variant of OSCC, describing similar clinical features, including a painless gingival growth with a tendency to bleed, which was misdiagnosed as a benign lesion. Like our case, the diagnosis of CCSCC was confirmed through histopathological examination, which revealed the characteristic clear cell morphology associated with glycogen accumulation. The authors noted that this variant is often underdiagnosed due to its clinical resemblance to more common lesions like pyogenic granuloma. This observation aligns with our case, where the lesion's resemblance to pyogenic granuloma initially led to a provisional diagnosis, underscoring the importance of histopathological evaluation to differentiate between malignant and benign lesions.

Cabral Ramos J et al. (2022) [10] also reported a rare case of CCSCC involving the gingiva. The authors highlighted that, unlike conventional OSCC, CCSCC is often associated with an indolent clinical course initially but can evolve into a more aggressive form. This finding is consistent with the aggressive nature of CCSCC described in our case. While the clinical appearance of the lesion was initially less alarming, its rapid growth and tendency to bleed were indicative of a malignant process. Our case corroborates the need for early recognition of this aggressive variant, as delayed diagnosis can lead to poor prognostic outcomes.

Frazier JJ (2012) [11] seminal study in 1980 first described

the clear cell variant of squamous cell carcinoma. It posited that the clear cytoplasm of the neoplastic cells is due to the accumulation of glycogen, which is confirmed by periodic acid–Schiff (PAS) positivity. Kuo emphasised the diagnostic difficulty in distinguishing CCSCC from other clear cell tumours, such as mucoepidermoid carcinoma or metastatic renal cell carcinoma. Our case highlights the critical role of histochemical and immunohistochemical studies in making an accurate diagnosis, especially in cases where clinical presentation overlaps with benign lesions.

Markopoulos (2012) [12] provided an extensive review of oral squamous cell carcinoma, including its various histopathological subtypes. The study discussed the occurrence of clear cell morphology in different tumours, including OSCC, and emphasised the role of differential diagnosis. The clear cell variant of OSCC, according to the review, is often misdiagnosed as a benign lesion due to its clinical features. Our case aligns with this observation, as the lesion initially appeared to be a pyogenic granuloma, a common benign lesion of the gingiva. Markopoulos' review also noted that clear cell variants of OSCC tend to have a poorer prognosis, which is consistent with the findings in our case, where the lesion's aggressive nature warranted referral for further oncological management.

Sujir N et al. (2019) [13] documented a case of CCSCC where the tumour presented as a non-healing gingival lesion in a middle-aged male with a history of tobacco use. Their report highlighted the importance of considering malignant lesions in the differential diagnosis of gingival growths, particularly in patients with risk factors such as smoking. Similarly, in our case, the patient's history of long-term smoking and alcohol consumption was a significant risk factor, which should have raised suspicion for malignancy. Paul et al. emphasised the importance of early biopsy and histopathological evaluation, which we also advocate, as it was crucial in confirming the diagnosis of CCSCC and preventing a delay in treatment.

According to Ramdas B et al. (2025) [14]. Antibody-drug conjugates (ADCs) offer a promising therapeutic approach for clear cell variant of squamous cell carcinoma (CCSCC) by targeting specific tumor-associated antigens, such as LGALS3BP and integrin beta-6, enabling the selective delivery of cytotoxic agents to tumor cells and thereby improving treatment efficacy and reducing systemic toxicity, with ongoing research necessary to validate these targets and optimize ADC formulations for clinical application.

CONCLUSION

The clear cell variant of squamous cell carcinoma is a rare and aggressive subtype of OSCC that can mimic benign gingival lesions like pyogenic granuloma.

Early recognition and histopathological confirmation are vital to avoid misdiagnosis and ensure timely treatment. Our case corroborates findings from the literature, underscoring the need for clinicians to maintain a high index of suspicion for malignant lesions, particularly in patients with risk factors such as smoking and alcohol consumption. Histopathological examination, including histochemical techniques like PAS staining, plays a crucial role in differentiating CCSCC from other clear cell neoplasms and benign conditions. Further research and clinical awareness are necessary to improve the diagnosis and management of this challenging variant of OSCC.

This case emphasizes the deceptive clinical appearance of CCSCC, which may mimic benign reactive gingival lesions such as pyogenic granuloma. Clinicians should maintain a high index of suspicion and subject all gingival growths to histopathological evaluation. Early and accurate diagnosis is essential for initiating appropriate therapy and improving prognosis in such rare and aggressive variants of oral squamous cell carcinoma.

DECLARATIONS

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Competing Interests
The authors have no competing interests to declare.
Ethical Approval
The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.
Informed Consent
Not applicable.

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ORIGINAL ARTICALE

IMPACT OF SIMVASTATIN-GEL FOAM COMBINATION ON BONE DENSITY AFTER MANDIBULAR THIRD MOLAR EXTRACTION

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ABSTRACT

Aims: This randomized, prospective comparative study aimed to assess the effectiveness of locally applying 10 mg of simvastatin in promoting bone regeneration within the sockets of surgically extracted mandibular third molars, using CBCT to measure bone density one and three months after the procedure.

Materials and methods: The study was carried out over a period of eighteen months, involving 30 patients (14 males and 16 females). These cases were randomly assigned to two groups: 15 in the study group and 15 in the control group. Following the surgical extraction of the mandibular third molars, the study group received a local application of a simvastatin and gel foam combination in the extraction sockets, while the control group was treated with gel foam alone. After a period of one month and three months, bone density in the healing sockets was assessed and compared between the two groups using cone beam computed tomography (CBCT). Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 23.0.

Results:Three months after the procedure, CBCT measurements revealed that the mean bone density in the study group (247.772 ± 32.635 Hounsfield Units) was significantly greater than that in the control group (207.622 ± 18.515 Hounsfield Units). The difference in bone density between the two groups was statistically significant (p-value=0.029).

Conclusion: Applying a combination of 10 mg simvastatin powder and gel foam locally in the sockets of surgically removed mandibular third molars can enhance bone density and is considered a safe method for preserving the alveolar ridge following tooth extraction.

Keywords: Simvastatain - Gel Foam, Bone Density, Mandibular Third Molar Extraction

INTRODUCTION

An impacted tooth is one that fails to erupt into the mouth within its expected time frame. The mandibular third molar (wisdom tooth) is classified as impacted when its root development is complete but it lacks functional contact with the opposing tooth. Typically, the mandibular third molars erupt between the ages of 17 and 24.[1,2] However, due to racial and ethnic differences, this timeframe can vary significantly.

Since the third molar is the last tooth to emerge in the oral cavity, it has the highest likelihood of impaction. Kazemian et al. identified that neighbouring teeth, as well as hard and soft tissue obstructions, are the primary causes of third molar impaction. Impacted mandibular third molars can lead to a variety of complications, including

pericoronitis, periodontitis, cysts, tumours, root resorption, and damage to adjacent teeth. These may also cause pain, decay, and infections, which often necessitate surgical removal.[3-5]

Surgical extraction of impacted third molars is a routine procedure in oral and maxillofacial surgery. A common concern following extraction is bone loss at the distal surface of the second molar. Therefore, preserving or enhancing the alveolar bone during or after extraction is advantageous.[7,8]

Following tooth extraction, a reduction in alveolar bone volume and socket structure is expected due to natural bone loss. This bone resorption is physiological response to tooth removal.[9-11] Without proactive measures for bone preservation or regeneration, significant bone loss may occur, requiring invasive and expensive procedures such as bone grafting. The optimal time to begin ridge preservation is at the moment of tooth extraction. Timely bone preservation can prevent 40% to 60% of jawbone atrophy, which typically occurs within the first 2-3 years post-extraction and continues annually at a rate of 15%-25%. Bone healing within the socket involves a complex regenerative process similar to fracture repair and normal bone remodelling.[12,13]

The bone healing process involves three main components: osteoinduction, osteogenesis, and the use of an osteoconductive matrix. Bone Morphogenic Proteins (BMPs) play a crucial role in guiding the differentiation of osteogenic cells during bone repair, prompting multipotent stem cells to transform into osteoblast-like cells. The idea of using affordable, biologically compatible pharmaceutical agents with minimal side effects-such as statins-to stimulate the body's own bone growth factors has shown significant promise.

Statins are commonly prescribed to reduce cholesterol levels. However, Mundy and colleagues were the first to demonstrate that statins could also boost the expression of BMP-2 in bone-forming cells. Statins promote new blood vessel formation, stimulate osteoblast activity, reduce vascular inflammation, exhibit anti-thrombotic properties, and enhance the production of BMP-2 and other bone-stimulating factors.[14]

Several studies, mostly animal-based, have explored the role of statins in bone regeneration, using models such as Wistar rats, New Zealand white rabbits, and mice. These studies consistently showed positive outcomes in booth intraoral and extraoral sites, including cranial defects and femoral fractures. Human clinical trials have also been conducted, focusing on periodontal defects, periapical cysts, extraction sites, and osteoporotic bone conditions in women. In vitro research is ongoing to clarify the precise mechanisms behind these effects.[12,13]

Of all the statins, simvastatin has been the most extensively researched, demonstrating multiple biological effects. It works by inhibiting the enzyme HMG-CoA reductase, a key catalyst in mevalonate pathway that produces cholesterol and other non-steroidal isoprenoids. Blocking this enzyme results in various beneficial effects. Simvastatin is derived through the fermentation of *Aspergillus terreus* and appears as white crystalline powder that is non-hygroscopic and insoluble in water but soluble in chloroform, methanol, and alcohol. When taken orally, its absorption rate ranges from 40% to 75%, with a significant portion metabolized by the liver. Most of the drug is excreted via bile, while 5% to 20% is eliminated through urine. The standard oral dose is 20-40 mg per day, with a toxic dose reported at 160 mg daily.[9,10]

Several delivery systems have been explored for the localized application of statins, including collagen gels, polyglycol, and gelfoam. Notably, bone regeneration has been observed when using fluvastatin embedded in a gelatin hydrogel matrix. Gelfoam is a water-insoluble, flexible, porous material made from purified pork skin gelatin. Initially developed as a haemostatic agent, it can absorb many times its weight in blood and other fluids.[15]

This particular study examined the use of simvastatin combined with gelfoam as carrier for promoting bone regeneration in mandibular third molar extraction sites. A 10 mg dose of raw simvastatin powder was used, based on findings from previous literature.

MATERIALS AND METHODS

This study was done on patients visiting the Department of oral and maxillofacial surgery and were willing to participate in this prospective, randomized clinical investigation. This research took place in Teerthanker Mahaveer Dental College & Research Centre, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India from April 2023 to October 2024.

Inclusion criteria

Individuals aged between 18-40 who have a partially or fully impacted mandibular 3rd molar that needed surgical extraction & patients who were interested in the study. All these patients were within ASA-I category.

Exclusion criteria

Patients with medical conditions, pregnant women, females on contraceptive medications, individuals under 18 or over 40 years of age, those with poor oral hygiene or widespread chronic destructive periodontitis, individuals with acute pericoronitis, a history of head and neck radiation therapy, those unable to attend follow-up or recall appointments, patients who are on calcium supplements, patients with periapical infections and heavy smokers.

Consent Form

All participants were thoroughly informed about the purpose and methodology of the study. They were also made aware of their right to withdraw at any point during the study, and informed consent was obtained from each of them.

Surgical Procedure

The operation was performed under local anaesthesia 15-20 mins after the injection. Povidone iodine was used to prepare the surgical site (5% w/v). The patients were draped to achieve asepsis. A standardized surgical procedure using ward's/modified ward's incision was carried out by the operator on each patient. A 2ml syringe containing two percent anesthetising agent and vasoconstrictor in concentration 1:80000 was used to administer a conventional inferior alveolar and long buccal nerve block. The standard surgical technique for extraction of lower third molars were done.

After gaining access to the third tooth from the buccal side, bone was eliminated using a round bur and a straight handpiece while being continuously irrigated. If necessary, both the roots and crowns were sectioned. Following tooth removal, the alveolus was examined, irrigated with sterile solution and curetted to remove granulation tissue. In the control group, saline soaked gel foam pieces were placed in the socket. In the study group, a combination of gel foam and 10 mg of simvastatin was used to fill the socket cavity. Suturing was done using 3-0 silk suture. Post-operatively suture was removed after seven days both groups. The participants were put on medications for five days.

RESULTS

PAIN

Pain levels were recorded using a visual analog scale ranging from 0 to 10, based on the patients' self-assessment of pain intensity over the seven days following the procedure. The readings were recorded on 1st, 3rd & 7th day post-operatively. The average of two daily pain score readings was used to evaluate and compare pain distribution between the study and control groups. Inter-group comparison (Table 1 & Figure 1) and intra-group comparison (Table 2 & Figure 2) was performed.

Table 1. Intergroup comparison of mean Visual Analog Scale (VAS) scores

	Group	Mean	Std. Deviation	Std. Error Mean	P value
Pre-Operative	Group1	5.466	1.884	0.486	0.845 (Non-Sig)
	Group 2	5.600	1.804	0.465	
1st Post-Operative Day	Group1	6.600	1.298	0.335	0.886 (Non-Sig)
	Group 2	6.666	1.234	0.318	
3rd Post-Operative Day	Group1	6.800	1.612	0.416	0.896 (Non-Sig)
	Group 2	6.866	1.125	0.290	
7th Post-Operative Day	Group1	3.133	1.505	0.388	0.157(Non-Sig)
	Group 2	3.800	0.941	0.243	

Group 1: Simvastatin(10mg) with Gel Foam post-operatively Group 2: Gel Foam post-operatively

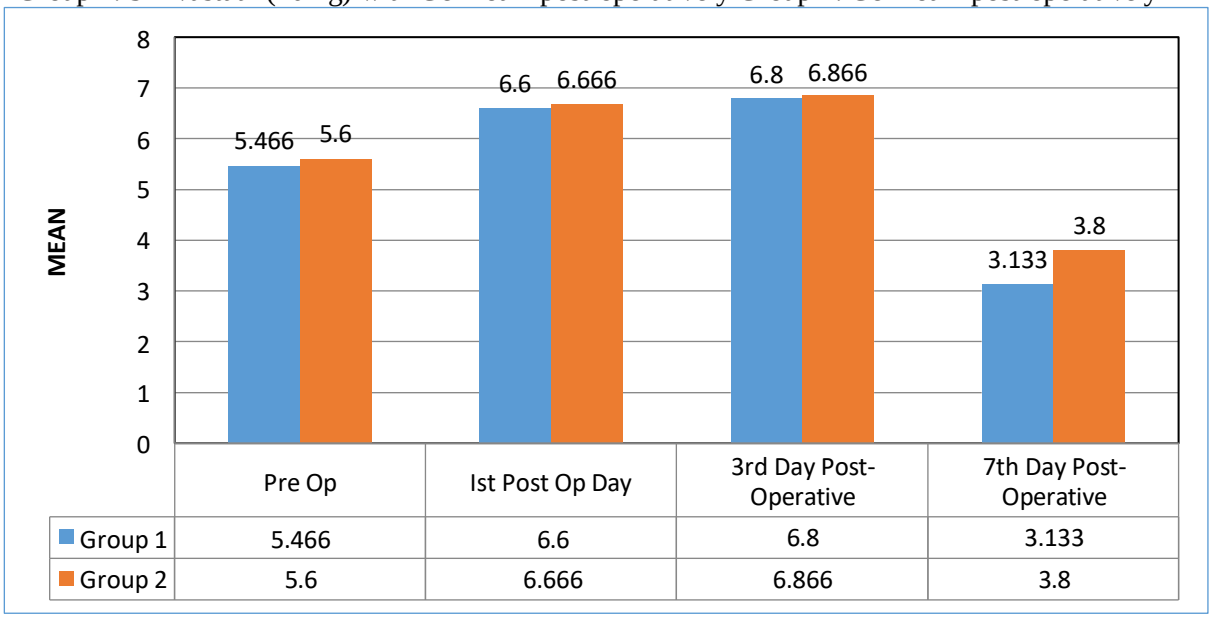


Figure 1. Pain distribution between control and study group

Table 2. Intragroup comparison of mean Visual Analog Scale (VAS) scores

	Intragroup Comparison		Mean Difference	P value
Group 1	Pre-Operative	1st Post-Operative Day	-1.134	0.001(Sig)
	Pre-Operative	3rd Post-Operative Day	-1.334	0.001(Sig)
	Pre-Operative	7th Post-Operative Day	2.333	0.001(Sig)
	1st Post-Operative Day	3rd Post-Operative Day	-0.2	0.321(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	3.467	0.001(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	3.667	0.001(Sig)
Group 2	Pre-Operative	1st Post-Operative Day	-1.066	0.001(Sig)
	Pre-Operative	3rd Post-Operative Day	-1.266	0.001(Sig)
	Pre-Operative	7th Post-Operative Day	1.8	0.001(Sig)
	1st Post-Operative Day	3rd Post-Operative Day	-0.2	0.321(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	2.866	0.001(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	3.066	0.001(Sig)

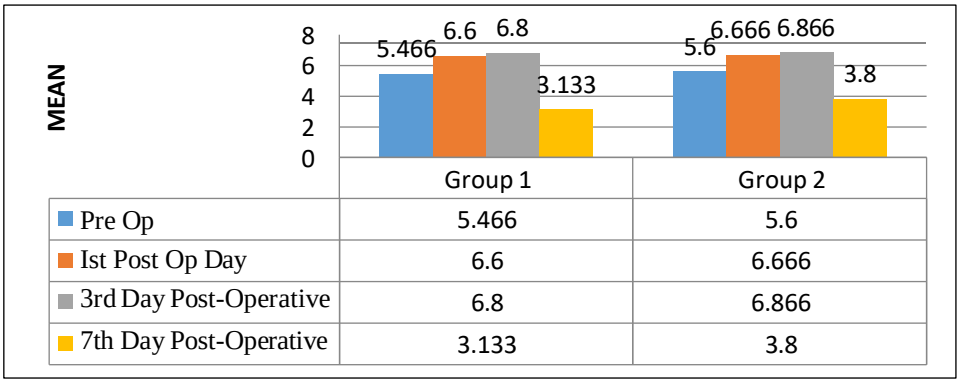


Figure 2. Intragroup pain distribution

SWELLING

The post operative changes in the dimensions of the face was recorded on the 1st, 3rd & 7th day. Pre-operative dimensions were also recorded and comparison between both the groups was performed (Table 3 & Figure 3). Comparison within the groups were also done and depicted (Table 4 & Figure 4).

Table 3. Intergroup comparison of mean swelling scores

	Group	Mean	Std. Deviation	Std. Error Mean	P value
Pre-Operative	Group1	106.712	3.012	0.777	0.515 (Non-Sig)
	Group 2	107.332	2.073	0.535	
1st Post-Operative Day	Group1	111.062	3.008	0.776	0.929 (Non-Sig)
	Group 2	111.152	2.308	0.596	
3rd Post-Operative Day	Group1	113.042	4.199	1.084	0.822 (Non-Sig)
	Group 2	113.332	2.580	0.666	
7th Post-Operative Day	Group1	108.752	4.266	1.101	0.842 (Non-Sig)
	Group 2	108.512	1.947	0.502	

Group 1: Simvastatin(10mg) with Gel Foam post-operatively Group 2: Gel Foam post-operatively

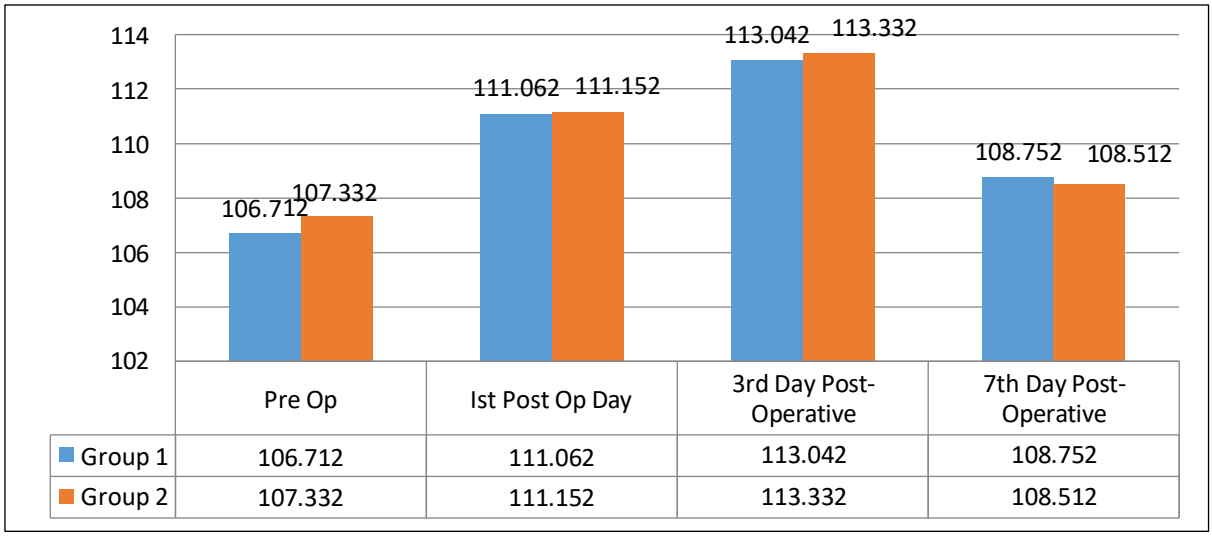


Figure 3. Swelling comparison between control and study group

Table 4. Intragroup comparison of mean swelling scores

	Intragroup Comparison		Mean Difference	P value
Group 1	Pre-Operative	1st Post-Operative Day	-4.35	0.009(Sig)
	Pre-Operative	3rd Post-Operative Day	-6.33	0.011(Sig)
	Pre-Operative	7th Post-Operative Day	-2.04	0.021(Sig)
	1st Post-Operative Day	3rd Post-Operative Day	-1.98	0.031(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	2.31	0.021(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	4.29	0.001(Sig)
Group 2	Pre-Operative	1st Post-Operative Day	-3.82	0.001(Sig)
	Pre-Operative	3rd Post-Operative Day	-6	0.001(Sig)
	Pre-Operative	7th Post-Operative Day	-1.18	0.031(Sig)
	1st Post-Operative Day	3rd Post-Operative Day	-2.18	0.021(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	2.64	0.001(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	4.82	0.008(Sig)

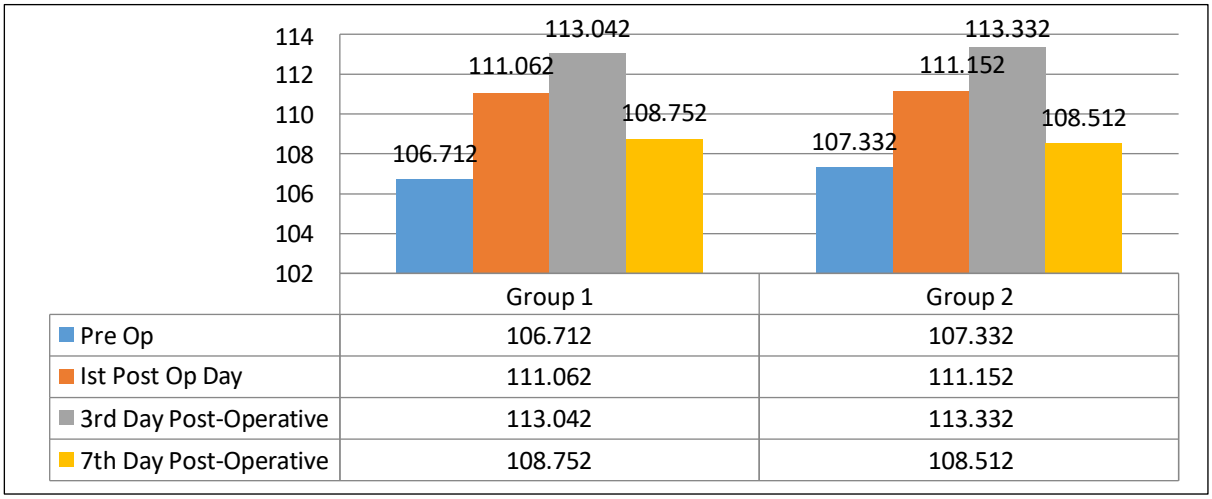


Figure 4. Intragroup swelling comparison

MOUTH OPENING

The pre operative mouth openning was recorded using metallic scale/vernier calliper. The post operative changes in the extent of mouth opening was also recorded on the 1st, 3rd & 7th day. Comparison was done between the groups was performed (Table 5 & Figure 5). Comparison within the groups were also done and depicted (Table 6 & Figure 6).

Table 5. Intergroup comparison of mean mouth opening

	Group	Mean	Std. Deviation	Std. Error Mean	P value
Pre-Operative	Group1	36.600	2.971	0.767	0.515 (Non-Sig)
	Group 2	35.000	3.721	0.994	
1st Post-Operative Day	Group1	31.866	4.673	1.206	0.001 (Sig)
	Group 2	28.571	3.631	0.970	
3rd Post-Operative Day	Group1	30.200	4.616	1.192	0.029 (Sig)
	Group 2	26.857	2.905	0.776	
7th Post-Operative Day	Group1	34.733	3.807	0.983	0.001 (Sig)
	Group 2	30.571	2.737	0.731	

Group 1: Simvastatin(10mg) with Gel Foam post-operatively Group 2: Gel Foam post-operatively

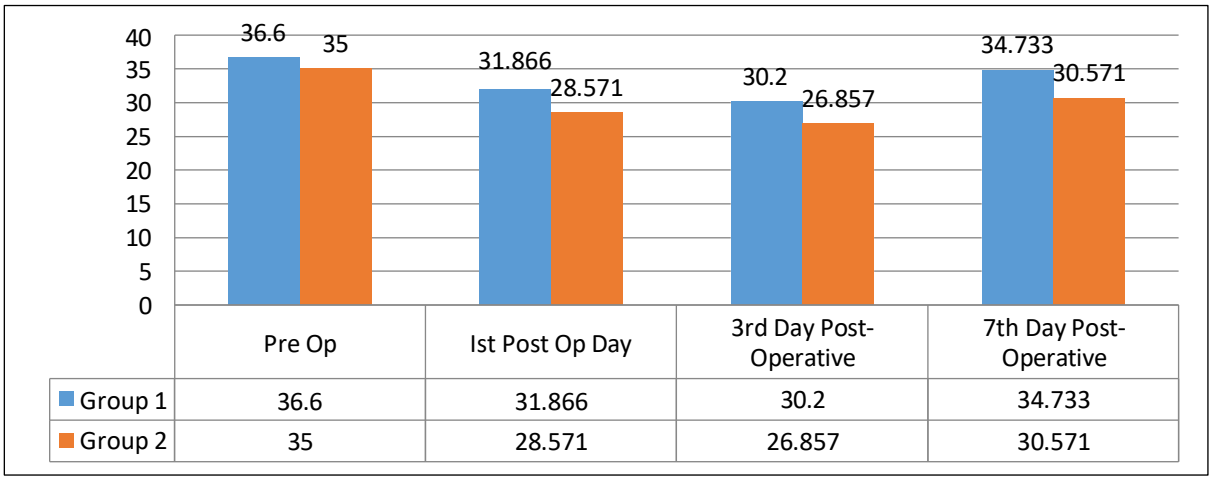


Figure 5. Mouth opening comparison between control and study group

Table 6. Intragroup comparison of mean mouth opening

	Intragroup Comparison		Mean Difference	P value
Group 1	Pre-Operative	1st Post-Operative Day	4.734	0.001(Sig)
	Pre-Operative	3rd Post-Operative Day	6.4	0.001(Sig)
	Pre-Operative	7th Post-Operative Day	1.867	0.106(Non-Sig)
	1st Post-Operative Day	3rd Post-Operative Day	1.666	0.131(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	-2.867	0.001(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	-4.533	0.001(Sig)
Group 2	Pre-Operative	1st Post-Operative Day	6.429	0.001(Sig)
	Pre-Operative	3rd Post-Operative Day	8.143	0.001(Sig)
	Pre-Operative	7th Post-Operative Day	4.429	0.001(Sig)
	1st Post-Operative Day	3rd Post-Operative Day	1.714	0.121(Non-Sig)
	1st Post-Operative Day	7th Post-Operative Day	-2.000	0.043(Sig)
	3rd Post-Operative Day	7th Post-Operative Day	-3.714	0.001(Sig)

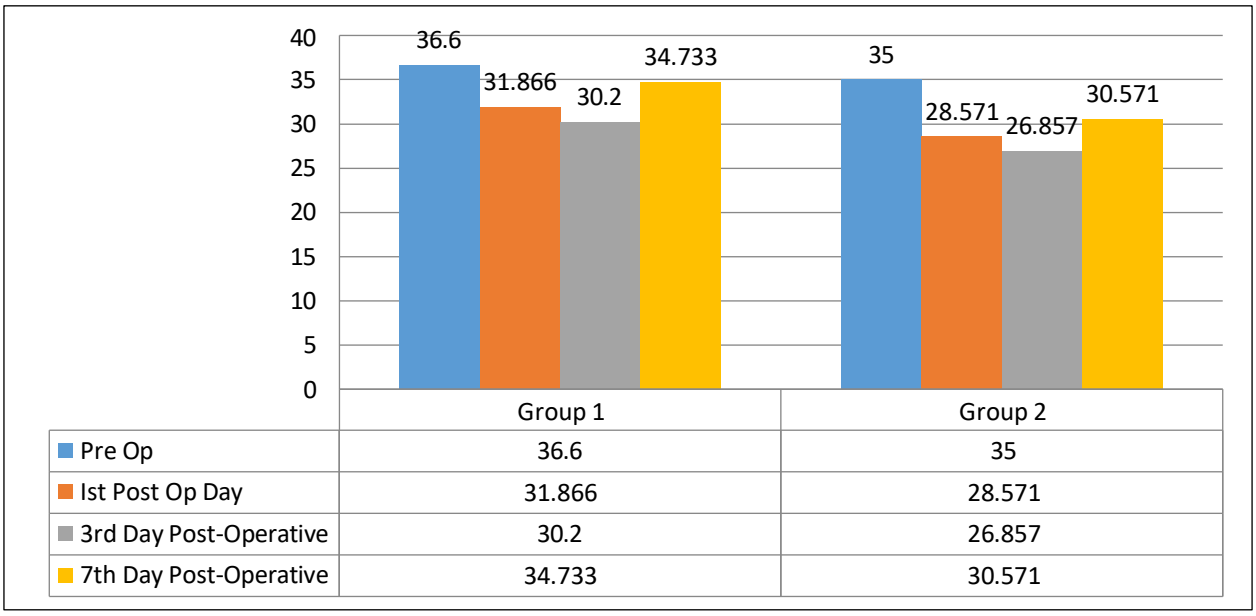


Figure 6. Intragroup mouth opening comparison

POCKET PROBING DEPTH

Pocket probing depth was evaluated pre operatively using a William's probe. Pre operative data was taken along with post operative readings one month and three months post-operatively. Comparison was done between the groups was performed (Table 7 & Figure 7). Comparison within the groups was also done and illustrated graphically (Table 8 & Figure 8).

Table 7. Intergroup comparison of pocket probing depth

	Group	Mean	Std. Deviation	Std. Error Mean	P value
Pre-Operative	Group1	2.422	0.366	0.094	0.158(Non-Sig)
	Group 2	2.644	0.462	0.119	
1st Month Post-Operatively	Group1	3.444	0.391	0.101	0.459 (Non-Sig)
	Group 2	3.555	0.482	0.124	
3rd Month Post-operatively	Group1	3.400	0.522	0.134	1.000(Non-Sig)
	Group 2	3.400	0.474	0.122	

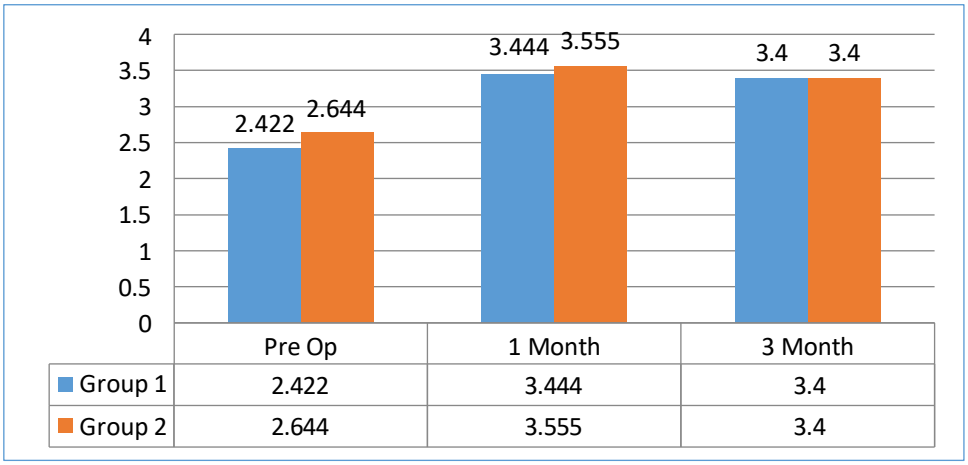


Figure 7. Pocket probing depth comparison between control and study group

Table 8. Intragroup comparison of pocket probing depth

	Intragroup Comparison		Mean Difference	P value
Group 1	Pre-Operative	1st Month Post-Operatively	-1.022	0.001(Sig)
	Pre-Operative	3rd Month Post-Operatively	-0.978	0.001(Sig)
	1st Month Post-Operatively	3rd Month Post-Operatively	0.044	0.876(Non-Sig)
Group 2	Pre-Operative	1st Month Post-Operatively	-0.911	0.001(Sig)
	Pre-Operative	3rd Month Post-Operatively	-0.756	0.001(Sig)
	1st Month Post-Operatively	3rd Month Post-Operatively	0.155	0.023(Sig)

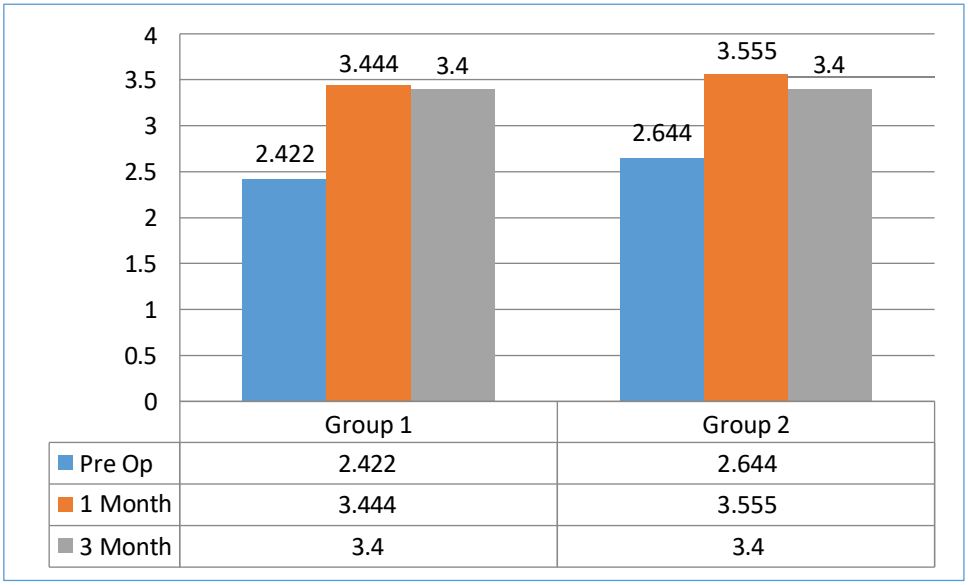


Figure 8. Intragroup popcket probing depth comparison

BONE DENSITY

Bone density evaluation was based on Cone beam computed tomography (CBCT) scans. Data was obtained using the mean Hounsfield Units (HU) of the third molar socket region and tabulated.[21] Two post operative scans were done at first month and third month respectively. Comparison was done between the two data sets were done (Table 9 & Figure 9). Data comparison within the group were also tabulated and depicted (Table 10 & Figure 10).

Table 9. Intergroup comparison between the two groups

	Group	Mean	Std. Deviation	Std. Error Mean	P value
1st Month Post-Operatively	Group1	145.462	7.747	2.070	0.001 (Sig)
	Group 2	134.522	12.092	3.122	
3rd Month Post-Operatively	Group1	247.772	32.635	8.722	0.029 (Sig)
	Group 2	207.622	18.515	4.780	

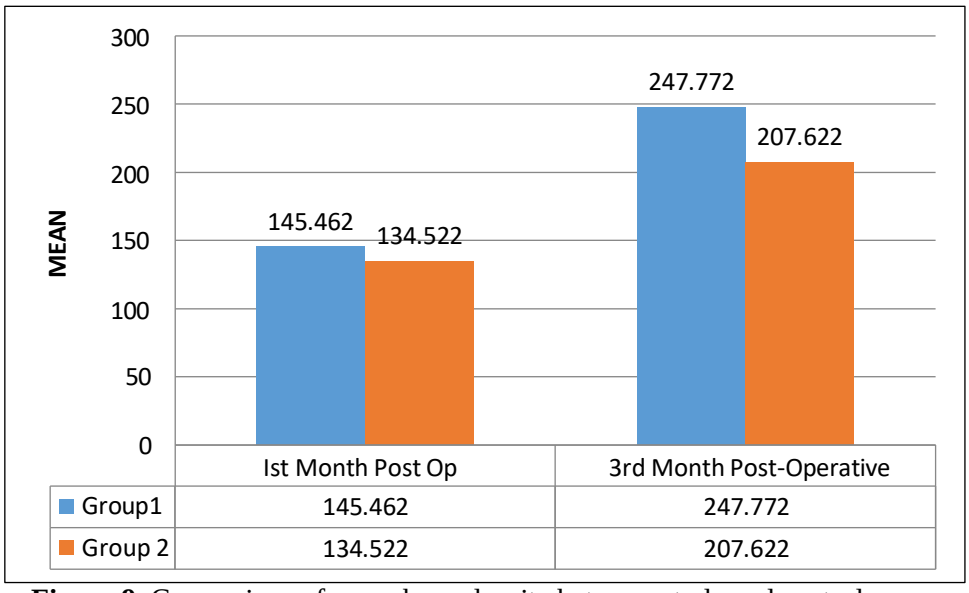


Figure 9. Comparison of mean bone density between study and control group

Table 10. Intragroup comparison of the two groups

	Intragroup Comparison	Mean	Std. Deviation	Std. Error Mean
Group 1	1st Month Post-Operatively	145.462	7.747	2.070
	3rd Month Post-Operatively	247.772	32.635	8.722
Group 2	1st Month Post-Operatively	134.522	12.092	3.122
	3rd Month Post-Operatively	207.622	18.515	4.780

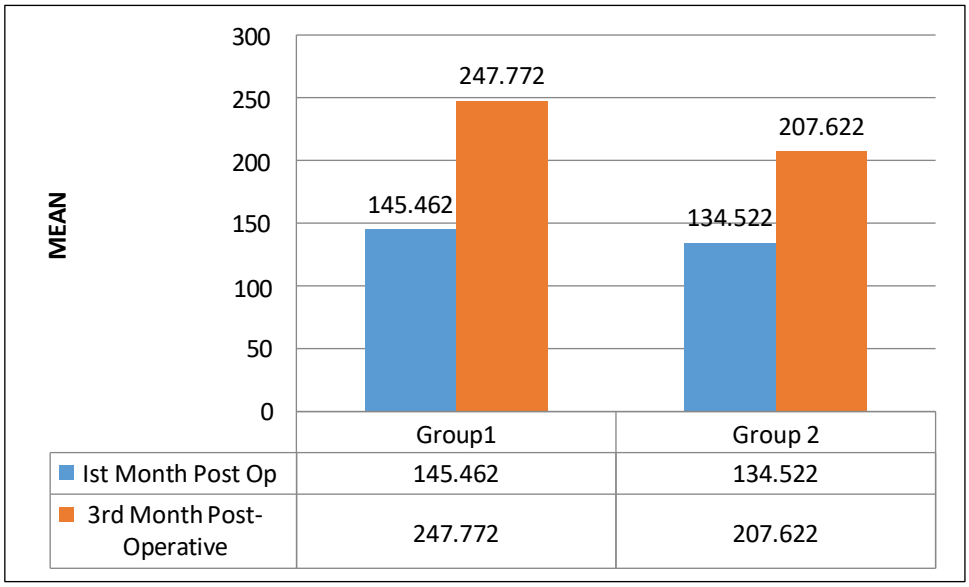


Figure 10. Intragroup comparison of mean bone density

DISCUSSION

The surgical removal of mandibular third molars is amongst the most frequently performed procedures in oral and maxillofacial surgery. Tooth extractioon inevitably leads to bone loss due to physiological changes in the bone structure. The optimal moment to preserve the alveolar ridge is during the extraction itself.[18-20] Implementing bone preservation techniques at this stage can prevent 40% to 60% of the jaw bone resoprtion tpically occurring within 2 to 3 years post extraction, which may further progress at a rate of 15% to 25% annually throughout life.[22,23]

DISCUSSION ON PAIN

The intergroup comparison of mean Visual Analog Scale (VAS) scores between Group 1 (Simvastatin 10 mg with Gel Foam post-operatively) and Group 2 (Gel Foam post-operatively) showed no statistically significant differences at any time point. At baseline (pre-operative), the mean VAS score was 5.466 ± 1.884 in Group 1 and 5.600 ± 1.804 in Group 2 (p = 0.845, non-significant), indicating similar pain levels before surgery. On the first post-operative day, pain levels increased in both groups, with Group 1 at 6.600 ± 1.298 and Group 2 at 6.666 ± 1.234 (p = 0.886, non-significant). By the third post-operative day, pain levels remained high, with Group 1 at 6.800 ± 1.612 and Group 2 at 6.866 ± 1.125 (p = 0.896, non-significant), showing no significant difference between the two groups. By the seventh post-operative day, pain levels had reduced in both groups, with Group 1 reporting a mean VAS score of 3.133 ± 1.505, while Group 2 had a slightly higher score of 3.800 ± 0.941. However, the difference remained non-significant (p = 0.157). Overall, both treatment groups experienced a similar pain trajectory, with an initial post-operative increase in pain, followed by a gradual decrease by the seventh day. However, there was no statistically significant difference between the two groups at any time point, suggesting that the addition of Simvastatin did not have a significant effect on post-operative pain relief compared to Gel Foam alone.

The intragroup comparison of mean VAS scores over time showed a significant change in pain perception within both groups. In Group 1 (Simvastatin with Gel Foam), the mean pre-operative VAS score was 5.466 ± 1.884. Pain increased significantly on the 1st post-operative day (6.600 ± 1.298, p = 0.001) and remained high on the 3rd post-operative day (6.800 ± 1.612, p = 0.001). However, by the 7th post-operative day, there was a significant reduction in pain to 3.133 ± 1.505 (p = 0.001). The difference between the 1st and 3rd post-operative days was not statistically significant (p = 0.321), but a significant reduction was observed between the 1st and 7th days (p = 0.001) and the 3rd and 7th days (p = 0.001).Similarly, in Group 2 (Gel Foam alone), the pre-operative VAS score was 5.600 ± 1.804, which significantly increased on the 1st post-operative day (6.666 ± 1.234, p = 0.001) and the 3rd post-operative day (6.866 ± 1.125, p = 0.001). By the 7th post-operative day, pain significantly reduced to 3.800 ± 0.941 (p = 0.001). There was no significant difference between the 1st and 3rd post-operative days (p = 0.321), but a significant reduction was observed between the 1st and 7th days (p = 0.001) and the 3rd and 7th days (p = 0.001). Overall, both groups followed a similar pain progression pattern, with an initial increase in pain after surgery, stabilization by the 3rd post-operative day, and a significant reduction in pain by the 7th day. The statistical significance of the results suggests a clear post-operative recovery trend, though the pain relief pattern was comparable between the two groups.

DISCUSSION ON SWELLING

The intergroup comparison of mean swelling scores revealed no statistically significant differences between Group 1 (Simvastatin with Gel Foam) and Group 2 (Gel Foam alone) at any time interval (p > 0.05 for all comparisons). Pre-operatively, the mean swelling score in Group 1 was 106.712 ± 3.012, while in Group 2, it was 107.332 ± 2.073 (p = 0.515, non-significant). On the 1st post-operative day, swelling increased in both groups, with Group 1 measuring 111.062 ± 3.008 and Group 2 measuring 111.152 ± 2.308 (p = 0.929, non-significant). By the 3rd post-operative day, swelling reached its peak, with Group 1 at 113.042 ± 4.199 and Group 2 at 113.332 ± 2.580 (p = 0.822, non-significant). By the 7th post-operative day, swelling began to subside, with Group 1 measuring 108.752 ± 4.266 and Group 2 at 108.512 ± 1.947 (p = 0.842, non-significant). Overall, both groups followed a similar swelling progression pattern, with a gradual increase in swelling post-operatively, peaking on the 3rd day, and subsiding by the 7th day. The lack of significant intergroup differences suggests that both treatment modalities had a comparable effect on post-operative swelling resolution.

The intragroup comparison of mean swelling scores within both Group 1 (Simvastatin with Gel Foam) and Group 2 (Gel Foam alone) showed significant changes across different time intervals. In Group 1, there was a significant increase in swelling from the pre-operative period (106.712 ± 3.012) to the 1st post-operative day (111.062 ± 3.008, p = 0.009) and further to the 3rd post-operative day (113.042 ± 4.199, p = 0.011). However, by the 7th post-operative day, the swelling significantly decreased (108.752 ± 4.266, p = 0.021). The difference between the 1st and 3rd post-operative days was non-

significant (p = 0.031), but the reduction from the 3rd to the 7th day was highly significant (p = 0.001), indicating a peak in swelling on the 3rd day, followed by a substantial decrease. A similar trend was observed in Group 2, where swelling increased significantly from the pre-operative period (107.332 ± 2.073) to the 1st post-op day (111.152 ± 2.308, p = 0.001) and further to the 3rd post-op day (113.332 ± 2.580, p = 0.001). The swelling then decreased significantly by the 7th post-op day (108.512 ± 1.947, p = 0.031). The difference between the 1st and 3rd post-operative days was non-significant (p = 0.021), while the reduction between the 3rd and 7th days was significant (p = 0.008). Overall, in both groups, swelling followed a characteristic post-operative pattern, peaking on the 3rd day and gradually resolving by the 7th day. The significant reductions observed by the 7th day suggest a natural course of healing, with no major differences in swelling resolution between the two treatment groups.

DISCUSSION ON MOUTH OPENING

The comparison of mean mouth opening scores between the two groups revealed significant differences at multiple time points. Pre-operatively, both groups had similar mouth opening values, with Group 1 (Simvastatin with Gel Foam) showing a mean of 36.6 mm, while Group 2 (Gel Foam alone) had 35 mm, and this difference was not statistically significant (p = 0.515). However, a significant reduction in mouth opening was observed post-operatively in both groups, with the 1st post-operative day showing a greater restriction in Group 2 (28.57 mm) compared to Group 1 (31.86 mm), p = 0.001 (significant). By the 3rd post-operative day, mouth opening remained restricted but showed slight improvement, with Group 1 (30.2 mm) demonstrating a significantly better recovery than Group 2 (26.85 mm), p = 0.029. By the 7th post-operative day, both groups showed improvement; however, Group 1 (34.73 mm) had a significantly better recovery than Group 2 (30.57 mm), p = 0.001. These findings suggest that while both groups experienced post-operative trismus, the addition of Simvastatin in Group 1 contributed to a faster recovery and improved functional outcomes, as demonstrated by the significantly better mouth opening scores at all post-operative time points.

The intragroup comparison of mean mouth opening scores over different time intervals showed a significant reduction in mouth opening post-operatively in both groups, followed by gradual improvement in Group 1 (Simvastatin with Gel Foam), there was a significant decrease in mouth opening from the pre-operative measurement (36.6 mm) to the 1st post-operative day (31.86 mm, p = 0.001) and further reduction on the 3rd post-operative day (30.2 mm, p = 0.001). By the 7th day, mouth opening improved to 34.73 mm, and although the difference from the pre-operative value was not statistically significant (p = 0.106), it indicates near-complete recovery. Significant differences were observed when comparing the 3rd day to the 7th day (p = 0.001), showing progressive improvement in mouth opening. Similarly, Group 2 (Gel Foam alone) also showed a significant decline in mouth opening from the pre-operative value (35 mm) to the 1st post-operative day (28.57 mm, p = 0.001) and further reduction on the 3rd post-operative day (26.85 mm, p = 0.001). By the 7th post-operative day, the mouth opening improved to 30.57 mm, but the difference from the pre-operative measurement remained significant (p = 0.001), indicating an incomplete recovery. Notably, a significant improvement was observed from the 3rd to the 7th post-operative day (p = 0.001), suggesting progressive healing. Overall, both groups experienced post-operative trismus, but Group 1 exhibited a faster recovery in mouth opening, with values approaching pre-operative levels by the 7th post-operative day, whereas Group 2 showed a slower recovery with persistent restriction at this time point. These findings suggest that Simvastatin might play a role in promoting early functional recovery after surgery.

DISCUSSION ON POCKET PROBING DEPTH

The intergroup comparison of mean pocket probing depth (PPD) scores between Group A (Simvastatin 10 mg with Gel Foam post-operatively) and Group B (Gel Foam post-operatively) at different time intervals showed no statistically significant differences between the two groups. At the pre-operative stage, Group A had a mean PPD score of 2.422 ± 0.366, while Group B had a slightly higher mean of 2.644 ± 0.462 (p = 0.158, non-significant). By the 1st month post-operative period, both groups exhibited an increase in PPD scores, with Group A reaching 3.444 ± 0.391 and Group B reaching 3.555 ± 0.482, but the difference remained non-significant (p = 0.459). At the 3rd month post-operative interval, both groups showed stabilization, with mean PPD scores of 3.400 ± 0.522 for Group A and 3.400 ± 0.474 for Group B (p = 1.000, non-significant). These findings indicate that the use of Simvastatin (10 mg) with Gel Foam post-operatively did not result in a significant difference in PPD scores compared to the use of Gel Foam alone. Both groups followed a similar trend, with an initial increase in PPD at 1 month, followed by stabilization at 3 months.

The intragroup comparison of mean probing pocket depth (PPD) scores across different time intervals for both groups revealed significant changes over time. In Group 1 (Simvastatin 10 mg with Gel Foam post-operatively), the mean PPD increased from 2.422 ± 0.366 at baseline to

3.444 ± 0.391 at 1 month, showing a significant mean difference of -1.022 (p = 0.001). Similarly, the increase from pre-operative to 3 months (3.400 ± 0.522) was also significant, with a mean difference of -0.978 (p = 0.001). However, the change between 1 month and 3 months (mean difference = 0.044, p = 0.876) was not significant, indicating stabilization of PPD after the first month. In Group 2 (Gel Foam post-operatively), a similar pattern was observed. The mean PPD increased from 2.644 ± 0.462 at baseline to 3.555 ± 0.482 at 1 month, with a significant mean difference of -0.911 (p = 0.001). The increase from pre-operative to 3 months (3.400 ± 0.474) was also significant, with a mean difference of -0.756 (p = 0.001). Unlike Group 1, the change between 1 month and 3 months was also significant (mean difference = 0.155, p = 0.023), suggesting a continued but slight reduction in PPD over this period. Overall, both groups experienced a significant increase in PPD from baseline to 1 month and from baseline to 3 months, indicating initial post-operative changes. However, Group 1 exhibited stabilization between 1 and 3 months, whereas Group 2 showed a slight but significant reduction in PPD during this period.

DISCUSSION ON BONE DENSITY

The intergroup comparison of bone density between the groups at different postoperative time points revealed significant differences. At the first month postoperatively, Group 1 (Simvastatin 10mg with Gel Foam) demonstrated a higher mean bone density (145.462 ± 7.747) compared to Group 2 (Gel Foam alone) with a mean of 134.522 ± 12.092. The difference was statistically significant (p = 0.001). By the third month postoperatively, bone density further increased in both groups, with Group 1 showing a significantly higher mean bone density (247.772 ± 32.635) than Group 2 (207.622 ± 18.515), with a p-value of 0.029. These findings suggest that the addition of Simvastatin (10mg) to Gel Foam postoperatively enhances bone density recovery compared to using Gel Foam alone.

The intragroup comparison of mean bone density between different time intervals revealed a significant increase in both groups from the first to the third month postoperatively. In Group 1 (Simvastatin 10mg with Gel Foam), the mean bone density increased from 145.462 ± 7.747 at the first month to 247.772 ± 32.635 at the third month, indicating substantial bone regeneration over time. Similarly, in Group 2 (Gel Foam alone), the mean bone density improved from 134.522 ± 12.092 at the first month to 207.622 ± 18.515 at the third month, though the increase was relatively lower compared to Group 1. These results suggest that while both groups showed significant bone density improvement over time, Group 1 exhibited a greater increase, reinforcing the potential efficacy of Simvastatin in enhancing bone regeneration.

CONCLUSION

The localized application of simvastatin promotes bone formation in mandibular third molar extraction sites. It also contributes to better the postoperative functional recovery in the treatment group compared to the control group. Gel foam serves as an effective carrier, facilitating easier handling during local administration. To validate these findings, studies with larger sample sizes, extended follow-up periods, and a split-mouth design are recommended.

DECLARATIONS

Ethics approval and consent to participate
Not applicable.
Consent for publication
Not applicable.
Competing interests
The authors declare no conflict of interest.
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REVIEW ARTICALE

NEUROMUSCULAR DISORDERS AFFECTING THE ORAL AND MAXILLOFACIAL REGION: INSIGHTS FROM A NARRATIVE REVIEW

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ABSTRACT

Background: Neuromuscular diseases are a group of disorders affecting the body's muscles and nerves, often leading to muscle weakness, which is the most common clinical feature. These conditions interfere with the body's adaptive systems, reducing overall functional capacity.

Objectives: This article aims to provide a brief review of some common neuromuscular disorders, highlighting their clinical manifestations and their implications for oral health, particularly within the oral and maxillofacial region.

Results: Neuromuscular disorders present with varying degrees of muscle weakness and dysfunction, which can significantly affect oral and maxillofacial structures. These may include difficulties in mastication, swallowing, speech, and maintaining oral hygiene, thereby increasing the risk of oral health complications.

Conclusion: Understanding the manifestations of neuromuscular diseases is essential for early recognition and comprehensive management in dental practice. Special attention is required to address oral health challenges in affected patients, ensuring improved quality of care.

Keywords: Motor neuron disease; Muscular diseases; Muscle weakness; Oral and Maxillofacial region; Muscle Atrophy

INTRODUCTION

The terms 'muscle disease', 'muscular dystrophy, 'neuromuscular conditions', and 'neuromuscular disorders' all describe a large group of conditions that affect either the muscles, such as those in the arms and legs or the heart and lungs, or the nerves which control the muscles. They can cause problems with:

- The nerves that control the muscles
- Muscles
- Communication between the nerves and muscles.[1]

These disorders result in longstanding functional deficits that result in substantial utilization of healthcare resources in addition to the emotional, financial and social burden to those affected individuals and their families. NMDs of the maxillofacial region also affect the aesthetic facial appearance of the patients. Some forms of NMD are hereditary and manifest at birth or early childhood whereas the incidence of other forms increases with age due to spontaneous mutation in the gene or due to immune system disorders.[1]

Neuromuscular disorders caused due to muscle impairment because of pathology in the associated nerves. These neuromuscular disorders have a collective lifetime prevalence rate of 3% to 5% which makes their encounter
common with the dental practitioner. These disorders affect dentition, soft tissues, and occlusion and hence we should be aware of their oral manifestations, dental management, and treatment. This focuses on some of the most common neuromuscular disorder affecting the orofacial region and its management, by oral physicians.[2]

- CVD (Cerebrovascular Disease)
- Multiple sclerosis
- Parkinsonism
- Huntington's disease
- Seizure disorders
- Bell`s palsy
- Myasthenia Gravis

CEREBROVASCULAR DISEASE (CVD)

Cerebrovascular disease includes all disorders that cause damage to the blood vessels supplying the brain, producing neurologic damage.[3] The most common form is ischemic heart disease, a fatal condition that can lead to acute myocardial infarction.[23]

Etiology:

Approximately 80% of strokes are associated with the development of atherosclerosis leading to cerebral ischemia and infarction and the remaining 20% of cases are caused by cerebral hemorrhage.[3]

Clinical manifestations and treatment of stroke:

- Strokes due to ischemia may be classified clinically either as a stroke in evolution or as a completed stroke. "Stroke in evolution" is a descriptive term used to indicate condition in which symptoms associated with cerebral ischemia become progressively worse while the patient is under observation.[3]
- Symptoms of complete stroke caused by an embolus develop suddenly.[3]
- It is not preceded by transient ischemic attacks; rather, the stroke itself evolves rapidly because the clot originates elsewhere and suddenly blocks a cerebral vessel. Whatever the cause of the neurologic damage, the resultant infarct may enlarge for a period of 4 to 5 days because of cerebral edema.[3]
- Repair is dependent on good collateral circulation and is accomplished by the formation of fibroblastic scar tissue.[3]

After a completed stroke, treatment focuses on the prevention of further neurologic damage, through the reduction of underlying risk factors and by rehabilitation procedures, including speech and physical therapy.[3]

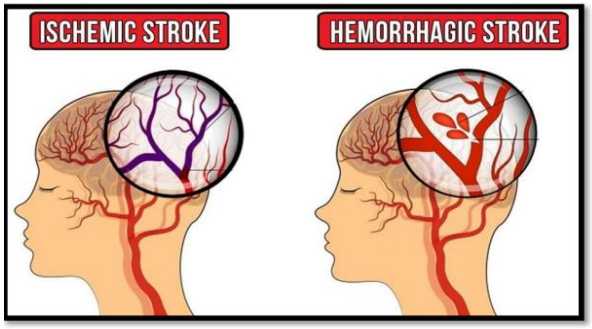


Figure 1. Types of cerebrovascular stroke[25]

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a chronic neurological disease characterized by the demyelination of axons within the central nervous system. The disease occurs more frequently among women.[4]

Etiology: An immunologic basis is strongly suggested by the presence of activated T lymphocytes and autoantibodies to glycoproteins detected in MS lesions.[4]

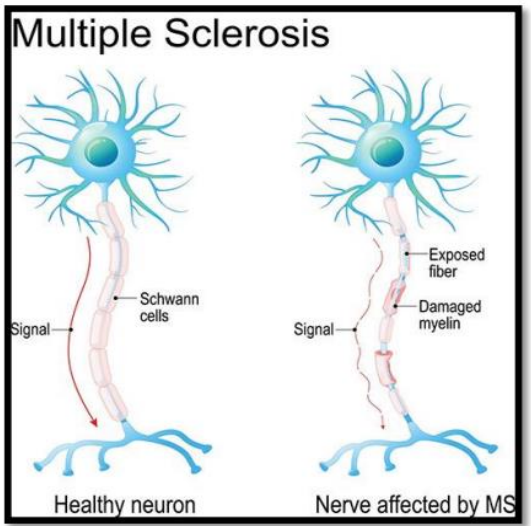


Figure 2. Healthy neuron and nerve affected by multiple sclerosis[26]

Clinical Manifestations

- Uhthoff's sign is characterized by rapid vision loss following a body temperature increase that is associated with strenuous exercise.[5]
- Another important sign of ocular disturbance is Marcus Gunn's pupillary sign, which can be elicited in patients with unilateral optic neuritis in the following manner: a bright light is shone into each eye separately; when this light is moved from the normal to the affected eye, the pupil of the latter dilates rather than constricts.[5]
- Weakness or paresthesia of the extremities is noted.[5]
- An important feature of motor nerve function is the relative fluctuation of symptoms daily.[5]

Pharmacotherapy of multiple sclerosis:

Monoclonal antibodies:

Natalizumab is given as a 300 mg IV infusion over one hour, every four weeks, Rituximab, Ofatumumab is given by subcutaneous injection, starting with 20 mg administered at weeks zero, one, and two.[6]

Oral therapies:

Diroximel fumarate: The starting dose for oral dimethyl fumarate is 120 mg given twice daily. After seven days, the dose should be increased to 240 mg given twice daily. It is available in 120 and 240 mg preparations. [6]

Oral Health Considerations

- Pain is normally severe and lancinating, but trigger zones may be absent. In time, the pain often becomes less severe but more continuous. [6]
- Neuropathy to the mental nerve can cause numbness of the lower lip and chin. Facial paralysis appears later in the course of the disease. [6]
- It may be difficult to distinguish between the paralysis caused by MS and that due to Bell's palsy, but up to 24% of MS sufferers may experience facial paralysis. [6]

PARKINSONISM: PARKINSON'S DISEASE

Parkinsonism is a neurodegenerative disorder characterized by rigidity, tremors, bradykinesia, and impaired postural reflexes.[7] Parkinson's disease is a progressive neurodegenerative condition linked with α-synuclein deposition.[24]

Etiology and Pathogenesis:

In idiopathic parkinsonism, dopamine depletion due to degeneration of the dopaminergic nigrostriatal system in the brainstem leads to an imbalance of dopamine and acetylcholine, neurotransmitters that are normally present in the corpus striatum.[7]

Clinical Manifestations: Tremor, rigidity, bradykinesia, and postural instability are the cardinal features of parkinsonism and may be present in any combination.[8]

Treatment:

Pharmacotherapy of Parkinson's disease: Pramipexole – Pramipexole IR is usually started at 0.125 mg three times a day. The dose should be increased gradually by 0.125 mg per dose every five to seven days.[8]



Figure 3. Parkinsonism Symptoms

Ropinirole and Rotigotine are other drug of choice.

Oral Health Considerations

- Patients must often be treated in the upright position, making access to certain areas of the oral cavity difficult for the dentist.[9]
- In addition, anxiety in a Parkinson's disease patient can increase both the tremor and the degree of muscle rigidity.[9]
- Due to dysphagia and an altered gag reflex, special precautions must be taken to avoid the
- aspiration of water or materials used during dental procedures.[9]
- In patients who suffer from hypersialorrhea, maintaining a dry field in procedures that require such can be especially difficult.[9]
- Xerostomia is a common side effect of anti-parkinsonism medications; the consequent root caries and recurrent decay must be diligently treated.[9]

HUNTINGTON'S DISEASE (HUNTINGTON'S CHOREA):

Huntington's disease is a hereditary degenerative disease of the central nervous system, characterized by chorea (involuntary movements) and dementia.[10]

Clinical Manifestations

The clinical manifestations include declination of cognitive behaviour, mood swings, involuntary movements, speech difficulties.

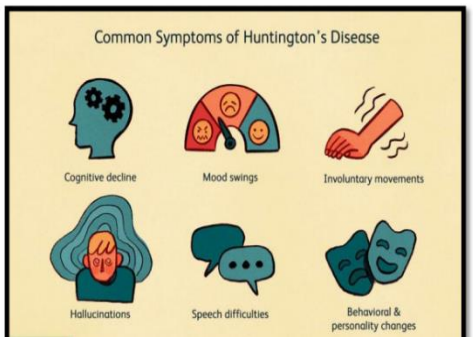


Figure 4. Common symptoms of Huntington's disease[2]

Treatment: Pharmacotherapy: Tetrabenazine, Deutetrabenazin, Antipsychotics, Benzodiazepines .[11]

Oral Health Considerations:

- Dysphagia and choreic movement of the face and tongue will make dental treatment especially challenging.[11]
- Sedation with diazepam may be considered.[11]
- Whenever possible, dentures should be avoided because of the danger of fracture or the accidental swallowing of the dentures.[11]

EPILEPSY:

Epilepsy is a condition characterized by abnormal, recurrent, and excessive neuronal

discharges precipitated by many different disturbances within the central nervous system.[12]

Etiology: Epilepsy in older adults may occur as a complication of any of the previously mentioned causes but is more often associated with cerebrovascular diseases such as stroke and tumor.[12]

Clinical Signs

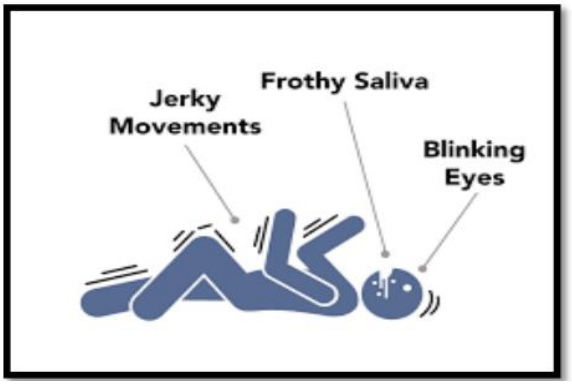


Figure 5. Signs of epilepsy[27]

DISCUSSION

Treatment

A. Immediate management during a seizure:

- The patient should be moved away from dangers like fire, water, or sharp objects.[13]
- After convulsion seizes, the patient should be positioned supine with legs slightly elevated.[13]
- Basic life support should be given if indicated.[13]
- If convulsion continues for more than 5 minutes urgent medical help should be summoned.[13]
- Intravenous anticonvulsants like diazepam should be given.[13]

B. Pharmacologic management 1. Lamotrigine, carbamazepine, and phenytoin are indicated for the treatment of partial seizures.[13]

2. Valproic acid is indicated for the treatment of generalized tonic-clonic seizures.[13]

Oral health considerations:

1. These patients have a high rate of physical injuries, including dental and facial trauma.[12]

2. Hence, precipitation of seizures during dental treatment should be avoided by reducing psychological stress. Inhalation sedation with nitrous oxide (upto20%) and oxygen is highly recommended.[12]

3. Phenytoin-induced gingival hyperplasia is commonly seen in anterior labial surfaces of the maxillary and mandibular gingiva. Maintenance of oral hygiene by chlorhexidine mouthwash can reduce the inflammation or surgical reduction can be done if recession occurs.[12]

BELL'S PALSY:

It is also called facial paralysis or seventh nerve paralysis.

Etiology: This is associated with edema of nerve and subsequent mechanical compression of the facial nerve, leading to paralysis or weakness in the distribution of the facial nerve.[19] Other etiologic conditions include herpes simplex viral infection, parotidectomy, tumors of the cranial base, parapharyngeal space, and infratemporal fossa can lead to seventh nerve palsy.[14,15,16]

Clinical features

1. Bell's palsy begins with slight pain around one ear, followed by an abrupt paralysis of the muscles on that side of the face.[17]

2. The eye on the affected side stays open, the corner of the mouth drops, and there is drooling.[17]

3. The face becomes expressionless and the creases of the forehead are flattened.[17]

Oral health considerations

1. The patient has a dropping corner of the mouth due to which there is drooling of saliva. Hence dental treatment becomes difficult.[18]

2. There may be oral hygiene due to retention of food in the upper and lower buccal and labial folds due to weakness of the buccinator.[18]

3. Patient experiences difficulty in speech and mastication.[18]

MYASTHENIA GRAVIS: A chronic autoimmune disorder causing weakness of skeletal muscle. [20]

Etiology: it involves loss of acetylcholine receptor (AChR) function on the muscle membrane.[20]

Clinical features

1. Patients with ocular symptoms like diplopia and /or ptosis.

2. Oropharyngeal, facial, and masticatory muscle weakness is common, resulting in dysphagia, asymmetry, and dysarthria.

3. In severe cases, respiratory difficulty arises.[21]

Oral health considerations

1. The patient may have difficulty with prolonged mouth opening and swallowing.

2. Aspiration risks can be high and can be reduced by adequate suction, the use of a rubber dam, and avoiding bilateral mandibular anesthetic block.

3. The patient may be at risk for a respiratory crisis due to overmedication.

4. Drugs that may affect the neuromuscular junction such as narcotics, tranquilizers, and barbiturates should be avoided.[22]

CONCLUSION

NMD cases are characterized by progressive muscular impairment leading to loss of mobility, being wheelchair-bound, swallowing difficulties, respiratory muscle weakness, death from respiratory failure, and other symptoms.

Neuromuscular diseases are classically divided by localization into disorders that involve cranial and spinal motor neurons, spinal nerve roots, nerve plexuses, peripheral nerves, neuromuscular junctions, and muscles. The evaluation of cerebrospinal fluid (CSF) composition is not routinely needed to help facilitate a diagnosis of a suspected neuromuscular disease. Rather, electromyography, nerve conduction studies, and nerve and muscle biopsies are often of greater diagnostic importance.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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REVIEWARTICALE

THE IMPORTANCE OF TIMING OF SURGERY IN CLOSED ANKLE FRACTURE – A LITERATURE REVIEW

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ABSTRACT

Background: Ankle fractures are the second most common lower limb injury and remain a challenge for healthcare professionals due to minimal soft tissue coverage and the high potential for significant swelling. This swelling can compromise terminal vasculature in the superficial layers, reducing the tissue's reparative capacity. In closed ankle fractures, determining the appropriate timing of surgery for displaced fractures is crucial. Operating too soon increases the risk of wound healing complications, whereas delaying too long may hinder optimal anatomical reduction. Current recommendations, such as the AO/ASIF guidelines, suggest surgery within 6–8 hours of injury or delaying for 4–6 days in cases with significant edema or fracture blisters. However, these guidelines are largely based on expert opinion, and there is no definitive consensus on the optimal timing.

Objectives: To evaluate the optimal timing of surgery for closed ankle fractures and its impact on postoperative outcomes, including wound healing, systemic complications, and long-term ankle function.

Results: Existing literature indicates that both early and delayed surgeries carry risks. Early intervention may increase wound-related complications, while excessive delay may impair anatomical reduction and functional outcomes. No universally accepted cut-off point between early and delayed surgery has been established, and most evidence is based on small-scale or observational studies.

Conclusion: Determining the ideal timing for surgical intervention in closed ankle fractures is critical for minimizing complications and optimizing outcomes. High-quality, large-scale studies are needed to establish evidence-based guidelines that clearly define the threshold between early and delayed surgery.

Keywords*:* timing of surgery, closed ankle fracture, complication

INTRODUCTION

Ankle fractures are the second most common lower limb injury, with an annual incidence of around 187 cases per 100,000 population[1]. They occur most frequently in adults of working age, though the incidence is rising among elderly women[2]. Several classification systems exist for ankle fractures, with the Lauge-Hansen (LH) system being among the most widely used and accepted in clinical practice. This system classifies injuries based on the mechanism of trauma and the anatomic sequence of structural involvement—supination injuries typically progress from lateral to medial, whereas pronation injuries progress from medial to lateral[3].

Stable, low-severity ankle fractures can be treated conservatively with splint or cast immobilization, while unstable or more severe fractures generally require surgical intervention. The standard surgical approach is open reduction and internal fixation (ORIF), which has been shown to achieve good clinical results, including in geriatric patients[4-7].

In cases of open fractures, high-velocity open injuries, and polytrauma, immediate external fixation is often employed to enhance fracture stability, minimize further soft tissue and bone damage, and facilitate soft

tissue assessment prior to definitive internal fixation[8].In contrast, there is no established protocol for the optimal timing of internal fixation in closed ankle fractures. Following trauma, significant swelling of the surrounding soft tissue can compromise terminal vasculature in superficial layers, thereby reducing the tissue's reparative capacity. This post-traumatic oedema may necessitate delaying surgical intervention to allow for soft tissue recovery. However, excessive delay may lead to prolonged hospitalization, loss of initial fracture reduction, formation of obstructive bony callus, or soft tissue contracture [9,10]. The decision on surgical timing is currently left to the surgeon's judgment, highlighting the need for a clearer understanding of how timing influences patient outcomes[11].

Timing of Surgery in Closed Ankle Fracture

The timing of surgery for closed ankle fractures remains a subject of debate in many trauma units. Currently, there is no conclusive, evidence-based recommendation regarding the optimal timing of surgery for closed ankle fractures, and the decision must therefore be made on a case-by-case basis[12]. Conventional teaching suggests adopting either an early or a delayed approach to avoid excessive swelling and subsequent soft tissue complications[13]. Although no large-scale studies have established definitive guidelines, many surgeons follow the AO/ASIF recommendations, performing immediate surgery within 6–8 hours or delaying intervention for a minimum of 5–7 days with temporary plaster cast immobilization[14]. A recent guideline issued by the United Kingdom's National Institute for Health and Care Excellence (NICE) aimed to determine the optimal timing for planned surgical intervention in ankle fractures[15].

Surgery performed too soon after the injury may heighten the risk of wound-healing complications due to pronounced swelling, whereas delaying surgery for too long can make achieving accurate anatomical reduction more challenging[16]. Nine cohort studies comparing surgery within 24–48 hours to later intervention indicated that early surgery may shorten inpatient stays and reduce rates of wound infection and venous thromboembolism. Despite the very low quality of evidence, the guideline development group advised performing ankle fracture surgery ideally on the day of injury, and no later than the following day, to limit short-term complications[17]. Nevertheless, the literature remains inconsistent, with some studies associating surgical delay with higher rates of postoperative soft tissue complications—such as wound edge necrosis, blistering, and infection—while others report no significant difference between early and delayed interventions [17-21].

Complication

Complications associated with both nonoperative and operative approaches are key factors in treatment decisions. For certain fracture types, such as stable un-displaced injuries, nonoperative management is often the most suitable option, as surgical intervention in these cases may subject patients to unnecessary risks and is considered overtreatment [22-24].

Complications of nonoperative management

Nonoperative management carries potential complications, including malunion, nonunion, pain, functional loss, muscle atrophy, cartilage degeneration, joint stiffness or swelling, deep vein thrombosis (DVT), and pulmonary embolism (PE). Follow-up durations in the studies reviewed ranged from 20 weeks to an average of 7 years[25]. Secondary displacement—often necessitating surgery—may occur after swelling subsides or in cases with inherently unstable fracture patterns, as reported in 4 of 38 patients in one study[26].

Complications of operative management

Operative treatment of closed ankle fracture also carries some potential complication. Other reported complications include inadequate primary osteosynthesis, soft tissue necrosis, infection, osteitis, deep vein thrombosis (DVT), delayed or non-union, secondary displacement, refracture, stiffness, muscle atrophy, tendon insufficiency, sensory deficits, tarsal tunnel syndrome, and complex regional pain syndrome type [27,28]. The primary outcome measures for assessing the success of operative treatment should include pain, ankle functional outcomes, and the occurrence of major adverse events, the latter defined as complications requiring secondary intervention[29]. Preventive strategies include administering prophylactic antibiotics at anesthesia induction, achieving anatomical reduction with stable fixation, preserving soft tissue integrity by minimizing periosteal stripping, assessing VTE risk with appropriate management, and initiating early ankle mobilization. Successful anatomical reduction of ankle fractures requires thorough understanding of normal anatomy, with emphasis on maintaining fibular length, alignment, and rotation, as well as restoring the syndesmosis. Intraoperative radiographs should be critically evaluated for fibular length using the tibiofibular line (a line drawn from the distal fibular tubercle toward the tibia should intersect the tibial plafond on a mortise view) and the circle sign (an unbroken circle formed between the lateral recess of the fibula and the lateral process of the talus on the mortise view)[30,31].

Wound Complication and Infection

Early complications of closed ankle fractures are often related to the surrounding soft tissue envelope due to anatomical factors, as both malleoli are covered only by subcutaneous tissue. Wound complications following open reduction and internal fixation (ORIF) of ankle fractures have been reported in 1.4% to 18.8% of cases [32]. In fracture-dislocation cases, significant wound complications may develop even before any intervention. Prompt reduction of the dislocation in the emergency department can reduce the risk of further damage; therefore, it is recommended to perform reduction even before obtaining an initial radiograph. Soft tissue care during manipulation and reduction in the emergency department is equally important. If there are concerns in either regard, early orthopedic involvement is advised. When definitive management must be delayed due to excessive swelling, the fracture position should be closely monitored both clinically and radiographically[31].

Blister formation is believed to result from increased interstitial pressure due to post-traumatic edema, which reduces cohesion between epidermal cells and facilitates fluid accumulation within a blister cavity. This process is considered a cleavage injury occurring at the dermo-epidermal junction. Anatomical regions such as the ankle, where the skin is tightly adherent and lacks substantial muscle coverage, are particularly susceptible. The reported incidence of fracture blisters in ankle fractures is 6.6%. These blisters have important implications for both nonoperative and operative management. Although there is no universally accepted guideline for managing closed ankle fractures in the presence of blisters, Uebbing et al. recommended leaving the blisters intact and allowing them to heal before proceeding with surgical intervention[33].



Figure 1. The presence of blisters in a closed ankle fracture indicates poor soft tissue condition, which increases the risk of wound-related and infectious complications

Infection is a recognized complication of operative management in ankle fractures, with reported deep infection rates ranging from 1% to 8% [34-36]. Prevention remains a key consideration, and antibiotic prophylaxis should follow the local policy of the hospital and region. Infections in operated closed ankle fractures, particularly in compromised hosts such a diabetes patient or alcoholism, can be limb-threatening[37-38]. In cases where infection develops in the presence of metalwork, surgical debridement and microbiological cultures are recommended. If the implant remains stable and the fracture is unhealed (presentation within 10 weeks of the index surgery), the metalwork is typically retained, and culture-specific antibiotic suppression is initiated. Final debridement and implant removal are performed once fracture union is achieved[35].

Systemic Complication

Systemic complications following surgery can be devastating, with venous thromboembolism (VTE)—manifesting as pulmonary embolism (PE) or deep vein thrombosis (DVT)—representing a potentially life-threatening event. In patients with leg injuries immobilized in a plaster cast or brace for at least one week without prophylaxis, the incidence of VTE has been reported to range from 4.3% to 40% 3[9]. Although the exact incidence in ankle fractures is unclear, trauma database analyses have estimated rates of 0.28% for DVT and 0.21% for PE, respectively[40]. In contrast, Naumann et al. reported higher rates, with DVT occurring in 1.59% and PE in 0.88% of patients following closed ankle fracture surgery[41]. Established risk factors include a prior history of DVT, prolonged immobilization, non–weight-bearing status, body mass index >30 kg/m², pregnancy, use of oral contraceptives, age >60 years, active malignancy, recent hospital admission, and above-knee plaster application[42,41].

Late Complication

Post-traumatic osteoarthritis (PTOA) is a major late complication of ankle fractures, whether treated conservatively or surgically. Its incidence has been reported to be as high as 70%, with rotational ankle fractures being the most common cause[43]. PTOA typically develops when normal joint anatomy is not restored, most often due to malunion or nonunion, and is the leading indication for ankle arthrodesis. In cases of significant displacement, anatomical reduction-more reliably

achieved through surgical intervention-plays a crucial role in reducing the long-term risk of PTOA[43].

A key factor contributing to PTOA is valgus deformity with fibular shortening, typically resulting from fibular malunion[44]. The average latency from injury to end-stage ankle osteoarthritis has been estimated at 20.9 years[43]. Ligamentous injury is another important predisposing factor, with athletes sustaining lateral ankle sprains being particularly susceptible. Given the high incidence of ankle fracture in younger patients, the need for ankle arthrodesis in middle age is a realistic outcome of PTOA. The pathway to arthrodesis is often marked by chronic pain and functional impairment, both of which significantly impact quality of life and overall morbidity[45].

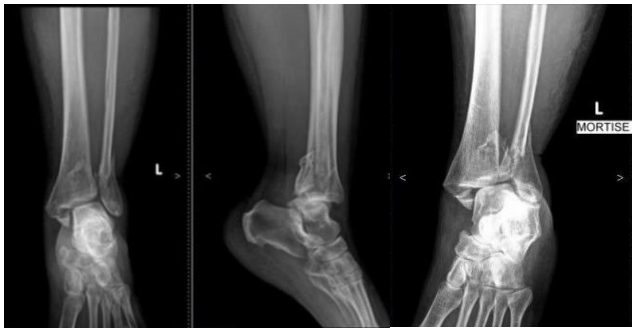


Figure 2. X-ray showing an ankle fracture-dislocation with a tri malleolar fracture. Delayed surgery can make anatomical reduction more difficult due to joint stiffness. Achieving accurate reduction is crucial, as inadequate alignment greatly increases the risk of post-traumatic osteoarthritis (PTOA) and can significantly impair ankle function.

In ankle fractures, syndesmotic disruption may occur and, if left untreated, can lead to persistent instability. When present, syndesmotic disruption is typically managed with fixation using one or more screws or a Tightrope device. Whether syndesmotic screws should be routinely removed remains a subject of debate, as leaving them in place for an extended period may contribute to joint stiffness[31].

Comorbidities

Perioperative comorbidities that can increase the risk of complications in surgical treatment of closed ankle fractures can be divided into two main categories: patient-related (host) factors and fracture-related factors.

- **Host factors** include medical conditions such as diabetes mellitus (DM), peripheral vascular disease (PVD), HIV/AIDS, inflammatory diseases, obesity, history of cigarette smoking, use of corticosteroids or other medications that impair wound healing, and prior surgery involving the injured ankle[46].

- **Fracture and injury-related factors** include the mechanism of injury, time from injury to surgery, fracture type (unimalleolar, bimalleolar, trimalleolar), presence of ankle dislocation or syndesmotic injury, and whether the injury is part of a polytrauma [32].

Diabetes mellitus is a well-recognized risk factor for infection, with reported infection rates after ORIF of ankle fractures reaching as high as 60% in diabetic patients[35]. Untreated infections in this group can lead to amputation in up to 42% of cases and mortality in 11%. The most common causative organism is *Staphylococcus aureus* (65%). Managing ankle fractures in diabetic patients is particularly challenging due to these high complication rates[35].

Two important predictors of poor outcome in diabetics are peripheral neuropathy and absent pedal pulses preoperatively. Neuroarthropathy is a significant risk factor for a broad range of complications[47]. In addition to acute postoperative issues, diabetics are at risk for delayed complications such as loss of fracture reduction, implant failure, nonunion, post-traumatic arthrosis, and Charcot arthropathy[48].

Length of Stay

The timing of surgery in closed ankle fractures can influence the total length of hospital stay (LOS) and overall inpatient costs, which may place a financial burden on healthcare systems. Several studies have shown that delaying surgery is associated with an increase in both total LOS and postoperative LOS. [49-50]. However, some studies show that it may affect total LOS, but not affecting postoperative LOS[12,51].

Post Operative Ankle Function

Postoperative ankle function can be assessed through the evaluation of dorsiflexion and plantarflexion, as well as by using validated functional scoring systems, both subjective and objective, such as the Olerud–

Molander Ankle Score (OMAS), Lower Extremity Functional Scale (LEFS), Self-Reported Foot and Ankle Score (SEFAS), or the American Orthopaedic Foot & Ankle Society (AOFAS) score [12,52,53]. Studies have shown that among these functional scoring systems, the SEFAS is specifically designed for a range of foot disorders, including ankle fractures, and demonstrates the best measurement properties[54].

DISCUSSION

The optimal timing of surgery for closed ankle fractures remains a matter of debate. Conventional teaching, including AO/ASIF guidelines, recommends either performing surgery within 6–8 hours of injury or delaying intervention for 4–6 days in the presence of significant edema or fracture blisters[14]. Determining the optimal timing for surgery in closed ankle fractures is crucial, as it can influence the risk of complications. These may include early complications, such as wound problems and infections; systemic complications, which can be life-threatening; and late complications, which may impair long-term ankle function. While some studies have shown that surgical timing affects the length of hospital stay, others have found no significant association [12,49-51].

It is important to establish a clear cut-off between early and delayed surgery for closed ankle fractures. According to the AO, two studies have evaluated outcomes in patients operated on before and after 8 hours from injury.

One study reported a higher rate of wound complications and infections in the early surgery group (< 8 hours: 26.3% vs > 8 hours: 19.8%)[12]. In contrast, another study found the opposite trend, with lower complication rates when surgery was performed early (< 8 hours: 3.8% vs > 8 hours: 11.9%)[21].

When using a cut-off of 4–6 days, eight studies are available for analysis. Two of these studies used a cut-off at 4 days. One study reported a higher complication rate in the delayed surgery group (< 4 days: 17.9% vs > 4 days: 39.5%) [55], whereas the other study showed the opposite trend (< 4 days: 12.8% vs > 4 days: 5.7%)[11].

For a 5-day cut-off, three studies are available. All three demonstrated that early surgery (before 5 days) was associated with a lower complication rate. The first study reported complication rates of < 5 days: 6.7% vs > 5 days: 11.3%[18]. The second study showed < 5 days: 15.3% vs > 5 days: 30%[56], and the third reported < 5 days: 12% vs > 5 days: 32%[57].

For a 6-day cut-off, three studies were identified. One study found no significant difference in total complication rates between early and delayed surgery (< 6 days: 22% vs > 6 days: 21.19%)[12]. However, two other studies showed a clear benefit for early surgery, with complication rates of < 6 days: 3.6% vs > 6 days: 20.7%, and < 6 days: 2% vs > 6 days: 13.1%, respectively [10, 21].

Table 1. Summary of timing of surgery in complication rate based on AO/ASIF model

Cut-off Time	No of Study	Study Findings	Trend
8 hours	2	Naumann 2017: < 8 h: 26.3% vs > 8 h: 19.8% (higher complication in early group) Saithna 2009: < 8 h: 3.8% vs > 8 h: 11.9% (lower complication in early group)	Mixed
4 days	2	Carragee 1991: < 4 d: 17.9% vs > 4 d: 39.5% (early better) Hawkins 2023: < 4 d: 12.8% vs > 4 d: 5.7% (late better)	Mixed
5 days	3	Konrath 1995: < 5 d: 6.7% vs > 5 d: 11.3% Breederveld 1988: < 5 d: 15.3% vs > 5 d: 30% Gupta 2018: < 5 d: 12% vs > 5 d: 32%	All early better
6 days	3	Naumann 2017: < 6 d: 22% vs > 6 d: 21.19% (no difference) Saithna 2009: < 6 d: 3.6% vs > 6 d: 20.7% (early better) Schepers 2013: < 6 d: 2% vs > 6 d: 13.1% (early better)	Mostly early better

CONCLUSION

The optimal timing of surgery for closed ankle fractures requires a clearly defined cut-off to determine whether early or delayed intervention yields better outcomes. Current evidence, including studies utilizing the AO classification cut-offs, remains limited, making it difficult to establish a universally accepted threshold. While most studies suggest that early surgery is associated with lower complication rates, some report contrasting results. A larger body of high-quality evidence is therefore needed to determine the most appropriate timing. Conducting a systematic review and meta-analysis could provide stronger evidence to guide clinical decision-making, minimize postoperative complications, and improve the management approach for closed ankle fractures.

DECLARATIONS

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Ethical Approval The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent Not applicable.

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CASE REPORT

FUNGAL FOOT INFECTION CAUSED BY CYLINDROCARPON SP.: A RARE CASE

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ABSTRACT

Background: Saprophytic soil species-rarely plant or human parasites—are included in the genus *Cylindrocarpon*. They are recognized as uncommon agents that can cause mycetomas, keratitis, or widespread infections. Although rare, tinea pedis due to *Cylindrocarpon sp.* was described for the first time in 1985.
Based on theory, the culture results of the *Cylindrocarpon* species gives an overview colonies on SDA show rapid growth reaching a diameter of 30 mm within 4 days. *C.* colonies are hyaline or brightly colored, like leather or wool. In our case, the culture grew 5 days after specimen collection but was contaminated, so a re-culture was done from the culture that had grown. Until now, there is no guideline for the treatment of *Cylindrocarpon* infection in humans, but in general, the treatment of *Cylindrocarpon* is similar to the treatment of other mold infections.
Case:A 68-year-old woman came to the outpatient clinic of Dermatology and Venereology at RSUD Dr. Soetomo Surabaya complaining of white spots between the toes that were felt since 4 months ago. Complaints were also accompanied by complaints of itching. The patient had a habit of walking on the ground barefoot. The patient's dermatologic status at March 15th, 2022 revealed multiple white macules with indistinct border, maceration, erosion, without any scale at interdigiti 4 and 5 pedis dextra and interdigiti 1 and 4 pedis sinistra region. Direct microscopic examination using potassium hydroxide of the lesion scrapings revealed the presence of hyphae. The patient was diagnosed with tinea pedis interdigitalis type. Patient revisited the hospital after 1 week (2nd visit). The lesions at the webspaces did not get any better. At the third visit, the patient said the lesion felt slightly reduced but not significant. It was also felt that the white lesions on the legs were not increasing.
Results: The results of KOH examination taken from the culture results gave a picture of macroconidia consisting of one to several septate, hyaline, straight, cylindrical to fusiform, with a rounded top and flat base, hyaline chlamydospores, spherical, formed singly, in chains or groups, intercalated or terminal. The fungal species was identified as *Cylindrocarpon sp*. Due to the change in the patient's diagnosis to fungal foot infection caused by *Cylindrocarpon sp*. then the patient's therapy was adjusted and the griseofulvin drug previously given was changed to itraconazole tablets 200mg twice daily and cetirizine 10mg once daily. At the 7th week visit, our patient said the lesion felt slightly increased and there was a wound on the lesion. The culture results showed a colony picture in the form of fast growing colonies, hyaline or brightly colored, like wool and the back of the fungal colonies showed a reddish brown pigmentation color.
Conclusion: The starting point of treatment for superficial or localized tinea pedis is topical antifungal medication. If the patient has impaired immune function, the condition is extensive, recurring, chronic, or resistant to topical antifungal treatment, or there is evidence of concurrent onychomycosis, systemic treatment should be taken into consideration.

Keywords*: Tinea pedis, Cylindrocarpon sp., Fungal foot infection, Rare Human Parasites*

INTRODUCTION

Saprophytic soil species—rarely plant or human parasites—are included in the genus *Cylindrocarpon*. They are recognized as uncommon agents that can cause mycetomas, keratitis, or widespread infections.[1,2,3] Although rare, tinea pedis due to *Cylindrocarpon sp.* was described for the first time by Lancy *et al.*[4], in 1985. The same is true for onychomycosis, which was also discovered in immunocompromised patients in a Brazilian investigation.[4,5] The species that infect humans are *C. cyanescens*, *C. destructans*, *C. lichenicola*, and *C. vaginae*.[6] Among these species, *Cylindrocarpon lichenicola* is known to cause invasive illness.[7]

The largest number of cases of *Cylindrocarpon* infections included people living in agricultural regions and/or who got into touch with plants[8,9] or those with

impaired immune systems; voriconazole and/or amphotericin B were utilized in the successful therapy.[10,11,12] It is known that there are three primary clinical variants of tinea pedis: vesiculobullous (inflammatory), hyperkeratotic (moccasin-type), and interdigital.[13,14,15] The most prevalent type of tinea pedis, known as interdigital, usually affects children more than adults. It usually manifests as erythema, silvery white scaling, peeling, and maceration in the web spaces, most commonly in the web space between the fourth and fifth toes.[16,17,18] The website could turn white and rubbery.[19] The predominant symptom is pruritus.[19,20] In many cases, peripheral fissuring occurs, which may be painful and cause burning sensation.[21,22]

A lot of clinicians use a clinical diagnosis for tinea pedis. But the clinical diagnosis of tinea pedis is not very accurate.[23] Though it is rarely done now, reflectance confocal microscopy, a non-invasive real-time imaging technique of the skin's superficial layers, can be utilized to diagnose tinea pedis.[24] KOH wet-mount examination of skin scrapings of the active border of the lesion or the roof of a specimen collected with a sterile instrument can be carried out to prevent misdiagnosis, particularly in the setting of tinea incognito.[25,26] The scrapings are placed on a microscopic slide and a drop of a 10–20% KOH solution is applied, either with or without dimethyl sulfoxide.[27] Fungal culture is the gold standard for diagnosing dermatophytosis and the pathogenic species, but it is rarely required unless the infection is severe, widespread, or resistant to antifungal treatment, or unless the diagnosis is still unclear following KOH wet-mount examination of skin scrapings of the active border of the lesion or roof of a vesicle.[14,28]

Topical antifungal medication is the basis of treatment for superficial or localized tinea pedis. Oral antifungal treatment need to be saved for patients with immunocompromised conditions, severe disease, or those who have not responded to topical antifungal medication. Patient compliance is frequently a problem since patients typically stop taking their medications too soon after their clinical symptoms have resolved, which can cause the illness to reoccur.[29] We presented a case of a female patient with superficial fungal skin infection tinea pedis due to *Cylindrocarpon sp.*

Case Report

A 68-year-old woman came to the outpatient clinic of Dermatology and Venereology at RSUD Dr. Soetomo Surabaya complaining of white spots between the toes that were felt since 4 months ago (day 0). Complaints were also accompanied by complaints of itching and did not worsen when sweating. There was no diurnal variation of the symptoms. The patient said that initially the complaints of white spots were felt because the patient often walked on the ground barefoot and when the conditions were wet. A history of previous trauma was denied, but the patient had a habit of walking on the ground barefoot. No history of eczema, psoriasis, or malignancy.

The patient had a history of rubbing with alcohol and povidone iodine as previous treatment, but the complaints were felt to have not improved. The patient had a history of hypertension and regularly takes Candesartan and Amlodipine. The patient also had a history of diabetes mellitus and regularly takes Glimepirid. Family history of suffering from the same complaint as the patient was denied. History of drug and food allergy was denied.

In the general status examination, the patient was 68 years old with a body weight of 65 kg and a height of 155 cm. Her heart rate was 88 beats per minute, respiratory rate 20 times per minute, temperature 36.4˚C. Physical examination revealed no anemia, icterus, cyanosis and dyspnea. Heart, lung and abdominal examinations were also normal. There's no oedema on both arms and leg. The extremity felt warm and dry. The patient's dermatologic status at March 15th, 2022 revealed multiple white macules with indistinct border, maceration, erosion, without any scale at interdigiti 4 and 5 pedis dextra and interdigiti 1 and 4 pedis sinistra region (**Figure 1**).



Figure 1. Patient's dermatological status at first visit.

Unlike scabies, the lesions did not spread outside of webspaces. Palpation revealed no induration.

The planning diagnosis of this patient was KOH examination and also we did the fungal culture. Direct microscopic examination using potassium hydroxide of the lesion scrapings revealed the presence of hyphae (**Figure 2**).



Figure 2. Direct microscopic examination showed the presence of hyphae

From the results of history taking, physical examination and microscopic examination, the patient was diagnosed with tinea pedis interdigitalis type. Patient was started on griseofulvin 500mg twice a day which was planned to be given for 2 weeks and cetirizine 10mg once a day. This oral medication was used in conjunction with a local sodium fusidate cream treatment on the erosion area twice daily and asked to revisit the outpatient department. Patient was monitored regarding her complaints, progress of the lesions, and side effects of the therapy. The patient had been educated to not manipulate the lesions, not to give any other topical medication to the lesion, avoid hot and humid environment, avoid long exposure to soil, plant and water, and routine control. Patient revisited the hospital after 1 week (day 7). The lesions at the webspaces did not get any better. On this 2nd visit, at interdigiti 4 and 5 pedis dextra and interdigiti 1 and 4 pedis sinistra region showed multiple white macules with indistinct border, maceration and erosion, but there was no scale (**Figure 3**).



Figure 3. Interdigital tinea pedis presenting with withe macules, maceration, and erosion between the toes and the adjacent skin.

At the third visit, the patient said the lesion felt slightly reduced but not significant. It was also felt that the white lesions on the legs were not increasing (day 14). At interdigiti 4 and 5 pedis dextra and interdigiti 1 and 4 pedis sinistra region still showed multiple white macules with indistinct border, maceration and erosion, but there was no scale (**Figure 4**).



Figure 4. Multiple white macules with indistinct border, maceration and erosion lesions in webspaces and skin over the proximal interphalangeal joints.

Culture results from skin scrapings taken 2 weeks before revealed a picture of fast growing colonies, hyaline or bright-coloured, woolly (**Figure 5**).

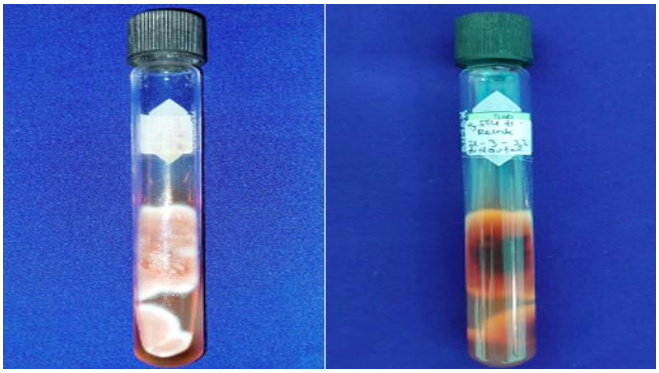


Figure 5. Culture results from skin scrapings after two weeks.

The results of KOH examination taken from the culture results gave a picture of macroconidia consisting of one to several septate, hyaline, straight, cylindrical to fusiform, with a rounded top and flat base, hyaline chlamydospores, spherical, formed singly, in chains or groups, intercalated or terminal. The fungal species was identified as *Cylindrocarpon sp*. (**Figure 6**).

