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ԲԱՆԲԵՐ ՍՏՈՄԱՏՈԼՈԳԻԱՅԻ ԵՎ ԴԻՄԱԾՆՈՏԱՅԻՆ ՎԻՐԱԲՈՒԺՈՒԹՅԱՆ
Գիտագործնական հանդես

Գլխավոր խմբագիր - Հակոբյան Գ.Վ.
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RESEARCH ARTICLE

USE OF THE ELECTRICAL DEVICE ON DENTAL IMPLANT'S BACTERIAL BIOFILM: A PRELIMINARY IN VITRO STUDY

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Abstract

Background. Mucositis and peri-implant disease are pathological conditions found following bacterial colonization on the peri-implant soft tissues and on the implant fixture during implant-prosthetic rehabilitation, from single edentulism to full-arch rehabilitation.
The therapeutic approaches to the two pathological conditions use surgical and non-surgical therapeutic protocols, with the aim of eliminating the bacterial biofilm from the implant surface, through the use of mechanical, chemical or photodynamic agents.
The aim was to evaluate the effect of the electric field generated by the Ximplant machine on the bacterial load and on the biofilm grown on the dental implants.
Materials and methods. Twenty-eight dental implants were contaminated with the saliva of a donor, and subsequently fifteen implants were treated with the electric field generating machine while twelve were not treated. The bacterial biofilm was then measured by resazurin assay, both on treated and untreated implants.
Results. The results revealed a difference between treated and untreated implants in terms of biofilm activity,as assessed by color change using the resazurin assay. Treated implants (n = 15) showed no color change across all observation time points (2 hours, 1 day, 2 days, 3 days), indicating an absence of bacterial activity or residual biofilm. Conversely, all untreated implants (n = 12) exhibited a consistentcolor change starting at 2 hours, suggesting persistent biofilm activity. A sterile implant used as a negative control (n = 1) showed no color change throughout the experiment, confirming the absenceof contamination
Conclusion. The study showed preliminary success of the electrofield in reducing microbial populations and destroying clinical biofilm, compared to a sterile implant as a control.

Keywords: Mucositis, peri-implantitis, bacterial load, dental implant

INTRODUCTION

Implant-prosthetic rehabilitation is the treatment of choice for functional and aesthetic restoration, both in cases of single edentulism and in cases of total arch rehabilitation [1-5].

Mucositis and peri-implant disease are pathologies that can be encountered during dental implant rehabilitation [6-10]. Mucositis is characterized by the distinctive signs of inflammation with the absence of radiographically visible loss of supporting alveolar bone. Peri-implant disease is also characterized by purulent exudate and radiographic signs of peri-implant bone loss. Peri-implant bone loss can have a bacterial etiology, determined by the action of the peri-implant bacterial biofilm, as well as by intraoperative and prosthetic surgical causes. This type of pathological bone resorption must be differentiated from biological factors, such as physiological remodeling or mechanical stress. The inflammatory-bacterial etiology determines the resorption between the bone-implant interface and its consequent loss [11-16].

In literature, the therapeutic strategies for the resolution of these two pathological conditions range from non-surgical to surgical treatment and aim at the elimination of the surface biofilm, through mechanical and/or chemical agents[7]. As demonstrated in many scientific works, these techniques present critical issues related to the partial elimination of bacteria and surface contaminants [46-52]. In recent years, the metallurgical industry has conducted studies on the electrochemical cleaning of metal surfaces to eliminate and decontaminate the biofilm and prevent its formation by acting on the electrochemical bonds of the biofilm layer, also breaking the bonds that determine adhesion to the surfaces[17]. This new technique would allow the decontamination of the surfaces of dental implants while maintaining their shape intact, unlike current mechanical procedures [10].

The aim of the work was to evaluate the effect of the electric field on the reduction and decontamination of bacterial plaque on the surface of the implant.

Materials and methods

The study protocol applied, regarding both the bacterial contamination of the fixtures and their electrical treatment, follows Falisi et al. [54].

Bacterial contamination of dental implants.

Twenty-eight grade 4 titanium dental implants (sandblasted and double acid etched) with a length of 13 and a diameter of 4.0 (In-Kone® by Global D, France) were used.
This study was conducted in accordance with the principles and guidelines of the Declaration of Helsinki. Five ml of saliva was collected from the volunteer patient with active peri-implant disease, with signs of inflammation, suppuration and radiographic signs of peri-implant bone loss. On the morning of collection, he was asked not to practice his usual home oral hygiene routine. Implant contamination was performed using a bacterial culture in the logarithmic phase of growth, prepared by culturing ten colonies of saliva in 5 ml of Brain Hearth Infusion (BHI) broth (Oxoid ThermoFisher Scientific, USA) supplemented with 5% defibrinated sheep blood in an anaerobic environment for 96 hours at 37 °C. The bacterial suspension was adjusted to the OD of 0.5 McFarland scale and subsequently diluted 1:1000. Bacterial biofilm formation on the implants occurred by incubating the devices in a sterile vial (Eppendorf Safe-Lock Tubes, Eppendorf Italia) with 900 µL of bacterial suspension prepared as described above. The samples were incubated in a vertical position for 48 h at 37 °C. After incubation, the implants were washed three times in a sterile 0.9% NaCl solution to remove the planktonic form of non-adherent bacteria.

Electrical treatment of implants.

After bacterial contamination, five implants were transferred to the treatment chamber with the addition of 100 µl of 0.9% NaCl solution and treated using the “Peri-implantitis Protocol” of the X-IMPLANT instrument (LED S.P.A., Aprilia, Italy) (fig 1, 2).

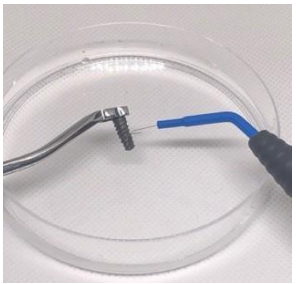




Fig.1 Treatment chamber **Fig.2** Device

This protocol consisted of four cycles of electrical current (alternating electrical current at 625 kHz, 260 Vpp, 15 W and 180 mA) performed on the implant according to the programmed times of the machine, the electrode was positioned in 4 tangential positions peripherally at 90 ° from the previousposition. Once the treatment phase with the Ximplant instrument was completed, the implants were further washed with 0.9% NaCl solution. Four implants were not treated. One implant was sterile and incubated with 900 µl of BHI was used as a negative control. Both treated and untreated implants were added to a reagent, resazurin (Labbox italia srl) and incubated for visual evaluation at 2 hours, one day, two days and the final third day of theexperimental procedures[19] (Table 1).

Table 1. Row data. Negative = no color change; Positive= color change

Implants #	After 2 hrs	After 1 day	After 2 days	After 3 days
C 1	Negative	Negative	Negative	Negative
2	Negative	Negative	Negative	Negative
3	Negative	Negative	Negative	Negative
4	Negative	Negative	Negative	Negative
5	Negative	Negative	Negative	Negative
6	Negative	Negative	Negative	Negative
7	Negative	Negative	Negative	Negative
8	Negative	Negative	Negative	Negative
9	Negative	Negative	Negative	Negative
10	Negative	Negative	Negative	Negative
11	Negative	Negative	Negative	Negative
12	Negative	Negative	Negative	Negative
13	Negative	Negative	Negative	Negative
14	Negative	Negative	Negative	Negative
15	Negative	Negative	Negative	Negative
16	Negative	Negative	Negative	Negative
17	Positive	Positive	Positive	Positive
18	Positive	Positive	Positive	Positive
19	Positive	Positive	Positive	Positive
20	Positive	Positive	Positive	Positive
21	Positive	Positive	Positive	Positive
22	Positive	Positive	Positive	Positive
23	Positive	Positive	Positive	Positive
24	Positive	Positive	Positive	Positive
25	Positive	Positive	Positive	Positive
26	Positive	Positive	Positive	Positive
27	Positive	Positive	Positive	Positive
28	Positive	Positive	Positive	Positive

Statistical analysis

Descriptive statistics was performed. Chi-squared test was used to assess significant differences between the two groups (treated vs not treated) in each reference time with $p<0.05$.

Results

The results revealed a difference between treated and untreated implants in terms of biofilm activity, as assessed by color change using the resazurin assay. Treated implants (n = 5) showed no color change across all observation time points (2 hours, 1 day, 2 days, 3 days), indicating an absence of bacterial activity or residual biofilm. Conversely, all untreated implants (n = 4) exhibited a consistent color change starting at 2 hours, suggesting persistent biofilm activity. A sterile implant used as a negative control (n = 1) showed no color change throughout the experiment, confirming the absenceof contamination (fig. 2).

	T1=after 2hr		
PP	Negative	Positive	Total
No	0	12	12
Yes	15	0	15
Total	15	12	27

	T2=after 1day		
PP	Negative	Positive	Total
No	0	12	12
Yes	15	0	15
Total	15	12	27

	T3=after 2 days		
PP	Negative	Positive	Total
No	0	12	12
Yes	15	0	15
Total	15	12	27

	T4 after 3 days		
PP	Negative	Positive	Total
No	0	12	12
Yes	15	0	15
Total	15	12	27

Fig. 2. Contingency tables. PP= peri-implantitis protocol yes/no.

The χ^2test demonstrated significant differences between treated and untreated groups at all time points, with $\chi^2 = 9.000$, $p = 0.003$. These findings confirm the effectiveness of the electric field treatment in significantly reducing bacterial activity. (Table 2).

Table2.Chi-square analysis.dF=degree of freedom

Time	χ^2 value	dF	P value
T1 =after 2 hrs	9000	1	0.003
T2 = after 1 day	9000	1	0.003
T3= after 2 days	9000	1	0.003
T4= after 3 days	9000	1	0.003

The absence of biofilm activity in treated implants contrasts sharply with the consistent biofilm activity in untreated ones.

Table 1 and Figure 1 summarize these findings, illustrating the significant difference in bacterial activity between the two groups. In conclusion, all treated implants did not show any color change, as the control sterile implant and all not-treated implants showed a color change already after two hours.

As demonstrated by scientific studies on biofilm, the presence of bacteria leads to the formation of biofilm on all surfaces, both biological and non-biological [12-15]. The first layer of biofilm to form is made up of beneficial bacteria called commensals. Due to changes in the intraoral habitat and the reduced host response, a state of dysbiosis is triggered that determines a shift of the commensal microbial flora towards the development of pathogenic species. Dysbiosis causes an increase in the production of inflammatory mediators, which induces the production of toxic products in the host cell that in turn lead to the destruction of the tissues around the implant [43-46]. In the literature, several surgical and non-surgical strategies have been introduced for the elimination of pathological biofilm from surfaces. [20-24]. Both are based on periodontal treatments and prevention because it is considered essential to give the patient the appropriate hygiene instructions to reduce the bacterial load while maintaining healthy peri-implant tissues [25-27].

In some scientific works in which the use of oral antiseptics such as 12% chlorhexidine was used after adequate mechanical debridement, it did not improve the scores of gingival bleeding after probing (BOP) compared to the control groups in which only mechanical debridement was used.

Even the potential beneficial effects (reduction of BOP and deep bleeding) hypothesized using systemic antibiotics (azithromycin) failed three/six months after treatment, as well as the use of probiotics had no benefit compared to mechanical therapy[28, 29].

On the other hand, the use as an alternative to mechanical therapy such as the use of ultrasonic instruments, glycine spray sandblasting or YAG laser has a good clinical outcome with BOP reduction, compared to mechanical debridement alone [40,43]. The use of both photonic and laser techniques, however, mostly control the progression of peri-implant pathology rather than resolve it [30,31].

The poor results of bacterial decontamination compared to these techniques could be attributed to the difference in the titanium surface compared to that of the dental root. This implies that the re-osseointegration phase is deficient with the interposition of fibrous tissue between the bone and the implant as demonstrated by histological studies [32, 33]. A strategy that seems to show advantages in the prevention and treatment of peri-implantitis is the ultraviolet (UV) photofunctionalization of the implant fixture surface. UV irradiation of surfaces has shown an antimicrobial effect, as it converts the hydrophilicity of the implant surface, increasing attachment, retention, proliferation and osteogenic cells. However, in recent years, electrochemical treatments for biofilm decontamination have appeared. They cause a polarization of the metal surfaces, preventing microorganisms from attaching and breaking the anchoring bonds to the structures. In addition, the electrochemical activity determines a change in pH with the formation of oxidizing ions that reduce the number or kill the bacteria present [40.53.]

Recently, some scientific works have dealt with the decontamination of plants from biofilm using low intensity direct currents. They have given good results since there were no live bacteria at the anode, while at the cathode the colonies were reduced threefold [40,41,43].

Since our study aimed to evaluate the alternating current on a contaminated plant surface, the results allow us to evaluate the good response of bacterial decontamination.

Conclusions

Considering the limits of this scientific work, the results push us to continue and follow the path of using electric current in peri-implant treatment therapy. Expanding new treatment strategies.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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RESEARCH ARTICLE

CHANGES IN THE WIDTH OF THE KERATINISED MUCOSA IN THE AREA OF ONE-STAGE DENTAL IMPLANTATION WHEN USING A SOFT TISSUE CUFF REINFORCED WITH BONE GRAFTING MATERIAL

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Abstract

Objectives: The aim of the paper is a follow-up comparison of the xenogenic collagen matrix and soft-tissue cuff reinforced with bone grafting material (STCRBGM) for an increase in the keratinized mucosa's width in the one-stage dental implantation area.

Materials and Methods: The main observation group consisted of 25 patients who, after tooth extraction, had the implant placed in a prepared bed where the socket was preliminarily filled with Sensobone xenograft, after which the STCRBGM was formed with subsequent fixation of a temporary crown. The comparison group included 26 patients in whom, after tooth extraction, the implant was placed in the prepared bed where the socket was preliminarily filled with Sensobone xenograft, after which the soft tissue area was filled with Sensobone xenograft, and the temporary crown was fixed. The width of the keratinized mucosa (KM) was determined from the free gingival margin to the mucogingival junction before implantation, then 3-month and one-year follow-up after implantation. The study results were processed using the statistical package of the licensed software "Statistica, version 13".

Results: Comparing the follow-up use of xenogenic collagen matrix and STCRBGM to increase the width of the KM in the field of one-stage dental implantation, it was found that the use of STCRBGM provided a significant increase in the width of the KM in 3-month follow-up after implantation by 0.87 mm, and in one-year follow-up by 0.94 mm, which is significantly 1.25 mm more than in the group where only xenogenic collagen matrix was used. Besides, a significant increase in the width of the KM was observed in one-year follow-up in the area of all teeth and in the group with xenogenic collagen matrix there was a significant decrease. The KM width does not depend on the age and gender of the patients, as well as on the type of teeth and jaws.

Conclusion: The effectiveness of one-stage dental implantation is facilitated by the adequate width of the KM provided by STCRBGM.

Keywords: *One-moment dental implantation, Keratinized mucous membrane, Sensobone xenograft, Free connective tissue autograft.*

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INTRODUCTION

One-stage dental implantation in patients with single anterior tooth loss can shorten the treatment period and provide better restorative and aesthetic effects.[26] After minimally invasive extraction, both one-stage and two-stage dental implantations can guarantee good clinical results, one-stage implantation, however, ensures more satisfaction, better aesthetic effect, and good prospects for clinical use.[16]

The mucous membrane around the implant is covered with keratinized epithelium, followed by a 1-1.5 mm thick barrier epithelium that fills the space up to the bone ridge. Studying the width of the keratinized mucosa (KM) around the implant is important. According to the literature, an increase in the width of the KM in the implant area is significantly associated with an improvement in the condition of soft tissues, and to avoid peri-implant inflammation, it should be at least 2 mm[4,13,14] wide, since a width of less than 2 mm is associated with higher rates of gingival recession, gingival index, modified gingival index, and plaque index.

The mucous membrane around the implant is covered with keratinized epithelium, followed by modified plaque index, bleeding on probing, modified bleeding index, and bone loss.[11,17,19,22] It has been established that the stability of soft tissues after implantation depends on the height of the keratinized tissue, periodontal phenotype, and papilla height.[9,20] Covani U. et al.[6] found that in one-stage dental implantation with a xenograft, in addition to positive final aesthetic results, during a one-year follow-up, early growth was maintained in the tissues around the implant, and a five-year follow-up revealed that the bone level had minimally changed.

Methods of preserving the volume of hard and soft tissues around the implant increasing the gingival KM and the thickness of soft tissues (creating gingival volume from the bone ridge to the edge of the mucous membrane).[3,10] One of the key stages in dental implantation is using a connective tissue autograft.[8] The use of individual anatomically designed immediate temporary restorations after the extraction of one tooth and immediate implant placement minimises the loss of tissue volume, which optimises the final aesthetic result.[2]

Thus, ensuring an increase in the gingival KM in the implant area is an important task in dental implantology, as it is one of the factors affecting the long-term implantation result from both a functional and aesthetic point of view.

AIM

A follow-up comparison of the xenogenic collagen matrix and soft-tissue cuff reinforced with bone grafting material (STCRBGM) for an increase in the keratinised mucosa's width in the one-stage dental implantation area.

MATERIALS AND METHODS

Clinical trials were housed by our private dental clinics (DNIPRO DENTAL HUB LLC and Dr. Niezhentsev's Clinic LLC) and the Department of Propaedeutic and Surgical Dentistry of Zaporizhzhia State Medical and Pharmaceutical University. The study included 51 patients who underwent one-stage dental implantation.

Depending on the implantation technique, all patients were divided into two groups. The main observation group consisted of 25 patients who, after tooth extraction, had the implant placed in a prepared bed where the socket was preliminarily filled with Sensobone xenograft, after which the STCRBGM was formed with subsequent fixation of a temporary crown. The comparison group included 26 patients in whom, after tooth extraction, the implant was placed in the prepared bed where the socket was preliminarily filled with Sensobone xenograft, after which the soft tissue area was filled with Sensobone xenograft, and the temporary crown was fixed. Patients of both groups were divided by age and gender (Table 1).

Patients of both groups had 35 dental implants installed (Table 2). There was no significant difference between the groups in the number of implants installed in the selected teeth.

Table 1. Division of patients by gender and age

Feature	Main observation group (n=25)	Comparison group (n=26)
Men	16 (64%)	15 (57.7%)
Women	9 (36%)	11 (42.3%)
Average age	48.2 (44.0; 54.0)	47.1 (39.0; 54.0)

Table 2: Number of dental implants installed in patients of the study groups

Implant placement	Main observation group (n=25)	Comparison group (n=26)
Central incisor (CI)	5 (14.3%)	5 (14.3%)
Lateral incisor (LI)	6 (17.1%)	7 (20%)
Canine (C)	3 (8.6%)	3 (8.6%)
1 premolar (1PM)	5 (14.3%)	5 (14.3%)
2 premolar (2PM)	6 (17.1%)	4 (11.4%)
1 molar (1M)	10 (28.6%)	11 (31.4%)
Total	35 (100%)	35 (100%)

The KM width around the implant was determined according to the method described by Nalbantoğlu A. M. et al.[15] To indicate the mucogingival junction (the boundary between the mobile and fixed mucosa), the anterior part of the gingiva was stained with 5% Lugol's iodine solution using a cotton swab and a brush with light pressure, and the solution was applied several times until a clear demarcation line was achieved. Once a clear line was obtained, a soft tissue retractor was placed to facilitate scanning and minimize mucosal displacement. The KM width was determined from the free edge of the gum to the mucogingival junction. The KM width around the implant was determined before implantation (before tooth extraction), and then during 3-month and a one-year follow-up.

3D scanning with obtaining optical impressions was performed using an intraoral scanner "Medit i500" (Manufacturer: Medit, Korea). Medit i500 is an open real-time CAD/CAM system that allows exporting .stl files that can be easily transferred and tracked throughout the entire technological process.

The results of the study were processed using the statistical package of the licensed software "Statistica, version 13" (Copyright 1984-2018 TIBCO Software Inc. All rights reserved. License No. JPZ8041382130ARCN10-J). The reliability of differences in the compared values was confirmed by Student's t-test. The normality of the distribution of quantitative traits was analyzed using the Shapiro-Wilk test. When the parameters had a distribution that differed from the normal one, the descriptive statistics were presented as the median with interquartile range – Me (Q25; Q75). The significance of differences in the compared values for unrelated samples was determined by the Mann-Whitney test, and for related samples – by the Wilcoxon test. All tests were two-sided. The difference at $p<0.05$ was considered statistically significant. Relationships between groups of studied parameters were identified with correlation analysis, by calculating Spearman's rank correlation coefficients between quantitative features (r).