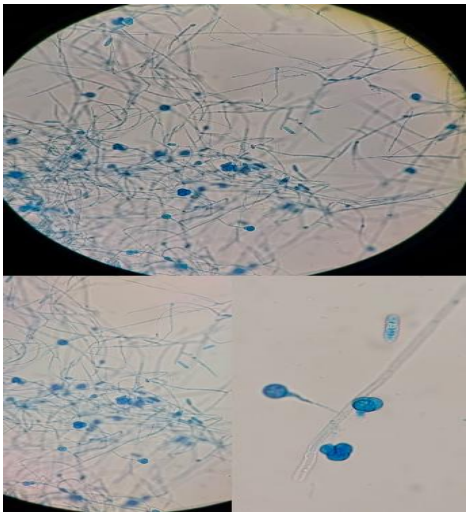


Figure 6. KOH examination from culture: macroconidia which are one to several septate, hyaline, straight, cylindrical to fusiform, with a rounded apex and flat base, chlamydospores hyaline, spherical, formed singly, in chains or in clumps, intercalary or terminal.

Due to the change in the patient's diagnosis to Fungal foot infection caused by *Cylindrocarpon sp*. then the patient's therapy was adjusted. The griseofulvin drug previously given was changed to itraconazole tablets 200mg twice daily and cetirizine 10mg once daily. Our patients monitored regarding her complaints, progress of the lesions, and side effects of the therapy. She educated to not manipulate the lesions, not give any other topical medication to the lesion, avoid hot and humid environment, avoid long exposure to soil, plant and water, and routine control too.

At the 5th visit (day 27), the patient said the complaints of white spots were felt to be reduced, moreover complaints of itching were also felt to be reduced (**Figure 7**).



Figure 7. Interdigiti 4 and 5 pedis dextra and interdigiti 1 and 4 pedis sinistra region still showed multiple white macules with indistinct border, maceration and erosion, but there was no scale.

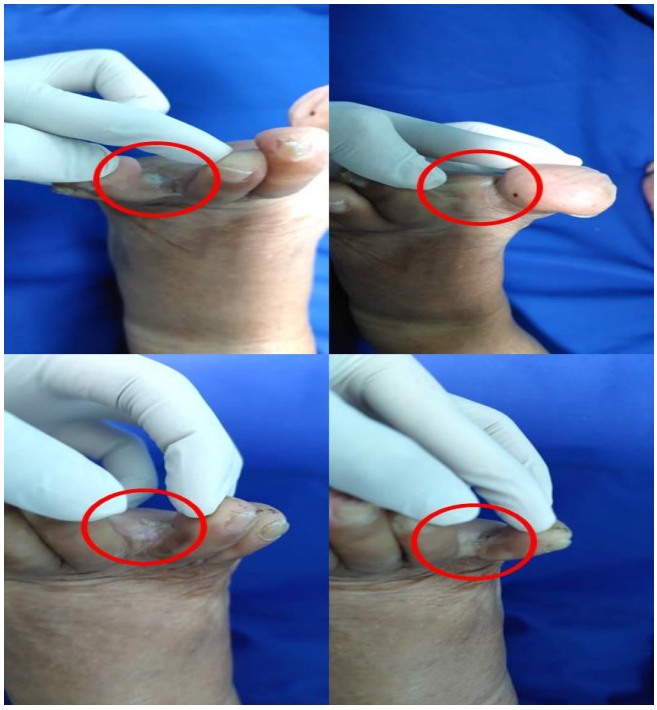


Figure 8. Increased multiple white macules with wound on the lesion, maceration, and erosion.

DISCUSSION

Saprophytic soil species-rarely plant or human parasites-are included in the genus *Cylindrocarpon*. They are recognized as uncommon agents that can cause mycetomas, keratitis, or widespread infections.[1,2,3] Although rare, tinea pedis due to *Cylindrocarpon sp.* was described for the first time by Lancy *et al*., in 1985. The same is true for onychomycosis, which was also discovered in immunocompromised patients in a Brazilian investigation.[4,5] Therefore, due to their anatomical proximity, the connection between these infections may have started at one point.[30]

Numerous pathogenic fungus belonging to the *Nectriaceae* (Hypocreales) genera *Cylindrocarpon*, *Fusarium*, and *Cylindrocladium* reveal a tight taxonomical connection to *C. destructans*.[31] Because of their similar macroscopic features, the genera *Cylindrocarpon* and *Fusarium* are sometimes confused with one another.[32,33] The genus *Cylindrocarpon* was stated by Mantiri *et al*.[34] to have about 125 species. Booth[35] further classified this genus into four groups based on the presence of chlamydospores and microconidia: *C. magnusianum*, *C. cylindroides*, *Nectria mammoidea*, and *C. destructans*. Species that infect humans are *C. cyanescens*, *C. destructans*, *C. lichenicola*, and *C. vaginae*.[6] Among these species, *Cylindrocarpon lichenicola* is known to cause invasive illness.[7]

Based on theory, the culture results of the *Cylindrocarpon* species gives an overview colonies on Sabouraud Dextrose Agar (SDA) show rapid growth reaching a diameter of 30 mm within 4 days. *C.* colonies are hyaline or brightly colored, like leather or wool (**Figure 9**). The opposite of fungal colonies on SDA showed diffuse pale reddish brown pigmentation.[8]

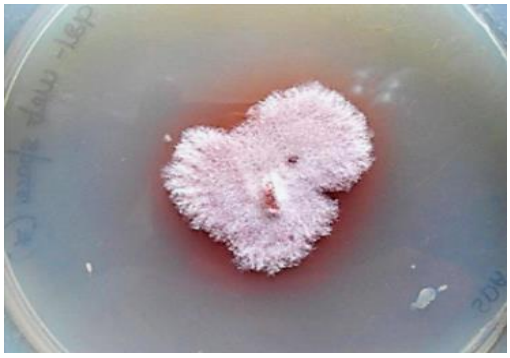


Figure 9. Colony of *C. lichenicola* on SDA after 4 days of incubation at 25˚C

In our case, the culture grew 5 days after specimen collection but was contaminated, so a re-culture was done from the culture that had grown. The culture results showed a colony picture in the form of fast growing colonies, hyaline or brightly colored, like wool and the back of the fungal colonies showed a reddish brown pigmentation color (**Figure 5**).
Based on the theory of KOH Microscopic examination results obtained the presence of macroconidia consisting of one to several septates, hyaline, straight or curved, cylindrical to fusiform, with rounded apex and flat base. Chlamydospores can be present or absent, hyaline to brown, spherical, formed singly, in chains or clusters, intercalated or terminal Figure (**Figure 6**).[8]

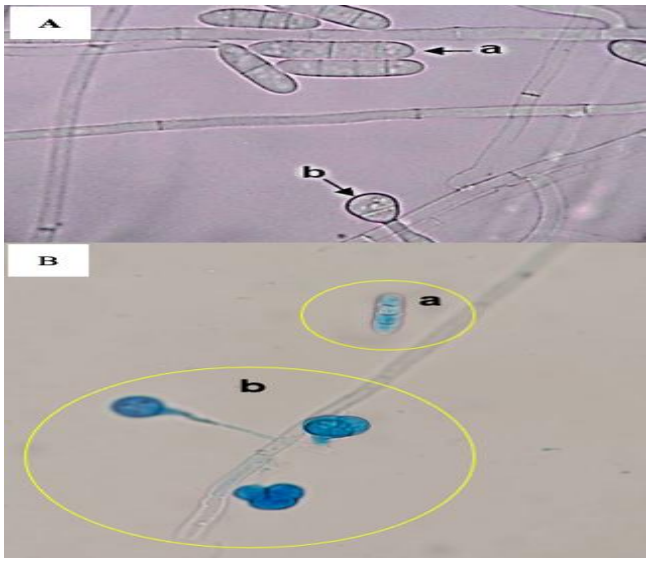


Figure 10. A) Slide culture showing (a) macroconidia and (b) terminal multicelled chlamydospore. Magnification, ×400.[8] B) KOH examination of the culture results in our case.

This description is in accordance with the results of the KOH examination of the culture results in our case (**Figure 6**).
The starting point of treatment for superficial or localized tinea pedis is topical antifungal medication.[21,36]

If the patient has impaired immune function, the condition is extensive, recurring, chronic, or resistant to topical antifungal treatment, or there is evidence of concurrent onychomycosis, systemic treatment should be taken into consideration.[16,26] Until now, there is no guideline for the treatment of *Cylindrocarpon* infection in humans, but in general, the treatment of *Cylindrocarpon* is similar to the treatment of other mold infections. James *et al.*[3] reported a clinical improvement in a previous case of disseminated infection caused by *C. lichenicola* after marrow regeneration and therapy with 1 mg of AmB per kg. In our case patient was given itraconazole tablets 200mg twice daily and cetirizine 10mg once daily.

DECLARATIONS

Ethics approval and consent to participate
Not applicable.
Consent for publication
Not applicable.
Competing interests
The authors declare no conflict of interest.
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ORIGINAL RESEARCH

INFLUENCE OF THE ADDITION OF NANO CERIUM OXIDE/CHITOSAN COMPOSITE ON THE MECHANICAL CHARACTERISTICS OF POLYMETHYLMETHACRYLATE RESIN

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ABSTRACT

Background: Cerium oxide and chitosan (Ce/CS) nanoparticles have garnered significant interest due to their remarkable properties, including antioxidant activity, biocompatibility, antibacterial effectiveness and anti-inflammatory activities. This study evaluates the impact of incorporating a Ce/CS nanocomposite into polymethylmethacrylate (PMMA) resin on its mechanical properties. The composite consisted of 30% cerium oxide and 70% chitosan by weight (wt), with varying percentages incorporated into the PMMA resin selected according to a pilot study.

Material and Methods: Ninety PMMA specimens were fabricated and categorized into three groups according to the Ce/CS nanocomposite percentage in the PMMA resin: control (0 wt%), group A (1 wt%), and group B (5 wt%). Transverse strength, impact strength, and surface hardness were assessed, with 10 specimens for each test. Fourier transform infrared spectroscopy (FTIR) and scanning electron microscope (SEM) were used to examine the chemical and surface alterations of PMMA resin. The collected data were analyzed using one-way ANOVA and Tukey HSD test, with a significance level of $P \leq 0.05$.

Results: The resulting data revealed a significant difference among all groups ($P \leq 0.05$). Group A exhibited the highest values in transverse and impact strength compared with the other groups. Group B showed the highest values in surface hardness compared with group A and the control group. The FTIR graph indicated changes in the material's chemical structure, suggesting the formation of new functional groups. SEM image showed an even distribution of Ce/CS nanocomposite inside the PMMA matrix of group A compared with group B.

Conclusion: The study concludes that incorporating 1 wt% of a nano cerium oxide/chitosan composite into PMMA denture base resin significantly enhances its transverse and impact strength compared with 5 wt%. Furthermore, both 1 wt% and 5 wt% Ce/CS nanocomposites resulted in a notable improvement in the surface hardness of the PMMA resin.

Keywords*:* Cerium oxide; Chitosan; Polymethylmethacrylate ; Transverse strength; Impact strength; Surface hardness.

INTRODUCTION

The Denture base, typically made of polymethylmethacrylate (PMMA), is a non-toxic and inexpensive material with low water absorption and aesthetically pleasing features. It is easy to process, finish, polish and repair[1]. However, despite fulfilling cosmetic requirements for dental prostheses, PMMA resin lacks the mechanical performance needed for long-term durability[2]. Its primary drawback lies in its poor mechanical properties, including low flexural strength, hardness, and limited fracture and impact strength. Therefore, improving PMMA resin involves enhancing its mechanical properties.

In recent years, nanotechnology has been increasingly applied in dental materials, with numerous studies exploring its benefits and clinical applications[3].

Polymeric nanocomposites, composed of nanoscale fillers dispersed within a polymer matrix, have emerged as promising candidates for this purpose[4]. One of the most

practical and cost-effective strategies for improving the mechanical, thermal, chemical, and physical properties of PMMA is the incorporation of suitable nanofillers[5]. These nanoscale reinforcing agents can impart unique physical, mechanical, and biological properties, resulting in advanced nanocomposites with superior performance [6].

Previous studies have explored various filler materials, including glass ceramics, alumina (Al_2O_3), hydroxyapatite, yttria-stabilized zirconia, nitrile rubber, polyethylene fibers, fiberglass, and stainless steel, all of which have significantly enhanced the properties of PMMA [7].

Chitosan (CS), a linear polysaccharide, offers exceptional biological properties, including antimicrobial activity, biodegradability, non-toxicity, and biocompatibility[8]. Similarly, Cerium oxide (CeO_2) nanoparticles have garnered considerable interest due to their remarkable characteristics, such as redox activity, biofilm inhibition, antibacterial efficacy, and anti-inflammatory effects[9]. Furthermore, incorporating nano CeO_2 into denture base resins has improved their mechanical properties [10].

This study evaluates the effect of incorporating cerium oxide and chitosan (Ce/CS) nanocomposite into PMMA on its mechanical properties. It uses a fixed Ce/CS ratio applied at different percentages designated by a pilot study.

MATERIALS AND METHODS

Specimen grouping

A total of 90 specimens of PMMA material (PROCRYLA® / Fast Heat-Polymerizing Acrylic Resin, PD, Germany) were prepared and categorized into three groups (30 specimens each) based on the percentage composition of the Ce/CS nanocomposite. A composite ratio of 30 wt% Ce and 70 wt% CS was incorporated into the PMMA resin, selected from a pilot study that included both transverse strength and surface hardness tests. For each test, nine PMMA specimens were prepared with varying percentages of CS/Ce fillers into the PMMA: 1 wt%, 3 wt% and 5 wt%, and three control specimens without filler. The study comprised three groups: a control group (C) consisting of PMMA specimens without filler, group (A) with PMMA containing 1 wt% of Ce/CS nanocomposite and group (B) with PMMA containing 5 wt% of Ce/CS nanocomposite. Three mechanical tests were conducted: transverse strength, impact strength, and surface hardness. For each test, 10 PMMA specimens were used.

Specimen patterns preparation

Plastic patterns were fabricated using laser-cutting machines, with dimensions specified according to the requirements of each mechanical test. For the transverse strength test, the specimens measured 65 × 10 × 2.5 mm in length, width and thickness, respectively, following ADA (1999) guidelines [11]. For the impact strength test, the specimens were measured 80 x 10 x 4 mm in length, width, and thickness, respectively, following ISO 179-1:2000 standards[12]. For the surface hardness test, the specimens measured 35 x 35 x 6 mm in length, width and thickness, respectively, prepared according to ISO 868:2003 standard [13], as shown in Fig. 1.

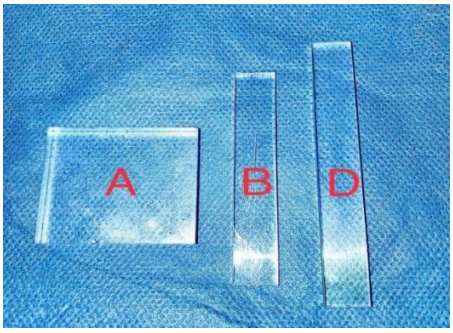


Figure 1. Transparent plastic patterns. A: For hardness test, B: For Transverse strength test, D: For impact strength test.

The plastic patterns were coated with a separating medium and invested in a metal flask using Type 4 dental stone (Zhermack®, Italy), prepared according to the manufacturer's instructions at a water-to-powder ratio of 25 mL/100 g. After the dental stone had set, the two halves of the flask were separated and the patterns were removed to form mold cavities for the PMMA resin.

Calculating the mixing amount of PMMA and Ce/CS nanocomposite

The PMMA resin was prepared according to the manufacturer's instructions by mixing 21 grams of polymer with 10 ml of monomer. The quantities of polymer and Ce/CS nanocomposite used in this study are detailed in Table 1. The volume of monomer used was consistently 10 ml for all groups.

Table 1. Mixing amount of Ce/CS nanocomposite and PMMA resin powder.

Groups	Amount of Ce+CS (gm)	Amount of Polymer (gm)
Control	0	21
A	0.21= 0.063 + 0.147	20.79
B	1.05= 0.315 + 0.735	19.95

Mixing and packing of Ce/CS nanocomposite and PMMA resin

A probe sonication machine was used to mix Ce/CS nanocomposite and PMMA powders with the monomer, utilizing a clean and dry glass mixing bowl to ensure uniform dispersion of the fillers and resin powders within the monomer. The mixing process continued for five minutes, using 120 watts of power at a frequency of 60

kilohertz. These parameters were selected based on a pilot study, demonstrating their effectiveness in breaking the fillers into individual nanocrystals and achieving a homogeneous mixture. The mixture was left for five minutes until it reached the dough stage. The PMMA resin was then packed and inserted into the mold cavity within the flask. A polyethylene sheet was placed over the resin to achieve a smooth surface. The two halves of the flask were sealed and placed under a hydraulic press at 100 psi to ensure uniform distribution of the PMMA resin inside the mold. Excess resin was removed, and the flask was placed in a water bath for curing. Following the manufacturer's recommendations, a short curing cycle with a two-step process was initially carried out for 1.5 hours at 74°C, followed by an additional 0.5 hours at 100°C.

Transverse strength test

A three-point bending test was proposed to evaluate the transverse strength of PMMA specimens using an Instron universal testing machine. Each specimen was placed on two opposing support wedges, separated by 50 mm. A load was then applied at the center of the specimen using a loading rod positioned midway between the two supports (Fig. 2). The transverse strength was calculated according to the following equation:

$$\textit{Transverse strength} = 3FL/2bd^2$$

Where: P = Maximum force exerted on specimen (N), L = Distance between the supports (mm), b = The specimen width (mm) and d = specimen depth (mm)

The load was applied with a crosshead speed of 1 mm/min, bending the specimens until fracture occurred. The fractured surfaces were examined using a scanning electron microscope (SEM).

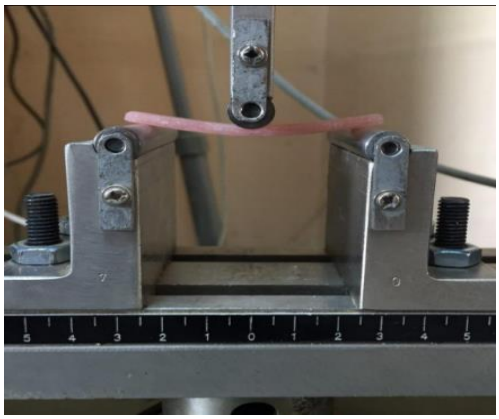


Figure 2. Instron universal testing machine and the specimen is under test.

Impact strength test

The impact strength test was conducted using a Charpy impact testing device, which applies a pendulum to calculate the impact load on the PMMA specimen (13). The impact strength was calculated using the following formula:

$$\textit{Impact strength} = E/bd10^3$$

Where: E = absorption of impact energy in joules, b = width of the specimen (mm) and d = thickness of the specimen (mm).

Surface hardness test

The Shore D hardness device measures the depth of penetration of the durometer indenter foot into the specimen surface. For each PMMA specimen, hardness measurements were taken at five locations: one in the center and four in the margins. The surface hardness value for each specimen was determined by calculating the mean of these five measurements, following the ASTM D2240 and ISO 868:2005 (14).

Fourier transform infrared spectroscopy (FTIR) and SEM were used to examine the chemical and surface alterations of PMMA resin.

Statistical analysis

Data description, analysis, and presentation were conducted using the Statistical Package for the Social Sciences (SPSS, version 22; Chicago, IL, USA). The Shapiro–Wilk test was applied to assess the normality of the variables, confirming that all were normally distributed across the groups. A one-way analysis of variance (ANOVA) was conducted, followed by Tukey's post hoc test for pairwise comparisons among the groups, with a significance level of $P \leq 0.05$.

RESULTS

Cross-sectional examination of the fractured PMMA specimens using SEM at 1000× magnification revealed a smooth and homogeneous resin matrix in the control group (Fig. 3A). In contrast, specimens from group A exhibited a uniform dispersion of Ce/CS nanoparticles within the resin matrix (Fig. 3B), while in group B, filler particles were unevenly distributed, forming aggregated clusters in the matrix (Fig. 3C).

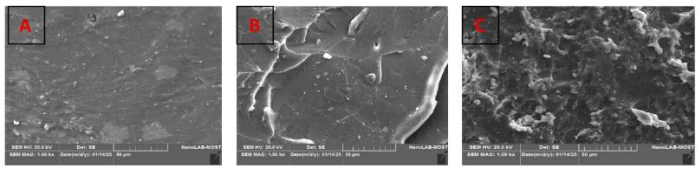


Figure 3, Control (A), 1% by vol. (B), 5% by vol. group (C) specimen under the scanning electron microscope at a magnification scale of 50µm.

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectrum study reveals chemical interaction between cerium oxide/chitosan nanofiller powder and PMMA, indicating the formation of new functional groups (Fig. 4A, 4B, and 4C). From a chemical perspective, these interactions suggest a reaction between the acrylic resin and the cerium oxide/chitosan nanofiller, as demonstrated by observable changes in the FTIR spectra.

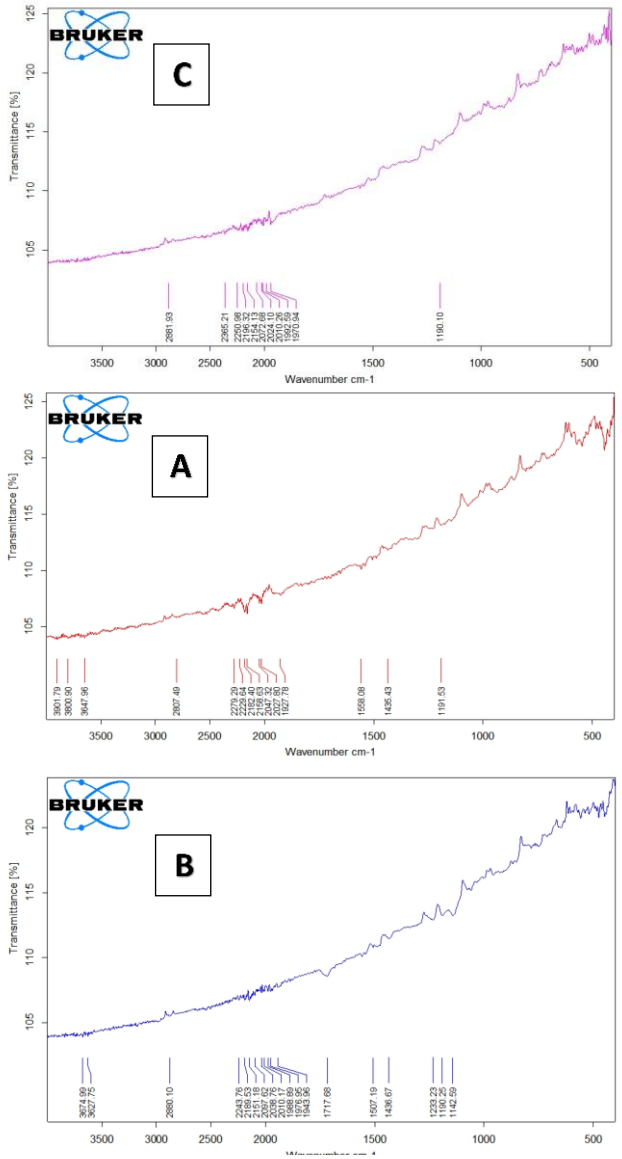


Figure 4. FTIR graph for the control (C) and experimental group (A) and (B).

Transverse strength statistics

Descriptive analysis of transverse strength values showed that group A exhibited the highest mean value (104.54 N/mm²), followed by the control group (93.15 N/mm²) and group B (89.76 N/mm²). One-way ANOVA revealed a statistically significant difference among the tested groups (P value ≤ 0.05), as shown in Table 2. Post hoc comparisons using Tukey's HSD test indicated a significant difference at P≤0.05 between group A and the control group; however, no significant difference between the control group and group B. Moreover, a significant difference (P≤0.001) was observed between groups A and B.

Table 2. The descriptive statistics and One-way ANOVA test of the transverse strength value in (N/mm²).

Groups	N	Mean	± SD	F	Sig. P≤0.05
Control	10	93.15	2.69		
A	10	104.54	2.66	103.22	0.00
B	10	89.76	1.74		

Impact strength statistics

The mean value of group A exhibited the highest impact strength value (11.33 KJ/m²), followed by the control group (10.04 KJ/m²), while group B displayed the lowest value (9.63 KJ/m²). Furthermore, the one-way ANOVA test revealed a significant difference at P≤0.05 among the tested groups, as shown in Table 3. The Tukey's HSD test showed a significant difference between groups A and the control group and group B. However, no significant difference was observed between Group B and the control group.

Table 3. Descriptive statistics and One-way ANOVA test of the impact strength test of all experimental groups in (KJ/m²).

Groups	N	Mean	±SD	F	Sig. P≤0.05
Control	10	10.04	0.68		
A	10	11.33	0.87	11.20	0.00
B	10	9.63	0.93		

Surface hardness statistics

Group A exhibited the highest mean value (88.07), followed by group B (85.80), while the control group had the lowest value (84.46). A one-way ANOVA revealed a statistically significant difference among the groups (P≤0.05), as shown in Table 4. Post hoc analysis using Tukey's test indicated significant differences between the experimental groups A and B compared to the control group and between groups A and B.

Table 4. The descriptive statistics and One-way ANOVA test for the surface hardness test of all groups.

Groups	N	Mean	±SD	F	Sig. P≤0.05
Control	10	84.46	0.60		
A	10	88.07	0.75	49.99	0.00
B	10	85.80	1.03		

DISCUSSION

Numerous researchers have proposed that the mechanical and physical properties of PMMA resin can be improved by incorporating various additives [15]. The null hypothesis of the current study was rejected. A mixture of nanosized cerium oxide and chitosan particles was added to the PMMA resin in a specific amount, determined through a pilot study, to improve its mechanical and physical properties. The filler particles are significantly smaller than the PMMA resin powder, allowing them to fill the interstitial spaces within the PMMA polymer matrix. This leads to a heterogeneous composite without disturbing the segments of the polymer chain. Furthermore, the filler proportion must remain minimal to ensure proper interlocking with the PMMA resin and maintain the PMMA matrix's structural integrity [15].

The transverse strength test evaluates a material's resistance to bending and its stiffness, providing insight into its mechanical behavior under flexural stress [16]. High flexural strength is critical for denture base materials, as they face repeated flexing during mastication, resulting in fatigue and potential failure [17]. The three-point bending test is often used to replicate the functional stresses experienced by dentures during chewing and other oral activities [18].

In this study, incorporation of 1 wt% Ce/CS nanocomposite into PMMA increased the transverse strength value to 104.54 N/mm², compared with adding 5 wt%, which exhibited the lowest value at 89.76 N/mm². This improvement is attributed to the uniform distribution of Ce/CS nanoparticles within the PMMA matrix, as shown in Fig. 4, which shows the incorporation of 1 wt% Ce/CS nanoparticles into PMMA. Furthermore, the enhanced transverse strength is attributed to the formation of interconnections across the linear macromolecular chains, promoted by the nanoparticles. These findings are consistent with the observations of Alnamel and Mudhaffer, who reported that transverse strength diminished with increased concentrations of SiO_2 nanoparticles, reinforcing the importance of optimizing filler content for mechanical performance [19].

Several studies have reported that incorporating carbon-based nanomaterials, such as graphene oxide, into PMMA resins enhances their mechanical properties [20] and reduces the degree of polymerization shrinkage. This reduction in shrinkage restricts the segmental motion of the macromolecular chains, increasing the material's strength and rigidity, thereby improving both fracture resistance and transverse strength [21].

The tendency of nanoparticles to agglomerate can lead to a reduction in transverse strength when 1 wt% Ce/CS nanocomposites are incorporated, as this aggregation induces stress concentrations at the agglomerated sites, thereby diminishing mechanical properties [22]. Once the PMMA resin reaches its filler saturation point, it cannot incorporate additional nanoparticles without compromising the integrity of the resin matrix, resulting in reduced performance. This alteration is statistically significant and will influence the performance of the PMMA-Ce/CS nanocomposite. Xia et al. (2008) emphasized the significance of uniform dispersion and reported that transverse strength improved with an optimal distribution of nanofiller particles (100 nm) [23].

Impact strength test measures the energy required per unit area to fracture a material under sudden force, such as the impact from a falling denture. Therefore, denture base materials must possess sufficient impact strength to prevent breakage in such situations [24]. In this study, a Charpy impact testing machine was employed, one of the most commonly used methods for assessing a material's toughness [25]. High-impact denture base resins are especially useful for individuals at a high risk of dropping their dentures, such as patients with physical limitations or cognitive impairments. This study demonstrated that incorporating a 1 wt% Ce/CS nanocomposite significantly increased the impact strength value compared with the control group. Statistically, no significant differences were observed among the other tested groups. The interfacial shear strength between the nanofiller and the matrix significantly enhances the impact strength due to the formation of cross-links or supramolecular bonds. The nanofillers act as a shield, preventing the propagation of fractures. Furthermore, ensuring strong bonding between the nanofiller and the resin matrix can effectively alter the fracture propagation path [26].

Additionally, the critical stress value for particle/matrix debonding increases as particle size decreases, which may also contribute to enhanced impact strength. This improvement results from the increased total particle/matrix interfacial surface area available for energy dissipation [27]. The decrease may be attributed to the agglomeration of nanoparticles, which possess high surface energy and tend to adhere to one another, forming clumps. Agglomeration likely results from difficulties dispersing nanofillers uniformly in the polymer matrix using conventional methods such as probe sonication apparatus, leading to inhomogeneity and promoting nanoparticle aggregation as illustrated in Fig. 4. Consequently, increasing in nanoparticle concentration to 5 wt% correlates with a decrease in impact strength, likely due to poor distribution within the acrylic matrix (28). This clarifies why the impact strength of the 5 wt% nanoparticles group is inferior to that of the 1 wt% group.

Another explanation is inadequate bonding at the interface between the inorganic CeO2 nanoparticles and the organic polymer matrix in the PMMA-containing nanoparticle fillers. This weak interfacial bonding leads to stress concentration at the filler–matrix interface. The ineffective transmission of stress across the filler–matrix interface results in localized stress concentrations, which facilitate crack initiation and ultimately lead to material failure. The PMMA matrix demonstrates brittle behavior, characterized by rapid crack propagation and sudden fracture of the specimen. This behavior indicates a low resistance to crack growth and suggests that only a small amount of energy is required to initiate and propagate fractures within the material [29].

Surface hardness refers to a material's resistance to surface penetration or indentation. The Shore D hardness test was employed in this study because it is more suitable for PMMA resins [30]. The results showed a significant improvement in surface hardness with the addition of

Ce/CS nanocomposite compared to the control group. This enhancement is attributed to the reduced interparticle distance within the polymer matrix facilitated by Ce/CS nanoparticles. The decreased spacing promotes stronger interparticle bonding, leading to nanoparticle aggregation and the accumulation of hard Ce/CS nanoparticles on the surface of the PMMA matrix, thereby improving the material's hardness performance [31].

Furthermore, a high concentration of nanocomposite group (5 wt%) resulted in a considerable increase in hardness due to the denser network of reinforcing particles. In contrast, the low concentration group (1 wt%) produced a modest increase in hardness, probably due to the lower network density and reduced accumulation of hard particles within the PMMA resin matrix [32].

The current study recommends that future research be conducted to investigate the effects of the Ce/CS nanocomposite on the color, polishability, and clinical performance of denture bases fabricated from PMMA resin.

CONCLUSION

Within the limitations of this study, the 1 wt.% of a nano cerium oxide/chitosan composite incorporated into PMMA denture base resin significantly enhances transverse and impact strength compared with 5 wt.%. Furthermore, both 1 wt.% and 5 wt.% Ce/CS nanocomposites led to a notable improvement in the surface hardness of the PMMA resin.

DECLARATIONS

Competing interest

The authors declare that there are no competing interest.

Funding

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Ethical Approval

None declared.

Competing interests

The authors declare no competing interests.

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ORIGINAL RESEARCH

THE GLOBAL CHALLENGE OF CHEMOTHERAPY TOXICITY: RETHINKING SUPPORTIVE CARE IN MODERN ONCOLOGY

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ABSTRACT

Chemotherapy remains a central component of cancer treatment, yet its therapeutic efficacy is frequently overshadowed by a broad spectrum of systemic toxicities that severely compromise patient quality of life. This adverse effect – ranging from nausea, vomiting, and anorexia to mucositis, diarrhea, fatigue, and alopecia, are driven by complex molecular and cellular mechanisms that extend far beyond the direct cytotoxicity to malignant cells. Emerging evidence highlights the role of inflammatory cytokine cascades, oxidative stress, neurotransmitter imbalance, mitochondrial dysfunction, and epithelial barrier disruption in mediating these side effects. For instance, serotonin release and 5-HT_3 receptor activation underlie chemotherapy induced emesis, while hypothalamic dysregulation contributes to anorexia. Mucositis results from ROS mediated NF-κB activation and epithelial apoptosis, whereas diarrhea is linked to SN-38 induced enterocyte damage, tight junction disruption, and microbiome imbalance. Fatigue stems from altered HPA axis signalling and mitochondrial energy deficits, while alopecia arises from p53 mediated apoptosis in hair follicle keratinocytes. Understanding these multifaceted mechanisms provides a foundation for the development of targeted adjunct therapies, particularly those driven from biocompatible and multifunctional natural agents. This review presents an integrated molecular perspective on chemotherapy induced toxicities and explores innovative strategies for their prevention and management.

Keywords: Chemotherapy, toxicity, Nausea and vomiting, Anorexia, P53 pathway, Oncology, Inflammatory cytokines

INTRODUCTION

significant challenges to healthcare systems globally. Despite the considerable progress made in prevention, early detection, and treatment modalities, cancer continues to account for substantial morbidity and mortality[1]. According to the World Health Organization (WHO), over 19 milllion new cancer cases are diagnosed annually, and this number is expected to rise in the coming decades due to aging populations, lifestyle changes, and environmental exposures. While advances in immunotherapy, targeted therapy, and precision medicine have revolutionized oncologic care, chemotherapy remains a cornerstone of cancer treatment, especially in settings where advanced or metastatic disease precludes localized interventions[2].

Chemotherapy refers to the systemic administration of cytotoxic agents that are designed to kill or inhibit the proliferation of rapidly dividing cells. The rationale behind its use stems from the high mitotic activity that characterizes most malignancies[3]. Agents such as alkylating compounds, antimetabolites, topoisomerase

inhibitors, and mitotic spindle poisons have been staples in oncologic pharmacology for decades. These drugs interfere with various stages of the cell cycle, therby arresting tumor growth or inducing apoptosis in neoplastic cells. However, the lack of specificity toward malignant cells remains chemotherapy's greatest shortcoming[4]. Normal cells that also possess high proliferative rates- such as those in the bone marrow, gastrointestinal tract, hair follicles, and reproductive organs- become inadvertent targets, leading to the well documented toxicities associated with chemotherapy[5].

The toxicity profile of chemotherapeutic drugs is broad and varies depending on the class of agent, dose, duration of treatment, and individual patient susceptibility. Acute side effects include nausea, vomiting, mucositis, diarrhea, and myelosuppression, which can culminate in anaemia, leukopenia and thrombocytopenia. These hematologic toxicities, in turn, increase the risk of infection, bleeding, and fatigue. Furthermore, alopecia, skin rashes, and altered taste perception can significantly affect body image and self-esteem. Long term and late effects are of particular concern for cancer survivors and may include cardiotoxicity, neurotoxicity, nephrotoxicity, pulmonary fibrosis, secondary malignancies, infertility, and cognitive impairments often described as "chemo brain". Each of these sequelae carries profound implications for quality of life and functional independence[6].

The paradox of chemotherapy lies in its duality- it is both life saving and life altering. While it remains indispensable in many cancer treatment protocols, its impact extends far beyond tumor cytoreduction. The physiological toll is often compounded by psychological distress, including anxiety, depression, and post-traumatic stress. Social isolation and financial toxicity are also frequently reported, particularly in low- and middle-income countries where health insurance coverage and access to supportive care may be limited[7]. Caregivers, too, bear a significant emotional and physical burden, further underscoring the ripple effects of cancer treatment. In this context, the quality of survivorship has become an essential metric alongside traditional outcomes such as progression free and overall survival. Over the years, numerous strategies have been employed to ameliorate chemotherapy associated toxicity. These include the development of supportive medications such as antiemetics (e.g., 5HT3 receptor antagonists), growth factors (e.g., G-CSF), and cytoprotective agents (e.g., dexrazoxane for anthracycline- induced cardiotoxicity). Advances in pharmacogenomics have allowed for more personalized dosing regiments, aiming to minimize toxicity without compromising efficacy. However, these approaches are often reactive rather than preventive and may not sufficiently address the multifactorial nature of chemotherapy induced damage[8].

In light of these challenges, nanotechnology and targeted drug delivery systems have emerged as promising alternatives or adjuncts to traditional chemotherapy. By encapsulating chemotherapeutic agents in nanoparticles or conjugating them with ligands that recognize tumor-specific antigens, it is possible to increase drug accumulation in tumor tissues whiles sparing normal cells[3,9]. This selective delivery can reduce systemic exposure, thereby minimizing off-target effects. Furthermore, such platforms can be engineered to release their payload in response to specific stimuli in the tumor microenvironment, such as pH, enzymes, or temperature. Several nanocarrier systems – including liposomes, dendrimers, micelles, and polymeric nanoparticles- are currently under investigation or have received regulatory approval, marking a paradigm shift in the way chemotherapeutics are administered[10]. Phytochemicals and natural compounds are also gaining attention for their potential to modulate the toxic effects of chemotherapy. Substances such as curcumin, resveratrol, quercetin, and thymoquinone exhibit antioxidant, anti-inflammatory, and cytoprotective properties. These agents may enhance the therapeutic index of chemotherapy by sensitizing tumor cells to its effects while simultaneously protecting normal cells from collateral damage. Some compounds even possess intrinsic anticancer activity and can be used in combination with conventional drugs to achieve a synergistic effect. This has paved the way for the exploration of integrative oncology, which seeks to harmonize conventional and complementary therapies for a more holistic approach to cancer care[11].

An emerging area of focus involves the tumor microenvironment (TME), which plays a critical role in cancer progression, metastasis, and response to therapy. The TME comprises not only cancer cells but also stromal cells, immune cells, extracellular matrix components, and signalling molecules. Chemotherapy can inadvertently remodel the TME, sometimes enhancing the invasive or drug-resistant properties of residual cancer cells. Strategies that concurrently target the TME- such as inhibiting angiogenesis, modulating immune checkpoints, or reprograming cancer associated fibroblasts-may improve therapeutic outcomes and reduce recurrence rates. Understanding these intricate cellular interactions is vital for designing next generation chemotherapeutic regiments with improved efficacy and tolerability[12].

Moreover, the psychosocial and supportive care dimension of chemotherapy is garnering increased recognition. Effective communication between clinicians and patients, adequate symptom management, nutritional support, psychological counselling, and palliative care are all crucial for enhancing the overall treatment experience. Patient reported outcome measures (PROMs) are increasingly being integrated into clinical trials and

routine practice to capture the subjective experience of chemotherapy, ensuring that therapeutic decisions are aligned with patient preferences and values. Thus, chemotherapy continues to be a mainstay of cancer treatment, offering hope and extended survival for millions of patients worldwide. However, its use is marred by a host of adverse effects that compromise patient well being and can lead to treatment delays or discontinuation. Addressing these challenges requires a multifaced approach, including innovations in drug design and delivery, incorporation of complementary therapies, improved understanding of the tumor microenvironment, and enhanced supportive care, As the field of oncology moves toward more precise and personalized interventions, the goal must be not only to prolong life but to preserve its quality, ensuring that the fight against cancer does not come at the cost of the patient's dignity, functionality, and overall health[13].

The following table outlines the major side effects induced by chemotherapy, emphasizing the specific molecular mechanisms involved such as neurotransmitter activation, inflammatory cytokine release, oxidative stress and apoptosis. These representative chemotherapeutic agents are also known to trigger each and or the entire symptom as mentioned in the table. A mechanistic understanding of these toxicities is critical for guiding the development of effective, multi-targeted supportive care interventions to mitigate patient burden and enhance treatment adherence (Table 1).

Table 1. Chemotherapy Induced Side effects: Molecular mechanisms and Representative drugs

Symptom	Molecular Mechanism	Example Drug
Nausea/Vomiting	5-HT_3 receptor stimulation via serotonin → CTZ activation	Cisplatin[13]
Anorexia	Cytokine-induced hypothalamic and dopaminergic disruption	Doxorubicin[14]
Mucositis	ROS → NF-κB → cytokines/MMPs → mucosal damage	5-Fluorouracil[15]
Diarrhea	Enterocyte loss, microbiome shift, COX-2/IL-6 upregulation	Irinotecan[16]
Fatigue	Mitochondrial dysfunction + HPA axis/cytokine imbalance	Paclitaxel[1,17]
Alopecia	p53-mediated apoptosis of hair follicle keratinocytes	Cyclophosphamide[18]

2.Molecular Mechanism of the Chemotherapeutic induced side effects

2.1 Nausea and Vomiting: A Molecular Mechanistic Perspective in Chemotherapy

Nausea and vomiting are among the most distressing and commonly reported adverse effects associated with chemotherapy. These symptoms result from a complex interplay of peripheral and central nervous system mechanisms, primarily mediated by the stimulation of neurochemical receptors and signalling pathways in response to cytotoxic insult[19]. The emetogenic potential of chemotherapeutic agents particularity drugs like cisplatin is attributed to their ability to damage gastrointestinal tissues and induce neurochemical cacades that ultimately activate the vomiting center in the brainstem. The process begins in the gastrointestinal (GI) mucosa, where chemotherapeutic agents such as cisplatin induce cellular stress and damage. Specifically, they act on enterochromaffin cells, specialized epithelial cells found in

the lining of the small intestine, which contain large quantities of serotonin (5-hydroxytryptamine or 5-HT) stored in secretory granules. Upon damage or stimulation, these cells release 5-HT into the surrounding tissue and bloodstream (Figure 1)[20].

The released 5-HT binds to 5-HT3 receptors, which are ligand gated ion channels located on the terminals of vagal afferent neurons that project to the brainstem. Activation of these receptors causes neuronal depolarization and the initiation of action potentials that travel along the vagus nerve to the nucleus tractus solitarius (NTS) and area postrema, the latter of which contains the chemoreceptor trigger zone (CTZ). The CTZ is one of the few areas in the brain without a well-developed blood brain barrier, making it highly sensitive to circulating emetogenic substances, including chemotherapeutic agents and their metabolites. Once the CTZ is activated, it communicates with the central pattern generator (CPG) in the medulla oblongata, integrating multiple afferent inputs. This leads to coordinated efferent signals that stimulate the somatic and autonomic systems responsible for the vomiting reflex. Importantly, the CTZ and NTS contain multiple nueroreceptors that modulate this process, including dopaminergic D_2 rceptors, neurokinin-1 (NK-1) receptors, and muscarinic and histaminergic receptors[21,22].

Chemotherapy induced nausea and vomiting (CINV) can be divided into acute and delayed phases. Acute CINV occurs within the first 24 hours of chemotherapy and is predominantly mediated by the 5-HT_3 pathway, while delayed CINV, which occurs 24-72 hours later, is more associated with substance P and activation of NK-1 receptors. This biphasic response underscores the need for combination antiemetic therapies, often involving 5-HT_3 receptor antagonists (e.g., ondansetron), NK-1 receptor antagonists 9e.g., aprepitant), and dopamine antagonists (e.g., metoclopramide). Among all chemotherapeutic agents, cisplatin is considered the most emetogenic, with nearly 90% of patients experiencing significant nausea and vomiting without prophylactic antiemetic therapy. Cisplatin's high emetogenicity is due to its potent activation of enterochromaffin cells and subsequent massive serotonin release. Overall, the pathophysiology of chemotherapy induced nausea and vomiting is rooted in the serotonergic activation of vagal afferents, central dopaminergic and neurokinin pathways, and integrated reflex control by the brainstem. Understanding these pathways has led to the development of targeted pharmacological interventions that have dramatically improved patient outcomes, yet the complexity and multifactorial nature of CINV still present significant challenges in cancer care[23,24].

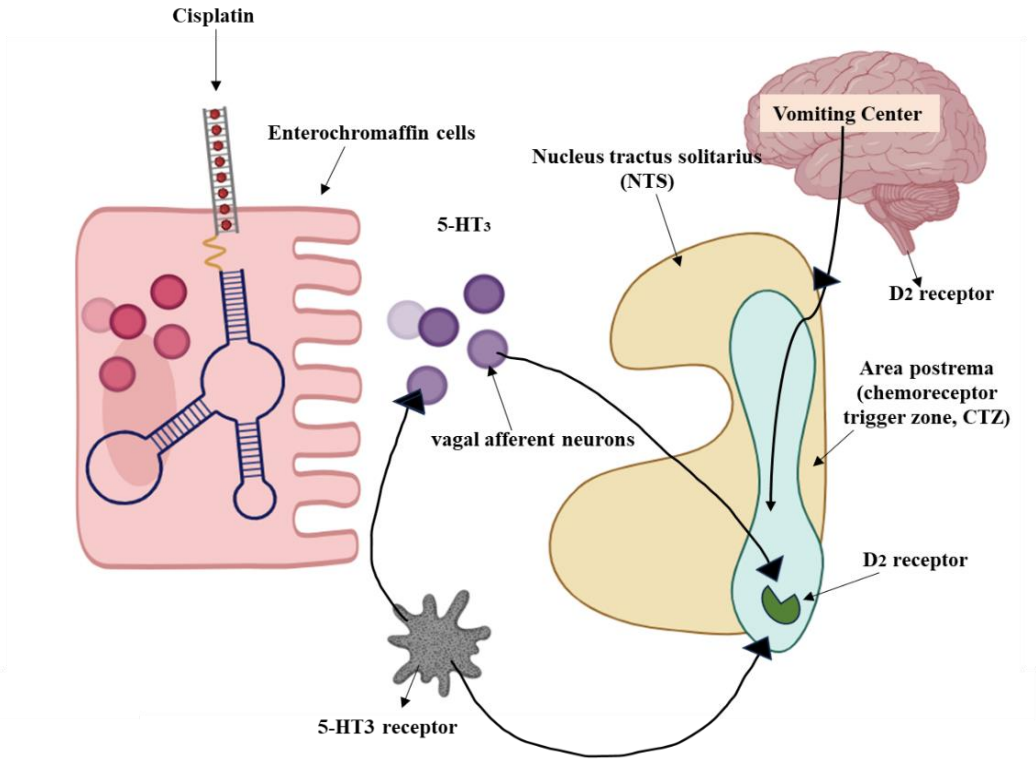


Figure 1: Molecular Mechanism of Chemotherapy Induced Nausea and Vomiting

Cisplatin induced damage to gastrointestinal epithelial cells stimulates enterochromaffin cells to release serotonin (5-HT). Serotonin activates 5-HT_3 receptors on vagal afferent nerves, transmitting signals to the nucleus tractus solitarius (NTS) and the chemoreceptor trigger zone (CTZ) in the medulla oblongata. The CTZ integrates these inputs and activates the vomiting center via dopaminergic (D_2) and neurokinin-1 (NK-1) receptors, resulting in the emetic reflex. The actute phase is primarily 5 HT_3 mediated, while the delayed phase involves NK-1 receptor activation.

2.2 Anorexia (Loss of Appetite): Molecular Mechanisms in Chemotherapy

Anorexia, or the pathological loss of appetite, is a prevalent and debilitating side effect of chemotherapy. It contributes significantly to cancer cachexia, impaired immune response, delayed healing, and reduced quality of life. While often perceived as a simple reduction in food intake, chemotherapy induced anorexia is a complex neuroimmunology disorder orchestrated by the interaction between pro-inflammatory cytokines, neuroendocrine dysregulation, and neurotransmitter imbalances within the brain, especially the hypothalamus and mesolimbic system[25].

The hypothalamus plays a central role in appetite regulation by integrating peripheral signas related to energy status and coordinating hormonal and neural inputs. Under normal conditions, orexigenic (appetite stimulating) signals such as neuropeptide Y (NPY) and agouti related peptide (AgRP) stimulate food intake. In contrast, anorexigenic (appetite suppressing) signals like pro-opiomelanocortin (POMC) and leptin reduce appetite. Ghrelin, a hormone secreted by the stomach, activates NPY/AgRP neurons, promoting hunger[26].

Chemotherapy disrupts this tightly regulated system primarily through the elevation of systemic pro-inflammatory cytokines, including tumor necrosis factor -alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). These cytokines are released in response to cellular damage and oxidative stress induced by cytotoxic drugs like doxorubicin, and they easily cross the blood brain barrier (BBB) or signal via vagal afferents to the hypothalamus. Once in the brain, these cytokines inhibit the expression and activity of NPY, thereby suppressing orexigenic signals. Simultaneously, they enhance the leptin like anorexigenic pathways, even in the absence of actual leptin increase. For example, IL-1β inhibits food intake by increasing POMC activity melanocortin signalling through MC4R receptors [27].

Beyond the hypothalamus, chemotherapy induced anorexia also involves the mesolimbic dopamine system, which governs the reward value of food. This pathway includes key region like the ventral tegmental area (VTA) and the nucleus acumens (NAc). Dopamine release in this circuit is essential for the motivation to eat. Chemotherapeutic drugs and inflammatory cytokines disrupt dopaminergic neurotransmission by impairing dopamine synthesis (Via tyrosine hydroxylase inhibition) and altering dopamine receptor sensitivity. The resulting anhedonia (inability to feel pleasure) diminishes the hedonic drive to eat, even when energy reserves are low[28].

Moreover, peripheral signals like gastric emptying delays and altered taste/smell perception, both mediated by cytokines effects and direct mucosal toxicity, further reduce the appeal and anticipation of eating. Chemotherapy also affects the vagal signaling to the brainstem, altering satiety thresholds and reinforcing early satiation. An illustrative example is doxorubicin, which increases circulating levels of TNF-α and IL-6, both centrally implicated in anorexia. Animal models treated with doxorubicin show profound reductions in food intake accompanied by hypothalamic downregulation of NPY and ghrelin receptors and reduced dopaminergic tone in the NAc. Ultimately, chemotherapy induced anorexia is a multifaced condition mediated by inflammatory, neuroendocrine, and neurochemical alterations. The cytokine driven suppression of orexigenic pathways, enhancement of anorexigenic signalling, and blunting of reward mechanisms together contribute to a profound and persistent loss of appetite, often resistant to standard nutritional support. Understanding these mechanisms paves the way for targeted interventions, such as ghrelin agonists, anti-inflammatory agents, and dopamine modulators, to compact anorexia and improve patient wellbeing during cancer therapy (Figure 2)[29].

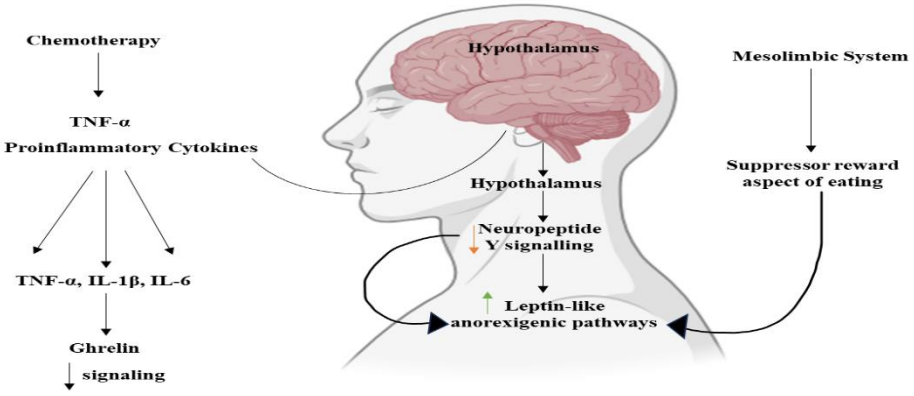


Figure 2. Molecular mechanism of chemotherapy induced Anorexia.

Chemotherapy elevates systemic pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), which disrupt hypothalamic appetite regulation. These cytokines suppress orexigenic signals and enhance anorexigenic pathways. Ghrelin signalling is impaired, further reducing hunger drive. Additionally, cytokines and chemotherapeutic agents disrupt dopaminergic signalling in the mesolimbic system, diminishing reward perception and motivation to eat. Altered vagal input, taste perception, and gastric motility also contribute to appetite suppression.

2.3 Mucositis: Molecular Mechanisms of Chemotherapy Induced Mucosal Injury

Mucositis is a severe and painful inflammatory condition of the mucous membranes lining the gastrointestinal (GI) tract, especially affecting the oral cavity. It is a common and dose limiting side effect of cytotoxic chemotherapy, particularly with agents like 5-flurouracil (5-FU). Clinically, mucositis manifests as erythema, ulceration, pain, dysphagia, and increased risk of systemic infections due to barrier breakdown. At the molecular level, mucositis arises from a series of interconnected biological events, beginning with epithelial stem cell damage and culminating in inflammatory amplification, tissue breakdown, and ulceration[30].

Chemotherapeutic agents such as 5-FU target rapidly proliferating cells, which include not only tumor cells but also the basal epithelial progenitor cells in the mucosal lining. These cells are essential for continuous mucosal regeneration. Damage to these cells initiates the first phase of mucositis-epithelial injury. DNA damage caused by chemotherapy induces a cascade of oxidative stress, with the overproduction of reactive oxygen species (ROS) within mucosal tissues. ROS play a dual role: while they directly damage cellular structures (lipids, proteins , DNA), they also serve as secondary messengers that activate downstream signaling pathways, most notably nuclear factor kappa B (NF-κB). NF-κB is a redox sensitive transcription factor that translocates into the nucleus upon activation and binds to promoter regions of genes involved in inflammation and cell death[31].

This leads to the second phase – upregulation of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin -6 (IL-6). These cytokines create a positive feedback loop by further activating NF-κB and recruiting immune cells like neutrophils and macrophages into the mucosal tissue. The resulting inflammatory amplification promotes the release of matrix metalloproteinases (MMPs), particularly MMP-1 and MMP-9, which degrade the extracellular matrix and basal membrane components, destabilizing the mucosal structure[32].

Simultaneously, apoptosis of mucosal epithelial cells is triggered through both intrinsic (mitochondrial) and extrinsic (death receptor) pathways. ROS cause mitochondrial dysfunction and cytochrome c release, activating caspase-9 and downstream executioner caspases, while TNF-α binds to TNFR1, initiating FADD dependent caspase 8 activation. Together, these lead to widespread epithelial cell death and sloughing of the mucosal surface.

The third phase is characterized by ulceration, where the mucosal integrity is lost, exposing underlying submucosa to mechanical injury and microbial invasion. Bactrial components like lipopolysaccharide (LPS) further exacerbate inflammation by engaging Toll-like receptors on immune and epithelial cells, sustaining NF-κB activity and cytokine production. A prominent example eis 5-fluorouracil (5-FU), which interferes with thymidylate synthase and incorporates into RNA/DNA, leading to cell cycle arrest and apoptosis in epithelial stem cells. In preclinical models, 5-FU has been shown to increase ROS levels and activates NF-κB, resulting in significant upregulation of TNF-α, IL-1β, MMPs, directly correlating with ulcer severity.Taken together, chemotherapy induced mucositis is a multi phase pathological process involving epithelial stem cell damage, oxidative stress, NF-κB mediated inflammation, matrix degradation, and apoptosis. The breakdown of the mucosal barrier not only causes significant morbidity but also compromises nutrition, drug delivery, and infection control. Understanding these molecular underpinnings has paved the way for targeted interventions, including antioxidants, NF-κB inhibitors, cytokine blockers, and growth factors like palifermin, aimed at preventing or mitigating mucosal damage in cancer patients[33] (Figure 3).

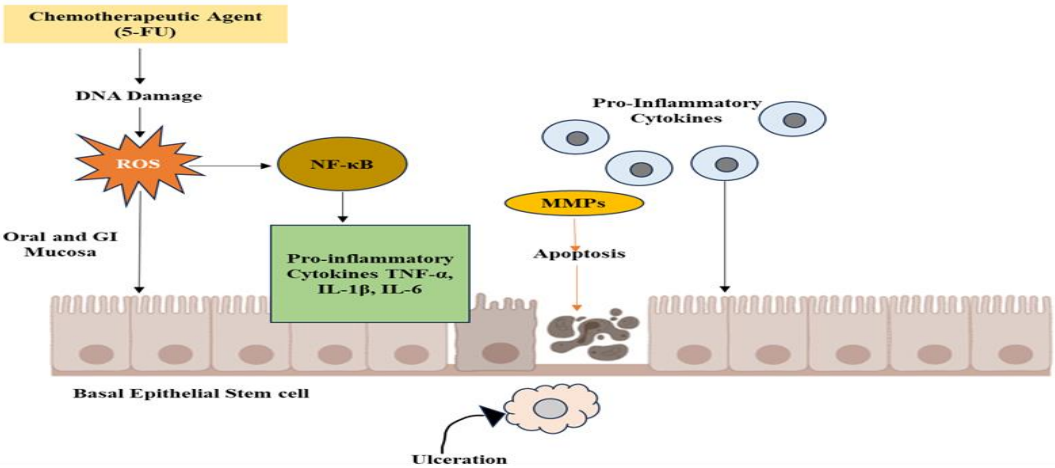


Figure 3. Molecular Mechanism of Chemotherapy Induced Mucositis

Chemotherapy agents like 5-fluorouracil (5-FU) damage basal epithelial cells, intitaiting oxidative stress and generation of reactive oxygen species (ROS0. ROS activate NF-κB, leading to the upregulation of pro-inflammatory cytokines and matrix metalloproteinases , which degrade the extracellular matrix. Apoptosis is triggered via both mitochondrial and extrinsic pathways. Barrier breakdown results in ulceration and microbial invasion, sustaining inflammation and worsening mucosal injury.

2.4 Chemotherapy Induced Diarrhea: Molecular Mechanism of Gastrointestinal Toxicity

Diarrhea is a common and potentially severe gastrointestinal side effect of many chemotherapeutic agents. It results from complex disruptions in intestinal epithelial integrity, inflammation, secretory function, and microbiome balance, leading to increased fluid secretion and reduced absorption. Among chemotherapeutic agents, irinotecan is notorious for causing severe, often delayed onset diarrhea, primarily due to its active metabolite SN-38. The molecular mechanisms behind chemotherapy induced diarrhea involve DNA damage, inflammatory signalling. Tight junction disruption, and microbiota alterations.At the core of this toxicity is epithelial cell damage. Chemotherapy targets rapidly dividing cells, including the intestinal crypt stem cells responsible for regenerating the epithelial lining. DNA damage induced by drugs such as irinotecan, 5-fluorouracil, and methotrexate causes apoptosis of enterocytes. This leads to villous atrophy, decreased absorptive surface area, and malabsorption of water and nutrients, which are primary contributors to diarrhea[34].

Irinotecan is converted in the liver to its active metabolite SN-38, which is responsible for both anti-tumor efficacy and gastrointestinal toxicity. SN-38 exerts its effects by inhibiting topoisomerase I, leading to accumulation of DNA strand breaks, activation of P53, and apoptosis of intestinal epithelial cells. SN-38 is detoxified in the liver via glucuronidation, but it can be reactivated in the gut by bacterial β-glucuronidase enzymes, leading to prolonged exposure of the intestinal mucosa to SN-38, resulting in epithelial injury and inflammation. This epithelial damage leads to the release of pro-inflammatory cytokines, particularly interleukin-6 and TNF-α. These cytokines activate downstream pathways such as the cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2) axis, which promotes inflammation, vasodilation, and chloride secretion, therby enhancing intestinal fluid loss. IL-6 also activates STAT3, contributing to mucosal inflammation and impaired mucosal regeneration.

In addition to inflammatory cytokines, epithelial barrier dysfunction is exacerbated by disruption of tight junction proteins, such as claudins, occludins, and zonula occludens-1 (ZO-1). Chemotherapy induced ROS and cytokines lead to the internalization or degradation of these proteins, increasing paracellular permeability. The compromised barrier permits luminal antigens and bacteria to infiltrate the mucosa, further amplifying inflammation and contributing to secretory diarrhea. Furthermore, chemotherapy induces gut microbiome dysbiosis, characterized by a reduction in commensal bacteria and overgrowth of pathogenic strains. These microbial changes enhance mucosal inflammation and reduce production of short chain fatty acids (SCFAs) like butyrate, which are essential foe enterocyte health and water reabsorption. In irinotecan treated models, pathogenic bacteria with β glucuronidase activity increase reactivation of SN-38G, creating a toxic positive feedback loop (Figure 4).

In the delated phase of irinotecan induced diarrhea, which occurs 2-10 days post treatment, the main pathological event is epithelial apoptosis, sustained inflammation, and impaired regenerative capacity. In severe cases, this can progress to life threatening colitis or dehydration, necessitating dose reduction or treatment discontinuation. Utimately, chemotherapy induced diarrhea is a multifactorial process involving enterocyte apoptosis, inflammatory cytokine release, barrier dysfunction, and microbiome disturbances. Irinotecan exemplifies this toxicity through its SN-38 metabolite and its interaction with the microbiota. Understanding these molecular mechanisms has led to the development of preventive and therapeutic strategies, including probiotics, COX-2 inhibitors, IL-6 blockers, and β-glucuronidase inhibitors, aimed at mitigating intestinal injury and improving patient outcomes during chemotherapy[35].

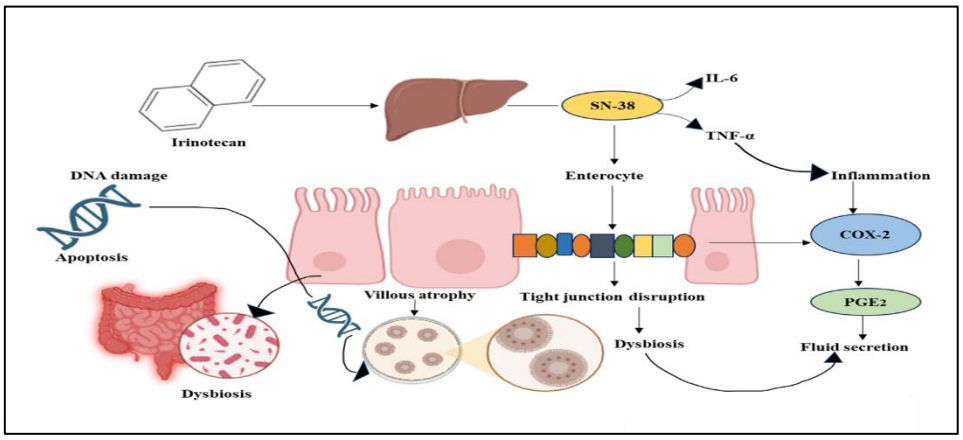


Figure 4. Molecular Mechanism of chemotherapy Induced Diarrhea

Irinotecan is metabolized to SN-38, which induces DNA damage and apoptosis in intestinal epithelial cells, leading to villous atropy and malabsorbtion. SN-38 also promotes the release of pro-inflammatory cytokines and activates the COX-2/PGE2 pathway, enhancing intestinal secretion. Disruption of tight junction proteins increases epithelial permeability. Gut dysbiosis and bacterial β-glucuronidase mediated reactivation of SN-38G amplify mucosal injury, resulting in delayed onset secretory diarrhea.

2.5 Chemotherapy – Induced Fatigue: Molecular Mechanisms of Energy Dysregulation

Fatigue is one of the most common and distressing symptoms experienced by cancer patients undergoing chemotherapy. It is characterized by a persistent sense of physical, emotional, and cognitive tiredness that s not relieved by rest and significantly impairs daily functioning. Unlike normal tiredness, chemotherapy-induced fatigue is rooted in cellular and molecular disturbances that affect energy production, inflammatory regulation, endocrine balance, and neurotransmitter signaling.

At the cellular level, chemotherapy leads to mitochondrial dysfunction, which ia a major contributor to fatigue. Mitochondria are the primary site of adenosine triphosphate (ATP) production through oxidative phosphorylation. Chemotherapuetic agents such as paclitaxel and doxorubicin generate reactive oxygen species (ROS) as byproducts of their action on rapidly dividing cells. These ROS cause oxdative damage to mitochondrial membranes, enzymes, and mitochondrial DNA (mt DNA), impairing the fuction of the electron transport chain (ETC). The inhibition of ETC complexes leads to reduced ATP synthesis and energy deficit at the cellular level, particularly in high demand tissues like skeletal muscle and the central nervous system. The resulting bioenergetic failure directly contributes to the feeling of physical exhaustion[36].

Simultaneously, chemotherapy induces chronic systemic inflammation, a process that amplifies fatigue through immune endocrine dysregulation. Cytotoxic agents trigger the release of pro-inflammatory cytokines, including interleukin-6, TNF-α, interleukin-1 beta. The cytokines can cross the blood brain barrier or signal through vagal afferent pathways, activating microglial cells in the central nervous system. The resulting neuroinflammation disrupts normal neuronal activity, particularly in the hypothalamic pituitary adrenal (HPA) axis[37].

The HPA axis is central to maintain circadian rhythms, stress response, and cortisol homeostasis. Chemotherapy induced cytokines interfere with the hypothalamic secretion of corticotropin releasing hormone (CRH) and arginine vasopression (AVP), leading to impaired release of adrenocorticotropic hormone (ACTH) and subsequent adrenal cortisol production. Disruption of this axis causes flattering of the diurnal cortisol rhythm, which is strongly associated with central fatigue, mood disturbances, and sleep disorders[38].

Neurotransmitter imbalance further exacerbates fatigue. Chemotherapy affects central neurotransmission, particularly involving serotonin (5-HT), dopamine (DA), and norepinephrine (NE). Inflammatory cytokines upregulate the enzyme indoleamine2,3 dioxygenase (IDO), which degrades tryptophan, the precursor for serotonin into kynurenine, reducing serotonin availability. Lower serotonin levels contribute to mood changes, lethargy, and disrupted sleep. Additionally, reduced dopaminergic signalling in the mesolimbic and prefrontal cortex leads to diminished motivation and reward sensitivity, a key feature of central fatigue.Both paclitaxel and doxorubicin have been shown to significantly increases ROS production in mitochondria and elevate systemic cytokines such as IL-6 and TNF-α.

In animal models and patients, these drugs impair mitochondrial respiration, decrease muscle strength, and alter cortisol dynamics- consistent with the multifactorial etiology of chemotherapy induced fatigue. together, fatigue during chemotherapy arises from a synergistic interplay between mitochondrial injury, inflammatory cytokine activation, HPA axis disruption, and neurotransmitter imbalance. These molecular and neuroendocrine alterations create a state of chronic energy insufficiency and emotional dysregulation that cannot be overcome by rest alone.

Targeted interventions aimed at restoring mitochondrial function, controlling inflammation, and regulating neuroendocrine signaling may offer promising avenues to alleviate fatigue and enhance quality of life in cancer patients (Figure 5)[39]

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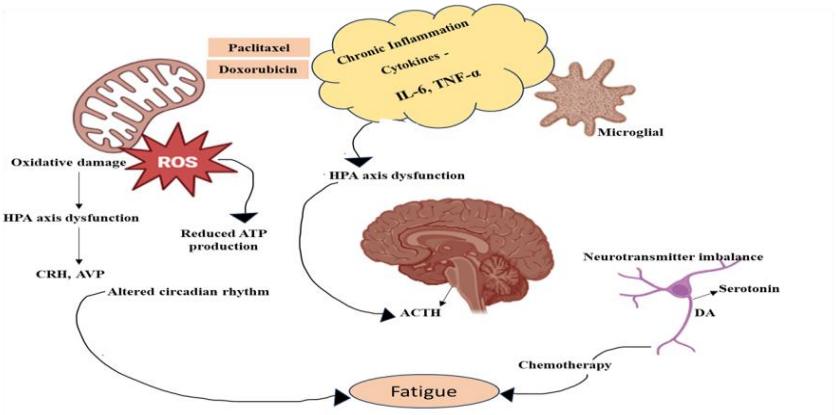


Figure 4. Molecular Mechanism of chemotherapy Induced Diarrhea.

Chemotherapy leads to mitochondrial dysfunction and reduced ATP production due to oxidative damage from reactive oxygen species (ROS). Concurrently, systemic inflammation elevates cytokines, disrupting the hypothalamic pituitary adrenal axis and flattening the diurnal cortisol rhythm. Inflammatory cytokines also alter neurotransmitter signalling by depleting serotonin and impairing dopamine synthesis, resulting in reduced motivation, sleep disturbances, and central fatigue. Together these pathways create a multifunctional disruption of energy regulation and emotional homeostasis.

2.6 Chemotherapy Induced Alopecia: Molecular Mechanisms of Hair Follicle Damage

Alopecia, or hair loss, is one of the most visible and psychologically distressing side effects of chemotherapy. It occurs primarily due to the targeted destruction of rapidly dividing cells- specifically, hair matrix keratinocytes- which share similar proliferative charcteristics with cancer cells. The pathophysiology of chemotherapy induced alopecia (CIA) is particularly associated with disruption of the anagen phase of the hair cycle, which is the active growth phase. This disruption involves complex molecular events, including DNA damage, p53 activation, mitochondrial mediated apoptosis, and dysregulation of cell survival pathways. During the anagen phase, hair follicle matrix keratinocytes at the base of the hair bulb divide rapidly to support the continuous elongation of the hair shaft. Chemotherapeutic agents, particularly alkylating agents like cyclophosphamide and microtubule stabilizing agents like docetaxel, are highly toxic to these cells due to their mechanism of action on DNA replication and mitosis[39,40].

Upon administration, drugs such as cyclophosphamide induce DNA cross linking and strand breaks, which are detected by the cell's DNA damage response (DDR) machinery. This activates the tumor suppressor protein p53, a master regulator of cellular stress responses. Once activated, p53 upregulates pro-apoptotic genes such as Bax and PUMA, a simultaneously downregulates anti-apoptotic proteins like Bcl-2, tipping the balance toward cell death.

This cascade triggers mitochondrial outer membrane permeabilization (MOMP), resulting in the release of cytochrome c into the cytosol. Cytochrome c forms a complex with Apaf-1 and procaspase-9, leading to the formation of the apoptosome, which subsequently activates executioner caspases. These caspases cleave structural and regulatory proteins, leading to controlled cellular demolition of their matrix keratinocytes.

In addition to the intrinsic pathway, extrinsic apoptotic signals also contribute to CIA. Chemotherapy agents have been shown to upregulate Fas receptor (CD95) and its ligand FasL on the surface of hair follicle cells. Binding of Fas to FasL activates caspace-8, which either directly initiates the executioner caspase or amplifies apoptosis by cleaving Bid, a pro-apoptotic Bcl-2 family protein that further engages the mitochondrial pathway.Importantly, these apoptotic events not only destroy the proliferative matrix cells but also didrupt the hair shaft formation and anchoring, leading to rapid shedding of hair- a process referred to as anagen effluvium. This typically begins with 1-2 weeks of chemotherapy intiation and becomes most noticeable by 1 month[41].

Cyclophosphamide is a classic example of an agent that causes alopecia through p53 mediated mitochondrial apoptosis. Docetaxel, a taxane derivative, causes mitotic arrest by stabilizing microtubules, leading to accumulation of DNA damage, activation of P53, and ultimately hair follicle apoptosis. Studies have shown that both drugs result in significant hair follicle regression and uncreased TUNEL-Positive cells in the hair bulb region, indicative of apoptosis.

Overall, chemotherapy induced alopecia results from the rapid induction of apoptotic pathways in hair follicle matrix cells, primarily mediated through p53 activation, mitochondrial cytochrome release, caspase activation, and Fas/FasL interactions. While this response is an unfortunate off target effect of anti-cancer therapy, understanding these molecular mechanisms has opened avenues for potential prevention strategies, such as scalp cooling, p53 pathway modulation, and cytokine-based protectants, aiming to preserve hair follicle integrity during treatment (Figure 6)[42].

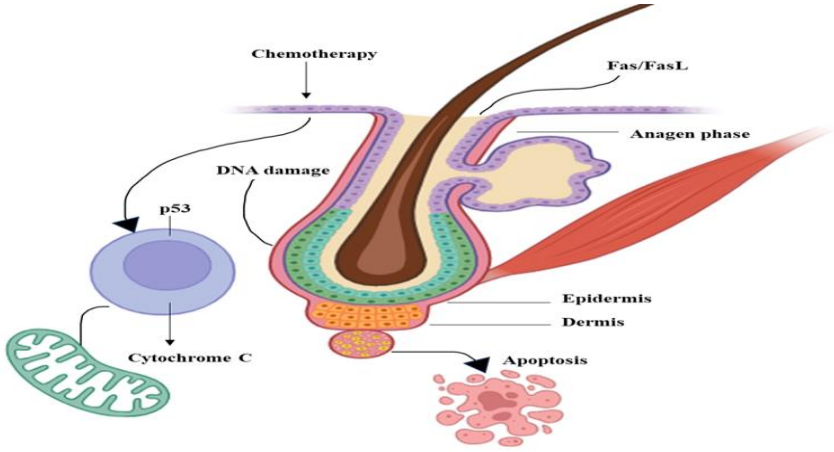


Figure 6. Molecular Mechanism of Chemotherapy Induced Alopecia

Chemotherapeutic agents such as cyclophosphamide and docetaxel damage rapidly dividing hair matrix keratinocytes during the anagen phase of hair growth. DNA damage triggers activation of the p53 pathway, leading to upregulation of pro-apoptotic proteins and downregulation of anti-apoptotic proteins. This activates mitochondrial mediated apoptosis through cytochrome c release and caspase cascade initiation. Additionally, Fas/FasL signalling contributes to extrinsic apoptosis. These pathways result in premature regression of hair follicles and hair shaft detachment, causing rapid hair loss known as anagen effluvium.

2.7 Beyond Cellular Damage: The broader Impact of Chemotherapy Induced side effects

Chemotherapy, while life saving, comes with a considerable burden that extends far beyond its cytotoxic action on tumor cells. The adverse effects of chemotherapy are not confined to physiological domains; they deeply affect the psychological, emotional, social, and financial well being of patients. For many individuals undergoing cancer treatment, the fear of chemotherapy related side effcets such as nausea, fatigue, mucositis, alopecia, and diarrhea- becomes more overwhelming than the fear of cancer itself. This intense apprehension can lead to delays in care seeking behavior, refusal to initiate chemotherapy, or premature termination of treatment cycles, all of which significantly compromise the overall therapeutic outcome[43].

These side effects are particularly distressing because they are often visible, painful, and persistent, eroding he patient's sense of identity and control. For example, alopecia, though not life-threatening, profoundly affects body image and self -esteem. Fatigue and gastrointestinal disturbances reduce the ability tp perform everyday tanks, leading to functional decline and social withdrawal. Over time, these physical symptoms contribute to anxiety, depression, and feelings of isolation, creating a feedback loop that worsens quality of life and psychological resilience during treatment[44].

Moreover, the economic implications of managing chemotherapy induced toxicities are substantial, especially in low- and middle-income countries. Patients often require hospital admissions for severe neutropenia, blood transfusions for anemia, antibiotics to control infections, and nutritional interventions for mucositis and anorexia. The cost of supportive medications, such as antiemetics, antidiarrheals, growth factors, and corticosteroids, adds significantly to the overall financial burden. In regions where health insurance is sparse and out of pocket expenses are high, these costs can be catastrophic, leading to treatment discontinuation and widening health inequities. This further undermines the objectives of national cancer control programs and accentuates global disparities in cancer outcomes.

Despite advances in oncology, current supportive care strategies remain largely reactive. Protocols now routinely include antiemetics, corticosteroids, and analgesics. These agents help mitigate acute symptoms but often fail to prevent the onset of toxicities or address their underlying causes. Additionally, many of these drugs are associated with secondary side effects, such as metabolic disturbances, immunosuppression, and drug-drug interactions, further complicating treatment[45].

One of the critical limitations of current supportive therapies lies in their single target mechanism of action, which is ill suited to manage the multifactorial nature of chemotoxicity. Chemotherapy induced side effects stem from oxidative stress, inflammatory cytokine cascaded, mitochondrial dysfunction, epithelial barrier breakdown, and apoptotic signaling in non-cancerous tissues. Addressing these complex, overlapping pathways with single agents offers only partial relief. Consequently, there is a pressing need for novel adjunct therapies that are multi-functional, biocompatible, and protective of normal tissues without compromising the antitumor efficacy of chemotherapy. Such agents should ideally possess antioxidant, anti-inflammatory, mitoprotective, and regenerative properties. Phytochemicals, nanoparticles, and bioengineered compounds are emerging as promising candidates, with the potential to redefine supportive care and transform the patient experience during chemotherapy[45].

2.8 Emerging Paradigms in Chemotoxicity: Molecular Insights and the promise of Biocompatible Adjuncts

The landscape of cancer therapy is evolving rapidly, not only in the direction of precision oncology and targeted agents but als in our growing understanding of the systemic toxicities associated with conventional chemotherapy. Traditionally, the adverse effects of chemotherapy have been attributed to its non-selective cytotoxicity against rapidly dividing normal cells- such as those in the gastrointestinal tract, bone marrow, and hair follicles. However, emerging molecular insights have unveiled a novel, secondary mechanism of chemotoxicity that challenges this simplistic view and highlights the need for more intelligent supportive interventions.

One of the most intriguing developments in the biology of chemotoxicity is the discovery of cell free chromatin particles (cfChPs) as active mediators of collateral tissue damage. These cfChPs are released from cancer cells undergoing apoptosis or necrosis following exposure to chemotherapeutic agents. Structurally, they consist of fragmented nucleosomes, comprising DNA wrapped around histone proteins, which upon release into the extracellular milieu and systemic circulation, become unintended messengers of toxicity. Healthy cells, including non-dividing or slow dividing somatic cells, can inadvertently internalize these cfChPs through processes such as endocytosis or micropinocytosis[46]. Once inside, cfChPs integrate into host genomic DNA, creating genomic instability, including double strand DNA breaks which activate DNA damage responses and potentially lead to mutagenesis, apoptosis, or senescence.

The downstream consequences of cfChP internalization are not limited to direct DNA injury. These particles also trigger inflammatory pathways, activate Toll like receptors, induce oxidative stress, and upregulate pro-apoptotic signaling cascades. The resulting cellular stress response is a self amplifying loop that recruits immune

cells, further increases the production of reactive oxygen species, and generates a bystander effect, where tissues uninvolved in the original tumor site become collateral targets of toxicity. This paradigm shift implies that chemotherapy induced tissue injury is not merely a result of drug exposure, but a delayed and systemic phenomenon, perpetuated by molecular remnants of dying cancer cells.

This deeper understanding necessitates a shift in the philosophy of supportive oncology. Historically, supportive care has been reactive, focused on symptom management after damage has occurred. While interventions such as antiemetics, corticosteroids, growth factors, and antidiarrheals remain essential, they offer limited protection against the underlying molecular cascade initiated by chemotherapy. Furthermore, these agents come with their own spectrum of side effects and often target single pathways in a multifactorial process[47].

In response to these challenges, there is a growing scientific and clinical interest in natural origin, biocompatible compounds that offer multi modal protection without interfering with the anti-cancer efficacy of chemotherapy. Polyphenols such as curcumin, resveratrol, epigallocatechin gallate (EGCG), and quercetin, as well as plant derived terpenoids, alkaloids, and flavonoids, have demonstrated promising antioxidant, anti-inflammatory, immunomodulatory, and cryoprotective activities in preclinical studies. These compounds can scavenge free radicals, inhibit pro-inflammatory cytokines, upregulate endogenous antioxidant systems like Nrf2, and even modulate apoptosis pathways selectively in normal versus cancerous tissues.

Unlike synthetic pharmacological agents, natural origin compounds are generally well tolerated, non-immunogenic, and biodegradable, traits that are crucial for their safe long term use, particularly in immunocompromised cancer patients. Moreover, these agents do not typically interfere with the DNA damaging mechanisms of chemotherapeutics and may even enhance therapeutic outcomes by improving cellular resilience in healthy tissues[48].

The limitation of natural compounds has historically been their poor bioavailability, rapid metabolism, and low tissue specificity. However, the advent of nanotechnology-based delivery systems has revolutionized this field. Carriers such as liposomes, chitosan nanoparticles, polymeric micelles, alginate beads, and dendrimers can encapsulate bioactive compounds, protect them from degradation, and deliver them in a controlled manner to target tissues. These nanocarriers can be further engineered to respond tp specific environmental cues, such as pH changes in the tumor microenvironment or temperature gradients allowing site specific drug release and minimizing systemic exposure[49].

For example, chitosan-based nanoparticles have been used to deliver curcumin with significantly improved bioavailability and sustained release, resulting in reduced mucosal damage and enhanced antioxidant defences during chemotherapy. Similarly, EGCG loaded polymeric micelles have shown potential in protecting cardiac tissue from doxorubicin induced cardiotoxicity without altering its antineoplastic effects. The integration of natural origin therapeutics with advanced nanocarriers represents a cutting-edge approach in cancer supportive care. It enables prophylactic intervention at the molecular level, reducing oxidative damage, preserving tissue function, and preventing long term complications. More importantly, its envisions a future of integrative oncology where cytotoxic therapy is paired with tissue protective adjuncts, allowing patients to receive full dose chemotherapy with fewer interruptions, improved quality of life, and reduced treatment abandonment. Ultimately, the biology of chemotoxicity is more complex and far reaching than previously understood. The systemic propagation of damage through cfChPs and inflammatory signalling demands a shift from reactive to proactive protection strategies. By leveraging biocompatible, multi-targeted natural compounds and precision nano delivery platforms, the next generation of supportive care can mitigate the collateral damage of chemotherapy, making cancer treatment not only more effective but also more humane[49].

3 CONCLUSION

Chemotherapy has revolutionized cancer treatment, but its adverse effects continue to limit its full potential. The emergence of cfChPs as mediators of systemic toxicity has introduced a new therapeutic target, one that lies not in the tumor, but in the spaces between cells and signals. As we advance toward more personalized and less toxic cancer therapies, the need for innovative, protective, and biocompatible agents becomes urgent. The future of supportive oncology lies in intervention, not reaction. We must seek compounds that pre-emptively shield healthy tissues, interrupt molecular cascades of damage, and preserve organ function without compromising cancer control. In this evolving landscape, there is immense potential for bioactive natural molecules delivered through smart nanocarriers to redefine what it means to survive and thrive through chemotherapy.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

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ORIGINAL ARTICALE

GINGIVITIS: ISOLATION AND DIAGNOSIS OF THE CAUSATIVE BACTERIA AND ITS RELATIONSHIP TO OBESITY IN AL -DIWANIYAH GOVERNORATE

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ABSTRACT

Background: Seventy clinical samples were collected from gingivitis patients between 3/1/2025 and 30/3/2025 under the supervision of a specialized physician. Samples were obtained from professional dental facilities in Al-Diwaniyah Governorate. The study included 29 male patients (41.43%) and 41 female patients (58.57%), with ages ranging from 7 to 80 years.
Objectives: The aim of this study was to investigate the prevalence and types of bacterial isolates in gingivitis patients and to examine the relationship between gingivitis and obesity.
Results: Out of 70 clinical samples, 55 bacterial isolates (78.57%) demonstrated growth. Microscopic examination with Gram staining showed that 44 isolates were Gram-positive (80% growth rate), including 28 streptococci, 11 staphylococci, and 5 Enterococcus faecalis. Eleven isolates were Gram-negative, with a growth rate of 20%. The findings indicated that bacteria associated with gingivitis were more prevalent in obese patients, with a bacterial growth rate of 70.91%, compared to 29.09% in patients with gingivitis only.
Conclusion: The study demonstrates a clear relationship between gingivitis and obesity, indicating that bacterial prevalence is higher in obese patients with gingivitis. These findings highlight the importance of considering obesity as a risk factor in the management and prevention of gingivitis.

Keywords: Enucleation, Healing Time, Marsupialization, Pediatric Dentistry, Recurrence Rates

INTRODUCTION

The mouth, like other areas of the body, or possibly more so, is distinguished by the presence of microorganisms in the majority of its components. These organisms have a balanced interaction with their hosts, but this relationship can worsen in the mouth, resulting in illness. This is frequently related with changes in the biology of the mouth. These alterations may be caused by external factors such as antibiotic treatment or an increase in the amount of fermentable carbohydrates in the diet. Or it could be internal sources, such as changes in the integrity of the host defenses following pharmacological treatment, which impact the usual presence of bacteria and possibly the existence of germs in difficult-to-reach areas. For example, when a person's teeth are pulled due to gum inflammation, the germs causing the inflammation are transmitted into the bloodstream and spread to other organs of the body, resulting in secondary disorders. This sort of bacteria is known as opportunistic pathogens. Many oral bacteria can behave this manner. At some time in their lives, many people suffer from an imbalance of the natural bacteria in their mouth [1]. Oral bacteria are ordinarily in a state of dynamic equilibrium, and when this balance is upset, the natural flora in the mouth is disrupted, resulting in oral disorders [2]. Gingivitis and tooth decay are the two most frequent and widespread oral illnesses in the world [3].

Periodontal disease refers to a range of disorders that affect the tissues surrounding a tooth, Gum disease is the major cause of tooth loss and is very prevalent in developing countries, Gingivitis is a reversible inflammatory response due to the presence of dental

plaque. The gums usually return to their normal state before the infection if oral hygiene is taken care of. The infection is chronic and more severe in people who suffer from hormonal disorders, such as during pregnancy and puberty[4]. Gingivitis is a chronic inflammatory illness caused by the interaction of gum bacteria and the host's reaction to that contact[5]. This raises the risk of obesity, diabetes, and perhaps rheumatoid arthritis [6,7]. In 2010, [8] proposed a relationship between gingivitis and obesity. In 2011, [9-12] shown the tight relationship between obesity and gingivitis. Obesity is a chronic metabolic condition characterized by the abnormal buildup of fat [13]. Poor eating habits, as well as genetic, behavioral, cultural, social, and technological influences, all contribute to weight gain [14]. Obesity has a number of immediate life-altering repercussions, including stroke, osteoporosis, diabetes, gout, gallbladder disease, and coronary heart disease [15,16] demonstrated that non-vital gut microorganisms have a significant role in obesity by enhancing insulin resistance produced by Gram-negative bacteria.

MATERIALS AND METHODS

2-1 "Clinical specimen collection"

70 clinical samples were gathered from patients with varying weights and disease lesions from specialized dental centers and private clinics in Al- Diwaniyah Governorate. The collection cases included inflammation and swelling of the gums of both sexes and of different ages.

Samples were gathered with sterile cotton swabs under the supervision of a specialized physician before being transferred to the scientific laboratories at Al-Diwaniyah Teaching Hospital.

2-2 "Isolation and identification of bacteria" 2-2-1 'Culture diagnosis'

The initial stage in identifying bacteria was to culture clinical samples on different medium using a planned approach appropriate to each bacterial species being studied. The plates were then incubated at 37°C for 18-24 hours. The diagnosis is made based on the morphological properties of bacterial development, such as colony size, shape, color, odor, and the ability to ferment lactose and hemolyze [17].

2-2-2 ' Microscopic examination' A typical bacterial colony was transferred onto a glass slide on which a drop had previously been deposited. It was then spread across the slide and allowed to dry. Following that, the slide was exposed to a flame and stained with Gram stain. Following that, the bacterial cells were inspected using a light microscope at a magnification of 1000 to see the color, shape, and reactivity to the dye [18].

RESULTS AND DISCUSSION

'Clinical specimen collection'

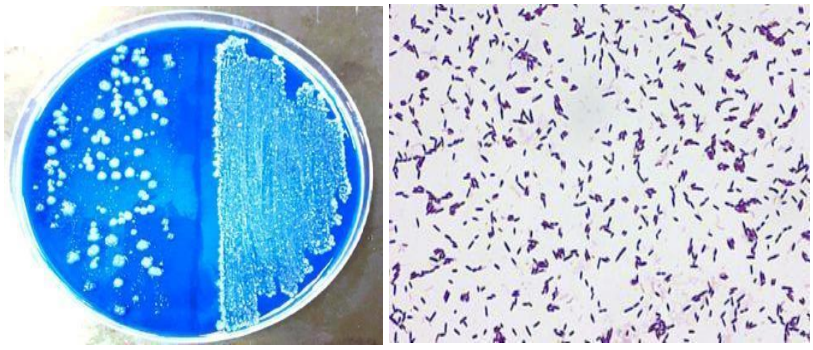
70 clinical samples were taken from gingivitis patients between 3/1/2025 and 30/3/2025, under the observation of a specialized physician. Samples were gathered from professional dental facilities in Al- Diwaniyah Governorate. The collecting process includes 29 clinical samples from men (41.428% of the total sample) and 41 clinical samples from women (58.571% of the total sample). Males and females' ages ranged between (7-80) years, as seen in Table 1. And, with varied weights, it was discovered during isolation that those with obesity and excessive weight gain are more vulnerable to gum inflammation than others, which is consistent with the findings of the researcher [19].

Table 1. The collection of clinical samples from persons with gingivitis of both sexes, of various ages and weight.

Number of clinical samples	Females	The age	The weight	Males	The age	The weight
10	6	7-10	30-55	4	8-11	25-50
11	7	10-12	35-60	4	9-12	30-45
9	4	13-15	50-70	5	15-17	45-70
8	5	16-22	60-85	3	17-20	65-90
11	5	23-30	80-90	6	25-40	80-105
11	9	40-70	75-85	2	70-75	95-100
10	5	50-75	90-100	5	75-80	90-107
70						

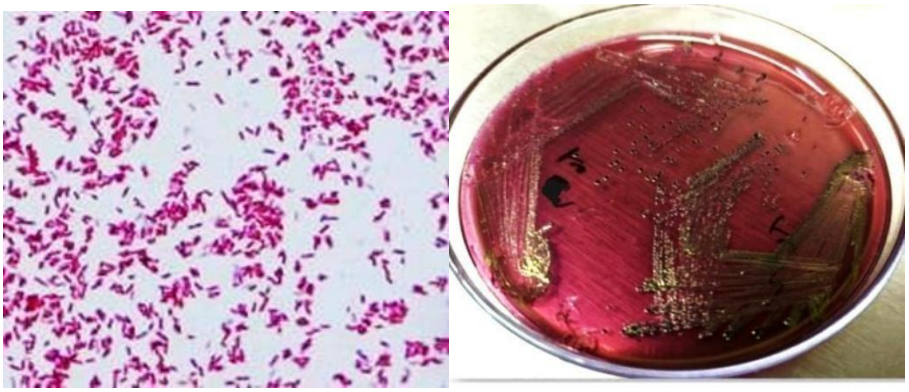
'Culture diagnosis and microscopic examination'

The findings of the culture diagnosis showed the growth of 55 bacterial isolates out of 70 isolates, with a growth rate of (78.571%), there were isolates, including anaerobic, spherical growth in the form of short chains, single and double spheres. This demonstrated its capacity to grow in the selective medium Mitis Salivarius agar, which is used to isolate streptococci. These colonies grew clearly on the medium and had a transparent blue tint. The size ranged from 0.5 to 2 mm, and they were both regular and irregular in shape, with some adhering to the medium and others not adhering (figure 1). The longer the anaerobic incubation period, the easier it was to identify the bacteria. This is consistent with the findings of the researcher [20], who identified Staphylococci, Streptococci, Corynebacterium, Lactobacillus, and other anaerobes as the bacteria responsible for gingivitis and oral illnesses. Other bacterial colonies demonstrated the ability to grow on a medium Eosin methylene blue and under aerobic circumstances, forming small, flat, dark-green colonies with a metallic shine due to their ability to ferment lactose. These colonies were Escherichia coli (Figure 2), which is comparable to what was achieved by [21]. Another bacterium was characterized by its capacity to grow in medium MacConkey agar, a differential medium. The bacteria that live on it can digest lactose and generate vivid pink mucous colonies. It was demonstrated that they are K. pneumoniae (Figure 3). This is what the researcher [22] demonstrated. Other bacterial colonies demonstrated their ability to thrive on the medium Cetrimide agar, producing bacterial colonies with blue-green and greenish-yellow colors and shapes. They were smooth, with a high core and flat corners, and smelled like grapes. After diagnosis, it was determined that they were P. aeruginosa (Figure 4). This outcome corresponds to what the researcher described [23]. Other bacteria grew in the medium Mannitol salt agar and formed smooth, elevated, circular colonies. Based on the physical characteristics of the colonies developing on the medium, the bacteria were identified as (staphylococcus). In addition to their ability to withstand salt concentration, yellow colonies emerged. After diagnosis, it was discovered that they were (S. aureus) and other pink-colored colonies that did not ferment lactose sugar. It was discovered that these were (S. epidermidis) (Figure 5) [24]. The bacterial isolates that were able to grow on the medium Esculin Agar, forming small white colonies with a circular shape, have the ability to turn the color of the medium to black due to their ability to secrete an enzyme that breaks down the esculin substance in this medium, forming the esculin compound, which combines with the iron ions present in the medium in the form of iron citrate, forming a black compound indicating the growth of Enterococcus faecalis. (Figure 6) [25,26].



"A", "B"

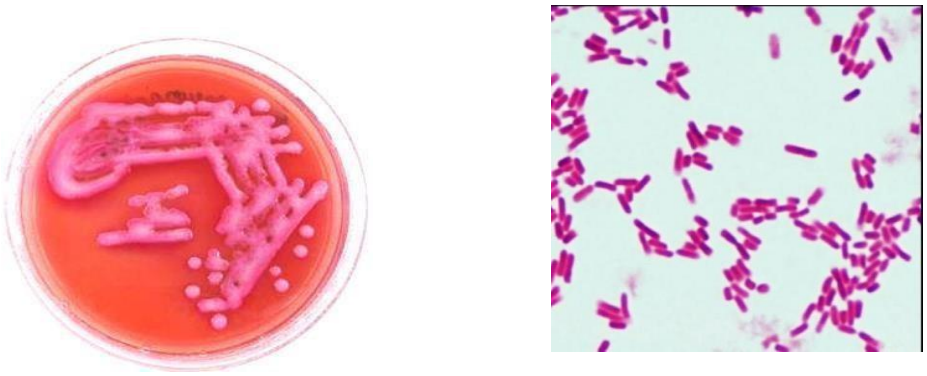
Figure1. 'A' S. mutans on mitis salivarius agar 'B' S. mutans under the microscope.



A B

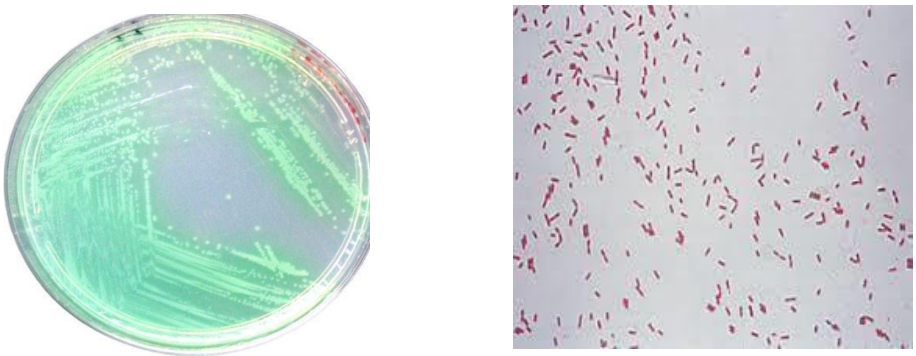
Figure2. 'A' E. coli on Eosin methylene blue 'B' E. coli under the microscope.

Khadija Mousa Abd Al-Jabar, Zahraa aheem alzamiliy alzamiliy, Majida Mohammad Abid Falhy ,Zahraa Falah Azeez Gingivitis: Isolation and diagnosis of the causative bacteria and its relationship to obesity in Al -Diwaniyah Governorate.Bulletin of Stomatology and Maxillofacial Surgery.2025;21(8).281-287doi:10.58240/1829006X-21(8).281



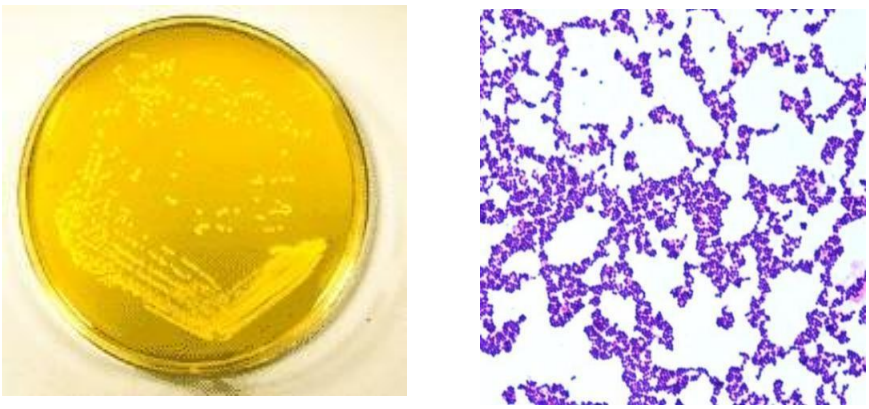
"A" "B"

Figure 3. 'A' K. pneumoniae on MacConkey agar 'B' K. pneumoniae under the microscope.



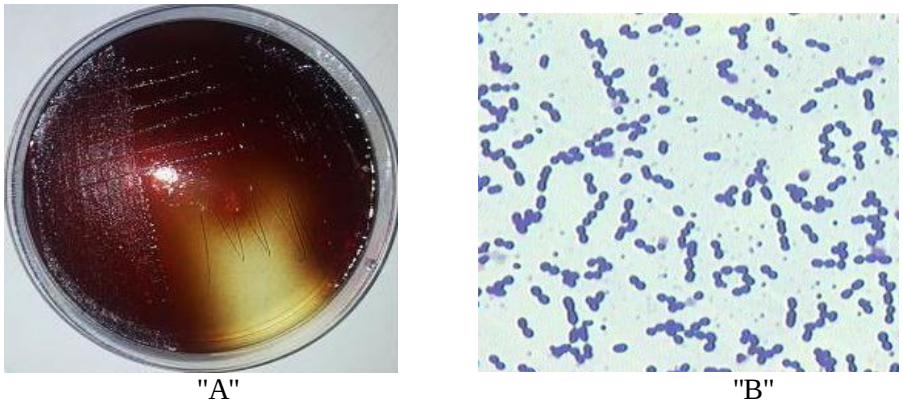
"A" "B"

Figure 4. 'A' P. aeruginosa on Cetrimide agar 'B' P. aeruginosa under the microscope.



A B

Figure 5. 'A' S. aureus on Mannitol salt agar 'B' S. aureus under the microscope.



"A" "B"

Figure 6. 'A' Enterococcus faecalis on Esculin Agar ' B' Enterococcus faecalis under the micro

Following the culture diagnosis, a microscopic inspection with Gram stain was done on all of the developing isolates, which numbered 55 out of 70 and had a growth rate of 78.571%. Microscopic investigation, as shown in Table 2, revealed that 44 bacterial isolates tested positive for Gram stain, with a growth rate of 80%. 28 of the isolates were streptococci. This finding is consistent with [27], which concluded that streptococci are the primary bacterial cause of gingivitis and tooth decay. 11 isolates were staphylococci, which contradicts the researcher's [28,29] claim that staphylococci are the predominant bacteria in gingivitis. Furthermore, Streptococcus bacteria induce opportunistic infections when combined with other Streptococcus species found on the skin, digestive tract, and nose [30,31]. They also cause serious hospital infections [32]. This is owing to bacteria having quick resistance mechanisms that allow them to spread easily, such as plasmids during conjugation and transformation, it also has enzymes and surface antigens that allow it to infiltrate the body's tissues, similar to staphylococcus bacteria [33]. Gram-negative bacteria were found among the bacteria causing gingivitis, but at a lower rate than Gram-positive bacteria. Microscopic investigation revealed that 11 of the 55 bacterial isolates are Gram-negative, with an average growth rate of 20%. This is consistent with previous research, which has shown that the majority of Gram-negative bacteria originate from digestive and respiratory tract illnesses [27,34].

Table 2. Number of bacterial isolates diagnosed by microscopic inspection and isolated from pathological illnesses characterized by gingivitis

Bacterial isolates organized by genus and species	Microscopic examination		number
S. mutans	Gram positive		28
S. aureus	Gram positive		11
E. faecalis	Gram positive		5
E. coli	Gram negative		6
P. aeruginosa	Gram negative		4
K. pneumonia	Gram negative		1
Total number of isolates	Gram positive 44	Gram negative 11	55

Table 3 shows that bacteria that cause gingivitis are more prevalent in patients who are obese and have gingivitis. The growth rate of bacteria causing inflammation in people with gingivitis and obesity was 70.909%, which is higher than the rate of bacteria isolated from people with gingivitis only, which was 29.090%. The current investigation demonstrated the existence of a relationship between gingivitis and obesity. Obese people are more likely to develop gingivitis. This finding was reinforced by early research, including the claim [35] that obesity increases the chance of developing gingivitis, indicating a faster and more visible development in overweight individuals. This is similar to what was stated by [36], where it was proven that the risk of developing gingivitis is linked to an increase in the body mass index, [37] also reported that excessive obesity increases the causes of diseases, [38] suggested that obese individuals have adipose tissue that is a storehouse of inflammatory cytokines, which increases the likelihood of developing periodontitis, whereas [39] reported difficulty in interpreting the association between obesity and gingivitis based on several observational studies.

Table 3. Depicts the connection between gingivitis and obesity

Isolated bacterial species	Gingivitis + obesity	Gingivitis
Gram-positive bacteria	Number of isolates	
S. mutans	20	8
S. aureus	8	3
E. faecalis	3	2
Gram-negative bacteria	Number of isolates	
E. coli	4	2
P. aeruginosa	3	1
K. pneumonia	1	__
The total	39 70.909%	16 29.090%

CONCLUSIONS

Among the many bacterial genera that live in the mouth, gram-positive streptococci are the most common cause of gingivitis. When conditions are favorable, they secrete acids, which cause a decrease in Hp levels and gingivitis. Obese and overweight individuals are also more likely to develop gingivitis and tooth decay.

Recommendations

We advocate performing a study on the wrong eating habits that contribute to gingivitis. We also recommend conducting a comprehensive study on foods that cause obesity and avoiding them due to their impact on oral health in particular and overall health, as well as conducting a comprehensive study similar to the current one to detect other types of bacteria that may cause oral infection. Raising knowledge about the importance of the mouth and how to protect it from gum inflammation and tooth decay by regular cleaning, avoiding foods that trigger inflammation, and frequent dental checkups.

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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ORIGINAL RESEARCH

AGE ESTIMATION BASED ON PULP / TOOTH VOLUME BY CONE BEAM COMPUTERIZED TOMOGRAPHY IMAGE

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ABSTRACT

Background and Objectives: Accurate age estimation is essential in forensic and clinical dentistry, with the pulp/tooth volume ratio (PTVR) emerging as a promising morphological marker. This study aimed to evaluate the relationship between PTVR and chronological age using cone beam computed tomography (CBCT) in a Kurdish adult population, and to develop a population-specific regression model for age estimation.

Methods: A cross-sectional study was conducted on 246 Kurdish adults aged 16–60 years who underwent CBCT imaging at a dental clinic in Sulaimaniah, Iraq. PTVR was measured in central incisors and canines using standardized CBCT protocols and volumetric analysis software. Stratified random sampling ensured proportional representation across age groups.

Results: A strong, statistically significant negative correlation was found between PTVR and chronological age in both central incisors and canines ($r = -0.94$, $p < 0.001$). Linear regression models demonstrated high predictive accuracy ($R^2 > 0.90$) for age estimation in both sexes. Sex-based differences in PTVR were observed in canines but not in central incisors. The predictive strength of the models varied across age groups, with the highest accuracy in 25-29 years ($R^2 = 0.706$, $P \leq 0.001$) and 55-60 years ($R^2 = 0.654$, $P \leq 0.008$) group.

Conclusion: PTVR measured via CBCT is a highly reliable indicator for age estimation in Kurdish adults, with strong predictive accuracy. The developed regression models can assist in forensic identification and legal documentation, highlighting the importance of population-specific data in forensic odontology.

***Keywords*: Age Determination by Teeth, Pulp Cavity, Secondary Dentin.**

INTRODUCTION

Oral health is closely linked to systemic well-being, with poor dental status associated with conditions such as cardiovascular disease and diabetes (Kaushik et al., 2018). Teeth, essential for mastication and as a barrier to pathogens, undergo significant structural changes throughout life [1]. Humans possess two dentitions: 20 primary teeth and 32 permanent teeth, each with distinct anatomical features [2]. The tooth's crown is covered by enamel, the hardest tissue in the body, while underlying dentin and pulp play critical roles in sensory function and defense [3,4]. With age, secondary dentin deposition reduces pulp chamber volume, compromising regenerative capacity and increasing susceptibility to necrosis [5].

Traditional age estimation in forensic dentistry relied on two-dimensional (2D) radiographs, which are limited by anatomical overlap and distortion, often resulting in inconsistent pulp/tooth ratio (PTVR) measurements [6]. While biochemical methods such as aspartic acid racemization have been explored, their invasiveness limits practical application [7].

The introduction of cone beam computed tomography (CBCT) has revolutionized dental imaging, enabling high-resolution three-dimensional (3D) visualization of pulp and tooth structures with reduced radiation exposure [8, 9]. Studies have demonstrated strong correlations between CBCT-derived PTVRs and chronological age, supporting its use in forensic age estimation [10, 11]. However, challenges remain,

including variability in imaging protocols and a lack of population-specific data, particularly for underrepresented groups such as the Kurdish population [12].

Given the scarcity of research on dental age estimation in the Kurdish population and the limitations of previous methods, this study is necessary to provide accurate, population-specific age estimation models. The novelty lies in applying CBCT-based PTVR analysis to a homogeneous Kurdish sample in Sulaimaniah, addressing both single- and multi-rooted teeth. The aim was to establish a reliable, non-invasive method for chronological age estimation, enhancing forensic and clinical applications in this unique demographic.

METHODS AND MATERIALS

Study design and setting

This cross-sectional observational study was conducted at the Family Dental Clinic, Chwarbax Street, Sulaimaniah, Iraq, over a 13-month period (February 2024–March 2025).

Participants

Participants were Kurdish adults aged 16–40 years who underwent CBCT imaging at the clinic for routine dental diagnostics. Eligible individuals were identified through retrospective review of archived scans and prospective recruitment during the study period. Stratified sampling ensured proportional representation across nine age groups (16–19, 20–24, 25–29, 30–34, 35–39, 40-44, 45-49, 50-54, 55-60, years).

A stratified random sampling method was used. Sample size was calculated using G*Power (v3.1.9.7) based on a pilot correlation (r=0.52) between age and PTVR, yielding a minimum of 194 participants (α=0.05, power=80%). Allowing for attrition, 246 participants were included.

Participants were included if they were aged >16 years, self-identified as Kurdish, had at least one fully erupted and intact permanent tooth (excluding third molars), provided high-quality CBCT scans in DICOM format, and gave informed consent for the use of anonymized data. Individuals were excluded if they had dental trauma, caries, or restorations affecting the pulp, a history of orthodontic or periodontal surgery, systemic diseases influencing dentine deposition, previous endodontic treatment on the examined teeth, or poor-quality CBCT images.

Data Collection

CBCT scans were acquired using a standardized protocol (90 kVp, 5 mA, 8.9 s, voxel size 0.2 mm³, FOV 8×8 cm). DICOM files were imported into OnDemand 3D Dental software for segmentation. Individual teeth were isolated in axial, coronal, and sagittal planes. Grayscale thresholding (1,400–3,000 HU for dentine; 200–1,200 HU for pulp) differentiated tissues, with manual refinement to exclude non-tooth structures. 3D reconstructions enabled volumetric measurement of pulp and tooth, and PTVR was calculated as (pulp volume/tooth volume) × 100. Demographic and PTVR data were recorded in a secure, anonymized database.

Ethical Considerations

The study was approved by the Institutional Review Board of the College of Medicine, University of Sulaymaniyah (3170-29/09/2024). Written informed consent was obtained from all participants. Data were anonymized and stored securely, adhering to the Declaration of Helsinki.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics v27. Descriptive statistics summarized age and PTVR. Pearson's correlation assessed the relationship between age and PTVR. Multiple linear regression and one-way ANOVA (with Tukey post-hoc tests) evaluated predictors and group differences. Statistical significance was set at $p<0.05$.

RESULTS

The total number of participants examined was 246, among whom 117 were male and 129 were female. The mean age for males was 36.623 ± 11.594 years, while for females it was 36.379 ± 12.384 years. No statistically significant difference was observed in the mean age between males and females (Table 1).

Table 1. Mean ± (SD) of age by sex in in study participants

Sex	N	Age (Mean ±SD)	Min	Max	P-Value
Male	117	36.623 ± 11.594	16	58	0.873
Female	129	36.379 ± 12.384	16	60	
Total	246	36.495 ± 11.991	16	60	

The overall mean PTVR for central teeth was 0.033 ± 0.014. For central teeth in males, the mean PTVR was 0.033 ±0.013, and for females, it was 0.033±0.014. This difference in the mean PTVR for central teeth between genders was not statistically significant. The overall mean PTVR for canine teeth was 0.040 ± 0.015. In males, the mean PTVR

for canine teeth was 0.043 ± 0.016, while in females, it was 0.037 ± 0.013. A notable significant difference was observed in the mean PTVR for canine teeth between genders (P ≤ 0.001) (Table 2).

Table 2. Mean ± (SD) of PTVR in central and canine tooth by sex in in study participants.

Tooth Type	Total	Male	Female	P
Central	0.033 ± 0.014	0.033 ±0.013	0.033±0.014	0.659
Canine	0.040 ± 0.015	0.043 ± 0.016	0.037 ± 0.013	0.001

Table 3 shows the mean pulp-tooth ratio in central and canine teeth based on the participants' age groups. The most frequent age groups were 40–44 and 45–49 years. For the 45–49 years age group, the mean PTVR for central teeth was 0.022 ± .002, while for canine teeth, it was 0.029 ± 0.002. In the 40–44 years age group, the mean PTVR for central teeth was 0.026 ± 0.003, while for canine teeth, it was 0.034 ± 0.004.

Table 3. Mean ± (SD) of PTVR in central and canine tooth by age group in in study participants.

Age group (year)	N	PTVR (central teeth)	N	PTVR (Canine teeth)
16-19	24	0.057 ± 0.009	24	0.068 ± 0.011
20-24	26	0.049 ± 0.007	26	0.055 ± 0.011
25-29	30	0.043 ± 0.005	30	0.048 ± 0.005
30-34	29	0.034 ± 0.002	29	0.042 ± 0.004
35-39	29	0.031 ± 0.003	29	0.037 ± 0.005
40-44	32	0.026 ± 0.003	32	0.034 ± 0.004
45-49	35	0.022 ± .002	35	0.029 ± 0.002
50-54	26	0.017 ± 0.003	26	0.022 ± 0.005
55-60	15	0.015 ± 0.003	9	0.020 ± 0.009

A strong negative connection was detected between age and PTVR in central teeth among men (r = -0.94, P < 0.001). A significant negative connection was seen between age and PTVR in male canine teeth (r = -0.94, P < 0.001). This strong inverse Correlation was consistently observed across all tooth types in males (r = -0.94, P ≤ 0.001). In females, a significant inverse correlation was also observed between age and PTVR in central teeth (r = -0.94, P ≤ 0.001), as well as in canine teeth (r = -0.92, P ≤ 0.001). This significant inverse correlation was similarly evident across all tooth types in females (r = -0.94, P ≤ 0.001) (Table 4).

Table 4. Correlation between age and PTVR by sex.

Tooth Type	Male		Female	
	Pearson Correlation Coefficient	P-value	Pearson Correlation Coefficient	P-value*
Central	- 0.94	0.001	- 0.94	0.001
Canine	-0.94	0.001	-0.92	0.001
Total	-0.94	0.001	-0.91	0.001

*P-value calculated based on Spearman correlation coefficients

The correlation between age and PTVR according to tooth type is presented in Table 5. In central teeth, significant inverse correlations were observed between age groups and PTVR: for the 20–24-year group (r = -0.446, P ≤ 0.022), the 25–25 (r = -0.729, P ≤ 0.001), the 30–34 (r = -0.466, P ≤ 0.011), the 40–44 (r = -0.417, P ≤ 0.017), the 45–49 (r = -0.438, P ≤ 0.009), and the 55–60-year group (r = -0.687, P ≤ 0.005). No notable correlation was found between age and PTVR in the 16–19, 35-39, and 50-54 age groups. In canine teeth, significant inverse correlation were observed between age group 55–60-year and PTVR (r = -0.685, P ≤ 0.042), in other age groups, there was no correlation between age and PTVR.

Table 5. Correlation between age and PTVR by tooth type.

Age group (year)	Central tooth		Canine tooth	
	Pearson Correlation Coefficient	P-value	Pearson Correlation Coefficient	P-value
16-19	0.243	0.253	- 0.285	0.177
20-24	- 0.446	0.022	- 0.090	0.661

25-29	- 0.729	0.001	- 0.147	0.438
30-34	- 0.466	0.011	- 0.171	0.376
35-39	- 0.155	0.422	- 0.223	0.244
40-44	- 0.417	0.017	0.053	0.773
45-49	- 0.438	0.009	- 0.181	0.299
50-54	0.150	0.465	- 0.261	0.198
55-60	- 0.687	0.005	- 0.685	0.042

*P-value calculated based on Spearman correlation coefficients

The PTVR was used to estimate age using a linear regression model. Age and pulp perimeter had a substantial negative association ($P < 0.001$), as shown by the Pearson correlation coefficient between them, which had an R2 value of 0.929. Based on this, the regression line was validated, and the regression equation was utilized for age estimation. Due to the strong association between age and PTVR in central teeth, age estimation was conducted for men ($R^2 = 0.932$, $P \leq 0.001$) and females ($R^2 = 0.927$, $P \leq 0.001$) using the regression equation. Similarly, for canine teeth, age estimation was conducted for males ($R^2 = 0.918$, $P \leq 0.001$) and females ($R^2 = 0.902$, $P \leq 0.001$) based on the regression equation (Table 6).

Table 6. Estimating age in male and female. With the pulp–tooth volume ratio in the related equation of that tooth.

Tooth Type	Male	Female
	Estimating Age	Estimating Age
Central	Y = 36.623 – 62.786 PV/TV	Y = 36.379 – 63.348 PV/TV
Canine	Y = 36.623 – 63.716 PV/TV	Y = 36.379 – 66.207 PV/TV
Total	Y = 36.495 – 63.072 PV/TV	Y = 36.459 – 63.236 PV/TV

Due to the significant correlation between age and PTVR in central and canine teeth, age estimation for different age groups was performed using a regression equation. Age estimation in age groups based on PTVR in central teeth was as follows: In the age group 25-29 years ($R^2 = 0.706$, $P \leq 0.001$), In the age group 45-49 years ($R^2 = 0.403$, $P \leq 0.016$), and the age group 55-60 years ($R^2 = 0.654$, $P \leq 0.008$). Age estimation in age groups based on PTVR in canine teeth was as follows: In the age group 55-60 years ($R^2 = 0.649$, $P \leq 0.059$) (Table 7).

Table 7. Age estimation in age groups. With the pulp–tooth volume ratio in the related equation of that tooth.

Age group (year)	Central tooth	Canine tooth
	Estimating Age	Estimating Age
16-19	Y = 17.333 – 18.253 PV/TV	Y = 17.333 – 19.252 PV/TV
20-24	Y = 22.076 – 25.330 PV/TV	Y = 22.076 – 23.388 PV/TV
25-29	Y = 26.866 – 34.905 PV/TV	Y = 26.866 – 28.743 PV/TV
30-34	Y = 31.965 – 39.576 PV/TV	Y = 31.965 – 33.712 PV/TV
35-39	Y = 37.034 – 38.824 PV/TV	Y = 37.34 – 39.381 PV/TV
40-44	Y = 41.843 – 45.435 PV/TV	Y = 41.843 – 43.305 PV/TV
45-49	Y = 46.685 – 50.652 PV/TV	Y = 46.685 – 49.794 PV/TV
50-54	Y = 51.846 – 52.309 PV/TV	Y = 51.846 – 53.246 PV/TV
55-60	Y = 57.333 – 61.822 PV/TV	Y = 57.333 – 57.976 PV/TV

DISCUSSION

Teeth are recognized as highly resilient to environmental and systemic influences, making them ideal for forensic age estimation, especially when other skeletal markers are compromised [13]. The present study demonstrated a significant negative correlation between PTVR and chronological age in both central incisors and canines among Kurdish adults, confirming that PTVR decreases as age increases [14]. This finding aligns with previous research, which consistently reported an inverse relationship between PTVR and age, supporting the use of secondary dentin deposition as a reliable marker for age estimation [15, 16]

Historically, 2D radiographic methods such as panoramic and periapical radiographs were used for age estimation, but these techniques are limited by image distortion and anatomical overlap [17]. The advent of CBCT has enabled more accurate, three-dimensional assessment of pulp and tooth volumes, overcoming the limitations of 2D imaging [18]. Comparative studies have shown that CBCT-based volumetric analysis provides higher predictive accuracy for age estimation than 2D methods [19].

The use of CBCT in this study provided a significant

methodological advantage, as three-dimensional volumetric analysis offers greater accuracy and reproducibility compared to traditional two-dimensional radiographic techniques, which are prone to distortion and anatomical overlap [18]. This is in line with the findings of Mangulkar et al. [19], and Santos et al.[20], who reported that CBCT-based PTVR measurements yield higher predictive accuracy for age estimation than 2D methods. The high coefficient of determination ($R^2 > 0.90$) observed in our regression models further underscores the robustness of volumetric PTVR as an age predictor, echoing results from Anjani et al. [21], and Salma and Abdelfatah [22].

Sex-based differences in PTVR were observed in canine teeth, with males exhibiting higher mean values than females, a trend also reported by Manan et al.[23]. However, no significant sex difference was found in central incisors, which aligns with the findings of Safaei et al. [24], and Shafiei Rad et al. [25]. These results suggest that while sex may influence pulp volume in certain tooth types, central incisors remain a stable marker for age estimation across genders.

Notably, the strength of the correlation between PTVR and age varied across age groups. The association was weaker in younger participants, likely due to greater biological variability and less pronounced secondary dentin deposition in early adulthood [26]. This highlights the need for age-specific calibration of regression models and suggests that volumetric PTVR analysis may be most reliable in middle-aged and older adults.

Overall, this study provided a high-precision, population-specific model for age estimation in Kurdish adults, reinforcing the necessity of tailored approaches that consider genetic and environmental factors. Future research should expand sample diversity and explore advanced modeling techniques to further enhance accuracy.

While focusing on a specific ethnic population allowed for the development of a regionally tailored regression model, this approach limits the generalizability of the findings to other populations. The predictive strength of the regression model varied across age groups, likely due to small sample sizes in certain strata and the non-linear nature of secondary dentin deposition at different life stages. Furthermore, the study did not account for potential confounding factors such as systemic health conditions, subtle prior dental treatments, dietary habits, or orthodontic interventions, which may influence secondary dentin formation and thus affect the accuracy of age estimation models.

CONCLUSIONS

This study demonstrated that the PTVR in central incisors and canines, as measured by CBCT, is a highly reliable and effective parameter for age estimation in adults, showing a strong negative correlation with chronological age. The linear regression models developed exhibited excellent predictive accuracy, confirming PTVR as a valuable tool for forensic and legal age assessment in the Kurdish population. These findings highlight the importance of using population-specific models and support the practical application of CBCT-based PTVR analysis in forensic and anthropological contexts.

DECLARATIONS

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Ethics approval and consent to participate

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ORIGINAL RESEARCH

THE IMPACT OF CAFFEINE ON SLEEP QUALITY AND MENTAL HEALTH AMONG DENTAL STUDENTS IN ERBIL CITY, KRG/IRAQ

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ABSTRACT

Background: Caffeine is a widely consumed psychoactive substance, often used by university students to enhance alertness and cognitive performance. However, excessive caffeine intake may negatively impact sleep quality and mental health, particularly among students in demanding academic fields such as dentistry.

Objective: This study aims to assess the impact of caffeine consumption on sleep quality and mental health among dental students in Erbil City, Kurdistan Region of Iraq. It examines caffeine intake patterns and their association with sleep disturbances and psychological well-being.

Methods: A cross-sectional study was conducted among 450 dental students from universities in Erbil. Data were collected through a self-administered questionnaire consisting of four sections: socio-demographic characteristics, caffeine intake assessment (Modified Caffeine Intake Questionnaire), sleep quality evaluation (Pittsburgh Sleep Quality Index), and mental health assessment (Depression, Anxiety, and Stress Scale-21). Statistical analysis was performed using SPSS version 28, with significance set at $p \leq 0.05$.

Results: The majority of participants (68.2%) were female, and most (65.6%) were aged 21-23 years. About 62% consumed ≤400 mg of caffeine daily, with coffee and tea being the most common sources. Sleep disturbances were prevalent, with 46% of students reporting ≤6 hours of sleep per night. Mental health assessment revealed that 42.9% of participants experienced varying degrees of dysphoria, hopelessness, and anxiety. A significant association was found between high caffeine intake and poor sleep quality, as well as increased symptoms of depression, anxiety, and stress ($p < 0.05$).

Conclusion: Excessive caffeine consumption among dental students in Erbil is associated with poor sleep quality and negative mental health outcomes. Awareness programs and strategies promoting healthier sleep hygiene and responsible caffeine use are recommended to mitigate these effects.

Keywords: Caffeine, Sleep Quality, Mental Health, Dental Students, Erbil, Iraq

INTRODUCTION

Caffeine, a widely consumed psychoactive substance, plays a significant role in the daily routines of many individuals worldwide. It is commonly found in beverages such as coffee, tea, energy drinks, and soft drinks, as well as in certain medications. While moderate caffeine consumption is often associated with enhanced alertness and improved cognitive performance, excessive intake can have adverse effects, particularly on sleep quality and mental health.[1] University students, especially those in demanding academic fields such as dentistry, frequently consume caffeine to combat fatigue and maintain focus during long study hours. However, this coping mechanism may lead

to disrupted sleep patterns and contribute to mental health issues, including anxiety and depression.[2, 3]

Studies have indicated that chronic sleep deprivation can exacerbate mental health challenges, creating a potentially harmful cycle for students relying on caffeine to manage their academic demands.[4] Sleep quality is a critical determinant of overall health and well-being, directly influencing cognitive performance, emotional regulation, and physical health. Poor sleep hygiene and insufficient rest are associated with a range of negative outcomes, including reduced academic performance and increased risk of developing psychiatric disorders.[5, 6] Caffeine, while beneficial in small doses, can interfere with the ability to achieve restorative sleep by delaying sleep onset, reducing sleep duration, and altering sleep architecture.[7] Mental health is another vital concern, particularly among students who face the dual pressures of academic and personal responsibilities. Research suggests a bidirectional relationship between caffeine consumption and mental health, where high intake levels may exacerbate symptoms of stress and anxiety, while individuals with existing mental health issues may consume caffeine to self-medicate,further complicating their conditions.[8, 9] Moreover, studies highlight that gender differences may influence caffeine's effects, with females reporting greater sensitivity to its impact on sleep and mood compared to males.[10] The timing and frequency of caffeine intake also play a significant role, as late-day consumption is more likely to disrupt sleep patterns and increase daytime fatigue.[11] Evidence suggests that students with pre-existing poor sleep hygiene are more prone to excessive caffeine use, compounding their sleep and mental health challenges.[12] In addition, heavy caffeine users often report higher levels of academic-related stress, indicating a complex interaction between lifestyle factors and psychological well-being.[13]

This study aims to assess the impact of caffeine consumption on sleep quality and mental health outcomes among dental students in Erbil City, Kurdistan Region of Iraq. The objectives were to characterize the habitual caffeine intake within this group. It will further investigate the potential association between these caffeine consumption patterns and sleep quality and mental health status, according to researchers' knowledge no similar study had been done in Erbil city among this group of population.

MATERIALS AND METHODS

Study design and setting: Cross sectional study was designed for the current study in which a convenience sample of students aged 18 years or older presented with the impact of caffeine on sleep quality and mental health. The study conducted at dentistry colleges in Erbil-Kurdistan region of Iraq and carried out from 5th of July 2024 to 15th of December 2024.The researchers investigated the potential association between caffeine consumption patterns and sleep quality and mental health status among dental students.

Method and data collection: The study conducted with enrolling a convenience sample size of from medical university students across Erbil city. The process of data collection was done via using self- administered questionnaire including four sections first section A: socio-demographic data comprising (gender, age, year of study, household income, marital status), following by section B: modified caffeine intake (MCI) questionnaire, section C: Pittsburgh sleep quality index (PSQI) for measuring sleep quality and finally section D: depression, anxiety, and stress 21 scale (DASS-21) for assessing negative emotional states. Caffeine intake was assessed using MCI, with daily caffeine intake calculated based on total consumption of coffee, tea, caffeinated beverages, and energy drinks. PSQI measured sleep quality over the previous four weeks, while DASS-21 evaluated depression, anxiety, and stress levels. Data were collected using a convenience sampling technique to collect information on target population in an approachable manner.

Data management and statistical analysis: The data recorded on a specially designed questionnaire, collected and entered in the computer via Microsoft Excel worksheet (Excel 2016) and then analyzed using appropriate data system which is called Statistical Package for Social Sciences (SPSS) version 28 and the results were compared between patients with different variables, with a statistical significance level of ≤ 0.05. The results presented as rates, ratio, frequencies, percentages in tables and figures and analyzed using t-test, and Chi square tests.

Inclusion criteria: Inclusion criteria comprised of medical students aged more than 18 years who were intaking caffeine regardless of their gender were enrolled. Participants who were interested in taking part in the study and those who met the specified criteria were included in the study.

Exclusion criteria: Exclusion criteria included students outside medical fields who aged less than 18 years old. Respondents who did not give consents to participate in the research, furthermore students who did not meet the criteria were excluded in the study.

Ethical considerations: This study was submitted to the Ethics and Scientific committees of Family Medicine Research Ethics Committee at Kurdistan Higher council of Medical Specialties for scientific and ethical approval. This study was explained and a verbal consent was obtained from each student. Confidentiality and anonymity of data were ensured.

RESULTS

A total of 450 participants enrolled in our study, most (68.2%) of them were female and 21-23 year group had the highest (65.6%) age amount following by 26.7% of them were 18-20 years old and the least amount (0.7%) categorized under 27 years and above, the vast majority (97.3%) of cases were single, more than one third 34.2% of them were studying at fourth grade and only 8.7% were fifth graders, more than half (52.2%) of students had high (more than 1 million IDQ) income and lowest income (Less than 250.000 IDQ) was for 14.2% of students, the majority (82%) of them were unemployed, 46% of them were sleeping for ≤6 hours and finally 17.3% of students had normal schedule of sleep (6-8 hours) (Table 1 and Figure 1).

Table 1. Sociodemographic characteristics of participants.

Variables	Categories	Frequency	Percent
Gender	Male	143	31.8
	Female	307	68.2
Age	18 - 20	120	26.7
	21 - 23	295	65.6
	24 - 26	32	7.1
	27 and above	3	0.7
Marital status	single	438	97.3
	married	12	2.7
Grade	First	56	12.4
	Second	86	19.1
	Third	115	25.6
	Fourth	154	34.2
	Fifth	39	8.7
Income	Low (Less than 250.000) IDQ	64	14.2
	Moderate(250-1Million) IDQ	151	33.6
	High (More than 1Million)	235	52.2
Job	Yes	81	18
	No	369	82
sleeping	≤6 hours	207	46
	6 - 8 hours	78	17.3
	>8 hours	165	36.7
Total		450	100%

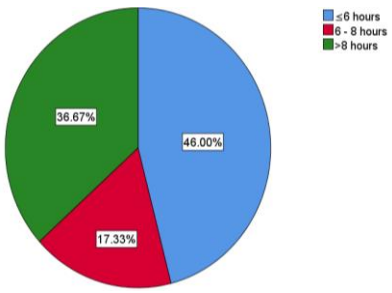


Figure 1. Sleeping hours of participants.

Table 2 shows that most (72.7%) of students were smokers, 62% of them were drinking caffeine (MCI) ≤ 400mg/day, 28.7% of participants were drinking coffee four times/day and 19.5% were consuming only one time/day, the highest tea consumption was 37.6% among students one time/day and lowest consumption was three times/ day for 2.7% of students, 23.6% of respondents were involved with energy drinks four times a day and only 7.8% had energy drinks twice a day, 23.6% of the sample size were having carbonated drinks four times a day and finally only 3.3% of them had soft drinks once a day.

Table 2. Smoking and consuming beverages among students.

Variables	Categories	Frequency	Percent
Smoking	Yes	327	72.7
	No	123	27.3
Caffeine (MCI)	0 mg/day	57	12.7
	≤ 400mg/day	279	62
	> 400mg/day	114	25.3
Coffee consumption	0 times a day	95	21.1
	1 Time/ day	88	19.6
	2 Times/day	60	13.3
	3Times/day	78	17.3
	4 Times/day	129	28.7
Tea consumption	0 times a day	122	27.1
	1 Time/ day	169	37.6
	2 Times/day	41	9.1
	3Times/day	12	2.7
	4 Times/day	106	23.6
Energy drinks	0 times a day	256	56.9
	1 Time/ day	52	11.6
	2 Times/day	35	7.8
	3Times/day	1	0.2
	4 Times/day	106	23.6
Carbonated drinks	0 times a day	262	58.2
	1 Time/ day	15	3.3
	2 Times/day	58	12.9
	3Times/day	9	2
	4 Times/day	106	23.6
Total		450	100%

Table 3 reveals that dysphoria condition applied to 19.8% of students to some degree, and 9.3% of them dysphoria applied most of the time, hopelessness, devaluation, self-deprecation, Anhedonia and inertia applied to 20.9% of students to some degree following by applied to 12.7% to a considerable degree and 9.3% of them experienced the conditions most of the time or very much, finally more than half 57.1% of respondents did not apply any sort of mental issues on them.

Table 3. Mental issues among participants.

Variables	Categories	Frequency	Percent
Dysphoria	Did not apply to me at all	262	58.2
	Applied to me to some degree, or some of the time	89	19.8
	Applied to me to a considerable degree or a good part of the time	57	12.7
	Applied to me very much, or most of the time	42	9.3
Hopelessness	Did not apply to me at all	257	57.1
	Applied to me to some degree, or some of the time	94	20.9
	Applied to me to a considerable degree or a good part of the time	57	12.7
	Applied to me very much, or most of the time	42	9.3
Devaluation	Did not apply to me at all	257	57.1
	Applied to me to some degree, or some of the time	94	20.9
	Applied to me to a considerable degree or a good part of the time	57	12.7
	Applied to me very much, or most of the time	42	9.3
Self-deprecation	Did not apply to me at all	257	57.1
	Applied to me to some degree, or some of the time	94	20.9
	Applied to me to a considerable degree or a good part of the time	57	12.7
	Applied to me very much, or most of the time	42	9.3
Anhedonia	Did not apply to me at all	257	57.1
	Applied to me to some degree, or some of the time	94	20.9
	Applied to me to a considerable degree or a good part of the time	57	12.7
	Applied to me very much, or most of the time	42	9.3
Inertia	Did not apply to me at all	257	57.1
	Applied to me to some degree, or some of the time	94	20.9
	Applied to me to a considerable degree or a good part of the time	56	12.4
	Applied to me very much, or most of the time	43	9.6
Total		450	100%

Table 4 shows that autonomic arousal, muscle effect and situational anxiety appealed to 18.2% of students some of the time, 12.2% of cases had autonomic arousal also 12.7% for each muscle effect and situational anxiety applied most of the time, more than half (53.1%) of respondents did not experience any subjective anxiety, difficulty relaxing and nervous arousal while 18.2% of students faced all three conditions to some degree, 14% of cases had subjective anxiety to a considerable degree following by difficulty relaxing had a population of 9.3% and nervous arousal 10.2% to a considerable degree.

Table 4. Mental disorders among students

Variables	Categories	Frequency	Percent
Autonomic arousal	Did not apply to me at all	247	54.9
	Applied to me to some degree, or some of the time	82	18.2
	Applied to me to a considerable degree or a good part of the time	66	14.7
	Applied to me very much, or most of the time	55	12.2
Muscle Effect	Did not apply to me at all	247	54.9
	Applied to me to some degree, or some of the time	82	18.2
	Applied to me to a considerable degree or a good part of the time	64	14.2
	Applied to me very much, or most of the time	57	12.7
Situational anxiety	Did not apply to me at all	247	54.9
	Applied to me to some degree, or some of the time	82	18.2
	Applied to me to a considerable degree or a good part of the time	64	14.2
	Applied to me very much, or most of the time	57	12.7
Subjective anxiety	Did not apply to me at all	239	53.1
	Applied to me to some degree, or some of the time	89	19.8
	Applied to me to a considerable degree or a good part of the time	63	14
	Applied to me very much, or most of the time	59	13.1
Difficulty relaxing	Did not apply to me at all	285	63.3
	Applied to me to some degree, or some of the time	89	19.8
	Applied to me to a considerable degree or a good part of the time	42	9.3
	Applied to me very much, or most of the time	34	7.6
Nervous arousal	Did not apply to me at all	285	63.3
	Applied to me to some degree, or some of the time	89	19.8
	Applied to me to a considerable degree or a good part of the time	46	10.2
	Applied to me very much, or most of the time	30	6.7
Total		450	100%

Issues as upset agitated, irritable and impatient appealed to 19.6% of cases to some degree tracking the situation applied a good part of the time to 10.2% of them, most of the time all three mentioned experienced by only 6.9% and finally most (63.3%) of the sample size did not have the conditions at all. (Table 5)

Table 5. Psychological problems among respondents

Variables	Categories	Frequency	Percent
Upset agitated	Did not apply to me at all	285	63.3
	Applied to me to some degree, or some of the time	88	19.6
	Applied to me to a considerable degree or a good part of the time	46	10.2
	Applied to me very much, or most of the time	31	6.9
Irritable	Did not apply to me at all	285	63.3
	Applied to me to some degree, or some of the time	88	19.6
	Applied to me to a considerable degree or a good part of the time	46	10.2
	Applied to me very much, or most of the time	31	6.9
Impatient	Did not apply to me at all	285	63.3
	Applied to me to some degree, or some of the time	88	19.6
	Applied to me to a considerable degree or a good part of the time	46	10.2
	Applied to me very much, or most of the time	31	6.9
Total		450	100%

Results of Table 6 discover that there was a statistically significant association between sleeping and caffeine, most (59.6%) of those who consumed > 400mg/day had ≤6 hours while 48.7% of ≤ 400mg/day group consumers had the same amount of sleeping. There was a statistically significant association between sleeping and coffee consumption, most (59.1%) of students with one time a day drinking coffee had >8 hours of sleeping while only 4.7% of four times a day coffee drinkers had the same sleeping hours.

According to tea consumption there was a significant statistical association with sleeping hours, those who were drinking tea four times a day were divided into first the majority (95.3%) who slept ≤6 hours and second only 4.7% of them had more than eight hours of sleep. There was a significant statistical association between sleeping and energy drinks, all (100%) of participants who consumed energy drinks three and four times a day had ≤6 hours of sleep while none (0%) of them had regular 6-8 hours or more than eight hours of sleep.

There was a significant statistical association between sleeping and carbonated drinks, 46.7% of those who were drinking soft drinks once a day had 6-8 hours of sleep while only 6.9% of those who were drinking carbonated drinks twice a day had regular 6-8 sleeping hours. Chi square test was significant and p-value was < 0.05.

Table 6. Association between sleep disturbance and coffee, caffeine, energy and carbonated drinks

Variable	Categories	Sleeping			p-value
		≤6 hours	6 - 8 hours	>8 hours	
Caffeine (MCI)	0 mg/day	3 (5.3%)	12 (21.1%)	42 (73.7%)	0.001
	≤ 400mg/day	136 (48.7%)	51 (18.3%)	92 (33%)	
	> 400mg/day	68 (59.6%)	15 (13.2%)	31 (27.2%)	
Coffee consumption	0 times a day	4 (4.2%)	28 (29.5%)	63 (66.3%)	0.001
	1 Time/ day	5 (5.7%)	31 (35.2%)	52 (59.1%)	
	2 Times/day	15 (25%)	17 (28.3%)	28 (46.7%)	
	3Times/day	60 (76.9%)	2 (2.6%)	16 (20.5%)	
	4 Times/day	123 (95.3%)	0 (0%)	6 (4.7%)	
Tea consumption	0 times a day	28 (23%)	43 (35.2%)	51 (41.8%)	0.034
	1 Time/ day	63 (37.3%)	26 (15.4%)	80 (47.3%)	
	2 Times/day	10 (24.4%)	6 (14.6%)	25 (61%)	
	3Times/day	5 (41.7%)	3 (25%)	4 (33.3%)	
	4 Times/day	101 (95.3%)	0 (0%)	5 (4.7%)	
Energy drinks	0 times a day	53 (20.7%)	64 (25%)	13 (54.3%)	
	1 Time/ day	14 (26.9%)	14 (26.9%)	24 (46.2%)	
	2 Times/day	33 (94.3%)	0 (0%)	2 (5.7%)	
	3Times/day	1 (100%)	0 (0%)	0 (0%)	
	4 Times/day	106 (100%)	0 (0%)	0 (0%)	
Carbonated drinks	0 times a day	73 (27.9%)	67 (25.6%)	122 (46.6%)	0.001
	1 Time/ day	6 (40%)	7 (46.7%)	2 (13.3%)	
	2 Times/day	17 (29.3%)	4 (6.9%)	37 (63.8%)	
	3Times/day	5 (55.6%)	0 (0%)	4 (44.4%)	
	4 Times/day	106 (100%)	0 (0%)	0 (0%)	
Total		207 (46%)	78 (17.3%)	165(36.7%)	

DISCUSSION

The findings of this study highlight several important sociodemographic and behavioral factors associated with sleep patterns and mental health among university students. The majority of participants were female (68.2%), single (97.3%), and aged between 21–23 years (65.6%). A significant proportion (46%) reported sleeping ≤6 hours per night, which is below the recommended 7–9 hours for young adults.[14] Only 17.3% had a normal sleep duration (6–8 hours), suggesting widespread sleep deprivation in this population.

The findings of this study provide valuable insights into the impact of caffeine consumption on sleep quality and mental health among dental students in Erbil. The results suggest a significant relationship between caffeine intake and various sleep disturbances, including reduced sleep duration, increased sleep latency, and poorer overall sleep quality this was inline with many other studies.[15, 16] Additionally, higher caffeine consumption was associated with increased levels of anxiety and stress among students. These findings are consistent with previous studies indicating that excessive caffeine intake can disrupt sleep patterns and negatively affect mental well-being.[17]

A strong association was found between high caffeine intake (>400 mg/day) and short sleep duration (≤6 hours), with 59.6% of high caffeine consumers reporting insufficient sleep. This aligns with previous research indicating that excessive caffeine intake, particularly in the afternoon or evening, disrupts sleep latency and quality.[18]

Additionally, coffee consumption frequency was significantly linked to sleep disturbances; 95.3% of students drinking coffee four times a day slept ≤6 hours,

whereas those consuming it once a day were more likely to sleep >8 hours (59.1%). This supports evidence that caffeine's half-life (5–6 hours) can delay sleep onset and reduce total sleep time.[7] This aligns with our findings, which indicate that dental students who consume caffeine regularly report difficulty falling asleep and experience fragmented sleep.

Furthermore, studies have established a link between caffeine and increased anxiety levels due to its stimulant effects on the central nervous system.[19] This was also observed in our study, where students with higher caffeine intake reported elevated stress and anxiety levels, supporting the hypothesis that caffeine exacerbates mental health challenges.

The impact of caffeine on sleep can be attributed to its antagonistic effects on adenosine receptors, which play a crucial role in promoting sleep. By blocking these receptors, caffeine increases alertness and reduces the sensation of fatigue, leading to prolonged wakefulness and disrupted sleep cycles.[20] Additionally, caffeine consumption, particularly in high doses, is associated with increased secretion of stress hormones such as cortisol, which may contribute to heightened anxiety and stress levels in students facing academic pressure.[21]

Energy drink consumption showed a particularly strong correlation with poor sleep, as all students consuming energy drinks 3–4 times daily reported ≤6 hours of sleep. This is consistent with studies linking energy drinks to increased insomnia and sleep fragmentation.[22] Similarly, carbonated drink intake was associated with reduced sleep duration, with 100% of those consuming them four times a day sleeping ≤6 hours. The high sugar and caffeine content in these beverages may contribute to sleep disturbances.[23]

A concerning proportion of students reported mental health issues, including dysphoria (19.8%), hopelessness (20.9%), and anxiety-related symptoms (18.2%). Poor sleep has been consistently linked to depression and anxiety in young adults.[24] The high prevalence of ≤6-hour sleepers (46%) may exacerbate these conditions, as sleep deprivation impairs emotional regulation and cognitive function.[25]

Implications for Dental Students

Given the demanding nature of dental education, students often rely on caffeine to enhance alertness and sustain academic performance. However, the findings of this study highlight the potential drawbacks of excessive caffeine consumption, particularly its detrimental effects on sleep quality and mental health. Poor sleep hygiene can negatively impact cognitive function, concentration, and academic performance, creating a vicious cycle where students resort to even higher caffeine intake to compensate for sleep deprivation.

Limitations and Future Directions

Despite the valuable insights provided by this study, certain limitations must be acknowledged. First, the cross-sectional nature of the study limits the ability to establish causality between caffeine consumption and sleep/mental health outcomes. Longitudinal studies are recommended to explore the long-term effects of caffeine on sleep patterns and mental well-being. Additionally, self-reported data on caffeine intake and sleep quality may be subject to recall bias. Future research could incorporate objective measures, such as actigraphy or polysomnography, to obtain more precise sleep assessments.

CONCLUSION

Sleep disturbances among university students are strongly associated with high caffeine intake, frequent energy drink consumption, and poor mental health. Interventions promoting sleep hygiene, caffeine moderation, and mental health support could mitigate these issues.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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REVIEW ARTICALE

EVOLUTION OF DENTAL IMPLANT AND IMPLANT SURFACE TREATMENTS- A NARRATIVE REVIEW

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ABSTRACT

Dental implants have undergone remarkable evolution over the past decades, transforming from simple experimental devices to highly predictable treatment modalities in modern dentistry. The earliest concepts of implantology were rooted in the search for biocompatible materials and mechanical stability, eventually leading to the revolutionary discovery of osseointegration. Since then, continuous advancements in implant design, surface morphology, and surface treatments have greatly enhanced clinical success rates. Early implants relied on smooth, machined surfaces, but clinical limitations such as longer healing times and unpredictable outcomes drove the development of modified surfaces. Techniques including sandblasting, acid etching, anodization, plasma spraying, and bioactive coatings have been introduced to improve bone–implant contact, accelerate osseointegration, and increase long-term stability. Recent innovations focus on nanostructured modifications, biomimetic approaches, and surface functionalization with growth factors, aiming to integrate biological and technological principles for superior clinical performance. This review highlights the historical progression of dental implants, the scientific rationale behind different surface treatments, and their clinical implications. Understanding these developments provides valuable insight into current trends and future directions in implant dentistry, emphasizing the role of surface engineering in optimizing osseointegration and enhancing patient outcomes.

Keywords*:* Dental implants, Osseointegration, Surface modification, Nanotechnology, Implantology

INTRODUCTION

Tooth loss has long been a challenge for humans, inspiring restorative attempts across civilizations. From ancient prosthetic practices using shells and ivory to today's sophisticated titanium implants, the pursuit of stable, functional tooth replacement reflects centuries of innovation [1,2].

A crucial turning point occurred with the discovery of osseointegration, establishing dental implants as a predictable therapeutic option. The role of implant surface design and modification has since become central to enhancing bone-implant interaction, reducing healing times, and improving long-term clinical performance. This review traces the historical development of dental implants, with emphasis on the evolution of surface treatments and their clinical significance. [3,4]

Historical Background

Early Civilizations and Primitive Restorations:

Archaeological evidence shows that Egyptians, Etruscans, and Mayans experimented with tooth replacement. Seashells, ivory, and stones were placed in alveolar sockets, while gold wires stabilized mobile teeth. The Mayans, around 600 AD, are credited with some of the earliest functional dental implants using carved shell fragments [5, 6].

Early Scientific Attempts (16th–19th Century): During the Renaissance, attempts to transplant cadaveric teeth became common. In 1809, Maggiolo reported placing a gold tube into an extraction site, though it resulted in severe inflammation. Later efforts included implants made of porcelain, silver, and iridium, reflecting ongoing trials with material compatibility [7, 8].

20th Century Innovations: Significant progress occurred in the early 1900s. In 1913, Dr. EJ Greenfield introduced a lattice-style iridio-platinum implant. The Strock brothers later tested Vitallium screw-type implants in both animals and humans. The mid-20th century saw the introduction of subperiosteal implants and early endosseous designs such as spiral and screw-shaped implants, laying the foundation for modern systems. [9, 10]

The Branemark Revolution: The defining milestone came in the 1950s when Per-Ingvar Brånemark discovered osseointegration while studying bone healing in rabbit models. By the 1960s, he successfully applied titanium screw implants in humans, establishing a long-lasting and predictable solution. His work formalized osseointegration as a direct structural and functional connection between living bone and titanium, revolutionizing implant dentistry [11, 12].

Milestone era of Dental implants

A two-stage threaded titanium root-form implant was introduced by Dr. P. Branemark in 1978. He also created and tested a method using pure titanium screws, which he referred to as fixtures.[13] These were the earliest, best-documented, and longest-lasting dental implants to date when they were originally implanted in his patients in 1965. Severe chin and jaw abnormalities, congenitally absent teeth, and misaligned teeth were present in Branemark's first case. The mandible underwent four implants. These implants took six months to integrate and stayed in place for the following 40 years. [13,14] When he implanted titanium chambers in rabbit femurs to study blood flow, he made this discovery by accident in 1952; over time, the chamber became firmly affixed to the bone and could not be removed.[12] In fact, the titanium surface connected with the bone. In reality, if a fracture did take place, it always happened between bones rather than between the bone and the implant. He used this concept to the field of dentistry. With the help of his implant, the term "osseointegration" and the belief that dental implant education may be added to dentistry school curricula were created. Branemark clarified and extended this phrase further, defining it as "a direct structural and functional relationship between organized, living bone and the surface of a load-bearing implant." The Branemark implant was first designed as a cylindrical one; later variations took on tapered shapes. After the Branemark implant, numerous other implant types were developed, such as the IMZ implant, the Stryker implant, the CoreVent implant. [14, 15] and the ITI-sprayed implant.



Trending of titanium implants

The endosseous root form implant was the type of implant that many dental professionals employed in the middle of the 1980s. In the early 1980s, Dr. Tatum developed the omni-R implant, which has horizontal titanium alloy fins. [16] Core-Vent Hollow Threaded Implant and Screw-Vent Implant with Hydroxyapatite Coating were both developed by Dr. Niznick. He began adding new technologies, such as Micro-Vent and Bio-Vent. [17] The root form endosseous implant was soon after introduced by Dr. Driskell in the 1980s in two variations: one coated with titanium alloy and the other with hydroxyapatite. Early in the 1980s, the calcite firm began producing calcitite, a synthetic polycrystalline ceramic hydroxyapatite. [18] The Straumman Company first offered an integral ITI implant system in 1985. The device comprises of plasma sprayed cylinders and screws which are designed to be placed in one stage procedure.

The use of titanium (Ti) dental implants and the procera (Nobel Biocare, Zurich, Switzerland) computer-aided design and computer-aided manufacture (CAD/CAM) method of high precession were both approved by the US Food and Drug Administration in 1982 and 1983, respectively. The development of materials and methods to increase quality and anchoring has made remarkable progress. In order to improve osseointegration, ceramic surface treatments have been integrated by manufacturer companies since the advent of contemporary ceramics in 1992. [19,20]

Evolution of Dental implant Surface coatings

The nature of the implant surface determines the response and has an impact on the mechanical strength of the implant tissue interface since the surface of dental implants is the only component that comes into contact with the bio-environment. The first osseointegrated dental implants had a machined or smooth machined surface.

These implants have surface markings from the devices used in their development and were cleaned and decontaminated. These surface flaws aid in the bonding of bone cells to the metal. Dental implants with machined surfaces have the drawback that bone-forming cells frequently migrate to the surface grooves. [21-23] The major goal of modifying dental implant surfaces is to speed up osseointegration healing. The surface treatment increases the functional surface area of the implant bone interface so that the stress is effectively distributed. Moreover, the surface treatment promotes bone apposition and influences the cytokine and growth factor production. [24,25] Various surface treatments include mechanical treatments; that is machining and grit blasting, acid etched chemical treatments, anodic oxidation through electrochemical treatments, thermal treatments and laser treatments.[26]



Hydroxyapatite coating and titanium plasma sprayed coatings

Hydroxyapatite (HA) has the ability to create robust connections between the implant and the bone. Recent research suggests that nano-hydroxyapatite-coated surfaces in the transmucosal area are just as compatible as pure titanium surfaces. [27,28] However, the possibility that the hydroxyapatite may experience resorption and additional deterioration, ultimately leading to the loosening of the titanium particles, has been documented in situations with plasma sprayed coatings. Composite coatings, titanium nitride coatings, carbon, glass, and ceramic coatings are examples of additional coating surfaces.

The thickness of the coating on the implant can be controlled to be between 40 and 50 micrometres using plasma spraying coating, which includes injecting powdered forms of titanium into the plasma torch at high temperatures. On the implant surface, this particle subsequently condenses and fuses together, increasing the production of TGF-beta 1 and inducing mineralization nodule. However, the plasma sprayed approach has a number of disadvantages, including irregular layer thickness and poor long-term coating adhesion.

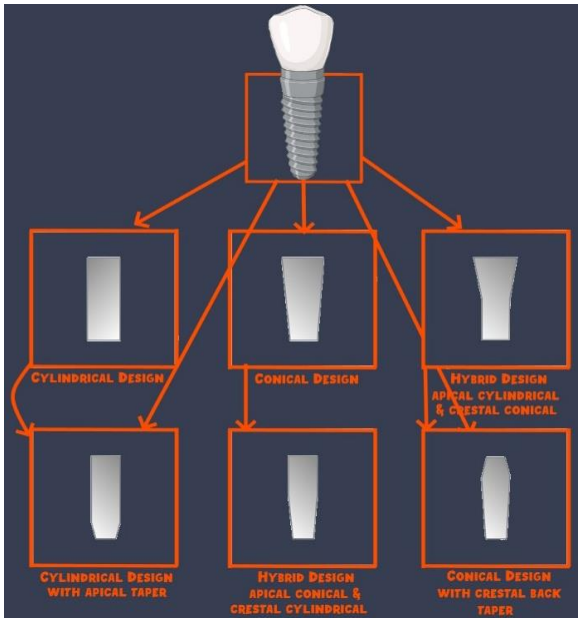


Sandblasted and etched implants

The formation of sandblasted and acid-etched implants involves a protracted blasting procedure, followed by etching with sulfuric and hydrochloric acids. For the blasting process, large grit titanium or alumina particles are utilized. This leads to surface abrasion with excellent bone integration. Compared to machined implants, titanium implants with alumina and titanium particles of 25 micrometre and 75 micrometre diameter promoted superior bone growth. [31-34]

Electrochemical dental implant surface treatment

Electrochemical anodic oxidation works first began in the 1950s. Using anodic oxidation, ceramic TiO_2 layers with thicknesses ranging from hundreds of nanometers to hundreds of micrometres can be formed on titanium substrates. Currently, titanium-based devices that have calcium phosphate molecules added to them have been used in clinical settings. Due to its many benefits, including its ease of use and low cost, ability to improve coating adhesion, interfacial bonding, and corrosion resistance, and ability to increase mechanical compatibility of the coating by creating porous structures with excellent cell colonization potential, anodic oxidation has gained popularity in recent years in the surface modification of titanium. [35,36]



Laser and growth factor treatments

Another technique to improve bone-to-metal interactions is surface preparation by laser ablation of dental implants. This process produces titanium microstructure surfaces that are extremely hard, highly resistant to weakening, have exceptional roughness, and have an enhanced oxide layer.[37] According to biological studies, there are grooved surfaces that facilitate cell adhesion and control how they grow [38].

On titanium implant surfaces, growth factors include bone morphogenetic proteins (BMPs), platelet-derived growth factor (PDGF), and TGF-beta 1 promote bone repair.[39] Goats have been used to study the effects of applying TGF- beta1 to calcium-phosphate implant surfaces.[40-43] The disadvantage in the use of growth factors in treating the surfaces of implants is that the active growth factor has to be released over a period of time.[44]

Current implant design trends

1. Analyzing with finite elements (FEA)

In order to analyze the jaw bone and the boning-implant interface and to optimize implant design so that it functions in accordance with bone stress distribution, FEA has become a widely used technique in implant dentistry. To forecast the properties of the stress distribution in bone within physiological bounds, it comprises of three-dimensional models. [45]

2. CAD/CAM modern dental implant technology

Employing three-dimensional printing, a personalized implant (3DP) was initially applied to quick prototyping and tooling. In the beginning, 3DP produced unique, customized items for restorative dentistry. Dental labs can generate dental prostheses (crowns, bridges) and plaster/stone models more quickly and with good precision by integrating oral scanning with a CAD/CAM design and employing 3DP thanthe majority of traditional techniques carried out by lab staff. [46]

The use of CAD/CAM as a supportive tool to enhance the outcomes of implant therapy has increased with the development of implant dentistry. For challenging circumstances where traditional abutments might not offer a good choice for a future prosthesis, customized implant abutments have been successfully manufactured utilizing CAD/CAM

Complex shaped implants and abutments have been produced using CAD-CAM technology. The accuracy of these methods is improved. [47-48]

The use of cone beam computed tomography (CBCT) combined with CAD/CAM was suggested to produce a surgical guide for implant placement

3DP and CAD/CAM have been involved in practically every area of implant dentistry. When a patient needs an implant to replace a single tooth, the tooth must be extracted during the initial procedure, and only then may the implant be placed during a subsequent procedure. To avoid the need for a second surgery and to allow for quick implantation, it would appear more efficient to have the personalized implant ready before tooth extraction. [49]

3. Implants made with nanotechnology

For dental implants, nanotechnology-based developments include biomimetic calcium phosphate coatings, the addition of growth hormones to speed up bone repair, and surface roughness modification at the nanoscale level to improve protein adsorption and cell adhesion. [50]

Only a few research have revealed changes to the roughness as well as the chemistry at the nanoscale scale in a repeatable manner, despite the fact that most attempts to obtain Nano roughness have used processing techniques such lithography and surface laser-pitting. Another strategy is to coat Ti surfaces with nanoparticles such as biomimetic calcium phosphate, alumina, titania, zirconia, and other minerals. Additionally, to boost up the local bone-healing process, Ti dental implants can also be coated with bone-stimulating substances like growth factors (such as transforming growth factor-, bone morphogenetic proteins [BMPs], platelet-derived growth factors, and insulin-like growth factor [IGF]-1 and 2) and antiresorptive medications (bisphosphonates). [50-51]

Various nanoparticles used in dental implants and their applications are shown in table 1.

Table 1. Various Nanoparticles and its applications in Dental Implants

Nanoparticle	Utilization method	Application	References
Silver	1. A layer of 9.3, 21.3, and 98 nm thickness coated on the enamel surface 2. Coated as a colloidal. 3. Coating of Sliver and amorphous nanoparticles of the synthetic calcium phosphate. 4. Improved by chitosan with fluoride mixture, and placed as a colloidal suspension yearly one-time	Anti-bacterial treatments Antibacterial treatment Resin-composite fixatives Mouth-freshener	Espinosa-Cristóbal et al., 2013[52] Huang et al., 2011[53] Cheng et al., 2012. [54] Dos Santos et al., 2014[55]
Zirconium oxide	1. Coating material + Nano-hydroxyapatite 2. Coated with Ca/PO4 3. Inclusion into dental resins 4. Anti-bacterial agents for peri-implantitis 5. Inclusion into dental cement	Dental implant Cement sealants Resins-composite fixatives Dental cement Treatments of antibacterial implant	Memarzadeh et al., 2015 [56] Osorio et al., 2014[57] Kasraei et al., 2014[58] Vargas-Reus et al., 2012[59] Guerreiro-Tanomaru et al., 2014 [[60]
Titanium dioxide	1. conjunction with bright-healing orthodontic paste 2. nanotubes integrated into ZnO NPs on Ti surfaces 3. Adhered in the same liquid to improve hydrogen peroxide bleaching performance	In Resins composites fixatives Implant. Bleaching agents	Poosti et al., 2013[61] Liu et al., 2014[62] Martín et al., 2015[63]
Cuprous oxide	1. Relative to TiO2, Ag + CuO, Ag + ZnO & also WO4 which compositions had anti-microbial impact.	Resins-composite fixatives	Vargas-Reus et al., 2012[64]
Chitosan-particles	1. Combined with silver NPs 2. It's being used as a chelating agent in a nano-hydroxyapatite-coated Ti implant	Resins-composite fixatives Implants	Targino et al.,2014[65] Kim et al., 2013[66]
QAC Nanostructures	1. Coated as a quatemarian ammonium compound with 2. An organosilane, silicon NPs, and epoxy silicate 3. Resin composite materials as a cross-linking quintenary ammonium polyethyleneimine (QPEI)	Resins composite fixatives Resins composite-materials	Gong et al., 2014 [67] Beyth et al., 2010[68-70]

The journey of dental implants reflects a rich convergence of material science, biomechanics, and clinical ingenuity. What began with primitive attempts using natural substances has evolved into highly engineered titanium systems that define modern implantology.[1-10] A turning point came with Brånemark's discovery of osseointegration, which laid the biological groundwork for predictable and long-lasting implant success.

Among the many factors influencing implant performance, surface modification stands out as particularly impactful. Techniques like sandblasting, acid etching, anodization, and plasma spraying has each contributed to improving bone–implant contact and speeding up integration.[10-20]

Yet, none are without drawbacks—plasma-sprayed coatings, for example, may struggle with adhesion over time, while hydroxyapatite layers can degrade under certain physiological conditions.[20-25] Emerging technologies such as nanostructured surfaces and

biomimetic coatings are pushing the boundaries of implant design. By incorporating nanoparticles, growth factors, and bioactive agents, researchers aim to recreate the bone's natural microenvironment and enhance cellular interactions. These innovations are promising, but they also raise important questions about long- term safety, cost, and clinical viability questions that demand thorough investigation.[25-40]

Despite the growing array of surface treatments, direct comparisons between them remain scarce. Few studies have rigorously evaluated different approaches under consistent clinical conditions. Meanwhile, digital tools like CAD/CAM and finite element analysis has refined implant design, but their influence on biological outcomes is still being explored.[40-70]

This review highlights the importance of bridging laboratory advances with clinical realities. Moving forward, collaborative research efforts should focus on well-designed clinical trials, longitudinal studies, and systematic reviews to guide evidence-based decisions in surface treatment selection.

Summary and future research

In conclusion, the history of dental implants has been a stunning and fascinating journey of growth and progress. One can only pause and marvel at how inventive man has been throughout the ages in this area of research and investigation. A variety of materials, including gold ligature wire, shells, ivory, chromium, cobalt, iridium, and platinum, were initially used to create dental implants. The gaps once held by natural teeth have been filled with a range of structures, from spiral stainless steel implant designs to double helical inventions and endosseous root shapes, thanks to the swift and tenacious work of dental researchers and doctors. Dental surfaces were also modified to hasten the healing of osseointegration.

Hydroxyapatite, composites, carbon, glass, ceramic, and titanium oxide were all used to create changed surfaces. Dental implant research has advanced over time, and new materials, shapes, and surface coatings have been developed to offer people the greatest tooth replacement options for their immediate and long-term need.

DECLARATION

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

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ENHANCING COLLEGE STUDENTS' COMPETENCIES THROUGH COURSE ASSESSMENT, STUDENT ACTIVITIES, AND TEACHING SERVICES: EVIDENCE FROM A CHINESE PRIVATE UNIVERSITY

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ABSTRACT

The enhancement of students' general and professional competencies has become a key indicator of educational quality in higher education. This study investigates the influence of course assessment, student activities, and teaching services on competence enhancement, drawing on the customer satisfaction theory (ACSI) and expectation disconfirmation theory (EDT). Using 5,853 valid questionnaires collected from undergraduates at a Chinese private university, we constructed an empirical model to examine the relationships among these factors. Reliability and validity analyses confirmed the robustness of the measurement instruments (Cronbach's $\alpha = 0.958$; cumulative variance explained = 88.9%). Pearson correlation and multiple regression analyses revealed that all three factors significantly and positively affect students' perceived enhancement of general and professional competencies ($R^2 = 0.848$, $p < 0.01$). Among them, student activities demonstrated the most substantial impact, highlighting the pivotal role of the "second classroom" in fostering comprehensive skills such as leadership, teamwork, and communication. The findings validate the applicability of ACSI and EDT in educational contexts and emphasize the importance of diversified course assessments and high-quality teaching services in promoting student development. This study offers theoretical insights and practical implications for higher education reform, particularly for private universities seeking to optimize curriculum evaluation, strengthen student engagement, and improve service quality.

Keywords*:* competence enhancement; course assessment; student activities; teaching services; private university

INTRODUCTION

In the era of global transformation in higher education, improving students' general and professional competencies has become a crucial indicator for evaluating the effectiveness of talent cultivation. The shift from a quantity-oriented to a quality-driven educational paradigm, especially under the Outcome-Based Education (OBE) framework, emphasizes not only the mastery of disciplinary knowledge but also the development of critical thinking, problem-solving, teamwork, and leadership. In China, the Ministry of Education has further highlighted the concept of "value-added evaluation" in its 2021–2025 review scheme, urging universities to assess how educational processes enhance students' comprehensive abilities rather than focusing solely on academic achievements. Against this backdrop, research on the factors influencing competence enhancement has gained increasing attention.

Prior studies have consistently shown that three key dimensions—course assessment methods, student activity participation, and the quality of teaching management and services—play pivotal roles in shaping students' learning outcomes and personal growth[1]. Diverse and process-oriented assessment models can stimulate continuous learning and creativity. At the same time, extracurricular activities, often referred to as the "second classroom," serve as an essential platform for developing interpersonal and leadership skills. Similarly, efficient teaching services and support systems create a favorable learning environment that strengthens students' motivation and engagement. However, existing empirical research on the combined effects of these three dimensions remains limited, especially in the context of Chinese private universities. Most prior studies either focused on single factors or conducted macro-level policy analysis, leaving a gap in micro-level evidence that connects student satisfaction with measurable competence enhancement.

Harbin Cambridge University, as a representative private institution with strong curriculum innovation and extracurricular programs, provides an ideal setting for exploring this relationship. To address these gaps, this study employs a large-scale questionnaire survey (n = 5,853) and statistical modeling to examine how course assessment, student activities, and teaching services jointly affect students' self-perceived improvement in general and professional competencies. By integrating customer satisfaction theory (ACSI) and expectation disconfirmation theory (EDT), this research aims to develop a comprehensive explanatory framework for understanding competence enhancement and to provide practical insights for quality improvement in private higher education.

2. Literature Review

The enhancement of students' competencies has evolved into a critical measure of educational quality in higher education worldwide. Competence enhancement is often defined as the process through which students acquire, develop, and integrate a wide range of knowledge, skills, attitudes, and values that enable them to succeed in academic, professional, and social environments[1]. This multidimensional concept includes both general competencies—such as critical thinking, problem-solving, communication, collaboration, and creativity—and professional competencies that are specific to students' fields of study[2]. Recent studies highlight that universities must move beyond the narrow evaluation of knowledge acquisition to adopt holistic approaches that consider how educational experiences shape students' comprehensive abilities and personal development[3,4]. Internationally, a growing body of research has employed value-added approaches to assess student competencies by comparing outcomes at different points in the learning journey[2]. For instance, the National Survey of Student Engagement (NSSE) and related longitudinal studies have shown that student engagement—both in and out of the classroom—significantly predicts improvements in competencies over time[1]. In the Chinese context, the Ministry of Education has integrated the "value-added evaluation" concept into national quality assurance frameworks (MOE, 2021), emphasizing that universities must evaluate not only academic performance but also how effectively they foster students' general and professional abilities during their studies [5]. Despite its importance, the determinants of competence enhancement **re**main underexplored, particularly in private universities. While prior research has examined aspects such as curriculum design, teaching innovation, and learning support services, few studies have systematically assessed the combined influence of course assessment, student activities, and teaching services on students' self-perceived competence growth[6]. This study builds upon the existing literature to fill this gap. Course assessment is widely acknowledged as a powerful tool for influencing students' learning behaviors, motivation, and competence development[7]. Traditional summative assessments—typically in the form of final exams—often prioritize rote memorization and knowledge reproduction, which may not adequately foster higher-order thinking or real-world problem-solving abilities. In contrast, formative and process-oriented assessment approaches, such as project-based learning, case analysis, peer evaluation, and continuous feedback mechanisms, have been shown to improve critical thinking, collaboration, and innovation significantly8,9.

International studies emphasize that diversity in assessment methods not only improves academic outcomes but also contributes to students' confidence and lifelong learning attitudes. For example, research by Bahadur et al. (2024)[10] demonstrates that when students perceive assessment methods as transparent, fair, and constructive, their motivation to engage in deep learning increases substantially. Similarly, in the context of Chinese higher education, Zhuang and Liu (2022)[11] argue that curriculum reforms emphasizing formative assessment and real-world application tasks have led to measurable improvements in students' problem-solving and teamwork skills. Moreover, course assessment is not merely an evaluation mechanism but also a pedagogical strategy for guiding learning. Elliott and Healy (2018)[12] suggest that well-designed assessments can act as "learning scaffolds," providing students with structured opportunities to apply theoretical knowledge, reflect on their progress, and develop competencies that are transferable to professional contexts. Therefore, understanding students' satisfaction with course assessment is crucial for identifying how assessment systems contribute to the value-added enhancement of both general and professional competencies. Student activities, often conceptualized as the "second classroom," play a fundamental role in complementing academic curricula and fostering holistic student development[13]. These activities—ranging from campus cultural events, volunteer services, and academic competitions to student clubs and entrepreneurship projects—provide students with opportunities to develop soft skills such as leadership, teamwork, communication, and time management.

Astin's (2017)[14] student engagement theory underscores the importance of active participation, arguing that the time and effort students devote to extracurricular activities strongly correlates with their learning outcomes and personal growth. International

evidence supports this view: studies conducted in the United States, Europe, and Asia show that students who participate actively in non-academic activities demonstrate higher self-confidence, stronger interpersonal relationships, and better career readiness[15,16].

In the Chinese context, extracurricular programs have received renewed emphasis under the "Three-Wide Education" model, which integrates ideological education, academic learning, and practical experiences to cultivate well-rounded graduates[5]. However, while the value of the second classroom is widely acknowledged, few empirical studies have quantitatively examined how satisfaction with student activities directly impacts students' perceived enhancement of general and professional competencies in private universities. Teaching services and administrative support are essential for creating an environment conducive to student learning and personal development. According to Elliott and Shin (2002)[17], educational service quality encompasses factors such as accessibility of learning resources, responsiveness of administrative staff, timeliness of feedback, and overall student support systems. When students perceive teaching services as reliable, efficient, and student-centered, they are more likely to experience a sense of belonging and satisfaction, which in turn positively influences their motivation and competence growth[18].

In Chinese private universities, teaching services often include digital learning platforms, online consultation, academic advising, and extracurricular support, all of which have been increasingly adopted to improve teaching efficiency and responsiveness[19]. For example, Chen et al. (2023)[20] found that the integration of online feedback systems and interactive teaching tools significantly enhanced students' academic satisfaction and engagement. Yet, empirical evidence on how students' satisfaction with teaching management and services contributes to competence enhancement remains limited.

This study draws upon customer satisfaction theory (ACSI) and expectation disconfirmation theory (EDT) to frame the relationship between institutional practices and students' perceived competence enhancement [21,22]. ACSI highlights the role of perceived quality and value in shaping satisfaction, while EDT posits that satisfaction arises when actual experiences exceed prior expectations. By applying these theories to higher education, student satisfaction with course assessment (X1), student activities (X2), and teaching services (X3) can be conceptualized as key mediators that influence competence growth (Y).

While previous research has examined these dimensions individually, few studies have explored their combined effects within a single, integrated model. Moreover, existing literature is dominated by research on public universities, leaving a knowledge gap concerning private institutions in China, which have unique characteristics in curriculum design, teaching practices, and student engagement strategies. To address these gaps, this study constructs a three-dimensional analytical model**.** It proposes hypotheses to test the joint effects of X1, X2, and X3 on Y, thereby extending the application of ACSI and EDT in educational contexts. Building on the literature review and theoretical foundations of the American Customer Satisfaction Index (ACSI) and Expectation Disconfirmation Theory (EDT), this study conceptualizes course assessment (X1)**,** student activities (X2)**,** and teaching services (X3) as key institutional factors influencing students' perceived enhancement of general and professional competencies (Y)**.** Prior studies have shown that these factors can significantly affect students' satisfaction and development outcomes (Kuh, 2020; Elliott & Shin, 2020). However, their relative impact remains unclear, particularly in the context of Chinese private universities. To address this gap, the study proposes the following hypotheses:

H1: Satisfaction with course assessment methods **(X1)** has a significant positive impact on students' perceived enhancement of general and professional competencies (Y).

H2: Satisfaction with student activity participation (X2) has a significant positive impact on students' perceived enhancement of general and professional competencies (Y).

H3: Satisfaction with teaching management and services (X3) has a significant positive impact on students' perceived enhancement of general and professional competencies (Y).

H4: Among the three factors (X1, X2, X3), student activity participation (X2) exerts the most substantial positive influence on students' competence enhancement (Y).

The conceptual framework (Figure 1) illustrates the hypothesized relationships among X1, X2, X3, and Y. The model assumes that all three factors positively influence Y, with X2 expected to have the most significant standardized regression coefficient.

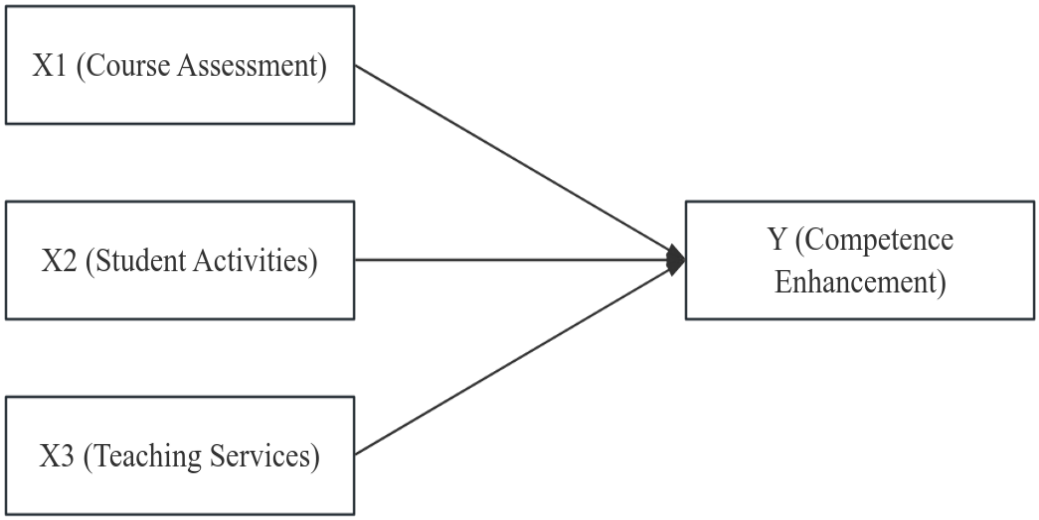


Figure 1. Research Conceptual Model

3. MATERIALS AND METHODS

3.1 Research Design and Subjects

This study adopts a quantitative research design to explore how course assessment (X1), student activities (X2), and teaching services (X3) influence students' perceived enhancement of general and professional competencies (Y). A structured questionnaire survey was administered to undergraduate students from the 2020, 2021, and 2022 cohorts of Harbin Cambridge University, a representative private university in China known for curriculum innovation and active student engagement programs.

A stratified sampling strategy was employed to ensure the representativeness of the sample across grades and majors. A total of 7,200 questionnaires were distributed, and 5,853 valid responses were collected, yielding an effective response rate of 81.29%. Among the respondents, 26.1% were male and 73.9% were female. By grade, 34.4% were from the 2020 cohort, 34.1% from the 2021 cohort, and 31.6% from the 2022 cohort, indicating a well-balanced sample structure.

3.2 Questionnaire Design and Variable Measurement

The questionnaire was designed based on a comprehensive review of established scales and frameworks, including the **American Customer Satisfaction Index (ACSI)** [21], the **SERVQUAL model** [23]and student engagement frameworks[1]. To ensure content validity, the initial draft underwent expert review by three educational scholars and two specialists in survey design. A pilot test (n = 150) was then conducted to refine wording, eliminate redundant items, and improve clarity.

The final questionnaire comprised four sections, each corresponding to one latent construct: **Y (Competence Enhancement):** Measures students' self-perceived improvement in general abilities, professional skills, and overall competencies.**X1 (Course Assessment Satisfaction):** Evaluates students' satisfaction with the diversity, fairness, and formative aspects of course evaluation systems.**X2 (Student Activity Participation Satisfaction):** Assesses students' engagement in extracurricular activities such as cultural events, volunteer services, and competitions.**X3 (Teaching Management and Service Satisfaction):** Reflects students' perceptions of teaching support, administrative efficiency, and responsiveness of feedback mechanisms.

All items were rated on a **5-point Likert scale** (1 = very dissatisfied, 5 = very satisfied) to ensure consistency and comparability of responses.

3.3 Test of reliability and validity

Reliability Analysis: Internal consistency was assessed using Cronbach's α. The overall α value was 0.958, with all constructs exceeding the threshold of 0.9, indicating excellent reliability and stability.

Validity Analysis: The structural validity of the instrument was evaluated through the **Kaiser-Meyer-Olkin (KMO)** test and Bartlett's test of sphericity. The KMO value was 0.868, and Bartlett's test was significant at $p < 0.01$, confirming the suitability for factor analysis. Principal Component Analysis (PCA) showed that the cumulative variance explained reached 88.9%. All factor loadings were above 0.9, further demonstrating strong construct validity.

3.4 Data collection and analysis methods

Data were collected via the **Wenjuanxing** online platform, which ensured efficient distribution and retrieval of responses. Invalid or incomplete questionnaires were excluded.

The data analysis was conducted using **SPSS 27.0**, following these steps: **Descriptive Statistics:** To summarize demographic information (gender, grade). **Reliability and Validity Testing:** To verify the measurement properties of the questionnaire.**Correlation Analysis:** Pearson correlation coefficients were calculated to examine relationships between X1, X2, X3, and Y.**Multiple Regression Analysis:** A regression model was built to test the hypotheses and evaluate the explanatory power of the three factors.**Model Fit and Residual Analysis:** Residual histograms and VIF statistics were used to confirm normality and multicollinearity assumptions.

The regression model is formulated as:

$$Y=\beta_0+\beta_1X_1+\beta_2X_2+\beta_3X_3+\epsilon$$

4. RESULTS

4.1 Descriptive Statistical Analysis

A descriptive analysis was performed to outline the demographic characteristics of the sample. Among the 5,853 valid respondents, 1,529 (26.1%) were male and 4,324 (73.9%) were female. By grade distribution, students from the 2020 cohort accounted for 34.4% (n = 2,011)**,** the 2021 cohort accounted for 34.1% (n = 1,995)**,** and the 2022 cohort accounted for 31.6% (n = 1,847) (see Tables 1 and 2).

The balanced distribution across gender and grade levels indicates that the dataset adequately represents the undergraduate population of Harbin Cambridge University, ensuring reliability for subsequent statistical analysis.

Table 1. Gender distribution Statistics

	Frequency	Percentage	Effective percentage
male	1529	26.1	26.1
female	4324	73.9	73.9
Total	5853	100	100

Table 2. Distribution Statistics of Grades

	Frequency	Percentage	Effective percentage
Grade 2022	1847	31.6	31.6
Grade 2021	1995	34.1	34.1
Class 2020	2011	34.4	34.4
Total	5853	100	100

4.2 Reliability and Validity analysis

(1) Reliability analysis

Cronbach's α reliability test was performed on the questionnaire using SPSS 27.0. The results showed an overall alpha value of 0.958, greater than 0.9, indicating extremely high internal consistency and reliability of the questionnaire (see Table 3).

Table 3. Cronbach's α reliability test Results

Cronbach Alpha	Number of items
0.958	4

(2) Validity analysis

By KMO and Bartlett's sphericity test, the KMO value was 0.868, the Bartlett test approximate chi-square value was 26,651.254, and the significance level was less than 0.01, indicating that the data were suitable for factor analysis (see Table 4).

Principal component analysis results showed that the cumulative variance contribution rate reached 88.9%, which could effectively explain most of the variable information (see Table 5). In addition, the factor loadings for each dimension were all greater than 0.9, verifying the good structural validity of the questionnaire (see Table 6).

Table 4. Results of the KMO and Bartlett's sphericity tests

KMO sampling appropriateness measure		0.868
Bartlett sphericity test	Approximate chi-square	26651.254
	Degrees of freedom	6
	Saliency	<0.01

Table 5: Total variance interpretation Rate

Components	Initial eigenvalues			Extract the sum of squares of the loads.		
	Total	Percentage of variance	Cumulative %	Total	Percentage of variance	Cumulative %
1	3.557	88.924	88.924	3.557	88.924	88.924
2	0.191	4.776	93.7			
3	0.146	3.659	97.359			
4	0.106	2.641	100			

Table 6 Component Matrix (Factor Loading)

Variables	Loadings
Y	0.954
X1	0.945
X2	0.944
X3	0.928

4.3 Correlation Analysis

The results showed that the three independent variables (X1: Course Assessment Satisfaction, X2: Student Activity Participation Satisfaction, X3: Teaching Management Satisfaction) were all significantly and positively correlated with the dependent variable (Y: Value-added of General and Professional Abilities) ($p < 0.01$) (see Table 7). Specifically, the correlation coefficient between satisfaction with course assessment methods and satisfaction with student ability enhancement was $r = 0.873$, the correlation coefficient between satisfaction with student activity participation and satisfaction with student ability enhancement was $r = 0.889$, and the correlation coefficient between satisfaction with teaching management and service was $r = 0.836$.

Table 7. Pearson Correlation Coefficient Matrix

		X1	X2	X3	Y
X1	Pearson Correlation r	1	847 * *	845 * *	873 * *
	Significance (two-tailed)		<0.01	<0.01	<0.01
X2	Pearson Correlation r		1	823 * *	889 * *
	Significance (two-tailed)			<0.01	<0.01
X3	Pearson Correlation r			1	836 * *
	Significance (two-tailed				<0.01

These results preliminarily support H1-H3, suggesting that improvements in course assessment methods, student activities, and teaching services are all associated with higher perceived competence enhancement.

4.4 Regression analysis results. To validate the research hypothesis, this study established multiple linear regression models with student ability enhancement satisfaction as the dependent variable and satisfaction with course assessment methods (X1), student activity participation satisfaction (X2), and teaching management and service satisfaction (X3) as independent variables.

(1) Model

Fit The R^2 value of the regression model was 0.848, indicating that the three types of independent variables could account for 84.8% of the variation in student competency enhancement satisfaction, indicating a high model fit (see Table 8).

Table 8. Regression Model Fit (R^2 Values)

Model Summary				
Model	R	R squared	Adjusted R-squared	Error in standard estimates
1	.921[a]	.848	.848	.265

(2) **The F value of the ANOVA**

The regression equation is 10,903.366, and the significance level is less than 0.01, indicating that the overall regression model is statistically significant (see Table 9).

Table 9. ANOVA Analysis of Variance Results

ANOVA[a]					
Model	Sum of squares	Degrees of freedom	Mean square	F	Significance
Regression	2301.106	3	767.05	10903.366	.000[b]
Residual	411.468	5849	.070		
Total	2712.574	5852			

(3) Regression coefficient test

The results of the regression coefficient test show that all three types of independent variables have a significant positive impact on the dependent variable ($p < 0.01$), among which:

The regression coefficient β = 0.334 for X1 means that for every additional unit, the satisfaction with student ability enhancement increases by 0.334 units; The regression coefficient β = 0.451 of X2 is the most influential factor; The regression coefficient β = 0.160 for X3 also showed a positive promoting effect.

In addition, the variance inflation factor (VIF) of each variable was all below 5, indicating that the problem of multicollinearity was not significant. Based on the results, the regression equation for this study is:

$$Y = 0.058 + 0.334X_1 + 0.451X_2 + 0.160X_3$$

Table 10. Regression Coefficients Table

Coefficients							
Variables	Unstandardized coefficients		Standardized coefficient	t	Significance	Collinearity statistics	
	B	Standard error	Beta			Tolerance	VIF
(Constant)	.058	.008		7.147	.000		
X1	.334	.011	.335	30.501	.000	.215	4.653
X2	.451	.010	.466	45.017	.000	.242	4.128
X3	.160	.010	.170	16.475	.000	.245	4.082

(3) Residual analysis of the model

Verified the normality and good fit of the regression residuals through the residual histogram (see Figure 1), indicating that the assumptions of the model are valid.

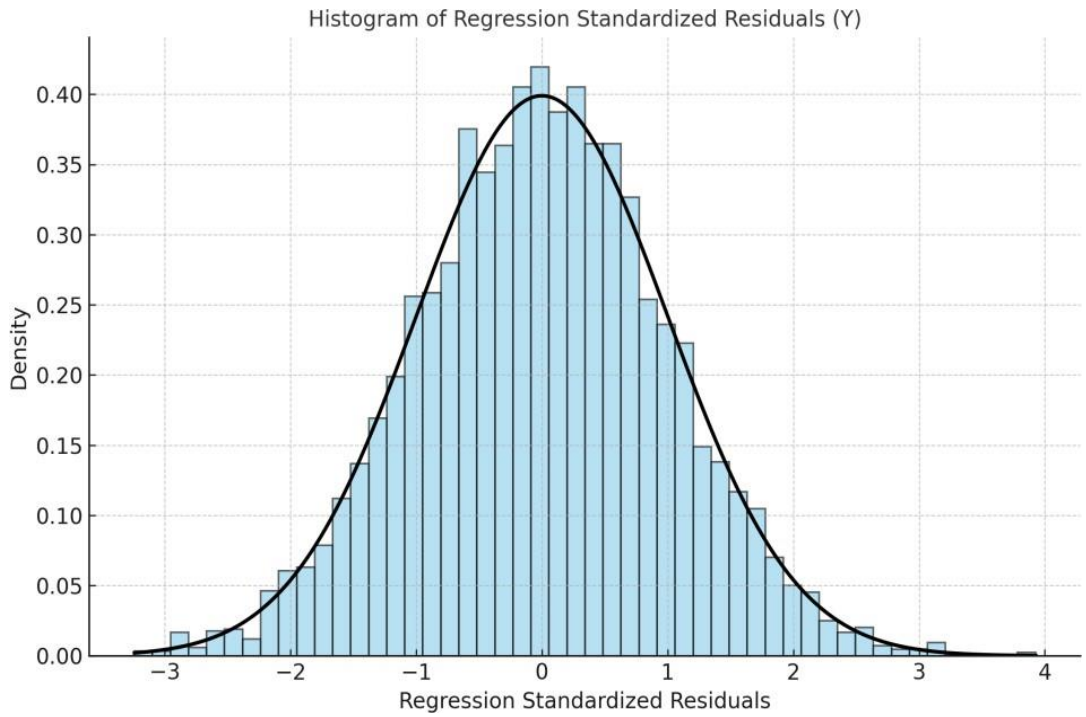


Figure 2. Histogram of Regression Standardized Residuals (Dependent Variable: Y)

4.5 Summary of Research Findings

The results strongly support all four hypotheses (H1–H4). Specifically, course assessment satisfaction (X1), student activity participation satisfaction (X2), and teaching management and service satisfaction (X3) all significantly contribute to the perceived enhancement of students' general and professional competencies (Y). Among these factors, student activities (X2) play the most dominant role, followed by course assessment (X1) and teaching services (X3). These findings underscore the multifaceted nature of competence enhancement, highlighting that classroom learning, extracurricular engagement, and institutional support work synergistically to improve students' overall capabilities.

5. Discussion and Implications

5.1 Research findings and Theoretical validation

The empirical results of this study provide robust evidence supporting the hypotheses (H1–H4) and offer new insights into how course assessment (X1), student activities (X2), and teaching services (X3) contribute to the enhancement of college students' general and professional competencies (Y).

First, course assessment satisfaction (X1) exhibits a significant positive effect on competence enhancement, validating H1. The standardized regression coefficient (β = 0.334) indicates that improvements in students' perceptions of assessment fairness, diversity, and formative feedback are strongly associated with perceived growth in general abilities, such as critical thinking and communication skills, as well as professional competencies. This aligns with Outcome-Based Education (OBE) principles, which emphasize that well-designed assessment systems not only measure learning outcomes but also drive learning behaviors and foster skill development (Biggs & Tang, 2011)[24]. The results are also consistent with Liu et al. (2023), who found that diversified assessments such as project-based tasks and collaborative evaluations significantly improve students' ability to apply knowledge in practical contexts.

Second, student activities (X2) emerge as the strongest determinant of competence enhancement, confirming H2 and H4. With the highest standardized coefficient (β = 0.451), X2 demonstrates that extracurricular participation—ranging from cultural events and volunteer services to academic competitions—serves as a vital platform for cultivating leadership, teamwork, and interpersonal communication. This finding resonates with Astin's Student Engagement Theory (2017)[14], which emphasizes that student involvement in non-academic activities is directly linked to their holistic development. Similar results were observed by Hong and Park (2024)[15], who highlighted that active engagement in campus activities strengthens problem-solving skills and boosts confidence. The prominent role of X2 also reflects the unique importance of the "second classroom" in Chinese higher education, where extracurricular experiences complement formal academic instruction and enhance students' employability.

Third, teaching services (X3) also significantly contribute to competence enhancement, supporting H3. Although its standardized coefficient (β = 0.160) is relatively minor, X3 remains statistically significant ($p < 0.01$), indicating that high-quality teaching management and responsive administrative services provide a supportive learning environment that reinforces students' motivation and satisfaction. This aligns with the **American Customer Satisfaction Index (ACSI)** model, which posits that service quality directly affects customer (or student) satisfaction and outcomes[21]. Prior research by Elliott and Shin (2020) similarly confirmed that efficient academic services, timely feedback, and accessible learning resources significantly enhance students' perceptions of institutional quality.

Fourth, the overall regression model explains 84.8% of the variance in Y, confirming the synergistic effects of X1, X2, and X3. This high explanatory power suggests that competence enhancement is **multifactorial** and that these three dimensions collectively shape students' learning experiences and outcomes. The findings also extend the applicability of **Expectation Disconfirmation Theory (EDT)** to educational contexts, demonstrating that students' satisfaction—and their perceived competence growth—are strongly influenced by whether institutional practices exceed their expectations in assessment, engagement, and service.

In summary, the results validate the integrated research model proposed in this study, supporting all four hypotheses. The evidence underscores that student activities are the most influential factor, followed by course assessment and teaching services. This finding is consistent with both international and domestic studies[1], highlighting the importance of fostering a balanced ecosystem that integrates classroom learning, extracurricular engagement, and administrative support to maximize students' overall competence development.

5.2 Comparison with Existing Studies

The findings of this study are broadly consistent with prior research on competence enhancement, while also providing new evidence that addresses gaps in the existing literature, particularly concerning private universities in China.

The positive effect of course assessment (X1) on competence enhancement aligns with global research on the role of diversified and formative evaluations. International studies have widely emphasized that formative assessment and continuous feedback are essential for improving students' critical thinking, application skills, and problem-solving abilities. For example, Croxton (2021)[8] and Bahadur et al.[10] (2024) found that students who experience transparent and constructive assessments are more motivated to engage in deep learning and self-reflection. Similarly, in the Chinese context, Zhuang and Liu (2022)[11] reported that universities implementing project-based assessments and peer evaluations observed a significant increase in students' practical competencies and teamwork skills. The results of this study echo these conclusions, highlighting that students at Harbin Cambridge University perceive a higher level of competence growth when they are evaluated through diverse, fair, and process-oriented methods**.**

However, this study also reveals that while assessment is essential, it is not the strongest predictor of competence enhancement**.** This finding contrasts with some prior research focused on public universities, where curriculum assessment often plays a dominant role due to the standardized teaching structures.

The significant and most substantial effect of student activities (X2) validates previous studies on the role of the "second classroom."Astin's (2017) student engagement theory asserts that students' involvement in extracurricular activities directly contributes to their personal and professional growth. The finding that X2 ($\beta = 0.451$) has the largest effect size aligns with Wu and Li (2020), who found that participation in campus cultural events, academic competitions, and volunteer services significantly improves students' leadership, communication, and problem-solving skills**.** International research further supports this, as Hong and Park (2024)[15] demonstrated that extracurricular engagement correlates positively with students' career readiness and social adaptability.

Notably, this study's evidence suggests that private universities may rely more heavily on extracurricular programs to compensate for the limitations of classroom instruction**.** Unlike some public universities with standardized curricula and rigorous academic systems, private institutions often have greater flexibility to design student-centered activities that enhance real-world competencies.

The impact of teaching management and services (X3) is consistent with studies on service quality in higher education, but adds new insights into the private university context. Previous research (Elliott & Shin, 2020)[17] has demonstrated that service quality—including academic advising, administrative efficiency, and digital learning platforms—is a critical driver of student satisfaction and academic success. This study corroborates such findings by showing that X3 ($\beta = 0.160$, $p < 0.01$) significantly contributes to competence enhancement. However, its relatively minor coefficient compared to X2 and X1 suggests that, although teaching services are essential, they act more as an enabling factor rather than a direct driver of competence growth. This observation aligns with Pan et al. (2022)[19], who emphasized that administrative services provide the foundation for effective teaching and student engagement but may not directly build competencies unless integrated with experiential learning initiatives.

The overall explanatory power of the model ($R^2 = 0.848$) exceeds that reported in many earlier studies. While previous research often examined each factor separately, this study adopts an integrated three-dimensional model**,** demonstrating that course assessment, student activities, and teaching services work synergistically to shape competence enhancement. This integrated approach advances existing literature by showing that the relative influence of student activities is the highest**,** a finding that is underreported in prior studies focusing on public universities or single-factor analyses.

This study contributes a unique perspective by focusing on a private university in China. Most previous research on competence enhancement in China has concentrated on public universities or elite institutions (Li & Huang, 2023)[5]. The results of this study show that private universities, despite facing resource constraints, can still achieve high levels of student satisfaction and competence growth by leveraging innovative assessment systems, diverse extracurricular activities, and responsive teaching services**.** This reinforces the idea that institutional characteristics, such as flexibility and student-centered management, may allow private universities to adopt more customized and holistic approaches to student development.

5.3 Theoretical Implications

This study provides several theoretical contributions by integrating multiple conceptual frameworks—namely, the **American Customer Satisfaction Index (ACSI)**,

Expectation Disconfirmation Theory (EDT), **Outcome-Based Education (OBE)**, and **Astin's Student Engagement Theory**—to explain how course assessment, student activities, and teaching services jointly influence students' competence enhancement.

The findings extend the application of ACSI in higher education. Traditionally, ACSI has been widely used in consumer behavior research to evaluate customer satisfaction and its impact on loyalty and perceived value (Fornell et al., 1996)[21]. By conceptualizing students as key stakeholders and "service recipients" in the educational process, this study demonstrates that students' satisfaction with academic assessment, extracurricular engagement, and institutional services can be analogized to customer satisfaction in service industries. The high explanatory power of the model ($R^2 = 0.848$) indicates that satisfaction is a robust predictor of competence enhancement. This supports the notion that educational quality can be effectively analyzed through a service-oriented lens, thus broadening the theoretical scope of ACSI.

The results provide empirical evidence for EDT by linking students' perceived expectations with competence growth. EDT posits that satisfaction is determined by the degree to which actual experiences exceed or fall short of prior expectations (Oliver, 1980)[22]. The findings of this study show that when students perceive course assessments to be diverse and transparent**,** student activities to be enriching and well-structured**,** and teaching services to be efficient and responsive**,** their sense of competence enhancement improves significantly. This confirms that the positive disconfirmation of expectations—where the actual educational experience is better than anticipated—can foster not only satisfaction but also perceived personal development**.** By applying EDT in the academic context, this study expands its relevance beyond consumer research and validates its utility in measuring student outcomes.

The study reinforces and enriches OBE principles.OBE emphasizes that teaching and assessment should focus on observable outcomes and students' ability to apply knowledge in real-life scenarios (Spady**,** 1994). The finding that course assessment (X1) significantly affects competence enhancement highlights the importance of the evaluation as both a measurement and a learning tool**.** The positive association between process-oriented assessment and students' self-perceived skill development aligns with the OBE principle that "assessment drives learning" (Biggs & Tang, 2011)[24].

Moreover, the strong influence of student activities (X2) suggests that OBE frameworks should incorporate non-academic learning experiences as critical components of outcome measurement.