RESULTS

Before implantation in patients of both groups, the KM width in the area of one-stage dental implantation was almost the same and had no significant difference (Table 3). In the patients of the main study group, a significant increase in the KM width relative to the index before implantation was determined by 0.87 mm after a 3-month ($p<0.00001$) and by 0.94 mm ($p<0.000004$) after a one-year follow-up. While in the comparison group, there was no significant difference in the follow-up dynamics of the index, there was only a tendency to a slight decrease in the KM width relative to the index before implantation: by 0.11 mm ($p=0.548$) after a 3-month and by 0.2 mm ($p=0.261$) after a one-year follow-up. Relative to the comparison group in the main study group, the KM width was significantly larger by 1.09 mm ($p<0.0000001$) 3 months after implantation, and by 1.25 mm ($p<0.0000001$) in a year.

Table 3. Follow-up dynamics of KM width in the area of one-stage dental implantation, Me (Q25; Q75), mm

Stage of implantation	Main observation group (n=25)	Comparison group (n=26)	p
Before implantation	3.64 (2.94; 4.38)	3.53 (2.89; 4.06)	p = 0.545
3-month follow-up	4.51 (3.94; 5.16) *	3.42 (2.90; 4.04)	p < 0.0000001
One-year follow-up	4.58 (3.94; 5.11) *	3.33 (2.85; 3.84)	P < 0.0000001
Notes. * - a significant difference in the values at a 3-month and one-year follow-up after implantation compared to the value before implantation within the same observation group, p<0.05.			

Having studied the KM width in the area of one-stage dental implantation depending on the jaw (Table 4), no significant difference was found in both observation groups before implantation and in the follow-up (3 months and one year after implantation). However, in both groups, there was a tendency for the KM to be wider in the upper jaw than in the lower jaw by an average of 0.5 mm: in the main study group this was by 0.59 mm before implantation, by 0.52 mm 3 months after implantation and 0.44 mm in a year, and in the comparison group this was by 0.59 mm, 0.54 mm and 0.52 mm, respectively. Before implantation, the KM width in the area of one-stage dental implantation in both the upper and lower jaw was almost the same in patients of both groups and did not differ significantly. In the patients of the main study group, the KM width was significantly greater than in the comparison group 3 months after implantation on the upper jaw by 1.08 mm (p<0.0004) and on the lower jaw by 1.1 mm (p<0.000001), and in a year – on the upper jaw by 1.22 mm (p<0.00009) and on the lower jaw by 1.3 mm (p<0.000000). In the patients of the main study group, a significant increase in the KM width was determined relative to the value before implantation after 3 months on the upper jaw by 0.86 mm (p<0.00007) and after a year by 0.44 mm (p<0.0001). In the comparison group, there was no significant follow-up difference in the value, there was only a tendency to reduce the KM width relative to the value before implantation by 0.54 mm (p=0.635) after 3 months and by 0.52 mm (p=0.344) after a year.

Table 4. Follow-up CSR width in the area of one-stage dental implantation depending on the jaw, Me (Q25; Q75), mm

Stage of implantation	Main observation group (n=25)		Comparison group (n=26)		p
	Upper jaw	Lower jaw	Upper jaw	Lower jaw	
	1	2	3	4	
Before implantation	3.76 (3.11; 4.48)	3.17 (2.87; 3.87)	3.66 (3.12; 4.28)	3.07 (2.80; 3.27)	1-2=0.102 3-4=0.053 1-3=0.731 2-4=0.649
3-month follow-up	4.62 (3.99; 5.21) *	4.10 (3.66; 4.58) *	3.54 (3.06; 4.11)	3.00 (2.73; 3.15)	1-2=0.069 3-4=0.067 1-3<0.0004 2-4<0.000001
One-year follow-up	4.67 (4.21; 5.34) *	4.23 (3.78; 4.62) *	3.45 (3.00; 4.12)	2.93 (2.61; 3.13)	1-2=0.149 3-4=0.064 1-3<0.00009 2-4<0.000000
Notes. * - a significant difference in the values at a 3-month and one-year follow-up after implantation compared to the value before implantation within the same observation group, p<0.05.					

Having analyzed the follow-up indicators of the KM width in the area of one-stage dental implantation by type of tooth (after 3 months and after a year) (Table 5), it was found that in the main observation group, there was a significant increase in the KM width in the area of all teeth. Thus, the index of the KM width relative to the index before implantation in the CI area increased by 0.96 mm ($p<0.02$) after 3 months and by 1.12 mm ($p<0.003$) after a year; in the LI area by 1.12 mm ($p<0.0009$) and 0.97 mm ($p<0.0002$), respectively; in the area of CC by 0.8 mm ($p<0.009$) and 0.92 mm ($p<0.008$), respectively; in the area of 1PM by 1.21 mm ($p<0.0009$) and 1.15 mm ($p<0.0003$), respectively; in the 2PM area by 1.01 mm ($p<0.004$) and 1.05 mm ($p<0.001$), respectively; in the 1M area by 0.53 mm ($p<0.00005$) and 0.68 mm ($p<0.0007$), respectively. No significant difference was found between the values 3 months after implantation and one year later between all teeth.

Table 5. The follow-up KM width in the area of one-stage dental implantation by tooth type in the main observation group (n=25), Me (Q25; Q75), mm

Tooth type	Number of implants	Before implantation	3-month follow-up	One-year follow-up	p
		1	2	3	
CI	5	3.99 (3.99; 4.67)	4.95 (4.38; 5.64)	5.11 (4.93; 5.57)	1-2<0.02 1-3<0.003 2-3=0.244
LI	6	3.70 (3.14; 4.38)	4.79 (4.01; 5.31)	4.67 (4.27; 5.41)	1-2<0.0009 1-3<0.0002 2-3=0.295
CC	3	3.72 (3.12; 4.22)	4.52 (3.97; 5.11)	4.64 (4.16; 4.98)	1-2<0.009 1-3<0.008 2-3=0.446
1PM	5	2.64 (2.28; 2.87)	3.85 (3.62; 3.88)	3.79 (3.66; 3.84)	1-2<0.0009 1-3<0.0003 2-3=0.204
2PM	6	3.21 (2.87; 3.79)	4.22 (3.94; 4.72)	4.26 (3.94; 4.68)	1-2<0.004 1-3<0.001 2-3=0.699
1M	10	4.17 (3.87; 4.72)	4.75 (4.33; 5.21)	4.85 (4.46; 5.28)	1-2<0.00005 1-3<0.0007 2-3=0.502
Total	35	3.64 (2.94; 4.38)	4.51 (3.94; 5.16)	4.58 (3.94; 5.11)	1-2<0.00001 1-3<0.00001 2-3=0.135

It was also found that before implantation in patients of the main observation group, the smallest KM width was in the area of 1PM, which amounted to 2.64 (2.28; 2.87) mm and was significantly less compared with these indicators in the CI region by 1.35 mm ($p<0.02$), in the LI region by 1.06 mm ($p<0.03$), in the CC region by 1.08 mm ($p<0.01$), in the 2PM region by 0.57 mm ($p<0.01$) and in the 1M region by 1.53 mm ($p<0.0002$). Even though the KM index width in the area of absolutely all teeth after implantation significantly increased, it remained significantly smaller in the area of 1PM compared to the same index: in the CI area by 1.1 mm after 3 months ($3p<0.02$) and by 1.32 mm after a year ($p<0.006$); in the LI area by 0.88 mm after a year ($p<0.03$); in the CC area by 0.85 mm after a year ($p<0.03$); in the 1M area by 0.9 mm after 3 months ($p<0.02$) and by 1.06 mm after a year ($p<0.03$) mm.

In the comparison group, the follow-up of the KM width indicators in the area of one-stage dental implantation by tooth type showed a completely

different picture (Table 6). Thus, in the CI area, no significant change in the KM width was found during the follow-up, but there was a tendency to reduce its width relative to the pre-implantation value by 0.16 mm after 3 months and by 0.2 mm after a year. In the areas of LI, CC and 2PM, a year after implantation, a significant decrease in the KM width was determined by 0.17 mm (p<0.001), 0.16 mm (p<0.04) and 0.29 mm (p<0.001). In the 1PM area, the KM width decreased by 0.12 mm, and a significant difference was determined between the indicators after 3 months and a year by 0.1 mm (p<0.01). In the 1M area, a significant difference was determined both after 3 months by 0.12 mm (p<0.00001) and after a year - by 0.22 mm (p<0.00001), while the indicator after a year significantly differed from that after 3 months by 0.1 mm (p<0.04).

Table 6. The follow-up KM width in the area of one-stage dental implantation by tooth type in the comparison group (n=26), Me (Q25; Q75), mm

Tooth type	Number of implants	Before implantation	3-month follow-up	One-year follow-up	p
		1	2	3	
CI	5	3.19 (2.79; 3.46)	3.03 (2.58; 3.25)	2.99 (2.51; 3.22)	1-2=0.719 1-3=0.646 2-3=0.924
LI	7	3.56 (2.89; 4.31)	3.46 (2.90; 4.22)	3.39 (2.85; 4.16)	1-2=0.252 1-3<0.001 2-3=0.078
CC	3	3.39 (2.81; 3.69)	3.33 (2.89; 3.58)	3.23 (2.72; 3.50)	1-2=0.477 1-3<0.04 2-3=0.128
1PM	5	2.76 (2.46; 3.11)	2.74 (2.38; 3.06)	2.64 (2.33; 2.97)	1-2=0.649 1-3=0.084 2-3<0.01
2PM	4	3.64 (3.59; 3.70)	3.49 (3.40; 3.58)	3.35 (3.24; 3.46)	1-2=0.165 1-3<0.003 2-3=0.167
1M	11	4.00 (3.27; 4.67)	3.88 (3.15; 4.36)	3.78 (3.11; 4.36)	1-2<0.003 1-3<0.0002 2-3<0.04
Total	35	3.53 (2.89; 4.06)	3.42 (2.90; 4.04)	3.33 (2.85; 3.84)	1-2<0.00001 1-3<0.00001 2-3=0.803

We compared the follow-up values of KM width by tooth type between the groups (Table 5, Table 6). It was found that in the area of all teeth in patients of the main observation group, a significant increase in the value was determined relative to the comparison group. Thus, the KM width in the CI area after 3 months was increased by 1.92 mm (p<0.003), and after a year by 2.12 mm (p<0.001); in the LI area by 1.33 mm (p<0.01) and 1.28 mm (p<0.006), respectively; in the CC area by 1.19 mm (p<0.03) and 1.41 mm (p<0.01), respectively; in the 1PM region by 1.11 mm (p<0.0009) and 1.15 mm (p<0.0007), respectively; in the 2PM region by 0.73 mm (p<0.04) and 0.91 mm (p<0.01), respectively; in the 1M region by 0.87 mm (p<0.01) and 1.07 mm (p<0.002), respectively.