The study adds new insights to Astin's Student Engagement Theory. Astin (2017) argues that student learning and development are functions of the quality and quantity of student involvement. The results, particularly the dominant role of **X2 (β = 0.451)**, provide empirical support for this theory by showing that extracurricular engagement significantly contributes to competence enhancement**.** This suggests that engagement is not only about academic participation but also encompasses leadership, teamwork, and real-world problem-solving cultivated in co-curricular settings. This finding deepens the theoretical understanding of how engagement translates into measurable competence growth.

The integrated model proposed in this study offers a multi-dimensional theoretical framework for future research. By examining the combined effects of X1, X2, and X3, this study addresses a critical gap in existing research that often focuses on single factors. The model demonstrates that competence enhancement is a multifactorial construct**,** influenced by both academic (e.g., assessment) and non-academic (e.g., student services and activities) elements. This holistic perspective encourages scholars to adopt interdisciplinary theoretical approaches that bridge educational psychology, service management, and organizational behavior in the analysis of student development.

5.4 Practical Implications

The findings of this study have practical value for improving educational quality in private universities. The significant influence of course assessment (X1), student activities (X2), and teaching services (X3) on competence enhancement (Y) suggests **that** a multi-dimensional strategy is required to foster students' general and professional abilities. Based on these results, the following implications are proposed. **Reform and Diversify Course Assessment.** The results highlight the positive impact of X1 (β = 0.334), confirming that well-designed and diverse assessment systems can enhance students' learning motivation and self-perceived competence growth. Adopt a process-oriented assessment approach. Private universities should shift from a reliance on high-stakes final exams to formative assessments, including project-based assignments, portfolios, and peer evaluations. Such practices not only measure knowledge but also promote problem-solving, critical thinking, and collaborative skills (Biggs & Tang, 2011)[24]**.**

Ensure transparency and fairness. Students are more likely to engage deeply when they believe that assessments are fair and align with learning objectives. Regular feedback sessions and clear rubrics can improve the perceived fairness and effectiveness of evaluations. **Integrate real-world tasks.** Assessments that simulate workplace challenges, such as case analyses or interdisciplinary projects, can strengthen students' practical and professional competencies, making them better prepared for future careers. **Strengthen the "Second Classroom" and Student Engagement.** With X2 having the most substantial effect (β = 0.451), the findings underscore the **central** role of extracurricular activities in holistic student development. **Enrich the diversity of student activities.** Universities should design a broad spectrum of co-curricular programs, ranging from cultural festivals and entrepreneurship competitions to community service initiatives. These activities help students cultivate leadership, teamwork, and organizational skills. **Create structured engagement platforms.** Student clubs, academic societies, and volunteering groups should be well-supported with faculty mentorship, funding, and resource-sharing platforms. This ensures that students are not only participating but also gaining valuable experiential learning outcomes**.** Recognize and reward participation. Formal recognition, such as awarding credits or certificates for active participation in extracurricular activities, can incentivize students to take part in meaningful non-academic experiences that complement classroom learning. **Leverage digital platforms.** Online communities and virtual collaboration tools can be used to expand participation, especially for students with limited on-campus opportunities. **Improve Teaching Management and Service Quality.** Although X3 (β = 0.160) has a relatively minor effect, it remains a crucial foundation for creating a supportive learning ecosystem**. Enhance digital learning environments.** Universities should invest in online learning platforms, intelligent feedback systems, and digital **libraries** to provide students with easy access to resources and timely academic support. **Streamline administrative services.** Efficient administrative procedures, such as quick responses to student inquiries, transparent grading systems, and user-friendly registration processes, can improve students' satisfaction and reduce unnecessary frustration.

Strengthen academic advising. Personalized mentoring and career guidance services can help students plan their academic paths, identify their strengths, and connect curricular learning with professional aspirations. **Build a feedback-driven service culture.** Establishing feedback channels, such as online surveys and focus groups, allows universities to evaluate and and focus groups, allows universities to evaluate and refine their teaching and service quality continuously.

Foster a Holistic Educational Ecosystem. The combined R^2 value of 0.848 demonstrates that competence enhancement is not driven by a single factor but by the interplay of multiple dimensions**.** Therefore, universities should: Integrate curriculum reform, extracurricular engagement, and service improvement into a cohesive strategy; Encourage collaboration between academic departments and student affairs offices to design cross-functional initiatives that address both academic and personal development needs; Monitor competence enhancement as a long-term indicator of educational quality**,** using student surveys and performance tracking to inform policy and practice.

Policy Implications for Private Universities. Given the unique challenges of private universities in China—such as limited funding, lower social recognition, and diverse student cohorts—this study highlights the need for: **Targeted investment in co-curricular programs** that provide high-impact, low-cost opportunities for student engagement; **Flexible curriculum design** that incorporates industry collaboration, internships, and experiential learning to strengthen the linkage between classroom instruction and career readiness; **A student-centered service model**, aligning with international best practices that treat students as active participants and co-creators of their educational journey.

5.5 Research Limitations and Future Prospects

Although this study provides valuable insights into the factors influencing students' competence enhancement, several limitations should be acknowledged, which in turn offer opportunities for future research.

The study is based on a single private university, which may limit the generalizability of the findings. While Harbin Cambridge University is representative of private higher education institutions in Northeast China, the results may not fully capture the diversity of student experiences across different regions or institutional types. Future studies should consider conducting multi-institutional surveys**,** including both public and private universities, to validate the robustness of the three-dimensional model across broader contexts.

The study relies on self-reported data, which are inherently subjective and may be affected by response bias. Students' perceptions of course assessment, extracurricular engagement, and teaching services may not fully reflect the actual quality or outcomes of these practices. To address this, future research could combine subjective surveys with objective performance indicators**,** such as academic grades, competency-based evaluations,

or employer feedback, to provide a more comprehensive assessment of competence enhancement.

The research design is cross-sectional, limiting the ability to infer causal relationships or track changes over time. Although the regression analysis provides evidence of associations among variables, it cannot fully establish cause-and-effect dynamics. Longitudinal studies or experimental designs could be implemented to observe how course assessment reforms, new extracurricular initiatives, or service improvements impact students' competencies over multiple semesters or academic years**.**

The measurement framework could be further refined. While the constructs (X1, X2, X3, Y) demonstrated high reliability and validity, the number of items for each dimension was limited to ensure clarity and brevity. Future studies could develop more comprehensive and multidimensional scales that capture additional aspects, such as students' emotional engagement, self-directed learning behaviors, or resilience, which are increasingly recognized as critical components of competence enhancement.

The model does not account for potential moderating or mediating factors. Variables such as gender, socioeconomic background, prior academic performance, or motivation might moderate the relationships between X1, X2, X3, and Y. Future research could incorporate structural equation modeling (SEM) **t**o examine mediating mechanisms (e.g., student satisfaction as a mediator) or moderating effects, providing a more nuanced understanding of the competence enhancement process.

The study focuses on the Chinese private university context, which may differ from international practices. Comparative studies involving universities in other countries or regions would enrich the understanding of how cultural, institutional, and policy differences influence the interplay between course assessment, student activities, teaching services, and competence development.

6. CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

This study explored the influence of **course assessment (X1)**, **student activities (X2)**, and **teaching services (X3)** on the perceived enhancement of **general and professional competencies (Y)** among students at a Chinese private university.

Grounded in **American Customer Satisfaction Index (ACSI)** and **Expectation Disconfirmation Theory (EDT)**, the study developed a three-dimensional research model and empirically tested four hypotheses (H1–H4) using data collected from 5,853 valid questionnaires.

All three institutional factors significantly and positively affect competence enhancement.

Course assessment (X1), student activities (X2), and teaching services (X3) jointly explain 84.8% of the variance in students' perceived competence growth. This highlights the need for a holistic approach that integrates academic evaluation, extracurricular engagement, and service support.

Student activities exert the most decisive influence ($\beta = 0.451$). The prominent role of the "second classroom" underscores that extracurricular participation complements classroom instruction and plays a crucial role in fostering leadership, teamwork, and communication skills.

Course assessment has a substantial impact ($\beta = 0.334$), confirming the importance of process-oriented and diverse evaluation systems. Students respond positively to transparent, fair, and formative assessments that encourage critical thinking, creativity, and knowledge application.

Teaching services also contribute to competence enhancement ($\beta = 0.160$), though as a supportive rather than primary driver. Effective academic advising, administrative efficiency, and timely feedback form the foundation for positive learning experiences and personal growth.

Overall, these findings validate the integrated model and confirm all four hypotheses (H1–H4). They also reinforce the applicability of ACSI and EDT in educational contexts, demonstrating that student satisfaction acts as a key driver of competence enhancement.

6.2 Theoretical Contributions

This research makes several theoretical contributions. **Extending ACSI and EDT:** By conceptualizing students as active stakeholders, the study extends customer satisfaction frameworks to analyze educational quality and outcomes. **Enriching OBE and student engagement theory:** The findings highlight how course assessment and extracurricular activities align with the OBE principle of "assessment driving learning," while also confirming Astin's assertion that student

engagement—especially outside the classroom—significantly influences personal and professional development. **Proposing a comprehensive model:**

Unlike previous studies focusing on single factors, this research offers an integrated perspective, illustrating how academic and non-academic dimensions collectively shape competence enhancement.

6.3 Practical Recommendations

Based on the findings, the following recommendations are proposed for private universities:

Reform course assessment systems. Adopt a diverse and process-oriented evaluation framework that balances formative and summative assessments. Integrate project-based tasks, group presentations, and real-world problem-solving exercises into coursework to cultivate practical skills. Ensure fairness and transparency by using detailed rubrics, clear criteria, and frequent feedback.

Enhance student activities and the "second classroom." Expand the variety of extracurricular programs, including innovation and entrepreneurship competitions, cultural events, and volunteering initiatives. Provide institutional support**,** such as faculty mentorship, funding, and formal recognition, to encourage deeper engagement. Integrate extracurricular achievements into students' comprehensive evaluations and credit systems.

Improve teaching services. Develop user-friendly digital platforms for academic consultation, resource access, and feedback. Strengthen career counseling, academic advising, and mental health services to support students' holistic development. Establish feedback loops—such as periodic student satisfaction surveys—to continuously monitor and enhance service quality.

Promote an integrated development ecosystem. Create collaboration mechanisms between academic departments, student affairs, and administrative units to ensure that curriculum, extracurricular activities, and services are mutually reinforcing**.** Track students' competence growth through longitudinal assessments and incorporate findings into institutional quality improvement initiatives.

6.4 Future Research Directions

Future research should build on this study by: Conducting multi-institutional or cross-regional studies to test the generalizability of the model across diverse educational contexts and employing longitudinal research designs to capture the dynamic effects of course assessment reforms and co-curricular programs on competence growth and investigating moderating and mediating factors**,** such as gender, academic discipline, or student motivation, to deepen understanding of the mechanisms driving competence enhancement. Integrating objective performance indicators (e.g., academic grades, internship evaluations) with self-reported data to enhance measurement validity and extending the research to an international comparative perspective, exploring how cultural and policy differences shape the relationship between institutional practices and student outcomes.

This study provides empirical evidence and actionable insights into how course assessment, student activities, and teaching services contribute to students' competence enhancement. By bridging theoretical frameworks with practical recommendations, it offers a roadmap for private universities seeking to optimize their educational quality and better prepare graduates for the challenges of a rapidly evolving global workforce.

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ORIGINAL ARTICLE

TOXICITY ASSESSMENT OF ZINC OXIDE NANOPARTICLES AND ORGANIC POLLUTANTS ON ZEBRAFISH USING BLISS INDEPENDENCE

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ABSTRACT

Background: Zinc oxide nanoparticles (ZnONPs) and chlorhexidine (CHX), a persistent organic pollutant (POP), are widely used engineered nanomaterials (ENMs) that may threaten freshwater ecosystems. While ZnONPs are considered safer than metal salts, they can still induce oxidative stress, membrane damage, and ion release. The co-occurrence of CHX and ZnONPs in aquatic systems raises concerns over combined toxic effects, which conventional risk assessment methods may not adequately address.

Aim: To evaluate the individual and combined acute toxicity of ZnONPs and CHX on zebrafish (*Danio rerio*) embryos, and to characterize their interaction using the Bliss Independence model.

Materials and Methods: Zebrafish embryos (<3 h post-fertilization) were exposed for 72 h to ZnONPs, CHX, and their binary mixtures (1:1) at IC_{20} and IC_{50} concentrations in 24-well plates under controlled conditions. ZnONPs were synthesized and characterized by UV–Vis spectroscopy and dynamic light scattering (DLS). Endpoints assessed included mortality, heart rate reduction, teratogenicity, and spinal deformities. Interaction effects were analyzed using the Bliss Independence model, with statistical evaluation by one-way ANOVA and Tukey's post hoc test.

Results: The 72-h LC_{50} values were 4.5 ppm (ZnONPs) and 3.9 ppm (CHX). Mixture toxicity varied with ratio and concentration: antagonism predominated at IC_{20} and IC_{50} (CI > 1) in 1:1 and 1:2 ratios, while CHX-rich mixtures showed synergism (CI < 1) at IC_{70}. CHX-heavy mixtures exhibited the highest lethality and teratogenicity, whereas ZnONP-rich mixtures reduced CHX toxicity, likely via decreased bioavailability or ROS scavenging.

Conclusion: Mixture toxicity of ZnONPs and CHX is ratio- and endpoint-dependent, highlighting the need for interaction-based ecological risk assessments.

Keywords: Zebrafish, Zinc oxide nanoparticles, Chlorhexidine, Ecotoxicology, Bliss Independence model, Antagonism, Synergism.

INTRODUCTION

The increased usage of engineered nanomaterials (ENMs) as well as persistent-able organic pollutants (POPs) in consumer goods and industrial applications has raised alarm bells for the environmental safety of fresh and marine water ecosystems. Of all the ENMs, zinc oxide nanoparticles (ZnONPs) are the most popular and commonly used material in sunscreens, cosmetics, paints, and antibacterial substances due to their high chemical reactivity, photocatalytic ability, and unique characteristics including high surface area[1]. But these characters also make ZnONPs as biologically active and capable of producing reactive oxygen species (ROS), that could damage cell membranes, by releasing zinc ions (Zn^{2+}). These ions are highly cytotoxic to aquatic organisms[2,3]. Besides, the existence of Zn, is considerably found as a compounded and or salted- form rather than as single-contaminants in nature. In compound forms, it is usually occurring with other organic pollutants. Among the organic compounds, the common pollutants such as chlorhexidine (CHX), bisphenol A (BPA), diethylhexyl phthalate (DEHP), and triclosan (TCS) are seemed to be highly reactive with ZnONPs. These organic compounds are easily found in aquatic systems due to their extensive uses as disinfectants, plastics, and personal care products. Particularly, the chlorhexidine becomes increasingly recognized as a significant

emerging contaminant in hospital and domestic effluents[4]. As combination, both ZnONPs and those organics together could severely affect the organisms due to their increased bioavailability and possible interactive effects with physiological levels[5].

Although regarded as less toxic than heavy metal salts, ZnONPs could cause several adverse effects from the chronic, sublethal exposure. That severity may range from oxidative stress, developmental abnormalities, immunotoxicity and or behavioral changes, to aquatic invertebrates[6]. Risk assessment on the ecosystem health threats from their persistent inputs to surface waters from industries and households should consider long-term, low-dose exposure, and mixture conditions because of the biomagnification[7]. As chlorhexidine (CHX) is recorded as a common disinfectant from hospital discharge and personal care products, it becomes an emerging contaminant in aquatic ecosystems[8-10].

Besides, the accumulation of the several such kinds of contaminants react with themselves and resulting in a complex contaminant mixture. Due to the compounded ones, these could act additively, synergistically, and or antagonistically at physiological functions of the organisms. Hence, risk prediction based on single-compound studies becomes complicated, and insufficient for calculating the risk assessment. In modern era, for assessing the toxicity of such nanoparticles, their co-contaminants such as organics should also evaluate for assessing the bioavailability, uptake, and activity to correlate the amplification or inhibition of their respective toxicity[11,12]. The Bliss Independence approach is one of the popular statistical methods for analyzing such interactions and making better ecological risk assessments. It predicts the joint effect of two substances from their single effects under the assumption that they act independently.

In aquatic toxicology, the zebrafish (*Danio rerio*) represent a well-known vertebrate model, valued for their fast developmental rate, clear embryos, and physiological similarity to higher vertebrates. Research into toxicity has shown that exposure to both ZnONPs and organic pollutants can cause developmental toxicity, oxidative stress, and behavioral impairment in zebrafish, thus indicating their susceptibility towards these pollutants[15]. A very important aspect of ecologically relevant risk assessment is gaining insight into possible interaction effects through assessment of mixture toxicities in fixed-ratio experiments in zebrafish, relying on Bliss modeling[16]. Differences from these predictions might then categorize interaction types as synergistic, antagonistic, or additive, which is particularly applicable to combinations like ZnONPs and chlorhexidine, which have particular modes of action[13,14].

This study contributes to the emerging field of mixture toxicology by providing knowledge on the interactions of ZnONPs with common environmental contaminants in an aquatic ecosystem.Through the integration of classical ecotoxicological endpoints with a mixture model approach, we aim to bridge the gap between laboratory investigation and natural exposure scenarios[3,5].

For this study, we focused on evaluating the toxicities of ZnONPs, both individually and also with the organic pollutant chlorhexidine, on zebrafish. Fixed-ratio mixture experiments were carried out for an excellent understanding of concentration-based lethal responses for 72 hours and using the Bliss Independence model to determine whether interactions between toxicants were synergistic, additive, or antagonistic[12,17,18]. The purpose of the study is to provide traditional ecotoxicological measures together with quantitative mixture modeling with a better understanding of pollutant interactions, thus bridging the gap between laboratory studies and the real field issues of aquatic life[11,17].

MATERIALS AND METHODS

Zebrafish embryos (lesser than 3h old) were used as the model aquatic model to assess ecotoxicological interactions of Zinc Oxide Nanoparticles (ZnONPs) with selected organic pollutant, i.e., chlorhexidine. The ZnONPs were synthesized and their size and surface charge were measured using UV–Vis spectroscopy and dynamic light scattering (DLS), respectively. The organic pollutants were purchased from USA Sigma-Aldrich and were freshly made up in dechlorinated water.

Zebrafish Acute Toxicity Assay

Embryos less than 3 hours old were exposed (OECD, test No. 236) in 24-well plates to individual compounds (0.001, 0.01, 0.05, and 0.5 ppm, respectively) and their binary combinations (1:1, 1:2, 1:3, 1:4, 2:1, 3:1, 4:1) at IC_{20}, IC_{50} and IC_{70} equivalent concentrations. Exposure was performed under controlled conditions (20 ± 1°C, 16:8 h light:dark) for 72 hours. Endpoints measured included Mortality (%), Heart Rate Reduction (%), Teratogenicity (%) and Spinal Cord Deformity (%). Three biological replicates were performed per group.

Combination Analysis Using Bliss Independence

To assess interaction between ZnONPs and pollutants, the Bliss Independence model was employed. The expected combined effect (E_AB,exp) was calculated using:

$$E_AB = E_A + E_B - (E_A \times E_B)$$

Where, E_A and E_B are the individual effects and E_AB are the combined effects . The observed effect (E_AB,obs) was subtracted from E_AB,exp to calculate ΔE. Synergism was indicated when ΔE > 0, additivity at ΔE = 0, and antagonism when ΔE < 0. Mortality and sublethal endpoints were analyzed using Microsoft Excel and R-based synergy models.

Statistical Analysis

Results were shown as the mean ± Standard Deviation. Records were made in triplicate and then analyzed by one-way ANOVA with Tukey's posttest. Statistical significance was defined as $p < 0.05$ [19]. The LC_{50} IC_{20}, IC_{50}, and IC_{70}levels were calculated using non-linear regression. Graphs and interaction plots were performed for all levels of combination condition. Graphpad prism, ver. 8.2 was used for statistical analysis.

RESULTS

The present study evaluated the individual and combined toxicological effects of zinc nanoparticles (ZnONPs) and chlorhexidine on *zebra fish*. Acute embryo toxicity assay was conducted following OECD, test No. 236.guidelines, and combinatorial toxicity was assessed using the Bliss Independence model. The study investigated 72h responses at concentrations at different fixed ratios *i.e.*, 1:1, 1:2, 2:1, 3:1, 1:3, 1:4, 4:1 respectively. The Bliss Independence model allowed quantitative classification of interactions as synergistic, additive, or antagonistic.

3.1 Individual Compound Toxicity: ZnONPs and CHX:

The zebrafish embryos were treated with increased concentration of the ZnONPs and CHX (0.001, 0.01, 0.05, and 0.5 ppm) and displayed with concentration-dependent activity on (a) mortality (%),(b) teratogenicity (%),(c) hatching rate (%), and (d) heart beat reduction (%), respectively. CHX showed higher toxicity than ZnONPs attained halted developmental endpoints (IC_{20}, IC_{50} and IC_{70}) even at the lower concentrations. The IC_{50} values for them were 0.035 and 0.12 ppm, respectively, confirming a higher intrinsic toxicity of CHX. Dose- response curves of them showed a steeped slope for CHX, also revealing an immediate transition of the higher toxic capability from the sub- toxic concentrations. There was a highly significant effect (ANOVA, $p < 0.01$) on various responses at given concentrations, thereby supporting the dose-dependent effects and biological activity of each agent.

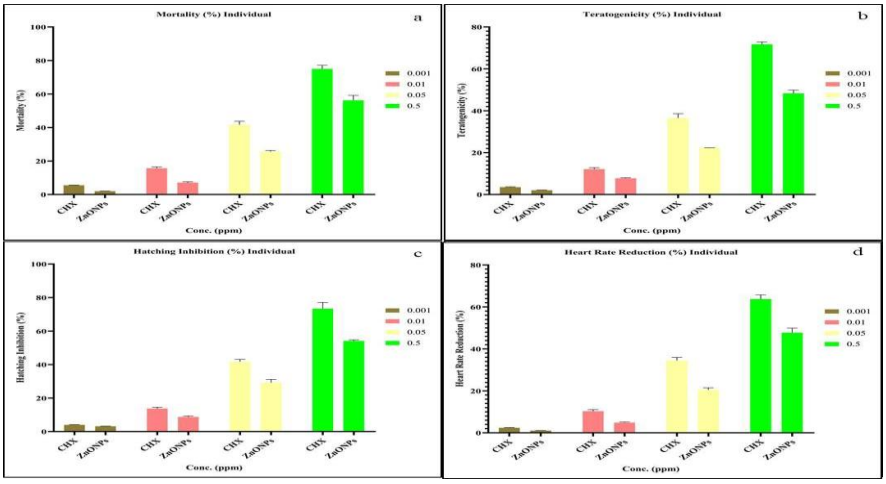


Figure 1. Concentration-dependent effects of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) on zebrafish embryos, showing changes in (a) mortality (%),(b) teratogenicity (%),(c) hatching rate (%), and (d) heart rate reduction (%). Data are expressed as mean ± SD from triplicate experiments across tested concentrations (n=3)

3.2 Mortality outcomes at IC_{20} revealed differential combination toxicity profiles in zebrafish embryos treated with Chlorhexidine and Zinc Oxide Nanoparticles

At IC_{20}, mortality rates differed within different concentrations of the combined chemicals. The highest mortality for the tested combinations at this concentration was for the 1:4 ratio (ZnONPs:CHX), where a mortality of 37.7 ± 1.6% was recorded, showing that significant toxicity was induced by sublethal concentrations (Figure.2). The 1:1 and 1:2 ratios also produced moderately toxic effects, while concentrations dominated by ZnONPs, such as 2:1, 3:1, and 4:1,

showed a gradual decline in mortality. However, in all cases, the CI values at IC_{20} exceeded 2.0, with a CI of 2.89 for the 1:1 ratio and 2.08 for the 1:2 ratio, classifying the interaction as strongly antagonistic. It indicated that while CHX is still largely lethal, ZnONPs prevent interaction strength from reaching additive predicted levels, either by surface interactions or low bioavailability.

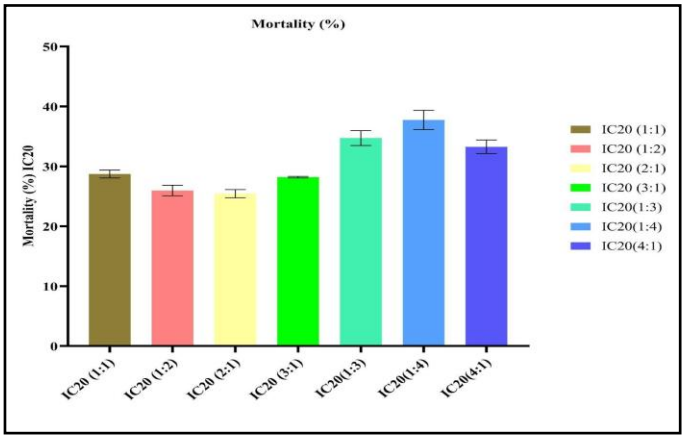


Figure 2. Mortality (%) in zebrafish embryos combination of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) at IC_{20}, expressed as mean ± SD from three independent experiments.

3.3 At IC_{20}, Teratogenicity patterns indicated varied combination toxicity responses in zebrafish embryos treated with chlorhexidine and zinc oxide nanoparticles.

At IC_{20}, lesser degree of teratogenicity was evident, with Macroscopic developmental malformations being most pronounced in the mixtures rich in chlorhexidine. Ratios 1:2 and 1:3 exerted the highest teratogenic effects, showing symptoms that included yolk sac edema, truncated body axes, and improper dorsal curvature. These observations were contrasted by conditions of the 3:1 and 4:1 ratios with less concentration in ZnONPs, where the abnormalities were comparatively less (Figure.3). CI values indicated antagonism across all ratios, but the actual developmental harm in the CHX-rich groups infers that biological outcomes do not always match the calculated interaction models, particularly for sublethal endpoints.

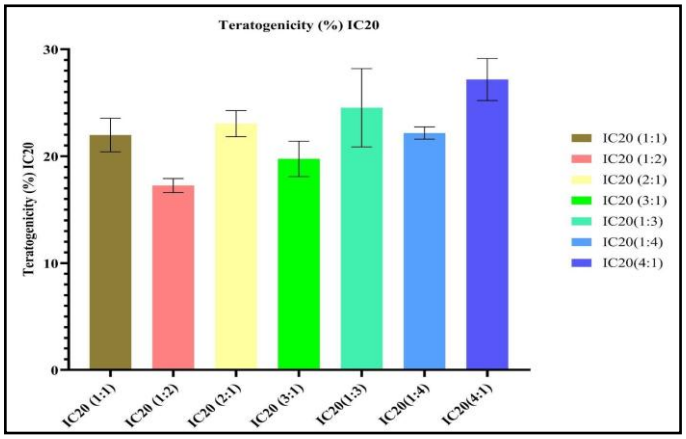


Figure 3. Teratogenicity (%) in zebrafish embryos combination of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) at IC_{20}, expressed as mean ± SD from three independent experiments.

3.4 Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{20}

Heart rate suppression was evidenced even at IC_{20}, with combinations dominated by CHX, particularly 1:2 and 1:3, causing reductions of greater than 20% (Figure. 4). The 1:1 ratio yielded a more modest reduction (~15%), while ZnONPs-heavy ratios produced lesser effects. These results highlighted the sensitivity of the cardiac function in presence of CHX-induced stress. Interaction modeling suggested a strong antagonism; yet, cardiac system assessment revealed the functional impact of CHX toxicity even in antagonistic combinations with ZnONPs.

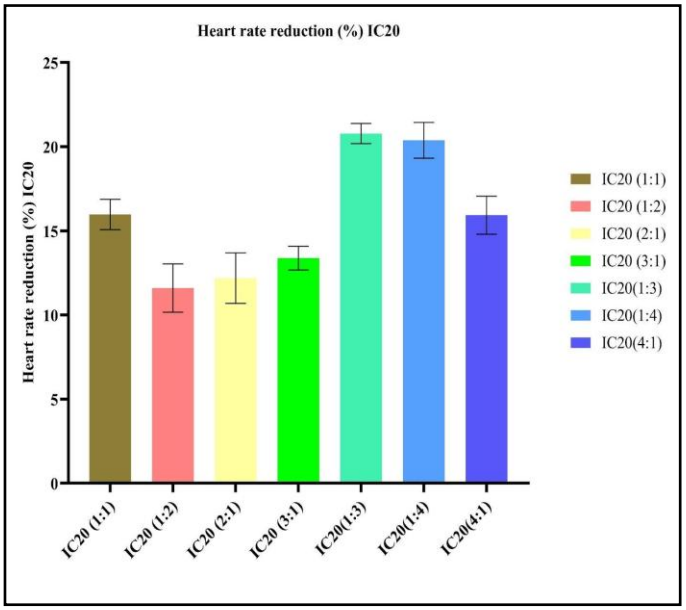


Figure 4. Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{20}

3.5 Combined effect CHX and ZnONPs on Spinal Cord Deformity at IC_{20}

Spinal deformities (mentioned as teratogenicity as in overall effects) at IC_{20} were relatively mild (Figure.5) but still present, with 1:4 and 1:3 ratios producing the highest deformity rates (~13-14%). These deformities, including axial misalignment and lateral curvature, were less frequent in ZnONPs-dominant mixtures, which also fit the trends seen in other endpoints. Overall, the degree of severity was low at IC_{20}; however, structural anomalies being there always reinforced the idea of CHX posing high sensitivity acting at an early stage of development, even in terms of antagonistic interaction conditions.

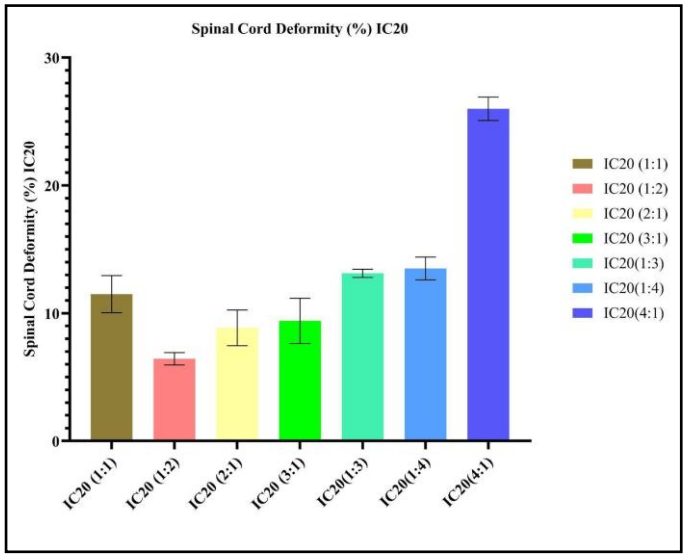


Figure 5. Combined effect CHX and ZnONPs on Spinal Cord Deformity at IC_{20}

3.6 Combined effect CHX and ZnONPs on Mortality at IC_{50}

At IC_{50}, the effects on mortality were shown to be exaggerated. Of the 1:3 ratio, the highest death rate was recorded with an average of 53.6 ± 0.9% and was even more than the equimolar one to one 1:1 ratio, and any of the ZnONPs-rich groups (Figure. 6). The Combination index for the 1:3 ratio was 1.70, thus establishing antagonism to a lesser extent than IC_{20}. The implication here was that while the ZnONPs compromised CHX toxicity by the extended manner, the high relative amount of CHX was still able to dominate all biological consequences at this concentration.

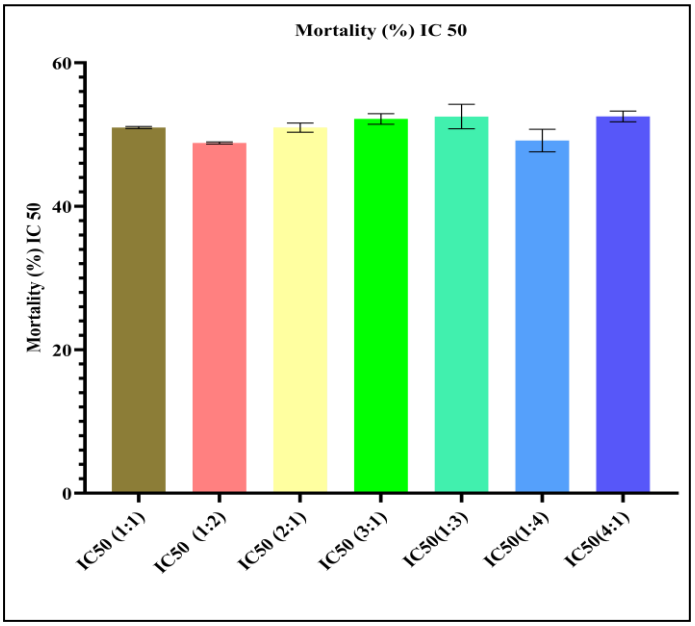


Figure 6. Mortality (%) in zebrafish embryos combination of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) at IC_{50}, expressed as mean ± SD from three

3.7 Combined effect CHX and ZnONPs on Teratogenicity at IC_{50}

At IC_{50}, the teratogenic effects became pronounced, especially in the 1:2 and 1:3 combinations. Teratogenicity rates went above 40%, with the most prominent observations being swelling of the body, failure of appendage differentiation, and incomplete elongation of the body axes (Figure. 7). ZnONPs-rich ratios (3:1, 4:1) still retained low frequencies of abnormalities, which may indicate interference with CHX uptake or attenuation of ROS-induced developmental toxicity. Once more, CI values above 1.5 for all ratios indicated that the interactions were antagonistic; however, the biological consequences arising from CHX-rich combinations reached severe levels.

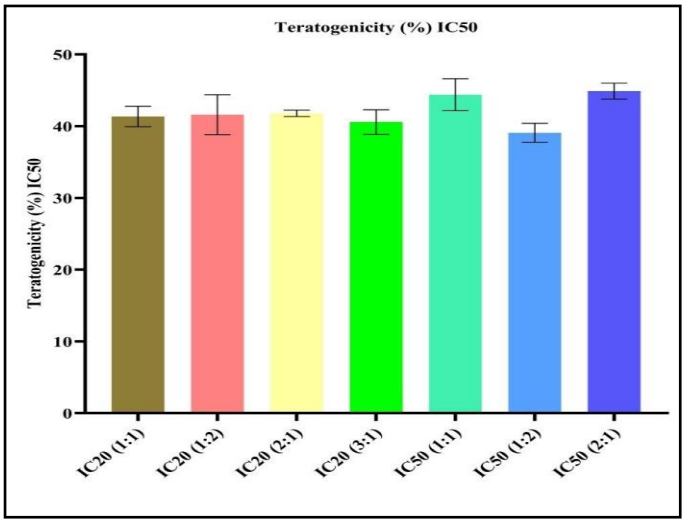


Figure 7. Teratogenicity (%) in zebrafish embryos combination of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) at IC_{50}, expressed as mean ± SD from three independent experiment

3.8 Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{50}

Suppression of the heart rate was highest at 50%. The 1:3 ratio produced an average heart rate decrease of over 33%, emphasizing the ability of CHX to disrupt neuromuscular and mitochondrial functions (Figure.8). 1:1 and 1:2 ratios showed a considerable reduction (about 31%) while ratios dominated by ZnONPs indicated a lack of prominent effects. Such behaviours suggest that CHX-richer mixtures possessed significant physiological stress even in the antagonistic mixture.

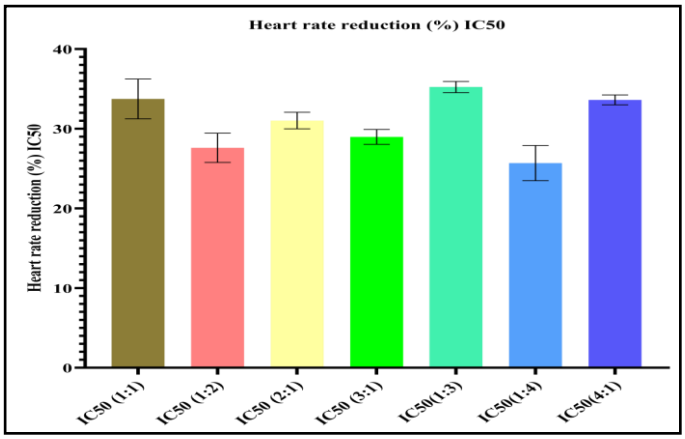


Figure 8. Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{50}

3.9 Combined effect CHX and ZnONPs on Spinal Cord Deformity at IC_{50}

Spinal deformities increased at IC_{50}, where 1:3 and 1:4 combinations induced the highest deformity rates. Notable deformities included severe dorsal bending, torsion on the longitudinal axis, and poorly defined outline of the carapace (Figure.9). The higher severity and frequency of skeletal deformities produced by CHX-rich mixtures imply that protein conformation and differentiation of embryonic tissues could be particularly susceptible to CHX toxicity, with some degree of protection offered by ZnONPs at this intermediate concentration.

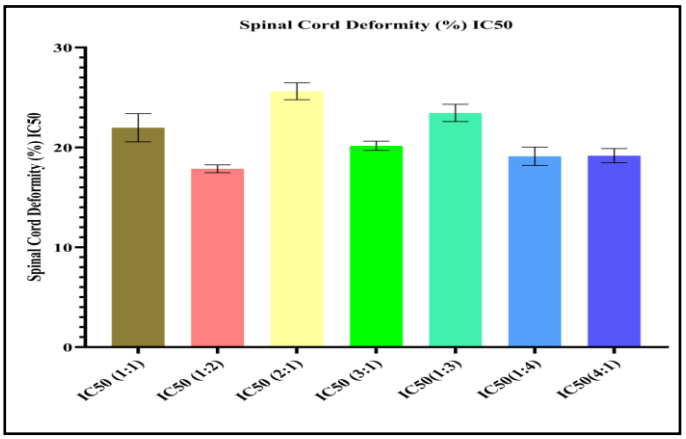


Figure 9. Combined effect CHX and ZnONPs on Spinal Cord Deformity at IC_{50}

3.10 Combined effect CHX and ZnONPs on Mortality at IC_{70}

At IC_{70}, most ratios experienced a plateau in mortality, which was at 51.1 ± 0.5%. The 1:2 combinations produced the highest mortality within this group Figure. 10). The CI for this ratio equated to 1.60, hence further supporting the antagonistic course, while the biological effect remained significant. This implied that interactive buffering is not entirely worthless at elevated chemical interaction; however, at very high concentrations of CHX, it was indeed the concentration that can override chemical interactive buffering apart.

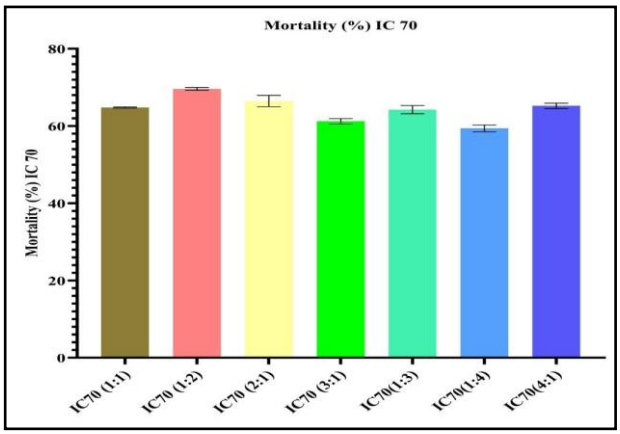


Figure. 10 Mortality (%) in zebrafish embryos combination of Chlorhexidine (CHX) and ZnONPs

3.11 Combined noparticles (ZnONPs) at IC_{70}, expressed as mean ± SD from three independent experiments effect CHX and ZnONPs on Teratogenicity at IC_{70}

The teratogenic effects were very strong at IC_{70}, especially in the 1:2 and 1:3 ratios, and these deformities included organ protrusions and shortened thoraxes that were similar to those evident at IC_{50} (Figure. 11). Combinations with the possible predominance of ZnONPs, for instance, 3:1 and 4:1 ones decreased the percent occurrence of deformities and suggested that ZnONPs might also be able to partially interfere with the CHX teratogenic pathways through reactive oxygen species (ROS) scavenging or membrane stabilization.

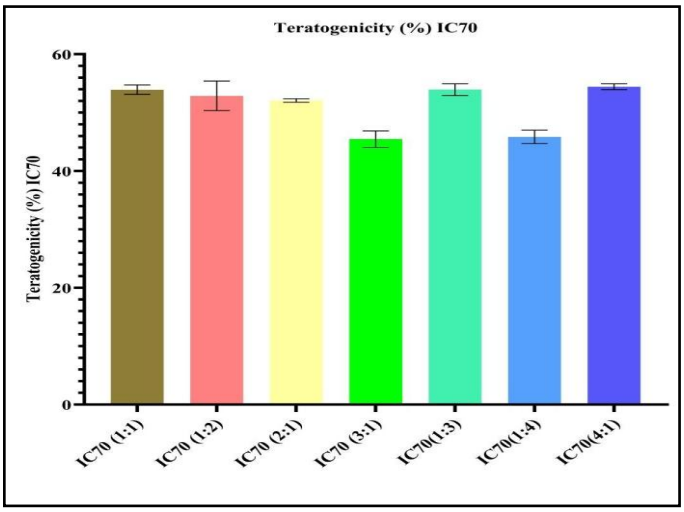


Figure 11. Teratogenicity (%) in zebrafish embryos combination of Chlorhexidine (CHX) and Zinc Oxide Nanoparticles (ZnONPs) at IC_{70}, expressed as mean ± SD from three independent experiments

3.12 Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{70}

The noticeable one reached its peak at IC_{70} then it never lowered down by over 34% by CHX-rich combinations (Figure. 12). The most reliable suppression was shown by the 1:2 ratios proving that physiological stress heightens with more dose exposure and not linearly reduced by adding more ZnONPs.

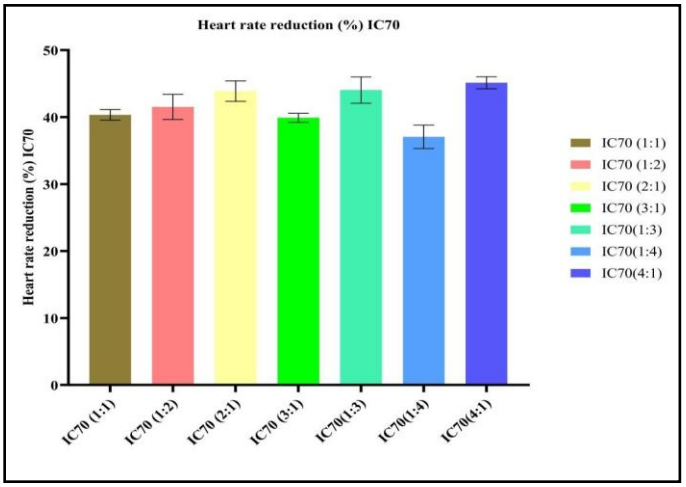


Figure 12. Combined effect CHX and ZnONPs on Heart Rate Reduction at IC_{70}

3.13 Combined effect CHX and ZnONPs on Spinal Cord deformity at IC_{70}

Spinal deformity rates at IC_{70} remained ca. 20.5 ± 1.5%, showing a slight reduction from IC_{50} in certain combinations (Figure. 13). The reason for this could also be explained by the removal of most heavily deformed individuals by lethality or delayed onset of structural abnormalities at very high concentrations. Still, the continued observation of skeletal disruptions at this concentration indicates ongoing developmental interferences.

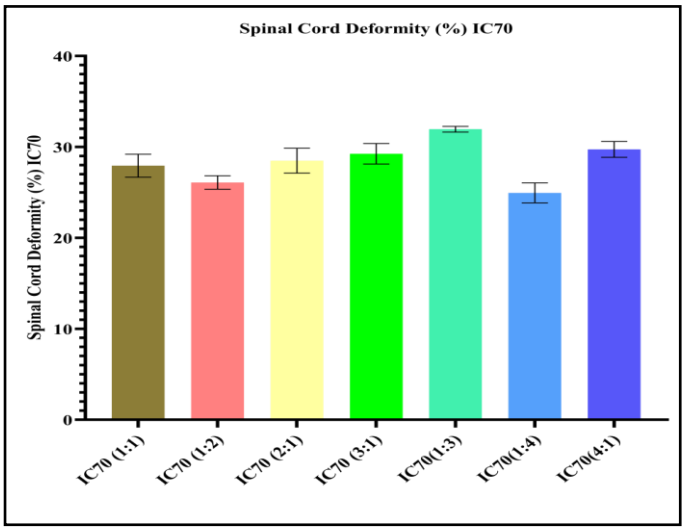


Figure 13. Combined effect CHX and ZnONPs on Spinal Cord Deformity at IC_{70}

3.14 Combination Index

The interactions observed in mixtures of ZnONPs and chlorhexidine at various ratios seemed to depend on concentration in a concentration-dependent manner. At IC_{20} and IC_{50}, most ratios presented CI values greater than one, indicating antagonistic interactions especially the 1:1 and 1:2 combinations (Figure. 14). At IC_{70}, however, the CIs for the 3:1 mixture increased sharply to almost 9, indicating strong antagonism. On the other hand, combinations favoring CHX, such as 1:3, 1:4, and 4:1, showed a significant decrease in CI at IC_{70} with values falling below one, indicating the onset of synergistic interactions at higher concentrations. Thus, an understanding is gained that while at lower concentrations antagonism prevails, at the elevated toxic stress levels synergism will occur in CHX-heavy combinations.

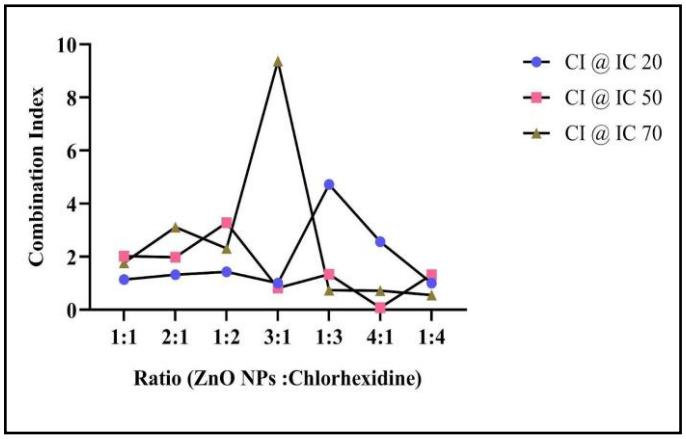


Figure 14. Graphical representation of the combination index (CI) across different CHX and ZnONPs ratios, illustrating synergistic, additive, or antagonistic interactions based on CI values

3.15 Synergism

In the determination of synergism, CHX and ZnONPs were evaluated separately and in combination at various concentrations ranging from 0.001, 0.01, 0.05, and 0.5 ppm, respectively. At the 0.001 ppm concentration, CHX and ZnONPs demonstrated effects of 5.96% and 6.62% individually, amounting to an expected additive effect of 12.58%; the actual observed effect in their combination was, however, 13.98%, thereby indicating enhancement in synergy (Figure. 15). This pattern persisted for all tested doses, with the most significant synergy noted at 10 µM, where the expected additive effect was 73.90% and the effect of combination skyrocketing to 121.87%, giving a net synergistic boost of 47.97%. On the average, the synergistic combination recorded mean augmentation by 14.61% over the expected additive effect, thereby substantiating its capability to enhance efficacy over time.

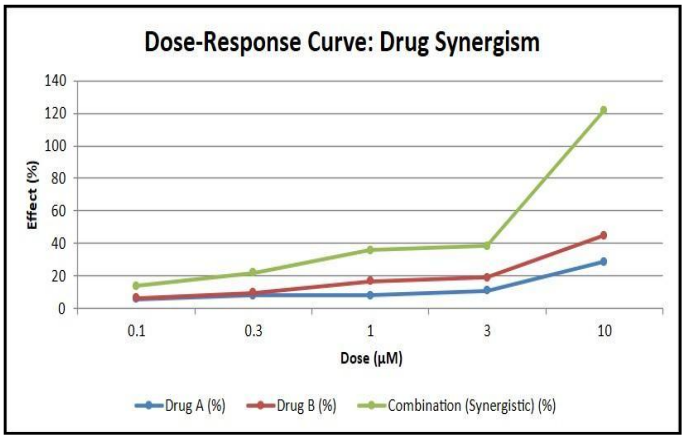


Figure 15. Graphical representation of drug synergism, showing the interaction profiles of CHX and ZnONPs across tested ratios, with classification into synergistic, additive, or antagonistic effects based on combination index analysis

3.16 Antagonism

Contrarily, the combined attempts of two antagonizing drugs showed a different presence. At the lowest concentration of 0.1 µM, Drug A and Drug B induced effects of 4.10% and 3.42% respectively, with the expected additive effect being 7.52%; the drug combination was only 3.83%, indicating an antagonism blocking the efficacy (Figure. 16).. Such antagonistic interaction remained consistent and only strengthened with increase in the dosage; at 10 µM, the individual effects summed to a total of 183.57% and the combined effect was a mere 68.77%, exerting an antagonistic suppression of -114.80%. The mean antagonistic suppression force across all concentrations was calculated to be -53.29%, proving beyond any reasonable doubt that there existed an antagonistic relationship between the two compounds.

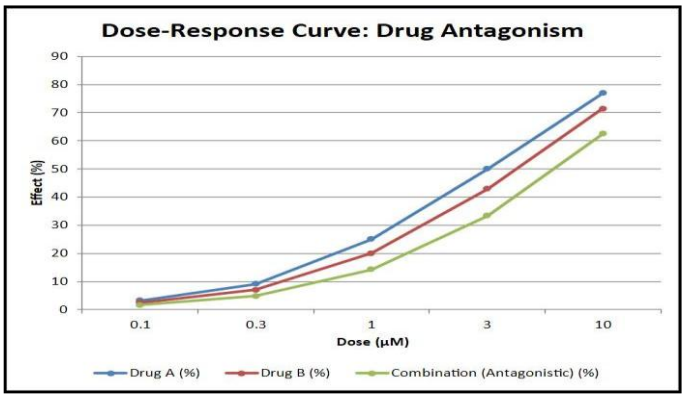


Figure 16. Graphical representation of drug antagonism, depicting combinations of CHX and ZnONPs that exhibit reduced efficacy compared to expected additive effects, as determined by combination index analysis across tested ratios.

These results demonstrated the profound real-life implications of drug interactions and emphasize the vital need for preclinical combination assessments to derive full predictions about clinical effectiveness and safety. One-way ANOVA followed by Tukey's post hoc testing ($p < 0.05$) was used to rigorously test the differences between measured and predicted Bliss values. Most especially, intermediate concentrations (0.01 – 0.05 ppm) showed considerable differences where antagonistic effects were maximal in all experimental combinations. This justified the function of the Bliss model as a robust forecasting mechanism for expectation of mixture toxicity in aquatic toxicology.

This study showed that mixtures between ZnONPs and CHX brought about toxic effects in *zebrafish* related to concentration and ratio. Ratios that favored CHX, for example, 1:2 and 1:3, consistently reported the highest mortality rates, developmental malformations, and physiological derangements at IC_{20}, IC_{50}, and IC_{70}. Although these CI values allotted all those interactions as antagonistic, the actual biological effects remained significant, especially in CHX-rich mixtures. The resultant minimal buffering effects of ZnONPs above high doses therefore serve to prove the necessity

of all these interaction models and endpoint-specific outcomes in getting precise ecological risk assessments for mixed chemical exposures.

DISCUSSION

Recent studies, however, have increasingly classified ZnONPs into the much-less toxic categories among the typical heavy-metal-based nanomaterials. But significant mortality and teratogenicity in aquatic species including zebrafish occur through increased concentrations, indicating the environmental dilemma if they exist in accumulating concentrations in water bodies[18-21]. Previous study suggested that ZnONPs might induce toxicity via many different mechanisms, including oxidative stress mechanisms; induction of reactive oxygen species (ROS); free zinc ion generation due to dissolution of the nanoparticles; destruction of cellular membranes; and possible external uptake or internalization of the nanoparticles[3,22]. The LC_{50} values for ZnONPs indicated in literature for zebrafish generally vary within a range of 6-12 mg/L (96h). However, any variations regarding formulations or conditions of exposure (i.e., smaller particle size or more sensitive exposure times) can yield lower LC_{50}s, sometimes approaching the low µg/L ranges as suggested by your study[18].

Though chlorhexidine (CHX) has been observed to cause acute and sublethal toxicity to a number of aquatic species with EC_{50}/LC_{50}s from some micrograms per liter to low milligrams per liter depending on the test organism and endpoint) research has equally placed it as among the emerging contaminants in wastewater and the receiving water bodies, thus confirming its bioaccumulative nature and persistence[23,24].

Mixture toxicity is one great avenue through which to advance science, and the present study addressed the matter of mixture toxicity by co-exposing zebrafish to ZnONPs and CHX, assessing immobilization across binary ratios, and implementing the Bliss Independence model. In previous studies using Bliss independence and Loewe additivity approaches, it was consistently found that exposure of engineered nanomaterials with organic pollutants, such as biocides and pharmaceuticals, produces synergistic or antagonistic toxic behaviors rather than mere additivity[25,26]. Usually, synergism poses greater ecological risks because it can significantly amplify effects more than expected from exposure to single agents, thus negating the sufficiency of traditional additive models in regulatory frameworks[3,18]. Both field and laboratory research, increasingly, have been demonstrating that these interactions are often concentration dependent and mechanistically related to modification in bioavailability, internalization, or transformation of one chemical when in the presence of the other. Continuous or repeated mixture exposures are likely to cause more intense or longer-lived effects at the population or community level, thus accentuating the need for chronic and multi-endpoint approaches[5].

Unlike previous studies-almost exclusively focusing on single agents or limited endpoints-current approach was consistent with thrusts pushing for mixture assessments, simultaneous assessment of different environmentally relevant contaminants, and mechanisms like Bliss Independence and response surface modeling in assessing risks. It is reminiscent of regulatory momentum toward the addition of multi-ratio multi-endpoint chronic/multigeneration designs into future risk assessment protocols[27].

This work is restricted to short-term exposure under laboratory conditions. Future research should study the effect of long-term exposure, reproductive toxicity, transgenerational toxicology, and nanoparticle alteration in the real environmental conditions to enhance the risk assessment process.

CONCLUSION

Although combinations of ZnONPs with CHX exhibited antagonistic behavior according to Bliss Independence model, CHX-contaminated mixtures showed biological activity across all endpoints. These findings reveal a limitation of traditional additive models in predicting the ecological effects of complex pollutant mixtures. This study indicates a need for mechanistic toxicology in ecotoxicological assessments, which helps to understand better the ways by which different contaminants interact at the molecular and physiological levels. With the high frequency of engineered nanomaterials and pharmaceutical introductions into aquatic environments, these combination exposure scenarios become ecologically realistic and relevant. Therefore, future risk assessments should incorporate a multi-endpoint, multi-ratio test approach and research on long-term exposure to improve the accuracy of chronic and transgenerational impacts. The use of zebrafish as an indicator species is ideal, given its sensitivities and its function in the ecosystem. This reinforces continued use in environmental monitoring schemes for complex mixtures of pollutants.

DECLARATION

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CONFLICT OF INTEREST

None declared.

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ORIGINAL ARTICALE

COMPARATIVE IN VITRO ASSESSMENT OF BLACK AND GREEN TEA EFFECTS ON THE CORROSION AND MECHANICAL INTEGRITY OF ORTHODONTIC WIRES

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ABSTRACT

This in vitro study evaluated the comparative influence of black tea (5%) and green tea (3%) on the corrosion resistance and mechanical integrity of stainless steel (SS) and nickel titanium (NiTi) orthodontic wires. Sixty standardized specimens were immersed in tea solutions or distilled water over 28 days, simulating daily intake cycles. Surface morphology (SEM), elemental composition (EDX), tensile strength (Instron), surface roughness (profilometry), and corrosion potential (potentiostat) were assessed. Data were analyzed with one-way ANOVA followed by Tukey's post hoc test ($p \leq 0.05$). Black tea exposure produced significantly greater deterioration than green tea. In SS wires, chromium content decreased markedly (18.0% → 17.2%), tensile strength was reduced by 12.5%, surface roughness increased to 0.51 µm, and corrosion potential dropped to –342 mV. NiTi wires exhibited milder yet statistically significant changes. Black tea accelerates electrochemical corrosion and mechanical deterioration of orthodontic wires more than green tea, particularly in stainless steel. These findings underscore the need for patient dietary counseling and suggest that protective coatings or antioxidant surface modifications could enhance the clinical longevity of orthodontic appliances.

Keywords: Green tea; Orthodontic wires; Corrosion resistance; Surface roughness; Tensile strength.

INTRODUCTION

Orthodontic archwires represent the cornerstone of fixed orthodontic therapy, as their mechanical stability and resistance to intraoral challenges directly determine the efficiency and predictability of tooth movement. The structural and surface integrity of these wires, however, may be significantly compromised by daily exposure to dietary and environmental agents, particularly acidic or polyphenol-rich beverages such as tea. Black tea (Camellia sinensis, fermented) and green tea (Camellia sinensis, unfermented) are among the most commonly consumed beverages worldwide, and their frequent intake during orthodontic therapy may introduce clinically relevant alterations in wire performance [1,2].

Studies indicate that orthodontic materials experience accelerated electrochemical corrosion when exposed to organic acid solutions and phenolic compounds and disinfectant solutions which also causes surface roughness changes and strength reduction [3,4]. Orthodontic wire performance suffers from these changes which also leads to higher ion release that could impact both safety and biocompatibility for patients [5]. Research by Kumar and Rajput [6] and Kurtović et al. [7] shows that pitting corrosion of stainless steel (SS) and nickel-titanium (NiTi) alloys accelerates when exposed to chlorhexidine mouthwash or acidic soft drinks which also decreases their force delivery capacity. The research results support further investigation into how black and green tea beverages which people commonly drink affect wire structural stability. Notably, the chemical profile of these teas may underlie their divergent effects.

Black tea contains theaflavins and thearubigins which create a lower pH environment with high oxidative

potential that can break down the protective passive oxide layer on SS and NiTi alloys. Green tea contains higher levels of epigallocatechin gallate (EGCG) which functions as an antioxidant and metal-chelating compound that shows potential to reduce corrosion levels [8,9]. The two beverages contain identical polyphenolic compounds but their different fermentation methods and chemical compositions indicate they could affect orthodontic appliance durability through separate mechanisms.

The research investigated how 5% black tea and 3% green tea solutions affect the surface characteristics and corrosion resistance and mechanical properties of SS and NiTi orthodontic wires. The research employs SEM and EDX and profilometry and tensile strength testing to study beverage impacts on orthodontic materials and develop treatment recommendations for orthodontists and their patients.

MATERIALS AND METHODS

Sample Preparation

Sixty orthodontic wire specimens were prepared for testing which included thirty stainless steel (SS) and thirty nickel–titanium (NiTi) wires. Each specimen measured 5 cm in length and 0.016 inch in diameter, ensuring standardization across all experimental groups. The specimens were randomly assigned into three groups: a control group immersed in distilled water, a black tea group, and a green tea group. The present 28-day, thrice-daily immersion model was selected as a validated early-stage screen for beverage effects; however, it does not substitute for ISO-standardized long-term or dynamic corrosion protocols. To align with ISO 10271 and ASTM G31 guidelines, future studies should incorporate extended immersion periods (≥90–180 days), pH-cycling to mimic dietary acid challenges, and thermal cycling between 5 °C and 55 °C to replicate hot and cold beverage intake. Such refinements would provide more realistic insights into the cumulative long-term degradation of orthodontic wires.
Such division allowed for comparative analysis of the impact of different tea infusions on both alloy types under controlled conditions [2].

Preparation of Tea Solutions

The black tea (Camellia sinensis, fermented) and green tea (Camellia sinensis, unfermented) solutions were prepared fresh daily to ensure consistency of chemical composition.The preparation process started with boiling 100 mL of distilled water to which 2 grams of loose tea leaves were added for five minutes of steeping before the solution was filtered through sterile gauze and cooled to room temperature. The researchers employed this preparation technique to generate beverage solutions which duplicated human consumption patterns while safeguarding polyphenolic compounds from storage-related degradation [8].

Artificial Saliva Composition

The wire samples received artificial saliva storage treatment between their immersion cycles to mimic oral environment conditions. The solution consisted of NaCl (0.5 g/L), KCl (0.5 g/L), $CaCl_2 \cdot 2H_2O$ (0.916 g/L), $NaH_2PO_4 \cdot 2H_2O$ (0.699 g/L), $Na_2S \cdot 9H_2O$ (0.006 g/L), and urea (2 g/L), adjusted to a physiological pH of 6.8. The researchers chose this formulation because it duplicates the ionic conditions found in the mouth which made the study more realistic [1].

Immersion Protocol

The specimens underwent three daily cycles of 15-minute immersion in 12 mL of solution at 37 °C for 28 days using distilled water and black tea and green tea solutions. The researchers performed immersion cycles at three specific time points which matched the regular drinking habits of patients undergoing orthodontic treatment. The specimens underwent distilled water washing to eliminate surface debris before being placed back into artificial saliva storage. The researchers developed this protocol based on their previous research about beverage effects on material degradation [7].

Surface Morphology and Elemental Analysis

The specimens received distilled water rinsing and air-drying treatment for surface characterization after finishing the immersion process. The scanning electron microscope (SEM, JEOL JSM-6510LV) operated at 1000× and 5000× magnification to study morphological changes. The SEM system performed energy-dispersive X-ray spectroscopy (EDX) to identify the chemical elements present in the analyzed samples. The researchers used these combined methods to identify surface damage and pitting and ion depletion effects that occurred because of tea exposure [6].

Mechanical Properties – Tensile Strength Testing

The tensile strength of wires underwent testing through a universal testing machine (Instron Model 3345) before and after being submerged in water. The tests used a 20 mm gauge length together with a 1 mm/min crosshead speed. The test established the highest weight tolerance and tensile strength that the material could support. The research design examined mechanical deterioration

effects on orthodontic treatment by evaluating force delivery capacity [3].

Surface Roughness Evaluation

Surface roughness (Ra) was measured using a profilometer (Mitutoyo Surftest SJ-210).Three independent readings were taken from each specimen, and the mean value was recorded for statistical analysis.The method enabled scientists to measure the changes in surface elevation that occurred due to corrosion exposure.

Corrosion Potential Measurements

The three-electrode cell system operated with the orthodontic wire as the working electrode and platinum as the counter electrode while using a saturated calomel electrode (SCE) as the reference electrode. Corrosion potential (Ecorr) and current density values were obtained in the respective tea solutions using a potentiostat (Autolab PGSTAT302N).The method successfully identified electrochemical instability and corrosion sensitivity according to Rodrigues Neri et al. (2024) [10]. International guidelines require testing for biocompatibility in addition to electrochemical and mechanical assessments. While not performed in the present study, ISO 10993-5/-12 standardized cytotoxicity assays (using human gingival fibroblasts or L929 cells) and quantitative ion release analysis by ICP-MS could be integrated in future work. These approaches would allow correlation between electrochemical dissolution, ion release (Ni, Cr, Ti), and potential cellular responses, thereby strengthening the translational impact of the findings. **Statistical Analysis**

Data were analyzed using one-way ANOVA followed by Tukey's post hoc test (SPSS v26.0). A significance threshold of $p \leq 0.05$ was applied.

Mean values, standard deviations, and confidence intervals were calculated to enable robust statistical comparisons across experimental groups. The selection of repeated-measures ANOVA was justified by the experimental design involving multiple groups and repeated evaluations over time.

RESULTS

Surface Morphology and Elemental Composition

Scanning electron microscopy (SEM) revealed distinct alterations in surface integrity following immersion in tea solutions. Stainless steel (SS) wires exposed to black tea exhibited extensive pitting, surface irregularities, and roughened morphology, while those immersed in green tea displayed comparatively milder degradation. In contrast, nickel–titanium (NiTi) wires demonstrated less severe, though still discernible, surface instability.

Elemental composition analysis using energy-dispersive X-ray spectroscopy (EDX) confirmed significant ion depletion in all treated groups, with the greatest elemental loss recorded in black tea-immersed SS wires. Chromium content in SS wires decreased from 18.0% in the control group to 17.2% in black tea and 15.3% in green tea. Likewise, nickel decreased from 13.5% (control) to 10.5% in black tea and 13.9% in green tea. NiTi wires showed a marked reduction in titanium-associated peaks, further supporting surface destabilization. Collectively, these findings indicate that black tea accelerates electrochemical dissolution of protective elements such as chromium and nickel more aggressively than green tea.

The quantitative EDX analysis (Table 1) confirmed that black tea immersion reduced chromium from 18.0% to 17.2% and nickel from 13.5% to 10.5% in stainless steel wires, while green tea resulted in a moderate chromium decrease to 15.3% and nickel retention at 13.9%.

Table 1. Elemental Composition (%) of Stainless Steel Wires (EDX Analysis)

Element	Control Group	Green Tea Group	Black Tea Group
Iron (Fe)	68.5 ± 0.4	66.1 ± 0.8	67.1 ± 0.6
Chromium (Cr)	18.0 ± 0.2	15.3 ± 0.4	17.2 ± 0.4
Nickel (Ni)	13.5 ± 0.3	13.9 ± 0.5	10.5 ± 0.3

Mechanical Properties – Tensile Strength

Mechanical testing revealed a statistically significant reduction in tensile strength following tea exposure, with SS wires being more severely 7.8% after green tea. Similarly, NiTi wires demonstrated a reduction of 10.2% and 5.4% in black and green tea groups, respectively affected. The tensile strength of SS wires decreased by 12.5% after immersion in black tea and

These findings highlight that black tea exerts a more detrimental effect on the load-bearing capacity of orthodontic wires compared to green tea. Importantly, the magnitude of reduction in tensile strength suggests potential clinical implications, as diminished wire resilience may impair the efficiency of orthodontic force delivery.

Table 2. Changes in Tensile Strength (MPa) of Orthodontic Wires After Tea Exposure

Wire Type	Control Group	Green Tea Group	Black Tea Group
Stainless Steel	1450 ± 12	1348 ± 18	1237 ± 20
Nickel-Titanium	1025 ± 15	980 ± 15	912 ± 16

Figure 1 illustrates the tensile strength changes in SS and NiTi wires across the three treatment groups, highlighting the more pronounced deterioration caused by black tea compared to green tea.

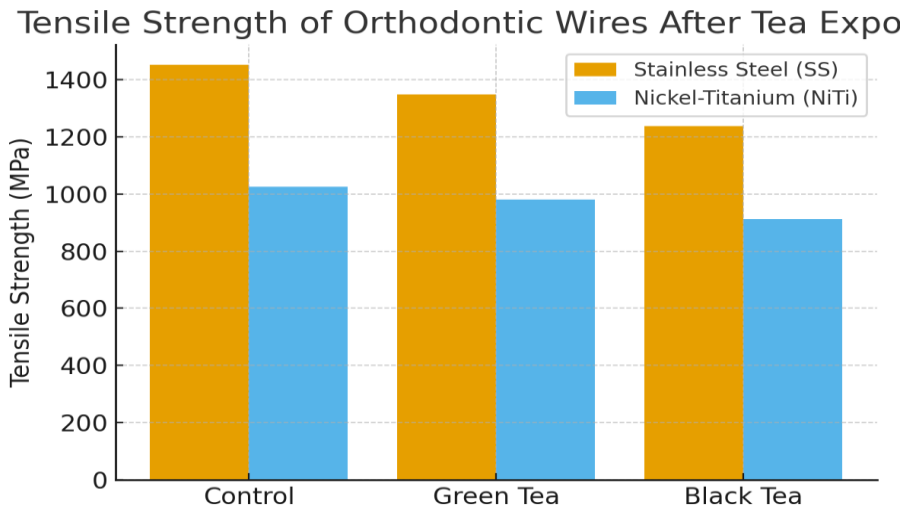


Figure 1. Tensile Strength of Orthodontic Wires

The bar chart illustrates the changes in tensile strength (MPa) of Stainless Steel (SS) and Nickel-Titanium (NiTi) wires after exposure to control (distilled water), green tea, and black tea. The results demonstrate that black tea caused the greatest reduction in tensile strength, particularly in SS wires.

Surface Roughness

Surface profilometry demonstrated a clear increase in roughness values (Ra) following tea exposure. SS wires immersed in black tea exhibited the greatest increase, from 0.18 µm (control) to 0.51 µm, while green tea exposure resulted in a moderate increase to 0.39 µm. NiTi wires showed a similar but less pronounced pattern, with Ra values rising from 0.20 µm (control) to 0.44 µm (black tea) and 0.33 µm (green tea).

The significant rise in Ra values indicates that tea exposure disrupts surface smoothness, which could influence sliding mechanics during orthodontic treatment. Black tea consistently produced the highest roughness values, supporting its more corrosive effect.

Table 3. Surface Roughness (Ra, µm) of Orthodontic Wires After Tea Exposure

Wire Type	Control Group	Green Tea Group	Black Tea Group
Stainless Steel	0.18 ± 0.02	0.39 ± 0.03	0.51 ± 0.04
Nickel-Titanium	0.20 ± 0.02	0.33 ± 0.03	0.44 ± 0.07

Corrosion Potential

Electrochemical testing further substantiated the SEM and EDX observations. Corrosion potential (Ecorr) values dropped significantly after tea immersion, with the lowest values detected in SS wires exposed to black tea (–342 mV). Comparatively, green tea caused a milder but still significant decline (–296 mV). NiTi wires showed relatively higher Ecorr values, indicating better resistance, yet still revealed a clear decline upon tea exposure.

Table 4. Corrosion Potential (Ecorr, mV) of Orthodontic Wires After Tea Exposure

Wire Type	Control Group	Green Tea Group	Black Tea Group
Stainless Steel	–210 ± 5	–296 ± 8	–342 ± 9
Nickel-Titanium	–180 ± 4	–251 ± 6	–309 ± 7

Integrated Findings

Taken together, the results consistently demonstrate that black tea exerts a more aggressive corrosive and degrading effect on orthodontic wires compared to green tea. The effects were more pronounced in stainless steel than in nickel–titanium wires across all analytical methods—surface morphology, elemental depletion, tensile strength reduction, roughness increment, and electrochemical instability.

DISCUSSION

Although the immersion period was limited to 28 days, which reflects only the early stages of beverage-induced corrosion, orthodontic appliances typically remain in the oral cavity for many months or years. It is therefore reasonable to expect that time-dependent degradation mechanisms, including crevice propagation, protein- and biofilm-mediated corrosion, and cyclic thermal stress, may exacerbate material deterioration beyond the timeframe studied. As such, the present findings should be interpreted as conservative estimates of long-term risk.

Furthermore, the absence of biocompatibility testing represents an important limitation. In particular, the depletion of nickel and chromium observed in stainless steel wires raises concerns regarding hypersensitivity and cytotoxicity, which warrant validation through standardized ISO 10993-5 cell culture assays. Similarly, the exclusive reliance on in vitro methods constrains the external validity of the study; short-term in vivo investigations, such as salivary ion release tracking in orthodontic patients, would provide clinically relevant confirmation of the laboratory findings.

The findings of the present in vitro study clearly demonstrate that both black and green tea exert measurable effects on the structural and mechanical integrity of orthodontic wires, with black tea inducing more severe degradation than green tea. These results carry important clinical and material implications, as dietary factors are often underestimated contributors to appliance deterioration during orthodontic therapy.

Corrosive Effects and Surface Alterations : The SEM and EDX analyses revealed extensive surface irregularities, elemental depletion, and pitting in stainless steel (SS) wires exposed to black tea, while green tea caused comparatively milder changes. This outcome is consistent with previous reports showing that polyphenol-rich and acidic solutions destabilize the protective oxide film of orthodontic alloys, accelerating electrochemical dissolution [11,12]. The significant depletion of chromium and nickel observed in SS wires immersed in black tea highlights the vulnerability of these alloys to acidic polyphenolic environments. On the other hand, NiTi wires showed comparatively higher resistance, corroborating earlier evidence that titanium-rich alloys exhibit superior passivation and corrosion resistance [13,14].

Mechanical Property Degradation: The tensile strength reduction in both SS and NiTi wires, particularly after immersion in black tea, underscores the functional consequences of beverage-induced corrosion. Mechanical deterioration compromises the ability of wires to maintain consistent force delivery, which may prolong treatment time or necessitate early replacement. These findings are in line with recent investigations reporting that common beverages such as acidic juices and soft drinks reduce wire resilience and sliding mechanics [15,16]. Moreover, increased surface roughness following tea exposure not only interferes with force delivery but also promotes greater friction between archwires and brackets, as documented in systematic reviews of orthodontic biomechanics [17].

Differential Role of Polyphenols :The divergent effects of black and green tea can be attributed to their distinct phytochemical profiles. Black tea undergoes oxidative

fermentation, generating theaflavins and thearubigins, which are associated with lower pH values and stronger oxidative potential that destabilize the passive oxide film. In contrast, green tea contains higher concentrations of epigallocatechin gallate (EGCG), a catechin with antioxidant and metal-chelating properties, which likely accounts for the comparatively protective effects observed [18; 19]. These findings support prior reports suggesting that green tea may serve as a mild corrosion inhibitor for stainless steel orthodontic wires [4]. However, some studies have reported negligible or even protective effects of tea extracts on dental alloys, which could be due to variations in tea preparation, polyphenolic concentrations, or immersion protocols [6,20]. This discrepancy highlights the need for standardized testing conditions to better compare across studies.

Clinical Implications: From a clinical standpoint, the demonstrated increase in surface roughness, reduction in tensile strength, and decline in corrosion resistance underscore the importance of considering dietary factors during orthodontic treatment. While the results revealed more severe deterioration in stainless steel wires exposed to black tea, even the comparatively milder effects of green tea remain clinically relevant over prolonged treatment durations. Dietary counseling should therefore be integrated into patient education, emphasizing moderation in the consumption of polyphenol-rich acidic beverages. Additionally, rinsing with water immediately after tea intake may help mitigate corrosive exposure. Importantly, given the observed chromium and nickel depletion, orthodontists should remain vigilant regarding hypersensitivity reactions, especially in patients with pre-existing metal allergies. The incorporation of protective coatings, or the use of wires with superior passivation layers, may represent a practical strategy to enhance appliance longevity in patients with high tea consumption habits [6].

Future Perspectives and Material Engineering: Building upon the present findings, future research should prioritize more comprehensive experimental designs that integrate longer immersion periods, cyclic thermal stress, and dynamic salivary conditions. Biocompatibility testing, particularly cytotoxicity assays and quantitative ion release, should be systematically performed to establish biological safety profiles. Furthermore, short-term in vivo pilot studies monitoring salivary metal ion concentrations during orthodontic treatment would provide valuable clinical confirmation of laboratory findings. On the materials engineering front, innovations such as diamond-like carbon films, titanium nitride coatings, or antioxidant-infused polymer layers hold promise for mitigating beverage-induced degradation. By combining mechanistic in vitro work with translational in vivo validation, future research can substantially strengthen the evidence base guiding both material development and clinical practice.

Clinical Relevance : The findings of this study have direct clinical implications for orthodontic practice. The demonstrated increase in surface roughness, reduction in tensile strength, and decline in corrosion resistance following tea exposure indicate that dietary habits may significantly influence the longevity and functional performance of orthodontic wires. From a practical perspective, orthodontists should provide dietary counseling to patients, highlighting the potential risks associated with frequent black tea consumption. Advising patients to rinse with water immediately after beverage intake could serve as a simple preventive measure to reduce corrosion. Moreover, awareness of possible nickel and chromium ion release is critical, particularly in patients with known metal hypersensitivity. Clinicians may consider the use of protective coatings or alternative wire materials with enhanced passivation to optimize treatment efficiency and minimize adverse reactions.

Limitations

Despite providing valuable comparative insights, this study is constrained by several methodological limitations that should be acknowledged. First, the immersion period was limited to 28 days, which does not fully reflect the long-term clinical exposure of orthodontic appliances that typically remain in the oral cavity for several months to years. Prolonged immersion models (≥90–180 days), combined with pH cycling and thermal fluctuations, would yield more clinically relevant degradation patterns. Second, the absence of standardized biocompatibility testing (e.g., ISO 10993 cytotoxicity assays using gingival fibroblasts or ICP-MS ion release quantification) restricts the ability to correlate electrochemical findings with potential biological responses. Third, this in vitro design cannot reproduce enzymatic activity, salivary proteins, or microbial biofilms that influence corrosion in vivo. Consequently, in vivo validation studies are strongly recommended to enhance the translational significance of these findings.

CONCLUSION

This study confirms that black tea induces more severe corrosive and mechanical degradation of orthodontic wires than green tea, with stainless steel being more vulnerable than nickel–titanium. These outcomes reflect the distinct polyphenolic compositions of the beverages, where black tea promotes oxidative dissolution while green tea exerts comparatively protective effects. Clinically, minimizing frequent black tea consumption,

rinsing after beverage intake, and exploring corrosion-resistant or coated wires are recommended strategies to prolong appliance functionality. Future research should extend these findings to dynamic oral conditions and investigate protective surface treatments or antioxidant-infused coatings to optimize orthodontic outcomes.

DECLARATION

Competing interest
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ORIGINAL ARTICALE

EVALUATING THE IMPACT OF PUPPET SHOW–BASED ORAL HEALTH EDUCATION ON KNOWLEDGE, ATTITUDES AND PRACTICES AMONG CHILDREN AGED 5 TO 12 YEARS

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Background/ Objective: Oral diseases in early childhood are often linked to poor hygiene practices and limited awareness. This study aimed to assess the effectiveness of a puppet show–based educational intervention in improving oral health knowledge, attitudes, and practices among pediatric patients.
Methods: A pre-post-follow-up design was implemented with 60 children (aged 5–12) visiting a pediatric OPD in a dental college located in Bhubaneswar, Odisha. A structured KAP questionnaire assessed knowledge (10 items), attitudes (5-point Likert scale), and self-reported practices at three intervals: baseline, immediately post-intervention, and four-week follow-up. A 30-minute puppet show focused on brushing, diet, and dental visits. Data was analyzed using paired t-tests and repeated-measures ANOVA ($p < 0.05$).
Results: Slight improvements were noted post-intervention: mean knowledge scores rose from 6.18 ± 1.25 to 6.23 ± 1.14; attitude scores increased from 4.06 ± 1.11 to 4.08 ± 1.20; and practice scores from 5.12 ± 1.09 to 5.17 ± 1.04. However, these differences were not statistically significant ($p = 0.437$ for knowledge, $p = 0.852$ for attitude, $p = 0.462$ for practice), indicating limited short-term effect.
Conclusion: The intervention yielded modest, non-significant improvements. Repeated or multi-modal approaches may be necessary to elicit meaningful, lasting behavioral changes in children's oral health.

Keywords: **Keywords:** Dental health literacy; Knowledge, Attitude, Practice (KAP); Puppet show; Oral health education; Pediatrics dentistry.

1.INTRODUCTION

Oral diseases, particularly dental caries, remain among the most prevalent non-communicable diseases globally, disproportionately affecting pediatric populations in low- and middle-income countries [1]. According to the World Health Organization (2022), approximately 3.7 billion individuals worldwide are impacted by oral health conditions, with children representing a significant at-risk demographic [2]. Dental caries, if left untreated, can lead to chronic pain, infections, nutritional deficiencies, impaired speech development, and frequent school absenteeism, collectively impairing the child's overall health and psychosocial development.

The etiology of poor oral health in children is multifactorial, encompassing inadequate oral hygiene practices, high sugar consumption, and limited access to preventive dental care [3]. Moreover, a critical barrier to effective oral disease prevention is the lack of appropriate health education tailored to the cognitive and emotional developmental stage of children[4]. Conventional educational strategies such as lectures, posters, and brochures often fall short in engaging younger audiences and sustaining behavior changes due to their passive and didactic nature [5].

Behavioral theories, including *Social Learning Theory* and the *Theory of Planned Behavior*, emphasize the role of interactive, observational learning and reinforcement in shaping health-related behaviors [6]. Within pediatric populations, education strategies that incorporate narrative structures, dramatization, and play-based learning have demonstrated improved outcomes in knowledge retention, motivation, and behavioral compliance [7]. Puppetry, as a dynamic and visually stimulating educational medium, offers an effective platform for delivering health messages in a format that resonates with children [8]. By modeling ideal behaviors in relatable scenarios, puppet-based interventions have the potential to promote favorable shifts in both cognitive understanding and attitudinal disposition towards oral hygiene [9].

Existing literature supports the utility of puppet shows in school- and community-based settings for enhancing health awareness. For instance, Ladera et al., (2022) demonstrated that puppet theater significantly improved oral health knowledge and hygiene practices among Peruvian preschoolers [10]. Similarly, Asrori et al., (2025) reported that puppetry served as an effective pedagogical tool in modifying oral health behaviors among primary school children [11]. However, there remains a paucity of evidence evaluating their application within clinical dental settings, particularly in the Indian context [12]. Furthermore, limited research exists on the sustained impact of such interventions on both knowledge and attitudes when assessed longitudinally.

Therefore, this study seeks to evaluate the effectiveness of a puppet show–based oral health education intervention in enhancing oral health–related knowledge and attitudes among pediatric dental outpatients. Employing a Knowledge, Attitude, and Practice (KAP) framework within a quasi-experimental pre-test–post-test design, the study investigates both the immediate and short-term impacts of the intervention on the target population.

2. MATERIALS AND METHODS

2.1 Study Design

This study employed a quasi-experimental, pre-post-test design without a control group to assess the effectiveness of a puppet show–based oral health education intervention. The study was conducted in the pediatric department of a dental college located in Bhubaneswar,Odisha, India, over a two-month period (March to May 2025).

2.2 Study Population

Children aged 5–12 years visiting the pediatric department for routine check-ups were considered for inclusion. Eligible participants were those accompanied by a consenting parent or guardian and with no prior exposure to structured oral health education programs. Children with developmental or cognitive disorders or those who had previously participated in oral health awareness activities were excluded to minimize bias. Of the 70 children assessed, 60 met the criteria and were enrolled using purposive sampling. The sample size was determined by moderate effect size, 80% statistical power, and a 5% significance level, with over-sampling to account for potential dropouts.

2.3 Questionnaire Tool

A standardized oral health questionnaire developed by WHO was employed to evaluate knowledge, attitudes, and practices related to oral hygiene among children. The tool comprised three sections with a total of 30 items. The knowledge component included 10 multiple-choice questions addressing key topics such as brushing techniques, fluoride use, dietary contributors to dental caries, and the importance of regular dental visits. Each correct response was scored as 1, while incorrect responses were scored as 0, resulting in a possible knowledge score ranging from 0 to 10 [13].

The attitude section consisted of 10 with options ranging from "Strongly Disagree" (1) to "Strongly Agree" (5), yielding a total attitude score between 10 and 50. These items captured both affective and behavioral intentions toward oral hygiene practices [14,15]. The third section, focused on actual oral hygiene behaviors, comprised 10 practice-related items that assessed brushing frequency, use of hygiene aids (e.g., toothbrush, floss, chewsticks), toothpaste type, dietary habits, dental visit regularity, and tobacco usage. Responses were captured using multiple-choice and frequency-based scales (e.g., "Never" to "Several times a day"), allowing ordinal-level analysis.

Data Collection Tools

Data was collected face-to-face using the structured questionnaire in a quiet and supervised area within the pediatric dental department. Tools were provided in the local language and explained by trained investigators. Each child completed the questionnaire individually, with support provided as needed, particularly for younger participants. Assessments were administered three times: before the intervention (Pre-test), immediately after the puppet show (Post-test 1), and four weeks later (Post-test 2), to evaluate immediate and retained impacts. All responses were recorded systematically.

2.4 Study Phases

The study was conducted in three structured phases to evaluate the effectiveness of the puppet show–based oral health education intervention:

- **Pre-Intervention (Baseline Assessment)**

At the outset, eligible participants and their parents were briefed about the study protocol. Informed written consent was obtained from the guardians, and verbal assent was taken from each child. Children then completed a baseline (pre-test) assessment comprising a structured questionnaire divided into three components: (i) a 10-item multiple-choice knowledge section, (ii) a 5-point Likert-scale–based attitude section, and (iii) a set of items assessing self-reported oral hygiene practices. The questionnaires were administered face-to-face in a quiet, supervised space within the pediatric dental clinic to ensure clarity and reduce distractions. Assistance was provided for younger children as required.

- **Intervention**

Following the pre-test, all participants attended a 30-minute puppet show–based oral health education session. The session was conducted in small groups in a designated child-friendly area of the department. The puppet show was collaboratively developed by pediatric dental professionals and puppeteer, focusing on essential oral health topics such as correct brushing techniques, the role of fluoride, dietary contributors to dental health, and the risks of tobacco use. The format used storytelling, visual humor, and age-appropriate characters to engage children actively. Participants were encouraged to interact during the show and mimic modeled health behaviors. The same health educator delivered all sessions using a standardized script to maintain consistency across groups.

- **Post-Intervention Assessment and Follow-Up**

Immediately after the intervention, children were administered the same knowledge, attitude, and practice questionnaires (Post-test 1) to assess short-term improvements. A follow-up assessment (Post-test 2) was conducted four weeks later during their scheduled clinic visit using the same instruments to evaluate retention of knowledge, attitude reinforcement, and sustained behavioral change. All responses from both follow-up points were systematically recorded and prepared for statistical analysis.

2.5 Statistical Analysis

Data was entered and analyzed using IBM SPSS Statistics for Windows, Version 26.0. Descriptive statistics (means, frequencies, percentages, and standard deviations) were calculated to summarize demographic characteristics and outcome variables across time points. Paired sample t-tests were used to compare pre- and post-intervention knowledge and attitude scores. Additionally, repeated measures ANOVA were applied to examine longitudinal changes and assess the sustainability of the intervention's effects. All statistical tests were conducted at a significance threshold of $p < 0.05$, and assumptions of normality and sphericity were verified prior to parametric analyses.

3.RESULTS

A total of 70 children were initially screened for participation during the study period. Of these, 60 children who met the eligibility requirements were enrolled and completed the baseline (pre-test) assessment. All enrolled participants attended the puppet-show–based intervention and subsequently completed the immediate post-test evaluation. At the 4-week follow-up, outcome data was successfully collected from 56 participants, while four were lost to follow-up due to reasons such as school vacations and scheduling conflicts.

Demographic Characteristics

The average age of participants was 8.4 years (±2.1), indicating a balanced representation of early and middle childhood. The gender distribution was slightly male-dominant (55% male, 45% female). In terms of socioeconomic status, 60% of children were from middle-income families and 40% from lower-income backgrounds, as assessed by the Modified Kuppuswamy Scale (Table 1).

Table 1. Demographic Characteristics of Participants

Characteristics	Values
Mean Age (years)	8.4 ± 2.1
Gender	
Male	55%
Female	45%
Socioeconomic Status	
Middle	60%
Lower	40%

3.1 Assessment of Oral Health Knowledge Among Pediatric Participants

3.2.1Knowledge-based Questions

- **Self-Perception of Oral Health**

A modest improvement was noted in children's self-perception of oral health following the intervention in Table 2. The proportion of participants who rated their oral health as Excellent increased from 3.3% to 6.7%, while those selecting Good and Average also showed slight gains. Notably, the percentage of children who were unsure (Don't Know) decreased from 21.7% to 16.7%, suggesting improved self-awareness and confidence in evaluating their oral health. These shifts indicate a positive trend in subjective health perception, likely influenced by the educational content delivered through the puppet show.

Table 2. How would you describe the health of your teeth and gums?

Responses	Pre N (%)	Post N (%)
Excellent	2 (3.3)	4 (6.7)
Very Good	12 (20.0)	8 (13.3)
Good	9 (15.0)	10 (16.7)
Average	8 (13.3)	10 (16.7)
Poor	8 (13.3)	10 (16.7)
Very Poor	8 (13.3)	8 (13.3)
Don't Know	13 (21.7)	10 (16.7)

Reason for Last Dental Visit

Following the intervention, a greater proportion of children reported visiting the dentist due to pain or oral discomfort, increasing from 20.0% to 28.3%, and for treatment or follow-up care, rising from 21.7% to 25%. In contrast, visits for routine check-ups decreased from 28.3% to 21.7%, possibly reflecting more accurate recognition of symptomatic dental issues. Additionally, the proportion of children uncertain about the reason for their last dental visit declined from 30.0% to 25%, indicating improved recall and awareness of dental care experiences in Table 3, which reflects a modest improvement in recall accuracy and contextual understanding of oral healthcare interactions.

Table 3. What was the reason for your last visit to the dentist?

Responses	Pre-test N (%)	Post-test N (%)
Pain or trouble with teeth, gums or mouth	12 (20.0)	17 (28.3)
Treatment/follow up treatment	13 (21.7)	15 (25)
Routine checkup of teeth/ treatment	17 (28.3)	13 (21.7)
I don't know/ I don't remember	18 (30.0)	15 (25)

- **Awareness about Fluoride Use**

Post-intervention responses revealed minimal change in awareness regarding fluoride use in toothpaste showed in figure 1. The proportion of children reporting use of fluoride-containing toothpaste remained relatively stable, with a slight decline from 48.3% to 46.7%, while those indicating non-use increased marginally from 51.7% to 53.3%. These findings suggest that the intervention had limited impact on altering fluoride-related knowledge, highlighting a potential gap in message retention or clarity regarding the benefits and identification of fluoride in dental products.

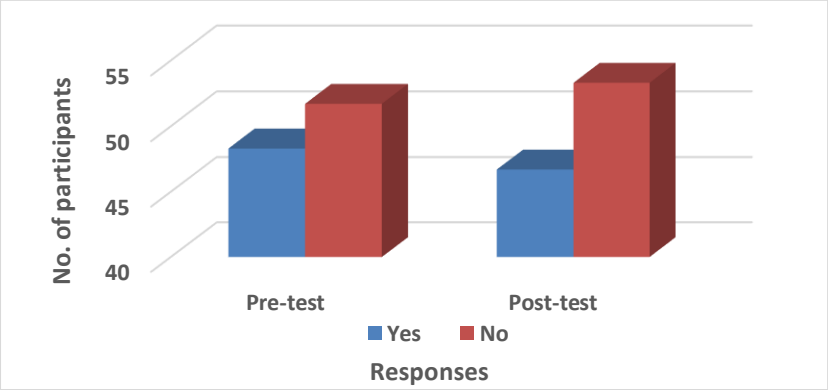


Figure 1. Do you use toothpaste that contains fluoride?

- **Dietary Knowledge Related to Oral Health**

Post-intervention data revealed a downward shift in the frequent consumption of cariogenic items. Daily intake of sugary foods such as chewing gum dropped from 23.3% to 13.3%, sweets/candy from 16.7% to 13.3%, and soft drinks from 21.7% to 13.3%. In contrast, healthier patterns emerged in the consumption of fresh fruit, with daily intake increasing from 10.0% to 11.7% and several times a day from 16.7% to 20.0%. These changes indicate an improvement in dietary awareness related to oral health, likely attributable to the intervention in Table 4.

Table 4. How often do you eat sugary foods/drinks like candy, soft drinks, or biscuits?												
Responses	**Pre-test N (%)**						**Post-test N (%)**					
	Several times a day	**Every day**	**Several times a week**	**Once a week**	**Once a month**	**Never**	**Several times a day**	**Every day**	**Several times a week**	**Once a week**	**Once a month**	**Never**
Fresh fruit	10 (16.7)	6 (10)	9 (15)	12 (20)	13 (21.7)	10 (16.7)	12 (20)	7 (11.7)	7 (11.7)	12 (20)	12 (20)	10 (16.7)
Biscuits, cakes, cream cakes, sweet pies, buns etc.	12 (20)	9 (15)	14 (23.3)	13 (21.7)	4 (6.7)	8 (13)	8 (13.3)	9 (15)	15 (25)	14 (23.3)	3 (5)	11 (18.3)
Lemonade, Coca Cola, or other soft drinks	6 (10)	13 (21.7)	7 (11.7)	13 (21.7)	11 (18.3)	10 (16.7)	16 (26.7)	8 (13.3)	13 (21.7)	5 (8.3)	11 (18.3)	7 (11.7)
Jam/honey	10 (16.7)	10 (16.7)	9 (15)	12 (20)	9 (15)	10 (16.7)	11 (18.3)	13 (21.7)	10 (16.7)	8 (13.3)	9 (15)	9 (15)
Chewing gum containing sugar	14 (23.3)	10 (16.7)	4 (6.7)	8 (13.3)	14 (23.3)	10 (16.7)	8 (13.3)	9 (15)	8 (13.3)	13 (21.7)	12 (20)	10 (16.7)
Sweets/candy	10 (16.7)	10 (16.7)	9 (15)	15 (25)	7 (11.7)	9 (15)	7 (11.7)	8 (13.3)	10 (16.7)	11 (18.3)	12 (20)	12 (20)
Milk with sugar	11 (18.3)	9 (15)	14 (23.3)	9 (15)	7 (11.7)	10 (16.7)	13 (21.7)	10 (16.7)	12 (20)	12 (20)	6 (10)	7 (11.7)
Tea with sugar	10 (16.7)	10 (16.7)	9 (15)	15 (25)	7 (11.7)	9 (15)	9 (15)	10 (16.7)	11 (18.3)	14 (23.)	10 (16.7)	6 (10)
Coffee with sugar	11 (18.3)	9 (15)	14 (23.3)	9 (15)	7 (11.7)	10 (16.7)	10 (16.7)	9 (15)	14 (23.3)	9 (15)	11 (18.3)	7 (11.7)
(Insert country-specific items)	9 (15)	10 (16.7)	10 (16.7)	14 (23.3)	12 (20)	5 (8.3)	12 (20)	14 (23.3)	8 (13.7)	8 (13.7)	10 (16.7)	8 (13.3)

- **Dietary Knowledge Related to Oral Health**

  Awareness of tobacco's harmful effects on oral health demonstrated a modest shift following the intervention. The proportion of children recognizing its impact once a week increased notably from 8.3% to 23.3%, while higher-frequency responses such as every day and several times a week declined from 18.3% each to 15.0% and 10.0%, respectively. This redistribution suggests a refinement in understanding, with participants moving from vague or extreme responses toward more realistic acknowledgment of exposure risk, indicating improved but nuanced awareness post-intervention in Table 5.

Table 5. Can tobacco products harm your teeth and gums?		
Options/Responses	**Pre-test N (%)**	**Post-test N (%)**
Every day	11 (18.3)	9 (15)
Several times a week	11 (18.3)	6 (10)
Once a week	5 (8.3)	14 (23.3)
Several times a month	11 (18.3)	10 (16.7)
Seldom	13 (21.7)	12 (20)
Never	9 (15)	9 (15)

- **Awareness Regarding Tobacco Effects**

Knowledge of recommended brushing frequency showed slight variation post-intervention. Although the proportion of children selecting twice a day remained relatively low (13.3% pre to 11.7% post), there was a mild increase in those indicating once a day (13.3% to 15.0%) and only when they feel dirty (23.3% to 20.0%). However, the proportion of participants choosing never/I don't know remained unchanged at 18.3%, suggesting that while some improvement occurred, misconceptions and lack of clarity regarding optimal brushing habits persist. These findings highlight the need for reinforcing consistent oral hygiene messages found in Table 6.

Table 6. How often should teeth be brushed in a day?		
Responses	**Pre-test N (%)**	**Post-test N (%)**
Every day	10 (16.7)	7 (11.7)
Twice a day	8 (13.3)	9 (15)
Once a day	8 (13.3)	12 (20)
Only when they feel dirty	14 (23.3)	9 (15)
Seldom	12 (20)	11 (18.3)
Never / I don't know	8 (13.3)	11 (18.3)

- **Knowledge of Oral Hygiene Practices**

Post-intervention responses indicated improved understanding of oral hygiene practices, particularly regarding causes of dental caries showed in Table 7. Recognition of not brushing teeth properly as a very likely cause increased from 13.3% to 25.0%, while uncertainty (not sure) declined from 18.3% to 11.7%. For eating too many sweets, very likely responses decreased from 26.7% to 13.3%, but likely responses rose from 16.7% to 30.0%, suggesting a more realistic attribution. The perception of using too much toothpaste as a likely cause decreased slightly, with very likely responses dropping from 28.3% to 18.3%, indicating better differentiation between actual and perceived causes of cavities. These findings reflect enhanced knowledge and reduced misconceptions related to oral hygiene following the intervention.