Similar to patients of the main observation group, the patients in the comparison group before implantation demonstrated the smallest KM width in the 1PM area, which was 2.76 (2.46; 3.11) mm and was significantly less than in the LI area by 0.8 mm (p<0.03), in the 2PM area by 0.88 mm (p<0.003) and

the 1M area by 1.24 mm ($p<0.01$). Following up after implantation, the index of KM width in the area of all teeth decreased, in the area of 1PM it remained significantly lower compared to the same index: in the LI area by 0.72 mm in 3 months ($p<0.004$) and by 0.75 mm in a year ($p<0.03$); in the 2PM area by 0.75 mm ($p<0.004$) and by 0.71 mm ($p<0.03$), respectively; in the 1M area by 1.14 mm ($p<0.004$) and ($p<0.03$), respectively.

The correlation analysis revealed no dependence of the KM width on the age and gender of patients and the type of teeth and jaws.

During the year of follow-up, there were no dental implant failures in both groups, and the survival rate of implants one year after their installation was 100%.

DISCUSSION

As obvious from the presented research results in patients who used STCRBGM for one-time dental implantation, there was a significant follow-up increase in the KM width (after 3 months of implantation and after surgery). Thus, before implantation, the KM width was 3.64 (2.94; 4.38) mm, and after a 3-month follow-up it significantly increased to 0.87 mm (4.51 (3.94; 5.16) mm), and after a one-year follow-up it increased by 0.94 mm (4.58 (3.94; 5.11) mm), which was significantly larger at 1.25 mm, than in the group where only xenogeneic collagen matrix was used (3.33 (2 .85; 3.84) mm). In the group with the xenogenic collagen matrix, there was a tendency to a slight decrease in the KM width to 0.11 mm after a 3-month, and to 0.2 mm after a one-year follow-up.

According to Temmerman A. et al. [23], using a connective tissue graft increases the KM width around the implants by 1.3 ± 0.9 mm, more than in the presented study. Perhaps this is related to the age of the patients, since the younger the patient, the greater the initial value of the KM. In our other study, the average age of the patients was 48.2 (44.0, 54.0) and 47.1 (39.0, 54.0) years, which was the reason for the initial smaller value of the KM width.

It was established that the KM width in the area of one-moment dental implantation in both groups, before implantation and in the follow-up, did not depend on the jaw. However, it was found that in both groups, the KM width was on average 0.5 mm larger on the upper jaw than on the lower.

The study revealed that depending on the type of teeth, the follow-up values of KM width in the area of one-moment dental implantation in the group with the use of STCRBGM reliably increased, and a year after implantation, a reliable increase in the KM width in the area of all teeth was determined (CI by 1.12 mm, LI by 0.97 mm, CC by 0.92 mm, 1PM by 1.15 mm, 2PM by 1.05 mm, and 1M by 0 0.68 mm), and in the group with xenogenic collagen matrix there was a significant decrease (LI by 0.17 mm, CC by 0.16 mm, 2PM by 0.29 mm, 1PM by 0.12 mm, 1M by 0.22 mm). Simultaneously, in the group with the use of STCRBGM, compared to the group with xenogenic collagen matrix, after a one-year follow-up, the KM width in the CI region was larger by 2.12 mm, in the LI region – by 1.28 mm, in the CC region – by 1.41 mm, in the 1PM region – by 1.15 mm, in the 2PM region – by 0.91 mm, and in the 1M region – by 1.07 mm.

It was also established that before implantation in patients of both groups, the smallest KM width value was in the area of 1 PM, which was 2.64 (2.28; 2.87) mm in the group with the use of STCRBGM and 2.76 (2.46; 3.11) mm in the group with xenogenic collagen matrix.

In our study, we did not find any correlation between the KM width and the age and gender of the patients. Similar results were obtained by Nalbantoğlu A.M. & Yanık D.,[15] although there are contrary data in the literature.[21]

Literature data demonstrate that soft tissue augmentation methods reliably improve the quantity and quality of soft tissue around the implant. Among augmentation procedures, connective tissue graft is associated with better changes in keratinized tissue thickness compared to xenogenic collagen matrix,[5, 7,12,25] which is confirmed in the presented study.

Qiu X. et al. found that a xenogenic collagen matrix in combination with an apically located flap has the same clinical effectiveness in increasing the KM width as a free connective tissue graft in combination with an apically located flap but with higher shrinkage.[18] Comparing the effect of different autogenous grafts on the soft tissue thickness and the KM width, Tommasato G. et al. found that it was the connective tissue graft that showed the best performance in all comparisons, increasing the KM width of the KSO,[24] which is confirmed in our study.

CONCLUSION

Comparing the follow-up data of the use of xenogeneic collagen matrix and STCRBGM to increase the KM width in the area of one-time dental implantation, it was established that the use of STCRBGM provided: a reliable increase in the KM width 3 months after implantation by 0.87 mm, and after a year – by 0.94 mm, which is significantly larger by 1.25 mm than in the group where only the xenogenic collagen matrix was used; a significant increase in the width of KSO after a year in the area of all teeth (CI by 1.12 mm, LI by 0.97 mm, CC by 0.92 mm, 1PM by 1.15 mm, 2PM by 1.05 mm, 1M by 0 0.68 mm), and in the group with xenogenic collagen matrix there was a significant reduction (LI by 0.17 mm, CC by 0.16 mm, 2PM by 0.29 mm, 1PM by 0.12 mm, 1M by 0 .22 mm). Simultaneously the KM width in the area of one-moment dental implantation in both groups, before implantation and during the follow-up, did not depend on the jaw and was on average 0.5 mm larger on the upper jaw than on the lower jaw. Before implantation in patients of both groups, the smallest KM width value was in the area of 1PM. The KM width does not depend on the age and gender of patients, as well as on the type of teeth and jaws. During a one-year follow-up period, there was no dental implant failure in both groups, and the survival rate of the implants one year after their installation was 100%.

Thus, the effectiveness of one-stage dental implantation is facilitated by the adequate KM width, ensured by STCRBGM.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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RESEARCH ARTICLE

MARGINAL BONE LOSS,BIOLOGICAL WIDTH AND GEOMETRIC SHAPE OF THE ABUTMENT:7-YEAR FOLLOW-UP OF AN ABUTMENT CALLED Trumpet R

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Abstract

Background. Marginal bone resorption observed around osseointegrated implants after the first year is particularly dangerous, especially if the implants are sandblasted and etched. In this case, this MBL can open the way to bacteria that, by colonizing the implant surface, can trigger peri-implantitis and the loss of the implants and the prosthesis screwed onto them.

The aim of this work was to evaluate the MBL around implants inserted with a mathematical protocol and prostheticized with a one-time abutment called Trumpet.

Materials and Methods: 10 patients were considered who needed an all-on-six rehabilitation (5) and single rehabilitations (5). Measurements of the soft tissue thickness and the distance between the crest and the implant neck (CI) were performed at the time of surgery and at a distance of 1.3 and 7 years.

Results: Clinical and radiographic controls performed at a distance of 1.3 and 7 years of the treated patients showed the same CI distance (Crest - Implant) in all patients without observing marginal bone loss.

Conclusions: The use of a mathematical model that takes into account the soft tissue thickness for the positioning of the implant with respect to the bone crest and the use of abutments that give more space to the soft tissues to respect the biological width seems to be the correct way to avoid the loss of marginal bone around the implants.

Keywords: Cholesterol, serum, lipids, mouth, dyslipidemias

INTRODUCTION

The use of osseointegrated implants is now a consolidated practice with a scientific literature that is very abundant and in agreement on the medium and long-term efficacy. It is possible to find consensus both for traditional implantology performed with cylindrical implants[1-4], and that performed with the new Rex blade implants [5] or the new generation subperiosteal ones [6].

During the first surgical phase, it is possible that different aspects can influence optimal healing; on the one hand, the way in which the implant site is prepared and on the other, the materials with which the implants are constructed and the way in which their surface is conditioned.

With regard to the implant site, the results of a study [7] are interesting, in which the role of the shape of the drills and the way in which the temperature generated during the preparation of the implant site changes are highlighted. This factor, often underestimated, could cause bone necrosis in the deepest part of the drill and far from irrigation and cooling. Always in this perspective, we emphasize the published works regarding the great advantages of preparing the implant site with the piezosurgery method [8].

The piezoelectric method has in fact been demonstrated by the research group of Trisi et al [9] not to generate heat unlike the drills and the cut performed with reciprocating saws that instead generate heat in the areas furthest from cooling. For this reason, the use of piezosurgery in the preparation of the implant site is desirable and advisable.

As regards the materials used for the construction of the implant, there are many studies supporting different technologies that over the years have tried to improve the BIC (Bone Implant Contact); in this regard, important works are those regarding the Nano Tite surface [10], those supporting TiUnite [11] and those related to the use of SLA Active hydrogen peroxide by Straumann [12].

Also very interesting in the literature are the scientific works that concern the modification of the surface with Raloxifene [13-15], with Bisphosphonates [16] and with the use of static magnetic fields applied using magnetically charged neodymium iron boron cap screws and healing screws [17-19].

While in the latter we mainly observe a greater differentiation of the osteoblasts, not cell multiplication but with an increase in matrix production, in the majority of the modified surfaces we want to obtain a greater response of the osteoblasts in terms of cell recruitment. Therefore, while with static magnetic fields we observe a simple effect linked to the physical presence of the cap screw or the healing screw in the presence of the same titanium surface, in all other ways we observe a substantial and definitive modification of the implant surface with all the risks that this can entail in the medium and long term.

However, very recent studies [20-21] demonstrate that the best surface, i.e. the one capable of obtaining the highest BIC, has not yet been found, and many mechanisms that are at the basis of the production of the matrix are still unknown. Immediate loading, for example, is able to have a stimulating effect on undifferentiated osteoblasts [22] and to be able to increase the BIC. Having made this fundamental premise, the loss of marginal bone is strictly correlated to the type of surgery [23], to the respect of the biological width, to the type of material used to construct the abutments, to the way in which the conditioning of the soft tissues is carried out and to the position of the implant with respect to the bone crest.

As regards the type of surgery, the immediate post-extraction implant performed with the one time abutment technique respects the concept of the Chamber Concept expressed by Degidi et al [24-25]; in particular the shape of the abutment and the incarceration of the clot seem to be important for the neo angiogenesis and in the maintenance of the vascular support to the vestibular and palatine or lingual bone crests.

Berglundh et al in 1996 with the famous experiment on Beegle dogs [26-27] demonstrated that it is essential to have 3 millimetres of soft tissue above the implant, of which 2 millimetres of epithelium and 1 millimetre of connective tissue. In particular, Abrhansoon demonstrated in 1998 [28-29] that titanium stimulates a hemi-desmosomal junction by epithelial cells and in particular the loosening and tightening maneuvers of the healing screws [30] as well as those related to the impression taking [31-33] trigger an inflammatory response that ends up producing keratin and reduces the possibility of a hemi-desmosomal attack; Kawahara et al [34-35] define this attack as a biological seal that appears to be particularly valid with the epithelium and zirconium with a reduced production of pro-inflammatory cytokines [36-40].

Based on the work of Bergludh, it is important to cite the scientific work [41] regarding the exact position of the implant that must be sunk in proportion to the reduction in the thickness of the soft tissues. In practice, considering with X the thickness of the soft tissues, with K the biological width that must be 3 (mm), the position of the implant with respect to the bone Y will result from the following formulaY=X-3. To respect the biological width, we can therefore move the implant away in an intra-osseous position so as to be able to obtain those 3 millimeters of biological width necessary to be able to maintain the implant without observing Marginal Bone Loss. Always in this vein, studies on platform switching are important[42-44] which in fact distribute the biological width on a horizontal area of the implant collar.

The aim of this work is to evaluate the Marginal Bone Loss at 7 years on a sample of 30 implants in which an abutment called Trumper was used and designed to increase the surface available to the soft tissues in compliance with the biological width [45-50].

Materials and methods

The study was conducted at one clinical center in conformity with the Good Clinical Practice Guidelines, following the recommendations of the World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects, as revised in Fortaleza (2013).

10 patients were considered who had to have implants inserted both in single areas and for works with multiple implants; they were used.

The inclusion criteria were as follows:

Age >18 years old;

General good health (ASA I–II);

Adequate oral hygiene (full mouth plaque score

≤20%, full mouth bleeding score ≤20%);
Presence of one or more hopeless teeth requiring extraction.
The exclusion criteria were as follows:
Pregnancy or lactation;
Untreated periodontitis;
Osteometabolic disease;
Intravenous bisphosphonate therapy;
History of chemotherapy or radiation therapy in the neck–head area;
Heavy smoking (>15 cigarettes per day);
Absence of buccal bone plate.
The selected population was as follows:
Age 31–77 years old;
7 men and 3 women.
Written informed consent was provided by all patients for both the clinical procedure and participation in this study. Preoperative CBCT was performed. Patients were administered antibiotic prophylaxis starting the day before extraction with amoxicillin and clavulanic acid at 2 g per day for 6 days.
The implants used were TTi (Biosaf In, Ancona Italy) with a diameter of 4 mm and variable length; for all the implants, Trumpet type abutments were used (Biosaf In, Ancona Italy). This abutment patented by Biosaf In and designed by Fabrizio Bambini has the peculiar characteristic of having a 3 mm surface that is not straight but curvilinear; the curved surface has therefore developed a larger surface compared to the straight surface (fig. 1,2).



Figure 1.TTi implant by Biosaf In and Trumpet Abutment.

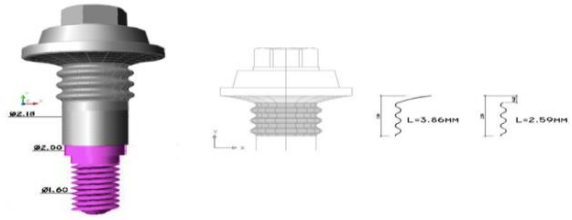


Figure 2. Trumpet concept

Surgery was performed following the above protocol:
• Non-traumatic extraction of the terminal tooth, flap less
• Preparation with a dedicated Biosaf In kit for insertion of TTi type implants and under preparation of the implant
• Positioning of the implants using the formula Y=X-3 where X represents the thickness of the soft tissues measured with the CBCT by increasing the contrast
• Measurement of the distance between the crestal bone peak and the crestal point of the implant (Crestal-Implant CI)
• Simultaneous insertion of the Trumpet and tightening to 30 Ncm
• Tightening of Trumpet abutments (T Base) and blocking them with resin …. O
• Impression with Trumpet transfer
• Tightening of resin prosthesis within 24 hours and tightening of screws at 20 Ncm
• Delivery of definitive prosthesis after 60 days
• Measurement of CI segment at the time of radiographic checks (fig 4 and 5)
• Radiographic checks at 30 60 90 days, cbct check at 1 year, 3 years and 5 years

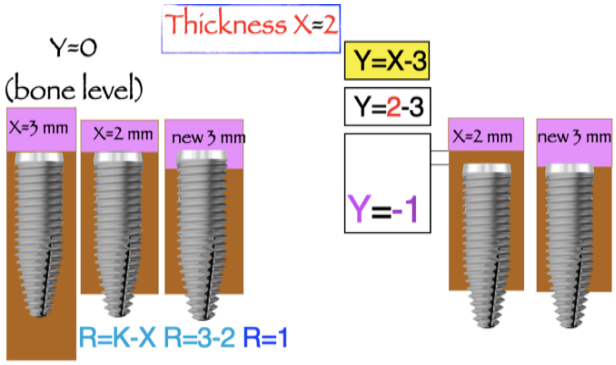


Figure 3. Example of position of implant

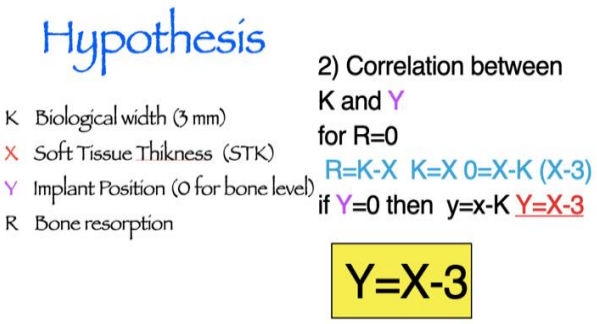


Figure 4. Mathematical rational of Hypothesis

In the figure 5 and 6 we describe the 2 red points on Crestal bone and on Implant neck: CI segment that we measure at time 0, and after 1, 3 and 5 years (table 1 of Reslts).



Figure 5. RX of CI Segment at time 0
Figure 6. RX of CI after 5 years

In the figures 7-12 the clinical situation and OPG of a female patient with an all on six executed with Biosaf-In implants, TTi type, with Trumpet abutment inserted ad modum "one time abutment" respecting Y=X-3 cresta implant position and with the provisional crowns screwed at 24 hours after surgery.

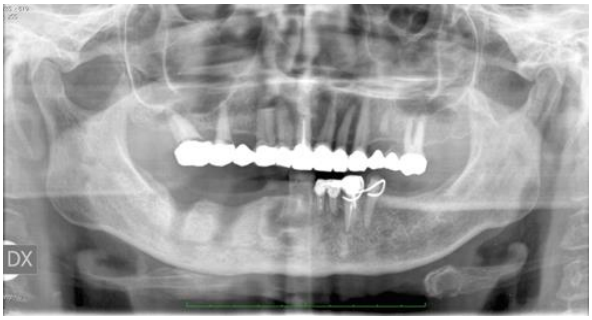


Figure 7. Pre Operative OPG

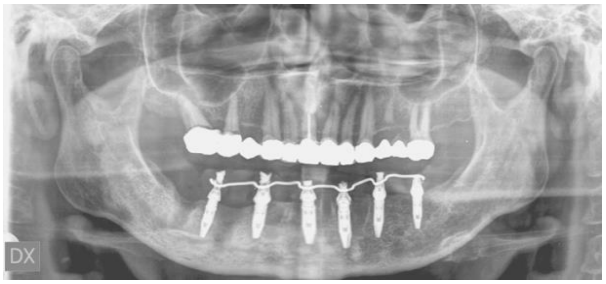


Figure 8. Post operative at 24 hours OPG



Figure9. Post operative with provisional crowns at 24 hours intra oral situation



Figure 10. Clinic Control after 1 year

Results
The 10 patients operated on inserted a total of 35 implants, of which 5 all on six and 5 single elements. The CI segments measured in the materials and methods were measured and were indicated in the table 1 and figure 5,6.
• Thickness of the soft tissues (X)
• Position of the implant with respect to the bone crest (Y), giving Y=0 the crestal position of the implant, negative values for subcrestal position of the implant
• Initial CI (distance from Crestal bone to Implant)
• CI at 0 days
• CI at 1, 3 and 5 years
• Prosthetic complications (screw loosening on Trumpet, fracture of the prosthesis, implant loss).

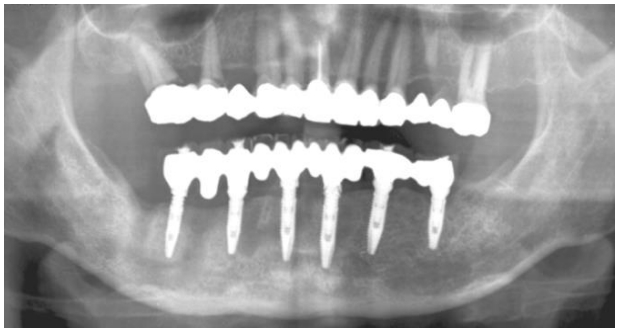


Figure 11. 1 year control OPG

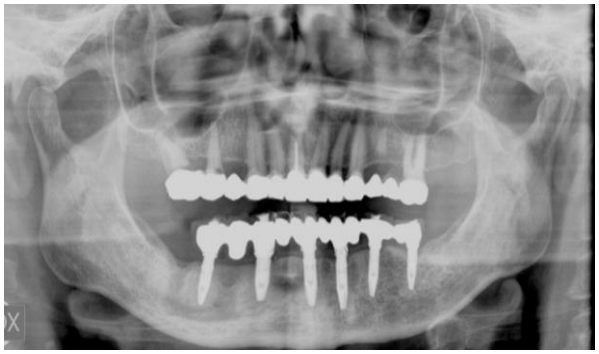


Figure 12. 5 years control OPG

Table 1. measurements in mm of X, CI after 1,3 5 years and type of complications

	X	Y	CI 0	CI 1	CI 3	CI 5	Complic
1 (Ao6)	2 (mean)	-1	1	1	1	3	Unscrew
2 (Ao6)	2 (mean)	-1	1	1	1	3	0
3 (Ao6)	2 (mean)	-1	1	1	1	3	0
4 (Ao6)	1 (mean)	-3	3	3	3	3	0
5 (Ao6)	1 (mean)	-3	3	3	3	3	0
6	2	0	0	0	0	0	0
7	1	-2	2	2	2	2	Unscrew
8	1	-2	2	2	2	2	0
9	1	-2	2	2	2	1	0
10	2	-1	1	1	1	0	0

The 5 patients subjected to all on six had the CI distance unchanged in % of cases while in 2 cases this segment was reduced by one millimeter (figure 4 and 5 with CI segment reduced).