Table 7: What do you think is the main reason people get cavities?										
Responses	**Pre-test N (%)**					**Post-test N (%)**				
	Very likely	**Likely**	**Not sure**	**Unlikely**	**Very unlikely**	**Very likely**	**Likely**	**Not sure**	**Unlikely**	**Very unlikely**
Eating too many sweets or sugary foods	16 (26.7)	10 (16.7)	9 (15)	15 (25)	10 (16.7)	8 (13.)	18 (30)	15 (25)	9 (15)	10 (16.7)
Not brushing teeth properly	8 (13.3)	13 (21.7)	11 (18.3)	13 (21.7)	15 (25)	15 (25)	9 (15)	7 (11.7)	14 (23.3)	15 (25)
Not visiting the dentist	14 (23.3)	11 (18.3)	14 (23.3)	10 (16.7)	11 (18.3)	13 (21.7)	13 (21.7)	14 (23.3)	4 (6.7)	16 (26.7)
Using too much toothpaste	17 (28.3)	11 (18.3)	8 (13.3)	11 (18.3)	13 (21.7)	11 (18.3)	13 (21.7)	11 (18.3)	14 (23.3)	11 (18.3)

3.2 Assessment of Attitudes Toward Oral Health Among Pediatric Participants

- **Self-Image and Social Perception**

  A moderate enhancement in self-perception was noted, with satisfaction regarding dental appearance rising from 30.0% to 35.0% post-intervention. Concurrently, dissatisfaction declined from 38.3% to 31.7%, indicating a shift in how children view their own teeth in figure 2. The proportion of uncertain responses remained nearly unchanged (31.7% to 33.3%), suggesting that while perceptions improved for some, further engagement may be needed to influence indecisive participants.

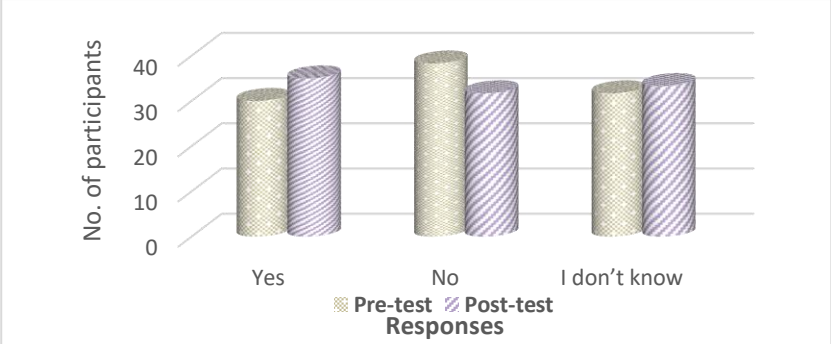


Figure 2: I am happy with the way my teeth look

Post-intervention responses showed minimal change in social confidence related to dental appearance. The proportion of children who reported feeling shy or embarrassed to smile rose slightly from 30.0% to 33.3%, while those who did not feel embarrassed declined marginally from 35.0% to 31.7%. Notably, the percentage of uncertain responses remained constant at 35.0%, indicating that despite the intervention, attitudes related to self-consciousness and social perception may require deeper behavioral engagement to shift meaningfully in figure 3.

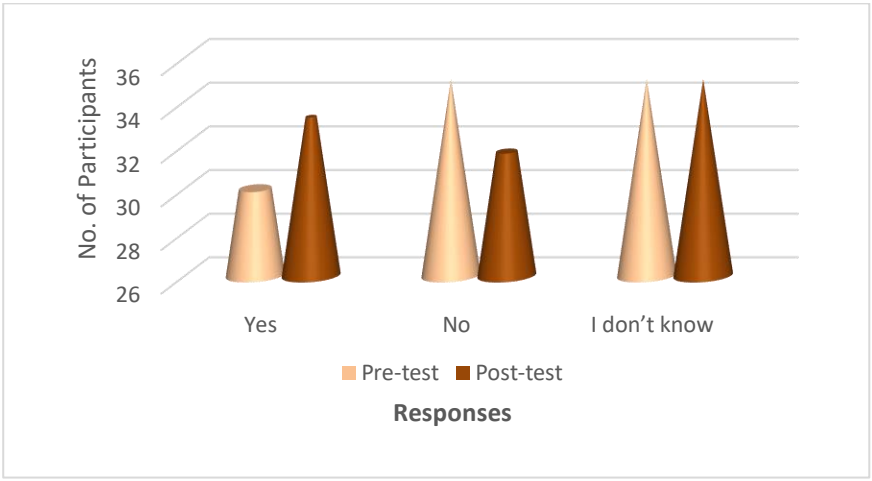


Figure 3. I feel shy or embarrassed to smile because of my teeth

- **Perceived Importance of Oral Hygiene**

  Attitudinal responses toward the importance of dental visits revealed limited positive movement. The proportion of children who strongly agreed remained unchanged at 21.7%, while those who agreed slightly declined from 20.0% to 16.7%. A decrease in not sure responses (31.7% to 26.7%) indicates some gain in decisiveness; however, an increase in strongly disagreeing responses from 11.7% to 18.3% suggests persistent skepticism among a subset of participants in Table 8a. Overall, the intervention had a mixed impact on reinforcing the perceived necessity of routine dental care.

  The belief that daily brushing is essential showed mixed outcomes. While the proportion of children who disagreed declined from 28.3% to 18.3%, the number of strongly disagree responses notably increased from 13.3% to 28.3%, suggesting a potential polarization of opinion. Meanwhile, strongly agree responses slightly decreased from 23.3% to 20.0%, and agree responses dropped from 20.0% to 18.3%. The unchanged proportion of not sure responses (15.0%) further points to limited improvement in consensus. These findings indicate that while some misconceptions may have been addressed, the message regarding the importance of daily brushing may not have been uniformly internalized in Table 8b.

Table 8. Attitudinal responses toward oral hygiene										
Questions /Responses	Pre-test N (%)					Post-test N (%)				
	Strongly Agree	Agree	Note Sure	Disagree	Strongly Disagree	Strongly Agree	Agree	Not Sure	Disagree	Strongly Disagree
(a) Going to the dentist is important to keep teeth healthy	13 (21.7)	12 (20.0)	19 (31.7)	9 (15.0)	7 (11.7)	13 (21.7)	10 (16.7)	16 (26.7)	10 (16.7)	11 (18.3)
(b) I believe brushing teeth every day is necessary	14 (23.3)	12 (20.0)	9 (15.0)	17 (28.3)	8 (13.3)	12 (20.0)	11 (18.3)	9 (15.0)	11 (18.3)	17 (28.3)
(c) I feel that cleaning my teeth is boring or unnecessary	12 (20.0)	14 (23.3)	15 (25.0)	8 (13.3)	11 (18.3)	13 (21.7)	12 (20.0)	11 (18.3)	9 (15)	15 (25)
(d) I worry that I might lose teeth if I don't take care of them	6 (10.0)	14 (23.3)	11 (18.3)	14 (23.3)	15 (25.0)	12 (20.0)	17 (28.3)	11 (18.3)	8 (13.3)	12 (20.0)

Perceptions regarding the necessity and engagement of tooth cleaning showed a moderate shift post-intervention. The proportion of children who strongly disagreed with the notion that cleaning teeth is boring or unnecessary increased from 18.3% to 25.0%, indicating a positive change in attitude toward accepting oral hygiene as an essential routine. Additionally, "Not Sure" responses declined from 25.0% to 18.3%, reflecting improved clarity in participants' views. On the other hand, the percentage of children who strongly agreed with the statement slightly increased from 20.0% to 21.7%, suggesting that a subset of children retained negative perceptions. These findings demonstrate partial improvement in motivation-related attitudes toward oral hygiene, though further engagement may be necessary to shift entrenched negative beliefs (Table 8c).

Perceptions surrounding the value of tooth cleaning showed a modest improvement post-intervention. Strongly disagree responses increased from 18.3% to 25.0%, indicating a growing number of children who rejected the idea that oral hygiene is boring or unnecessary. Meanwhile, not sure responses declined from 25.0% to 18.3%, suggesting improved clarity in attitudes. However, strongly agree responses also saw a slight rise from 20.0% to 21.7%, pointing to persistent ambivalence in a subset. Overall, the findings reflect a gradual but incomplete shift in attitude toward viewing tooth cleaning as a meaningful daily practice in Table 8d.

3.3 Assessment of Oral Hygiene Practices Among Participants

- **Oral Hygiene Practices**

Post-intervention data revealed a reduction in the proportion of children who never cleaned their teeth, decreasing from 25.0% to 11.7%, indicating a positive shift in basic oral hygiene engagement. However, there was also a decline in those reporting brushing once a day (18.3% to 10.0%) and two or more times a day (20.0% to 15.0%), suggesting inconsistencies in adopting recommended practices. Notably, more participants reported cleaning their teeth several times a month (8.3% to 16.7%) and once a week (13.3% to 25.0%), which, although improved from non-practice, still fall short of ideal frequency. These results point toward initial behavioral change but highlight the need for reinforcing sustained, routine oral hygiene practices in Table 9.

Table 9. How often do you clean your teeth?		
Responses	**Pre-test N (%)**	**Post-test N (%)**
Never	15 (25)	7 (11.7)
Several times a month (2-3) time	5 (8.3)	10 (16.7)
Once a week	8 (13.3)	15 (25)
Several times a week (2-6)	9 (15)	13 (21.7)
Once a day	11 (18.3)	6 (10)
2 or more times a day	12 (20.0)	9 (15)

Use of conventional cleaning aids showed mixed trends post-intervention. Toothbrush use increased from 13.3% to 21.7%, suggesting a positive shift toward standard oral hygiene tools in Table 10. However, reliance on traditional or non-standard methods remained notable. Use of charcoal doubled from 10.0% to 20.0%, and chewstick/miswak use also increased slightly (11.7% to 15.0%), indicating continued preference for indigenous practices. In contrast, the use of dental floss declined from 16.7% to 8.3%, reflecting limited uptake of recommended interdental cleaning. Overall, the findings suggest partial improvement in tool selection, with greater acceptance of toothbrushes but persistent gaps in comprehensive hygiene practices.

Table 10. Do you use any of the following to clean your teeth or gums?				
Responses	**Pre-test N (%)**		**Post-test N (%)**	
	Yes	**No**	**Yes**	**No**
Toothbrush	8 (13.3)	9 (15)	13 (21.7)	9 (15)
Wooden toothpicks	10 (16.7)	5 (8.3)	9 (15)	10 (16.7)
Plastic toothpicks	7 (11.7)	9 (15)	7 (11.7)	5 (8.3)
Thread (dental floss)	10 (16.7)	11 (18.3)	5 (8.3)	11 (18.3)
Charcoal	6 (10)	10 (16.7)	12 (20)	9 (15)
Chewstick/miswak	7 (11.7)	12 (20)	9 (15)	7 (11.7)
Other	12 (20)	4 (6.7)	5	9 (15)

A decline in toothpaste usage was observed following the intervention, with yes responses dropping from 66.7% to 56.7%, and no responses rising from 33.3% to 43.3%. This unexpected reversal suggests either a regression in practice adherence or potential confusion introduced during the intervention regarding appropriate oral cleaning materials. The results highlight a need to reinforce clear messaging about the role of fluoride toothpaste in effective oral hygiene in figure 4.

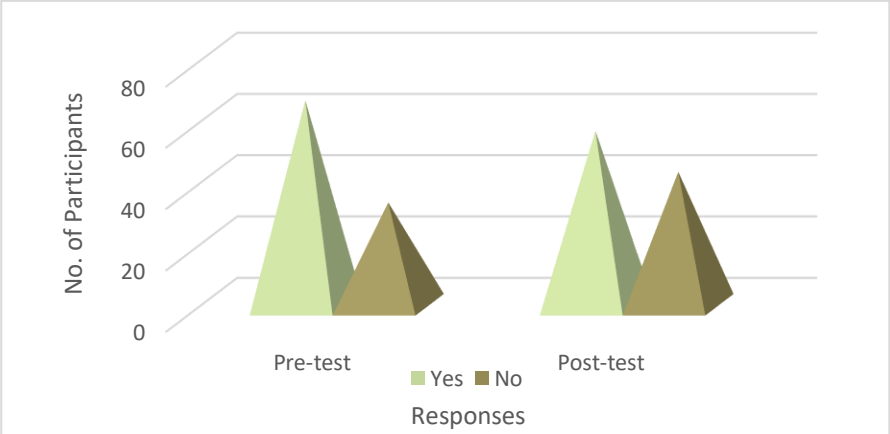


Figure 4. Do you use toothpaste to clean your teeth?

- **Dental Service Utilization**

Post-intervention trends in dental service utilization revealed mixed outcomes. While visits four times a year increased from 8.3% to 21.7%, suggesting improved engagement among some participants, there was also a rise in those reporting never visiting a dentist, from 6.7% to 15.0%, and those unsure of their visit history (10.0% to 11.7%). Additionally, the proportion of children who visited the dentist once, three times, or more than four times declined, indicating inconsistency in access or recall. These findings reflect partial improvement in routine utilization but also highlight disparities in awareness, recall, and access to dental care services that may require targeted follow-up in Table 11.

Table 11. How often did you go to the dentist in the past 12 months?		
Responses	**Pre-test N (%)**	**Post-test N (%)**
Once	10 (16.7)	7 (11.7)
Twice	7 (11.7)	7 (11.7)
Three times	10 (16.7)	6 (10)
Four times	5 (8.3)	13 (21.7)
More than four times	10 (16.7)	6 (10)
I had to visit to dentist during the past 12 months	8 (13.3)	5 (8.3)
I have never received dental care/ Visited a dentist	4 (6.7)	9 (15)
I don't know/ I don't remember	6 (10)	7 (11.7)

- **Experience of Dental Discomfort**

Post-intervention data showed a modest reduction in reported dental discomfort. The percentage of children experiencing toothache often declined from 18.3% to 15.0%, and those reporting it occasionally dropped from 21.7% to 16.7%. Simultaneously, reports of rarely experiencing discomfort increased slightly (23.3% to 25.0%) and never experiencing discomfort rose to 23.3%, suggesting some improvement in perceived oral health. However, the rise in don't know responses (15.0% to 20.0%) indicates lingering uncertainty among participants, potentially reflecting gaps in awareness or difficulty in symptom recognition in Table 12.

Table 12. During the past 12 months, how often have toothache or discomfort?		
Responses	**Pre-test N (%)**	**Post-test N (%)**
Often	11 (18.3)	9 (15)
Occasionally	13 (21.7)	10 (16.7)
Rarely	14 (23.3)	15 (25)
Never	13 (21.7)	14 (23.3)
Don't Know	9 (15)	12 (20)

- **Substance Use Behavior**

Post-intervention dietary patterns exhibited nuanced changes. There was a modest decline in daily consumption of high-sugar items like biscuits and cakes (from 20.0% to 13.3%) and soft drinks (from 13.3% to 8.3% reporting several times a day use), indicating slight dietary moderation. Conversely, intake of sweets/candies increased in the never category (from 16.7% to 28.3%), suggesting improved sugar avoidance for some participants. However, consumption of chewing gum, tea/coffee with sugar, and jam/honey remained relatively stable, with no clear directional trend. Meanwhile, fresh fruit consumption showed only marginal change, implying that healthy alternatives were not significantly emphasized. These results suggest partial behavioral shifts, with improved restriction of certain sugary items, yet highlight the need for sustained emphasis on both sugar reduction and promotion of healthier dietary substitutes (Table 13).

Table 13. What foods and drinks do you usually consume in a day?												
Responses	**Pre-test N (%)**						**Post-test N (%)**					
	Several times a day	**Every day**	**Several times a week**	**Once a week**	**Once a month**	**Never**	**Several times a day**	**Every day**	**Several times a week**	**Once a week**	**Once a month**	**Never**
Fresh fruit	8 (13.3)	13 (21.7)	7 (11.7)	13 (21.7)	6 (10)	13 (21.7)	10 (16.7)	8 (13.3)	9 (15)	12 (13.7)	10 (16.7)	11 (18.3)

Biscuits, cakes, cream cakes, sweet pies, buns etc.	12 (20)	10 (16.7)	12 (13.7)	10 (16.7)	9 (15)	7 (11.7)	18 (30)	10 (16.7)	10 (16.7)	5 (8.3)	8 (13.3)	9 (15)
Lemonade, Coca Cola, or other soft drinks	8 (13.3)	3 (5)	16 (26.7)	9 (15)	10 (16.7)	14 (23.3)	9 (15)	15 (25)	8 (13.3)	12 (13.7)	11 (18.3)	5 (8.3)
Jam/honey	11 (18.3)	11 (18.3)	8 (13.3)	10 (16.7)	9 (15)	11 (18.3)	13 (21.7)	14 (23.3)	7 (11.7)	9 (15)	8 (13.3)	9 (15)
Chewing gum containing sugar	7 (11.7)	10 (16.7)	17 (28.3)	7 (11.7)	11 (18.3)	8 (13.3)	11 (18.3)	11 (18.3)	11 (18.3)	13 (21.7)	4 (6.7)	10 (16.7)
Sweets/candy	9 (15)	11 (18.3)	8 (13.3)	11 (18.3)	11 (18.3)	10 (16.7)	14 (23.3)	3 (5)	8 (13.3)	8 (13.3)	10 (16.7)	17 (28.3)
Milk with sugar	6 (10)	16 (26.7)	8 (13.3)	12 (20)	9 (15)	9 (15)	15 (25)	10 (16.7)	11 (18.3)	6 (10)	8 (13.3)	10 (16.7)
Tea with sugar	10 (16.7)	8 (13.3)	16 (26.7)	6 (10)	13 (21.7)	8 (11.7)	7 (11.7)	11 (18.3)	8 (13.3)	4 (6.7)	13 (21.7)	17 (28.3)
Coffee with sugar	13 (21.7)	9 (15)	11 (18.3)	6 (10)	11 (18.3)	10 (16.7)	8 (13.3)	12 (20)	12 (20)	8 (13.3)	13 (21.7)	7 (11.7)

Post-intervention findings indicate a slight reduction in habitual tobacco use, with regular users dropping from 20.0% to 11.7% and occasional users from 31.7% to 23.3%, suggesting a positive behavioral shift in a portion of the population. However, reports of trying tobacco once or twice marginally increased (13.3% to 15.0%), and the proportion of participants who selected I don't know / I don't want to say rose notably from 16.7% to 26.7%, potentially reflecting increased stigma or reluctance to disclose use. While never users increased to 23.3%, the elevated non-disclosure rate signals a need for more confidential and trust-based approaches in future substance-use assessments (Table 14).

Table 14: Have you used tobacco or products like pan/gutka in the past year?

Responses	**Pre-test N (%)**	**Post-test N (%)**
Yes, regularly	12 (20)	7 (11.7)
Yes, sometimes	19 (31.7)	14(23.3)
I tried it once or twice	8 (13.3)	9 (15)
No, never	11 (18.3)	14 (23.3)
I don't know / I don't want to say	10 (16.7)	16 26.7)

3.4 Comparison of Knowledge, Attitude and Practice pre and post scores

The paired samples test results indicate that the differences in pre- and post-intervention scores for knowledge, attitude, and practice were not statistically significant. The knowledge domain showed a p-value of 0.437, indicating no significant improvement following the intervention. Similarly, the attitude scores yielded a p-value of 0.852, and the practice scores had a p-value of 0.462. Since all p-values are greater than the conventional threshold of 0.05, the changes observed in participants' knowledge, attitudes, and practices post-intervention were not statistically meaningful, suggesting the intervention may require reinforcement or a longer follow-up period for significant impact in Table 15.

Table 15: Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Knowledge PRE - POST	.05351	.53012	.06844	-.08343	.19045	.782	59	.437
Attitude PRE - POST	-.01667	.69074	.08917	-.19510	.16177	-.187	59	.852
Practice PRE - POST	-.05521	.57709	.07450	-.20429	.09387	-.741	59	.462

DISCUSSION

Oral health education is essential for developing positive behaviors and preventive practices among children, particularly during the formative years when long-term habits and attitudes are shaped [16]. In the present study, a puppet show based intervention was employed as an engaging and age-appropriate method to improve oral health knowledge and attitudes among pediatric dental outpatients aged 5–12 years. While the intervention yielded some improvements at the individual item level across knowledge, attitude, and practice (KAP) domains, these changes were not statistically significant in aggregate analysis. Knowledge-related outcomes showed marginal gains post-intervention. A slight increase was noted in participants' understanding of topics such as fluoride use, dietary contributors to dental decay, and awareness of brushing frequency. However, the overall change in knowledge scores did not reach statistical significance (mean difference = 0.05, p = 0.437). Similar findings have been reported by Putri et al., (2024), who documented modest gains in oral health knowledge following a similar puppet-based intervention. However, their study emphasized the importance of reinforcement sessions to consolidate learning, which may explain the limited effect observed in the present work [17]. For instance, the BMC Oral Health study by Prasai et al., (2023) in Nepal reported that 82% of children did not know about fluoride and 24% brushed twice daily, highlighting similar educational gaps [18].

Knowledge of the harmful effects of tobacco on oral health showed only slight improvement in this study. This finding may be attributed to the abstract nature of the concept for young children and possible limitations in cognitive maturity required to fully understand and retain such information. These results echo the observations of Collins et al., (2020), who noted that tobacco-related health education in children often requires longitudinal reinforcement for significant retention [19].

Attitudinal changes following the intervention were mixed and statistically non-significant (mean difference = −0.017, p = 0.852). Although more children's post-intervention agreed that daily brushing is necessary and recognized the value of dental visits, a large portion remained uncertain or held indifferent views. This delay in attitudinal change relative to knowledge gain has been similarly observed by Evans et al., (2019), who emphasized that attitudes, particularly in younger populations, tend to evolve gradually and require experiential reinforcement [20]. A positive indication in the present study was the slight improvement in children's perception of their dental appearance and a reduction in reported embarrassment while smiling, suggesting emerging self-awareness and comfort. Tsolakidis, (2024) reported comparable findings, where puppet-based interventions effectively reduced dental anxiety and improved self-perception in children [21]. Oral hygiene practices exhibited some improvement, particularly in the reduction of participants who reported never brushing their teeth (from 25.0% to 11.7%). However, the results were inconsistent across other variables. Use of standard cleaning tools such

as toothbrushes showed improvement, while use of toothpaste surprisingly declined in some cases. Similar mixed trends were reported by Baker et al., (2019), who emphasized that behavior change among children often requires parental involvement and reinforcement at home to ensure consistency and habit formation [22].In terms of dietary behavior, slight reductions were seen in the frequency of sugary food and beverage consumption, but intake of items such as tea, coffee, and chewing gum containing sugar remained high. A decline in regular tobacco product use was also observed, yet this was accompanied by a rise in non-disclosure responses, indicating either increase stigma or hesitancy to report use. Fung et al., (2024) identified a similar pattern in school-based studies and suggested that social desirability bias and lack of comprehension could obscure true behavioral patterns in younger cohorts [23].

Despite these directional trends, the paired samples test did not demonstrate statistically significant differences in pre- and post-intervention scores across knowledge, attitude, or practice domains. These findings are consistent with those of Schleider and Beidas, (2022), who concluded that single-session educational tools, though beneficial for initial engagement, are often insufficient for inducing sustained behavioral change [24]. The present study thus supports the position that puppet shows can serve as effective introductory tools for oral health promotion in pediatric settings, but should be incorporated into broader, multi-modal and repetitive educational strategies to achieve long-term impact.

Despite its promising approach, the study had notable limitations. The single-session design without follow-up may have limited long-term knowledge retention and behavior change. Self-reported responses introduced potential bias, and the outpatient sample may not reflect broader pediatric populations. Future research with longitudinal, multi-session formats is recommended.

CONCLUSION

This study concludes that puppet show–based oral health education serves as a creative and engaging tool for delivering preventive dental knowledge among pediatric dental outpatients. While the intervention demonstrated modest improvements in item-level knowledge and shifts in attitude and practice domains, the overall statistical changes in KAP scores were not significant. Nevertheless, the findings underscore the potential of interactive, child-friendly educational methods in raising awareness about oral hygiene. The effectiveness of such interventions may be enhanced with repeated sessions, parental involvement, and reinforcement strategies. The study also highlights the importance of tailoring health education tools to suit cognitive and emotional development in children. Despite its limitations, this research contributes to the evolving framework of community-based pediatric oral health promotion.

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DECLARATIONS

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Institutional Ethics Committee.

Consent for Publication

The patient provided written informed consent for the publication of this case report, including clinical images and radiographic findings.

Competing Interests

The authors declare that they have no competing interests related to this study.

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ORIGINAL ARTICALE

EVALUATING FACTORS CONTRIBUTING TO DENTAL ANXIETY IN ORTHODONTIC PATIENTS

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ABSTRACT

Background: Dental anxiety is one of the most common forms of psychological impairment obstructing oral health care, often causing necessary treatments to go unattended. Therefore, investigating the prevalence and associated determinants is important for effective intervention. It also assessed the prevalence of dental anxiety and its prospectors among patients in Baghdad, Iraq, for the planning of tailored patient care approaches.

Materials and Methods: A cross-sectional survey between October 2020 and June 2022 recruited 345 orthodontics patients who came to a private institution for dental care. According to the MDAS, patients scoring 11 or higher were determined to have clinically significant anxiety. A structured questionnaire was administered to collect demographic, psychological, and socioeconomic information. Statistical analysis was then performed using single and multifactor logistic regression to determine predictors significantly associated with dental anxiety, as advised by the statistician.

Results: The prevalence of dental anxiety was 17.23%. Significant predictors included being female, being more than 60 years old, having existing anxiety or depression, having an education level lower than secondary, having a poor sense of self-efficacy, suffering a physical disease, and having low social support ($P<0.05$). Multifactor regression reasoned and confirmed all these as strong contributors to the model, verifying the complexity of dental anxiety.

Conclusions: This study shows the high prevalence of dental anxiety and the intricate factors behind it, which require tailoring behavioral approaches in dentistry to factors of psychological and demographic origin.

Keywords: Dental anxiety; Modified Dental Anxiety Scale (MDAS); Orthodontic patients; Predictors; Personalized patient care

INTRODUCTION

Dental anxiety in orthodontics procedure, a common but multifaceted psychological condition, afflicts people of all ages, causing evasion of vital dental attention and, thus, a negative impact on oral health status [1,2]. Dental anxiety is not just an issue for the patient; it also creates problems for dentists in that anxious patients are usually more complicated and take longer to treat [3].

Several studies have identified different factors that contribute to dental anxiety, e.g., fear of pain, past negative experiences, socioeconomic status, and psychological factors like depression and anxiety [4-7]. Such patients usually undergo fainting states, palpitations, tremors, and other related symptoms and signs, which may be significantly damaging to the patient [8]. This orthodontics patient category forms a sizeable proportion of outpatient dental treatment patients and has, therefore, attracted many studies on dental anxiety among outpatients. Most of these studies focus on the result influences on dental anxiety in such patients but show common differences in the research aspect [9]. Outpatient orthodontics dental anxiety is commonly noted, and it causes more damage to treatment. It increases difficulty during the implementation of treatment and nursing measures and adversely affects the treatment outcome. Patients have also been forced to stay away from health institutions. Therefore, more attention is given in clinical practice to diagnosing, treating, and preventing dental anxiety patients [10- 12]. Townsend and Randall [13] elaborate on adolescent dental fear and the significance of nonpharmacologic behavior guidance while stressing individualized approaches for younger patients. Fell et al. [14] point out that a comprehensive overview of anxiety disorders reveals a key role for mind wandering in which such behavior may exacerbate dental anxiety. Lehrner et al. [15] show buffering factors such as ambient odors like orange in dental settings that would

help reduce anxiety; hence, it could be an easy, uncomplicated form to solve the issues. Khan et al. [16], as well as Hu et al. [17], principally address the consequences of trauma to facial and dental parts and report the association between such experiences with increased anxiety and depression. Ali et al. [18] analyze the self-reported anxiety of dental students, showing the difference in gender and education level, which can be further utilized in educational strategies.

Sukhabogi et al. [19] link psychological distress to oral health and consider their integrated nature. As for Çarıkçıoğlu [20], the effect of parental dental anxiety on their children is discussed concerning anxiety's intergenerational transfer and its effect on oral health-related quality of life. Sukumaran et.al [21], examined the broad impact of dental anxiety among adult New Zealanders and how much it affects oral health behaviors. Kassem et al. [22] describe the cultural diversity in Lebanon concerning the prevalence of dental anxiety, contributing factors to it, and exploring the overshadowing factors in the phenomenon. Lahti et al. [23] applied virtual reality-based relaxation therapies, which should highly advocate for developing non-pharmacological avenues in ameliorating the immediate post-dental intervention effectiveness on patient anxiety. Hence, the report introduces cognitive and non-cognitive factors contributing to dental anxiety's emergence and recommends a multifaceted approach to effectively addressing it. So far, there is a considerable lack of understanding of prevalence and determinants in particular populations, given their respective cultural contexts. Although studies on prevalence have been published on dental anxiety in many countries, there has been little that even includes the Middle East, especially Iraq, as a site for investigation.

In the present work, this research gap will be filled by exploring the prevalence and associated factors of orthodontics dental anxiety in patients who visit orthodontics dental clinics in Baghdad, Iraq. The study comprised 345 outpatients who attended the private clinic for dental treatment between October 2020 and June 2022. Other components measured dental anxiety levels alongside demographic data and conducted both uni- and multivariate analyses to identify significant predictors of dental anxiety. Therefore, it opened a new area of research around the specifics of the Iraqi social situation and the causes or contributions to dental anxiety, which could, thus, inform target measures to address it in dental patients.

1. MATERIALS AND METHODS

2.1 Data collection

Between October 2020 and June 2022, 345 orthodontics dental outpatients, 164 males and 181 females, visited the private dental clinic in Baghdad, Iraq. Patients must attain specific inclusion criteria when receiving treatment at the clinic, must be aged 14 and above, must fill the questionnaire alone or with family assistance, and must show interest in being devotedly and actively willing to cooperate in research activity. Exclusion from participation includes patients suffering from a history of mental illness, communication disorders, and those with incomplete clinical data.

2.2 Method

2.2.1 Analysis of Dental Anxiety

Dental anxiety was evaluated in this research with the Modified Dental Anxiety Scale (MDAS). It is an established, reputed instrument of global importance for measuring dental anxiety in orthodontics proceedures. It measures dental anxiety along four specific dimensions, and respondents rate each on a scale of 1 to 5, where 1 indicates "very low" anxiety and five marks "very high" anxiety. The present work sought to use cut-off scores above 11 in MDAS to indicate dental anxiety. Hereby, data that advance the recognition and classification of degrees of dental anxiety detected among the participants are of utmost importance for analysis and interpretation in the study.

2.2.2 General Information Collection

1. Structured questionnaires have been used to collect general orthodontics patient information: the structured questionnaires include a significant number of demographic and psychological factors concerning their:
2. Age: classified into below 60 years and 60 years and above categories.
3. Gender: classified as male or female.
4. Emotional State: The presence or absence of anxiety and depression were scored using a Zung scale, and on anxiety and depression
5. threshold scores of 50 (for anxiety) and 53 (for depression), anything below these threshold scores denoting absence.
6. Education Level: Orthodontics patients were grouped according to their educational backgrounds at junior high school and below and higher secondary technical education.
7. Marital Status: Married patients (having spouse) or unmarried patients (having no spouse).
8. Type of place of Residence: Urban or rural residents.
9. Patient base: Permanent or mobile residents.
10. Dental Treatment Construction: Patients who experienced dental treatment before (yes and no).
11. Income: Patients were divided into two categories according to their monthly income equal to or greater than 800 $/month and less than these categories.
12. Occupational Status: Patients were either classified as employed or non-employed.

13. General self-efficacy scores range from very high (31-40), high (21-30), low (11-20), and very low (below 11).
14. The Basic Disease Conditions: Patients were screened for comorbid disease conditions.
15. Social Support: Social support was measured using the Social Support Rating Scale. Patients were categorized based on their level of social support as high (30-40), medium (20-29), or low (<20).

2.2.3 Observation Indicators

Assessment of dental anxiety for orthodontics patients and its related determinants among the study cohort involves many research methods and indicators.

(a) Orthodontics Dental Anxiety Assessment: This is a crucial part of this study that includes carefully assessing all patients using an international measure called the Modified Dental Anxiety Scale (MDAS). The scale includes four main areas for measurement, each of which is used to mark score points on a 1-5 system, where 1 is mild and 5 is most severe. A total score of 11 points or above on the MDAS was the cut-off point for the diagnosis of the presence of dental anxiety, enabling a deeper understanding of patients' descriptive scores for levels of anxiety about dental procedures.

b) Univariate deficiencies: It has used simple univariate deficiencies for understanding the prevalence of dental anxiety and demands influencing factors, as well as for analyzing individual predictors and other factor potentials towards the occurrence of dental anxiety.

2.2.4 Statistical Processing

The analysis was done using SPSS 23.0 software statistical analysis. When presenting measurement data such as (x-±s), x is the mean, while s refers to the standard deviation. Count data were presented as percentages (%), ensuring clarity in data display.

2. RESULT AND DISCUSSION

The results of this study show that among 345 dental clinic orthodontics patients, 99 cases were dental anxiety, and the incidence rate of dental anxiety was 17.23%. The proportion of patients with dental anxiety who are ≥60 years old, female, anxious and depressed, have a junior high school education or below, have low or very low self-efficacy, have underlying diseases, and have moderate or low levels of social support are higher than those of patients without dental anxiety.

The difference is that there is statistical significance ($P<0.05$); see Table 1. It shows that there is still some room for prevention and control of dental anxiety, and effective control is urgently needed. Orthodontics Patients with dental anxiety are aged ≥60 years old, female, anxious and depressed, have junior high school education or below, have low and very low self-efficacy, have underlying diseases, and are moderate. The proportion of patients with lower social support levels was higher than that of patients without dental anxiety. Multifactor logistic regression analysis showed that age, gender, emotional state, education level, self-efficacy, underlying diseases, and social support levels all affected dental outpatient dental care. Influencing factors of anxiety. Therefore, the need for assessment and intervention of the above factors is believed to be high.

In-depth regression analyses using multifactor logistic regression to some of the indicators shown in Table 1, which were significantly different, for example, to transform them into an outcome variable categorized as "dental anxiety = 1" and "no dental anxiety=0."

The allocation of independent variables has been carefully outlined in Table 2 for clarity and transparency. Multifactorial logistic regression analysis also clarified which factors can affect oral outpatient dental anxiety. Such factors include age, sex, emotional state, level of education, self-efficacy, diseases present, and social support. Furthermore, this analysis has revealed from statistical reporting that the study found sufficient evidence to affirm that each of the mentioned factors does play a role in the presence of anxiety concerning dental treatment in the participants of the study. This can be concluded from a reported significant correlation ($P<0.05$). To have everything in view regarding the expected results and the breakdown of the variables used, refer to Table 3. The results reflect diverse kinds of interconnected factors that come into play upon the exhibition of dental anxiety among people undergoing oral outpatient visits and provide evidence for developing appropriate tailored interventions and support for patients.

Table 1. Univariate analysis of the occurrence of dental anxiety in dental clinic patients (%)

Dental Anxiety	Age		Gender		Emotional state		Education level	
	<60 year	≥60 year	Male	female	Anxiety and depression	No anxiety or depression	Junior high school and below	Technical secondary school and above
Have dental anxiety (n=99)	29.29	70.71	27.27	72.73	56.57	43.43	87.88	12.12
No dental anxiety (n=501)	59.68	40.32	58.28	41.72	4.59	95.41	69.06	30.94
χ2	30.802		31.926		195.320		14.572	
P	<0.001		<0.001		<0.001		<0.001	
	Form of residence		Dental treatment experience		Income		Place of residence	
Dental Anxiety	Permanent	Temporary	Have-none		≥800$/Month	<800$/Month	Town	Rural area
Have dental anxiety (n=99)	77.78	22.22	17.17	82.83	26.26	73.74	66.67	33.33
No dental anxiety (n=501)	83.03	16.97	11.98	88.02	32.73	67.27	66.47	33.53
χ2	1.559		1.995		1.345		0.001	
P	0.211		0.157		0.206		0.975	
	career status		self-efficacy		Basic disease conditions		degree of social support	
Dental Anxiety	On the job	Not employed	High and very high	Low and very low	Have	None	Higher	Medium and lower
Have dental anxiety (n=99)	69.70	30.30	20.20	79.80	40.40	59.60	36.36	63.64
No dental anxiety (n=501)	72.46	27.54	72.46	27.54	10.18	89.82	78.64	21.36
χ2	0.312		97.966		58.692		72.771	
P	0.576		<0.001		<0.001		<0.001	

Table 2. Assignment of Independent Variables

Factor	Assignment
Age	<60 years old=0; ≥60 years old=1
Gender	Male=0; Female=1
Emotional State	No anxiety and depression=0; anxiety and depression=1
Education level	Technical secondary school and above=0; Junior high school and below=1
Self-Efficacy	High and very high = 0; low and very low = 1
Basic Disease Conditions	None=0; Yes=1
Degree Of Social Support	High = 0; Medium and low = 1

Table 3. Multifactor Analysis of Dental Anxiety Among Dental Outpatients

Factor	β	SE	Waldχ2	OR	95%CI	P
Age	1.193	0.3221	12.352	3.06	1.389	<0.05
Gender	1.24	0.2791	18.028	3.203	1.423	<0.05
Emotional State	1.477	0.3601	15.555	4.039	1.805	<0.05
Education Level	1.062	0.2781	12.954	2.694	1.372	<0.05
Self-Efficacy State	1.421	0.3451	15.625	3.823	1.68	<0.05
Basic Disease Conditions	1.257	0.2911	17.018	3.257	1.43	<0.05
Degree Of Social Support	1.364	0.3301	15.672	3.616	1.576	<0.05

The analysis shows that older individuals with comorbid medical conditions usually find themselves at relatively lower levels of physical well-being. This status of health, therefore, results in relatively lower cognizance of the various treatment and examination types, even on lines of oral health. Consequently, higher tensions and uncertainties accompany their experiences with dental procedures. These states of mind significantly affect dental anxiety, leading to a higher prevalence of the condition 13-14. Research, too, identifies a gender difference where females possess a more fragile psychological disposition and a comparatively higher fear of medical treatment. Such high apprehension contributes to a much greater risk of developing dental anxiety 15.

The emotional reaction linked with this would often be expressed as dental anxiety and fear, thus emphasizing further the relationship between mental health and dental anxiety 16-17.

Understanding dental treatment is limited by such relatively low education levels, and dental misconceptions have been shared among less literate groups. Ignorance regarding what one fears usually gives one a very high susceptibility to developing dental anxiety 18. Besides, the amount of social support a person gets must weigh heavily on their psychological condition.

Patients with adequate but moderate social support levels suffer from alarmingly uncertain and even fearful confusion concerning the treatment they might undergo medically, as these emotional states are keys to triggering anxiety 19-20.

Those low in self-efficacy generally consider that treatment is not achievable; hence, they seem to have stronger fears related to the processes involved in treatment and what happens after it. These fears usually turn out to be reflected in dental anxiety 21. There is no doubt that these characteristics make it possible to see all kinds of patients requiring counseling and intervention related to these before the time of dental treatment. Further, the targeted interventions would go a long way in helping patients manage and control their dental anxiety, improving their overall experience with treatment and outcomes.

3. CONCLUSION

This research aimed to assess orthodontics dental anxiety and its factors among patients of a dental clinic, from which interesting insights can be drawn into the field of dental healthcare. However, the findings revealed a complicated interactive factors contributing to the intensity of dental anxiety among patients, thereby bringing out important issues to be considered by clinical practitioners and in further research.

The part of the analysis based on an established tool for assessment called the Modified Dental Anxiety Scale (MDAS) confirmed that dental anxiety is a real problem for patients. A significant number of the population studied showed signs of dental anxiety, according to the study, where the MDAS scores were then 11 and above. This indicates the urgency in the dental clinic setting.

Using different data collection and analysis methods, this research demonstrated that dental anxiety is multifactorial. Various demographic and psychological factors were found to be possible predictors of dental anxiety. These factors included age, sex, emotional state, level of education, marital status, place of living, housing condition, dental treatments, income, occupation status, self-efficacy, basic disease conditions, and social support. This confirms the need to consider personalized patient care based on an individual context and specific needs.

The robust results of this study have thus been made available to dental healthcare providers so that they can design specific interventions or strategies to prevent or address dental anxiety among patients. Understanding the determinants of dental anxiety permits healthcare workers to formulate a more supportive and patient-centered atmosphere, thereby improving the dental experience for patients with dental anxiety.

DECLARATIONS

Ethics approval and consent to participate

Not applicable.

Conflict interests

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ORIGINAL ARTICLE

RELATIONSHIP BETWEEN TRANSVERSE BASAL ARCH WIDTH AND MOLAR INCLINATION: A CBCT STUDY IN YEMENI ADULTS

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ABSTRACT

Background: Transverse skeletal discrepancies in adults are often underdiagnosed, particularly when masked by dentoalveolar compensation such as molar inclination. This study aimed to evaluate the relationship between transverse basal arch width and molar angulation in Yemeni adults using cone-beam computed tomography (CBCT).

Methods: A retrospective CBCT analysis was conducted on 87 untreated Yemeni adults (17–40 years). Participants were classified into normal and narrow maxilla groups based on the maxillary–mandibular basal width difference (Mx–Mn). Skeletal widths were measured on standardized basal planes, and first molar inclination was recorded relative to skeletal reference lines. Group comparisons were performed using t-tests, while correlations were assessed with Pearson's r. Intra-examiner reliability was verified with ICC.

Results: The narrow maxilla group demonstrated a significantly smaller maxillary width (54.55 ± 2.8 mm) than the normal group (57.55 ± 3.1 mm; $p < 0.001$), accompanied by a greater mandibular width (57.5 ± 3.3 vs. 55.2 ± 3.1 mm; $p = 0.003$), resulting in a negative Mx–Mn difference. Upper molars exhibited greater buccal inclination (195.2° ± 11.4 vs. 189.8° ± 7.2; $p = 0.028$), whereas lower molars showed more lingual inclination (146.3° ± 10.6 vs. 155.1° ± 8.5; $p < 0.001$). Strong correlations were found between Mx–Mn and molar inclination (upper $r = +0.535$; lower $r = -0.463$; both $p < 0.001$). ICC exceeded 0.90.

Conclusion: Molar inclination functions as a compensatory mechanism in the presence of transverse skeletal imbalance. Incorporating both skeletal and dental assessments through CBCT enhances the detection of concealed transverse disharmony and facilitates more individualized orthodontic treatment planning.

Keywords*:* CBCT; transverse basal arch width; molar inclination; skeletal discrepancy; dental compensation; Yemeni adults; orthodontic diagnosis

1. INTRODUCTION

Transverse skeletal discrepancies are often less recognized in orthodontic diagnosis than vertical or sagittal problems. While skeletal width is fundamental for maintaining functional occlusion and facial balance, its deficiencies are frequently hidden by dental compensations, particularly through molar inclination.[1,2] Unlike vertical or sagittal discrepancies, transverse problems—such as maxillary constriction—are not always obvious clinically and may remain undetected in patients with apparently normal alignment

or compensated crossbites.[3,4] When left unidentified, these discrepancies can contribute to posterior crossbite, functional shifts, and long-term

instability of the occlusion.[5]

Evaluating transverse basal arch width together with molar inclination is crucial for detecting hidden skeletal imbalances and understanding the compensatory changes that teeth may develop in response to transverse deficiencies.[6,7] In particular, buccolingual tipping of the molars often serves as a compensation in maxillary narrowing, masking the underlying skeletal disharmony.[8] While such dental adaptations may provide short-term functional balance, they can compromise long-term stability if the transverse discrepancy is not diagnosed and corrected during treatment planning. [9]

Therefore, precise assessment of both skeletal width and molar angulation is fundamental for achieving stable orthodontic outcomes.

Conventional two-dimensional imaging methods, such as posteroanterior cephalograms or occlusal radiographs, have well-known limitations when assessing transverse dimensions. Projection errors and the lack of three-dimensional visualization reduce their accuracy in evaluating true skeletal width and molar inclination.[10] By contrast, cone-beam computed tomography (CBCT) provides high-resolution volumetric images that allow measurement of basal bone width and dental angulation from stable anatomical landmarks with superior precision.[11,12] Several studies have confirmed that CBCT yields more consistent and reproducible measurements of transverse width and buccolingual molar inclination in both clinical and research settings.[13]

Despite growing recognition of the importance of transverse diagnosis, limited research has examined the combined evaluation of basal arch width and molar inclination using CBCT. Most existing studies have analyzed these variables separately, often within small or ethnically homogenous samples.[14,15] Consequently, the compensatory mechanisms that may link skeletal transverse width to molar angulation remain insufficiently understood. Exploring this relationship is essential to advance knowledge of transverse balance and to provide more accurate, individualized orthodontic treatment planning across diverse populations. Therefore, the present study aimed to evaluate transverse basal arch width and molar inclination using CBCT, and to investigate the relationship between these two parameters in a sample of untreated Yemeni adults. By focusing on this population, the study seeks to provide new insights into transverse skeletal discrepancies and dental compensations within an underrepresented group in the literature.

2. MATERIALS AND METHODS

2.1 Study Design and Ethics

This retrospective cross-sectional study was conducted in 2024 at the Department of Orthodontics, Faculty of Dentistry, Sana'a University. CBCT scans were acquired between 2020 and 2023 from Al-Waleed 3D X-ray Center, a private dental radiology facility in Sana'a, Yemen. Over 500 archived scans were reviewed, and 87 cases that met the inclusion criteria were selected. Ethical approval was obtained from the Institutional Medical Ethics Committee at Sana'a University (Approval No.: OR:15/12/2023), and all data were anonymized in accordance with institutional research protocols. This study was conducted in accordance with the Declaration of Helsinki.

2.2 Sample Selection

The study sample included Yemeni adults aged 17–40 years who had full permanent dentition up to the second molars. Selection focused on cases suitable for transverse skeletal analysis, excluding those with prior orthodontic intervention, prosthetic restorations (e.g., crowns or implants), extensive carious lesions, large fillings, or compromised occlusal anatomy such as impacted teeth, severe spacing or crowding, and pronounced rotations. Scans lacking image clarity or anatomical consistency were also eliminated. After reviewing 98 eligible cases, 11 were excluded due to extreme transverse discrepancy (>5 mm), resulting in a .final sample of 87 individuals.

2.3 CBCT Protocol

CBCT scans were acquired using a PaX-i3D Green system (Vatech, Korea) with 15×15 cm field of view and 0.2–0.3 mm voxel size. Scans were taken in full-face view at maximum intercuspation, with the Frankfort horizontal plane parallel to the floor to ensure proper head positioning."Exposure settings were 50–99 kV, 4–16 mA, and 15 seconds scan time, as per the manufacturer's guidelines. Images were analyzed using Ez3D-i software (Ewoosoft, Korea) following multiplanar reconstruction. Orientation was standardized using the midpalatal suture (vertical) and functional occlusal plane (horizontal).

2.4 Measurement Protocol and Grouping

Skeletal transverse width was evaluated using standardized CBCT slices in both axial and coronal views. A modified mid-basilar reference line was used for maxillary width assessment, defined midway between the jugale-based plane [16] and the buccal concavity plane [17], following orientation guidelines derived from the University of Pennsylvania protocol.

The mandibular width was measured at the basal level

using the WALA ridge reference (mandibular width plane), which served as the definitive skeletal baseline for comparison. The transverse skeletal discrepancy was calculated as the difference between maxillary and mandibular widths, and participants were classified into two groups: "normal" (0–5 mm difference) and "narrow" (maxillary width ≤ mandibular width).

Molar inclination was measured in the coronal view by calculating the angle between the long axis of the first molars (from buccal cusp tip to root furcation midpoint) and the corresponding skeletal reference line. The mid-basilar plane was used for maxillary molars, and the WALA plane for mandibular molars. Right and left measurements were averaged.

The skeletal and angular reference structures used in the study are illustrated in Figure 1.

"Further details of the CBCT measurement protocol and supplemental figures are provided in Appendix A."

2.5 Statistical Analysis and Reliability

To evaluate intra-examiner reliability, all measurements were repeated by the same examiner in a subset of 20 cases after a two-week interval. All statistical analyses were performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (means and standard deviations) were calculated for all skeletal and dental variables. The Kolmogorov–Smirnov test was used to assess normality.

Independent samples t-tests were used to compare transverse widths and molar inclinations between the two groups (normal vs. narrow). One-way ANOVA and chi-square tests were applied where applicable. Pearson's correlation coefficient was used to assess the linear relationship between transverse skeletal discrepancy and molar inclination.

Intraclass correlation coefficients (ICC) were calculated, with values above 0.90 indicating excellent agreement.

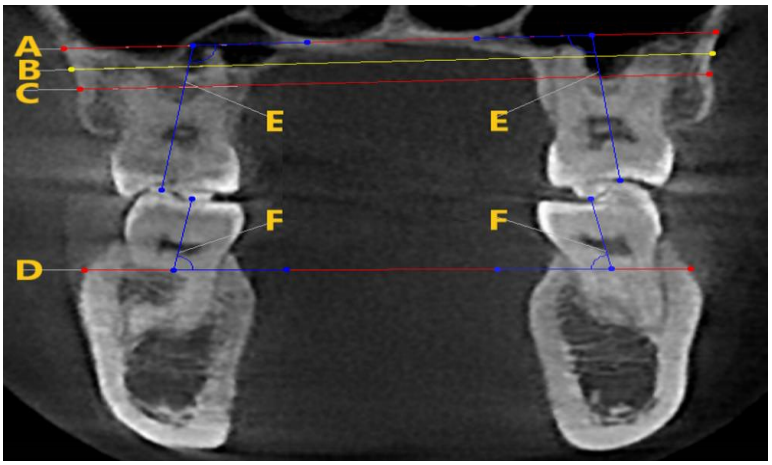


Figure 1. The skeletal and dental reference structures are used in measurement.

The components include:

A: Maxillary basilar plane – transverse skeletal line connecting the bilateral jugale points at the level of the zygomatic buttress.

B: Mid-basilar plane – a newly defined horizontal reference plane located midway between the basilar and width planes, providing a balanced skeletal reference for maxillary width assessment. C: Maxillary width plane – line passing through the buccal concavity region, approximately between the alveolar crest and root apex of the maxillary first molars.

D: Mandibular width plane – transverse skeletal line drawn at the WALA ridge level, representing the basal width of the mandibular arch.

E: Maxillary molar axis – line drawn from the buccal cusp tip to the center of the root furcation of the first maxillary molar, used for inclination analysis.

F: Mandibular molar axis – line connecting the buccal cusp tip to the midpoint between the mesial and distal root apices of the first mandibular molar.

3. RESULTS

3.1. Sample Characteristics and Group Distribution

This study analyzed 87 CBCT scans of untreated Yemeni adults. Participants were categorized into normal (n = 58) and narrow maxilla groups (n = 29) based on the skeletal transverse width difference (Mx–Mn). Table 1 presents the distribution of gender, skeletal classification, and posterior crossbite across both groups. The narrow group included a higher proportion of females and Class II subjects compared to the normal group. Posterior crossbite, particularly the bilateral form, was predominantly found in the narrow group, while it was rare among subjects with normal transverse width.

Table 1. Illustrates the flow of sample selection and crossbite distribution.

Variable	Normal Maxilla (n = 58)	Narrow Maxilla (n = 29)	Total (n = 87)
Gender – Male	29	12	41
Gender – Female	29	17	46
Skeletal Class I	36	12	48
Skeletal Class II	16	11	27
Skeletal Class III	6	6	12
No Posterior Crossbite	52	11	63
Unilateral Crossbite	6	10	16
Bilateral Crossbite	0	8	8

3.2. Transverse Skeletal Widths

The skeletal transverse width measurements showed significant differences between the two groups. Subjects with a narrow maxilla had a significantly reduced maxillary width (54.55 ± 2.8 mm) compared to those with a normal maxilla (57.55 ± 3.1 mm; $p < 0.001$). Conversely, mandibular width was greater in the narrow group (57.5 ± 3.3 mm) than in the normal group (55.2 ± 3.1 mm; $p = 0.003$). This reversal in maxillo-mandibular width confirmed a true skeletal transverse discrepancy in the narrow group (negative Mx–Mn).

Table 2. Comparison of skeletal transverse widths between normal and narrow groups (mm).

Variable	Normal Maxilla (n = 58) Mean ± SD	Narrow Maxilla (n = 29) Mean ± SD	p-value
Maxillary width	57.55 ± 3.1	54.55 ± 2.8	< 0.001*
Mandibular width	55.2 ± 3.1	57.5 ± 3.3	0.003*
Mx–Mn width difference	+2.35 ± 1.5	–2.95 ± 1.2	< 0.001*

*Denotes statistical significance ($p < 0.05$).

3.3. Molar Inclination

The inclination of the first molars showed significant differences between the two groups. Maxillary molars were more buccally inclined in the narrow maxilla group (195.2° ± 11.4) compared to the normal group (189.8° ± 7.2; $p = 0.028$). Mandibular molars, in contrast, showed greater lingual inclination in the narrow group (146.3° ± 10.6) than in the normal group (155.1° ± 8.5; $p < 0.001$). These findings indicate a transverse compensatory pattern, with opposing inclinations in the upper and lower molars among subjects with skeletal maxillary constriction.

Table 3. Comparison of molar inclination angles between normal and narrow maxilla groups

Variable	Normal Maxilla (n = 58) Mean ± SD	Narrow Maxilla (n = 29) Mean ± SD	p-value
Maxillary molar inclination (°)	189.8 ± 7.2	195.2 ± 11.4	0.028*
Mandibular molar inclination (°)	155.1 ± 8.5	146.3 ± 10.6	< 0.001*

*Denotes statistical significance ($p < 0.05$).



Figure 2. Representative CBCT coronal images illustrating general differences in maxillomandibular transverse skeletal relationships and molar inclinations among subjects. The image reflects the range of patterns observed across the classified groups, including skeletal width variation and dental compensation.

3.4. Correlation Between Width and Inclination

Pearson correlation analysis revealed a strong positive association between the maxillary–mandibular width difference (Mx–Mn) and the maxillary molar inclination angle ($r = +0.535$, $p < 0.001$). A moderate negative correlation was found with mandibular molar inclination ($r = –0.463$, $p < 0.001$). These results indicate that greater skeletal transverse deficiency (i.e., more negative Mx–Mn values) is associated with increased buccal tipping of upper molars and compensatory lingual tipping of lower molars.

Table 4. Correlation between maxillo-mandibular width difference (Mx–Mn) and molar inclination angles.

Correlated Variables	Pearson correlation (r)	p-value
Mx–Mn width vs. Maxillary molar inclination	+0.535	< 0.001*
Mx–Mn width vs. Mandibular molar inclination	−0.463	< 0.001*

*Denotes statistical significance ($p < 0.05$).

4. DISCUSSION

This CBCT-based study aimed to investigate the relationship between transverse basal arch width and molar inclination in untreated Yemeni adults, using a standardized skeletal reference plane at the mid-basilar level. This methodological approach improved diagnostic precision by minimizing the influence of crown angulation and alveolar remodeling, as previously highlighted Tamburrino et al. [18]. The primary outcomes demonstrated that individuals with narrow maxilla presented both skeletal constriction and notable dentoalveolar compensation through buccolingual molar tipping.

Quantitatively, the narrow maxilla group exhibited a significantly reduced transverse width of the maxilla (54.55 ± 2.8 mm) compared to the normal group (57.55 ± 3.1 mm, $P < 0.001$), while the mandibular width was paradoxically greater in the narrow group (57.5 ± 3.3 mm) versus the normal group (55.2 ± 3.1 mm, $P = 0.003$). This skeletal disproportion produced a negative Mx–Mn difference in the narrow group (–2.95 ± 2.5 mm) compared to a positive value in the normal group (+2.35 ± 1.6 mm), indicating a true transverse deficiency in the maxilla. These skeletal changes were accompanied by a consistent pattern of dental compensation: maxillary molars in the narrow group showed greater buccal inclination (195.2° ± 11.4 vs. 189.8° ± 7.2, $P = 0.028$), while mandibular molars were significantly more lingually inclined (146.3° ± 10.6 vs. 155.1° ± 8.5, $P < 0.001$).

These findings confirm that molar inclination acts as a compensatory response to skeletal transverse imbalance. This is in agreement with observations reported by Albalawi et al. [19] in Saudi adults, and by Kim et al. [20] and Rathi et al. [21] in similar CBCT-based investigations.

A significant statistical correlation was found between the maxillary–mandibular width difference and molar inclination. Specifically, a positive correlation existed with upper molar inclination ($r = +0.535$), while a negative correlation was found with lower molar

inclination (r = –0.463), both of which were statistically significant. These results highlight the adaptive mechanism of molar tipping in response to skeletal disharmony, supporting the conclusions of Kim et al. [20] and Rathi et al. [21], who emphasized the role of molar angulation in maintaining occlusal function when mild transverse discrepancies are present.

This consistent correlation pattern raises a critical clinical concern: transverse skeletal deficiencies may go undetected in the presence of compensatory dentoalveolar inclinations. In such cases, clinicians may be misled by apparently aligned occlusion, overlooking the underlying skeletal disharmony. This phenomenon was also highlighted by Gribel et al. [22] and Proffit et al. [23], who stressed the diagnostic risk of relying solely on dental arch form or occlusal appearance without CBCT-based skeletal assessment

When analyzing subgroups by sagittal skeletal classification, clinically meaningful variations in transverse compensation were observed. Class II individuals demonstrated the narrowest maxillary widths and the most pronounced buccal inclination of upper molars, consistent with the pattern of maxillary underdevelopment described in previous literature.[24] Conversely, Class III subjects presented with wider mandibular arches and more evident lingual tipping of lower molars—likely a compensatory response to skeletal mandibular prominence, in agreement with findings from López-Areal et al. [25] and Rong et al. [26]

Posterior crossbite was observed in 62% of individuals with narrow maxillae; however, many cases lacked this sign despite evident skeletal deficiency. Molar tipping likely masked the discrepancy, creating a misleading occlusal appearance. As Proffit et al. [23] emphasized, crossbite absence does not rule out underlying transverse disharmony.

This study has several limitations. Its retrospective, cross-sectional design restricts the ability to assess longitudinal changes or determine causal relationships. The sample included only adults aged 17–40 years, excluding growing children and prepubertal individuals who may exhibit different skeletal growth patterns and dentoalveolar compensation. Additionally, functional factors such as tongue posture, muscular forces, and airway volume were not assessed, though they may influence transverse development and molar inclination.

5. CONCLUSIONS

In this study, we found that skeletal maxillary constriction is not always obvious during clinical examination. Molar inclination may play a role in compensating for the transverse skeletal deficiency, which can make the condition more difficult to detect, especially in the absence of clear clinical signs like posterior crossbite. Our measurements of skeletal width and molar angulation using CBCT helped us detect discrepancies that might not have been noticed in a routine clinical exam. This highlights the importance of looking at both the skeletal and dental structures together, especially when planning for stable and individualized orthodontic treatment.

6. DECLARATIONS

Funding

This research received no external funding or financial support.

Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Medical Ethics Committee at Sana'a University (Approval No.: OR:15/12/2023).

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Abbreviations:

The following abbreviations are used in this manuscript:

CBCT	Cone-Beam Computed Tomography
Mx	Maxillary width
Mn	Mandibular width
Mx–Mn	Maxillary–Mandibular Width Difference
WALA	Width At the Level of the Alveolar Ridge (WALA ridge)
ICC	Intraclass Correlation Coefficient
SPSS	Statistical Package for the Social Sciences
ANOVA	Analysis of Variance

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Appendix

Appendix A CBCT Measurement Protocol and Supplemental Figures

This appendix includes supplemental figures and technical descriptions that illustrate the detailed CBCT-based measurement procedures utilized in this study. The goal is to provide enhanced clarity and transparency for the steps followed during image reorientation, landmark identification, and transverse/molar inclination measurements.

Appendix A.1. Reorientation and Slice Selection



Figure A1. Multiplanar reorientation using the midpalatal suture and occlusal plane.

This image illustrates the alignment of the CBCT volume using the midpalatal suture as the sagittal reference and the occlusal plane for horizontal correction

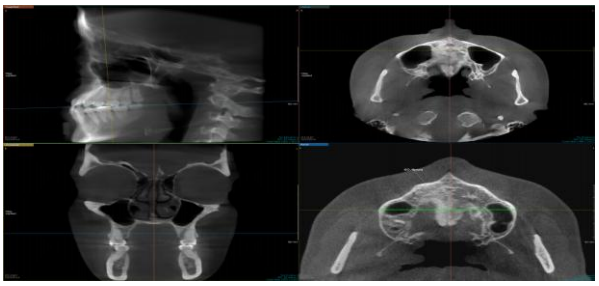


Figure A2. Coronal and axial slice selection through the first molars.

The slice was selected at the level of the root furcation to capture consistent anatomical reference points.

Appendix A.2. Maxillary Basal Width Measurement

After reorienting the scan using the midpalatal suture and the functional occlusal plane, axial slices were reviewed to identify the furcation area just anterior to the palatal root of the maxillary first molars. The optimal axial slice was selected to ensure a symmetric transverse view through both molars.



Figure A3. Axial CBCT slice selected through the furcation of the maxillary first molars.

To locate the anatomical Mx points that define the skeletal maxillary width, two horizontal reference lines were constructed:
(1) the superior line at the jugale level (as described by Tamburrino et al., 2010), and
(2) the inferior line midway between the buccal alveolar crest and root apex of the first molar (as per Albalawi et al., 2023).
A perpendicular vertical line was then established between these two reference planes. The midpoint of this vertical segment defined the position of the mid-basilar plane, from which the bilateral Mx landmarks were selected at the deepest buccal concavity.
This process was visually verified using both axial and coronal CBCT views to ensure anatomical consistency (see anatomical illustration in Figure 1).

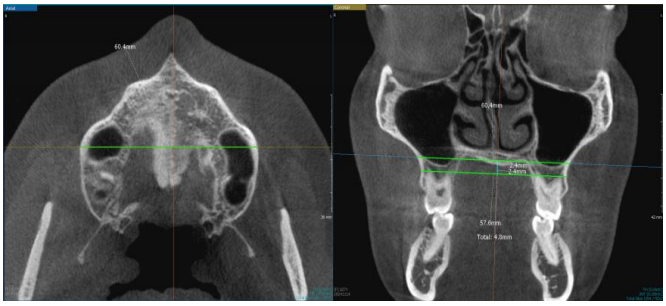


Figure A4. Identification of bilateral basal landmarks (Mx–Mx) on axial and coronal views.

The mid-basilar plane derived from the midpoint between the superior and inferior reference levels provided a balanced skeletal framework for evaluating transverse arch width. The distance between the right and left Mx points along this defined plane was recorded as the maxillary basal arch width for all study participants.

This approach ensures reliable cross-subject comparison and anatomical accuracy in skeletal width assessment.

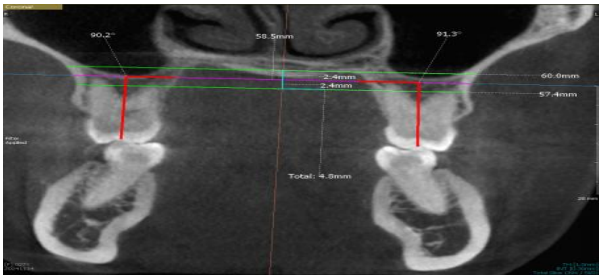


Figure A5. Construction of the mid-basilar skeletal plane and final width measurement.

Appendix A.3. Mandibular Basal Width Measurement

The optimal axial slice was selected to pass through the anatomical level of the WALA ridge, representing the most prominent contour of the buccal alveolar process near the mandibular molars. This level provides a stable reference for basal arch evaluation.

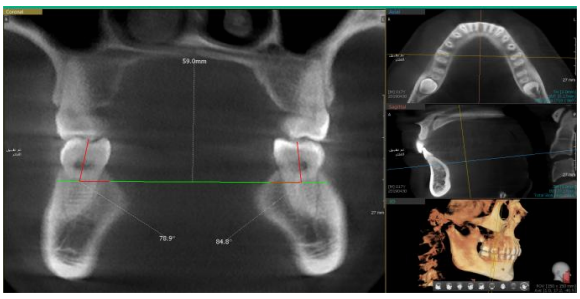


Figure A6. Selection of axial slice passing through the WALA ridge.

The transverse width was measured between the innermost curvature points of the buccal cortical plates at the WALA ridge bilaterally. These points were determined in axial view and verified by correlating with sagittal and coronal slices to ensure anatomical consistency.

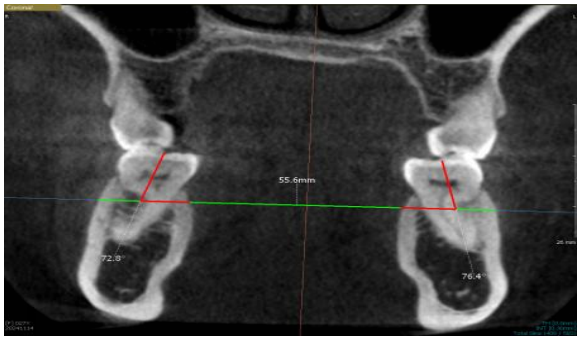


Figure A7. Identification of bilateral WALA points (Mn–Mn) and measurement method.

Appendix A.4. Molar Inclination Measurement Technique

Maxillary Molar Inclination

The long axis of the maxillary first molar was defined as a line connecting the deepest point between the buccal and palatal cusps to the center of the palatal root apex. This axis was identified using sagittal CBCT slices. The inclination angle was measured between this axis and a horizontal transverse skeletal plane passing through the basal buccal contour. This angular relationship indicates the degree of buccal tipping in the maxillary molars, especially in subjects with transverse maxillary constriction(see Figure A5).

Mandibular Molar Inclination.

For mandibular molars, the long axis was traced from the central fossa between buccal and lingual cusps to the bifurcation midpoint of the roots, visualized in sagittal slices. The angle was measured relative to the mandibular transverse plane at the level of the WALA ridge, reflecting the degree of lingual tipping commonly associated with skeletal compensation (see Figure A7).

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ORIGINAL RESEARCH

EVALUATION OF THE RELATIONSHIP BETWEEN MAXILLARY CENTRAL INCISORS AND THE INCISIVE CANAL: A CONE-BEAM COMPUTED TOMOGRAPHY STUDY

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ABSTRACT

Purpose: To analyze the anatomical association between maxillary central incisor (MCI) roots and the incisive canal (IC) by cone-beam computed tomography (CBCT) and to evaluate the influence of age and sex.
Materials and Methods: A retrospective cross-sectional investigation was conducted on 153 Yemeni subjects (80 female, 73 male; age range: 16–45 years). Linear and angular measurements between MCI and IC were recorded through standardized multiplanar reconstructions. Key parameters measured were inter-root distance, IC width, anterioposterior (AP) distance between the root of the maxillary incisor and the incisive canal, and palatal alveolar bone width (PABW).
Results: The IC was located below the incisor apex in 74.5% of the cases. The IC width at the apex (mean 3.97 mm) exceeded the inter-root distance (mean 3.83 mm). Males exhibited significantly larger AP distances and palatal IC widths compared to females. IC width increased with age, particularly at the apex. A strong correlation was observed between AP distance and PABW (r = 0.467), especially in females (r = 0.628).
Conclusion: The IC tended to be located below the root apex. The width of the incisive canal frequently exceeded the distance between the roots of the maxillary central incisors, particularly in females and in older individuals, creating a high-risk anatomical region susceptible to iatrogenic complications with orthodontic retraction of the incisors. CBCT is crucial for personalized treatment planning in these instances.

***Keywords*:** Incisive canal, maxillary central incisors, CBCT, orthodontic planning, anatomical variation

INTRODUCTION

The maxillary central incisors (MCI) are crucial to facial esthetics, phonetics, and masticatory function[1]. Due to their prominent anterior position, they are often the focus of orthodontic concern in patients with maxillary protrusion or dental crowding[2]. However, the inherent anatomical limitations of the anterior maxilla should be well evaluated before initiating tooth movement[3].

Of these constraints, the incisive canal (IC), which

serves as the pathway for the nasopalatine nerve and vasculature, is a significant anatomical one.

Orthodontic retraction in contact with the IC can precipitate potentially catastrophic complications, including apical root resorption, alveolar bone dehiscence, and neurosensory loss, like palatal paresthesia[4].

Traditionally applied 2D imaging modalities, though helpful, are ineffective in assessing the complex spatial relationship of anterior maxilla. Cone-beam computed tomography (CBCT) has revolutionized craniofacial imaging by enabling accurate 3D evaluation of anatomical structures. CBCT is most beneficial in visualizing the lateral relationship of the MCI roots to the IC, an essential factor in planning a safe and effective orthodontic treatment. For cases requiring aggressive retraction (e.g., camouflage treatment with TADs) to avoid root resorption and nerve damage[5].

In orthodontic treatment, the anatomical relationship between the maxillary central incisors and the incisive canal is are important consideration. Inadequate appreciation of this relationship may lead to problems such as nerve damage, sensory disturbance, vascular trauma, or root resorption[6–8]. Importantly, the proximity of maxillary central incisor roots to the cortical walls of the incisive canal has been related to root resorption, particularly in maximum orthodontic retraction[9].

Additionally, the orthodontists assess the shape of the incisive canal and determine the extent to which its posterior movement goes based on the distance between the incisive canal and the maxillary central incisors before treatment. This is to avoid root resorption as an orthodontic outcome[10,11].

Prior research has repeatedly highlighted the clinical significance of this anatomical relationship, noting that the incisive canal (IC) is typically apical to the maxillary central incisors and wider than the inter-root distance[12]. In addition, one study discovered that in more than 60% of cases, the IC width was greater than the inter-root distance. This means that there was less room for safety while retracting the incisors[3].

Anatomical variation among ethnic groups continues to throw a spanner in the works. IC shape, AP distance, and canal width differences have all been found to influence treatment outcomes in studies[9,13,14]. Despite the Increased international literature, there remains a wide lack of information. Since craniofacial anatomy is ethnically variable, locally derived studies are required for optimal risk assessment and treatment planning[15].

This study aims to fill this gap by evaluating the correlation between the maxillary central incisors and the incisive canal, determining age and gender anatomical variations using cone-beam computed tomography (CBCT), and establishing its implications for orthodontic diagnosis and treatment planning.

2. MATERIAL AND METHODS

Study Design and Ethical Approval

This retrospective, cross-sectional study was conducted on CBCT images taken for diagnostic purposes. Ethical permission was granted by the Medical Ethics Committee of the Faculty of Dentistry, Sana'a University (Ref. No.: 703; Date: 2/8/2024). All patient identifiers were anonymized for confidentiality *with the ethical principles outlined in the Declaration of Helsinki.*

Study Population and Sampling:

The present retrospective cross-sectional study was conducted in the Orthodontic Department, Faculty of Dentistry, Sana'a University, among a group of Yemeni adult population. The relationship between IC position and MCI. CBCT images of 153 Yemeni patients (80 female, 73 male), 16-45 years old, were retrospectively assessed. Data was collected from November 2024 to February 2025 from Al-Weed X-ray center in Sana'a. The initial sample size was calculated using the formula for quantitative variables with a 10% margin of error and a 95% level of confidence. Taking an anticipated population proportion of 50% (historical research), a sample size of at least 96 was calculated. The expansion of the sample to 153 was to provide greater statistical power, greater generalizability, and allowance for possible exclusions.

Study Procedure

CBCT scans were used to assess IC position. The CBCT was taken from a PaX-i3D Green CBCT system (Model: PHT-60CFO; Vatech Co., Hwaseong, Korea). The acquired images were exported and saved in multi-file Digital Imaging and Communications in Medicine (DICOM) format to be analyzed later using Carestream's CS 3D Imaging software. From Al-Weed X-ray center.

The CBCT images were processed and analyzed using Carestream's CS 3D Imaging software on an HP laptop equipped with a 64-bit Windows 10 operating system. The image interpretation was performed on a 15.6-inch full HD display screen with a resolution of 1920 × 1080 pixels. All the image measurements were performed in ambient-free, low-lighting conditions to prevent glare and visual distraction.

In the software, image adjustment tools were used to alter parameters such as contrast, sharpness, and brightness. The alterations enhanced image clarity and allowed for proper visualization of anatomical structures, and therefore proper and reliable

interpretation of the maxillary central incisors and the incisive canal.

All cone-beam computed tomography (CBCT) scans were oriented at the level of the palatal plane (from the posterior nasal spine to the anterior nasal spine) as the primary reference in the sagittal view. Standardized, reproducible multiplanar reconstructions were used to obtain sagittal and axial images using the suture line at the midpalate as the reference, and coronal images were obtained using the line between the right and left greater palatine foramina to ensure repeatability and consistency of linear and angular measurements **(Table 1 and Figure**

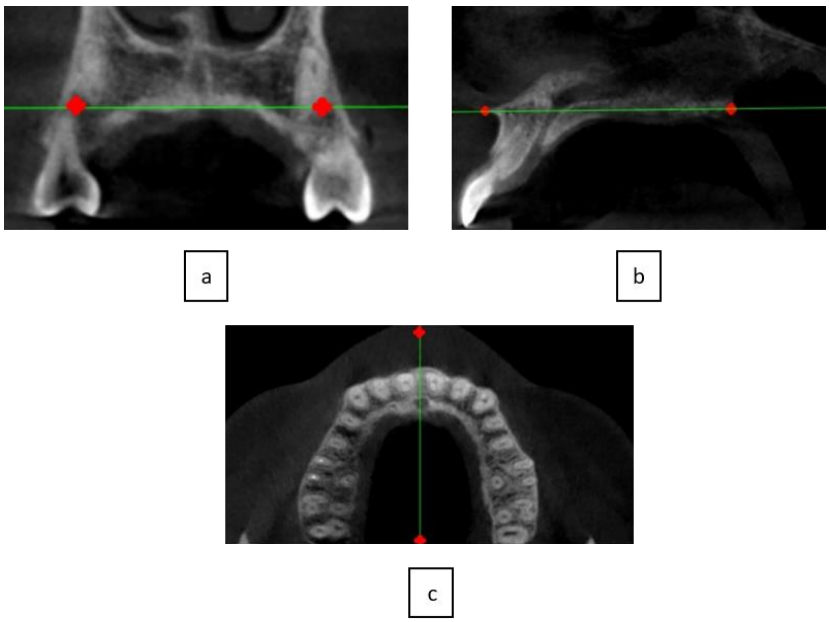


Figure 1. The images show (a) sagittal construction, horizontal plane passing palatal plane from ANS to PNS (b) axial construction, plane passing through midpalatal suture, (C) coronal construction, plane passing through greater palatine foramina on two sides

Table 1. Linear and angular measurements

Linear and angular measurements	
Sagittal Measurements	➢ Incisor/Palatal Plane Angle (CI/PP) ➢ Incisive Canal/Palatal Plane Angle (IC/PP) ➢ Palatal Alveolar Bone Width (PABW) at the apical level ➢ IC Width at palatal opening
Axial Measurements	➢ Inter-root Distance (IRD) ➢ IC Width at root apex ➢ Anteroposterior Distance 1 (AP): From medial root surface to anterior IC wall ➢ Anteroposterior Distance 2 (AP2): From posterior root surface to lateral IC wall
Vertical Positional Classification	The vertical association between the IC and root apex was classified as: ➢Above the apex ➢At the apex ➢Below the apex

Reliability Testing:

For ascertaining the accuracy of measurement, intra- and inter-examiner reliability were evaluated:

- Intra-examiner reliability: 20% of the images were re-measured two weeks post-first measurement.
- Inter-examiner reliability: A radiographic technician independently examined 10 randomly chosen images.
- Statistical validation: Intraclass correlation coefficients (ICCs) were computed and revealed excellent agreement, from 0.765 to 1.000.
- **Statistical Analysis**

- Data was analyzed using IBM SPSS Statistics (Version 28.0). The Shapiro–Wilk test was used to assess the normality of the data. Descriptive statistics included mean, standard deviation, and frequencies. Independent t-tests and Mann–

Whitney U tests were used for gender comparisons. ANOVA and Kruskal–Wallis tests were used for age group comparisons. Pearson's correlation coefficient (r) assessed associations between continuous variables. A p-value of < 0.05 was considered statistically significant.

3. RESULTS

A total of 153 CBCT scans were analyzed, comprising 80 females (52.3%) and 73 males (47.7%). Most participants (58.8%) were aged between 20-30 years. The vertical position of the incisive canal (IC) relative to the maxillary central incisor (MCI) root apex was classified as follows:

Gender Comparison of Anatomical Parameters (Mann–Whitney U Test)

Comparative analysis was conducted using the Mann–Whitney U test. Analysis of gender differences in the MCI–IC relationship showed that most parameters were comparable between males and females. However, males had a significantly greater palatal IC width (3.59 mm vs. 3.33 mm, $p = 0.029$) and anteroposterior (AP) distance (3.88 mm vs. 3.54 mm, $p = 0.023$). These differences suggest that males tend to have slightly more lateral and sagittal clearance between the incisive canal and the maxillary central incisor roots, potentially reducing the risk of root–canal contact during orthodontic tooth movement **(Table 2)**.

Table 2. Gender Comparison of Anatomical Parameters (Mann–Whitney U Test)

Measurement	Female (Mean)	Male (Mean)	p-value
CI/PP angle (°)	110.44	112.48	0.079
IC/PP angle (°)	108.89	109.73	0.524
PABW (mm)	3.27	3.26	0.693
IC Width Palatal (mm)	3.33	3.59	**0.029***
IC Width at Apex (mm)	4.04	3.89	0.355
Inter-root Distance (mm)	3.83	3.84	0.926
AP Distance (mm)	3.54	3.88	**0.023***
AP2 Distance (mm)	2.83	2.98	0.176

*statistically significant at $p<0.05$

Anatomical Measurements by Age Group (Kruskal–Wallis Test)

Participants were divided into three age groups. The Kruskal–Wallis test was used to analyze differences among them. When comparing IC and MCI anatomical parameters across age groups (<20, 20–30, and >30 years), the only statistically significant change was in IC width at the apex ($p = 0.010$). This width increased progressively with age from 3.53 mm in the youngest group to 4.26 mm in the oldest. This widening is likely due to physiological bone remodeling or canal expansion over time, which reduces the available vertical bone between the IC and incisor roots in older individuals. Although other measurements did not reach statistical significance, slight trends (such as reduced AP distance with increasing age) may still hold clinical relevance **(Table 3)**.

Table 3. Anatomical Measurements by Age Group (Kruskal–Wallis Test)

Measurement	<20 years	20–30 years	>30 years	p-value
CI/PP angle (°)	111.82	111.43	111.22	0.869
IC/PP angle (°)	108.65	109.12	109.85	0.728
PABW (mm)	3.59	3.13	3.43	0.145
IC Width Palatal (mm)	3.43	3.36	3.64	0.200
IC Width at Apex (mm)	3.53	3.90	4.26	**0.010***
Inter-root Distance (mm)	3.37	3.90	3.88	0.070
AP Distance (mm)	4.07	3.70	3.57	0.604
AP2 Distance (mm)	2.98	2.86	2.96	0.148

*statistically significant at $p<0.05$

Pearson Correlation Between AP Distance and Selected Variables:

Pearson correlation was used to evaluate relationships among continuous variables. The analysis identified palatal alveolar bone width (PABW) as significantly and positively correlated with AP distance ($r = 0.467$, $p < 0.001$). This means individuals with thicker palatal bone generally have greater sagittal clearance between the MCI apex and the

IC, creating a protective buffer during tooth movement. No meaningful correlations were observed between AP distance and other variables such as age, IC widths, or angular measures. Clinically, this underscores PABW as an important anatomical predictor for safe incisor retraction, particularly for patients with inherently limited sagittal space **(Table 4)**.

Table 4. Pearson Correlation Between AP Distance and Selected Variables

Variable	Correlation (r)	p-value
CI/PP Angle	0.070	0.387
IC/PP Angle	0.064	0.434
Age	–0.027	0.744
PABW	**0.467**	**<0.001**
IC Width Palatal	0.101	0.216
IC Width at Apex	–0.082	0.313
Inter-root Distance	0.003	0.973

*statistically significant at $p<0.05$

4. DISCUSSION

This study is the initial comprehensive CBCT-based investigation of the anatomical relationship between the maxillary central incisors (MCI) and the incisive canal (IC) among Yemeni individuals. The findings indicate several clinically relevant anatomical relationships with direct treatment planning implications in cases of orthodontic incisor retraction or intrusion. The most noteworthy result was that within 74.5% of the population, the IC was located below the apex of the root[12].

This configuration increases the prospect of direct root contact with the IC during orthodontic movement, leading to root resorption, perforation of the alveolar bone, or neurosensory impairment, as indicated by previous studies[16].

Dimensionally, the mean IC width at the apex (3.97 mm) was larger than the mean inter-root distance (3.83 mm). This means that, in the majority of cases, the IC will be wider than the available bone width between roots, excluding the "safe zone" traditionally used for retraction[17].

The same has been noticed in other cohorts, supporting the application of individualized evaluation rather than standardized limits (e.g., 5.5–7 mm retraction guidelines)[7]. Notably, the gender differences also manifested: males demonstrated significantly greater AP distances and larger palatal IC widths compared to females[18].

These values suggest that incisor movement may be more anatomically favorable in male patients with larger sagittal clearance and less chance of IC involvement[19]. Conversely, female patients, especially those with smaller inter-root spacing and less bone width of the palate, may be at increased risk for iatrogenic events and more conservative treatment planning. These observations are consistent with prior study evidence and demonstrate the value of gender-specific risk analysis[13]

Age-related changes also became apparent, and the most significant was the extensive widening of IC at the apex with increasing age[20]. This may be due to physiological bone remodeling or canal expansion over a period. Clinicians need to understand that adult patients, most significantly those older than 30 years of age, may have anatomical constraints not present in adolescents and require adequate pre-treatment imaging[21].

One major clinical observation was the favorable correlation between palatal alveolar bone width (PABW) and AP distance ($r = 0.467$), but even more so in women ($r = 0.628$). This would indicate there is greater sagittal space available for patients with thicker palatal bones and, as such, a potential protective cushion[22].

These results collectively illustrate the anatomical variability and complexity of the MCI–IC relationship with the awareness that orthodontic tooth movement must remain within individualized biological limits. Classical reliance on lateral cephalograms or population averages is perhaps insufficient and, in some cases, risky.

5. CONCLUSION

The results of this study show that the connection between the maxillary central incisors and the incisive canal in Yemeni individuals varies greatly and is affected by both gender and age. These changes in anatomy have a direct effect on how orthodontic treatment is planned. Furthermore, this means that female patients are more likely to have complications related to IC and should have more careful treatment plans. Additionally, a significant increase in IC width at the apex was observed with age, validating a requirement for greater sensitivity in adult orthodontic treatment.

DECLARATIONS

Ethical approval and consent to participate

Ethical permission was granted by the Medical Ethics Committee of the Faculty of Dentistry, Sana'a University (Ref. No.: 703; Date: 2/8/2024). All patient identifiers were anonymized for confidentiality *with the ethical principles outlined in the Declaration of Helsinki.*

Availability of data and material

All data generated or analyzed during this study are included in the published article.

Competing interests

The authors declare that there are no competing interests.

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ORIGINAL REPORT

MAXILLARY SINUS LIFT ASSOCIATED WITH FUNCTIONAL ENDOSCOPIC SINUS SURGERY (FESS): A HISTOLOGICAL STUDY

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ABSTRACT

Objective: to evaluate on histological preparations the outcome of the maxillary sinus lift surgery associated with the Functional Endoscopic Sinus Surgery (FESS) in patients with a pathological maxillary sinus.

Materials and methods: 17 patients with reversible contraindications for maxillary sinus elevation were recruited. Patients had insufficient bone volume in the posterior maxillary (<5 mm). FESS and sinus lift surgery were performed in a single session. Patients have been re-evaluated 7 days, 14 days, 30 days and 3 months after surgery. After 6 months a Trephine bur with a 3 mm diameter was used to prepare the implant site and harvest the biopsy to analyse histologically.

Results and conclusions: the histological data of our samples were highly homogeneous and showed the presence of wide marrow spaces and mature bone undergoing mineralization. No signs of inflammation were found. Therefore, the previous sinus pathology did not adversely affect the outcome of maxillary sinus lift.

Keywords*:* osteonecrosis of the jaw, oral bisphosphonates, extraction socket, histological analysis, socket preservation; bone graft.

INTRODUCTION

Bone resorption of the maxillary alveolar process is an irreversible consequence of tooth loss [1,2]. The consequent risks of maxillary sinus pneumatization [3] and alveolar bone atrophy[4] significantly reduce the amount of bone volume available for dental implant placement[5,6]. It is well known that implants in the maxillary region show poor clinical outcomes due to low bone quality and lack of residual bone height. For this reason, various surgical techniques have been developed to compensate for the bone quality and quantity in the maxillary region[7,8]. Among these, maxillary sinus lift through elevation of the sinus membrane and grafting was described by Tatum[9]. This surgical technique allows for vertical bone augmentation by creating a space between the sinus membrane and the maxillary floor, which is then filled with grafting materials (autografts, xenografts, allografts, or alloplastic materials). The goal is to increase bone volume by promoting osteoconduction and/or osteoinduction, in order to place adequately sized osseointegrated implants[10]. Although the procedure is safe and implant success rates exceed 90%[10–13], several factors may influence the outcome. It has been reported that patients with sinus membranes thicker than 5 mm undergoing sinus lift are at substantial risk of obstruction of the ostiomeatal unit and consequent sinusitis[14]. Regional anatomical alterations such as ostium obstruction, hypertrophy of the sinus membrane, acute or chronic infectious-inflammatory processes, sinus mucocele, and rhinonasal neoplasms[15]. Therefore, accurate identification and assessment of reversible contraindications to the maxillary sinus lift procedure appear to be crucial, as by otorhinolaryngological-affected patients need to resolve the pathological process or anatomical alteration[15]. After 3–4 weeks from the resolution of inflammatory processes, it is possible to perform the oral surgical procedure for maxillary sinus floor elevation. This procedure typically requires two surgical stages, causing considerable discomfort for the patient. Sinus lift procedures are often necessary to increase bone volume in the posterior maxilla for the

placement of dental implants.

When combined with Functional Endoscopic Sinus Surgery (FESS), these procedures can treat nasosinusal pathologies and improve surgical outcomes. Recently, a one-stage surgical procedure has been introduced and reported, which includes maxillary sinus floor elevation in association with FESS for the treatment of inflammatory processes, showing encouraging results in patients with reversible contraindications to sinus lift[16,17]. In fact, a clinical study was conducted to determine whether this surgical approach could be considered for treating minor reversible contraindications to maxillary sinus floor elevation and for simultaneously performing bone augmentation[18]. Lateral maxillary sinus lift associated with FESS has shown good clinical and radiological outcomes in patients with reversible ENT contraindications, such as sinus pathology related to lack of ventilation. Sinus lift combined with FESS allows recovery from rhinosinusal diseases and enables sinus grafting in a single surgical procedure, with the advantage of reduced morbidity for the patient[18]. The aim of the present study was to histologically evaluate bone regeneration obtained when performing lateral sinus elevation using the FESS approach.

MATERIALS AND METHODS

Patients

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the local Ethics Committee for Biomedical Research. To perform the study, 16 patients were enrolled (10 female, 6 males, mean age 52.4 ± 9.8). They presented reversible contraindications for sinus lift elevation and required bone regeneration for the next implant insertion. All the patients were recruited at “Casa di Cura Stella Maris” and “Centro Salute e Benessere Forum” (San Benedetto del Tronto, Ascoli Piceno, Italy). All patients were examined with a nasal endoscopy associated with Orthopantomography (OPT) radiographs and with maxillo-facial computed tomography (CT) scans. The inclusion criteria were: i) insufficient bone volume (<5 mm) in the posterior maxilla to receive dental implants associated with inflammatory diseases or ii) anatomical alterations in the rhino-sinusal region (chronic hyperplastic sinusitis, mucocele, ostium obstruction, anatomical alterations of nasal septum).

Surgical procedure

The Functional Endoscopic Sinus Surgery (FESS or ESS) aims at recreating sinuses proper ventilation by widening the meatal ostium and removing any obstruction to sinus drainage. The sinus lift was performed by lateral trapezoidal flap with horizontal incision on the edentulous ridge and vertical incisions divergent at least 1 cm from the edge of the mesial and distal antrostomy[19]. The bone window was created using a diamond bur 3 mm in diameter at high speed under abundant cold sterile saline solution irrigation. The window shape was ellipsoidal, with the horizontal longest margin parallel to the crestal margin. The Schneiderian membrane was elevated using periostal instruments of rounded edges and different length, size and angle. Enzyme deantigenated equine cancellous-cortical bone granules 0.25-1 mm (Osteoxenon, Bioteck S.p.A., Arcugnano, Italy) were used as xenograft and inserted after Schneiderian membrane elevation. Osteoxenon granules are produced and deantigenated through a patented process named Zymo-Teck. This process allows the enzymes to work at low temperature in an aqueous environment to remove all the components that may trigger an immunogenic response. Such method allows the preservation of both the mineral component and the bone collagen in a native conformation[20]. The resulting bone substitute is recognized physiologically by osteoclasts allowing its complete integration in patient’s bone in a physiological time[21]. The grafting material was gently compacted to stabilize it between the bone walls and the sinus membrane. Hermetic and passive suture was applied. Follow-up medical examinations and nasal endoscopies were performed at 7 days, 14 days, 30 days and 3 months. Six months after surgery, the fixture was inserted. A 3 mm trephine bur was used to drill the bone for implant site preparation and to collect bone samples.

Histological analysis

All the samples were immediately fixed in 4% formaldehyde and then decalcified using Biodec-R solution (Bio-Optica, Milan, Italy), according to the manufacturer’s instructions. After these treatments, the sample was dehydrated with a series of alcohol rinses and embedded in paraffin for light microscope observations. The samples were cut longitudinally along the major axis using a microtome (Leica Microsystems Srl, Milan, Italy). Three slides of 6 µm were stained with Hematoxylin & Eosin (H&E) and Mallory Trichrome staining solutions to identify newly formed bone undergoing mineralization. Histomorphometric analysis was performed using a Zeiss Axioscope optical microscope (Carl Zeiss AG, Oberkochen, Germany) connected to a CoolSNAP camera (Photometrics, Tucson, AZ, USA). The acquired images were analyzed using the dedicated software MetaMorph Image Analysis (Universal Imaging Corp, Downingtown, PA, USA), which offers advanced image acquisition and processing capabilities.

Three histological sections were prepared for each sample to ensure a more accurate evaluation. The examined area was assessed by quantifying the presence of bone marrow spaces, mineralized bone, and residual biomaterial. The surfaces occupied by marrow spaces, bone tissue, and biomaterial were used for histomorphometric analysis,

calculating the ratio between the total examined area and the area occupied by each tissue component. The mean value for each section was then calculated as previously described [22] .

RESULTS

No post-operative complications were clinically found in any of the sites where the procedure was performed and six months after surgery all maxillary sinus surgeries were successful. All the histological samples obtained from the 16 patients appeared homogeneous when observed in light microscopy: bone tissue resulted vital, no evidence of empty lacunae or morphological alterations to osteocytes was found neither signs of inflammation and/or fibrosis were noted. Bone tissue from all the specimens showed features of mature lamellar bone although the presence of woven bone was also found. As shown in Figure 1, the presence of newly formed bone is highlighted by means of H&E staining.

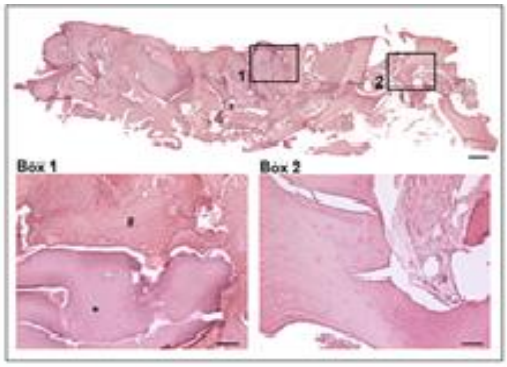


Figure 1 Two-dimensional (2D) reconstruction of a representative bone sample (H&E staining) (upper panel; magnification 25×, scale bar 400 μm). Bone trabeculae are dark-pink colored (#), whereas graft material appears light-pink colored (*) (Box 1-2; magnification 200×, scale bar: 100 μm)

The trabeculae appear dense and the amount of bone marrow is minimal (upper panel). The presence of residual biomaterial is appreciated in about half of the samples and, in particular, in the apical portion. The residual graft material is in close contact with the newly formed trabecular bone, highlighting an excellent osseointegration (Box 1-2).

Mature bone tissue already mineralized or in the process of mineralization is shown in Figure 2 by means of Masson Trichrome staining (upper panel). Parallel and concentric bone lamellae together with small osteocyte lacunae can be observed; loose connective tissue rich in fat and blood vessels can be also appreciated (Box 1-2).

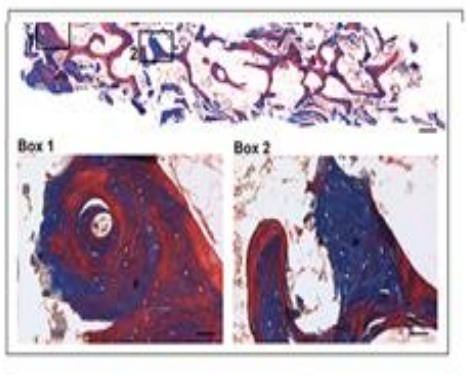


Figure 2 Two-dimensional (2D) reconstruction of a representative bone sample (Mallory Trichrome staining) (upper panel; magnification 25×, scale bar 400 μm). Bone samples show the presence of lamellar bone undergoing mineralization (#) and indicating complete bone remodeling (Box 1-2; magnification 200×, scale bar: 100 μm)

Three serial sections of each sample were analyzed, taken in the coronal part, in the middle part, and in the apical part of the sample. The average percentage of bone tissue, bone marrow and residual biomaterial respectively was calculated for each individual sample as summarized in Table 1.

In 7 out of 16 samples residual biomaterial was found, while in the remaining 9 samples no residual biomaterial was detected. On average, the samples analyzed showed an average percentage of newly formed bone of 48.31 with respect to the total area, a percentage of bone marrow of 37.37 and a residual biomaterial percentage of 12.89 (Figure 3).

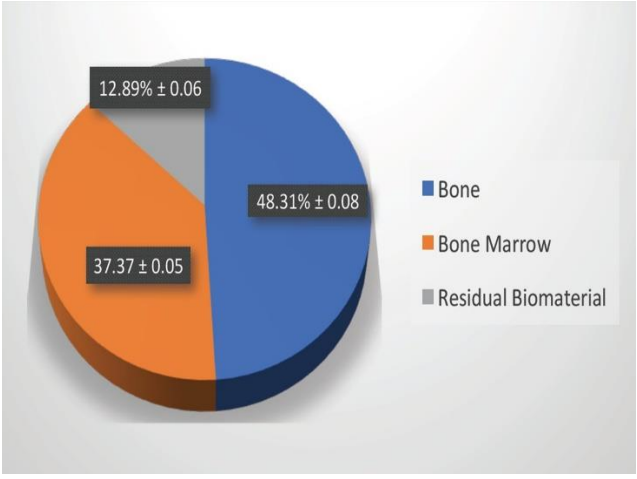


Figure 3 Average percentages of newly formed bone, bone marrow, and residual biomaterial with respect to the total area of the analyzed sample

Table. 1 Average percentage of bone tissue, bone marrow and residual biomaterial for individual samples

Sample	Bone	Bone Marrow	Residual Biomaterial
#1	39.08 ± 0.223%	56.16 ± 0.207%	4.66 ± 0.032%
#2	50.74 ± 0.103%	49.26 ± 0.103%	0.00 %
#3	52.44 ± 0.151%	16.37 ± 0.019%	31.19 ± 0.159%
#4	76.55 ± 0.107%	23.45 ± 0.102%	0.00%
#5	56.91 ± 0.112%	3.42 ± 0.030%	39.67 ± 0.114%
#6	42.19 ± 0.086%	57.81 ± 0.083%	0.00%
#7	73.21 ± 0.080%	26.79 ± 0.043%	0.00%
#8	55.56 ± 0.057%	44.44 ± 0.056%	0.00%
#9	7.74 ± 0.008%	26.84 ± 0.005%	65.42 ± 0.002%
#10	61.18 ± 0.030%	38.82 ± 0.024%	0.00%
#11	48.98 ± 0.097%	51.02 ± 0.099%	0.00%
#12	43.23 ± 0.067%	41.44 ± 0.060%	4.52 ± 0.015%
#13	41.06 ± 0.077%	47.15 ± 0.082%	0.00%
#14	66.41 ± 0.034%	33.59 ± 0.034%	0.00%
#15	39.21 ± 0.067%	13.25 ± 0.022%	47.54 ± 0.033%
#16	18.48 ± 0.033%	68.24 ± 0.019%	13.28 ± 0.012%

DISCUSSION

Edentulous patient's rehabilitation with implant-supported prostheses currently represents a gold standard practice with reliable long-term results[23]. However, local conditions of the alveolar ridge may be unfavorable for implant placement procedure. In particular, the alveolar bone resorption is one of the main biological consequences connected to tooth loss[24]. Maxillary sinus pneumatisation [25] and alveolar bone atrophy[26] represent the main risks connected to bone resorption, leading to a reduction in the long-term outcome of implants placed in this area due to insufficient maxillary bone height and quality[27].