In the 5 patients who underwent therapy for the replacement of a single element, the CI segment remained unchanged, while in one patient it was necessary to re-tighten the crown due to the fracture of the crown tightening screw on Trumpet.

Discussion

The possibility of solving simple and complex cases with osteo-integrated implants is now a widespread therapy and the insertion protocols are within the reach of all dental clinicians. However, the long-term maintenance of the implants seems to be more linked to the fundamental role that the soft tissues play in protecting the implants from bacterial insult. The initial thickness of the soft tissues is a fundamental point that is often not considered by the clinician in such a fundamental way.

When the patient presents for the visit to insert osseointegrated implants, he is subjected to the evaluation with CBCT to establish if the hard tissues can be sufficient to support an implant therapy; many scientific works are aimed at the use of computer-guided surgery. Although in fact the causes that can lead the clinician to propose implant therapy, there is always the problem of the biotype that the patient has and that can influence the medium and long-term not good prognosis of the proposed implant therapy. Patients with a thin biotype are more exposed to marginal bone loss and exposure of the first thread of the implant and the initial peri-implant mucositis is difficult to control.

Peri-implantitis that follows simple mucositis is a pathology whose resolution becomes very unpredictable. It is also true that the marginal bone resorption that is observed starting from the first year onwards often places the clinician in front of the need to perform connective tissue grafts that are not always within the technical reach of all clinicians. The initial idea was to design an abutment that could have a longer transmucosal path than a traditional abutment in line with the indications given by Bergludh in 1996 regarding the biological width. Trumpet and platform switching can represent a simple strategy and in the hands of all dentists to protect the implant from bacterial invasion by actually increasing the amount of soft tissue for implantation without resorting to additional mucogingival surgery.Furthermore, being able to calculate with a simple mathematical formula the correct position of the implant with respect to the bone crest, thus having precise and non-arbitrary references, appears to be, for the data in our possession, a simple and safe clinical conduct.

The possibility of solving simple and complex cases with osteo-integrated implants is now a widespread therapy and the insertion protocols are within the reach of all dental clinicians. However, the long-term maintenance of the implants seems to be more linked to the fundamental role that the soft tissues play in protecting the implants from bacterial insult. The initial thickness of the soft tissues is a fundamental point that is often not considered by the clinician in such a fundamental way. It is also true that the marginal bone resorption that is observed starting from the first year onwards often places the clinician in front of the need to perform connective tissue grafts that are not always within the technical reach of all clinicians. Prospective studies with a large number of patients will be necessary to consolidate this data which, although limited, we can consider non-preliminary

Conclusions

The use of a mathematical model that takes into account the soft tissue thickness for the positioning of the implant with respect to the bone crest and the use of abutments that give more space to the soft tissues to respect the biological width seems to be the correct way to avoid the loss of marginal bone around the implants.

DECLARATIONS

Conflicts of interest and financial disclosures

No conflict percentage and there was no external source of funding for the research in question.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

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CASE REPORT

EVALUATION OF THE EFFECTIVENESS OF IMMEDIATE DENTAL IMPLANTS PLACED IN EXTRAXTION SOCKETS WITH PERIAPICAL PATHOLOGY. A CONTROLLED CASE SERIES

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Abstract

Background: Immediate placement of implants in post-extraction sockets is a common and well-established treatment modality. However, extraction sockets with periapical pathology may negatively impact the outcome of this treatment procedure.

Objective: The aim of this study was to evaluate the clinical outcomes of immediate placement of dental implants in infected extraction sockets with periapical pathology.

Materials and Methods: The study included 37 patients who underwent tooth extraction with periapical pathology and immediate 151 Bio3 GmbH (Germany) implants placement.

Postoperative results; implant survival, implant failure, marginal bone loss (MBL), and patient-reported function of the implants were assessed clinically and radiographically.

Results: There were no complications during implant placement and in the postoperative period, no signs of infection around the implants were detected at the follow-up visit 4 weeks after implant placement, the soft tissues were in good condition, as evidenced by their healthy color and texture. The mean RFA for151 implants was 63.7 ISQ (implant stability), and after 3-5 months, respectively, 72.4 ISQ. The mean MBL after 12 months was 0.94, after 36 months the mean MBL was 1.28, at 60 months follow-up the mean MBL was 1.42.

The functional and aesthetic results of prosthetic restoration were satisfied by the patients, as chewing function was restored, the esthetics of the facial profile and occlusion improved. The success rate of immediate implants after 5 years was 96.8%, and shows a similar survival rate to the published success rates for immediate implants placed in non-infected sites.

Conclusion: Evidence suggests that immediate placement of implants in areas with periapical infections is a predictable and effective treatment protocol if the areas are thoroughly debrided prior to implant placement, high implants stability is achieved during implant placement, and systemic antibiotics are used.

Keywords: post-extraction sockets, periapical infections, immediate implants, Bio3 GmbH implants

INTRODUCTION

Currently, immediate placement of implants in fresh post-extraction sockets is an accepted established treatment option and has been shown to be a predictable and successful procedure when proper protocols are followed. Immediate implant placement has several advantages over delayed placement, such as reduced healing time and number of surgeries[1,2].

Immediate implant placement has a number of contraindications, and among them, the presence of active infection at the extraction site is considered one of the main contraindications due to the risk of infection spreading, which can lead to implant failure or retrograde peri-implantitis[3,4].

Some studies suggest that immediate implant procedures should be avoided in cases of periapical pathosis[5-9].

According to several publications, the survival rate of immediately placed implants in sites with endodontic infections ranges from 92-98.7%[10-12].

Several studies have evaluated the survival rates of dental implants placed directly in infected sockets compared to those placed in healthy sites and have not found significant differences in outcomes[13-15].

Immediate placement of the implant after tooth extraction and immediate loading of the implant with a fixed temporary reconstruction is preferred by the patient as postoperative pain after flapless surgery is significantly reduced compared to the traditional open approach[16,17].

With computer-aided design/computer-aided manufacturing (CAD/CAM) temporarily and the final designs provide high quality and esthetics of permanent prostheses[18,19]. Although computer-assisted implant placement and CAD/CAM have contributed to simplifying the patient rehabilitation workflow, the combination of immediate implant placement and immediate loading protocols is complex and requires a high level of organization between the implantologist, technician, and patient[20,21].

The aim of this study was to evaluate the clinical outcomes of immediate placement of dental implants in infected extraction sockets with periapical pathology.

Materials and Methods

The study included 37 patients who underwent immediate dental implants placement in areas with periapical lesions between 2020 and 2024. All patients underwent a comprehensive clinical and radiographic diagnosis.

Demographic Distribution

37 patients, the ages (38 -64 year) with a mean age of 64.7 ± 10.6 years old, (21 males and 17 females).

Inclusion criteria

- Good health (ASA I or II).
- Presence of four bony walls of the alveolus.
- Periapical teeth pathology could not be treated.

Exclusion criteria

- severely poor oral hygiene;
- uncontrolled chronic systematic disease;
- severe osteoporosis;
- patients using bisphosphonates;
- patients using antiresorptive drugs;
- patients who received radiotherapy from the head and neck region;
- alcohol or drug abuse;
- acute/chronicauto-immune mucosal diseases.
- smoker.

All patients included signed the informed consent forms according to the latest edition of the World Medical Association's Declaration of Helsinki and declared their commitment to participate for the full duration of the study.

All patients underwent complex clinical and radiographically diagnostics. Chronic periapical pathology was defined as periapical radiolucency lesions larger than 2 mm observed in the apical part of decayed teeth, teeth with failed endodontic treatment.

CT scan allowed to assess the quality and quantity of bone characteristics. The DICOM (digital imaging and communication in medicine) files acquired with CT were also imported in a three dimensional reconstruction software. Based on anatomical conditions and prosthetic planning, the position of the implants was virtually planned using 3D computer-aided design software (3Shape implant Studio).

Surgical protocol

Informed consent was obtained from all patients for extraction and immediate placement of dental implants. Patients were prescribed antibiotics (Augmentin-GlaxoSmithKline) 1 day before surgery. The teeth were extracted atraumatically, in some patients using a minimally invasive technique with a piezotome without flap elevation. The affected tissues of the extracted tooth were removed by careful needle curettage, treated with an antiseptic aqueous solution of 0.2% chlorhexidine digluconate, and then washed several times with sterile saline.

Implants were placed via standard protocols in the bone beyond the root apex and in the extraction sites, providing primer stability using a one-stage surgical technique, and CT was obtained.

151 Bio3 implants GmbH (GmbH, Germany) were placed was minimum of 30-35Ncm insertion torque upper (65) and lower (86) jaw, anterior or posterior sites (table 3). Implant stability was measured using Osstell Mentor during implant installation and after 3-5 months before fixation final prosthetic structur then, multi-unit abutments were immediately placed their height adjusted and suturing was done using 3/0 black silk sutures (Ethicon Mersilk, Johnson & Johnson Pvt Ltd). es.

Prosthetic protocol

Immediate functional loading using precise temporary prostheses was applied to 58 implants.

The impression transfer was fixed before scanning. The scanner is a data acquisition system that records the 3D geometry of the infrastructure and converts the actual dental model into a virtual dental model.

After 6 hours temporary prosthetic structures fitting in the oral cavity, they were fixed onto multiunit abutments using screws with 25Ncm.

The functional load on dental implants was performed with 62> ISQ values above 2-4 months after implantation with CAD/CAM using metal-ceramic or zirconium dioxide restorations and was fixed with screws of 25 Ncm.