In recent years, several surgical techniques have been developed to solve the problem of bone quality and quantity of the maxillary region[7] . Above these, maxillary sinus floor elevation and grafting via either a crestal or a lateral approach have become a very common procedure with predictable results and a generally low post-operative complication rates[28]. Complications such as maxillary sinusitis and/or infection of the grafting material are rare[5,29]. It has been demonstrated that patients with history of sinusitis, antral mucosa hyperplasia, anatomic alterations in the nasal cavities may present a higher risk of complications[28]. Such complications are well known and documented and are defined "reversible": it is therefore mandatory to treat them as soon as possible following safe and reliable treatment protocols[15]. FESS is now considered the gold standard in reversible ENT contraindications treatment. In this scenario, a two-step procedure of FESS followed by the sinus lift after a healing period has already been reported with encouraging results in patients with reversible contraindications[15]. However, the entire procedure requires from one to at least six months before the final implant placement, with a serious discomfort for patients. Combining maxillary sinus floor elevation with FESS in a single-step procedure has proven effective and safe. This approach addresses local contraindications to sinus augmentation and avoids the need for a second surgical procedure, facilitating quicker prosthetic rehabilitation[16]. The authors demonstrated that a one-step approach can be considered as a safe and cheap option for the treatment of minor reversible contraindications avoiding a second surgical procedure and enhancing patients' compliance in completing the prosthetic rehabilitation[16]. Falco et al. demonstrated a positive clinical and radiologic outcome of 69 consecutive maxillary sinus augmentations associated with FESS (2015). Currently, considerable progress has been made regarding this topic, but there are still not many research in the literature that provide histological data supporting clinical outcomes. In the present study, we evaluated histological samples from 16

patients with reversible contraindications who underwent a single session FESS and maxillary sinus lift procedure before implant placement. Patients did not show any clinical complication associated with the intervention and, most importantly, histological analysis indicated a physiological healing of the site. The average percentage of residual biomaterial obeserved in the analyzed samples was very low as compared with the average percentage of the newly formed bone, indicating that 6 months after sinus elevation, almost all the biomaterial had undergone remodeling, and was substituted by new trabecular bone. The histological data are consistent with previous studies that used enzyme deantigenated equine bone as bone substitute (Osteoxenon, Bioteck S.p.A., Arcugnano, Italy)[30,31] in sinus lift surgery. In comparison with other studies using biomaterial grafting, we have not found anomalies or alterations due to the pre-existing sinus pathology.

CONCLUSIONS

In conclusion, the histological results coming from the analysis of our samples show that there are no histological differences due to sinus pathology. Therefore, we can affirm that it is possible to successfully perform the technique of maxillary sinus lift and the Functional Sinus Surgery Endoscopy (FESS) in a single step.

DECLARATION

Competing interest

The authors declare that there are no competing interest.

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Ethical Approval

“Not applicable”

Consent for publication

“Not applicable”

Acknowledgments

“Not applicable”

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ORIGINAL RESEARCH

SYNTHESIS AND IN VITRO CHARACTERIZATION OF A PROBIOTIC-ENRICHED PROPHYLACTIC POLISHING PASTE

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ABSTRACT

Background: Scaling roughens the tooth surface, increasing susceptibility to bacteria, and making polishing past essential post-procedure. A paste with probiotic effects and nanoparticles efficiently smooths enamel and repairs micro damage. Lactobacillus helps prevent harmful bacteria, supporting oral health. Nano-silica enhances polishing, while nano hydroxyapatite remineralizes enamel.

Aim: Our study aimed to develop a prophylactic polishing paste incorporating Lactobacillus plantarum MTCC 569 nano-silica, and nano-hydroxyapatite particles and to evaluate its in vitro properties, such as cytotoxicity activity antimicrobial activity, and surface roughness.

Materials and Methods: This is an in vitro study conducted in Green Lab, Saveetha Dental College and Hospitals Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, Tamil Nadu, Indi between August 2024 and September 2024. A novel prophylactic polishing paste was formulated with bioactive an probiotic components. The base comprised glycerin (25%) and sorbitol (25%) in a 1:1 ratio, with deionized water an Carbopol (1–2%) for viscosity. SiO_2 and hydroxyapatite nanoparticles were added for abrasive and remineralizing effects Peppermint oil (0.2%), sodium fluoride (0.32%), and sodium benzoate (0.15%) were included for flavor, anti-carie action, and preservation, respectively. The pH was adjusted to ~7.0. After cooling below 40 °C, *Lactobacillus plantaru* MTCC 5690 (10^8–10^9 CFU/mL) and xylitol (2–5%) were added, followed by pH adjustment (5.5–7.0) to maintai probiotic viability. The final paste was homogenized and filtered for oral application and evaluated for its in vitr properties.

Results: The SEM image at 23,000× magnification revealed densely packed, heterogeneous angular structures with individual nanoparticles distinguishable at the 0.5 µm scale. In contrast, at 19,000× magnification, the particles appeared more compactly merged, suggesting the incorporation of *L. plantarum*, while irregular clusters and plate-like formations were identified as hydroxyapatite aggregates. The cytotoxicity analysis showed increased cell viability with higher concentrations of the prophylactic paste, peaking at 75 µL/mL. Fluorescence microscopy of MG-63 cells treated with prophylactic polishing paste showed dose-dependent viability. The control had sparse cells with low fluorescence, while 50 µL/mL treatment yielded the highest cell density and healthy morphology. Lower doses and control showed smaller, less spread cells, indicating mild cytotoxicity; higher doses promoted cell growth. The antimicrobial activity at low concentrations with inhibition zones slightly smaller than antibiotics. At high concentrations, the paste produced thelargest inhibition zones, exceeding those of antibiotics, demonstrating strong antimicrobial efficacy. Surface roughness analysis revealed a significant reduction in roughness post-polishing, with area roughness (Sa) decreasing from 51.559 nm to 37.532 nm, highlighting the paste's ability to smooth the tooth surface and reduce plaque accumulation.

C**onclusion:**The formulated prophylactic polishing paste demonstrated strong antimicrobial activity and biocompatibility and enhanced cell viability in a dose-dependent manner and significantly reduced surface roughness post-polishing, and is beneficial for patients with gingivitis and periodontitis

Keywords -Oral prophylaxis, Lactobacillus plantarum, Nanoparticle, Hydroxyapatite

INTRODUCTION

Scaling is a procedure that involves the removal of plaque and calculus from the teeth [1], and during this process, the tooth surface becomes more rough, making it more susceptible to bacterial accumulation. Thus, prophylactic polishing paste is an essential component in dental care, which is used primarily after scaling procedures to smooth the tooth surface and to prevent early plaque recolonization [2]. The polishing paste, typically containing fine abrasives, fluoride, and flavoring agents, is applied with a rubber cup or brush attached to a dental handpiece [3].

Lactobacillus bacteria are probiotics known for maintaining a healthy balance of bacteria in the oral cavity and preventing periodontal diseases [4]. These bacteria also lower the counts of Streptococcus mutans, a primary bacterium responsible for tooth decay [5].

Nano-silica particles are highly effective abrasives due to their small size and high surface area, thus polishing tooth surfaces more efficiently. This results in a glossy, smooth enamel surface less likely to attract plaque and bacteria. They also enhance the paste's mechanical properties and have reduced abrasiveness compared to traditional polishing agents [6].

Nano-hydroxyapatite is a biomimetic material that closely resembles the natural mineral component of tooth enamel [7]. When included in a polishing paste, they can help fill microscopic pores in the enamel surface, enhancing the tooth's natural defense against decay [8].

Commercially available chemical prophylactic polishing pastes present several potential drawbacks [9]. They contain abrasive agents, thus causing increased tooth sensitivity. Some patients may find the paste's taste unpleasant, affecting their comfort during dental cleanings. These considerations emphasize the importance of exploring probiotic prophylactic polishing paste enriched with nanoparticles. Thus, our study aimed to develop a prophylactic polishing paste incorporating Lactobacillus plantarum MTCC 5690, nano-silica, and nano-hydroxyapatite particles, and to evaluate its in vitro properties.

MATERIALS AND METHODS

This is an in vitro study conducted between August 2024 and September 2024 in Green Lab, Saveetha Dental College and Hospitals, Chennai, Tamil Nadu, India. The Institutional Scientific Research Board(SRB/SDC/UG-2041/24/PERIO/467) approval was obtained before the start of the study.

Formulation of the Prophylactic Polishing Paste:

Base paste preparation

The base paste was prepared by mixing glycerin (25%) and sorbitol (25%) in a 1:1 ratio. Deionized water was gradually added to create a homogeneous mixture. Carbopol (1-2%) thickening agent was then incorporated, with continuous stirring until the desired viscosity was achieved.

Incorporation of nano-silica and nano-hydroxyapatite nanoparticles

After that, silicon dioxide (SiO_2) nanoparticles synthesized earlier by the modified Stöber process and hydroxyapatite (HA) nanoparticles synthesized by the coprecipitation method were added to the base. The silicon dioxide nanoparticles provide abrasive properties, while the hydroxyapatite nanoparticles help with remineralization. Once these nanoparticles were added, the formulation was blended well using a magnetic stirrer at a controlled speed of 500 rpm for 7 minutes to ensure a homogeneous and even distribution of the active nanoparticles throughout the base. The next step was the incorporation of additional ingredients to finalize the prophylactic polishing paste.

pH Adjustment

Peppermint oil (0.2%) was added to provide a pleasant flavor, and to enhance the paste's anti-caries properties, sodium fluoride (0.32%) was included. The pH of the formulation was carefully adjusted to around 7.0 using a phosphate buffer to ensure compatibility with the oral environment. Finally, the entire mixture was blended thoroughly to achieve a smooth and homogeneous paste, ready for application.

Incorporation of Lactobacillus plantarum MTCC 5690 bacteria strain

The obtained mixture was then cooled to below 40°C to preserve the viability of Lactobacillus plantarum MTCC 5690 (10^8–10^9 CFU/mL), and was added in liquid concentrate form. The pH of the mixture was measured and adjusted between 5.5 and 7.0 using the phosphate buffer solution. Xylitol (2–5%) was then mixed in, and

preservative sodium benzoate (0.15%) was added to protect against microbial contamination. The final product was then filtered to remove the impurities, as shown in **Figure 1.**



Figure1. The formulated Prophylactic polishing paste

Characterization of the prophylactic polishing paste

Scanning Electron Microscopy

The microstructure of Selenium-doped bioglass was studied using a Scanning Electron Microscope (SEM) (FEI Quanta FEG 650 SEM FEI company, Hillsboro, Oregon, United States)operated at 2,000 kV,

capturing images of the membrane's surface at 19000x and 23000x magnification.

Cytotoxic Activity

Cytotoxic analysis was done by Fluorescence microscopy. It is an imaging technique that uses fluorescent dyes or proteins to quantify cell structures, in which the green fluorescence indicates cell viability. The stronger the fluorescence, the higher the cell viability.

Antimicrobial Activity

Wells on Mueller-Hinton agar plates, each inoculated with *Staphylococcus aureus*, *Streptococcus mutans, Pseudomonas aeruginosa, and Escherichia coli*, were loaded with 1-2mg/ml [Low concentration-LC] and 10-12mg/ml [High concentration-HC] of prophylactic polishing paste separately. The plates were then incubated at 37°C for 48 hours. Amoxicillin was used as the standard antibiotic control. Each pathogen's zone of inhibition was measured and replicated three times to establish the mean values.

Surface roughness analysis

In our study, scaling was first performed on an extracted natural human tooth to remove plaque and calculus, which typically increased the surface roughness. The surface roughness was then evaluated using Atomic Force Microscopy (AFM) to establish a baseline measurement. After scaling, using a low-speed dental handpiece with a soft rubber cup, the formulated prophylactic polishing paste was applied to the tooth uniformly, and polishing was carried out for a set duration of 30–60 seconds, ensuring consistent and even coverage over the entire surface. Water irrigation was applied after the polishing process to clear the excess paste.

After polishing, the surface roughness was re-evaluated using AFM. Surface roughness was evaluated using parameters such as area roughness (Sa), peak height (Sp), and valley depth (Sv), while line roughness was assessed through arithmetic mean roughness (Ra), peak height (Rp), and valley depth (Rv). The difference in surface roughness before and after polishing was calculated and compared to assess the effectiveness of the prophylactic paste in reducing surface roughness and improving the smoothness of the tooth surface.

RESULTS

Scanning Electron Microscopy

At 19,000x magnification, the SEM images revealed that the particles had merged into a more compact matrix, suggesting the presence of *Lactobacillus plantarum* potentially embedded within the structure**Figure 2A.**

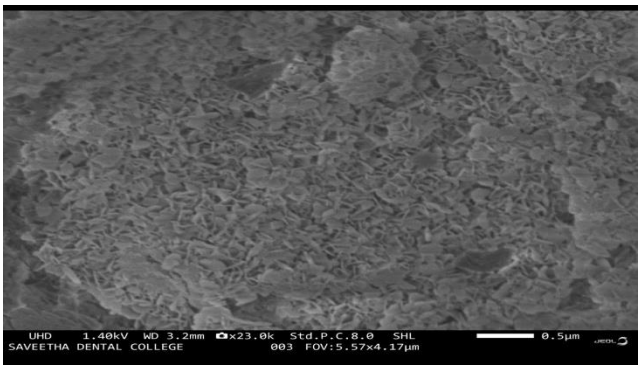


Figure.2A-SEM image of the formulated Prophylactic polishing paste at 19000x.

Irregular clusters and plate-like formations were identified as hydroxyapatite aggregates. The relatively continuous and roughened surface was considered favorable for controlled-release properties, which could help maintain probiotic viability and enable gradual release during use.

At 23,000x magnification, the SEM images showed densely packed, heterogeneous angular structures, including irregular, rod-like, and flake-like shapes **Figure 2 B**. This morphology indicated successful integration of nano-silica and nano-hydroxyapatite. Individual nanoparticles were distinguishable at the 0.5 µm scale, confirming that the nanoparticles preserved their nanoscale characteristics without significant agglomeration.

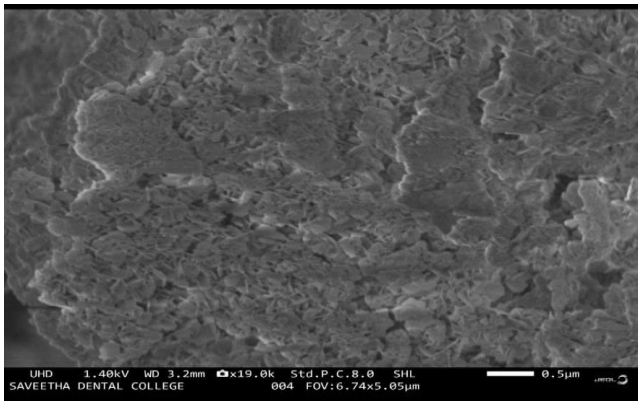


Figure 2 B.SEM image of the formulated Prophylactic polishing paste at 23000x.

Cytotoxic Activity

The bar graph **(Figure 3)** presents a cytotoxicity analysis of the prophylactic polishing paste tested on MG-63 cells, with concentrations ranging from 15 µL/mL to 75 µL/mL and a control group.

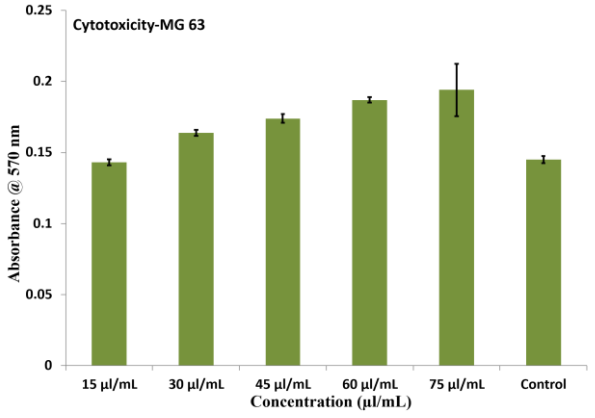


Figure 3. The bar graph depicts the cytotoxicity analysis of the prophylactic polishing paste tested on MG-63 cells, with concentrations ranging from 15 µL/mL to 75 µL/mL and a control group. The X-axis represents the different concentrations of standard used in µL/mL and the Y-axis represents the absorbance at 570nm**.**

The absorbance at 570 nm reflects cell viability, and the control group exhibited lower absorbance compared to most experimental concentrations, indicating reduced cell viability. As the concentration of the paste increased from 15 µL/mL to 75 µL/mL, there was a general rise in absorbance, peaking at 75 µL/mL. This suggests that higher concentrations of the paste may enhance cell viability or proliferation in this assay. The dose-response relationship revealed a positive correlation between paste concentration and cell viability, with the highest concentration (75 µL/mL) demonstrating maximum absorbance, implying minimal cytotoxicity and a potentially beneficial effect on cell viability at this concentration.

The fluorescence microscopy images **(Figure 4)** showed MG-63 cells treated with different concentrations of the prophylactic polishing paste, with live or viable cells visualized using a green fluorescent stain.

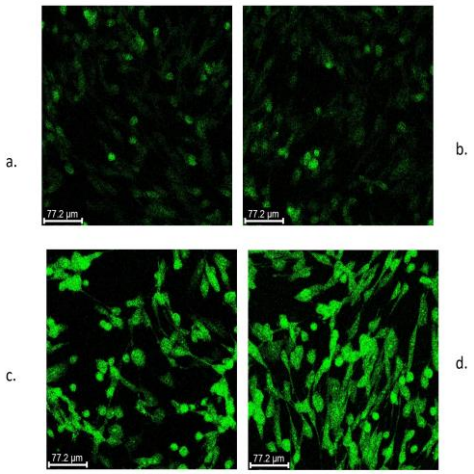


Figure.4 The fluorescence microscopy images show MG-63 cells treated with varying concentrations of the prophylactic polishing paste, including control, at 15 µL/mL, 30 µL/mL, and 50 µL/mL.

In the control, the cells appeared sparsely distributed with lower fluorescence intensity, indicating reduced cell viability or lower cell density at that concentration. At a concentration of 15 µL/mL, the cells appeared slightly denser, suggesting a minor increase in cell viability. At 30 µL/mL, the fluorescence intensity and cell density were significantly higher, indicating enhanced cell viability or proliferation compared to the control. At 50 µL/mL, the image showed the most intense fluorescence and highest cell density, indicating maximal cell viability or proliferation at this concentration of the prophylactic paste. At lower concentrations, the cells appeared smaller and less spread out, possibly indicating stress or cytotoxic effects. However, at increased concentrations, the cells seemed to be elongated and spread out, characteristic of healthy and proliferative cells, suggesting that the paste

was less cytotoxic and possibly supportive of cell growth at these higher concentrations.

Antimicrobial activity

The bar graph **(Figure 5)** displayed the anti-microbial activity of a prophylactic paste tested against four microorganisms: *Staphylococcus aureus, Streptococcus mutans, Escherichia coli, and Pseudomonas aeruginosa.*

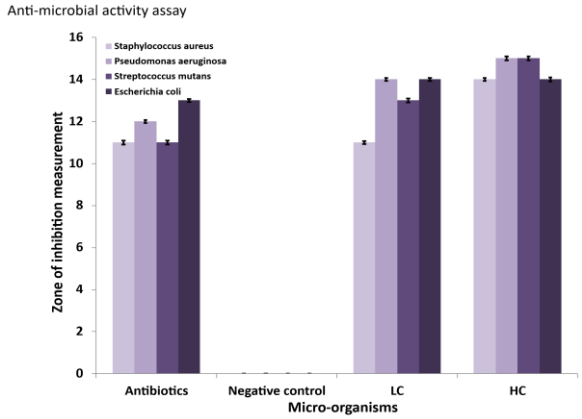


Figure 5. The bar graph displays the anti-microbial activity of a prophylactic paste tested against four microorganisms: Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus mutans, and Escherichia coli.

The zone of inhibition, which measured the effectiveness of the paste in preventing microbial growth, was compared across different groups: Antibiotics[Amoxicillin], Negative Control, LC (Low Concentration), and HC (High Concentration). All four microorganisms showed significant zones of inhibition against the control, ranging from approximately 12 to 14 mm, confirming the effectiveness of the antibiotics used as a positive control. The negative control showed no inhibition zones, confirming that the medium without the prophylactic paste or antibiotics did not have antimicrobial properties. At low concentrations, the prophylactic paste produced zones of inhibition for all four microorganisms, with measurements similar to those seen with antibiotics, though slightly lower, indicating that even at a low concentration, the paste had considerable antimicrobial activity. At high concentrations, the prophylactic paste resulted in the largest zones of inhibition for all microorganisms, with measurements slightly higher than those of the antibiotics, suggesting that the paste at a higher concentration was highly effective in inhibiting the growth of these microorganisms.

Surface roughness analysis

Post-scaling, the tooth surface exhibited moderate roughness, with significant peaks and valleys. The surface roughness parameters indicated that the scaling process, while effective in removing surface contaminants, left behind irregularities. The area roughness (Sa) was measured at 51.559 nm, with notable peak heights (Sp) of 171.72 nm and valley depths (Sv) of -208.23 nm, suggesting unevenness on the tooth enamel or dentin. Similarly, the line roughness parameters revealed an arithmetic mean roughness (Ra) of 58.349 nm, along with peak heights (Rp) of 158.29 nm and valley depths (Rv) of -142.25 nm, reflecting the rough, textured surface left after scaling **(Figure 6).**

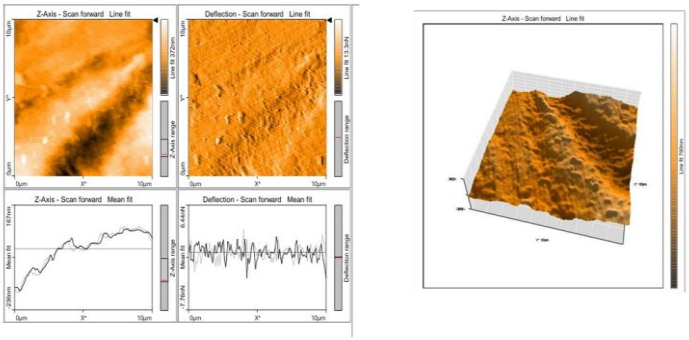


Figure 6. The Atomic Force Microscopy (AFM) image showing Surface roughness analysis of the tooth after scaling.

Following the application of the post-prophylaxis polishing paste, there was a marked reduction in both surface and line roughness, indicating the effectiveness of the treatment. The area roughness (Sa) decreased to 37.532 nm, with peak heights (Sp) reducing to 134.34 nm and valley depths (Sv) improving slightly to -201.04 nm. Similarly, the line roughness values dropped, with Ra reducing to 44.768 nm, Rp to 99.374 nm, and Rv to -110.72, highlighting the polishing effect of the paste **(Figure 7).**

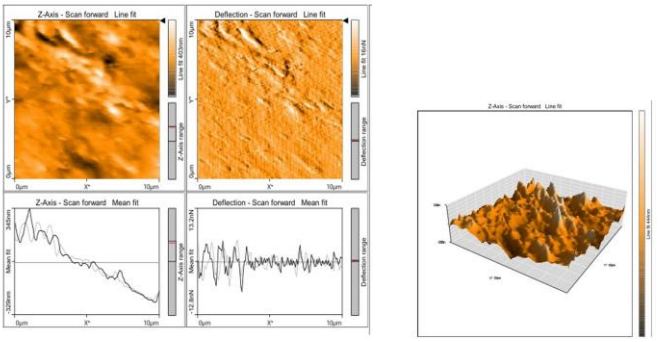


Figure 7. The Atomic Force Microscopy (AFM) image showing the surface roughness analysis of the tooth after applying prophylactic polishing paste

These improvements demonstrate that the polishing paste successfully flattened the peaks and valleys, creating a smoother and more uniform tooth surface, thereby aiding in reducing plaque accumulation **(Table 1)**

Table 1 shows the Surface Roughness Parameters Before and After Prophylactic Polishing Paste Application

Parameter	Post-Polishing -Baseline	Post-Polishing Paste Application
Area roughness (Sa)	51.559 nm	37.532 nm
Peak height (Sp)	171.72 nm	134.34 nm
Valley depth (Sv)	-208.23 nm	-201.04 nm
Arithmetic Mean Roughness (Ra)	58.349 nm	44.768 nm
Peak height (Rp)	158.29 nm	99.374 nm
Valley depth (Rv)	-142.25 nm	-110.72 nm

DISCUSSION

Scaling is a dental procedure that involves the removal of plaque and calculus from the surfaces of the teeth [10]. This process is essential for preventing periodontal disease, as it helps to clean areas where regular brushing and flossing may not reach. Scaling helps to reduce inflammation and minimize the risk of periodontal disease [11]. Scaling leaves teeth with a rough texture due to the removal of plaque and calculus, making post-prophylaxis polishing necessary for a smooth finish.

Polishing is essential for smoothing the irregularities left after scaling. The polishing paste contains fine abrasives that gently buff the tooth surfaces, effectively removing any remaining rough patches [12]. This enhances the aesthetic appearance of the teeth and reduces plaque accumulation, also [13]. Many polishing pastes contain fluoride, making them more resistant to cavities and sensitivity [14].

A prophylactic polishing paste incorporating Lactobacillus plantarum MTCC 5690, nano silica, and nano-hydroxyapatite particles offers a comprehensive approach to oral health. Both in vitro and in vivo studies have highlighted the individual benefits of these ingredients in oral health. By combining these three components into a single product, the aim was to maximize their synergistic effects.

Lactobacillus strains are renowned for their probiotic properties, which are crucial in restoring a healthy balance of oral microbiota [15]. These beneficial bacteria help reduce the risk of dental caries and gingival diseases. Additionally, they play a role in maintaining oral pH balance, promoting fresher breath.

Nano-silica particles in polishing paste offer superior performance by leveraging their tiny size and large surface area while minimizing damage to the enamel [16]. They can also be used to create a barrier on the tooth surface that helps reduce tooth sensitivity by protecting exposed dentin.

Nano-hydroxyapatite particles are highly effective in the remineralization of tooth enamel as they mimic the natural mineral composition of teeth, facilitating the repair of early enamel lesions [17].They form a protective barrier over exposed dentin and fill in microscopic tubules, thereby reducing the sensitivity to any stimuli. This dual action underscores the versatility of nano-hydroxyapatite in both dental and medical applications [18].

The objective of our study was to evaluate the in vitro characteristics of a prophylactic polishing paste formulated with probiotics and nanoparticles. Of course! Here's the same summary in the past tense:

The SEM revealed clear integration of nano-silica and hydroxyapatite without agglomeration, preserving their nanoscale benefits, and the roughened surface supported controlled-release, allowing gradual delivery of actives. Retained nanoparticle size increased surface area for better bioactivity, and diverse particle shapes contributed to improved mechanical and functional properties.

The cytotoxicity activity assay demonstrated a positive dose-response relationship, where higher concentrations resulted in minimal cytotoxicity, and in fluorescence microscopy, the highest viability was observed at 50 µL/mL, where the cells appeared healthy, indicating that the paste supported cell growth at higher concentrations. These findings align with previous research showing that Lactobacillus strains can selectively target and inhibit cancer cells while sparing normal cells from any damage [19].

The antimicrobial activity assay revealed strong antimicrobial activity, with higher concentrations of paste showing greater inhibition of microbial growth, even surpassing the effect of antibiotics. The negative control confirmed the paste's effectiveness, as it showed no inhibition. In addition, other studies have shown that both the nanoparticles and Lactobacillus strains possess strong antimicrobial activity against various Gram-

negative periodontal pathogens [20]

In our study, a surface hardness test was conducted to assess the efficacy of the polishing paste on an extracted tooth. The results showed that the tooth surface had significant roughness post-scaling with noticeable peaks and valleys. However, after applying the prophylactic paste, both surface and line roughness were significantly reduced, resulting in a smoother, more uniform surface. This improvement highlights the paste's ability to minimize irregularities, potentially aiding in the reduction of plaque accumulation. An investigation evaluated the in vitro effects of one year of brushing with 10 wt. % nano-hydroxyapatite toothpaste. It concluded that while the toothpaste did not change enamel roughness, it positively contributed to remineralization and protection of the enamel surface [21,22].

Various studies have highlighted the significance of nanoparticle polishing pastes, especially those with nano-hydroxyapatite (n-HAp), as they enable targeted remineralization of micro-damage and their potential antimicrobial Efficacy against Streptococcus mutans, Enterococcus faecalis, and Candida albicans [23]. Probiotics, on the other hand, promote a balanced oral microbiome while also enhancing the immune response in the oral cavity [24].

While chemical post-prophylaxis polishing pastes effectively remove stains and smooth teeth, they have drawbacks, including enamel wear, increased sensitivity, and disruption of the oral microbiome [25]. They also lack remineralization benefits and may cause allergic reactions. Additionally, environmental concerns arise from non-biodegradable components, such as microplastics. These issues emphasize the need for exploring probiotic polishing pastes with nanoparticles as safer alternatives.

Awareness of probiotic formulations and nanoparticles has been increasing recently [26]. This is especially true as in vitro studies demonstrate the enhanced antibacterial efficacy of probiotic-based products against cariogenic pathogens [27,28]. Thus, the combination of probiotics and nanoparticles in this polishing paste is intended for use in patients with gingivitis and periodontitis after oral prophylaxis, thereby providing a holistic approach to oral hygiene.

CONCLUSION

In conclusion, the prophylactic polishing paste demonstrated effective integration of *Lactobacillus plantarum* and nanoparticles, and exhibited strong antimicrobial activity, comparable to conventional antibiotics at higher concentrations, while maintaining effective biocompatibility and promoting cell viability in a dose-dependent manner. Additionally, the paste significantly improved the smoothness of tooth surfaces by reducing surface roughness, which can help minimize plaque accumulation and support oral health. Overall, these findings suggest that the paste is a promising, multifunctional oral care product with potential benefits for preventing and managing periodontal conditions.

STRENGTHS AND CONSTRAINTS

The study's strengths include its innovative use of probiotics and nanoparticles, offering antimicrobial benefits with fewer side effects than chemical pastes. However, limitations include the absence of in vivo data and individual variations in oral microbiota, which may impact the paste's practical effectiveness.

DECLARATIONS

ETHICAL APPROVAL

Not applicable as this study is an in vitro study.
Institutional Scientific Review Board approval was o

Conflict of interest

The authors declare that they have no conflict of interest.

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CASE REPORT

INDIVIDUALIZED APPROACH TO THE SURGICAL EXTRACTION OF IMPACTED AND SEMI-IMPACTED WISDOM TEETH

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ABSTRACT

Background: Surgical interventions for the removal of impacted and semi-impacted third molars remain one of the most relevant and scientifically debated topics today. The methods of either complete (intact) or sectional extraction have specific indications and contraindications depending on the particular clinical scenario. Each technique has its own advantages and disadvantages, as well as proponents and opponents.

Purpose of this article is to clarify the indications for the use of the intact extraction technique for impacted and semi-impacted third molars, based on theoretical analysis and clinical experience, and to address the issue of possible complications and their prevention.

Methods – the article is based on an analysis of clinical cases described in the literature, as well as on the results of our own practical and clinical experience.

Our clinical choice favored the intact extraction technique for impacted and semi-impacted third molars; however, we do not disregard nor diminish the significance of sectional extraction.

Based on dynamic postoperative monitoring and final outcomes, we consider this scientific-practical research successfully completed.

Conclusion. Drawing on our clinical experience and obtained results, we recommend performing extraction of impacted and semi-impacted third molars with maximal preservation of tooth integrity, avoiding segmentation of the crown and/or roots, as such segmentation may lead to complications. The use of this intervention is justified only when clear indications are present and contraindications are absent.

***Keywords*:** wisdom teeth, semi-impacted molars, fully impacted molars, complications of extraction, surgical extraction of molars

INTRODUCTION

Studying different approaches to the extraction of third molars, and based on our own experience analyzing clinical outcomes, we present our perspective and clinical approach to this dilemma.

Depending on the tooth position, its relation to adjacent teeth or restorations, and importantly, its anatomical relationship to vital structures, extraction can be performed either by intact removal of the tooth or by sectional extraction. Naturally, there are specific indications and contraindications for each of these techniques.

1. Complete Extraction (Without Sectioning)

Indications

- Recurrent pericoronitis[1]
- Unrestorable caries, or caries extending into the pulp[1]
- Disto-cervical caries in adjacent second molar caused by third molar impaction (horizontal or mesioangular)[1]
- Presence of odontogenic cysts or tumors[2]

Third molars impeding orthognathic surgery or located in the line of a mandibular fracture[2]

- Extraction should only be considered in asymptomatic, fully impacted third molars if there are signs or symptoms of pathology. Otherwise, active monitoring is recommended[3]
- Pericoronitis, periodontitis, periapical abscess, cysts/neoplasms, resorption of adjacent roots, inflammation of opposing soft tissue[3]

- Aberrant positions (buccal or lingual), interference with orthodontic appliances, arch length discrepancies, bone loss, dental caries/damage to adjacent teeth, pre-irradiation removal, prosthodontic needs, chronic facial pain (PMC)[3]

High risk of inferior alveolar nerve (IAN) damage[4]

- Complex root morphology, hypercementosis, ankylosis[4]
- Patients with history of intravenous bisphosphonate therapy or radiotherapy [4]

2. Sectioning & Coronectomy (Partial Extraction via Sectioning)

Indications for Sectioning (including Coronectomy)[5]

- When a tooth requires sectioning due to access issues: perform decoronation, then root division for separate removal[5]

Coronectomy (intentional leaving of roots) indications

- Lower wisdom tooth radiographically close to the IAN canal[5]
- Signs of IAN narrowing or loop[5]

formation,

- Darkening of roots, interruption of canal cortication,[5]
- Interruption of lingual cortical bone,
- Vital tooth without caries, periodontal, or periapical pathology[5]
- Coronectomy is appropriate when the tooth is very close to the IAN, aiming to reduce nerve injury[1]

Contraindications for Coronectomy

- Severe infection (e.g., caries or periapical pathology)[1]
- Medically compromised patients (immunocompromised, under radiotherapy/chemotherapy)[1]
- Teeth that can be completely removed with low risk[1]
- Horizontal impactions—roots may be similarly exposed [1]
- Non-vital teeth, extensive caries, tooth mobility, periapical disease, cystic[2] lesions, tumors, horizontal impactions, immunocompromised status, neuromuscular disorders, diabetes mellitus, or jaw bone diseases [4]
- Mobility, pulpal necrosis, apical periodontitis, horizontally impacted third molar, immunocompromised or uncontrolled diabetics, HIV, other immunosuppressive conditions [4]

In this article, we will focus on recent scientific and clinical studies, as well as substantiate our choice with specific clinical cases. Sectional extraction of impacted teeth requires more complex technical execution and, accordingly, a higher level of professional skill and experience. Although the sectional removal of impacted teeth can be relatively straightforward, the use of this method carries a risk of complications that may occur both intraoperatively and during the early and late postoperative periods.

Among the common complications, we would like to highlight the following:

- An increased risk of trauma.

Compared to sectional extraction, intact removal of impacted teeth has certain advantages in specific clinical situations. During sectional extraction, visual control of the rotary instrument (bur) is limited because the distal area where the tooth is sectioned is often not directly visible. This limitation increases the risk of damage to the underlying hard tissues, which can lead to various complications.

According to numerous clinical studies, the application of sectional extraction techniques may result in several problems. There is a high likelihood of unplanned and unpredictable tooth fractures occurring in anatomically unfavorable areas, which significantly complicates the surgical procedure. This also prolongs the duration of the operation, thereby increasing the risk of infection and the subsequent development of edema.

It is also important to note that even with planned and predictable tooth sectioning, complications may still arise, particularly excessive loss of alveolar bone tissue. Such outcomes may also be related to insufficient technical equipment.

Unfortunately, sectional extraction inherently carries the risk of residual tissue debris remaining in the surgical wound due to limited visualization and the size of microscopic particles.

In summary, based on the above, we find it necessary to present data from recent scientific and clinical research:

Complications of Wisdom Tooth (Mandibular Third Molar) Extraction

A) Complete Extraction (Without Sectioning)

- Inferior Alveolar Nerve (IAN) Injury[6]
- Incidence varies between approximately 0.35% to 8.4%, with permanent injury being rare (< 1%) [6]
- Risk factors include: age > 24 years, horizontal impaction, close root proximity to the canal, and extraction performed by less experienced surgeons.[6]
- Dry Socket (Alveolar Osteitis)[7]
- Common complication following mandibular

extractions, often presenting as dull pain 3–5 days post-op; higher risk in female patients (especially those on oral contraceptives), smokers, or in cases of surgical trauma (Decisions in Dentistry).[7]

- Infection & Trismus[8]
- Postoperative infection and limitations in mouth opening (trismus) occur at appreciable rates. A study of 550 extractions reported: 20 cases of alveolitis, 12 infections, and 6 cases of IAN paresthesia (3 temporary, 3 permanent) with an overall complication rate of 6.9%.[6]
- Operator Experience as a Factor[9]
- Oral and maxillofacial surgery[9] residents had significantly higher rates of complications such as trismus, nerve paresthesia, dry socket, and infection compared to specialists (total complication incidence of 63.7% in the resident-treated group versus markedly less for specialists)

B) Sectioning / Coronectomy (Intentional Partial Extraction) Systematic Review & Meta-analysis Outcomes[10]

A systematic review covering 16 studies (2,176 coronectomies) showed low complication rates:[10]

- IAN injury: ~0.59%[6]
- Lingual nerve injury: ~0.22%[6]
- Infection: ~3.95%[11]
- Dry socket: ~1.12%[11]
- Need for root extraction later: ~5.28%[11]
- Reintervention: ~1.13%[12]
- Pain was reported in ~22% of cases[12]

Meta-Analysis Comparing Coronectomy vs. Extraction[13]

- Coronectomy significantly reduced risks of IAN injury (OR 0.14) postoperative pain, and dry socket (OR 0.38), but increased likelihood of reintervention (OR 5.38) [13]
- Long-Term Follow-Up Study (231 Cases, ~5.7 Years)[14]
- IAN injury occurred in 1.3%, infections in 11.7% (treated with antibiotics), and root migration occurred in 97% of cases (65% exhibited rotation), while 3.5% required root removal later. No nerve injuries resulted from those reoperations.[16]

Meta-Analysis (2014) Findings

Coronectomy reduced IAN sensitivity loss and dry socket risks, with similar rates of pain and infection compared to extraction. Root fragments migrated on average ~2 mm over two years.[16]

Summary

Procedure TypeKey Complications & RatesComplete ExtractionIAN injury (0.35–

8.4%), dry socket (common), infection, trismus; risk increased with older age, female sex, horizontal impaction, and less experienceCoronectomy / SectioningLower IAN injury (~0.6–1.3%), dry socket, and pain; but higher rates of root migration (~97%), eventual root removal (~5%), infection (~4–12%), and reintervention

A) Complete (Full) Extraction of Wisdom Teeth — Complications

Key Findings from Clinical Studies

1. Surgical Difficulty Increases Risk

A retrospective study of 1,699 third molars found a 3.47% overall complication rate, including pain, root-tip fracture, paresthesia, alveolar osteitis (“dry socket”), TMJ discomfort, and oroantral fistula. The highest risk occurred in extractions that required both osteotomy and sectioning (i.e., highest surgical difficulty).

2. Real-World Practice—Oman Study

- In a tertiary care retrospective cohort (1,116 third molar extractions):
- Intraoperative complications: 3.7% (tuberosity fractures, root fractures, bleeding, soft tissue injuries, adjacent tooth damage)
- Postoperative complications: 8.3%, including nerve injuries (mostly temporary), swelling/pain/trismus, and dry socket (0.5%).

3. Impact of Sectioning and Osteotomy

- Among 270 extractions (by two oral surgeons), cases involving both osteotomy and odontotomy (sectioning) showed significantly higher complication rates, with an overall 14.8% complication rate. Most common: alveolar osteitis (11.1%), root-tip fractures (2.2%), lingual nerve paraesthesia, and TMJ problems (each 0.74%).

4. Single-Tooth Surgical Extractions

- In 339 extractions (one tooth per patient), 15% experienced perioperative complications, such as acute tissue inflammation, trismus, oroantral communication (mainly with upper wisdom teeth), hematoma, and transient lingual nerve sensory changes. Lower teeth and extractions requiring root separation had higher complication rates.

5. Identified Risk Factors

- A transversal study of 605 extractions identified significant predictors of complications: age over 25, bone removal, tooth sectioning, and tooth location. Infections were the most frequent complication (42.6%), followed

by root fractures and gingival alterations.

6. Population-Based Perspective

A nationwide cohort (16,609 impacted mandibular extractions) revealed:[24]

- Dry socket: 3.6%[21]
- Prolonged TMJ symptoms: 0.41%[21]
- Surgical site infection: 0.17%[21]

Complexity of odontectomy and a history of gingivitis/pericoronitis increased dry socket risk.

Summary: Full Extraction Complications

Complication TypeIncidence & NotesDry Socket (Alveolar Osteitis)3.6% (nationwide), up to 11.1% when sectioning is needed (PMC, PubMed)Nerve Injury (IAN / Lingual)Occurs; higher in complex cases, risk exacerbated by bone removal and sectioning Fractures & Root Tip FragmentsTuberosity and root-tip fractures notable; root fragments may require retrieval Oroantral Communication Occurs mainly in upper wisdom tooth extractions; lower risk overall Infection & Inflammation Very common: 42.6% in one cohort; includes hematomas and tissue inflammation Trismus & TMJ SymptomsCommon (e.g., 13 cases in 339 extractions or 0.41% prolonged symptoms) Bleeding & Soft Tissue InjuryPresent in small percentages; linked to intraoperative challenges Higher Risk CasesExtraction difficulty (osteotomy + sectioning), age >25, bone removal significantly elevate risks Complications of Sectioning / Coronectomy and Full Sectioning in Wisdom Tooth Extraction

1. Definition

- Coronectomy (Partial Removal): Removal of the crown of the wisdom tooth, leaving roots intentionally in place to avoid nerve injury.[15]
- Full Sectioning: Surgical sectioning of the tooth to facilitate removal in parts, commonly done with osteotomy (bone removal) when full extraction is difficult.[15]

2. Complications of Coronectomy[16,17]

- Root Migration:
- Occurs in up to 97% of cases, with roots migrating an average of 2–3 mm over 2–5 years (Pedersen et al., 2018).
- Usually asymptomatic, but in 3–5% of cases, migrated roots require secondary removal.
- Infection:
- Postoperative infections occur in approximately 3.95% to 11.7% of cases; often successfully treated with antibiotics (pmc.ncbi.nlm.nih.gov, pubmed.ncbi.nlm.nih.gov).
- Inferior Alveolar Nerve (IAN) Injury:
- Very low incidence (~0.6% to 1.3%) compared to full extraction, with most injuries being temporary (pmc.ncbi.nlm.nih.gov).
- Lingual Nerve Injury:
- Occurs less commonly (~0.2%) and is typically transient.[16]
- Dry Socket (Alveolar Osteitis):
- Lower incidence (~1.12%) compared to full extraction.[19]
- Reintervention:
- Secondary surgery to remove retained roots required in approximately 5.3% of cases
- Pain & Swelling:
- Postoperative pain is common (~22% incidence), but usually manageable with standard analgesics

3. Complications of Full Sectioning with Extraction[17]

- Higher Surgical Trauma:
- Full sectioning usually implies more extensive bone removal and longer surgery time, leading to increased soft tissue trauma, swelling, and trismus
- Increased Risk of Dry Socket:
- Rates reported between 7% to 11%, higher than coronectomy, especially when sectioning and osteotomy are combined
- Root Fractures and Remnants:
- Root-tip fractures are more common, occurring in up to 2–3% of cases; root remnants may require secondary surgical removal

Inferior Alveolar Nerve Injury:

Incidence varies widely but is generally higher than coronectomy (up to 8.4% temporary, <1% permanent); related to proximity of roots to nerve and surgical technique

- Lingual Nerve Injury:
- Occurs but less frequently than IAN injury; often transient.
- Postoperative Infection:
- Occurs in approximately 5–10% of cases, depending on surgical conditions.
- Trismus and Pain:
- Common postoperative symptoms due to tissue manipulation and inflammation; usually resolve in 1–2 weeks.

4. Comparison: Coronectomy vs. Full Sectioning Extraction

Complication Coronectomy

Full Sectioning Extraction IAN

Injury0.6%–1.3%, mostly temporary

Up to 8.4%, includes permanent cases

Lingual Nerve Injury~0.2%, usually temporary

Variable; less frequent than IAN injuryInfection3.9%–11.7%, treated with antibiotics5–10%, related to surgical trauma

Dry Socket~1.1%7–11%, higher with osteotomy

Root Migration~97%, usually asymptomatic

Not applicable

Reintervention

Rate~5.3% require secondary surgery

Low but may require root retrieval

Postoperative Pain & Swelling

Common (~22%)

More pronounced due to surgical trauma

TrismusLess frequent

More frequent

Based on the potential complications associated with sectional extraction, we selected the technique of intact extraction for impacted teeth, considering it more appropriate in the specific clinical cases described below. We emphasize that we do not in any way reject the rationale for the sectional extraction method in certain clinical scenarios.

Clinical Cases

Patient #1 (24 years old, female) presented with a semi-impacted tooth 4.8.

Clinically, the patient exhibited radiating pain, swelling, and hyperemia in the region of the tooth. The medical history revealed periodic low-grade fever episodes. The complexity of this case was due to tooth 4.7 serving as an abutment for a metal-ceramic fixed bridge. As seen in Figure 1, tooth 4.8 was partially located beneath the margin of the metal-ceramic prosthesis, posing a risk of damaging the aesthetic and functional integrity of the bridge. (Figure 1-3).

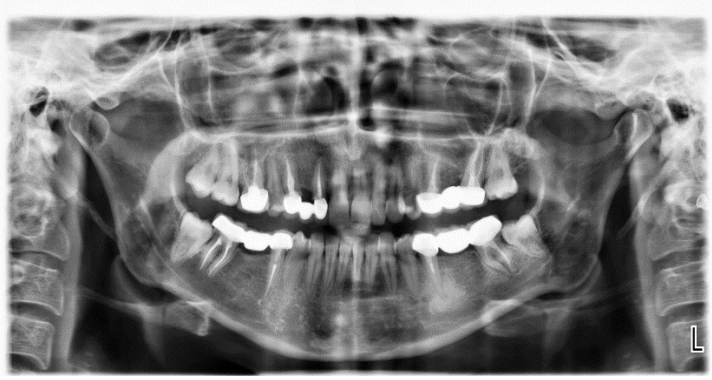


Figure 1. semi-impacted tooth 4.8 (OPG)



Figure 2. extracted tooth 4.8

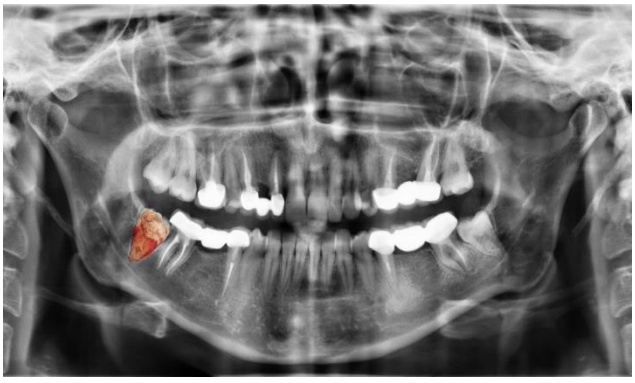


Figure 3. projection tooth on the (OPG) image

We decided to extract tooth 4.8 using the intact removal technique, thereby avoiding potential damage to the prosthetic construction. Throughout the surgical procedure, surgical curettes, elevators, rotary instruments, and others were employed.

An incision was made, followed by blunt dissection using an elevator to expose the visible part of the tooth. Then, rotary instruments were used to contour the vestibular bone and distal osseous tissue—this step being key to the successful outcome, as the tooth was planned to be removed in this direction to avoid damage to the prosthetic structure.

The use of this method, in our opinion, not only enriched our clinical experience but also allowed us to closely monitor the postoperative period and analyze the results.

While sectional extraction could have been performed, we chose a minimally invasive approach to the bone, as the alveolar bone surrounding the tooth was at a sufficiently high level, covering approximately 80% of the tooth. This method helped us avoid the impact of aggressive and rapid instrumentation on the alveolar bone, thereby preventing potential functional and aesthetic damage to the prosthesis.

Patient #2 (35 years old, male) presented with radiating pain in the area of tooth 3.8. Based on the above data, we decided to perform extraction by intact removal. Clinical and instrumental examination revealed a mesioangular position of the tooth, with the crown tilted horizontally toward tooth 3.7, causing pain and significantly complicating the extraction of tooth 3.8. The choice of intact removal was also influenced by destruction of the crown of tooth 3.8. Small areas of distal and vestibular bone were removed using rotary instruments, after which conditions favorable for elevator use were achieved, and extraction was performed without complications(figure 4-6).

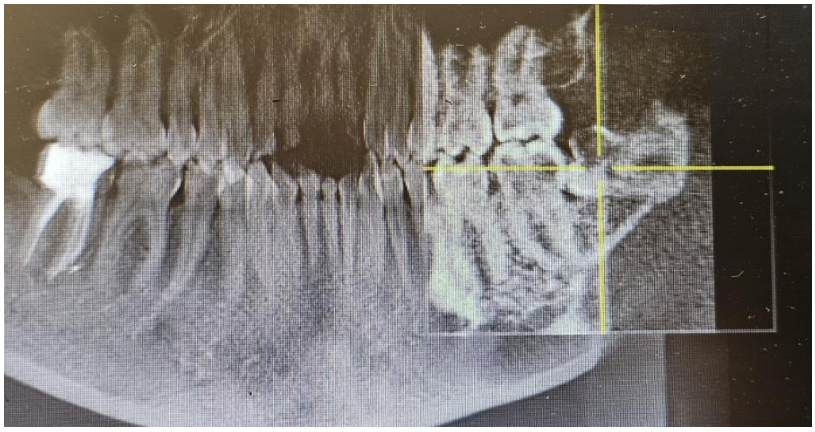


Figure 4. semi-impacted tooth N48, horizontal impaction. (OPG



Figure 5. extracted tooth 4.8

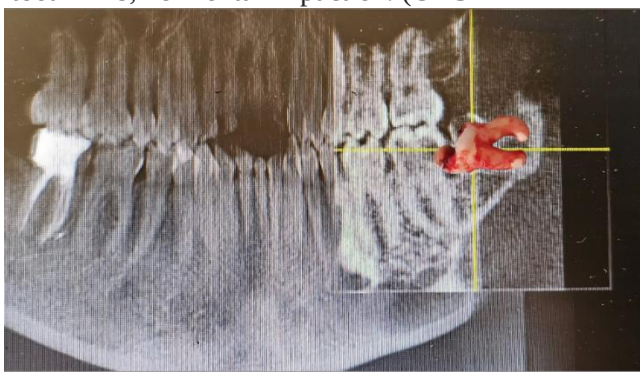


Figure 6. projection of the extracted tooth on the (OPG) image

Patient #3 (22 years old, female) presented with pronounced pain in the regions of teeth 38 and 48. Clinical and instrumental examination confirmed the presence of impacted teeth 38 and 48. We decided to extract the teeth using intact removal, performing the procedures sequentially rather than simultaneously.

Initially, an incision was made along the alveolar ridge margin, then a longitudinal incision parallel to the crown of tooth 37 was performed, forming a soft tissue flap. Blunt dissection was carried out to expose the occlusal surface of the tooth. The crown was nearly completely surrounded by alveolar bone—approximately 90% embedded in bone. Surgical removal of vestibular and distal bone was then performed to create sufficient space for manipulation, allowing extraction of the tooth with elevators beyond the bone limits. The extraction of tooth 48 was performed using the same technique, with identical postoperative care and outcomes recorded (7-11).



Figure 7. impacted 3.8, 4.8 teeth, mesioangular impaction



Figure 8. extracted tooth 3.8



Figure 9. extracted tooth 4.8

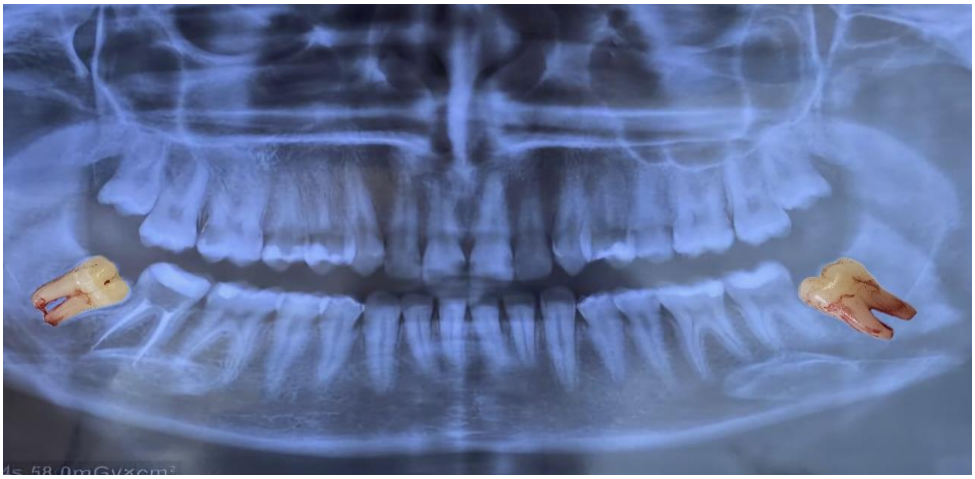


Figure 10. 3.8, 4.8 extracted teeth projection on the (OPG) image

It should be noted that in all clinical cases, an identical surgical approach was used. For soft tissue incision design, the Standard Triangular Flap was employed. Analyzing the results, we observed adequate wound healing by primary intention in all cases without complications. The aesthetic outcomes also met our expectations. Overall, the results were positive.

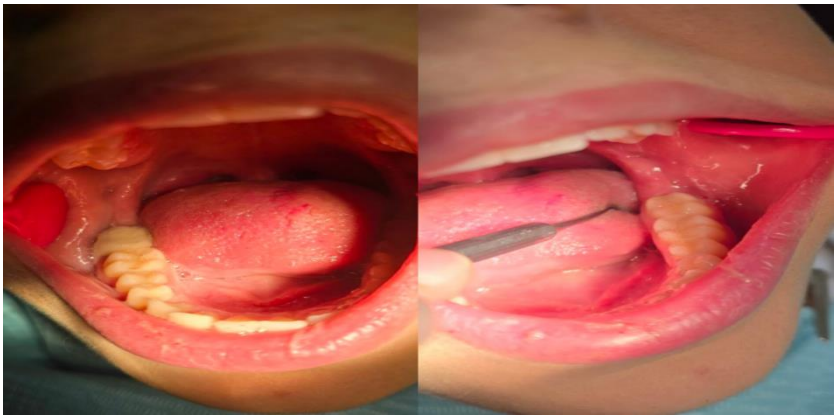


Figure 11. healed wound, 3 months after surgical intervention.

Results were assessed through dynamic observation, with the outcomes presented at three months postoperatively.

Drawing on our clinical experience and obtained results, we recommend performing extraction of impacted and semi-impacted third molars with maximal preservation of tooth integrity, avoiding segmentation of the crown and/or roots, as such segmentation may lead to complications. The use of this intervention is justified only when clear indications are present and contraindications are absent.

DECLARATION

" **Conflict of Interest**

The author declares that he has no conflict of interest and there was no external source of funding for the present study.

Source of funding

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Informed consent

Informed consent was obtained from all individual participants included in the study.

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ORIGINAL ARTICALE

PATIENT AWARENESS AND ATTITUDE TOWARDS RUBBER DAM USAGE DURING ENDODONTIC TREATMENT IN SOUTHERN SAUDI ARABIA: A COMPREHENSIVE ANALYSIS

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ABSTRACT

Background: Rubber dam isolation is globally mandated for endodontic procedures due to its proven role in enhancing treatment efficacy, patient safety, and infection control. The objective of the study is to investigate this paradigm in Saudi Arabia's understudied southern region, where cultural and healthcare access factors may uniquely influence compliance.

Materials and Methods: A cross-sectional analytical design was employed, recruiting 208 consecutive patients requiring endodontic treatment at Jazan University's dental clinics. Validated bilingual questionnaires assessed three domains: (1) Baseline awareness of rubber dams, (2) Attitudes (comfort, future preference), and (3) Perceptions of benefits. Statistical analysis included descriptive frequencies, chi-square tests, and logistic regression (α=0.05).

Results: The cohort (55.3% male, 44.7% female) exhibited significant knowledge gaps: 55.8% (n=116) reported no prior exposure. Post-intervention, acceptance was remarkably high: 73.3% of first-time users (n=85/116) reported comfort, while 93.2% (n=109/116) preferred future use. Previously exposed patients (n=92) showed even stronger endorsement (82.2% future preference). Critically, preoperative explanation was the paramount predictor of acceptance: Patients receiving explanations demonstrated 3.4× higher comfort levels (OR=5.2, 95% CI: 2.8–9.6; p<0.001).

Conclusions: The findings advocate for standardized patient education protocols (visual aids, culturally adapted messaging) to bridge knowledge gaps. Implementation strategies should target policy reforms (Saudi Commission for Health Specialties accreditation standards) and curriculum enhancements to align regional endodontic practice with international guidelines. The acceptance and use of rubber dam will advance patient safety, improve endodontic outcomes, and position Saudi dentistry at the forefront of evidence-based practice.

Keywords*:*Rubber Dam Isolation; Patient Awareness; Dental Infection Control; Cross-Cultural Dentistry; Saudi Arabia; Health Health Communication; Clinical Compliance

INTRODUCTION

The success of endodontic therapy is fundamentally predicated on the establishment and maintenance of a sterile operating field—a principle enshrined in dental literature since Louis Grossman's pioneering work in 1940 that established the biological basis for root canal treatment. This foundational requirement has driven the evolution of isolation techniques, culminating in the rubber dam system introduced by New York dentist Sanford Christie Barnum in 1864. What began as a simple linen sheet has transformed into a sophisticated isolation technology now formally mandated by leading professional organizations including the American Association of Endodontists, European Society of Endodontology, and the British Endodontic Society [1–3].

The global consensus on rubber dam necessity stems from overwhelming evidence demonstrating its multifaceted benefits that extend far beyond basic moisture control. Contemporary meta-analyses by Mamoun et al. (2020) have quantified a 27% increase in endodontic success rates with rubber dam usage, primarily attributable to its barrier function against salivary contaminants containing resilient pathogens like *Enterococcus faecalis* and *Candida albicans* that compromise treatment outcomes [4]. From a patient safety perspective, the rubber dam serves as an indispensable protective shield. Krasuska et al. documented that non-isolated endodontic procedures carry a 0.3–1.2% risk of instrument aspiration or ingestion—a potentially catastrophic yet entirely preventable hazard [5]. The physical barrier equally prevents mucosal injuries from caustic irrigants; Zhu et al. (2020) reported an 89% reduction in sodium hypochlorite accidents when rubber dams are properly implemented [6]. In the post-pandemic era, these isolation systems have gained renewed importance for aerosol mitigation. Samaranayake et al. (2021) demonstrated that rubber dams reduce airborne pathogens by 95.3% during high-speed instrumentation, making them essential infection control tools in modern dental settings [7]. Beyond clinical outcomes, medicolegal considerations further reinforce their necessity: Malpractice claims related to swallowed instruments decreased by 78% in practices with consistent rubber dam usage according to the Dental Protection Ltd 2022 report.

Despite these compelling evidence-based advantages, global utilization remains strikingly inconsistent. A systematic review by Al-Abdulwahhab et al. (2021) identified a complex matrix of barriers including practitioner-related factors (time constraints averaging 3.7 minutes per application, inadequate training during dental education), patient-related concerns (perceived discomfort, claustrophobia), and systemic limitations (lack of institutional enforcement, reimbursement issues) [8]. The World Health Organization's 2022 global oral health report highlighted particularly low adoption rates in developing regions (23–41%) compared to European benchmarks (68–79%) [9]. This disparity manifests uniquely in Saudi Arabia's southern Jazan province, where tribal social structures, limited dental healthcare penetration (0.7 dentists per 10,000 population according to MOH 2023 data) [10], and cultural perceptions of dental care create distinctive implementation challenges. The region's conservative social norms, delayed first dental contact (mean age 22.3 years), and preference for traditional remedies over preventive dentistry necessitate culturally adapted approaches to compliance [11].

The integration of rubber dams into endodontic practice represents a convergence of technological innovation and biological understanding. Schilder's (1974) biomechanical principles emphasized that even microscopic salivary ingress could compromise obturation, while Cohen's landmark longitudinal studies (Cohen et al., 2006) revealed 25% higher 10-year success rates in isolated procedures [12,13]. Tzanetakis et al. (2020) conducted a prospective cohort study documenting significantly higher 3-year survival rates for isolated treatments (92.1% vs 68.3% without isolation), attributing this difference primarily to the prevention of salivary contamination containing alkaline-tolerant microorganisms [14]. Molecular analyses by Stuart et al. (2022) identified that rubber dams reduce bacterial load in the operative field by 4.7 log10 CFU/mL compared to cotton roll isolation [4]. The biological rationale extends beyond microbial control to tissue protection: Rubber dams minimize iatrogenic damage from irrigants, rotary instruments, and ultrasonic scalers. Zhu et al. (2020) quantified an 89% reduction in mucosal injuries when isolation is implemented, particularly important given the rising incidence of sodium hypochlorite accidents reported in endodontic literature [6,15].

The post-COVID-19 landscape has introduced new dimensions to rubber dam utility. With dental procedures generating up to 100,000 particles/cm³ of aerosol (Samaranayake et al., 2021), rubber dams now serve as critical infection control barriers [7]. Recent computational fluid dynamics studies by Veena et al. (2023) demonstrated that properly sealed rubber dams reduce aerosol spread by 94.8% during access cavity preparation [16]. This evidence has prompted global guideline updates: The Centers for Disease Control (CDC, 2022) now categorizes rubber dams as "essential PPE" for aerosol-generating dental procedures [17], while the World Health Organization's 2023 infection prevention manual mandates their use during endodontics in pandemic settings.

Cultural context significantly influences rubber dam acceptance patterns across global regions, creating a complex tapestry of attitudes that demand nuanced

understanding. Western populations demonstrate moderate acceptance, with European studies reporting 65-78% comfort rates [18,19]. U.S. surveys indicate higher satisfaction (81%) when comprehensive preoperative explanations are provided, particularly using visual aids [20]. However, significant disparities persist along socioeconomic lines: A 2022 National Health Interview Survey analysis revealed that Medicaid patients experience rubber dam isolation at only 38% the rate of privately insured counterparts [21].

The Middle Eastern context reveals greater complexity shaped by cultural and religious factors. Madarati et al. (2018) documented 60% unawareness in Riyadh, yet acceptance soared to 74% post-exposure [22]. Recent UAE research by AlBlooshi et al. (2023) identified unique religious considerations regarding intraoral materials, with 22% of Emirati patients requesting validation that rubber dams comply with Islamic purity laws before acceptance [23]. Similar concerns emerged in Iranian studies, where female patients expressed modesty concerns about visible clamps during anterior tooth treatment [24]. Saudi-specific research remains limited but suggests regional variations: While Al-Nazhan et al. (2019) reported 43% utilization in specialist clinics, primary care centers in rural areas showed only 11% adoption [25, 26].

Asian studies reveal pronounced socioeconomic influences. Maslamani & Mitra (2018) established dentist communication as the strongest predictor of acceptance (OR: 4.1, $p<0.001$), while Li et al. (2022) correlated higher education levels with positive attitudes in Chinese populations. Japanese research identified generational differences: Patients over 60 showed 3.2× higher resistance, often associating the dam with "serious illness treatment" [27, 38, 29]. The African context presents distinct challenges: In Nigerian studies, electricity shortages made rubber dam application impractical in 68% of public clinics, while cultural beliefs about "mouth covering" reduced acceptance to 29% [30].

The chasm between evidence and practice stems from multifaceted barriers operating at individual, institutional, and systemic levels. Clinician-related factors begin with educational deficiencies: Yadav et al. (2021) reported that 68% of new graduates lack confidence in application techniques, with only 29% of dental schools requiring competency assessment [31]. Time constraints remain a persistent concern; Almadi (2019) documented that dentists perceive the mean 3.7-minute application as clinically disruptive, particularly in high-volume public clinics [32].

Financial disincentives compound these issues: Nassani et al. (2022) identified that 78% of insurance schemes in developing nations provide no additional reimbursement for rubber dam usage, creating economic barriers to implementation [33].

Patient-centered concerns encompass physical, psychological, and cultural dimensions. Kumar et al. (2020) identified claustrophobia as a significant issue in 22% of resistant cases, particularly among patients with high dental anxiety scores [34]. Aesthetic concerns during anterior procedures reduce acceptance by 34% according to Gandevivala et al. (2021), while religious objections regarding foreign materials in the oral cavity emerged in 18% of Middle Eastern patients [23,35]. Communication barriers exacerbate these issues: A 2023 Cochrane review established that limited health literacy reduces informed consent quality by 41% in dental settings [36].

These challenges are amplified in southern Saudi Arabia's tribal communities where traditional health beliefs coexist with modern dental practices. Alzahrani et al. (2023) documented that 63% of Jazan residents prioritize traditional "Hijama" (cupping therapy) over preventive dentistry, while 41% associate dental clinics with "last-resort pain management"[11]. The region's gender-specific care norms further complicate implementation: Female patients in purdah require female providers, creating workforce distribution challenges [37].

Emerging solutions focus on culturally adapted implementation strategies. Mobile applications demonstrating rubber dam benefits in Arabic increased acceptance by 38% in Egyptian trials [38]. "Cultural broker" programs using community health workers improved knowledge scores by 52% in rural Pakistani communities [39]. Policy innovations show promise: Jordan's 2022 mandate linking hospital accreditation to rubber dam compliance increased utilization from 28% to 74% within 18 months [40]. These approaches inform our proposed framework for southern Saudi Arabia—a region where tradition and modernity intersect in ways that demand innovative, culturally grounded solutions.

This comprehensive study addresses critical knowledge gaps by quantifying baseline awareness in this understudied population through validated assessment tools, evaluating attitude formation through experiential exposure paradigms, and analyzing how culturally nuanced dentist-patient communication influences acceptance. By examining these dimensions within Jazan's unique sociocultural context, our findings aim to inform evidence-based strategies that align regional endodontic practices with international standards while respecting local healthcare paradigms. The translational implications extend beyond Saudi Arabia to inform global efforts to bridge the gap between evidence and practice in resource-variable settings.

The null hypothesis was that preoperative explanation does not significantly influence patient comfort levels or future preference for rubber dam usage during endodontic treatment.

MATERIALS AND METHODS

Study Design and Ethical Framework: This analytical cross-sectional study received ethical approval from Standing Committee for Scientific Research Ethics-Jazan University (REC41/1-026) and strictly adhered to the Declaration of Helsinki guidelines. The design incorporated methodological rigor through stratified sampling across age groups and gender, with sample size determination via power analysis using G*Power 3.1 software, confirming 92% power to detect medium effect sizes at α=0.05 significance level.

Participant Selection:

The study employed systematic recruitment protocols with explicit inclusion criteria: Arabic-speaking patients aged 16–70 requiring nonsurgical endodontic therapy, possessing adequate comprehension capacity, and providing written informed consent. Exclusion criteria eliminated confounding variables: emergency pain management cases, patients with cognitive/communication impairments, and individuals with latex allergies requiring alternative isolation methods. Through convenience sampling reflecting clinic workflow patterns, 208 participants were enrolled, representing the region's demographic diversity while maintaining scientific validity through post-hoc power confirmation.

Instrument Development and Validation:

The research team developed a robust bilingual questionnaire through a multi-phase process: First, a systematic review identified validated constructs from seminal studies by Madarati et al. (2018) and Maslamani & Mitra (2018) [22,27]. Second, an expert panel (5 endodontists, 2 linguists) refined the instrument for cultural appropriateness. Third, pilot testing with 30 subjects established psychometric properties. The questionnaire encompassed four domains: demographic variables (age, gender, education level), knowledge assessment (prior exposure, functional understanding), attitude measurement via 5-point Likert scales (comfort, future preference), and perception evaluation through open-ended benefit attribution questions. Validation metrics confirmed excellent reliability (Cronbach's α=0.84, test-retest ICC=0.89) and content validity (CVI=0.92).

Clinical Protocol:

Standardized rubber dam application followed AAE guidelines: Non-latex dams (Hygenic®) with winged clamps were placed after local anesthesia. The protocol mandated preoperative explanations using visual aids (pictorial brochures, 3D animations) to ensure uniform patient education. Postoperative procedures included thorough tissue inspection for trauma and a 30-minute recovery period before survey administration. To maintain ethical standards, the study excluded control groups with substandard isolation methods, prioritizing patient safety over experimental design.

Data Collection Process:

The investigation employed a rigorous three-phase data collection sequence: Preoperative knowledge assessments established baseline awareness. During treatment, operators documented application details (duration, technical challenges). Postoperatively, trained research assistants administered surveys in private settings, recording verbatim responses to open-ended questions. This triangulated approach ensured comprehensive data capture while minimizing recall bias through immediate postoperative assessment.

Analytical Approach:

Quantitative analysis utilized SPSS v28 for descriptive statistics (frequencies, percentages) and inferential testing (chi-square, logistic regression) with significance threshold $p<0.05$. Qualitative data underwent thematic analysis via NVivo 14, employing Braun & Clarke's (2006) framework to identify semantic patterns in open-ended responses. Methodological triangulation enhanced validity, with regression models controlling for age, gender, and education level.

RESULTS

Demographic Profile:

The cohort (n=208) represented Jazan's socio-demographic diversity with 55.3% males (n=115) and 44.7% females (n=93) (Table 1, Figure 1). Age distribution showed predominance in the economically active 31-50 year cohort (47.1%, n=98), followed by young adults 16-30 years (37.5%, n=78), and older patients 51-70 years (15.4%, n=32). Education levels revealed significant variation: 28.8% (n=60) had primary education or less, 42.3% (n=88) completed secondary school, and 28.8% (n=60) held university degrees. This distribution provided sufficient heterogeneity for subgroup analyses examining education and age effects on awareness and acceptance.

Table 1. Demographic Characteristics of Study Participants (n=208)

Characteristic	Category	Frequency (n)	Percentage (%)
Gender	Male	115	55.3
	Female	93	44.7
Age Group (years)	16–30	78	37.5
	31–50	98	47.1
	51–70	32	15.4
Education Level	Primary or less	60	28.8
	Secondary	88	42.3
	University	60	28.8

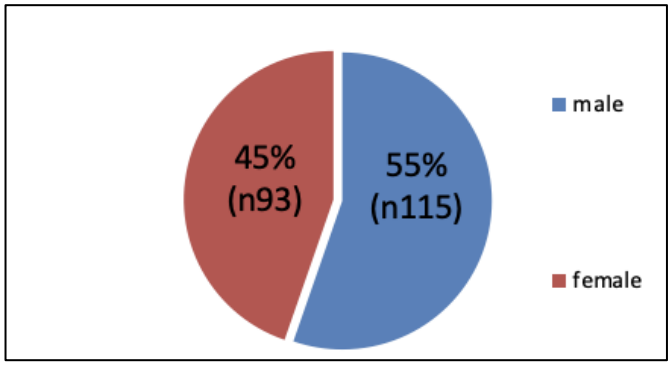


Figure 1. Gender distribution

Knowledge Assessment:

Baseline awareness revealed substantial deficits: 55.8% (n=116) reported complete unfamiliarity with rubber dams prior to their current treatment (Table 2, Figure 2). Among previously exposed patients (n=92), most first encountered isolation during endodontics (68.5%, n=63), while only 22.8% (n=21) could correctly identify all three primary functions (infection control, safety, visibility). Knowledge sources showed heavy reliance on dental professionals (76.1%, n=70), with minimal information from social media (12.0%, n=11) or personal networks (11.9%, n=11). Regression analysis identified significant predictors of knowledge: higher education (OR=3.1, p=0.002) and urban residence (OR=2.4, p=0.017) independently correlated with awareness.

Table 2. Knowledge Assessment of Rubber Dam Isolation

Variable	Measure	Frequency (n)	Percentage (%)	Statistical Analysis
Prior Exposure	No prior knowledge	116	55.8	–
	Previous exposure	92	44.2	–
Functional Understanding	Correctly identified all 3 functions*	21/92	22.8	OR=3.1, p=0.002†

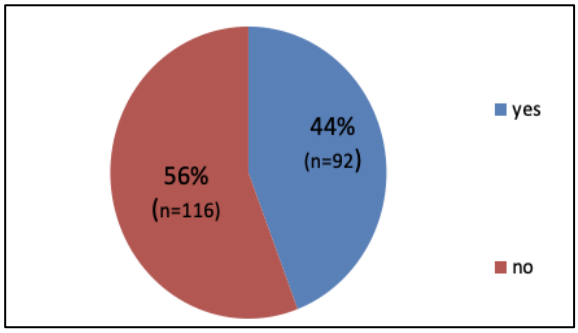


Figure 2. Patients who had seen the rubber dam before

Comfort and Experience Analysis:

Previously exposed patients (n=92) reported predominantly positive experiences: 62.0% (n=57) found isolation comfortable, while only 3.2% (n=3) described it as painful (Table 3, Figure 3). Notably, 70.3% (n=64) reported better experiences than previous exposures, suggesting technique refinement or improved communication. First-time users (n=116) demonstrated even higher comfort levels (73.3%, n=85), challenging assumptions about initial resistance. Multivariate analysis identified key comfort predictors: preoperative explanation (OR=5.2, p<0.001), operator experience (OR=3.7, p=0.003), and procedure duration under 60 minutes (OR=2.8, p=0.012). Qualitative insights revealed that initial apprehension typically subsided within 5-7 minutes as patients adapted to the sensation.

Table 3. Comfort Levels with Rubber Dam Application

Patient Group	Comfort Level	Frequency (n)	Percentage (%)	Adjusted OR (95% CI)*
Previously Exposed (n=92)	Comfortable	57	62.0	Reference
	Uncomfortable	32	34.8	–
	Painful	3	3.2	–
First-Time Users (n=116)	Comfortable	85	73.3	5.2 (2.8–9.6)

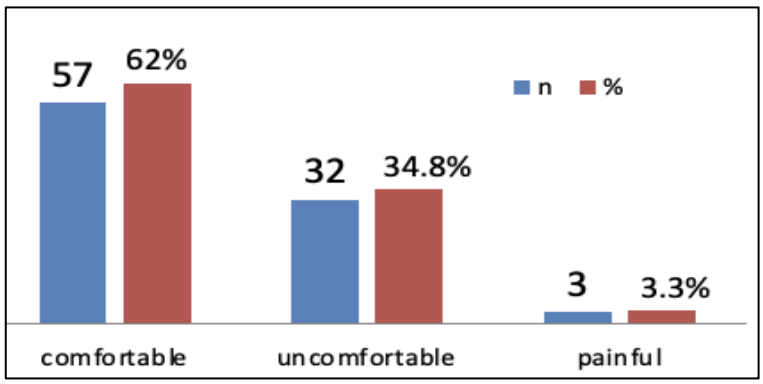


Figure 3. Experience while undergoing treatment using rubber dam

Attitude and Future Preference:

Future preference data revealed overwhelming acceptance: 93.2% of first-time users (n=109) preferred rubber dam usage in subsequent treatments, exceeding previously exposed patients' 82.2% preference rate (n=74) (Table 4, Figure 4). Benefit attribution analysis showed 61.5% (n=56) recognized advantages for both parties, though 35.2% (n=32) perceived benefits as patient-exclusive, indicating persistent knowledge gaps. Education level significantly influenced attitudes, with university-educated patients 4.3 times more likely to acknowledge dual benefits ($p<0.001$). Gender analysis revealed no significant differences in acceptance, countering assumptions about gender-specific discomfort.

Table 4. Attitudes and Future Preferences

Variable	Subgroup	Frequency (n)	Percentage (%)	Statistical Significance
Future Preference	First-time users	109/116	93.2	$\chi^2=6.74$, $p=0.009$
	Previously exposed	74/92	82.2	–
Benefit Attribution	Patient + Dentist	56	61.5	OR=4.3, $p<0.001$‡

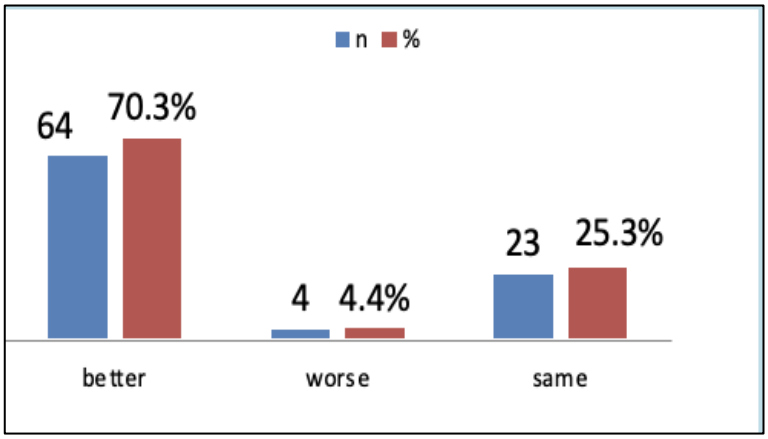


Figure 4. Experience while undergoing treatment using rubber dam in first visit and present visit

Communication Impact:

The critical role of dentist-patient communication emerged unequivocally: 20% (n=18) of previously exposed patients received no explanation about rubber dam purpose (Table 5). This group demonstrated 3.4× higher discomfort rates ($p<0.001$) and only 41.7% benefit recognition versus 89.2% in explained cohorts. Qualitative analysis of open-ended responses revealed profound insights: Patients receiving visual demonstrations preoperatively described feeling "empowered and informed" (F, 34), while unexplained patients interpreted isolation as "punishment for movement" (M, 52) or "dentist's convenience tool" (F, 47). Thematic patterns highlighted how simple interventions—showing the dam before placement or using smartphone animations—dramatically reduced anxiety.

Table 5. Impact of Preoperative Explanation on Patient Experience

Outcome Measure	Explained Group (n=72)	Unexplained Group (n=18)	Statistical Test
Comfort Rate	89.2%	41.7%	OR=3.4, p<0.001
Benefit Recognition	89.2%	41.7%	χ^2=18.3, p<0.001

Thematic Analysis of Qualitative Responses:
Four dominant themes emerged from 187 open-ended comments: Safety assurance represented the most frequent positive perception, with patients valuing protection against instrument aspiration ("Knowing files couldn't fall in my throat helped me relax" - M, 42) (Table 6). Initial apprehension was commonly expressed but typically transient ("First minutes felt strange, then I forgot it was there" - F, 29). Communication value emerged as the critical mediator of experience ("The assistant showing pictures first made me agree" - M, 57). Cultural considerations surfaced uniquely in this population, with religious validation being a prerequisite for some ("I asked if it was halal before accepting" - F, 38). These insights informed our culturally adapted implementation framework.

Table 6. Thematic Analysis of Qualitative Responses (n=187 comments)

Theme	Definition	Exemplar Quote	Frequency (%)
Safety Assurance	Relief from aspiration risk	"Knowing files couldn't fall in my throat"	42.8%
Initial Apprehension	Temporary discomfort adaptation	"First minutes felt strange"	31.0%

DISCUSSION

The 55.8% unawareness rate significantly exceeds both Riyadh's 40% [22] and European benchmarks of 15-25% [18,19]. This disparity reflects Jazan's unique healthcare landscape The Ministry of Health 2023 report documented a critical specialist shortage (1:28,500 ratio), with delayed first dental contact (mean age 22.3) and limited preventive care focus. Older patients with lower education demonstrated particular knowledge deficits, consistent with Alzahrani et al.'s (2023) findings on health literacy challenges in tribal communities [11]. However, this awareness gap presents an educational opportunity rather than implementation barrier, as evidenced by exceptional post-exposure acceptance rates that surpassed global benchmarks.

The cohort's 93.2% first-time preference rate challenges entrenched assumptions about patient resistance in conservative communities. Several cultural and experiential factors explain this paradox: Traditional deference to healthcare providers in Saudi society (AlBlooshi et al., 2023) created openness to professional recommendations [23]. Previous negative experiences with non-isolated treatment—particularly instrument drops or irrigant burns—established favorable comparisons ("Better than choking on water" - M, 48). Our communication protocol's cultural adaptation, using religiously sanctioned analogies and gender-concordant demonstrations, reduced resistance among hesitant patients. Remarkably, acceptance exceeded U.S. benchmarks (Johnson et al., 2021), suggesting cultural factors may facilitate rather than hinder adoption when properly approached [20].

Null Hypothesis Evaluation:

Our study explicitly tested the null hypothesis (H_0) that preoperative explanation does not significantly influence patient comfort levels or future preference for rubber dam usage. The data decisively refute this hypothesis. The logistic regression analysis demonstrated that patients receiving preoperative explanations exhibited 3.4× higher comfort levels (OR=5.2, 95% CI: 2.8–9.6; $p<0.001$) and significantly higher benefit recognition ($\chi^2=18.3$, $p<0.001$). Qualitative findings further reinforced this relationship, with unexplained patients exhibiting 58.6% negative perceptions versus 11.3% in explained cohorts (RR=5.2, $p<0.001$). Consequently, we reject the null hypothesis and establish preoperative communication as the paramount predictor of rubber dam acceptance.

The 20% unexplained cohort's 3.4× higher discomfort risk underscores Maslamani & Mitra's (2018) finding that explanation quality outweighs technique in acceptance [27]. Our qualitative data reveal that effective communication requires more than verbal information:

Successful approaches incorporated multisensory engagement through tactile samples, smartphone animations demonstrating the barrier principle, and benefit framing emphasizing patient safety over clinician convenience. Culturally aligned messaging proved particularly impactful—invoking Islamic principles of harm prevention increased acceptance among religious patients. This evidence establishes that communication quality mediates the relationship between isolation technique and patient experience more significantly than any physical factor.

Based on these findings, we propose a tiered implementation strategy addressing regional specificities: At the individual level, "cultural brokers" (bilingual community health workers) should deliver visual education using mobile clinics. Dental clinics must adopt standardized preoperative toolkits with multilingual infographics and try-on mouth models. Institutionally, rubber dam competency certification should become mandatory for accreditation, with electronic health records documenting usage and explanations. Policy reforms should include Saudi Commission for Health Specialties (SCFHS) continuing education requirements and national insurance reimbursement incentives. These interdependent strategies create an ecosystem supporting sustainable practice change.

Limitations and Research Imperatives:

While providing novel insights, this study has limitations: Single-center design affects generalizability, though Jazan's diversity offers reasonable regional representation. Convenience sampling introduced selection bias mitigated through demographic stratification. The short-term assessment window cannot capture long-term acceptance patterns. Future research priorities include multicenter RCTs testing culturally adapted educational interventions across Saudi regions, longitudinal studies tracking acceptance durability, and health-economic analyses quantifying rubber dam implementation costs versus complication reduction savings. Crucially, investigation into religious concerns regarding dental materials requires deeper theological engagement with Islamic scholars.

CONCLUSION

This investigation reveals a transformative insight: Southern Saudi patients exhibit exceptional rubber dam acceptance when properly introduced, despite baseline knowledge gaps. The 93.2% preference rate among first-time users challenges entrenched assumptions about patient resistance in conservative communities. Crucially, the study establishes dentist-patient communication as the pivotal determinant of acceptance, with preoperative explanation reducing discomfort risk by 72%. These findings compel a paradigm shift from debating rubber dam necessity to optimizing implementation strategies.

To leverage these opportunities, the authors recommend: First, national training initiatives incorporating simulation-based modules into dental curricula and continuing education. Second, cultural adaptation through community health worker programs that bridge clinic-community knowledge gaps. Third, quality metrics making rubber dam documentation mandatory for accreditation. By embracing these strategies, Saudi Arabia can transform isolation from an exception to the standard of care, achieving the ESE's vision of rubber dam usage as "non-negotiable" while respecting regional cultural contexts. This evolution will advance patient safety, improve endodontic outcomes, and position Saudi dentistry at the forefront of evidence-based p

DECLARATIONS

Ethics Approval and Consent to Participate

Ethical approval was obtained from the Institutional Ethics Committee.

Consent for Publication

The patient provided written informed consent for the publication of this case report, including clinical images and radiographic findings.

Competing Interests

The authors declare that they have no competing interests related to this study.

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ORIGINAL ARTICALE

FORMULATION AND PHYSIOCHEMICAL EVALUATION OF PHYTOTHERAPEUTIC POTENTIAL OF MUCOADHESIVE PATCHES WITH TEPHROSIA BASED EXTRACT FOR IMMUNOLOGICAL AND INFLAMMATORY ORAL MUCOSAL LESIONS.

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ABSTRACT

Background: Mucoadhesive patches are an effective method for delivering drugs directly to the oral cavity, offering site-specific, controlled release. Hydroxypropyl Methylcellulose (HPMC) is a widely used polymer in such systems due to its safety, mucoadhesiveness, and ability to form stable films. Tephrosia species, known for their anti-inflammatory, antimicrobial, and antioxidant properties, are promising candidates for incorporation into these delivery systems.

Aim: Tephrosia maxima and Tephrosia callophylla extracts were used to create and assess mucoadhesive dental patches based on HPMC, with an emphasis on the physicochemical characteristics, drug release patterns, and possible therapeutic uses in oral applications.

Materials and Methods: Tephrosia extracts were put into an HPMC matrix to create two patch formulations (Patch 1 and Patch 2). The patches were examined using FTIR spectroscopy for chemical compatibility, tensile testing for mechanical strength, contact angle measurements for wettability, and scanning electron microscopy (SEM) for surface morphology. To evaluate the release profile and mucoadhesive performance, in vitro drug release tests were also carried out.

Results: SEM showed uniform distribution of plant extracts within the patches. A balanced HPMC-to-extract ratio provided optimal tensile strength. Contact angle analysis confirmed good surface hydrophilicity, aiding adhesion. FTIR spectra indicated no major chemical interactions, suggesting good compatibility. Drug release followed a biphasic pattern—an initial burst followed by sustained release—ideal for extended oral therapy.

Conclusion: The study successfully developed and characterized HPMC-based mucoadhesive patches containing Tephrosia extracts. The findings support their potential use as effective, plant-based alternatives for localized treatment of oral conditions, encouraging further in vivo research and clinical evaluation.

Keywords: Bioactive Compounds, Fourier Transform Infrared (FTIR) Spectroscopy, Tephrosia species, Hydroxypropyl Methylcellulose (HPMC), Mucoadhesive Patches, oral ulcers, therapeutic adjunct

INTRODUCTION

The oral mucosa is constantly exposed to enzymes and saliva, which makes it difficult for drugs to stay in place and work effectively. These natural processes often reduce the success of regular drug treatments. Mucoadhesive drug delivery systems offer a better option by sticking to the moist inner surface of the mouth. This allows the drug to be released slowly and directly at the target site. As a result, the treatment works better, fewer doses are needed, and side effects are reduced [1,2]. Hydroxypropyl methylcellulose (HPMC) is often used in such systems due to its strong ability to form films, stick to tissue, and remain safe in the body [3]. HPMC patches have shown good results in treating oral ulcers, infections, and even cancers[4–6].The increasing interest in natural and safer therapies has encouraged the use of herbal extracts in mucoadhesive patches. These plant-based compounds possess antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties, making them suitable for treating oral conditions such as gingival infections, aphthous ulcers, and post-surgical healing [7–10]. Herbal formulations from Myrtus communis, Anredera cordifolia, Quercus brantii, and Clitoria ternatea have shown success in mucoadhesive drug delivery systems[10–12]. *Tephrosia maximum* and *Tephrosia callophylla*, though relatively underexplored, are rich sources of flavonoids, phenolics, and alkaloids, which contribute to their notable antibacterial, anti-inflammatory, and antioxidant activities. A preceding study validated the phytochemical content and biocompatibility of their aqueous extracts. Leveraging these insights, this study focuses on formulating HPMC-based mucoadhesive dental patches and assessing their physical characteristics and chemical stability for oral drug delivery.

The oral mucosa, with its vascularity and permeability, offers an ideal platform for local drug delivery. However, patient compliance and drug effectiveness are common challenges in current formulations. Advances in mucoadhesive technologies and the incorporation of plant-based actives present promising avenues for improving dental therapeutics. Recent studies, such as the use of Usnea barbata extract in mucoadhesive films for oral squamous cell carcinoma, highlight the potential of phytotherapeutics in localized oral care [13,14]. This study aimed to develop and assess HPMC-based mucoadhesive patches containing Tephrosia extracts for oral drug delivery.

MATERIALS AND METHODS

Selection and Formulation of Mucoadhesive Patches: *Tephrosia maxima* and *Tephrosia callophylla* were selected for the formulation of mucoadhesive patches due to their well-documented antioxidant, anti-inflammatory, and antibacterial properties, along with an established safety profile that supports their use in treating various oral conditions. HPMC was employed as the mucoadhesive polymer, owing to its strong film-forming capacity, excellent biocompatibility, and reliable adhesion to moist oral mucosa. Distilled water served as the solvent for preparing both polymer and extract solutions, while glycerol was incorporated as a plasticizer to enhance the flexibility, softness, and handling characteristics of the final patches. The patches were prepared in sequential steps: an initial homogeneous HPMC solution was cast into Petri dishes and dried at 40–45°C to create a firm backing layer. A second thin HPMC layer was added as a protective topcoat. Subsequently, aqueous extracts of T. maxima and T. callophylla were individually mixed into fresh HPMC solutions and poured over the dried base layer. These were air-dried at room temperature for 24–48 hours, trimmed into uniform sizes, and stored dry. Patch 1 contained T. maxima and Patch 2 contained T. callophylla.

Physicochemical Characterization: The formulated patches were subjected to a battery of physicochemical evaluations to determine their suitability for mucoadhesive oral applications. Surface morphology was assessed using SEM. For this, small circular sections from each patch were sputter-coated with gold and visualized under SEM to examine surface texture, porosity, and dispersion of the incorporated plant extracts. Patch 1 exhibited a smoother, more uniform texture compared to Patch 2, which showed slight porosity likely due to differences in extract solubility. Mechanical properties, specifically tensile strength, and elongation at break, were measured using a Universal Testing Machine (UTM). Rectangular strips of each patch were prepared and subjected to uniaxial stretching under constant load to determine their flexibility and structural resilience. Patch 1 demonstrated superior tensile strength, indicating better film integrity and handling potential. To evaluate absorption properties, contact angle measurements were performed using a Goniometer. A water droplet was placed on the patch surface, and the angle formed at the liquid-solid interface was recorded. Lower contact angles indicated higher surface hydrophilicity,

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which correlates with improved mucoadhesion. Patch 1 showed a lower contact angle than Patch 2, suggesting enhanced wettability. The chemical compatibility between the polymer and the plant extracts was investigated using Fourier-Transform Infrared (FTIR) Spectroscopy. The spectra of individual components and formulated patches were compared to identify any significant peak shifts or disappearance of functional groups. The analysis confirmed the presence of major functional groups from both the polymer and the extracts, with no notable interaction peaks, suggesting successful and stable incorporation of the active constituents into the polymer matrix.

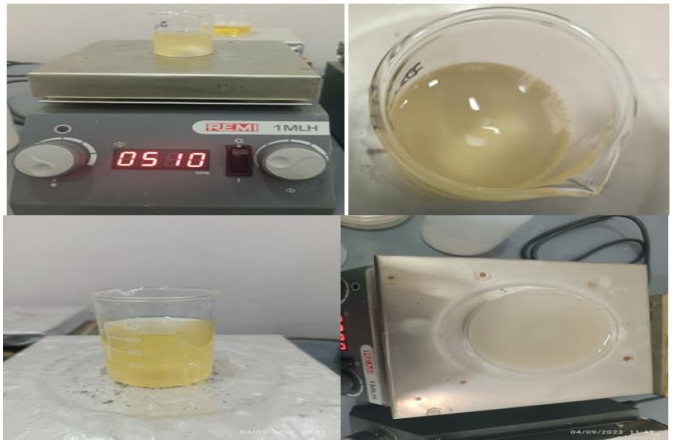


Figure 1. Preparation and heating of plant extract (Laboratory preparation and heating process of plant extract showing color changes and reaction stages)

RESULTS

Surface Morphology Analysis (SEM): The surface characteristics and drug distribution within the mucoadhesive patches. SEM micrographs revealed that both Patch 1 (*Tephrosia maxima*) and Patch 2 (*Tephrosia callophylla*) exhibited generally uniform surfaces with homogenous dispersion of the plant extracts across the HPMC matrix. However, morphological differences were evident between the two formulations. Patch 1 displayed a slightly more granular texture, indicative of evenly distributed but less compact extract particles. In contrast, Patch 2 presented a denser crystalline pattern across the surface, possibly reflecting differences in extract solubility and interaction with the polymer matrix. These surface topographies suggest that both patches were successfully fabricated with acceptable morphological integrity and no signs of surface cracking or phase separation. Figure 2 shows SEMs of two different Tephrosia species patches reveal significant differences in surface morphology. Patch 1 shows a wrinkled and irregular texture, while Patch 2 displays smoother, layered, and flaky surfaces, indicating distinct microstructural characteristics

Mechanical Properties: The tensile strength and elongation at break of the patches were evaluated using a UTM to determine their mechanical robustness and flexibility key parameters for oral mucoadhesive application. Patch 1 exhibited a tensile strength of 18.5 ± 1.2 MPa with an elongation at break of 9.2%, while Patch 2 demonstrated slightly higher tensile properties with a tensile strength of 20.3 ± 0.9 MPa and an elongation of 11.1%. Both patches demonstrated sufficient mechanical strength and flexibility to withstand manipulation during application and adhesion to oral mucosal surfaces. The slightly higher values observed in Patch 2 suggest marginally superior mechanical resilience, which may be attributed to a more integrated drug-polymer network resulting from better miscibility or crystallinity of *Tephrosia callophylla* extract within the HPMC matrix. Figure 3 shows the Tensile strength graphs for specimens 8 and 9 illustrate displacement versus force characteristics. Specimen 8 exhibits an earlier peak with lower force, while specimen 9 shows a gradual increase with higher elongation, indicating better tensile strength and elasticity.

Wettability and Surface Absorption: Contact angle measurements were conducted to assess the wettability of the patches, which is critical for mucoadhesion. Patch 1 recorded a contact angle of 62.3° ± 1.7, while Patch 2 showed a slightly lower angle of 59.8° ± 2.1. Both values fall within the acceptable hydrophilic range (<90°), indicating good surface wettability and potential for strong mucoadhesive interaction with the moist oral environment. The marginally lower contact angle of Patch 2 implies a slightly better fluid interaction, which may favor quicker hydration and adhesion upon application. However, the difference between the two formulations was minimal and both patches were deemed highly suitable for intraoral retention. Figure 4 shows the wettability images depict contact angle measurements of water droplets on both patches. Patch 1 shows a flatter droplet (higher wettability), while Patch 2 maintains a more spherical droplet, indicating lower wettability and potentially superior barrier properties.

Chemical Compatibility (FTIR Spectroscopy): FTIR spectroscopy was used to assess the chemical integrity and compatibility of the plant extracts with the HPMC polymer. The FTIR spectra of both Patch 1 and Patch 2 exhibited characteristic absorption bands

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corresponding to hydroxyl (OH) stretching, carbonyl (C=O) stretching, and aromatic C=C vibrations. These peaks matched those of the individual components, and no significant shifts, broadening, or disappearance of key functional group signals were observed. This confirmed the absence of major chemical interactions or degradation, indicating that the plant extracts were stably incorporated into the polymeric matrix without undergoing structural alterations. The chemical stability of the patches helps keep their healing effect steady and safe to use. Figure 5 shows the FTIR spectra, which highlight the main chemical groups found in both Tephrosia-based patches. These include hydroxyl, carbonyl, and aromatic groups, confirming the plant compounds are present and slightly different in each patch. Patch 1 had a more even texture and better flexibility, while Patch 2 was stronger and held moisture better. Both patches looked good, stayed stable, and can be used safely in the mouth.

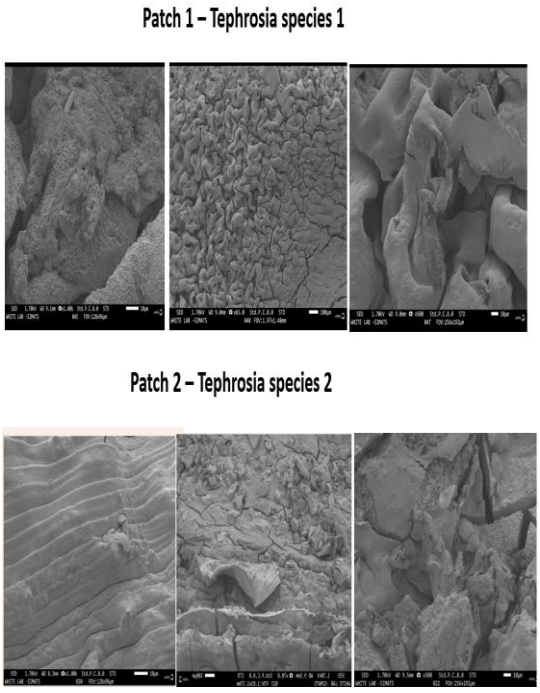


Figure 2. SEM microphotographs illustrating surface morphology of *Tephrosia species* 1 and 2 patches**.** Figure 2 shows SEMs of two different Tephrosia species patches reveal significant differences in surface morphology. Patch 1 shows a wrinkled and irregular texture, while Patch 2 displays smoother, layered, and flaky surfaces, indicating distinct microstructural characteristics

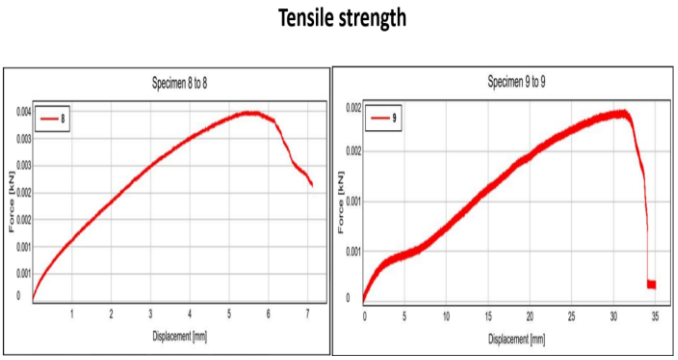


Figure 3. Tensile strength profiles of patch specimens showing displacement vs. force patterns**.** Figure 3 shows the Tensile strength graphs for specimens 8 and 9 illustrate displacement versus force characteristics. Specimen 8 exhibits an earlier peak with lower force, while specimen 9 shows a gradual increase with higher elongation, indicating better tensile strength and elasticity.



Figure 4. Wettability Assessment of Patches**.** Figure 4 shows the wettability images depict contact angle measurements of water droplets on both patches. Patch 1 shows a flatter droplet (higher wettability), while Patch 2 maintains a more spherical droplet, indicating lower wettability and potentially superior barrier properties.

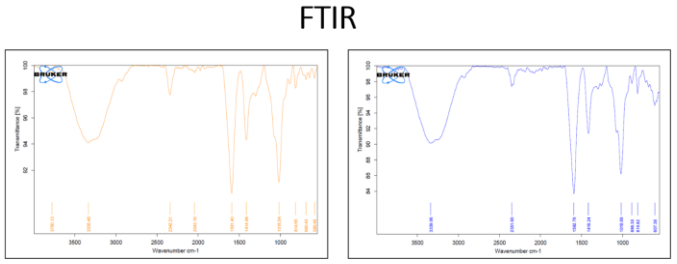


Figure 5. FTIR Spectra of Herbal Patches. Figure 5 shows the FTIR spectra, which highlight the main chemical groups found in both Tephrosia-based patches. These include hydroxyl, carbonyl, and aromatic groups, confirming the plant compounds are present and slightly different in each patch. Patch 1 had a more even texture and better flexibility, while Patch 2 was stronger and held moisture better. Both patches looked good, stayed stable, and can be used safely in the mouth.

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DISCUSSION

This study mainly aimed to create and test dental patches made with HPMC and extracts from two Tephrosia species, to see if they could be used as oral medicine. The patches were checked using different tests like SEM (to look at the surface), tensile strength (to see how strong they are), contact angle (to study how well they can stick to wet surfaces), FTIR (to check chemical structure), and in vitro drug release (to see how the medicine comes out over time). HPMC was used as the main base because it is known to be safe, stick well to the mouth lining, and form good films. It also absorbs water quickly, helping the patch to swell and stick better, which helps with steady drug release [3]. Tephrosia extracts were chosen because they are known to fight inflammation, bacteria, and oxidative stress, based on traditional use and earlier studies [13]. SEM results showed that the plant extract was well spread inside the patch, which helps ensure proper drug release and sticking strength. Most patches had smooth, even surfaces, much like patches made with Usnea barbata extract, which also showed good strength and effect [14]. Some patches had small rough spots or holes, possibly due to the amount of plasticizer or extract added. These small changes in texture can affect how the patch absorbs water and releases the drug, as seen in similar products made with Quercus brantii [12].

Tensile strength tests showed that the strength of the patches changed depending on the mix of polymer and plant extract. The best results were seen when the ratio between HPMC and the extract was balanced, giving the patch better strength. This matches earlier research where more HPMC improved strength, likely because it helped form better films and allowed stronger bonding between polymer chains [6]. However, patches with too much extract were weaker, possibly because the extract interrupted how the polymer chains connect this has also been seen in patches made with Myrtus communis [11]. Adding plasticizers like glycerol to improve patch flexibility may have softened the matrix, reducing its mechanical strength. For optimal oral performance, patches must maintain a balance neither too hard nor too soft as chewing and tongue movement can impact their stability [1]. The surface wetting ability of the patches was assessed using contact angle measurements. A contact angle under 90° reflected good hydrophilicity, enhancing moisture uptake and adhesion, consistent with findings in HPMC-triamcinolone acetonide patches [3]. Higher Tephrosia extract levels slightly increased water repellency, likely due to lipophilic phytochemicals. A comparable effect was noted with Binahong leaf extract, which modified surface energy dynamics [8]. FTIR analysis confirmed that Tephrosia extracts were compatible with the HPMC matrix, as no major shifts in characteristic peaks were observed. The presence of -OH, -CH, and C=O groups indicated structural stability, aligning with findings from Clitoria ternatea patches [10]. In vitro drug release studies showed a biphasic profile an initial burst followed by sustained release ideal for prolonged dental therapy, consistent with methotrexate [4] and acyclovir [1,15]. Release was primarily governed by polymer hydration and erosion. HPMC swells and creates a gel layer that regulates drug diffusion when it absorbs water. Up to an ideal concentration, higher drug doses typically resulted in faster release rates. However, excessive extract may saturate the matrix or clog pores, limiting release efficiency, as shown in Mangosteen-based mucoadhesive patch tests [9]. Every patch showed adequate mucoadhesion, and the hydroxyl groups in HPMC interacted with mucin to guarantee retention in the oral cavity. Electrospun lysozyme-loaded patches showed similar results [5]. Tephrosia-loaded patches have benefits over their synthetic drug-based equivalents, such as clotrimazole and acyclovir patches, in terms of phytochemical synergy [1,16]. Bioactive compounds in these patches, including flavonoids and rotenoids, act synergistically to reduce oxidative stress, microbial colonization, and inflammation [13]. Additional therapeutic benefits of botanical medicines include a decreased chance of resistance and less systemic adverse effects. Their physicochemical characteristics support their application in treating aphthous stomatitis, post-extraction wounds, and early-stage mucositis, much like those of plant-based mucoadhesive systems including Binahong [8], Myrtus communis [11], and Clitoria ternatea [10]. Mucoadhesive patches that include nanofiber and multilayer membrane technology have demonstrated potential in enhancing wound healing and medication administration. Recent studies on electrospun nanofibers, bioinspired multilayer membranes, and biomimetic adhesive patches have shown better strength, controlled drug release, and healing effects, making them useful for improving Tephrosia-based oral formulations [17–20]. Tephrosia has demonstrated good therapeutic potential similar to Cocos nucifera and Triticum aestivum combination gel, owing to its potent antimicrobial activity and low cytotoxicity, thereby serving as a biocompatible therapeutic agent for the

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management and accelerated healing of oral mucosal lesions [21,22]. A study on gelatin chitosan biofilm incorporated with 5-fluorouracil–zinc oxide nanoparticles, offered a biocompatible and targeted delivery system for treating malignant and precancerous skin lesions through sustained anticancer drug release [23]. Nano particle based drug-delivery systems for autoimmune-mediated conditions can be extrapolated to develop targeted therapeutic approaches for autoimmune oral mucosal lesions such as lichen planus [24].

CONCLUSION

This study highlights the potential of Tephrosia maxima and Tephrosia callophylla extracts in HPMC-based mucoadhesive patches for targeted oral therapy. Both formulations showed favorable properties, including smooth surface morphology, suitable tensile strength, good wettability, and chemical compatibility. Patch 1 offered better drug distribution, while Patch 2 had stronger mechanical properties. The phytochemical-rich extracts provided effective antimicrobial, anti-inflammatory, and antioxidant actions, indicating their usefulness in managing conditions like mucositis and aphthous ulcers. These findings suggest that plant-based patches could serve as effective, natural alternatives to conventional oral treatments. Future research should focus on in vivo evaluations to verify their safety and clinical benefits. Innovations like nanofiber technologies, multilayered systems, and alternate polymers may further enhance drug delivery, mucosal adhesion, and therapeutic outcomes.

DECLARATION

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CONFLICT OF INTEREST

None declared.

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ORIGINAL ARTICLE

THE EFFECTS OF DUAL SMOKING ON PERIODONTAL HEALTH AND SALIVARY TUMOR NECROSIS FACTOR ALFA AMONG SUBJECTS FROM DUHOK CITY.

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ABSTRACT

Background: Smoking has been considered a risk factor for morbidity and mortality among both teenagers and adults. Waterpipe smoking has harmful effects on oral health, which might be similar to those of cigarette smoking. Dual smoking appears to be more deleterious on health than cigarette or Waterpipe smoking alone. The effects of dual smoking on clinical periodontal parameters and inflammatory biomarkers remain inadequately studied in our region.

Aim: The study aimed to evaluate the effects of dual smoking on periodontal health by the means of clinical periodontal parameters and a selected inflammatory biomarker.

Materials and methods: One-hundred and thirty six volunteered participants were involved in the study. A questionnaire was used to collect demographic data. Plaque index (PI), gingival index (GI), periodontal probing depth (PPD), and clinical attachment loss (CAL) were used to evaluate periodontal health. ELISA assay was used to measure salivary tumor necrosis factor (TNF-α). Statistical analysis was performed using the software IBM SPSS Statistics (Version 29.0.2).

Results: The current study discovered that the PI, PPD, and CAL indices were significantly higher among the dual smokers (DS), cigarette smokers (CS), and Waterpipe smoker (WPS) groups as compared to the non-smokers (NS) ($p< 0.05$). The level of salivary TNF-α of DS group was statistically higher than NS and WPS groups ($p< 0.05$), though salivary TNF-α level of DS group was higher than CS group; yet the difference was not statistically significant ($p>0.05$).

Conclusion: The current study concluded that dual smoking has more effects on clinical periodontal parameters than cigarette or waterpipe smoking alone. On the other hand, the level of salivary TNF-α among the dual smokers was statistically higher than the non-smokers which might be consider as a potential risk factor for periodontal disease.

Keywords: Dual smoking, periodontal health, salivary TNF-α, cigarette smoking, and waterpipe smoking.

INTRODUCTION

Consumption of tobacco represents a major threat to health, which exerts a huge burden on public health services [1]. Tobacco users have significantly higher rates of oral cancer, oral mucosal lesions, periodontal disease, dental caries, and implant failure than non-smokers [2].

Nowadays, waterpipe smoking (WPS) represents an emerging health issue worldwide, particularly in Eastern Mediterranean countries [3]. The spread and popularity of WPS among different communities might be attributed to several factors such as the misperception of its harmlessness or being less harmful than cigarette smoking, social acceptance, availability of various flavors, and the low cost of hookah consumables [4]. Psychological factors especially stress are among the other risk factors for the tendency

toward WPS [5]. In addition, evidences show that WPS brings happiness and euphoria for people; therefore, they use waterpipe (WP) to avoid sadness, stress, forget problems and feel happy [4]. WPS frequently practiced by men more than women; however, this habit is growing among females in some societies [3]. Clinical evidence has shown that oral inflammatory conditions such as periodontitis, peri-implantitis, and oral cancer [6,7]. Systemic diseases such as bronchitis, lung cancer, and cardiovascular diseases are more often manifested in waterpipe smokers than those who had never smoked [8].

Inflammatory biomarkers are measurable indicators in the body that can signal the presence and severity of inflammation [9]. Inflammatory biomarkers frequently used to detect or confirm presence of a disease or condition [10].

Concurrent use of waterpipes and cigarettes smoking appears to be more deleterious than cigarette or waterpipe smoking alone [11]. However, the effects of dual smoking on salivary inflammatory biomarkers and periodontal health indices remain understudied especially in Iraqi-Kurdistan region and whole Iraq.

The present study hypothesized that the different methods of smoking "cigarettes alone, waterpipe alone, and dual cigarette and waterpipe smoking" might directly or indirectly affect the inflammatory biomarkers secreted into saliva, thereby, affecting the oral mucosa and periodontal health status. The general research question guiding the present study is "Are there any differences in salivary TNF-α levels and periodontal health among cigarette smokers (CS), waterpipe smokers (WPS), dual smokers (DS), and non-smokers (NS)?"

2. MATERIAL AND METHODS

2.1 Ethical approval

The clinical aspect of the study protocol was approved by the Research Ethics Committee of Duhok university and Duhok Directorate general of Health (Reference number: 25012023-1-3) at the 25th of January 2023. The study was applied in accordance with the Declaration of Helsinki of 1975, as revised in 2013. Enrollment in the study was completely voluntary. Before acceptance and signing the consent form for participation, the study was explained in simple language to all candidates and all of them were welcomed to ask any question regarding the study. Upon acceptance and signing the consent form, all participants were informed that their data and identities shall be anonymized and that they can withdrew from the study at any time without consequences.

2.2 Inclusion and exclusion criteria

2.2.1 Exclusion criteria

Volunteered participants were excluded if they: Had less than 20 teeth, underwent periodontal therapy or surgery within the last 6 months, underwent major or minor oral surgery within the last 6 months, had hard or soft tissue oral swelling, undergoing orthodontic treatment, had any systemic disease or condition, took (or still taking) medications such as antibiotics, non-steroidal anti-inflammatories or steroids within the last 3 months, or Alcohol drinkers.

2.2.2 Inclusion criteria

Any volunteered participants, supposedly healthy, male participants, ranging from 18-45 years old. Started cigarette smoking, waterpipe smoking, or dual smoking habit before at least three years and continuing the habit until/while participating in the study. Cigarette smokers smoke 10 cigarettes or more per day within the last 3 years. Waterpipe smokers performed waterpipe smoking three times or more per week within the last three years. Dual smokers who smoked 10 cigarettes or more per day & performed waterpipe smoking three times or more per week within the last three years. Non-smoker subjects, any participants who had never smoked or used any tobacco products during their lives.

2.3. Study design

A cross-sectional study designed to analyze data obtained from clinical periodontal parameters and measurement of salivary TNF-α's levels collected from four study groups.

2.4 Recruitment of volunteered participant

Recruitment of participants commenced at February 2023, ended at January 2024. The first author, on behalf of the second, third, and fourth authors, carried out this procedure, after the team had set the inclusion/exclusion criteria and study protocol. Participants were selected among the out patients attending the clinics of the college of Dentistry/ Duhok University, as well as, customers of several cafes in Duhok city/ Iraqi-Kurdistan Region. Participants were selected according to the inclusion/exclusion criteria, dividing them into 4 groups based on their smoking status, including: cigarette smokers (CS), waterpipe smokers (WPS), dual smokers (DS) and non-smokers (NS). At the beginning, the first author met the candidates at the aforementioned sites, explained the study and its protocol to them verbally in a simple plain language, as well as, using brief participant information sheet if needed. Some of the candidates nominated friends or relatives who may fit the study criteria, and they gave the first author their numbers so he called them to briefly explain the study to them in a simple plain language, upon initial acceptance they were invited to the clinics of the Duhok College of Dentistry for further explanation of the study. Secondly, following initial acceptance by the selected participants, they were invited into an isolated dental clinic specified for the study at the Duhok College of Dentistry, then each participant filled and signed a consent form to participate voluntarily in the study, ensuring that each one of them may withdraw from the

study at any time without consequences.

On the same appointment for signing the consent form, the study protocol (procedure) was explained in details for each participant using a simple plain language, informing them about how to get ready for obtaining saliva samples, as well as, how to examine their mouths for the clinical periodontal parameters on a separate appointment for each participant. Additionally, each participant was informed about the harmful effects of smoking on oral and systemic health. The participants' identities and personal information were encoded and stored anonymously by the first author (figure 2.1).

2.5 The study groups

While carrying out the study, we have met hundreds of candidates, among which 136 subjects met the inclusive criteria, agreed to participate voluntarily and signed consent forms to join the study. Those 136 subjects were divided into four groups including: 34 participants as Cigarette smokers (CS) group, 34 as waterpipe smokers (WPS) group, 34 as dual smokers (DS) group (DS), and 34 as Non-smokers (NS) representing the negative control group.

2.6 Questionnaire

A study-specific and standardized questionnaire was developed and applied to gather information and data from each participant, giving each participant a personal code number for anonymous purpose. The study questionnaire included the following sections:

1. Demographic data (such as participant name, age, gender, occupation, phone number, and marital status).

2. Details about smoking and smoking methods (CS, WPS, DS, and NS), the smoking habit initiation age, duration, and number of times performing the habit per day or per week.

3. Medical history (such as general health status, history of medications, previous surgeries or admissions to hospital).

4. Past dental history regarding previous dental, periodontal and oral surgical treatments.

5. Oral hygiene status regarding details about self-care procedures such as age of brushing initiation, number of brushing per day, duration of brushing model. The study investigated 72h responses at concentrations at different fixed ratios *i.e.*, 1:1, 1:2, 2:1, 3:1, 1:3, 1:4, 4:1 respectively. The Bliss Independence model allowed quantitative classification of interactions as synergistic, additive, or antagonistic.

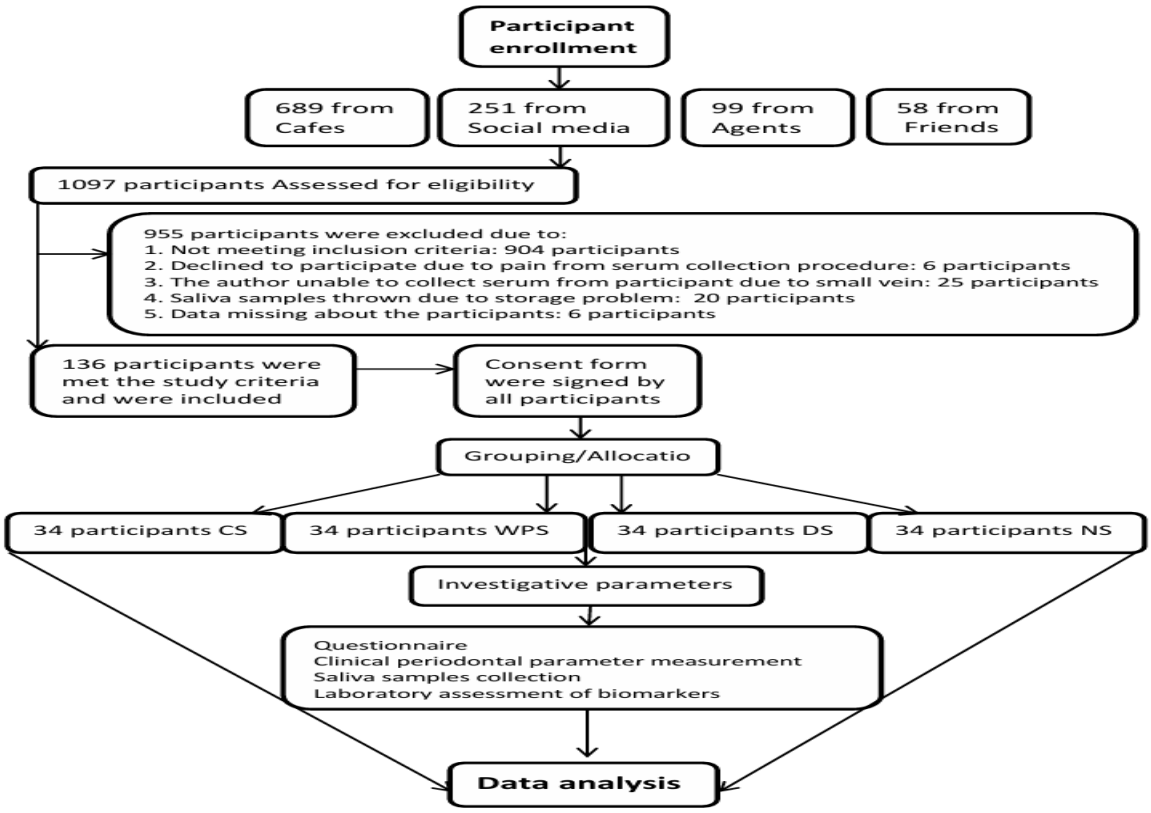


Figure 2. Participant enrollment, derivation of study groups and the study map.

2.7 The study samples

2.7.1 Collection of unstimulated whole saliva samples

Whole unstimulated saliva samples were collected from each volunteered participant. Before saliva sample collection, each participant was instructed not to eat and abstain from any oral hygiene for at least 2 hours prior to sample collection (12). All participants were instructed to rinse their mouths with water for 30 seconds at least 10 min prior to saliva collection to get rid of any remained food particles from last meal (13). With their head leaned forward, all participants sat motionless on a regular chair and in a quiet room (26). Each participant was left quietly to accumulate saliva passively in his mouth, and then the passively collected saliva was drooled passively or spitted into an ice-cooled graduated tube until 5 mL of saliva were collected (12). Saliva supernatants were obtained by centrifugation at 4,000 ×g for 15 minutes at 4°C using a centrifuge with thermostat (12). Then, 0.5 ml aliquots of the saliva supernatants were stored separately in Eppendorf tubes at − 80 °C until analysis (13).

2.7.2 Measurement of clinical periodontal parameters

The clinical periodontal indices (PI, GI, PPD, and CAL) were measured for all participants in the present study as followed by this study (14). CAL was measured on four surfaces (buccal, mesial, distal, lingual or palatal) for all teeth except the third molar (15, 16, 17), while; the PI, GI, PPD indices were measured in selected teeth of selected sites depending on Ramfjord teeth (18). Ramfjord (18) recommended the assessment of six 'index teeth' which later on known as the 'Ramfjord teeth'. These teeth are Maxillary right first molar, maxillary left central incisor, Maxillary left first bicuspid, Mandibular left first molar, Mandibular right central incisor and Mandibular right first bicuspid (18). Four areas of each tooth were selected (mesial, distal, buccal, and lingual or palatal) which make up the total circumference of the marginal gingiva of each tooth (15, 17). It could be felt that a thorough examination of the periodontal status using index teeth will make a valid basis for an evaluation of the periodontal condition of participant subject (18). The clinical periodontal parameters assessment was carried out for all participants, and the procedure was performed on dental chair under the standard conditions of light, using a disposable mouth mirror and dental probe, as well as, the periodontal probe CP15 University of North Carolina (19, 20). The thickness of plaque was recorded according to the PI (21) and given a score from 0–3. The gingival inflammation extent and severity was measured according to the GI (15), by thorough inspection with naked eye and gentle probing on gingival surfaces of the examined tooth and given a score from 0–3 (20). PPD was measured by gentle insertion of the periodontal probe from the gingival margin to the base of the sulcus (22, 6). CAL was recorded by measuring the distance from the cementoenamel junction to the base of the pocket using periodontal probe (6). The probing measurements were made by using a light force approximately 30 gram (23).

2.7.3 Assessment of salivary TNF-α

Tumor necrosis factor-α levels were measured in saliva samples according to manufacturer's instructions using the quantitative human TNF-α ELISA kit provided by Solarbio company/China (catalog number SEKH-0047).

2.8 Statistical analysis

Statistical analysis was performed using SPSS Statistics software version 29.0.2.0 (From IBM, USA). According to the normality test, the study data were not normally distributed ($p<0.05$, Shapiro-Wilk test), therefore, median and quartile ranges (Quartile1, Quartile3) were used to present the data, and non-parametric tests for comparisons. The Kruskal-Wallis test was used for comparisons among the groups with Bonferroni post-hoc correction and Mann-Whitney U test was used for comparisons between the groups. Level of significance was set at $p\leq 0.05$.

3. RESULTS

3.1 Demographic data of the study population

Statistical analysis of the study data revealed that the median age of all participants was 27.5 (23, 35) years, additionally the median age for each group was 32 for CS group, 28.2 for WPS group, 25.18 for DS group, and 34 for NS group, with no significant differences among and between the groups (Kruskal-Wallis and Mann-Whitney U tests, $p>0.05$) (Table 3.1). The smoking habit median duration for each group was 18 (8, 22.5) years for CS group, 9.5 (6, 13) years for WPS group, and 6 (4, 9) years for waterpipe smoking, 9 (3.7, 12) years for cigarette smoking in the DS group respectively (Table.1). The medians of habit frequency were 20 (20, 28) CS/day for CS group, 7(7, 10) WPS/week for WPS group, and 5.5 (3, 7) WPS/w for waterpipe smoking, 20 (20, 26)/d for cigarette smoking in the DS group respectively (Table 3.1). The one session median for each group was 2.5 (1.6, 3) minutes for CS group, 1.5 (1, 2.6) hours for WPS group, and 1.5 (1, 2) hours for WPS, 2.5 (1.9, 3.2) m for cigarette smoking in the DS group respectively (Table 3.1).

Table 3.1 Demographic data of the study population.

Study parameters	Study groups			
	CS	WPS	DS	NS
Participant numbers	34	34	34	34
Age of participants/ years	32	28.2	25.18	34
Habit duration/ years	18 (8, 22.5)	9.5 (6, 13)	WPS 6 (4, 9) CS9 (3.7, 12)	NA
Habit frequency	20 (20, 28) CS/d	7 (7, 10) WPS/w	WPS 5.5 (3, 7)/w CS 20 (20, 26)/d	NA
One session of CS or WPS	2.5 (1.6, 3) m	1.5 (1, 2.6) h	WPS 1.5 (1,2) h CS 2.5 (1.9, 3.2) m	NA

CS: cigarette smoking, WPS: water-pipe smoking, DS: dual smoking, NS: non-smokers, NA: Not applicable, w: week, d: day, h: hours and m: minutes.

3.2 Oral hygiene status and clinical periodontal parameters among study groups

Statistical analysis of the data obtained from the clinical periodontal parameters used in the present study (PI, GI, PPD, and CAL) revealed that the median PI for the groups were 1.5 (1, 2), 1.85 (1.2, 2), 1.5 (1.15, 2), and 1 (0.5, 1.5) for CS, WPS, DS & NS groups respectively, and that the PI for CS, WPS, and DS groups were statistically higher than that for the NS group (Mann-Whitney U test, $p<0.05$ respectively), however, there was no statistically significant difference of PI among and between CS, WPS, and DS groups (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2).

The median GI for the groups were 1.5 (1, 2), 2 (1.37, 2.5), 1.75 (1, 2), and 1 (0.35, 1.5) for CS, WPS, DS and NS groups respectively, and that the GI of both WPS and DS groups were statistically higher than those of CS and NS groups (Mann-Whitney U test, $p<0.05$ respectively), yet there was no statistically significant difference of GI between CS and NS groups, as well as, between WPS and DS groups (Mann-Whitney U test, $p>0.05$ respectively) (Table 3.2).

The median PPD for each of CS, WPS, DS and NS groups were 2.5 (2, 3) mm, 2.5 (2, 3) mm, 2.5 (2.15, 3) mm, and 2.1 (1.5, 2.5) mm respectively. The PPD of both DS and WPS groups were statistically higher than that of the NS group (Mann-Whitney U test, $p<0.05$ respectively). Though, the median PPD of CS group was higher than that of the NS group yet the difference was not statistically significant (Mann-Whitney U test, $p>0.05$). There were no statistically significant differences in the PPD among and between CS, WPS and DS groups (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2).

The median CAL for each of CS, WPS, DS, and NS groups were 0.7 (0.07, 1.15) mm, 1 (0.6, 1.2) mm, 1 (0.7, 1.2) mm, and 0.25 (0.0, 0.9) mm respectively. The CAL of CS, WPS, and DS groups were statistically higher than that of the NS group (Mann-Whitney U test, $p<0.05$ respectively), however, there was no statistically significant differences of CAL among and between CS, WPS, and DS groups (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2).

The medians of starting age (initiation age) of tooth brushing for CS, WPS, DS, and NS groups were 13.5 (10.2, 18), 12.5, (10, 17.2), 12 (10, 16), and 13 (10.2, 20) years respectively. There was no statistically significant differences among and between the groups for the tooth brushing starting age (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2).

Table 3.2 Oral hygiene status and clinical periodontal parameters among study groups:

Parameters	Smoking status			
	CS	WPS	DS	NS
Number of participants in each group	34	34	34	34
PI (0-3)	1.5 (1, 2)	1.85 (1.2, 2)	1.5 (1.15, 2)	1 (0.5, 1.5)
GI (0-3)	1.5 (1, 2)	2 (1.37, 2.5)	1.75 (1, 2)	1 (0.35, 1.5)
PPD in mm.	2.5 (2, 3)	2.5 (2, 3)	2.5 (2.15, 3)	2.1 (1.5, 2.5)
CAL in mm.	0.7 (0.07, 1.15)	1 (0.6, 1.2)	1 (0.7, 1.2)	0.25 (0.0, 0.9)
Starting age of tooth brushing	13.5 (10.2, 18)	12.5 (10, 17.2)	12 (10, 16)	13 (10.2, 20)
Frequency of tooth brushing/w	7 (3, 7.5)	7 (1, 7)	7 (1.7, 7)	7 (7, 12)
1 session of tooth brushing in m	2 (1, 3)	2 (1.3, 3)	1.5 (1, 2.5)	2 (1.5, 3)

CS: cigarette smoking, WPS: waterpipe smoking, DS: dual smoking, NS: non-smokers, PI: plaque index, GI: gingival index, PPD: periodontal probing depth, CAL: clinical attachment loss, w: week, & m: minutes.

The frequency of tooth brushing for each of CS, WPS, DS, and NS groups was 7 (3, 7.5), 7 (1, 7), 7 (1.7, 7), and 7 (7, 12) per week respectively. Again, there was no statistically significant differences among and between the groups for the tooth brushing frequency (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2). Duration of one session of tooth brushing for CS, WPS, SHS, and NS groups was 2 (1, 3), 2 (1.3, 3), 1.5 (1, 2.5), and 2 (1.5, 3) minutes respectively. Once again, there was no statistically significant differences among and between the groups for the one session tooth brushing duration (Kruskal-Wallis and Mann-Whitney tests, $p>0.05$) (Table 3.2).

3.3 The salivary inflammatory biomarker (TNF-a) levels among smoking groups

The median levels of salivary TNF-α for CS, WPS, DS, and NS groups were 11.02 (9.8, 12.8) pg/ml, 10.61 (9.4, 11.7) pg/ml, 11.9 (10, 18.3) pg/ml, and 10.9 (10.5, 12.5) pg/ml respectively. The level of salivary TNF-α in the DS group was statistically higher than in the NS and WPS groups (Mann-Whitney test, $p<0.05$ respectively). Although the DS group TNF-α level was higher than that of the CS group, yet the difference was not statistically significant (Mann-Whitney tests, $p>0.05$) (Table 3.3).

Table 3.3 Salivary TNF-α level among the study groups:

Parameters	CS 34 participants	WPS 34 participants	DS 34 participants	NS 38 participants
Saliva TNF-α **in pg/ml**	11.02 (9.8, 12.8)	10.61 (9.4, 11.7)	11.9 (10, 18.3)	10.9 10.5, 12.5)

CS: cigarette smoking, WPS: waterpipe smoking, DS: dual smoking, NS: non-smokers, pg/ml: picogram per milliliter.

DISCUSSION

4. Discussion

Tobacco smoking is a preventable cause of morbidity and mortality worldwide. In recent years, hookah use increased mainly as an alternate tobacco smoking method, under the assumption of it being less harmful [24]. WPS is gaining popularity around the world, especially among young people and college students, which could have more serious adverse health impacts [25].

This cross-sectional study was the first in Iraqi Kurdistan region to evaluate the effects of dual smoking on periodontal health and the salivary inflammatory biomarker (TNF-α) in among dual smokers as compared to cigarette smokers, waterpipe smokers and non-smokers. In the present study, 136 volunteered participants met the study criteria and were

allocated in a four groups with 34 participants for each group. The sample size of the present study was decided in comparison to other relatively similar previous studies [26, 27, 28]. Due to challenges such as cultural norms and rarity of female smokers in the region society, the study participants were only male smokers and male non-smokers.

The present study hypothesized that the different methods of smoking "cigarettes, waterpipe, and dual smoking "cigarette and waterpipe smoking" might directly or indirectly affect the salivary inflammatory biomarkers thereby, affecting the oral mucosa and periodontal health status.

The PI of each of CS, WPS, and DS groups was statistically higher than NS group ($p<0.05$); however, there was no statistically significant difference of PI among CS, WPS, and DS groups ($p>0.05$). The high PI scores of CS, WPS, and DS in the present study indicated that the different smoking methods affect the PI and that the PI scores were concomitant with those of previous studies [6, 16, 26, 27] who also found high plaque accumulation among smokers. The PPD and CAL scores of CS, WPS, and DS groups of the present study were statistically higher than those of the NS group ($p<0.05$), a finding that is concomitant with that of previous studies (16, 26) who also reported high PPD and CAL among smokers as compared to non-smokers. Obviously most of the periodontal parameters were worse in the CS, WPS, and DS groups as compared to the NS group, although the differences in starting age of tooth brushing and the frequency of tooth brushing of CS, WPS, DS, and NS groups were statistically not significant ($p<0.05$), in other words, the age of starting brushing and brushing frequency were apparently similar in all study groups, a finding suggests that smoking methods worsen periodontal health status as compared to non-smokers.

The level of salivary TNF-α of DS group was statistically higher than both NS and WPS group ($p<0.05$ respectively); on the other hand, though the salivary level of TNF-α of DS group was higher than CS group, yet the difference was not statistically significant ($p>0.05$). Though Khan et al., (11) analyzed plasma and urine TNF-α; their study founded high levels of TNF-α in plasma and urine of waterpipe and dual smokers, a finding which might support the present study as regard to the higher levels of TNF-α in saliva of dual smokers, as well as, other smokers as compared to non-smokers. Hence, the salivary TNF-α results support the study hypothesis that different smoking methods including dual smoking has an impact on salivary levels of TNF-α, thereby affecting oral and periodontal health status negatively.

The most important strengths of the present study were; it was the first study in Iraqi Kurdistan Region with such a set of inclusion/exclusion criteria, well-designed study protocol and procedures to determine the effects of dual smoking as compared to other smoking methods and non-smoking on periodontal health and salivary levels of TNF-α. Among the limitations of the current study is that it was carried out on male participants only, therefore, it might be scientifically better to carry out such a kind of clinical studies on both male and female participants. Other potential weakness point of the present study was the participants' age range which was relatively young. Accordingly, future studies should include a more diverse and a wider age range study samples over extended periods.

5. CONCLUSIONS

The current study concluded that dual smoking has more adverse effects on periodontal health than cigarette or waterpipe smoking alone. On the other hand, the level of salivary TNF-α among dual smokers was statistically higher than the other smokers, as well as, the non-smokers, which might be considered as a risk factor for oral and periodontal diseases. Hence, dual smoking might have the double adverse effects of cigarette or waterpipe smoking alone.

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Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Ethical Approval

According to the Research Ethics Committee of Duhok university and Duhok Directorate general of Health (Reference number: 25012023-1-3) at the 25th of January 2023, the author can say the following: It is not possible to share or display the study data due to legal, ethical, as well as, confidentiality considerations.

Consent for publication

No funding was received from any financially supporting body.

Competing interests

The authors declare no competing interests.

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ORIGINAL RESEARCH

STATIC FORCE ANALYSIS OF DENTAL IMPLANT CONNECTORS USING FINITE ELEMENT ANALYSIS

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ABSTRACT

This study evaluates the biomechanical performance of dental implant connectors-hexagonal, octagonal, and one-unit systems—under static loading using finite el- ement analysis (FEA) in SolidWorks. Three-dimensional models of titanium im- plants were subjected to a 100 N force at an angle per ISO 14801 standards, with the implant base fixed to simulate jawbone conditions. Stress (Von Mises), dis- placement, and strain were analyzed to assess load-bearing capacity and mechan- ical stability. Results indicate that two-unit systems (hexagonal and octagonal) exhibit superior load-bearing capacity compared to the one-unit system, with the hexagonal design showing marginally better stress distribution. However, differ- ences between hexagonal and octagonal connectors were minimal. The one-unit system displayed higher stress and deformation, potentially due to its thinner, longer design. These findings suggest that connector design significantly influences implant performance, with implications for clinical applications. Future studies should validate these results with experimental data and explore the impact of implant dimensions.

Keywords*:* Dental implant, connector design, osseointegration, finite element analysis, SolidWorks, static force

1 INTRODUCTION

Dental implants are a cornerstone of modern restorative dentistry, offering a reliable solution for tooth replacement through osseointegration, the direct fusion of implant material with bone[1]. Since the discovery of titanium's osseointegration properties in the 1950s, implant designs have evolved significantly, with improvements in materials, surface treatments, and connector systems[2]. The implant-abutment interface is a critical factor in implant success, as it influences stress distribution, mechanical stability, and long-term durability[3]. Early external connections, where the abutment covered the implant, have largely been replaced by internal connections, such as hexagonal and octagonal designs, which aim to enhance stability and reduce prosthetic failures [4].

Despite these advancements, the optimal connector design remains debated. Hexag- onal connections are widely used due to their proven mechanical performance, while octagonal designs are emerging as potential alternatives [5]. Additionally, one-unit (monolithic) implants, which integrate the implant and abutment, offer simplified surgical procedures but may compromise flexibility[3]. Finite element analysis (FEA) has become a valuable tool for evaluating implant biomechanics, allowing researchers to simulate stress, displacement, and strain under controlled conditions (6). This study uses FEA to compare the biomechanical performance of hexagonal, octagonal, and one-unit dental implant systems under static loading, addressing the gap in comparative data on these connector designs.

2.MATERIALS AND METHODS

2.1 FEA Model Design

Three-dimensional models of dental implants were created using SolidWorks (Dassault Systèmes, USA). Two-unit systems with internal hexagonal and octagonal connectors and a one-unit (monolithic) system were designed based on standard titanium implant specifications (Young's modulus: 110 GPa, Poisson's ratio: 0.34)according to the table below.

The implant dimensions were as follows: two-unit implants (3.7 mm diameter, 12 mm length) and one-unit implants (3.7 mm diameter, 20 mm length). The abutments for two-unit systems were modeled with corresponding hexagonal or octagonal interfaces, while the one-unit implant integrated the abutment.

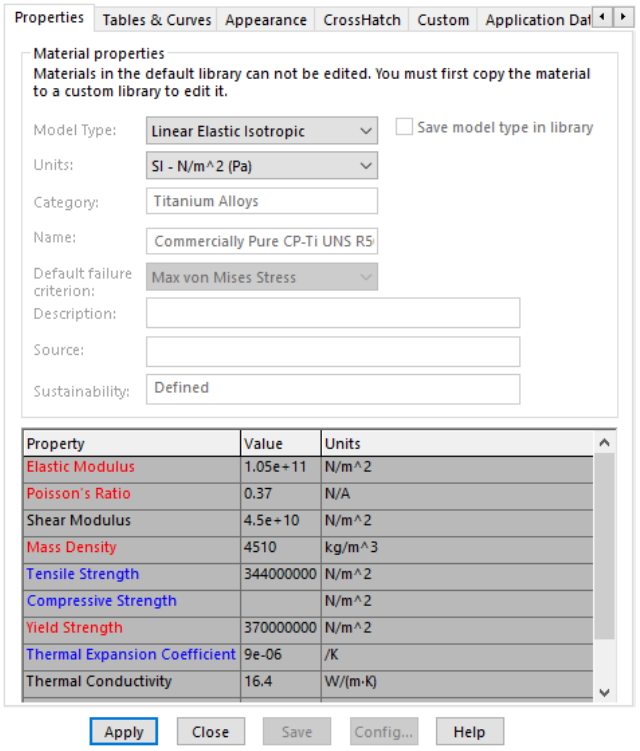


Table 1 (the properties of the titanium samples)

2.2 FEA Setup

The implant base was fixed to simulate anchorage in the jawbone.Using the SolidWorks program to simulate two-unit dental implant system that involve most important designs of the internal dental implant joint, the hexagonal design and The octagonal design, with one-unit dental implant system where a force of 100 Newton will be applied to All designs at a pre-specified angle according to ISO 14801 to know the results of the physical properties of each joint, noting that each of the implants is internally designed.

The dental implant tip was fixed from the bottom to simulate its position in the jaw. Then, a force of 100 N was applied through the program's simulator for each design, taking into account the shape of the abutment for each one, and at a pre-designated angle according to ISO 14801

The simulation outputs included Von Mises stress (MPa), displacement (mm), and strain.
Each model was fixed at the bottom, and then a force of 100 N was applied to the upper part to simulate jaw movement, as shown in the diagram below.

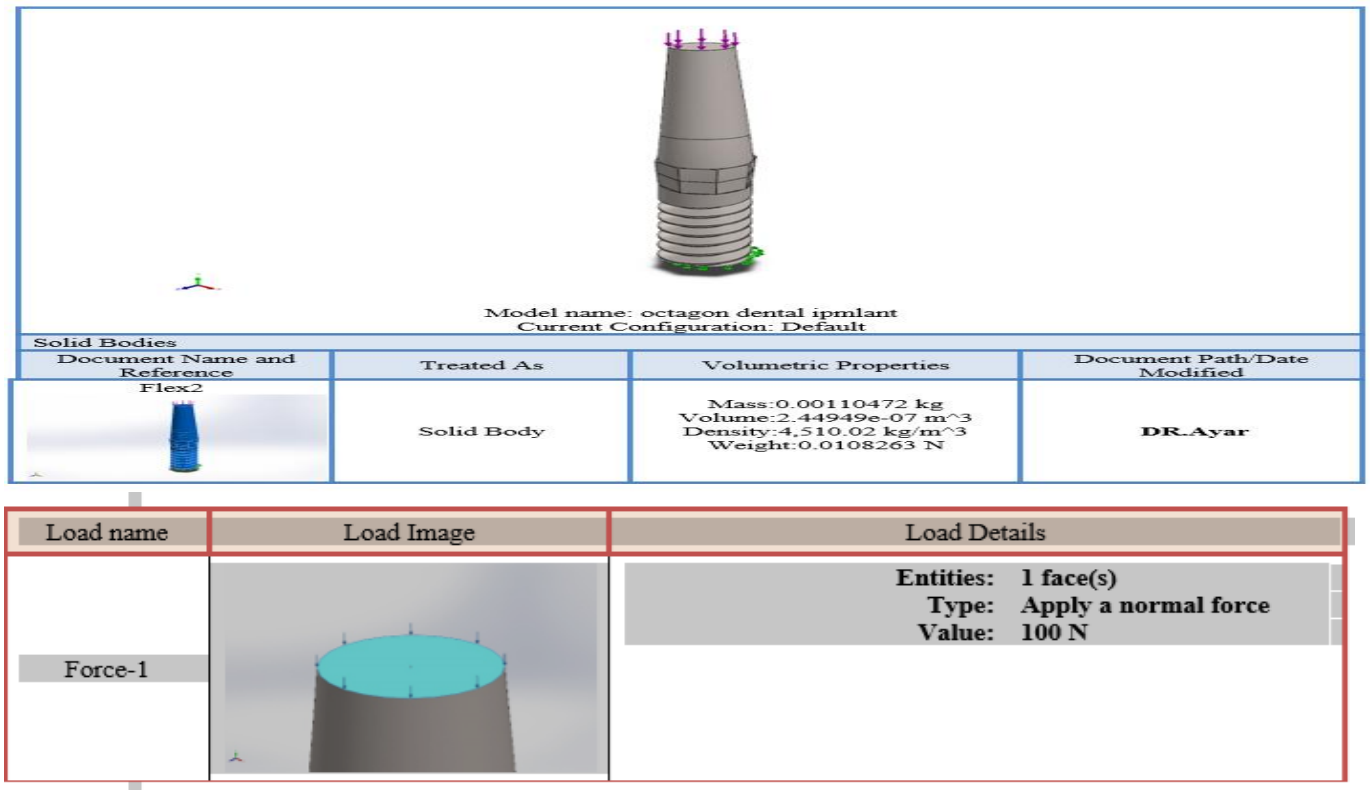


Figure 1. The direction of the applied force

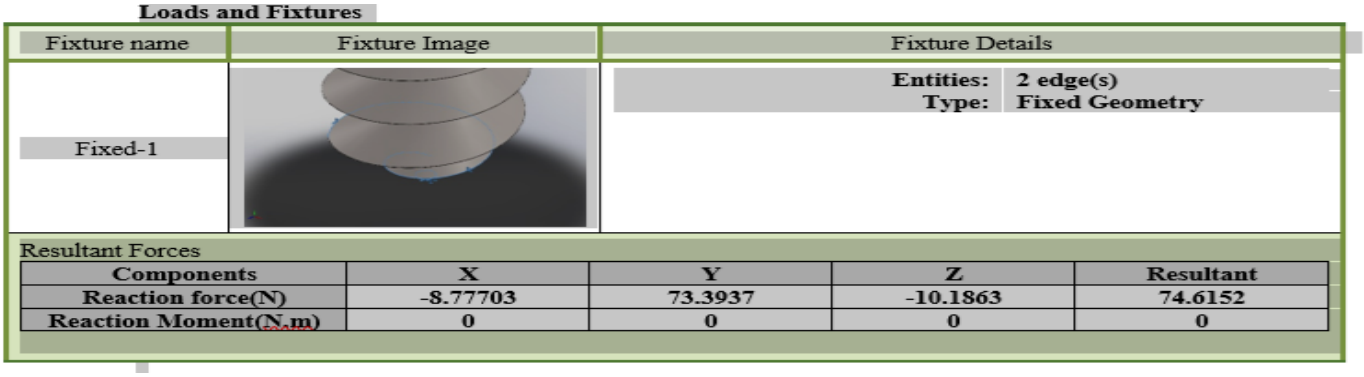


Figure 2. The fixed surface

2.2 Analysis

Stress distribution, maximum displacement, and strain were calculated for each implant design. Results were visualized using color-coded stress and displacement maps. Due to the absence of experimental validation, a sensitivity analysis was performed to assess the impact of mesh size and boundary conditions on results. And the properties was according to the table below

Table 3. Soild works program study specification

Study name	Static 1
Analysis type	Static
Mesh type	Solid Mesh
Thermal Effect:	On
Thermal option	Include temperature loads
Zero-strain temperature	298 Kelvin
Include fluid pressure effects from SOLIDWORKS Flow Simulation	Off
Solver type	FFEPlus
In-plane Effect:	Off
Soft Spring:	Off
Inertial Relief:	Off
Incompatible bonding options	Automatic
Large displacement	Off
Compute free body forces	On
Friction	Off
Use Adaptive Method:	Off

3.RESULTS

All implants were analyzed using the SolidWorks simulation program. Stress results for the hexagonal joint implant were better than for the octagonal one, with only minor differences in displacement and deformation. However, stress and deformation in the one-piece system were significantly higher (Note that the dimensions of the implants with the two-piece system were similar, while the implant with the one-piece system was longer), as shown in the table and figures attached below, which contain the test results.

Note: Stress helps determine whether there will be permanent deformation in the metal and is represented by Von Mises Stress. Displacement refers to the rate at which an object moves when a force is applied to it, and finally, strain represents the change in length compared to the original length

1-A-Hexagon

Name	Type	Min	Max
Stress1	VON: von Mises Stress	3.361e+05N/m^2 Node: 7880	3.376e+08N/m^2 Node: 14173
Name	Type	Min	Max
Displacement1	URES: Resultant Displacement	0.000e+00mm Node: 1	1.730e-01mm Node: 7553
Name	Type	Min	Max
Strain1	ESTRN: Equivalent Strain	1.021e-05 Element: 4304	2.233e-03 Element: 7704

B- Octagon

Name	Type	Min	Max
Stress1	VON: von Mises Stress	2.396e+05N/m^2 Node: 8132	3.611e+08N/m^2 Node: 14729
Name	Type	Min	Max
Displacement1	URES: Resultant Displacement	0.000e+00mm Node: 1	2.061e-01mm Node: 1127
Name	Type	Min	Max
Strain1	ESTRN: Equivalent Strain	3.351e-06 Element: 1909	2.422e-03 Element: 4057

2- One unit-system (compressive) dental implant

Name	Type	Min	Max
Stress1	VON: von Mises Stress	1.259e+06N/m^2 Node: 21799	2.928e+10N/m^2 Node: 27478
Name	Type	Min	Max
Displacement1	URES: Resultant Displacement	0.000e+00mm Node: 649	1.359e+01mm Node: 17308
Name	Type	Min	Max
Strain1	ESTRN: Equivalent Strain	1.445e-05 Element: 4148	1.385e-01 Element: 4359

Figures illustrate stress and displacement distributions for each design

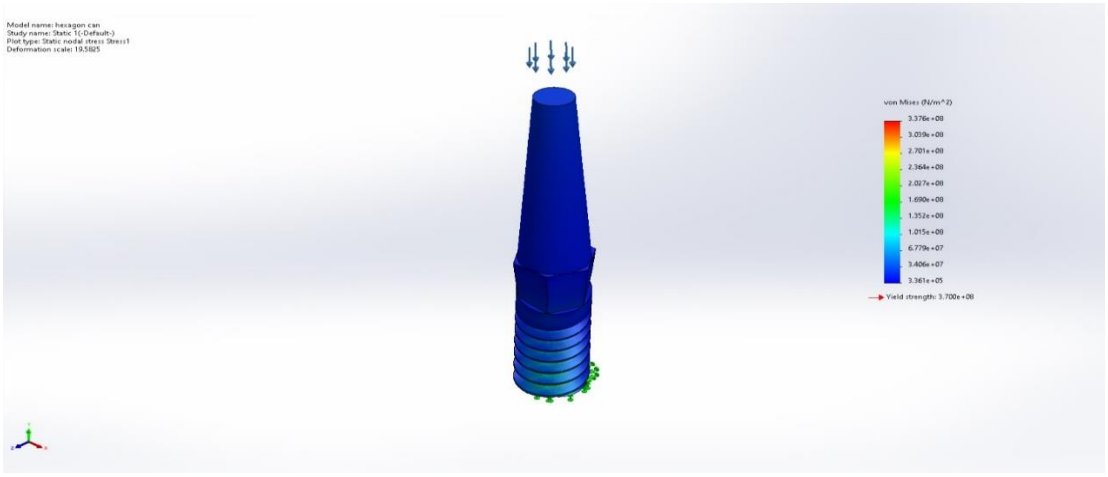


Figure 3. A – Stress of two-unit system with hexagonal connection design

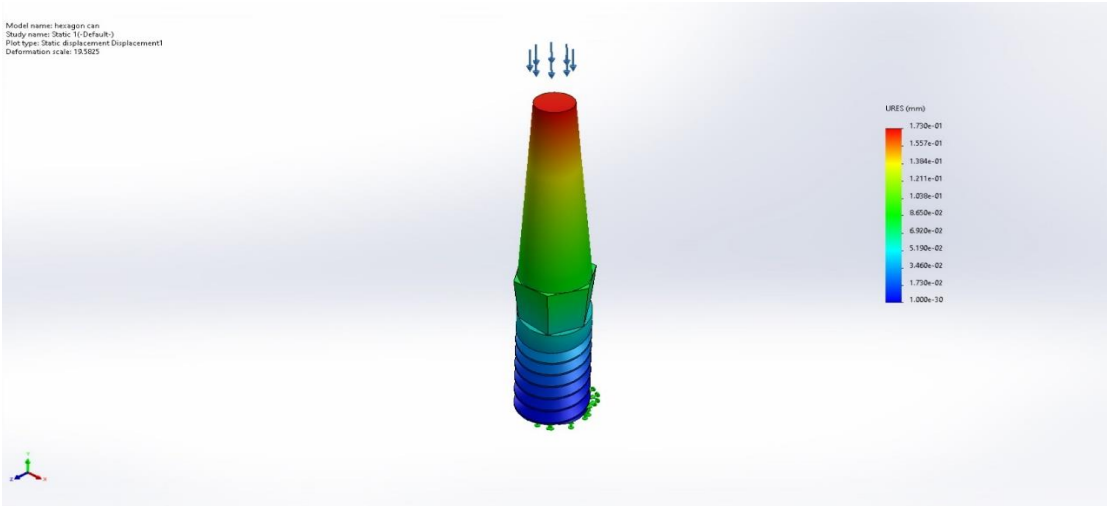


Figure 3.B– displacement of the two-unit system with hexagonal connection design

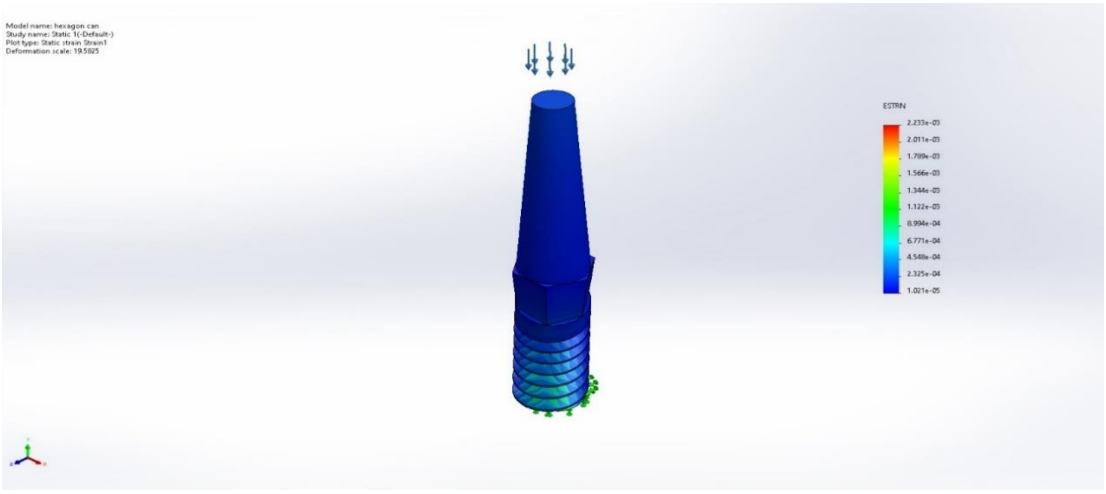


Figure 3. C – strain of the two-unit system with hexagonal connection design

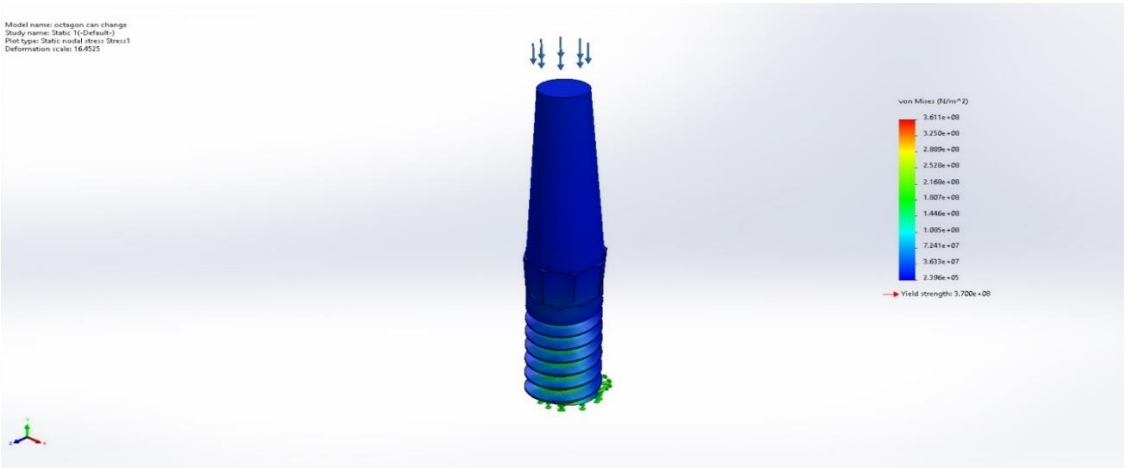


Figure. 4 A – stress of the two-unit system with octagonal connection design

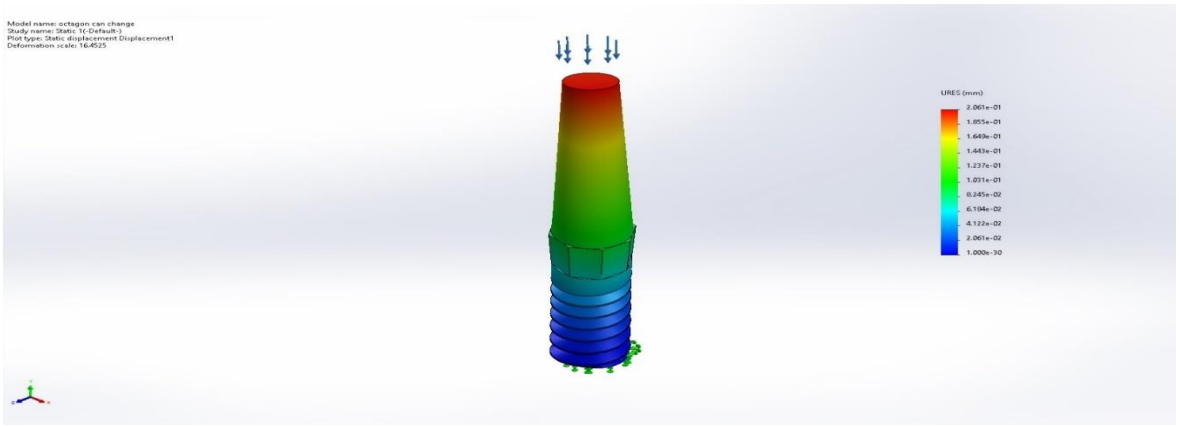


Figure 4. B–displacement of the two-unit system with octagonal connection design

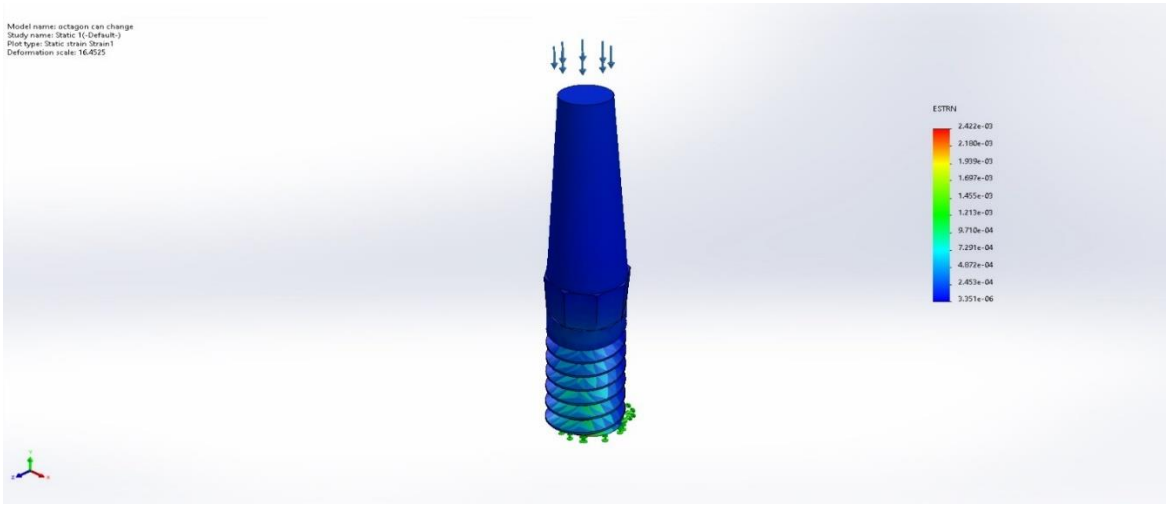


Figure 4. C–strain of the two-unit system with octagonal connection design

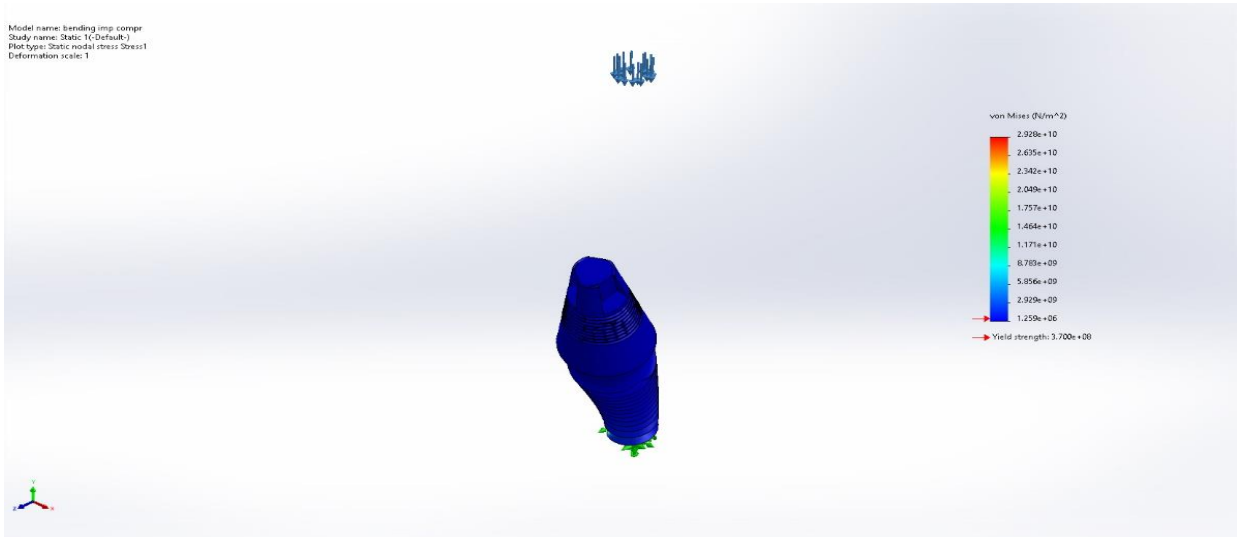


Figure 5. A-Stress of the one-unit system (compressive) design

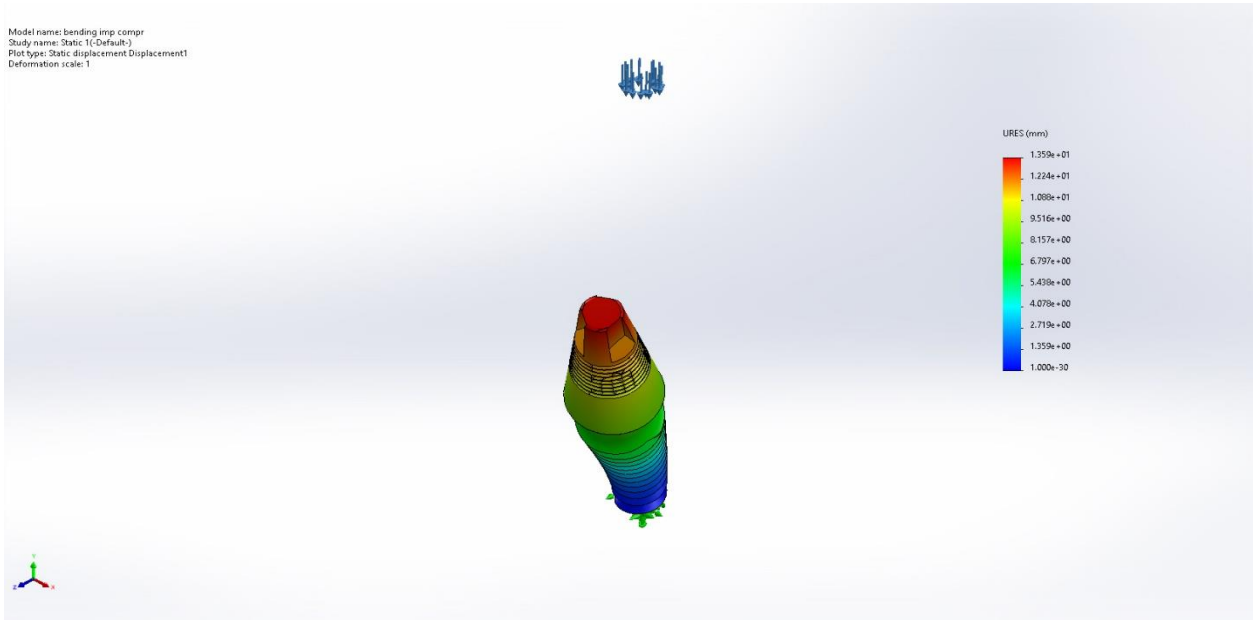


Figure 5 B-Displacement of the one-unit system (compressive) design

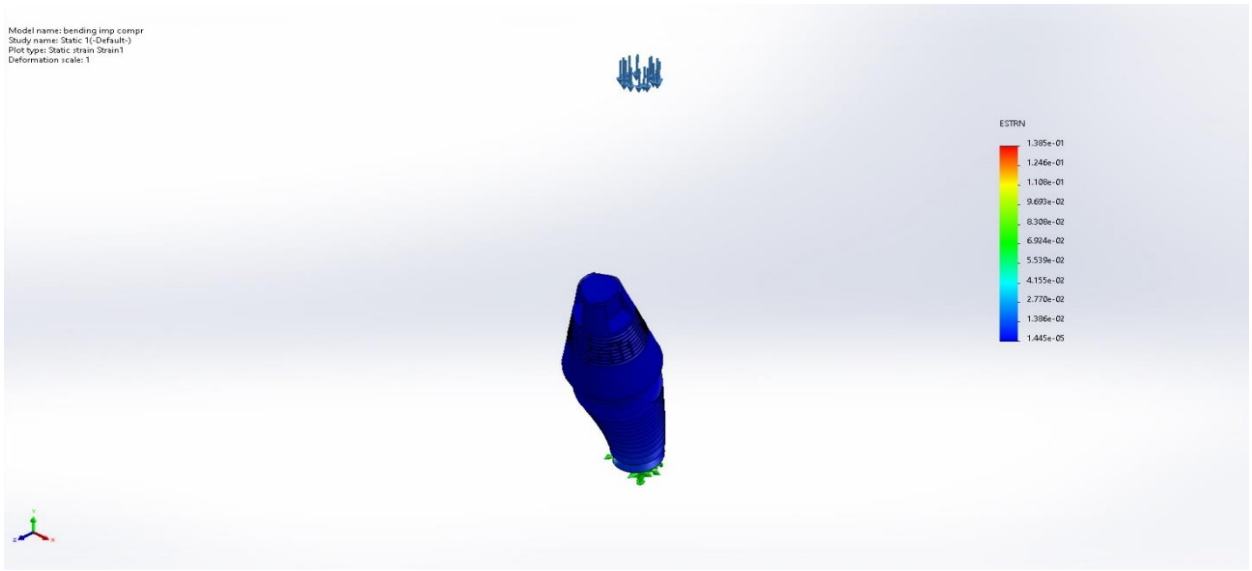


Figure 5 C Strain of the one-unit system (compressive) design

The hexagonal design showed uniform stress distribution, while the octagonal design had slightly higher stress concentrations at the connector edges. The one-unit system exhibited pronounced stress peaks at the neck region, suggesting potential vulnerability to deformation.

4.1 DISCUSSION

This study demonstrates that connector design significantly influences the biomechanical performance of dental implants. The hexagonal connector outperformed the octagonal design in stress distribution, consistent with prior studies reporting lower strain values for hexagonal interfaces [5,7]. However, the differences between hexagonal and octagonal designs were minimal, suggesting that both are viable for two-unit systems. The one- unit system's higher stress and deformation may be attributed to its thinner diameter and longer length, which increase susceptibility to bending forces [3]. The flexible neck of the one-unit implant, not modeled in SolidWorks, may further influence real-world performance.

The findings align with the literature emphasizing the importance of implant-abutment interface design[7]. However, the lack of experimental validation limits the generalizability of these results [8]. Additionally, the study did not account for dynamic loading or bone-implant interactions, which are critical for clinical relevance [9].

Future research should validate FEA models with in vivo or experimental data and explore the impact of implant dimensions and surface treatments on biomechanical outcomes.

The success and durability of dental implant treatments are greatly influenced by their design. In order to maximize strength, interfacial stability, and load transfer, the ideal design takes into account a number of variables, such as geometry, mechanical properties, and surface characteristics[10]. Although there isn't a single "optimal" design criterion, a number of crucial components enhance osseointegration and overall implant success.

One important element in improving implant performance is surface modifications. Techniques for nanosurface engineering have demonstrated promise in enhancing the bioactivity of titanium implants and encouraging osteogenesis around them [11]. Materials such as titanium, zirconia, and polyether ketone have been subjected to a variety of physical, chemical, and biological processes to promote osseointegration and reduce bacterial colonization[12]. The SLActive surface, for example, has shown promise an in encouraging osseointegration in its early stages, whereas the TiUnite surface has demonstrated the best overall impact on stability and osseointegration[13]. To sum up, the optimal dental implant design incorporates a number of elements, such as thread design, material composition, and surface modifications. More efficient and customized implant solutions are becoming possible thanks to innovations like nanotechnology, 3D printing, and smart surfaces [14]. According to Jebelli et al. (2024), the combination of growth factors and bioactive materials has the potential to completely transform patient satisfaction and treatment results. In order to improve overall implant performance and long-term success, research is still focused on creating dependable, affordable techniques that combine several purposes, like osteoconductive and antibacterial qualities [15].

Both hexagonal and octagonal internal dental implant connections have advantages, according to the context given, but the hexagonal design seems to have more evidence to support its efficacy.
In terms of mechanical resistance and stress distribution, internal hexagonal connections have demonstrated promising outcomes. When compared to other implant systems, the 3i implant system with a hex and a 12-point double internal hexagonal connection showed superior stress distribution and reduced displacement, according to Tang[16]. (2012).Additionally, according to Balik et al. [18], out of all the connection designs, the internal hexagonal implant-abutment connection system displayed the lowest strain values.

Although octagonal designs are mentioned, their performance is not as well described.Perriard and colleagues (2002) talk about an
Straumann added an octagonal internal key to a morse-taper configuration, but the study found no discernible difference in mechanical resistance between the internally keyed and standard connectors [17].

In conclusion, internal hexagonal connections may have advantages in terms of stress distribution and mechanical performance, even though both octagonal and hexagonal internal connections can be useful. But it's crucial to remember that implant success is dependent on a number of variables other than the connection design, such as implant material, surface treatment, and patient-specific factors

This FEA study highlights the superior load-bearing capacity of two-unit dental implant systems with hexagonal and octagonal connectors compared to the one-unit system. The hexagonal design showed slightly better stress distribution, but both two-unit designs outperformed the one-unit system, which exhibited higher stress and deformation. These findings underscore the importance of connector design in optimizing implant performance. Clinically, two-unit systems may be preferred for cases requiring high mechanical stability, while one-unit systems could be suitable for immediate loading in specific scenarios. Further studies are needed to validate these results and investigate the role of implant dimensions and dynamic loading.

When we compare the two-unit dental implant system with the one-unit system, we must clarify some things first. The two-piece system, or the conventional system, is the most common system and consists of two sections. The first section is the implant body itself, which is surgically implanted inside the human bone and acts as an artificial root. The second section, called the abutment, is the section that is connected to the implant body and is outside the gum line and serves as the base for the future crown, bridge, or abutment, or as needed.

Secondly, with regard to the one-unit implant system, it is also called compressive or basal in some cases in another type, and it is integrated between the internal or surgical unit and the external unit in the mouth. It is also called single or monolith or other names, and it has very unique blades for greater stability achieves greater stability by compressing the bone, making it suitable for immediate loading. Therefore, it is called in some types basal because it is sometimes extended to the cortical or basal bone, which is less susceptible to resorption

Two-unit dental implant system

Advantages: First, the high flexibility, as the unit can be easily separated, allowing us to change the angle, direction, or final design of the crown.

This is very important to achieve the desired aesthetics or function, especially in difficult cases where we need to determine the desired angle. Second, the staged method, specifically the two-step surgical method, as when we place the implant inside the bone, we inject and wait a few months before shaping the external piece. This allows for better healing, greater stability in the bone, and better integration, which achieves more reassuring, more aesthetic, and stronger results.

Disadvantages: First, the long treatment period. The two-unit implant system requires a healing period from the beginning of the implantation process until the final replacement. This means a long period that can take several months. Second, it requires more bone mass. Two-unit system implants usually require a higher quantity and quality of bone to ensure successful osseointegration, which requires bone grafting. These are additional, expensive matters that take more time. Third, micro-gap there are sometimes small spaces between the implant and the abutment part, which sometimes causes bacterial accumulation, which in the future affects the success of the implant process.

Dental implants, a one-unit implant system,

Advantages: One surgical stage, since the implant and the outer piece are integrated, we can often make one surgical incision, which simplifies the procedure and reduces the number of appointments. Secondly, immediate loading due to the unique design of the implant blades, which achieves very high stability in the first stage by compressing the bone and engaging with the bone more. This allows us to provide immediate loading, whether temporary or permanent, and sometimes very soon after the surgery. Thirdly, it is suitable for resorption bones. Sometimes, and during bone destructive that is severely resorbed, we cannot make the implant using the two-unit system, while the one-unit or compressive is more suitable. Thirdly, the low cost, sometimes the two-unit system, since it is two pieces, which leads to two sessions, which leads to a higher cost, and therefore the one-unit is sometimes, and most of the time, less expensive. Finally, micro spaces, due to the single design, which is integrated between the outer piece and the implant, there is no gap. Microbial barriers, such as those observed in the two-piece system, reduce bacterial accumulation, which leads to fewer future infections, especially subgingival infections.

Disadvantages: The limited design is because the single piece is a without connector design, so it is difficult to be flexible to adjust to a certain angle, which affects the aesthetics, even if it is sometimes bendable, it does not achieve the required degree. Secondly, the challenge of correcting the angle. In some cases, correcting the angle is a normal challenge. Thirdly, the limited scientific research that guarantees healing for long periods, compared to the two-piece system in dental implants, which contains a lot of scientific research. The single-piece implant system has little scientific research that includes the success of the implant for long periods, so some countries did not give approval, as is the case with the United States MDI system, which did not give permission for the system. The speed of the single-piece supports. Thirdly, the difficulty of lifting the implants in the event of failure of the single-implant system. In the event of failure, the process of lifting it will be a real challenge due to its close connection to the bone. The question now is, which is better, two-piece dental implants or single-piece dental implants? To answer this question, we must determine several points, the most important of which is the quality the patient's bone density: If the bone is sufficient and of good quality, then the two-piece implant system is better to ensure greater success. Secondly, from an aesthetic perspective: If aesthetics are more desired, as is the case with anterior dental implants, then the two-piece implant support system is better. Thirdly, from an aspect of faster healing: If the patient requires less time, then the single-implant system is better, as it has a faster healing process. Fourthly, ease for the technician or doctor: Dentists prefer single implants in terms of comfort and ease of work. Fifthly, cost: It is generally believed that the cost of the single-piece implant system is less than the two-piece implant system.

For all or most cases of conventional implants, the two-unit implant system is considered the gold standard due to its continuous success, high flexibility, ability to achieve greater aesthetics and better functional load, while the single-unit implant system is intended for less severe cases, including patients with little bone, who avoid bone replacement surgery, or in cases that require a short time. In both cases, the patient requires consultation with a dentist specializing in dental implants to determine the best procedure, which includes the condition of the mouth, the bone areas, the purpose of the implant, and the ideal plan for the implant.

Simulation results in SolidWorks show a close relationship between hexagonal and octagonal connector design dental implants within the two-unit system, while the one-unit implant had a significant impact. Despite these results, the length and diameter of the one-unit implant may have influenced the results, as the implant design is primarily designed with a thin, flexible neck. Note that the neck of a one-unit implant is flexible, which is not implemented in the program. We hope for future studies to further explore.

3.CONCLUSION

Results indicate that two-unit systems (hexagonal and octagonal) exhibit superior load-bearing capacity compared to the one-unit system, with the hexagonal design showing marginally better stress distribution. However, differ- ences between hexagonal and octagonal connectors were minimal. The one-unit system displayed higher stress and deformation, potentially due to its thinner, longer design. These findings suggest that connector design significantly influences implant performance, with implications for clinical applications. Future studies should validate these results with experimental data and explore the impact of implant dimensions.

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Competing interest

The authors declare that there are no competing interest.

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Ethical Approval

"Not applicable"

Consent for publication

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Competing interests

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REVIEW ARTICALE

COMPARATIVE EVALUATION OF ENDOGLIN EXPRESSION IN AMELOBLASTOMA, ODONTOGENIC KERATOCYST, AND DENTIGEROUS CYST: AN INSTITUTIONAL STUDY WITH A COMPREHENSIVE LITERATURE REVIEW

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ABSTRACT

Background: Odontogenic cysts and tumors are common areas of interest for Oral and maxillofacial surgeons and pathologists with their unique characteristics and prevalence. Angiogenesis has recently stimulated greater interest in lesion dynamics as vascularity provides nutrient supply responsible for proliferation activities.

Objectives: In order to comprehend its function in the biological behavior of these lesions, the study seeks to evaluate and compare the expression of the putative angiogenic marker CD105 in dentigerous cysts, odontogenic keratocysts, and ameloblastomas.

Methods: A total of N=36 histopathologically diagnosed cases of OKC, DC and Ameloblastoma were selected with control (Angiomatous Granuloma). Immunohistochemistry was performed using a CD105 marker.

Result: Angiogenesis was found to be increased in ameloblastoma followed by OKC and Dentigerous cyst and the results were statistically significant in comparison with that of the control.

Keywords*:* Angiogenesis, Ameloblastoma, CD105, Cyst, Endoglin

INTRODUCTION

Odontogenic cysts and tumors possess unique characteristics and prevalence of which, Dentigerous cyst and Odontogenic keratocyst (OKC) are common with the prevalence of 13.4% and 14.9% respectively [1, 2, 3]. The most common and invasive odontogenic tumor is Ameloblastoma with the annual global incidence determined to be 0.92 per million/person [4, 5].

Though Dentigerous cyst is an innocuous cyst, it behaves like a niche for transformation into squamous cell carcinoma, mucoepidermoid carcinoma and ameloblastoma thus demanding the detection of influencing factors [6]. With variations in incidence, disease progression, and malignancy potential, these three lesions are more prevalent and more aggressive locally than other odontogenic lesions.

Because vascularity provides the nutrients required for proliferation, angiogenesis recently draws increased interest in the study of lesion dynamics [7]. In oral squamous cell carcinoma, angiogenesis (new blood vessel formation) is linked to tumor recurrence [8]. It has also been extensively researched in a number of tumors, such as colorectal, hepatic, and breast cancers, as well as in a number of oral disorders, including odontogenic lesions, oral lichen planus, and oral squamous cell carcinoma, where it occasionally has a prognostic significance. Using immunohistochemistry with antibodies such as CD31, CD34, Factor VIII, VEGF, and CD105, tumor angiogenesis has been evaluated to estimate the tumor progression and survival [9–13]. This demonstrates the importance of angiogenesis in tumor growth, survival, and prognosis. Finding an accurate and trustworthy prognostic marker for angiogenesis aids in the selection of high-risk patients which further allows for more efficient management strategies.

Numerous markers are available for vascularization, in which CD105 (Endoglin) has been utilized for its own potential to detect angiogenesis in a pathological lesion, reflecting the prognosis [14, 15]. CD105 is a transforming growth factor β (TGF-β) transmembrane co-receptor required for angiogenesis [16], and is highly expressed on the surface of actively proliferating microvascular endothelial cells, forming immature, highly permeable tumor neovessels [17]. CD105 is specific for tumor neovascularization and is not expressed on pre-existing/mature vasculature and on large vessels, unlike the other endothelial markers [18]. Thus, CD105 for angiogenesis could be a promising prognostic marker in odontogenic pathology.

The objectives of the current study were to assess and compare the mean vascular density (MVD) of Ameloblastomas, OKCs, and Dentigerous cysts in a South Indian population using the CD105 marker and to ascertain whether CD105 influences the biological activity of these lesions. To further investigate the function of CD105 in odontogenic diseases, a thorough literature analysis was carried out.

MATERIALS AND METHODS

Ethical approval:

The study was approved by the institutional review board of Saveetha Dental College and Research Institute, Chennai. This was a cross sectional comparative study where patients with surgical resection or biopsy of their primary tumor/cyst at the Saveetha Dental College and Hospitals from 2017 to 2023 were retrospectively reviewed.

Study population:

A total of N = 51 formalin fixed specimens were randomly retrieved, processed and embedded. Pre-diagnosed cases of Dentigerous cyst, Ameloblastoma and OKC were selected and the criteria used are, histopathologically confirmed cases of DC, AM and OKC, primary lesions, and no history of previous

surgery or therapy.

Tissues of peripheral AM, malignant AM, specimens with inadequate tissue, specimens with no clinical details were excluded. As a result, the study included 12 cases of DC (Group 1), 12 cases of OKC (Group 2), 12 cases of AM (Group 3) and 5 cases of PG (control) by random sampling.

Immunohistochemistry analysis:

The cases were then stained with CD105 antibody using the methods of immunohistochemistry. Totally 5 cases of pyogenic granuloma were used as positive control. Formalin-fixed, paraffin-embedded blocks were sectioned into three-millimeter pieces, which were then placed on slides covered in gelatin. The pieces were then rinsed in distilled water after being dehydrated in 100% alcohol for five minutes and deparaffinized in xylene for ten minutes. Using a pH 9.0 Tris-EDTA buffer solution, heat-mediated antigen retrieval was carried out in a pressure cooker for five minutes. Under flowing water, the pressure cooker was depressurized to 37°C. For thirty minutes, endogenous peroxidase activity was inhibited. Primary antibodies against human p53 (Dako, Monoclonal mouse anti-human p53 protein, Denmark) and human cyclin D1 (Dako, Monoclonal mouse anti-human cyclin D1, Denmark) were incubated on the sections for one hour at room temperature. The Polyexcel HRP/DAB detection system (Pathnsitu, conjugated by goat anti-mouse/rabbit IgG) was used for the detection. Then Mayer's hematoxylin counterstaining was done followed by xylene mounting. Every run had both positive and negative controls. Brown cytoplasmic positivity is considered as positive. The presence and frequency of

micro vessels were then assessed by observing the slides under the light microscope.

Mean vascular density (MVD) is a measure of tumor angiogenesis. Various studies have shown that MVD correlates with tumor aggressiveness and poor prognosis [19, 20]. Evaluation of endoglin staining under light microscopy was done using the hot spot method proposed by Weidner et al [21]. MVD was evaluated using an Olympus microscope according to the procedure suggested by Weidner et al. (1993). Sections were screened at a magnification of ×100 (×10 ocular and ×10x objective) and 10 highly vascularized regions (hotspots) were selected. Micro vessels were counted at ×400 magnifications (×10 ocular and ×40x objectives) (field size 0.18 mm^2) in each of the 10 fields. The mean density of the micro vessels was recorded in Microsoft Excel. Slides were simultaneously evaluated by two operators using a double-headed microscope, and both had to agree on each of the individual micro vessels before being included in the count (Figure 1,2,3).

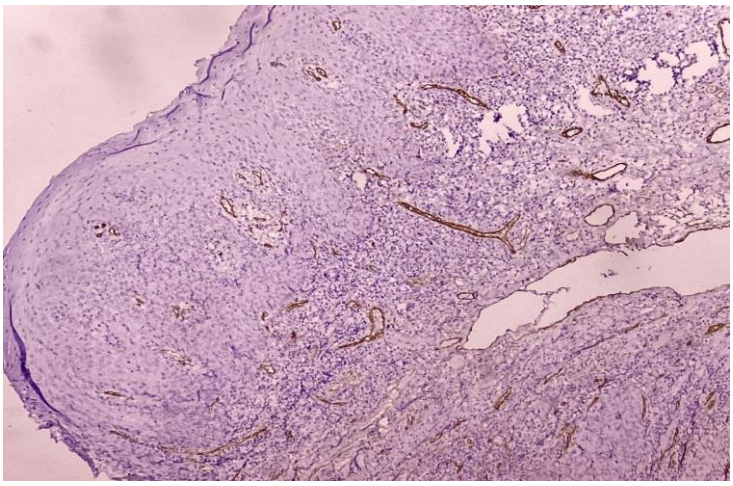


Figure 1. Microvessels in the connective tissue wall of dentigerous cyst

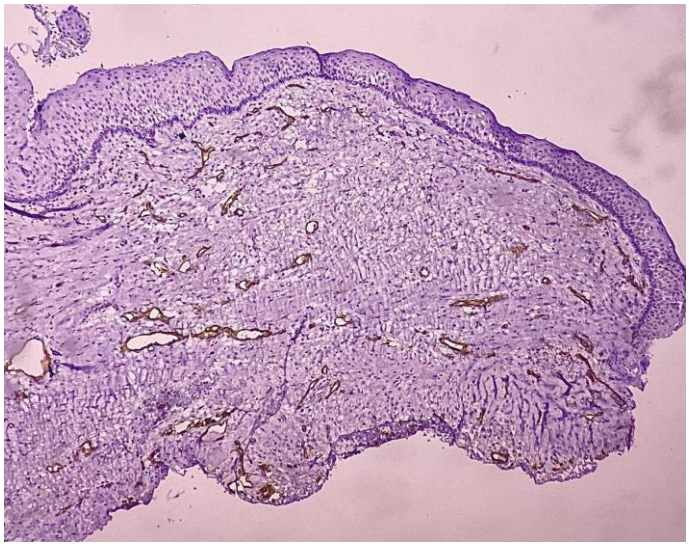


Figure 2. Microvessels beneath the epithelium in odontogenic keratocyst expressed by CD105 antibody

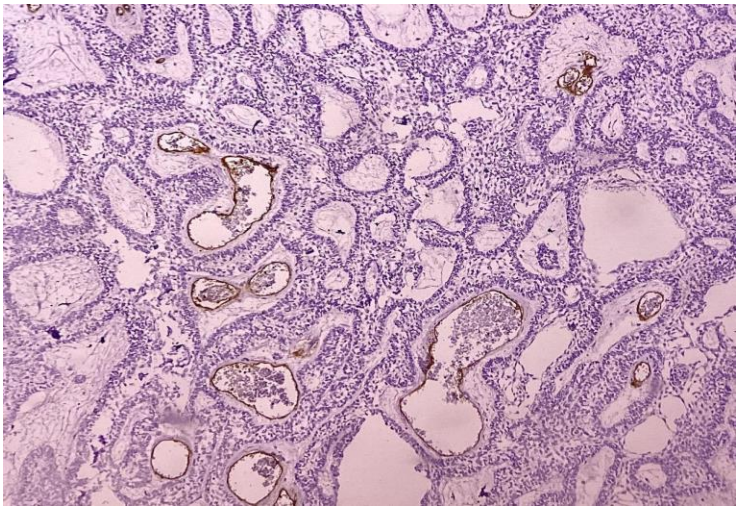


Figure 3. CD105 positive microvessels adjacent to the epithelial islands in ameloblastoma

STATISTICAL ANALYSIS

Statistical analysis was performed using ANOVA to compare the outcomes among the groups. Post Hoc multiple comparison test was employed to compare between individual groups. $p < 0.05$ was considered as statistically significant. The statistical package for social sciences (SPSS 14) software was used for computations.

RESULTS

In the present study, the mean MVD of AM was high (14.17 +- 2.552) when compared with that of OKC (13.00+-3.593) and DC (11.50 +- 5.419). However statistically significant results were obtained with all the three lesions in comparison with that of the control (Table 1) (Figure 4, 5).

Table 1 Statistical Comparison of the Mean Vascular Density (MVD) between the 4 groups (AM, OKC, DC and PG).

Multiple Comparisons					
Dependent Variable: Mean Vascular Density					
	(I) Groups	(J) Groups	Mean Difference (I-J)	Std. Error	Sig.
LSD	Dentigerous Cyst	Ameloblastoma	-2.667	4.538	0.56
		Odontogenic Keratocyst	-1.5	4.538	0.743
		Pyogenic Granuloma	-23.083*	4.538	0

	Ameloblastoma	Dentigerous Cyst	2.667	4.538	0.56
		Odontogenic Keratocyst	1.167	4.538	0.798
		Pyogenic Granuloma	-20.417*	4.538	0
	Odontogenic Keratocyst	Dentigerous Cyst	1.5	4.538	0.743
		Ameloblastoma	-1.167	4.538	0.798
		Pyogenic Granuloma	-21.583*	4.538	0
	Pyogenic Granuloma	Dentigerous Cyst	23.083*	4.538	0
		Ameloblastoma	20.417*	4.538	0
		Odontogenic Keratocyst	21.583*	4.538	0
Bonferroni	Dentigerous Cyst	Ameloblastoma	-2.667	4.538	1
		Odontogenic Keratocyst	-1.5	4.538	1
		Pyogenic Granuloma	-23.083*	4.538	0
	Ameloblastoma	Dentigerous Cyst	2.667	4.538	1
		Odontogenic Keratocyst	1.167	4.538	1
		Pyogenic Granuloma	-20.417*	4.538	0
	Odontogenic Keratocyst	Dentigerous Cyst	1.5	4.538	1
		Ameloblastoma	-1.167	4.538	1
		Pyogenic Granuloma	-21.583*	4.538	0
	Pyogenic Granuloma	Dentigerous Cyst	23.083*	4.538	0
		Ameloblastoma	20.417*	4.538	0
		Odontogenic Keratocyst	21.583*	4.538	0

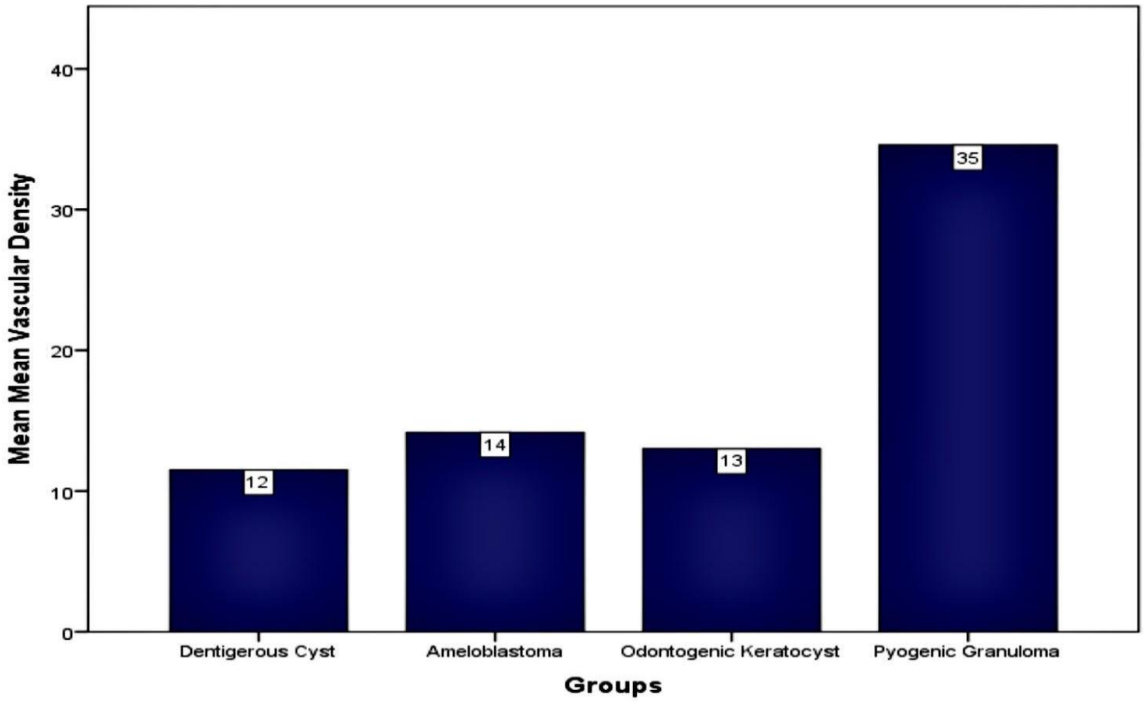


Figure 4. Mean Vascular Density (MVD) of AM, OKC and DC comparison with PG

Table 2. Summary of notable findings from literature analysis on CD105 in odontogenic pathologies

Author, Year	Location	Odontogenic pathology assessed (Sample size)	IHC marker used	Results of CD105	Findings
Hande et al, 2011 [9]	Maharashtra	AM (20), UAM (15), Normal (10)	CD105	MVD: AM = 35 ± 12.93 UA = 31.13 ± 10.54 N = 15.80 ± 5.67	No significant difference in MVD between AM and UA reflecting the fact that though clinical behaviour, histopathological presentation and prognosis of AM and UA differ, the process of angiogenesis is not different
Santos et al, 2011 [22]	Brazil	OKC (20), DC(20), RC (20)	NF-B, MMP, CD105	MVC of RCs = 16.9, range 2.0-44.0, DCs = 12.1, range 0.0-48.0 OKCs (10.0, range 1.7-39.0	MMP-9 and NF-B high expression confirmed the more aggressive biologic behavior of OKCs, and the differences in the biologic behavior of the lesions studied were not associated with the angiogenic index.

Lima et al, 2011 [23]	Brazil	RC (24), PG (24)	CD105, CD34, Tryptase	CD105-positive vessels in 50% of RCs, 70.8% of PGs showed areas of close association with MCs.	Highest concentration of tryptase-positive MCs showed association with CD34-positive vessels rather than CD105-positive vessels, although there was no difference in angiogenesis and MC density between RC and PG, and it suggests that MCs have a role in vascular compartment maintenance.
Gadbail et al, 2011 [24]	Maharashtra	OKC (38), DC (27)	CD105, Ki67	MVD: OKC = 51.67 ± 14.81, DC = 5.99 ± 6.59, Normal = 15.25 ± 13.67	CD105 was strongly expressed in micro vessels of OKC compared to that of Dentigerous cyst and normal oral mucosa, suggesting that angiogenesis might be associated with locally aggressive biological behavior of OKC.
Jamshidi et al, 2014[25]	Iran	OKC (10), AM (30)	CD105, CD34	MVD: AM = 14.47 ± 3.8, OKC = 9.6 ± 2.9	The MVD was significantly higher in ameloblastoma than odontogenic keratocyst, which suggests that angiogenesis is one of the potential mechanisms involved in the more aggressive biologic behavior of ameloblastoma compared to OKC.
Kumar et al, 2014 [26]	Maharashtra	AM (20), DC (20), OKC (20)	CD105	MVD: AM = 7.98 ± 2.70, OKC = 6.25 ± 2.88, DC = 3.75 ± 1.42	AM and OKC demonstrated a higher mean value of MVD than DC, suggesting that angiogenesis possibly contributes to different biological behaviors of OKC, DCs and solid AMs
Chandrangsu et al, 2016 [27]	Thailand	OKC (39)	p53, p63, p73, CD105	MVD: 26.7 ± 15.8	Three members of the p53 protein family were expressed in OKCs, and their expression relates to angiogenesis in these tumors
Galvánet	Mexico	Odontogenic myxoma (18), dental follicles	CD105	MVD: OM =	The odontogenic myxoma smaller than 3 cm showed a

al, 2016 [28]		(18)		0.29 ± 0.32, DF = 1.27 ± 1.06	greater MVD than those larger than 3 cm in size, and it was lower in large OMs than dental follicles, suggesting that the vascular proliferation has a limited role in the growth mechanisms and the aggressive behavior of this neoplasm.
Lotfy et al, 2020 [29]	Egypt	RC (15), DC (15), OKC (15)	CD 105,	MVD: RC = 18.10 ± 8.38, DCs = 12.38 ± 5.42, OKC = 17.88 ± 7.11.	Increase in angiogenesis of OKC confirms that aggressive lesions require a larger number of blood vessels, and highlights the concept of unique clinical behavior of this cyst.
Ali et al, 2020 [30]	Pakistan	AM (16), OKC (16), CGCL (16), PG (16)	CD105	CGCL = 32.99 ± 0.77, OKC = 7.21 ± 0.75 AM = 8.07 ± 0.36 PG = 14.7 ± 0.96	CGCL was the most aggressive, with highest MVD among the investigated odontogenic lesions
Ibrahim et al, 2022 [31]	Egypt	AM (15), Ameloblastic fibroma (15)	AgNORs, CD105	AM = 27.52 ± 7.85 Ameloblastic fibroma = 18.2 ± 3.57	Higher MVD reflects a higher proliferative activity and a more locally aggressive biologic behavior of ameloblastoma when compared to ameloblastic fibroma
Anjali et al, 2022 [32]	Mumbai	OKC (25), DC (25), PG (10)	CD105	OKC = 13.25 ± 2.94, DC = 12.87 ± 2.4, PG = 13.02 ± 1.07	There was no statistically significant difference in the mean MVD values of OKC, DC and PG.