Follow-Up

At intervals of 6 months to 60 months, the following parameters were taken into account: resonance frequency analysis (RFA), inflammatory processes in the peri-implant tissue, loss of marginal bone tissue in men (MBL), aesthetic and functional results.

Statistical analysis

Statistics were used to calculate and analyze the mean marginal bone loss of implants. The differences between follow-up periods were tested by paired Student's t test. All analyses were carried out using SPSS (SPSS Software Company, Chicago, IL, USA). Differences between observation periods were checked using the paired Student's t test. The p values < 0.05 were considered statistically significant.

Case series report presents a patients treated with immediate implants and implant-supported prosthesis.

Case 1.



Figure 1. Preoperative CT showing periapical lesions in the 12 tooth region

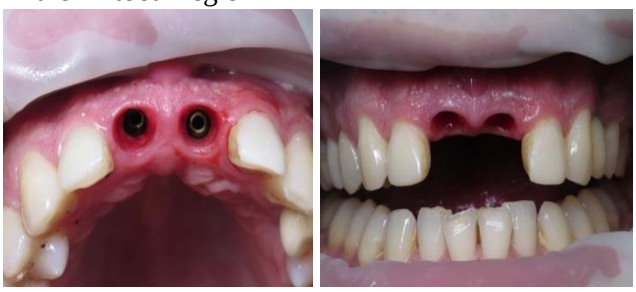


Figure 2. Intraoral view of 2 implants on the 11,21 tooth lower jaw before prosthetic rehabilitation.



Figure.3 Intraoral view after implant prosthetic rehabilitation



Figure 4.Extraoral view after implant prosthetic rehabilitation

Case 2.

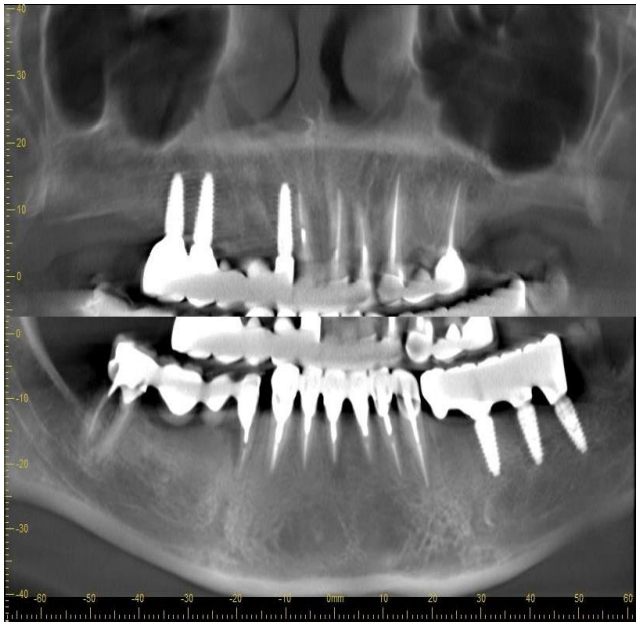


Figure 5. Preoperative CT showing periapical lesions in the 44 tooth region

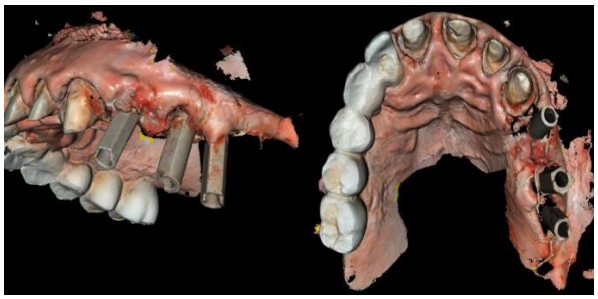


Figure 6. The impression transfers is installed on a multi- unit abutments on the upper jaw and scanned

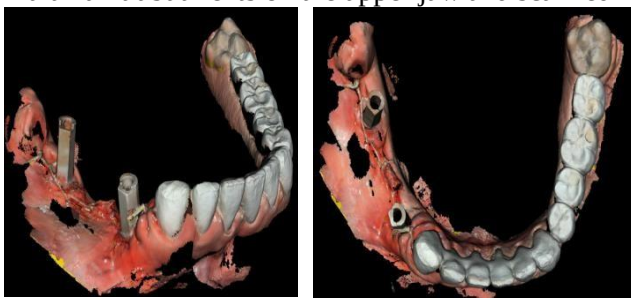


Figure 7. The impression transfers is installed on a multi- unit abutments on the lower jaw and scanned

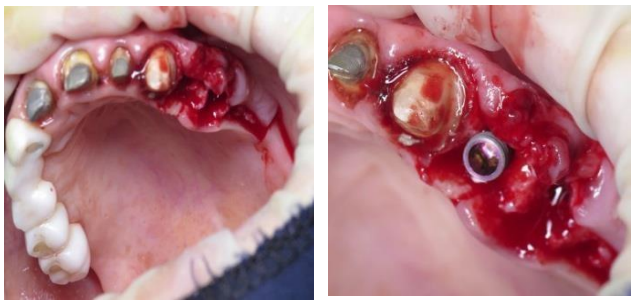


Figure 8. Intraoral view before and after implant placement



Figure 9. Intraoral view after implant placement



Figure 10 Screw-retained bridges on abutments before implant fixation



Figure 11 . Intraoral view after implant prosthetic rehabilitation

Case 3.

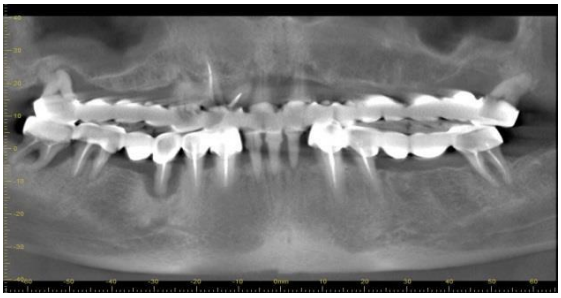


Figure 12. Preoperative CT showing periapical lesions in the 45 tooth



Figure 13. Postoperative CT after implant placement



Figure14. Intraoral view of 6 abutments on the upper jaw before prosthetic rehabilitation
Figure 15. Intraoral view of 6 abutments on the lower jaw before prosthetic rehabilitation



Figure 16,17 Prosthetic structures in upper jaw before prosthetic rehabilitation



Figure 18,19 Prosthetic structures in lower jaw before prosthetic rehabilitation



Figure 20,**21** Intraoral view after implant prosthetic rehabilitation

Case 5.

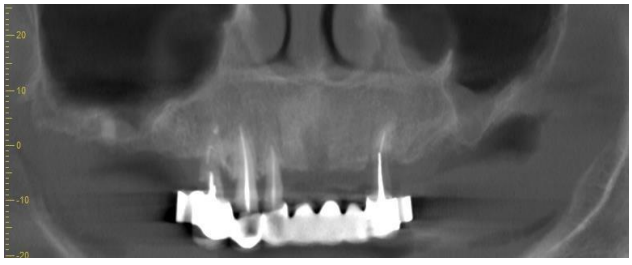


Figure 22. Preoperative CT showing periradicular lesions in the 14 tooth

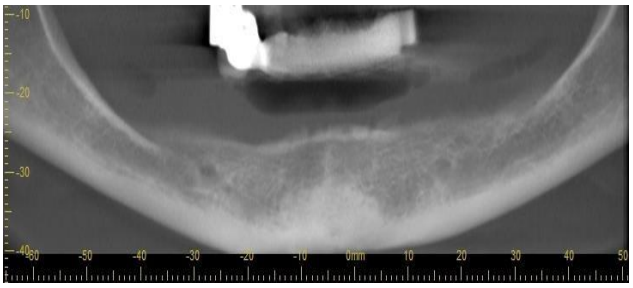


Figure 23. Preoperative CT upper jaw before implant placement

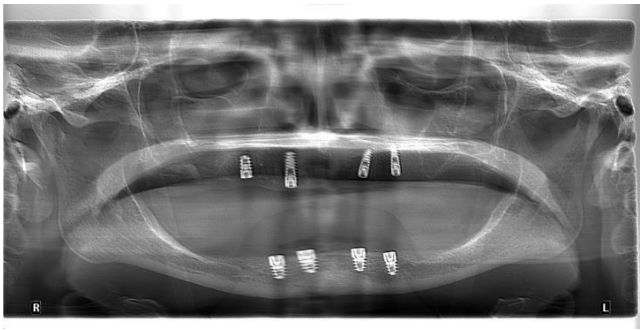


Figure 24. Postoperative CT after implant placement



Figure 25,26 Prosthetic structures in upper jaw and lower jaw before prosthetic rehabilitation



Figure 27,**28** Intraoral view after implant prosthetic rehabilitation

Results

There were no complications during implant placement, immediate postoperatively and the control visit.

4 weeks after implant placement, the soft tissues were in good condition, as evidenced by their healthy color and texture.

After 12 month, the average MBL was 0.94., after 36 month MBL was 1.28, the 60-month follow-up period, the MBL was 1.42(table 1).

Table 1. Average mean clinical index MBL after 1,3,5 year

Clinical index	Time after implant surgery			p-value
	after 1 year	after 3 year	after 5 year	
MBL	0.94	1.28	1.42.	<0.05

For 151 implants, the average RFA was 63.7 ISQ, after implant placement and 72.4 ISQ after 3–5 months (table 2).

Table 2.Average mean ISQ (Implant StabilityQuotient)

Implants	RFA ISQ (Implant Stability Quotient)		p-value
151	**after implant surgery** 63.7 ISQ	**after** 3–5 months **implant surgery** 72.4 ISQ.	<0.05

It was observed that 146 (96.8%) of 151 implants were successful and 5 (3, 2%) failed (table 3).

Table 3. Distribution of Implants Placed Across Sites

	Incisor		Canine		Premolar		Molar		Total	
	Number	Failed	Number	Failed	Number	Failed	Number	Failed	Number	Failed
Maxilla	27	0	18	0	16	1	14	2	65	3
Mandible	24	0	21	0	23	0	18	2	86	2
Total	51	0	39	0	39	0	32	4	151	5

The patients were satisfied, aesthetics and occlusion improved.

Discussion

The delayed dental implant protocol involves several stages after implant placement with an osseointegration healing period of 2 to 6 months followed by placement of the final prosthesis[22].

In recent times, there have been a significant number of clinical studies and systematic reviews that have positively assessed the immediate implants, and have shown a similar level of implant survival as with the delayed loading protocol[23].