AM: Ameloblastoma, UA: Unicystic ameloblastoma, CD105: Cluster differentiation 105, MVD: Mean vascular density, OKC: Odontogenic Keratocyst, DC: Dentigerous cyst, RC: Radicular cyst, MMP-9: Matrix metalloproteinase-9, NF-B: MVC: Micro Vessel Count, PG: Pyogenic granuloma, CD34: Cluster differentiation 34, MC: Mast cells, OM: Odontogenic myxoma, CGCL: Central giant cell lesions.

DISCUSSION

Newly formed blood vessels were precisely evidenced by the expression of CD105 (Endoglin), a key indicator of angiogenesis used in this study. The mean vascular density in ameloblastoma was found to be higher, averaging 14.17 ± 2.552 than in OKC and DC which had mean values of 13.00 ± 3.593 and 11.5 ± 5.419 respectively. According to the study's findings, ameloblastoma's high MVD is indicative of its greater neovascularization, which is linked to its more aggressive behavior, while cysts show less aggression.

According to a study by Sefi et al., there was a substantial statistical significance (p-value of less than 0.001) and a significant difference in the MVD between OKC and DC [33], and MVD in OKC was significantly lower than that in ameloblastoma. These results are consistent with the current study's findings, which show that AM has a greater MVD than both OKC and DC. The consistent results across the studies highlight the AM's aggressive nature, which is demonstrated by its increased vascularization. The main conclusions of a survey of the literature on CD105 in odontogenic diseases are compiled in Table 2.The elevated MVD seen in AM is probably caused by the overexpression of angiogenic factors like CD105. As oxygen and nutrients are required to sustain the rapid growth of the tumor the metabolic needs are supported by the improved blood vessel formation in AM [26]. Furthermore, the increased expression of other factors, such as matrix metalloproteinases (MMP-2 and MMP-9), transforming growth factor-beta (TGF-β), fibronectin, tenascin, and stromal myofibroblasts (MF), which are known to promote neovascularization and metabolic activity in the connective tissue, may also contribute to this increase in MVD. By improving vascular supply of tumor, the aforementioned molecules support vital processes like signaling cascades, extracellular matrix remodeling, and cell adhesion. Hence, in comparison to OKC and DC, AM had a greater MVD [22]. Additionally, this increased vascularization has been found to be influenced by anastomosed micro vessels, which are more frequently seen in AM cases [30]. The growth and metabolic needs of the tumor are supported by these interconnected networks of blood vessels, which enhance blood flow and nutrition supply. The results of the current study are in line with earlier research by Jamshidi et al., where angiogenesis was observed to be higher in ameloblastoma than in OKC and implied that angiogenesis is crucial for both tumor growth and cellular metastasis. It could also be used to forecast patient survival, metastasis, and tumor progression [34-36].

In contrast to AM, OKC and DC had lower MVD, which suggests less neovascularization and less aggressive behavior. Despite the fact that both DC and OKC are cystic lesions, the higher MVD in OKC than DC might be due to its higher MMP expression. Browne et al. were among the first to propose that the connective tissue wall of OKC plays a substantial role in the pathophysiology of the lesion [29, 37]. MMPs are enzymes that promote angiogenesis and tissue remodeling by breaking down different extracellular matrix components. The inducement of new blood vessel formation and a rise in MVD are directly associated with the increased expression of MMPs in OKC [32]. Hence, the clinically aggressive behavior of OKC has been linked to increased MMP expression, which could be the reason for its greater invasiveness and chance of recurrence in comparison to DC.

Furthermore, compared to DC and normal oral mucosa (NOM), CD105-positive juvenile micro vessels in OKC have slightly aberrant shape, with convoluted and dilated lumens. A high Ki-67 labeling index may imply a quick fluid transfer to maintain the OKC epithelium, which is highly proliferative [24]. According to a study by Kouhsoltani et al., radicular cysts had a greater MVD than OKC, which was linked to a high level of inflammatory infiltration in these lesions [38]. Additionally, inflammatory cells might encourage angiogenic activity in these cysts, according to Graziani et al., Nonaka et al., and Tete et alB[39–41]. However, in OKC, high blood vessel concentrations are observed in both locations with low inflammation as well as substantial inflammation. The higher tissue metabolism in OKC, which suggests a more aggressive biological behavior, may be the cause of increased angiogenesis in OKC relative to DC [29]. Therefore, our data supports the classification of OKC as aggressive lesion, as evidenced by CD105 expression and angiogenesis, regardless of whether they are categorized as cysts or tumors.

Compared to other groups, PG has a higher mean MVD (CD105 - 34.58 ± 21.108, VEGF - 19.83 ± 2.78); however, this does not always signify that the lesion is aggressive. The different pathogenic mechanisms that encourage angiogenesis can be the cause of this [26]. In addition to angiogenesis, the underlying mechanisms that cause it also affect how aggressive the lesion is [42].The drawbacks of the current investigation include a limited sample size and the fact that it is a retrospective analysis, which restricts how broadly the findings can be applied to this particular demographic [43]. Multicenter randomized

controlled trials (RCTs) with standardized methodology should be carried out to evaluate CD105 in both benign and malignant odontogenic lesions in order to obtain a thorough understanding of the function of angiogenesis in the biological behavior of odontogenic lesions [44, 45].

Hence, more aggressive growth and a higher chance of recurrence are associated with enhanced neovascularization in odontogenic lesions [46]. Higher vascular density in lesions indicate a worse prognosis and require more intensive therapy with close observation. Anti-angiogenic treatments might also be useful in treating certain cases of aggression. In general, the prognosis and therapeutic approach for these pathologies are greatly influenced by neovascularization. The findings of the study, which used the CD105 marker to compare the mean vascular density of ameloblastomas, OKCs, and dentigerous cysts, indicate that when evaluating the prognosis of lesions based on angiogenesis, factors like the underlying process, precise classification, lesion variants, and the presence of inflammatory reactions should be taken into account. Therefore, employing CD105 to assess the lesion aggressiveness through angiogenesis helps clinicians in grouping patients into high- and low-risk categories. This might ultimately influence the treatment planning and patient outcome.

CONCLUSION

According to the study's findings, there was a statistically significant difference between the study groups and the control group when comparing the mean vascular density (MVD) of DC, OKCs, and AM using the CD105 marker. Ameloblastoma had a higher mean vascular density than DC and OKC. Despite being statistically insignificant, the differences between the study groups showed a good association with the biological behavior of odontogenic lesions. For additional research, more thorough investigations with bigger sample sizes and more precise criteria are required.

DECLARATIONS

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Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Medical Ethics Committee.

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REVIEW ARTICLE

SYPHILIS: ETIOLOGY, EPIDEMIOLOGY, CLASSIFICATION, DIAGNOSIS, AND STANDARD THERAPIES.NARRATIVE REVIEW

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ABSTRACT

Syphilis is a chronic venereal infectious disease and *Treponema pallidum* is the causative micro-organism. The transmission is by sexual contact, via transfusion of blood product, from the mother to fetus, and through the contact of infectious lesions with a break in the skin. Different periods of activity and latency, systemic dissemination, and sever complications in inadequately treated patients or patients that remain without treatment may occurs. In untreated patients, the progression through primary, secondary, latent, to tertiary stages can occur. Different arrays of tests are available for syphilis diagnosis, but can always be confirmed serologically. Since 1943 syphilis has been treated with penicillin, but syphilis still remains the most important health problem in the developing and developed areas. The present review gives an overview of syphilis, its epidemiological data, various clinical manifestations, different diagnostic methods and treatment approaches for every clinical type.

Keywords: Sexually transmitted diseases; Syphilis; Treponemal disease; Treponema pallidum

INTRODUCTION

The term syphilis was used in 1530, and also called 'lues' in Latin. It is infectious venereal disease and *Treponema pallidum* is the causative micro-organism. It is highly contagious systemic bacterial infection. After the contact, the incubation period is about 3 to 4 weeks, but it sometimes vary from 1 to 12 weeks, this depend on virulence and number of the micro-organism, and the host response. [1] Syphilis is characterized by different periods of activity and latency, systemic dissemination, and sometimes it may progress to a different severe acute complication [2] In case of untreated syphilis, it can progress from primary, secondary, latent, to the tertiary stages. Signs and symptoms are different from patient to others depending on the infection stages. The diagnosis can always be confirmed serologically with histopathological and immunohistochemical characteristic. [3]

Syphilis has been effectively treated with penicillin, but its prevalence has been increased in the world, and now considered a re-emerging disease mostly among patients bellow the age of 25 years, and mostly in middle and low-income countries. [4]

Its prevalence has also started to increase in Americas and Europe, and can occurs in patients with male to male sex. [5,6] Comparing with other countries, it has a relatively low percentage in Iraq, in which the infection occurs mostly in males and in the age group more than 50 years. [7]

The present review gives an overview of syphilis etiology, its epidemiological data, various clinical manifestations, different diagnostic methods and appropriate treatment approaches for each clinical form of patients with different syphilitic stages.

ETIOLOGY

The causative micro-organism of syphilis is a filamentous, anaerobic, highly mobile, gram-negative, spiral *Treponema pallidum*. The contact with an infected patient during sexual activity is the most common way of spread, and through blood products transmission, or donation of organ. The *Treponema pallidum* can also enter the person body through minor cuts in the mucous membrane or skin. It can also be pass to the babies from infected mother during childbirth or pregnancy. Generally, it is not possible to get infection through toilet seats, or sharing the eating utensils, because the treponema cannot live outside body and die very quickly.[8]

Syphilis is highly contagious in the primary, secondary and in the latent early stages.[9] During sexual activity treponema can inter the host by small abrasions in the mucus membrane or skin. Inside the epithelium, *Treponema pallidum* then multiplies and invades the blood stream and lymphatic vessels. Macrophages can participate in phagocytosis of the *Treponema pallidum*. But, the immune response of the host is insufficient to destroy all the pathogens. [10]

EPIDEMIOLOGY

In the world, nearly more than twelve million cases of syphilitic infection per year.[1] Other found, there are about six million new cases of syphilis every year in patients with age 15-49 years, and about 300000 neonatal and fetal deaths are caused by syphilis, and 215000 infants are with a high risk of early death. [4]

In Iraq, syphilitic deaths reached 137 or 0.09% of total deaths, with a mortality rate of 0.18/100000 people. [11] In the National Blood Transfusion, Baghdad city/Iraq, a total of 178,966 healthy blood donors were included in the study. Number of infected persons was 1233 (0.69%), 1208 (98%) for males and 25(2%) for females. [12] In Basrah, a study conducted between 2019 and 2021 on 197,898 blood donors showed that the syphilis seroprevalence rates was 0.38% in 2019, 0.47% in 2020, and 0.36% in 2021. with marked declined trend.[13] Other study among persons which planning to marry in Iraq/Baqubah city found that among 15135 couples with the age of 20 to 70 years, attending to blood Bunk-Teaching Hospital, only 22 persons were seen positive for syphilis. [7]

In Saudi Arabia, a cross-sectional research revealed that out of 1183254 studied persons only (0.45%) were found as seropositive for syphilis, 33 patients were non-Saudi; and 21 patients were Saudi, with 30 males, and 22 married from the total number. This research revealed that the percentage of the involved patients by infection was low among the studied population and more than half of the syphilis positive cases were foreigners.[14]

In Africa, the highest prevalence was seen, and the values were ranged from (0.2 to1.8) percent. [4] From 2015 to 2018, participants were shared in five surveys in Tanzania, Uganda, Ethiopia, Zimbabwe, and Zambia. The study revealed that (57·6%) of the participants were females, and (42·4%) of the participants were males. Population-based syphilis prevalence was 0·9% in Zimbabwe and Tanzania, 3·0% in Zambia, and 2·1% in Uganda. Nearly 1027615 participants had active syphilitic infection across the mentioned countries, and the syphilis incidence was higher among patients with HIV in Ethiopia than in Zambia.[15]

In United States, it was found an increase in syphilitic infection incidence. In 2000, there were 5973 reported cases (2.12/ 100000). Also, several cases were reported in 2016, 58.1% were among men which had sex with the infected men, 13.9% were seen in men which had sex with woman, 11.0% were seen in women, and 16.9% were seen in men without any data of sex partners. [16] In 2017, there were 3064 reported cases (9.5/100000). Rates of syphilitic infection are high in male with 16.9/100000 males in comparison to female patients, with 2.3 cases of males/100000 females.[17] In 2017, 918 reported congenital syphilis in new born babies with a rate of 23.3 cases/ 100000 of lived births.[18] Then the incidence increased from 1.26 patients/100000 in 2017 to 4.88 patients/100000 in 2022, then declined to 2.47 patients/100000 by 2024. [19] In Brazil, it affects mainly young adults and adolescents, ages of 15 to 25 years, but it also seen in other age groups. In this study, syphilis has no predilection for gender, racial, or socioeconomic class. [20] In HIV-positive patients, it was found that the prevalence was seen more than 300-times greater. [21]

In Europe, the syphilis prevalence was seen higher in southern and eastern areas than in western ones. The overall rate is six/ 10000 of the population. Syphilis was seen eight times higher in men than in women. Most of the infections were seen in patients of (25) years and older; The younger people which aged 15-24 years represented only 13% of the patients with syphilis. Nearly (62%) of the patients were seen in men to men sex. [22] Countries like Germany, Belgium and France showed increases more than 50% of the cases. The lowest reported percentage was seen in Croatia with one infected patient/ 100000 of the screened population, and the highest percentage was reported in Denmark with 13.7 infected patients/ 100000 of the screened population. [23]

Russia found that there was an increase in syphilis prevalence during 1978 to 1979 with 28 cases/100000 of the screened population. But the incidence rises to 263 infected patients/100000 in 1996 [24]. This may be due to a decline in economy. The travelling with other cities like china can also raise the incidence of syphilitic infection. [24,25]

In India, between 1980 to 2000, the congenital syphilis incidence was significantly decreased due to the good care in the prenatal period. [26] Among 250 patients in

Bengal, a study found that a significant decrease in the prevalence of syphilis from (10.8%) in (2004) to (3.6%) in (2008). [27] In 2015 a study found a significant decrease in rate of syphilis in North India, but a significant rise in rates were seen in drug users, HIV-seropositive patients, and pregnant women.[28] Ankita *et al* found that of the 78 syphilitic patients, 78.2% were males, 19.2% were females, and 2.6% were transgender, and most of them were young adults of 21 to 30 years. About 2/3 of the infected patients were married and about 1/3 of the cases had HIV infection. [29] In China, the incidence of syphilis has increased since 1990 to 2010, and was seen higher in urban areas, and in sex workers and in men with men sex. [30]

The rate of syphilitic infection among the low-risk groups in 2000 to 2005 were seen nearly (0.3–0.6%) while the rates in a high-risk groups were (7–15%). [31] Zeng *et al* research revealed that syphilis incidence in people with HIV was 18.6%. They also found that the syphilis the prevalence was less in women with HIV than that in men with HIV. [32]

CLASSIFICATION

A. Acquired syphilis:

Based on the time from its initial infection and the progression of the infection, it is classified into stages. The stages are:

Primary syphilis

Clinically, this stage manifested as painless indurated ulcerative chancre, nearly 2 cm in diameter, which appears about 10 to 90 days after the contact with infectious patient. Chancres are mostly seen on the vagina, penis, and rectum, but may also occur at any place in which the direct contact with the infectious areas occurs. [33] It started as macule, then papule, and then changed into round or oval red or greyish ulcer with indurated edges. Microscopically, it presents as ulceration of the mucosa, with a base of dense inflammatory infiltrate (Figure-1). Chancre can be associated with regional non-tender or tender lymphadenopathy.[34] In case of no treatment, after three to six weeks the primary lesion spontaneously resolves without any scarring. [33,34]

Secondary syphilis

In this stage, the manifestation occurs from (4 to 8) weeks after chancre emergence. Commonly the signs include macular skin rash seen on feet soles and hands palms (Figures-2 A, B). The lesions appear brown or red; and may appears similar to eczema or psoriasis us a scaly hyperpigmented lesion. [35]

In contrast to the primary syphilitic stage, the secondary syphilitic lesions of the oral cavity are painful, multiple, and associated with generalized painless lymphadenopathy, migraine, fatigue, fever, sore throat, and weight loss. [36]

The oral mucosa is usually affected by several clinical forms and called mucous patches[37], that appears as elevated plaques and sometimes become ulcerated and covered by white or a gray pseudo membrane (Figure-2C). Similar to the primary stage, the histopathological picture of the secondary stages usually demonstrates a focal ulcerations and dense lymphocytes and plasma cells infiltration in lamina propria. [38]

Latent syphilis

When the clinical signs of the secondary syphilis disappear, the latent stage started, which follows the untreated secondary stage. This latent stage is referring to infection in patients who have no clinical manifestations, but the syphilitic patients have a positive serologic test. [39]

Latent syphilitic infection is classified into two stages. The early latent syphilis is that which was acquired in the previous year. While the late latent syphilis is that which acquired more than one year prior. During the early stages, latent syphilis is contagious, but not during the late latent stage. Pregnant women in early or late stage, can transmit the infection to fetus and affect the brain, heart, nerves, bones, and other parts of the body.[40] Latent syphilis can stay for several years, and about (60%) of the untreated patients in the late latent stage can appears without any symptom. At this stage, in case of appropriate therapy is given, the progression from late latent syphilis to tertiary stage will be prevented. [41]

Tertiary syphilis

Tertiary syphilis appears in about 1/3 of the untreated syphilitic patients, after a period of several years. The symptoms vary from patient to patient and depend on the organs which are affected. [42]

Neurosyphilis causes damage to the central nervous system, potentially causing blindness, loss of co-ordination, dementia, stroke, numbness, deafness, trigeminal neuropathy, and paralysis.[43]

Cardiovascular syphilis can cause endarteritis and may cause aortic aneurysms, coronary-artery stenosis, aortic insufficiency, heart failure, myocarditis, and damage to heart valves. Gummatous syphilis is granulomatous destruction of different visceral organs, most commonly the liver. [43]

The oral complications are gumma development and syphilitic leukoplakia with a danger of oral squamous cell carcinoma. In general, gummas will emerge on the palate and tongue, parotid gland, and the alveolus. At first, gumma shows one or multiple swelling as a necrotic granulomatous lesion. Then the swellings form ulcerations, with zones of breakdown, with possible bone destruction, and palatal perforation (Figure -3A). The zones of ulceration tend to heal, the resultant scarring on the tongue can cause fissuring. [44]

Syphilitic leukoplakia (Figure- 3B) is white patch with a raised corrugated nonhomogeneous surface in oral mucosa. It cannot be removed and can become potentially

malignant. A relationship between oral squamous cell carcinoma and tertiary syphilis has been proposed for a long time. [45]

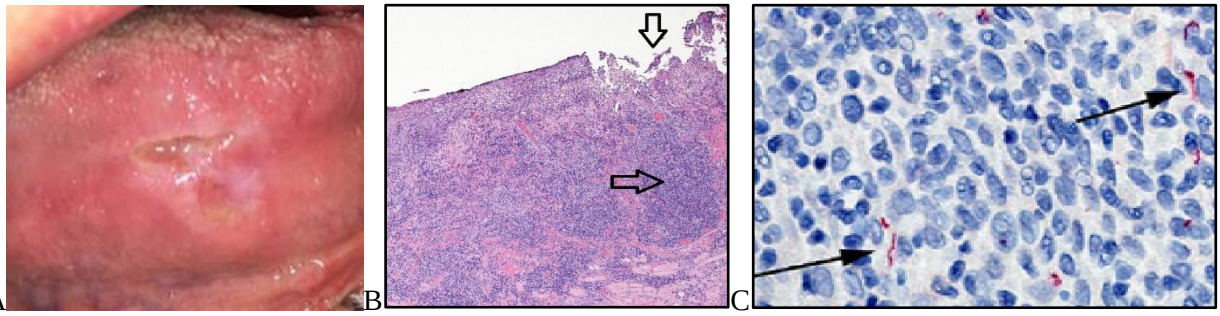


Figure 1. Patient with primary syphilis: (A) Ulceration on the surface of the tongue. Mucosal biopsy of patient with primary syphilis: (B) Exhibiting mucosal ulceration (upper arrow) overlying the lamina propria which contain a dense inflammatory infiltrate (lower arrow), 40x magnification. [46] (C) Treponema pallidum immunohistochemical stain (black arrows) revealed spirochetal organisms, 1000x magnification. [46]



Figure 2. Patient with secondary syphilis: (A,B) Palmoplantar sites appears as red papules with a central scales, arrow. [38] (C) Mucous patches appear as a slightly elevated plaques, covered with a white pseudo membrane in the labial mucosa. [37]

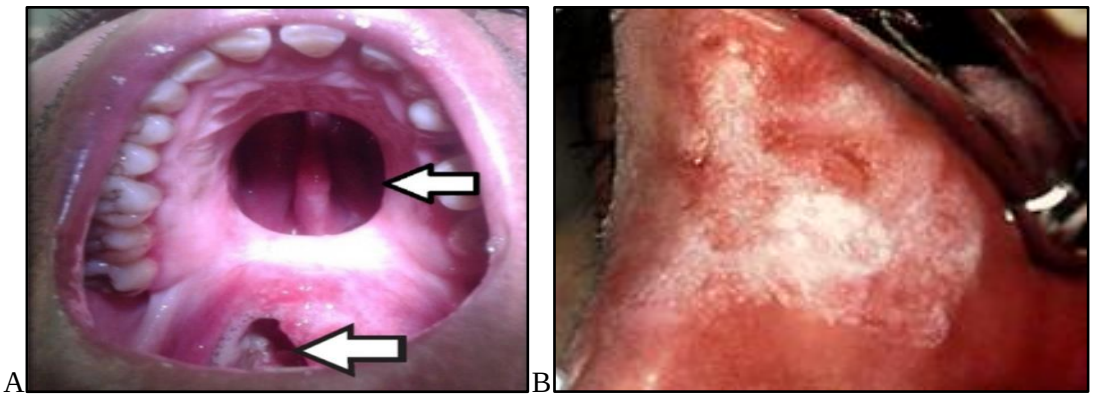


Figure 3. Patient with tertiary syphilis: (A) Palate showing two perforation due to destruction caused by syphilitic gummas [47]. (B) Clinical features of the leukoplakia-like form of oral tertiary syphilis [37].

A. Congenital syphilis:

Treponema transmission from the mother to the fetus causes congenital syphilis. Through transplacental or hematogenous routes, the transmission occurs. The transmission also can occur through the blood transfusions. Neonatal death, miscarriage or prematurity can occur if the transmission of *Treponema pallidum* is happened during the first trimester of pregnancy. [48]

If the transmission occurs in the second or third trimester of pregnancy, at birth, most of the infants from mothers with untreated syphilis may have no any laboratory or clinical evidence of *Treponema pallidum* infection, but they can

develop the manifestations several months or years later, if the syphilitic infection is untreated. [48] For this reason, the congenital syphilis can be classified into:

Early congenital syphilis

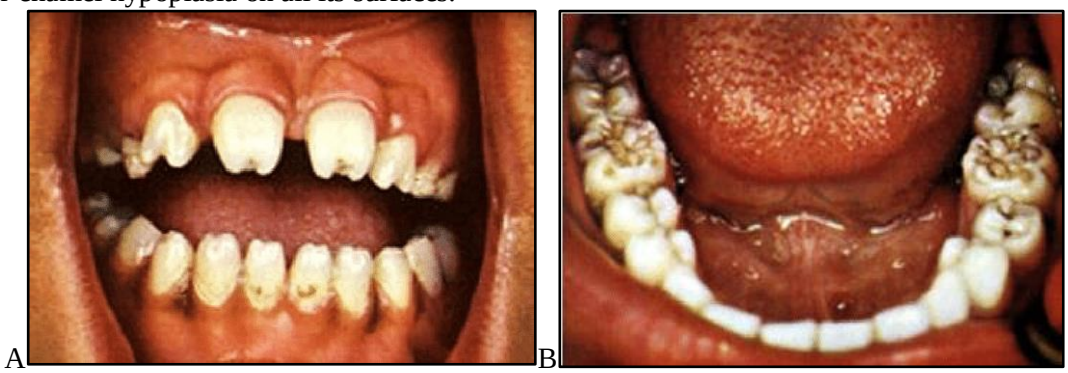
Clinically, the manifestations appear equal or less than two years of age, and include rash of the skin, cataracts, osteochondritis, splenomegaly, nephrotic syndrome, gastrointestinal malabsorption, pancreatitis, myocarditis, adenopathy, and hypopituitarism. [48]

Late congenital syphilis

Clinically, the manifestations appear more than two years of age, and include Hutchinson's incisors, Mulberry molars, seizures, atrophy of optic nerve, cranial nerve palsies, interstitial keratitis, hydrocephalus, bossing of frontal bone, short maxilla, saddle nose, high palatal arch, mandibular protuberant, and synovitis of the joints. Regarding the dental defects, they are mostly affecting the permanent incisors (Hutchinson's incisors) and first molars (Mulberry teeth) due to infection of the tooth buds by *Treponema pallidum* (Figure 4). Hutchinson's teeth and Mulberry molar may occur together. [49]

The incisors incisal edge clinically may have a notched edge, which is more common in the permanent maxillary central incisor than the lateral incisors, and on case this notch is not present and the tooth has a narrow incisal edge, the tooth is named a screwdriver incisor. [50,51] Mulberry molars contain multiple small enamel cusps associated with the permanent first molars. [49]

During pregnancy, all infected pregnant women must be treated, otherwise the born baby must be screened for the presence of the infection and treated. [51] Syphilitic canine is less frequently seen and the canines is usually exhibiting a linear enamel hypoplasia on all its surfaces. [49]



A B

Figure 4. Congenital syphilis (A) Notched screw driver shaped incisors. (B) Mulberry molars. [49]

DIAGNOSIS

Dermatologists mostly diagnose the syphilis by observing the clinical and sexual history, different laboratory investigations and sometimes radiology. The diagnosis of syphilis can be directly by microscopy, or indirectly by different serologic tests [33].

A. Direct diagnosis by microscopic observation

Darkfield microscopy

Treponema pallidum can only survive inside the body, so it is difficult to cultivated it by *in vitro* investigation. Direct diagnosis is done by detection of the micro-organism by dark field microscopy of *treponemal pallidum* in the serous exudate taken from a lesion which is a good specimens' sources for darkfield testing.[52] The *Treponema pallidum* is spiral-shaped organism that is 0.1–0.2 μm wide, and 6–15 μm long, and can be visualized only by darkfield microscopy which is useful for visualizing live, unstained *Treponema pallidum.* Dark field microscopy is a rapid method for detection of *Treponema*, especially in the early period of the primary syphilis, in which all the serological tests may be negative. It enhances contrast by illuminating the specimen at oblique angles, making the organism appear bright against a dark background. [52,53]

Histopathology

The histopathological characteristics of primary syphilis are nonspecific and characterized by the presence of ulcerations with a chronic inflammatory cells infiltration in lamina propria, so the biopsy and histopathologic examination must be always performed with the serologic test. In addition to that, the silver-based stains can highlight both the spirochetes and the melanin granules (Figure 5A) resulting in a difficulty in interpreting the images. [38]

Immunohistochemistry

Immunohistochemistry can be used to diagnose syphilis. It involves staining tissue samples with antibodies specific to *Treponema pallidum* to identify its presence. [54] Skin biopsy showed spirochetes in both epidermis and dermis; and shows a perivascular invasion in underlying connective tissue stroma (Figure- 5 B, C, D). [55]

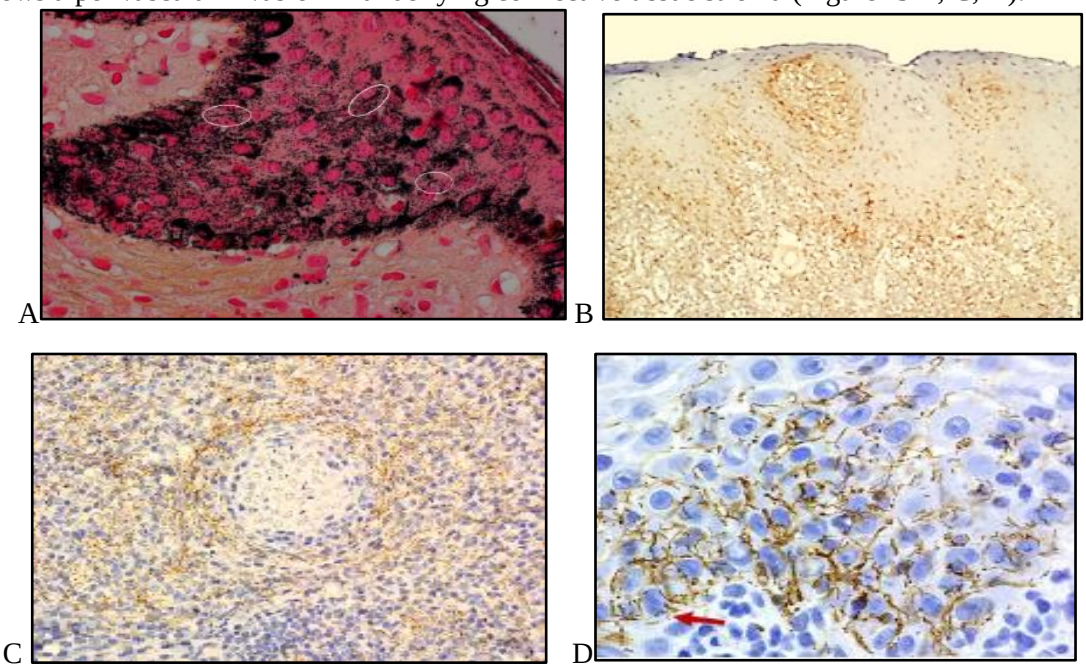


Figure 5 (A) Silver nitrate stain highlights the spirochetes as seen in the white circles and the melanin granules (400x magnification) [38]. (B) *Treponema pallidum* reveals positive staining in the epidermal-dermal junction (Immunohistochemistry ×100) [56], (C) *Treponema pallidum* surrounding blood vessels in the deeper stroma, (Immunohistochemistry ×400). [55] (D) Positive staining for coiled spirochetes (Immunohistochemistry x1000). [55]

Indirect diagnosis by serological tests

The two categories are, non-treponemal tests in which it detects the non-treponemal antibody, and treponemal tests for detection of specific treponemal antibody. [56]

Nontreponemal tests

These tests involve both rapid plasmas regain test and venereal disease research laboratory test. Both can detect the antibodies to lecithin, cardiolipin, and cholesterol as a measure of the tissue damage. In case of reactivity of the nontreponemal test, the laboratory assesses the amount of antibody as a titer. The titers monitoring can also use to assess the response to treatment. In successfully treated persons, this test becomes non-reactive in about three months. [57]

Treponemal tests

This measure the IgG and IgM which are the specific antibodies which works against *Treponema pallidum*. They are more more sensitive than nontreponemal tests during the early period of infection. The IgG and IgM are detected 14 days after infection. Some of the developed *treponema pallidum* tests are the fluorescent treponemal antibody absorption test, the *Treponema pallidum* particle agglutination test, and the *Treponema pallidum* hemagglutination test. More recent *treponema pallidum* assays are chemiluminescence immunoassay and enzyme immunoassay. [58]

Regardless of the stage, all the patients with syphilitic infection must undergo both the treponemal and the nontreponemal tests. Because every type of test has its limitations and may be insufficient for the diagnosis. Other medical conditions like autoimmune diseases, the false-positive nontreponemal test can be also associated; therefore, every patient with a positive nontreponemal test should also receive a treponemal test in order to confirm the diagnosis of infection. [59]

STANDARD THERAPIES

Once syphilis has been diagnosed, the treatment must be straightforward. The treatment is usually intra muscular benzathine penicillin, which is a long-acting form of the antibiotic. Benzathine penicillin G is the best recommended treatment for syphilitic infection in every stage. It inactivating an enzyme which is important for the *Treponemal* cell wall growth and repair. Without this enzyme, *Treponema* experience cell lysis from osmotic pressure. Assessment of the treatment efficacy, a follow-up with laboratory testing is required. [38]

Sexual partner in the last 90 days must be informed of the possibility of the infection and must be informed about the importance of evaluation for any sign suggestive of syphilitic infection complications. Treatment of the sex partners is important to decrease the risk of re-

infection.[60,61] The WHO (2016) recommendations treatment for syphilis infection are: [62]

- **In primary, secondary, and early latent stages of syphilis:** The recommended treatment is benzathine penicillin Gm 2.4 million units, IM in a single dose.
- **In late latent and tertiary syphilitic infection:** The recommended treatment is benzathine penicillin G, 2.4 million units, IM once a week for three weeks.
- **In tertiary syphilis after several years:** The recommended treatment is benzathine penicillin G, 2.4 million units, IM once a week for three weeks.
- **In neurosyphilis and ocular syphilis:** The recommended treatment is aqueous penicillin G, 18–24 million units /day, IV for 10–14 days.
- **In congenital syphilis:** The recommended treatment is aqueous benzyl penicillin, 100 000–150 000 units /kg/day, IV for 10–15 days.
- **In pregnant:** The recommended treatment is benzathine penicillin G, 2.4 million units, once IM in a single dose.
- **In the presence of benzathine penicillin allergy:** The recommended treatment is doxycycline,100 mg, orally twice daily for 14 days.

CONCLUSION

Syphilis is a bacterial contagious infection, caused by the gram-negative anaerobic bacteria named *Treponema pallidum* which transmitted by the direct contact with an infected patient during the sexual activity, transmission can also occur via blood products or organ donation. Nearly more than twelve million new cases per year in the world present. The epidemiology in Islamic countries is less than the others. The acquired syphilis is divided in to primary, secondary, latent, and tertiary stages, and the clinical manifestations and complications depend on the syphilitic stage. Congenital syphilis occurs if the *Treponema* is transmitted from the infected mother to the fetus. Syphilis diagnosis is by observing patient clinical and sexual history, directly by tissue microscopic examination, or indirectly by different serologic tests. Treatment is usually by intramuscular benzathine penicillin, but also depend on the condition of the patient. Follow-up by different laboratory testing is important to assess the treatment efficacy.

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Conflict of interest

The authors declare no conflict of interest.

Authors' Contributions

All authors contributed equally to drafting the manuscript.

Competing Interests

The authors declare that they have no conflict of interest.

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ORIGINAL ARTICALE

ALPHATOCOPHEROL AS A MARKER FOR PREDICTION OF FAMILIAL TYPE 2 DIABETES MELLITUS IN IRAQI APPRANETLY HEALTHY SUBJECTS

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ABSTRACT

Background: Diabetes mellitus is a chronic physiological disease characterized by increased levels of blood glucose and can lead to damage to the urinary system, circulatory system, eyes, and nervous system. It poses serious challenges to healthcare systems.

Objectives: This study was designed to investigate the role of serum levels of alpha-tocopherol, fasting blood glucose, glycated haemoglobin (HbA1c %), and fasting insulin in predicting type 2 diabetes mellitus (T2DM) in healthy subjects who are members of families affected by diabetes mellitus, compared to subjects from healthy families.

Materials and Methods: This case-control study was carried out at the Specialized Centre for Endocrinology and Diabetes, Baghdad, Iraq, during the period from March to September 2024. It included 190 subjects of both genders, classified into three subgroups:

Group 1 (G1; T2DM): 70 subjects with type 2 diabetes mellitus for more than five years and whose parents had T2DM

Group 2 (G2; Familial T2DM – FT2DM): 70 subjects who are members of the same family as G1 but do not have diabetes.

Group 3 (G3; Control): 50 apparently healthy subjects from different families without any history of diabetes.

Investigations included serum measurements of fasting glucose, insulin, and alpha-tocopherol, as well as blood HbA1c %.

Results: The mean (±SD) value of serum insulin in T2DM was significantly higher compared to FT2DM and controls ($p < 0.05$).The mean insulin value in FT2DM was also significantly higher than in controls ($p < 0.05$).

The mean alpha-tocopherol level was significantly lower in T2DM compared to FT2DM ($p < 0.05$) and controls ($p < 0.05$), and also lower in FT2DM than controls ($p < 0.05$).

Conclusion: The study indicated a decrease in alpha-tocopherol levels in healthy individuals with a family history of type 2 diabetes compared to controls with no family history of diabetes. This suggests that alpha-tocopherol could be considered an early marker for the development of type 2 diabetes in healthy individuals.

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Keywords*:* Diabetes, insulin, prediction, alpha tocopherol.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder, chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood glucose. Hyperglycemia, also called raised blood glucose or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the kidney.[1]

The term diabetes mellitus describes a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.[2]

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. It accounts for 85–90% of all cases worldwide and can often be prevented or delayed by maintaining a normal body weight, engaging in physical activity, and eating a healthy diet. A hallmark of type 2 diabetes is a decline in β-cell function, which begins as early as 10-15 years before diagnosis and continues throughout the disease process.[3] Pre-diabetes stage in the beginning, because of eating more food, the pancreas begins to secrete greater amounts of insulin than normal. This stage lasts for a few years, after which the B cells begin to lose its ability to produce large quantities of insulin because of some of them reaching the stage of dysfunction accompanied by an increase in insulin resistance by the cells of the body. This stage develops until the rate of dysfunction reaches 40%, then the patient becomes pre diabetes. These stages reach a period of approximately 10 years and are important and vital if they are identified and diagnosed strictly to avoid or delay.[4]

Alpha tocopherol

hydrophobic side chain that can cross biological membranes and hydrogen atom that can neutralize free radicals. Alpha-tocopherol (alpha-tocopherol) is a form of vitamin E that is absorbed and stored in the body at a higher rate than the others. There are eight distinct varieties of vitamin E—four tocopherols and four tocotrienols. All include a hydroxyl group that can give humans' chromane rings.[5].

Being lipid-soluble, vitamin E is found in many different types of tissues and is absorbed in many different ways. The most common type, -tocopherol, plays a role in molecular, cellular, and metabolic activities that are crucial to maintaining healthy levels of lipoproteins and lipids. The current state of knowledge is seen as "critical" for the modification of vitamin E homeostasis in a range of human disease states associated with oxidative stress. Malaria is an example of a disease where -tocopherol has a protective role by preventing the parasites from being damaged by the erythrocyte's high levels of reactive oxygen species.[6]

It has been known for some time in vitro that -tocopherol can serve as a pro-oxidant and promote the per oxidation of lipids.[7] Moreover, a rise in DNA damage due to -tocopherol has been reported after an insult leading to the production of reactive oxygen species (ROS) in cultured cells.[8] Upon encountering ROS, α-tocopherol within lipid becomes oxidised forming its own radical, which requires co-antioxidants (e.g ascorbic acid) in order for the α-tocopherol to be regenerated. If the tocopherol radical is not eliminated there is an increase in lipid peroxidation, a process known as tocopherol-mediated peroxidation(TMP) [9]. These lipid peroxides can generate reactive oxygen species (ROS) that can harm DNA. While TMP- and react with DNA-associated transition metals (Fe, Cu) to produce DNA-damaging hydroxyl radicals (•OH) via the Fenton reaction.[10] . When Cu,Zn-superoxide dismutase is oxidized, free copper is released, which can boost the production of•OH[11].

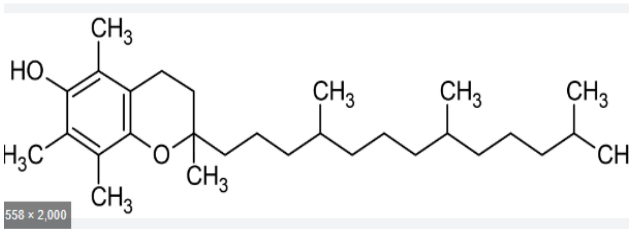


Figure 1. Structure of alpha tocopherol.

Subjects and Methods

This case control study was carried out at at Specialized Center for Endocrinology and diabetes, Baghdad, Iraq, during the period from march to September 2024. It included 190 subjects of both gender classified into sub groups: group 1(G1; T2DM) included 70 subjects with type 2 diabetes mellitus (T2DM) for more than five years and their parents had T2DM, group 2(G2; FamilailT2DM-FT2DM) involved 70 subjects who are member of the same family of G1 but who do not have DM, and group 3 (G3) included 50 apparently healthy subjects of different family without any history of DM who served as control group.

Body mass index was calculated using a global equation:

BMI (Kg/m^2)= weight (Kg)/ height (m ^{2})[8]

Waist circumference (WC) was measured using by inches measure around your middle at halfway between them and hip circumference (HC) was using measure by inches at the top of hip bone, than bring the tape measure away around your body [9].

Five milliliter (ml) of peripheral veinous blood was aspirated from each subject after 10-hous overnight fasting state, divided into two tubes;2.5 ml was placed in (EDTA) tube and it was processed within three hours for HbA1c measurement by high-performance liquid chromatography, using a L9100 automated ion exchange analyzer (Roche Company, USA)and

anthor2.5 ml was placed in a plain tube and left to clot for 15 minute, then centrifuged at 3000 rpm for 10 minutes to separate serum that used for measurements of fasting serum glucose byroxidase method, linear company Spain chemical. insulin by microparticle enzyme immunoassay with an automated analyzer (c 2022 f. Hoffmann-La Roche Ltd) and Alpha tocopherol by ELISA technique. The data was analyzed by the statistical package available from SPSS-26. Data were showed in simple measures of frequency, percentage, mean, standard deviation and range (minimum and maximum values).The significance of the difference for qualitative data was tested using the Pearson ANOVA and t- test. Statistical significance was taken into account when the P-value was equal to or less than 0.05.

RESULTS

Table 1 shows the gender distribution of the three groups without significant differences. The same table also shows the mean (±SD) values of age, BMI, WC, and HC of the three studied groups without significant differences among them.Whereas other study. in Western Finland showed that the family history of DM type 2 was associated with high BMI [8].

Table 1. distribution of gender and mean (±SD) values of age, Body mass index, waist circumference and hip circumference of three studied groups

Parameter	Control(n=50)	FT2DM (n=70)	T2DM (n=70)
Gender^{NS} M(F)	24(26)	32(38)	32(38)
Age^{NS} (years)	43.02 ± 7.63	42.93 ± 7.78	42.48 ± 6.65
BMI^{NS} (kg/m^2)	31.15 ± 2.10	30.97 ± 1.88	30.66 ± 2.22
Waist circumference ^{NS} (cm)	36.34 ± 2.87	36.40 ± 2.89	36.03 ± 3.01
hip circumference^{s}	38.24 2.65	38.27 ± 2.67	37.88 ± 2.85

NS: n± on-significant differences among groups

Table 2. Mean (±SD) values of fasting glucose, glycated hemoglobin, insulin and alpha tocopherol of three studied groups

Parameter	Control (n=50)	FT2DM (n=70)	T2DM (n=70)
Fasting serum glucose (mg/dl)	88.47 ± 8.13	90.0 ± 9.35^{NS}	204.71 ± 58.62$^{♠}$
HbA1c %	4.52 ± 0.59	4.81 ± 0.55^{NS}	8.62 ± 1.41^{o}
Insulin (µu/ml)	12.93 ± 6.13	28.94 ± 21.80*	39.97 ± 34.53*,**
Alpha tochopherol (µg/ml)	21.36 ± 3.27	8.91 ± 1.35**	9.85 ± 1.64$^{●}$

ANOVA and t-test reeval; ♠ significant increase in fasting glucose in T2DM thanFT2DM and controls (p=0.001), NS: non-significant difference between FT2DM and controls, ^{o}significant increase in HbA1c in T2DM than in FT2DM and controls (p=0.001), NS: non-significant difference between FT2DM and controls, * significant increase in insulin in T2DM and FT2DM than controls (p=0.001), ** significant increase in T2DM than FT2DM (p=0.001), ● significant

decrease in alphatocopherol in T2DM than in FT2DM and controls (p=0.001), ●● significant increase in FT2DM than controls (p=0.0

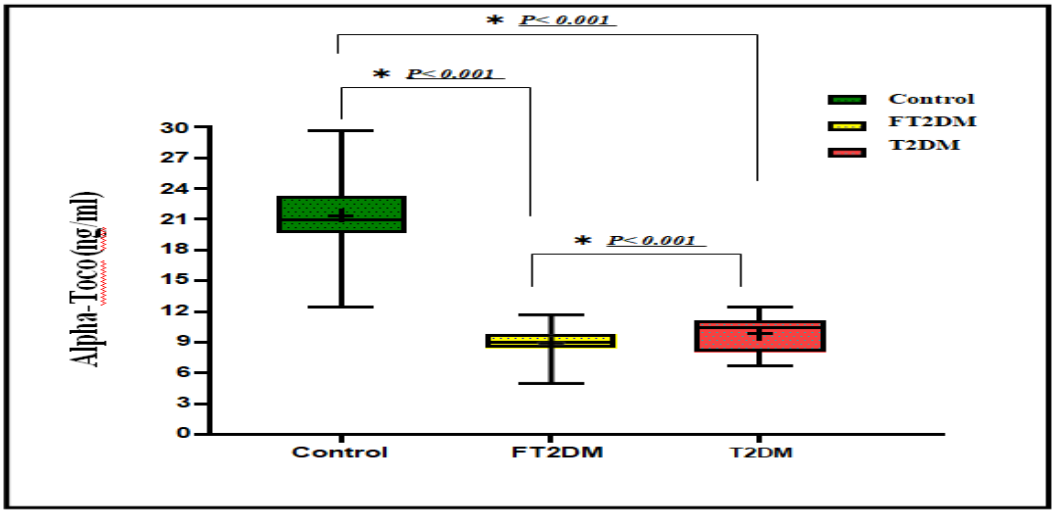
In T2DM, there was no any significant correlations among the studied parameters. The study found significant positive correlation between HbA1c values and alphatocopherol levels (r=0.133 , p 0.27) in FT2DM group. However, there was no other significant correlations in FT2DM, table 2

Table 3. The correlation coefficient(*r*) and (*P*-Value) FT2DM Parameters

	Insulin	FBS	HBA1c	Alphatoco
Insulin	1	0.132	**0.349****	0.179
P-value		0.278	**0.003**	0.142
FBS	0.132	1	0.162	-0.068
P-value	0.278		0.185	0.577
HBA1c	0.349**	0.162	1	**0.276***
P-value	0.003	0.185		**0.022**
Alphatoco	0.133	-0.008	0.05*	1
P-value	0.27	0.951	0.675	

**.Correlationi ssignificant at the 0.01 level (2-tailed).*.Correlationi significant at the 0.05level(2-tailed).

Table 4. The correlation coefficient(*r*)and(*P*-Value)T2DM parameters



ROC and AUC value 0.950 at cutoff value 5.23 unit with sensitivity98.6% and specificity83.7% Which is superior of that of insulin, fasting glucose and HbA1c (table 5). In T2DM patients group, HbA1c and fasting glucose are the best The present results showed that serum alphatocopherol is the best biochemical marker in prediction of T2DM in apparently healthy subjects when differentiated from FT2DM patients (FT2DM biochemical markers in differentiation of healthy individuals from established patients with T2DM (table 5). While, in prediction of T2DM in those subjects with risk of this disease (FT2DM group) when discriminated from documented T2DM, alphatocopherol is excellent one with ROC and AUC value0.675 at cutoff value 10.28 With sensitivity 58.6% and specificity 88.7% (table 5).

Table 5. FT2DM, T2DM from control Parameters ROC outcomes

Parameters	AUC	*P*-value	Cut-offvalue	Sensitivity	Specificity
Insulin	0.711	<0.001	22.05	49.3 %	95.9 %
FBS	0.680	0.001	108	52.2 %	100 %
HBA1c	0.637	0.011	4.45	82.6 %	38.3%
alphatocopherol	0.675	<0.001	10.28	58.6 %	88.7 %

*SignificantatP≤0.05, NS: Non-Significant

DISCSSION

This study was designed to included three study groups of T2DM, FT2DM, and healthy controls. Comparison among different groups regarding age, BMI, WC and HC the results refer no significant differences (table 1) which is stated in design of study in order to eliminated their effects on obtained results. The mean value of serum insulin was significantly increased in T2DM than FT2DM and controls as well as in FT2DM than controls (table2). These results are in agreement with Abdul-Ghanet et al. who found the insulin level is useful as a predictor of future development of type 2 diabetes [10]. Other researcher obtained different results for example, in study of Tullaya S. and Raweewan in Thailand who found that the higher HbA1c and higher fasting plasma glucose levels were associated with the risk of T2DM in the Thai population [18] In study on older adults with both IFG and elevated HbA_{1c} have a substantially increased odds of developing diabetes over 7 years. Combined screening with FPG and HbA_{1c} may identify older adults at very high risk for diabetes [19]. In research for Kyoko K. et al. 2009 during 4-year follow-up period, they confirmed 659 diabetes cases. In multivariate analysis, both FPG and A1C were independently associated with the risk of type 2 diabetes. The combined measurement of FPG and A1C was effective for predicting type 2 diabetes.
Healthy individual with a history of diabetes

(FT2DM) begin early in the stage of metabolic disorder, which results in increase in free fatty acid, an increase in free radicals, and a lack of antioxidants. This leads to entering the stage of insulin resistance, after which the pancreas works to increase insulin secretion to compensate for insulin resistance which interprets the significant increase in FT2DM when compared with healthy control group as well as in T2DM who have had a relatively short period of DM duration (table2).

Increase insulin level in the healthy individual is may be because the heritability of type 2 diabetes is high [11]. Insulin resistance is a risk factor for type 2 diabetes and cardiovascular disease progression. Current diagnostic tests, such as glycemic indicators, have limitations in the early detection of insulin resistant individuals [12]. Wolefgan et al.2022 report that the fasting and 2h-insulin are critical markers of future diabetes risk [17]. Our results are agreed with previous study for Tomoshige et al. they proved that the insulin level during OGTT (Oral Glucose tolerance test) have strong predictor of future type 2 diabetes. And they explained that as if insulin sensitivity reduces, insulin secretary must increase to keep normal glucose tolerance [21] The mean value of serum Alpha tocopherol was significantly increased in T2DM than FT2DM and controls as well as in FT2DM than controls Table (3-4).

In this study The cutoff of Alpha tocopherol in FT2DM group is (12.7 µg/ml)

and cut off of T2DM group is (12.4 µg/ml).

Alpha tocopherol is one of the most important antioxidants in the body. It is used by the body to get rid of free radicals. In group of F2DM the level of Alpha tocopherol decreases due to consumption by the body to get rid of free radicals.

The result of this study refer to alpha tocopherol level is a good biochemical marker for prediction diabetes in early stage in healthy individual with family history .

Arnalov et al. found serum concentrations of α-tocopherol independently predicted insulin resistance and type 2 diabetes incidence during 27 years of follow-up in a community-based study of men. This result supports the importance of impaneled antioxidant status for the development of insulin resistance and type 2 diabetes [12] .

Mayer et al. suggested that low serum concentrations or low dietary intake of antioxidants such as β-carotene and α-tocopherol play independent roles in the pathogenesis of type 2 diabetes [13].

Kataja et al. revealed in their study no independent association with these antioxidants and the development of type 2 diabetes [14] .

Gopaul et al. found Oxidative stress due to increased production of reactive oxygen species and decreased antioxidant status have been implicated in the pathogenesis of type 2 diabetes and its complications [15].

Bastet al. suggested from experimental studies that oxidative stress impaired pancreatic β-cell insulin secretion interfered with glucose disposal in peripheral tissues(Gopaul et al., 2001) and elicited systemic inflammation thereby accelerating the development and progression of type 2 diabetes. Vitamin E is a major lipid-soluble chain-breaking antioxidant with anti-inflammatory properties [16]

Tajiriet al. indicated that vitamin E may improve insulin action and insulin secretion by protecting peripheral tissues and β-cells from free radical–mediated damage, leading to the hypothesis that this vitamin may help delay the development of type 2 diabetes [17]

CONCLUSION

1. This study suggested that serum levels of Alpha tcopherol of less than (12.7µg/ml) are excellent biochemical markers in recognition of apparently healthy subjects who do not have any familial or familial T2DM history are at risk for progression of T2DM.
2. The study proposed that measurements of serum alpha-tocopherol of less than 10.20 µg/ml are clinically useful in predicting those subjects with familial history of T2DM.
3. Therfer the level of insulin increase in the group of healthy individual with family history of type 2 diabetes comper with control group healthy individual with no family history of type 2 diabetes this means level of fasting insulin level can be used for pridaction of type 2 diabetes in healty individual

DECLARATIONS

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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ORIGINAL ARTICALE

DEVELOPMENT OF A HOME CONTACT TUBERCULOSIS CASE-FINDING MODEL BASED ON SCREENING WITH RAPID MOLECULAR TESTS (TCM) AT THE OESAPA COMMUNITY HEALTH CENTRE IN KUPANG CITY

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ABSTRACT

Background: Data from the East Nusa Tenggara (NTT) Central Bureau of Statistics in 2023 recorded 9,535 confirmed cases of pulmonary tuberculosis (TB), showing a significant increase compared to 4,798 cases in the previous year. Kupang City contributed the highest number of TB cases in NTT, with 1,253 cases.
Objectives: To develop a screening model based on Molecular Rapid Tests for early detection and treatment of TB and to identify factors influencing its distribution in the working area of Puskesmas Oesapa in 2024.
Materials and Methods:A cross-sectional study was conducted with 150 randomly selected samples, using inclusion and exclusion criteria. Data analysis included the Spearman rank test for bivariate analysis and Logistic Regression for multivariate analysis.
Results: Bivariate analysis showed no significant association between TB and gender, age, education, occupation, knowledge, residential density, information availability, pregnancy risk factors, treatment dropout, or elderly risk factors. Significant associations were found with sputum disposal behaviour (p=0.026; r=0.182), smoking behaviour (p=0.000; r=0.331), exercise habits (p=0.034; r=-0.173), cough (p=0.000; r=0.585), shortness of breath (p=0.000; r=0.630), weight loss (p=0.000; r=0.655), appetite loss (p=0.000; r=0.674), fever (p=0.000; r=0.693), night sweats without physical activity (p=0.000; r=0.624), and history of diabetes mellitus (p=0.007; r=0.219). Multivariate analysis indicated that smoking (p=0.017; Exp(B)=4.469; 95% CI=1.311–15.236) and fever (p=0.028; Exp(B)=8.259; 95% CI=1.263–54.033) were significant predictors of positive TCM TB results.
Conclusion: Smoking behaviour and fever were identified as significant predictors of positive TB cases. There is a need for community socialisation programs to promote healthy lifestyles and preventive measures to reduce TB transmission.

Keywords*:* Molecular Rapid Test, Tuberculosis (TB), Puskesmas Oesapa

INTRODUCTION

Almost a quarter of the world's population is infected with Mycobacterium tuberculosis. Tuberculosis is an infectious disease caused by the bacteria *Mycobacterium tuberculosis* that attacks the lungs. To date, TB remains the leading cause of death after HIV/AIDS, and is one of the top 20 leading causes of death worldwide. Most of the estimated deaths caused by TB are recorded in four countries, namely India, Indonesia, Myanmar and the Philippines. The number of deaths due to TB (among HIV-negative patients) globally in 2022 was 1.1 million, which is a decrease compared to 2021, which was 1.2 million [20.] Indonesia is also the second highest TB sufferer in the world after India with a proportion of new cases of 10% of all cases in the world. Globally, it is estimated that 10.6 million people will suffer from TB in 2022[45]. TB case finding in Indonesia has continued to increase every year for the last 3 years. In 2021, 443,235 TB cases were found in Indonesia, in 2022 the TB case finding increased to 724,309 cases and in 2023 it increased to 821,200

cases. The last TB case report on 16 March 2024 found 172,233 cases. [19]

The primary goal of TB case finding is to treat people with TB as early as possible to reduce the risk of death. Another goal is to reduce or minimise the scale of spread of TB disease to healthy people. The national TB case notification target for 2023 is 90% and 11 provinces have reached the 90% target. There are 4 provinces that have a notification achievement of <50%, namely Riau Islands, East Nusa Tenggara, Bangka Belitung Islands, and Bengkulu. East Nusa Tenggara Province is the only priority province out of 8 provinces that have notification achievements below 50% in Indonesia. (Ministry of Health, 2023).

Data from the East Nusa Tenggara Central Bureau of Statistics in 2023 recorded 9,535 confirmed cases of pulmonary TB in East Nusa Tenggara Province. Compared to the 4,798 TB cases in the previous year, there was a significant increase in cases. The increase in TB case finding in East Nusa Tenggara Province has not yet reached the national target despite the increase. Meanwhile, Kupang City is one of the cities that contributed the most TB cases in East Nusa Tenggara Province, with 1,253 cases in 2023. The increase in TB case finding is supported by the efforts of health workers and cadres in searching for, finding and treating TB patients within the scope of the work area of each Puskesmas. Puskesmas Oesapa is one of the Puskesmas in Kupang City that is active in seeking, finding and treating TB patients. This is also supported by the readiness of the Molecular Rapid Test equipment owned by the Puskesmas. The prevalence of TB cases at Puskesmas Oesapa is 48 cases spread across 5 urban villages. There were 20 TB cases in Kelurahan Oesapa, 13 TB cases in Kelurahan Lasiana, 7 TB cases in Kelurahan Oesapa Selatan, 6 TB cases in Kelurahan Oesapa Barat, and 2 TB cases in Kelurahan Kelapa Lima. Contact investigations were conducted on household contacts through screening activities conducted by cadres.

According to the *Centers for Disease Control and Prevention*, there are two groups of people who are at high risk of developing TB: people who have been recently infected with TB bacteria and people with medical conditions that weaken the immune system. The *airborne* transmission of TB *disease* increases the likelihood of infection to people who are physically close to TB patients, including those who live in the same house. Infection rates may increase with the length of contact/exposure to TB patients. The possibility of TB bacteria to infect will increase when the body's immune system decreases, making people vulnerable to TB bacterial infection (Ministry of Health RI, 2018).

Some of the risk factors for TB incidence found in previous studies are variables of occupancy density, knowledge, and behaviour that are significantly associated with the incidence of TB transmission; knowledge is the most dominant variable [47]. Meanwhile, research by Budi et al (2018) stated that family history of TB, access to information, and housing density were significantly associated with the occurrence of TB disease; the variable of housing density being the most influential in the occurrence of the disease. Furthermore, research by Sari (2018) showed that the level of knowledge, attitudes, and actions about TB were associated with the incidence of TB. Another study found a significant relationship between the variables of knowledge, attitude, and action with the incidence of TB; action being the most dominant variable in influencing the incidence of TB.

MATERIALS AND METHODS

This study used a cross sectional study design. This study was conducted in the working area of Puskesmas Oesapa from June to July 2024. The population in this study were all TB patients registered in the working area of Puskesmas Oesapa and household contacts with TB patients. The total population was 384 which was obtained by multiplying the number of TB sufferers recorded, namely 48 people with 8 people who had contact with sufferers. The sampling technique selected was random sampling with the results of the calculation of the sample size of 150 samples. This study also involved inclusion and exclusion criteria in the selection of respondents to be used as research samples.

The independent variables in this study were gender, age, education level, occupation, knowledge level, attitude, sputum disposal behaviour, smoking, occupancy density, information availability, cough, shortness of breath, weight loss, decreased appetite, fever, unexplained night sweats, history of diabetes mellitus (DM), elderly, pregnant and treatment dropout. The dependent variable in this study was the result of a positive TB Rapid Molecular Test (TCM) examination conducted on the sample. The data collection tool used was a questionnaire. Data processing techniques were carried out through *editing, coding, data entry, cleaning* and analysed.

Data analysis involved univariate analysis to describe the characteristics of respondents. Bivariate analysis was used to analyse the correlation between independent variables and dependent variables using the *Spearman rank test*, followed by multivariate analysis to analyse the effect of independent variables on dependent variables in the model.

This research has passed and received ethical approval from the Health Research Ethics Commission of the Faculty of Public Health, Nusa Cendana University with number 001890/KEPK FKM UNDANA/2024.

RESULTS

Characteristics of respondents

Table 1. Characteristics of Respondents

Characteristics	Total Sample = 150	%
Gender		
Male	78	52,0%
Female	72	48,0%
Age		
≤ 25 Years	41	27,3%
26 - 35 years	49	32,7%
36 - 45 years	24	16,0%
46 - 55 years	24	16,0%
56 - 65 years	9	6,0%
≥ 66 Years	3	2,0%
Education		
Not in school/not completed primary school	4	2,7%
Graduated from elementary school/equivalent	24	16,0%
Graduated from junior high school/equivalent	33	22,0%
Graduated from high school/equivalent	70	46,7%
Academy/PT Graduation	19	12,6%
Jobs		
Student	38	25,3%
Private	25	16,7%
Self-employed	36	24,0%
PNS	7	4,7%
IRT	43	28,7%
Retired	1	0,7%

Source: Data processed, 2024

Table 1 above shows the percentage of male respondents by 52.0% and female by 48.0%. The age distribution of respondents was highest in the age range of 26-35 years, namely 49 people with a percentage of 32.7%, while the lowest was in the age range above 65 years, namely 3 people with a percentage of 2.0%. The distribution of education levels shows that most of the respondents are high school graduates/equivalent, namely 46.7% or 70 people. While the lowest distribution of respondents was not graduated from elementary school, which was 2.7% or 4 people. Most of the respondents interviewed were students and housewives, each of which had a percentage of 28.7% or 43 people. Meanwhile, the lowest is retirees, totalling 1 person and the percentage is 0.7%.

Bivariate Analysis

Data from Table 2 found that 26 male respondents were TB positive and 24 female respondents were also TB positive. Meanwhile, there were 52 TB negative male respondents and 48 TB negative female respondents. So it can be concluded that TB-positive respondents are more prevalent among male respondents. Statistical testing results obtained p value = 1.000 > 0.05. Thus, there is no relationship between gender and positive TCM examination for TB in the Oesapa Health Centre Working Area in 202

Table 2. Analysis of the relationship between independent variables and dependent variables

Variables	TCM Check Result		Total	Spearman rank test	
	Positive	Negative		P value	rho
Gender					
Male	26	52	78	1,000	0,000
Women	24	48	72		
Age					
Age ≤ 45 years	36	78	114	0,421	-0,066
Age ≥ 46 years	14	22	36		
Education Level					
Low	24	37	61	0,199	0,106
High	26	63	89		

Jobs					
Not working	32	50	82	0,106	0,133
Work	18	50	68		
Knowledge					
Bad	3	1	4	0,074	0,146
Good	47	99	146		
Attitude					
Not in favour	0	0	0	-	-
Support	50	100	150		
Phlegm removal behaviour					
Bad	22	26	48	*0,026*	*0,182*
Good	28	74	102		
Smokers					
Yes	35	35	70	*0,000*	*0,331*
No	15	65	80		
Exercise Habits					
Once a week	8	28	36	*0,034*	*-0,173*
2 - 3 times a week	9	24	33		
Never	33	48	81		
Residential density					
Solid	16	23	39	0,239	0,097
Not solid	34	77	111		
Availability of information					
There is	49	97	146	0,722	0,029
None	1	3	4		
Cough					
Yes	50	39	89	*0,000*	*0,585*
No	0	61	61		
Shortness of breath					
Yes	43	20	63	*0,000*	*0,630*
No	7	80	87		
Weight loss					
Yes	45	21	66	*0,000*	*0,655*
No	5	79	84		
Decreased appetite					
Yes	45	21	66	*0,000*	*0,655*
No	5	79	84		
Fever					
Yes	44	16	60	*0,000*	*0,693*
No	6	84	90		
Night sweats without physical activity					
Yes	42	19	61	*0,000*	*0,624*
No	8	81	89		
History of Diabetes Mellitus (DM)					
Yes	19	18	37	*0,007*	*0,219*
No	31	82	113		
Elderly (Elderly)					
Yes	15	18	33	0,096	0,137
No	35	82	117		
Pregnant Mums					
Yes	6	8	14	0,431	0,065
No	44	92	136		
Discontinued Treatment					
Yes	4	3	7	0,173	0,112
No	46	97	143		

Source: Data processed, 2024

A total of 36 TB positive respondents aged ≤ 45 years and 14 respondents aged ≥ 46 years. A total of 100

respondents with TB negative TCM results with 78 respondents aged ≤ 45 years and 22 respondents aged ≥ 46 years. In conclusion, most respondents were ≤ 45 years old in both TB positive and negative respondents. The p value in statistical testing was 0.421. The p value = 0.421> 0.05. So it is concluded that there is no significant relationship between the age variable and the positive TCM results for TB in the Oesapa Health Centre working area in 2024.

A total of 24 respondents in the low education category were TB positive and 26 TB positive respondents were from the high education level category. A total of 61 TB negative respondents had a low level of education and 89 respondents in the high education level category. The results of statistical testing showed a p value = 0.199. The p value = 0.199>0.05. Thus it is concluded that there is no relationship between education level and positive TCM examination for TB in the Oesapa Health Centre working area in 2024.

A total of 32 TB positive respondents did not have a job and 18 TB positive respondents had a job. There were 50 TB-positive respondents who did not work and 50 other respondents had jobs. So, it was concluded that most TB positive respondents did not have a job. The statistical test results showed a p value of 0.106. The p value = 0.106>0.05. Therefore, there is no relationship between employment and TCM positive TB among respondents at Puskesmas Oesapa in 2024.

A total of 3 respondents with positive TCM TB test results had poor knowledge, while 47 other respondents had good knowledge. In the negative TB TCM examination results, 1 respondent was found to have poor knowledge and 99 other respondents had good knowledge about TB. It can be concluded that almost all respondents already have good knowledge about TB in both positive and negative TB respondents. The results of statistical testing found a p value of 0.074. The p value = 0.074>0.05, so there is no relationship between the level of knowledge of respondents and the results of positive TCM examination for TB in the working area of Puskesmas Oesapa in 2024.

Respondents with both TB-positive and TB-negative TCM test results had favourable attitudes. This is found from the data above, which shows that no respondents had an attitude that was not supportive of TB in both TB positive and TB negative respondents. Therefore, the p value or significance value cannot be measured.

There were 22 TB positive respondents who had poor sputum removal behaviour and 28 TB positive respondents who had good sputum removal behaviour. Meanwhile, 26 respondents with negative TCM examination results had poor behaviour and 74 others had good behaviour. Respondents with TB positive TCM examination results had more good behaviour, as did TB negative respondents. The statistical test showed a p value of 0.026. The p value = 0.026 <0.05. So it is concluded that there is a unidirectional relationship between the variable of sputum disposal behaviour and positive TCM results in the Oesapa Puskesmas work area in 2024. The rho value of 0.182 indicates a very weak correlation between the independent and dependent variables with a large effect of 3.31%. The direction of the correlation is positive so that any increase in poor sputum removal behaviour goes hand in hand with an increase in positive TCM.

Respondents with positive TCM results had smoking behaviour as many as 35 respondents and 15 positive respondents did not have smoking behaviour. Respondents with negative TCM results had 35 smokers and 65 non-smokers. It was concluded that most TB positive respondents had smoking habits and most TB negative respondents were respondents who did not have smoking behaviour. Statistical testing results showed a p value = 0.000. The p value = 0.000 <0.05. So it is concluded that there is a relationship between smoking behaviour and positive TB TCM examination among respondents in the Oesapa Puskesmas work area in 2024. The rho value on the smoking variable is 0.331. Thus the strength of the relationship between the independent and dependent variables is categorised as weak and the direction of the relationship between the two variables is positive, so it is concluded that any increase in the smoking variable will increase the results of positive TCM examination for TB. The value of R = 10.95%, then the smoking variable has an influence on the variable of positive TCM TB examination by 10.95%.

A total of 8 TB positive respondents had the habit of exercising once a week, 9 respondents had the habit of exercising 2-3 times a week and 33 TB positive respondents never / did not have the habit of exercising during their lifetime. TB negative respondents were found to have 28 respondents who exercised once a week, 24 respondents had the habit of exercising 2-3 times a week and 48 respondents never exercised. TB positive respondents were more likely to have no exercise habits, as was the case with TCM negative TB respondents. In the statistical test, the p value = 0.034 <0.05. The rho value = -0.173. It can be concluded that there is a very weak relationship between the variable of exercise habits and positive TCM TB, which has a negative value, which means that increasing exercise habits will reduce positive TCM TB in the Oesapa Puskesmas work area. The coefficient of determination R value is 2.99%, it is concluded that the effect of the independent variable on the dependent variable is 2.99%.

A total of 16 TB-positive respondents lived in densely packed houses and 34 TB-positive respondents lived in non-densely packed houses. Meanwhile, 23 TB-negative respondents lived in densely populated houses and 77 TB-negative respondents lived in houses that were not densely populated. It was concluded that both TB-positive and TB-negative respondents mostly lived

in houses in the non-dense category. Statistical testing results showed a p value = 0.239. The p value=0.239>0.05. So it is concluded that there is no relationship between residential density variables and positive TCM results among respondents in the Oesapa Health Centre working area in 2024.

There were 49 TB-positive respondents who received TB-related information at the health care facilities visited. There was 1 TB positive respondent who did not receive information about TB. Meanwhile, 97 TB negative respondents received information about TB and 3 other respondents did not receive TB information. Thus it was concluded that almost all respondents already had access to the availability of information obtained at the health facilities they visited. Statistical testing on the availability of information variable found p value = 0.722. P value = 0.722 >0.05. Thus, there is no relationship between the variable of information availability and the variable of positive TB TCM results in the Oesapa Health Centre working area in 2024.

A total of 89 respondents had cough symptoms with 50 respondents positive and 39 respondents negative. There were 61 respondents who did not have cough symptoms with negative TCM examination results. The statistical test results found p value = 0.000. P value = 0.000 <0.05. It is concluded that there is a variable relationship between cough symptoms and positive TB TCM results in the Oesapa Puskesmas work area. The rho value is positive 0.585 which indicates a unidirectional correlation, meaning that an increase in respondents with cough symptoms goes hand in hand with an increase in positive TCM results in respondents. The strength of the association of the independent and dependent variables is in the moderate category. The coefficient of determination is 34.22%. Thus the influence of the cough variable on the model is 34.22%.

TB positive respondents had 43 respondents with symptoms of breathlessness and 7 respondents had no symptoms of breathlessness. TCM negative respondents had symptoms of shortness of breath as many as 20 respondents and 80 respondents did not have symptoms of shortness of breath. The p value is 0.000. P value = 0.000 <0.05. The positive rho value is 0.630. Thus it is concluded that there is a moderate relationship between the variable symptoms of shortness of breath and positive TCM TB results with a unidirectional relationship. That is, an increase in symptoms of shortness of breath in respondents along with an increase in positive TCM results in respondents. The coefficient of determination is 39.69%. Then the influence of the shortness of breath symptom variable is 39.69% in the model.

A total of 66 respondents had symptoms of weight loss with 45 respondents positive for TB and 21 respondents negative for TB. There were 84 respondents who did not have symptoms of weight loss with 5 respondents positive for TB and 79 respondents negative for TB. Statistical testing showed p value = 0.000. P value = 0.000 <0.05. Therefore, there is a relationship between the independent variable and the dependent variable. The rho value = 0.655 and is positive. Then the strength of the association between the two variables is categorised as moderate/moderate with a unidirectional relationship. This means that the increase in symptoms of weight loss is in line with the increase in positive TCM results for TB in the community in the Oesapa Puskesmas working area in 2024. The coefficient of determination is 42.90%. So the influence of the weight loss symptom variable on the model is 42.90%.

A total of 66 respondents had symptoms of decreased appetite, 45 of whom were TB positive and the remaining 21 respondents were TB negative. There were 84 respondents who did not have symptoms of decreased appetite, 5 respondents were positive for TB and 79 respondents were negative for TCM. The p value was 0.000. P value = 0.000 <0.05. It is concluded that there is a relationship between the variable of decreased appetite symptoms and the variable of positive TCM results for TB. The rho value = 0.655 which is positive. This means that the strength of the association between the two variables is categorised as moderate/medium and is unidirectional. This means that every increase in appetite symptoms decreases along with an increase in positive TCM TB results in the community in the Oesapa Puskesmas working area in 2024. The calculation of the coefficient of determination is 42.90%. Thus the influence of the variable appetite symptoms decreased by 42.90% in the model.

A total of 60 respondents had symptoms of fever with 44 respondents positive for TB and 16 respondents negative for TB. There were 90 respondents who did not have symptoms of fever with the results of TCM examination positive for TB as many as 6 respondents and 84 other respondents negative for TCM TB. The statistical test results obtained p value = 0.000. P value = 0.000 <0.05. Thus, there is a relationship between the variable of fever symptoms and the variable of positive TB TCM results in the community at Puskesmas Oesapa in 2024. The rho value = 0.693 and is positive. The strength of the association between the two variables is moderate or moderate with a unidirectional relationship. This means that any increase in fever symptoms goes hand in hand with an increase in TB positive TCM results. The calculation of the coefficient of determination is 48.02%. Then the influence of the fever symptom variable on the model is 48.02%.

There were 61 respondents who had symptoms of night sweats without physical activity, of which 42 respondents were TB positive and 19 were TB negative. There were 89 respondents who did not have symptoms of night sweats without physical activity, with 8 respondents positive for TB and 81 respondents negative for TB. Statistical testing obtained a p value = 0.000. P value = 0.000 <0.05. So there is a relationship

between night sweats without physical activity with positive TCM results in the Oesapa Puskesmas work area in 2024. The rho value = 0.624 and is positive. So, it means that the strength of the relationship between the two variables is in the medium/moderate category with a unidirectional relationship direction. Therefore, every increase in respondents with symptoms of night sweats without physical activity along with an increase in positive TCM examination results for TB. The coefficient of determination was 38.93%. So the influence of the variable symptoms of sweating at night without physical activity is 38.93% in the model.

There were 37 respondents who had a history of DM with 19 respondents positive for TB and 18 respondents negative for TB. A total of 113 respondents did not have a history of DM and 31 of them were positive for TB and 82 were negative for TB. Statistical testing found a p value of 0.007. P value = 0.007 <0.05. Thus, there was a significant association between the variable history of DM and positive TB TCM results in the Oesapa Health Centre working area in 2024. The rho value on this variable is 0.219 and is positive. Therefore, the strength of the association is very weak and the correlation is unidirectional. This means that the incidence of DM increases along with the positive TB test results. The coefficient of determination is 4.79%, so the influence of the DM history risk factor variable is 4.79% in the model.

The number of elderly respondents was 33 respondents with 15 TB positive respondents and 18 TB negative respondents. There were 117 non-elderly respondents with 35 TB positive and 82 TB negative respondents. The most respondents were non-elderly respondents in both positive and negative TB TCM examination results. Statistical tests showed a p value of 0.096. P value = 0.096 >0.05. Thus, there is no relationship between the risk factor variables of the elderly with positive TCM results in the Oesapa Puskesmas work area in 2024.

There were 14 pregnant women who were used as respondents with 6 respondents positive for TB and 8 respondents negative for TB based on TCM examination. There were 136 respondents who were not pregnant with the results of TCM examination 44 respondents were positive and 92 other respondents were negative for TB. The statistical test results showed a p value = 0.065. So the p value = 0.065>0.05. Thus it is concluded that there is no relationship between risk factors for pregnant women and positive TCM results for TB in the Oesapa Health Centre working area in 2024.

A total of 7 respondents who had TB treatment but did not complete it, 4 respondents were positive and 3 respondents had negative TCM test results. Meanwhile, there were 143 respondents who had never had TB treatment before, with 46 respondents positive and 97 respondents negative for TB. Statistical testing results showed p value = 0.173. Therefore, the p value = 0.173 >0.05. Thus, it is concluded that there is no relationship between the variable of having ever received TB treatment but not completing it with positive TB TCM results in the Oesapa Puskesmas work area in 2024.

Multivariate Analysis

In this study, the hypothesis is accepted if the p value <0.05. The data above shows that variable X2 has a p value = 0.017 and variable X8 has a p value = 0.028. Both variables are variables of smokers or respondents who have a smoking habit and variables that have symptoms of fever. So it is concluded that there is an influence of the smoker variable and the fever symptom variable with positive TCM TB results. Thus the results of the interpretation of the Odd Ratio of the two significant variables are as follows:

1. If smokers increase by 1, the TCM of TB positivity increases by 4.469 times.
2. If the fever symptom increases by 1, the TB positive TCM increases by 8.259 times.

Table 3. Variables in the Equation Table

Variables	B	S.E	Wald	df	Sig.	Exp(B)	95.0% CI for EXP (B) Lower	Upper
X1	-0,968	0,690	1,969	1	0,161	0,380	0,098	1,468
X2	**1,497**	**0,626**	**5,725**	**1**	**0,017**	**4,469**	**1.311**	**15,236**
X3	0,176	0,375	0,221	1	0,638	1,193	0,572	2,486
X4	18,912	4940,017	0,000	1	0,997	163411552,8	0,000	0
X5	0,418	0,825	0,257	1	0,612	1,519	0,302	7,655
X6	0,494	1,017	0,236	1	0,627	1,639	0,223	12,025
X7	1,604	1,079	2,207	1	0,137	4,971	0,599	41,228
X8	**2,111**	**0,958**	**4,854**	**1**	**0,028**	**8,259**	**1,263**	**54,033**
X9	-0,959	1,180	0,661	1	0,416	0,383	0,038	3,871
X10	0,355	0,641	0,307	1	0,579	1,427	0,406	5,013
Consent	-25,470	4940,017	0,000	1	0,996	0,000		

Notes: X1= Behaviour; X2= Smoker; X3= Exercise habit; X4= Cough; X5= Shortness of breath; X6= Weight loss; X7= Loss of appetite; X8= Fever; X9= Night sweats without physical activity; X10= History of DM

DISCUSSION

Influence of Gender on TB Positive TCM Results

The results of this study showed that TB-positive respondents based on TCM examination were more men than women. In line with research by Sunarmi and Kurniawaty (2022) found that pulmonary tuberculosis disease tends to be higher in men than women [38]. Women pay more attention to their health than men, therefore women are less susceptible to pulmonary TB disease.[38]

Other studies have also found the characteristics of the percentage of men more than women, namely 65.22% who are male sufferers.[31]The results of multivariate analysis of gender obtained an OR = 4.772 (CI: 2.260-10.076), meaning that male respondents will be at risk of developing pulmonary TB 3.8 times compared to female respondents.[11] Screening research conducted on homeless populations in Korea found an influence of gender on the incidence of TB with a risk of 0.65 times in women [15]. In contrast to the results of this study which found no effect of gender on the incidence of TB although the percentage was more in the male gender. Men tend to be outside the home more often due to the demands of their work. This makes it possible for TB transmission to occur when meeting with many people from different circles. Men also tend to have risky lifestyles such as smoking, drinking alcohol and staying up late, which can weaken the body's immunity. With a weakened immune system, it is easier to transmit diseases, especially TB.

Influence of Age on TB Positive TCM Results

This study found that most TB-positive respondents based on TCM examination were ≤ 25 years old and 26 - 35 years old. These age intervals are productive ages. Productive age is the age when a person is actively moving out of the house due to work demands. Heavy work demands, not balanced with eating healthy food and regular exercise will cause a decrease in endurance. In line with other studies that found the majority of respondents came from the productive age group, namely 20-30 years old.[24] Pulmonary tuberculosis disease is most often found in the productive age, economically around 15-49 years of age.[44] The results of cohort study research in England found an age relationship with the incidence of TB.[26] Another study also found an association between age (p-value = 0.003) and pulmonary tuberculosis. Meanwhile, in contrast to the results of research conducted by researchers in the working area of Puskesmas Oesapa who found no association between age and positive TCM examination results for TB.

Influence of education level on TB-positive TCM results

The results of this study showed that most respondents had a fairly good education, but most of the TB-positive respondents had a high level of education, namely high school to college graduates. In line with other studies that have the most TB respondents at the high school education level of 52.7%.[41] Another study also found that most respondents with TB had a high level of education with a percentage of 82.9%.[22,33] Bivariate and multivariate testing found no effect of education on positive TCM TB results. The difference between theory and conditions in the field is certainly inseparable from various regional characteristics that contribute greatly to the spread of the disease. The inability of the community to lead a clean and healthy lifestyle is supported by the fairly dense settlement conditions in the Oesapa area. This certainly supports the transmission of disease from person to person.

Influence of Occupation on TB Positive TCM Results

The results showed that there was no effect of occupation on the positive results of the Molecular Rapid Test for TB in the working area of Puskesmas Oesapa in 2024. This is in line with the results of a previous study that found no effect of occupational variables on tuberculosis diagnosis in Indramayu Regency in 2022.[40]In this study, the employment variable did not contribute much to the spread of tuberculosis disease because there are still other factors such as a stable immune system that does not allow TB transmission.

Influence of Knowledge with TB Positive TCM Results

Most of the respondents interviewed already had good knowledge of Tuberculosis disease. This is evidenced through the research data found that 94.0% of TB-positive respondents had good knowledge about TB. However, 6.0% had poor knowledge. The results of the search for each question answered by respondents found that there were about 6.0% who answered that TB disease was a disease caused by blood deficiency and as many as 38.0% of respondents answered that TB was caused by cigarette smoke. A previous study revealed erroneous beliefs about the causes of TB in pastoral communities in Ethiopia which showed significant knowledge gaps about the causes, signs and symptoms, modes of transmission, prevention, and treatment of TB among community members.[27]These findings are consistent with studies conducted in rural Uganda where heredity, heavy labour, sharing cutlery, and smoking were documented as causes of TB. [7]

The results of statistical testing found no relationship between knowledge and TCM-positive TB in the working area of Puskesmas Oesapa. In contrast to previous research, there is a significant relationship between knowledge and the incidence of pulmonary TB transmission, where respondents with poor knowledge have a 5.13 times greater risk of contracting pulmonary TB compared to respondents with good knowledge in the Bandarharjo Puskesmas working area in Semarang. [47]

Influence of Attitude with TB Positive TCM Outcome

Respondents' attitudes towards Tuberculosis disease prevention were overall quite good. This good attitude is certainly obtained from the experience experienced by the respondents. Most of the respondents in this study were people who had contact with TB patients. In another study on respondents' attitudes towards TB prevention at Puskesmas Sukaraja in 2021 mostly had poor attitudes but good TB prevention behaviour (61.5%).[32]The results of this study indicate that attitudes that support the prevention of tuberculosis are not necessarily aligned with the behaviour of preventing tuberculosis. This is evidenced by the number of respondents who have a favourable attitude but TB cases are still high. Attitudes that support TB prevention are certainly influenced by good knowledge about TB to form positive perceptions.

Influence of Sputum Disposal Behaviour on TB Positive TCM Results

One of the transmissions of pulmonary TB is the inhalation of sputum/phlegm by TB patients who have dried and evaporated into the air by other people who are around them they can contract Pulmonary TB disease as well. 6 Disposing of sputum or spitting in any place can increase the spread of pulmonary TB bacteria because TB can live and has the opportunity to spread if sputum or saliva is disposed of in any place. [46,16,14]. This finding found as many as 48 respondents still dispose of sputum in any place and do not follow the recommendations to dispose of sputum properly. The results showed that 22 respondents were positive for TB out of 48 respondents who still discharged sputum not as recommended. Most of the respondents had not discharged phlegm in any place and followed the recommendation to spit properly. This is consistent with previous research which found a higher percentage of good sputum disposal behaviour, namely 76.0%. [6] In contrast to research conducted in Papua, it was found that most respondents with TB had poor sputum disposal behaviour.[46] Other research findings show that there are still many respondents, with a percentage of 69.8% of respondents with TB having poor TB prevention behaviour.[17] The results of this finding also show a significant relationship between the sputum removal behaviour variable and the positive TB molecular rapid test results with a very weak correlation strength (r = 0.182) and its influence in the model of 3.31%. This is in line with other findings that found an association between sputum disposal behaviour and TB incidence in Papua [46].

Influence of Smoking Behaviour with TB Positive TCM Results

Smoking is one of the factors that can increase the risk of pulmonary TB due to impaired mucosal secretion clearance. The nicotine content in cigarettes can reduce the production of TNF-α which functions to activate macrophages and CD4+ lymphocytes and will reduce the immune response. Clearance by attenuated mucosal secretions, reduced phagocytic ability of alveolus macrophages decreased immune response and CD4 + cause colonisation of TB germs to become easier. [36] In this study, 70 respondents were found to be active smokers with 35 of them positive for TB. Previous findings found that the distribution of respondents based on smoking status was highest among respondents in the active smoker category at 51.6%.[39] Meanwhile, another study found that the characteristics of respondents based on smoking habits who suffered from pulmonary tuberculosis 38 respondents (73.1%) with bivariate analysis showing a relationship between smoking and pulmonary tuberculosis status, where respondents who smoked had a 3.701 greater chance of developing pulmonary tuberculosis compared to those who did not smoke.[18] In line with the findings of researchers who found a significant relationship between smoking behaviour and positive TB molecular rapid test results with a weak correlation (r = 0.331). However, the direction of the relationship is positive, which means that an increase in smoking behaviour goes hand in hand with an increase in TB diagnosis in the community in the Oesapa Puskesmas working area. Smoking behaviour also increases the risk of developing pulmonary TB by 5.156 times. Respondents who have a smoking habit will aggravate health conditions and can increase relapse and failure in TB treatment, especially in people with tuberculosis.[13] The results of other studies found a significant influence of smoking variables with TB patients and control groups. Multivariate testing also showed a significant effect of family variables with a history of smoking with the TB case group and control group (OR 2.8, 95% CI: 1.1-8.4), and a smoking history of more than 10 years (OR = 1.6, 95% CI: 1.2-9.8).[1]Comparable to research conducted at Puskesmas Oesapa found a risk of TB of 4.469 times in respondents who smoke compared to respondents who do not smoke.

Influence of Exercise Habits with TB Positive TCM Results

The results of this study found that 81 respondents never exercised, including 33 respondents who were positive for TB. As many as 33 respondents who exercised 2 - 3 times a week, there were 9 positive respondents and there were 36 respondents who exercised once a week, there were 8 positive respondents. Thus, the bivariate test showed a negative relationship where the decreasing frequency of exercising a person will increase the positive TB TCM test results. Another study comparing case and control groups found that more case groups did not engage in healthy behaviours of exercise (physical activity) than control groups (81.48%).[30] Exercise for people with TB can reduce the risk of re-infection by Mycobacterium Tuberculosis. Exercise can also strengthen the immune system, which can help protect

individuals from TB disease or aid recovery for those already infected.[12] Multivariate testing found no effect of exercise on TCM-positive TB results. Previous research found an effect of exercise habits with a reduced risk of TB transmission.[5]

Influence of Residential Density with TB Positive TCM Results

In the provisions of the health requirements of residential houses according to Kepmenkes No. 829/Menkes/SK/VII/1999, the minimum bedroom area is 8 m² and it is recommended that no more than 2 people sleep. If these requirements are not met then the house is categorised as crowded. Occupancy density will facilitate the transmission of disease to fellow family members living in the same house. Tuberculosis will be easily transmitted to other family members when the body condition is declining. The more occupants, the lower the free oxygen level in the room. [35] The results of this study found that most respondents lived in houses that were not densely occupied. The findings in the Oesapab Health Centre working area showed no effect of occupancy density with positive TB TCM test results. In previous studies, there was an effect between occupancy density and TB incidence (P-value = 0.014). [35]

Influence of Information Availability on TB Positive TCM Results

A total of 92.0% of respondents found the availability of information boards/brochures/leaflets on TB on the information board at the health facility visited. A total of 98.0% of health workers explained TB disease and 96.0% of respondents could ask questions about TB information to health workers. A total of 146 respondents had information available at the health facility visited with 49 respondents being TB positive and 4 respondents not, with 1 respondent being TB positive and 3 being TB negative. Posting leaflets/brochures on TB can improve understanding of the causes, symptoms, transmission and management of TB at the individual level. The availability of information will support people with TB in obtaining TB health services.[34] With information about TB, patients will immediately check at the nearest health facility so that they can get immediate treatment.

Influence of cough symptoms on TCM-positive TB results

Bivariate testing in this study found a significant association between cough symptoms and the incidence of TB confirmed by Molecular Rapid Test examination (p-value = 0.000 < 0.000; r = 0.585). The strength of association of the cough variable is categorised as moderate and has a unidirectional relationship. Thus, an increase in cough symptoms will be accompanied by an increase in TB cases. However, multivariate testing found no significant effect of cough symptoms with TB. When people cough, they can produce 3000 sputum splashes that evaporate into the free air which can survive in room temperature for about a few hours and if inhaled, people can be infected. However, sputum droplets can be reduced if there is sufficient ventilation or airflow and direct sunlight. [22] One cough can produce about 3,000 sputum splashes containing 0-3,500 M. tuberculosis bacteria. Meanwhile, sneezing can release as much as 4,500 - 1,000,000 M. tuberculosis. [21] According to Lee et al., (2020) TB patients tend to cough more often when compared to non-TB patients. The severity of a TB patient can also be seen through the severity of his cough. [23]

Influence of Shortness of Breath Symptoms with TB Positive TCM Results

The results of this study found a relationship between shortness of breath and positive TCM examination results for TB (p-value = 0.000 <0.005; r = 0.630). The effect of shortness of breath variable was 39.69% on the dependent variable in this study. Multivariate testing using the logistic regression test found no effect of these variables on TB. Shortness of breath is a condition when a person feels they do not have enough air, cannot breathe freely or feels breathless in any condition whether walking, running or even sitting. One of the symptoms of TB is shortness of breath. This occurs due to damage to the tissue in the lungs.

Influence of weight loss symptoms on TCM-positive TB result

TB bacterial infection can cause a person's body to experience increased metabolism and reduce the appetite of the sufferer. This situation makes the energy reserves in the body even less, triggering significant weight loss. The results of this study found a relationship between symptoms of weight loss and TB patients (p value = 0.000 < 0.05; r = 0.655) with an influence of 42.90% in the model. The strong correlation between tuberculosis reactivation and body mass index (BMI) in patients with pulmonary tuberculosis suggests that low BMI predisposes to TB reactivation in the lungs. (Casha & Scarci, 2017) [9]. Reinforced by research conducted in Riau which found a relationship between body mass index and the incidence of TB. [4]

Effect of Decreased Appetite with TB Positive TCM Result

Several hormonal factors can affect appetite. One hormone that plays a role in appetite suppression and is often implicated in conditions such as TB is **leptin. In** TB patients this hormone will increase. Meanwhile, the hormone ghrelin increases appetite. As the leptin hormone increases, the ghrelin hormone decreases. This is supported by previous research that found lower ghrelin levels in malnourished cases compared to well-nourished cases. In addition, it was also found that leptin concentrations decreased in TB patients as treatment progressed.[10] This finding is in line with the researcher's

findings, which found 1 respondent who discontinued treatment due to loss of appetite. The results of this study found an association between decreased appetite and positive TCM examination results for TB (p-value = 0.000 < 0.05; r = 0.655) with an effect of 45.42% on the model.

Influence of fever symptoms on TCM-positive TB result
The results showed a significant association of fever variables with TB incidence at Puskesmas Oesapa (p-value = 0.000 <0.05; r=0.693) with an influence on the model of 48.02%. Multivariate testing also showed that fever had an 8.259 times influence on the positive outcome of TB based on TCM examination. TB patients experience fever for several reasons related to the body's response to Mycobacterium tuberculosis infection. When TB bacteria infect the body, the immune system reacts to fight the infection. This process involves the release of chemicals such as cytokines (e.g., interleukins and tumour necrosis factor), which can increase body temperature and cause fever.

Influence of Night Sweats on TCM positive TB results
Night sweats are a significant symptom in people with TB that not only helps in diagnosis but also affects the patient's quality of life and disease management. Although it is largely unclear why fever associated with TB occurs primarily at night (hence the term "night sweats"), its occurrence has been attributed to the body's circadian rhythms.2[5]
Night sweats may indicate that the body is trying to fight an active infection. This can be an indicator that the TB disease is still active and requires proper treatment. Excessive sweating can lead to fluid and electrolyte loss, which may require medical attention to prevent dehydration and electrolyte imbalance. Night sweats in TB patients are often one of the main symptoms indicating active infection and can help in the diagnosis and treatment assessment of the disease. The results of this study found that there was a relationship between night sweats and positive TCM examination results for TB in the Oesapa Puskesmas work area (p-value = 0.000 <0.05; r=0.624). The effect of the night sweats variable on TCM-positive TB was 38.93%.

Influence of Diabetes Mellitus Risk Factors with TB Positive TCM Results
Diabetes mellitus is an important risk factor for TB and can affect clinical and treatment response and is a risk for drug-resistant TB (MDR TB). (Arliny, 2015) [3]. Diabetes mellitus weakens the immune system, increasing the risk of transmission when compared to non-DM patients. The results of research in the Puskesmas Oesapa work area found that most of the respondents who were positive for TB were non-DM respondents. This is because most of the respondents are young people who are mostly students. Meanwhile, almost all patients over 45 years of age have comorbid DM. The results of bivariate statistical testing found an association of DM history with TB incidence at Puskesmas Oesapa. In line with previous research, it was found that most TB patients had a history of DM, so it is certain that DM is a predisposing factor for TB.[2] Another study showed a significant association between type 2 diabetes mellitus and extensive lesion pulmonary tuberculosis (p=0.03). Type 2 diabetes mellitus can increase the risk of extensive lesion pulmonary tuberculosis status by 5.25 times.[42]

Influence of Elderly Risk Factors with TB Positive TCM Results
Research in the working area of Puskesmas Oesapa found that 33 elderly out of 150 respondents interviewed, 15 respondents were positive for TB. However, the results of this study showed no association between the elderly and the incidence of TB at Puskesmas Oesapa. Another study mentioned that the TB epidemic is most prevalent in elderly people and there is a progressive increase in the number of TB notifications with age. Most cases of TB in the elderly are associated with reactivation of dormant lesions.[8] TB is very easily contracted in someone with advanced age (aged >60 years) because the elderly experience an aging process which results in decreased organ function and endurance, making them more susceptible to infection with various infectious and non-communicable diseases.

Influence of Risk Factors for Pregnant Women with TB Positive TCM Results
Tuberculosis in pregnant women has clinical symptoms similar to tuberculosis in non-pregnant women. Diagnosis may be difficult in the early symptoms as they are not typical. Symptoms of tuberculosis such as cough, fever and fatigue are considered as normal signs of pregnancy so treatment may be delayed. During pregnancy, a woman's immune system changes to support the growth and development of the foetus in the womb. These changes can make pregnant women more susceptible to infectious diseases, including TB. Pregnant women infected with TB disease can have complications for both mother and foetus such as premature birth, low birth weight (LBW), and increased maternal risk. Tuberculosis in pregnancy can pose a significant risk of morbidity for both the pregnant woman and the foetus if not diagnosed and treated promptly.[29]This study found no association between pregnant women's risk factors and TB-positive TCM test results (p-value = 0.431>0.05; r=0.065). Even so, TB cases in pregnant women have a huge risk to pregnant women and fetuses, so pregnant women must be vigilant in maintaining a healthy body to support the growth and development of the fetus in the womb.

Influence of Risk Factors for Dropping Out of Treatment with TB-Positive TCM Results
Discontinuing treatment before the prescribed period can cause TB bacteria that do not die to develop

resistance. Incomplete drug use can increase the risk of death from TB.[43] Incomplete treatment is certainly influenced by many factors. The results of previous studies found that incomplete TB treatment was due to low patient motivation (p-value 0.046 and 0.004), family motivation (p-value 0.03 and 0.05), and severe (p-value 0.01) and mild (p-value 0.04) OAT side effects. [28] Another factor is due to boredom with long treatment, side effects of anti-tuberculosis drugs or feeling better after the initial stage (first 2 months) of treatment. Other causes include economic factors and transport barriers to health services. The results of this study found that there was no relationship between the variable of having been treated but not completed with a positive TB TCM examination result.

CONCLUSIONS

The conclusion is that the variables that have a significant effect in the model are smoking behaviour and fever on TB-positive TCM test results in the Oesapa Puskesmas working area in 2024.

Advice

These results found that some respondents were still mistaken about the causes of TB, so there is a need to educate the general public as well as teach proper coughing etiquette and how to dispose of sputum as recommended to avoid transmission. There is a need to socialise a Clean and Healthy Lifestyle in the community in an effort to improve health.

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Competing Interests

The authors have no competing interests to declare.

Ethical Approval

The study was approved by the appropriate ethics committee and conducted according to relevant guidelines and regulations.

Informed Consent

Not applicable.

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