The risk of implants immediately placed in sockets of teeth extracted with periapical pathology is that pathogenic bacteria in the socket can cause contamination of the implant during the early healing period[7,24].

Although studies published in recent years have

shown high success rates for immediate implant placement in sockets with chronic periapical pathology, the risks of this method are still a matter of debate in clinical practice[7,8,25].

To reduce the risk of infection, comprehensive curettage of granulation tissue and all soft tissue remnants in the sockets is necessary, irrigation with antiseptic agents for disinfection in mechanically difficult-to-reach areas, prophylactic use of antibiotics to disinfect the sockets of the extracted teeth[26-28].

Modern protocols offer immediate implantation and immediate loading, which is a predictable tooth replacement procedure that provides aesthetic and functional restoration[29-31].

Immediate loading of dental implants has several advantages such as reducing time, improving esthetic and occlusal function, eliminating temporary dentures, preventing reoperations and preserving residual alveolar bone and is considered a predictable procedure[32,33].

The use of preoperative virtual 3D is effective in controlling and immediate implant placement and immediate functional loading with the use of precise provisional prostheses[34,35].

This article describes the use of immediate implant placement protocol in areas with periapical lesions a technology that allows screw-retained and implant-supported temporary restorations using a completely digital protocol. With this accelerated digital treatment protocol, the transition to a restored dentition is achieved without the need for any physical impressions.

The use of CAD/CAM protocol in prosthetics on implants has three advantages: accuracy (or accuracy of fit), durability and simplicity of design. Each of these advantages is discussed as follows. With this protocol, the prosthetic sequence is significantly reduced, providing digital restoration of esthetics and function in one day.

Chronic odontogenic infection is a risk factor but not an absolute contraindication for immediate implants, the removal of teeth with periodontitis eliminates chronic odontogenic foci in the bone, which has a positive effect on the viability of the implants. In evaluated literature data there is no clear consensus on the grafting of the spaces between the implant and the socket.

According to the current research results, satisfactory survival rates (96.8%) were observed. Based on the results of this report, it can be concluded that immediate implant placement may be a favorable treatment option if careful selection of cases, the extracted tooth socket is debrided, antiseptically treated, and the implant has good primary stability in the extraction socket and correct prosthetic protocols. However, immediate implant placement requires a careful case selection and a specific treatment protocol. Although longer-term studies are needed, with a larger number of patients included.

DECLARATIONS

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Competing interests
Authors declare that they have no conflicts of interest to disclose.

Clinical trial number
Not applicable.

Ethical approval
This study was conducted in accordance with Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Patient consentment
The authors certify that they have obtained appropriate patient consent forms.

Authors contribution
All authors contributed equally to this manuscript. All authors participated significantly to the study design and execution, and have read, revised, and approved the final manuscript.

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RESEARCH ARTICLE

THE INFLUENCE OF VARIOUS FACTORS ON THE SUCCESS OF ORTHODONTIC MINISCREWS: RETROSPECTIVE STUDY

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Abstract

Objective: To assess the correlation between influencing factors such as patient age, gender, insertion side, and miniscrew length with the success and failure rates of orthodontic miniscrews.
Materials and Methods:A total of 142 miniscrews were placed in five different zones in 72 patients. Three different lengths of miniscrews were used. Patients were divided into three different groups according to their age.
Results: The highest success rate was observed in the upper right quadrant, while the lowest success rate was recorded in the lower left quadrant. Miniscrews with an 8mm length exhibited the highest success rate. Patients in group 1 showed the highest success rate; however, the chi-square test revealed no correlation with the success/failure rate of miniscrews.
Additionally, the success rate of miniscrews placed in female patients was higher than in male patients, with a significant correlation between gender and the success/failure rate of miniscrews.
Our findings highlight that the placement location (anterior palate vs. intraradicular) does not significantly impact the success rate of miniscrews. Instead, patient gender appears to be a more critical factor influencing miniscrew survival.
Conclusion: This retrospective study revealed that miniscrew success rate is not significantly influenced by insertion side, miniscrew length, or gender, but rather by patient age. Interradicular placement of miniscrews exhibits a success rate comparable to that of miniscrews placed in the anterior palate.
This knowledge can help orthodontists make more informed decisions about miniscrew placement and patient selection, ultimately improving treatment outcomes and advancing orthodontic practice.

Keywords: Key words: Orthodontic Miniscrew, Anchorage, Success rate, Stability

Introduction

Anchorage often plays a crucial and sometimes game-changing role in orthodontics. Prior to the invention of miniscrews, orthodontists had to rely on complicated and inconvenient appliances, which were not always well-received by patients. Due to the lack of patient compliance, the effectiveness of these methods was often minimal, resulting in alterations to the initial treatment plan.

Miniscrews, as anchorage devices, can be applied in various zones of the oral cavity, including interradicular sites in both the buccal and palatal regions, as well as extraradicular sites such as the infrazygomatic crest, buccal shelf, anterior palate, and ramus.

Different researchers have evaluated the success and failure rates of miniscrews in various regions. Topouzelis et al., stated that the overall success rate of miniscrews was 90.2%, with success rates of 93% in the retromolar triangle and 89% in the anterior palate, respectively[1]. Alharbi et al., in their systematic review, estimated the miniscrew failure rate to be 13.5%. The failure rate of short miniscrews was 12.7%, which is slightly higher than the failure rate of long miniscrews at 8.3%[2].

The stability of miniscrews can be influenced by various factors, including diameter, length, insertion torque, patient age and gender, poor oral hygiene, and insertion site.

In their study, G. Maino et al. reported that the mean overall success rate of the implants was 91.4%. They found that the length and shape of the miniscrews significantly influenced the success rate, while factors such as the side of insertion, screw diameter, and skeletal type showed no significant effects[3].

In orthodontic miniscrews of 1.6 mm diameter, regardless of the insertion method, the insertion torque increased with length. For orthodontic miniscrews of 1.4 mm diameter, and here was no statistical difference in the maximum ITV required for the continuous rotation insertion and intermittent rotation insertion methods between inserting orthodontic miniscrews of similar dimensions [4].

Sarul et al. compared the long-term stability of 6mm and 8mm miniscrews in the mandible within a homogeneous group of patients. They found that the 8mm orthodontic miniscrews were significantly more stable than the 6mm ones. The length of the TAD may be one of the factors affecting the long-term success rate in the mandibles of 20- to 29-year-old women, with the 8mm orthodontic miniscrews showing significantly greater stability in this group[5].

In a retrospective study, A. Manni et al. found that success rates were higher in male patients (88.1%) compared to female patients (76.4%). They also observed that a diameter of 1.3 mm was superior to a 1.5 mm screw diameter in achieving primary stability. Additionally, the success rates were significantly higher for miniscrews placed in the maxilla (86.9%) compared to those in the mandible (76.1%)[6].

Mohammadi et al., in their retrospective study, concluded that patients under 16 years of age and insertion torques exceeding 10 Ncm were associated with an increased failure rate of orthodontic miniscrews[7].

The aim of this retrospective study is to assess the correlation between influencing factors such as patient age, gender, insertion side, and miniscrew length with the success and failure rates of orthodontic miniscrews.

Materials and Methods

Data from the medical records of 72 patients from private clinic, who underwent miniscrew placement between 2021 and 2023 were retrospectively reviewed. A total of 142 miniscrews were inserted.The data extracted from the medical records included the date of miniscrew placement, the date of miniscrew removal or failure, the length and diameter of the miniscrew, the placement side, the age and gender of the patient. All patients and their parents were provided with detailed information and the consent was obtained through the signing of an agreement form.

Miniscrews of three different lengths (6mm, 8mm, and 10mm) were inserted, all with a diameter of 1.65 mm (Tomas, Dentaurum, Germany). These miniscrews were placed using the self-drilling method by the same surgeon, without prior drilling. Preoperative mouth rinsing with a 0.1% chlorhexidine solution occurred two days before and on the day of insertion.

Local terminal anesthesia, using an adrenaline-free anesthetic, preceded the placement of miniscrews. Following the surgery, patients were provided with standard postoperative care instructions, including gentle brushing of the surgical site to maintain oral hygiene. Additionally, patients were prescribed a 0.2% chlorhexidine mouth rinse to be used twice daily for one week.

A miniscrew was considered successful if it did not fail or show signs of mobility over a period of six months from the day of insertion. All miniscrews were loaded three weeks after insertion [8,9].

The failure of a miniscrew implant is defined as either the dislodgement of the miniscrew implant before loading or when a miniscrew becomes excessively mobile, thereby impeding the achievement of orthodontic anchorage objectives.

Patients were categorized into three groups based on their age: Group 1 (8-19 years), Group 2 (20-39 years), and Group 3 (40-60 years).

This research study has been conducted in full accordance with the World Medical Association Declaration of Helsinki.

Statistical Analysis

We used Logistic Regression model to analyze the relationship between various factors and the success-failure rate and descriptive statistics to summarize our findings. To assess the relationship between the categorical influencing factors and the miniscrew success/failure rate, the chi-square test was used.To compare the mean levels of different variables, the t-test was used.

The analysis was performed using SPSS 16.0 software (version 16; SPSS, Chicago, IL, USA). The level of significance was set at P = 0.05

Results

Totally 142 miniscrews were inserted in 5 different sides: Buccal Upper left, Buccal Upper right, Buccal Lower left, Buccal Lower right , Anterior Palate. Overall success rate was 90.14 % (128 miniscrews) and overall failure rate was 9.86 % (14 miniscrews). Amount of placed miniscrews in different zones with related success rates are shown in Table 1.

Table1.Success Rates of Different Insertion Si

Insertion Side	Overall amount	Success	Failure	SD(success)	SD(Failure)	Chi-square (p-value)
Total Miniscrew	142	128 (90.14%)	14 (9.86%)	13.27 %	12.6 %	
Buccal Upper Right	29	28 (96.5%)	1 (3.5%)	5.9 %	5.68 %	p>0.05
Buccal Upper Left	23	21 (91.3%)	2 (8.7%)			
Buccal Lower Left	14	11 (78.6%)	3 (21.4%)			
Buccal Lower Right	11	10 (90%)	1 (9%)			
Anterior Palate	65	58 (89.3%)	7 (10.7%)			

The lowest success rate was observed on the buccal left side of the mandible at 78.6%, while the highest success rate was observed on the buccal right side of the maxilla. The success rate of miniscrews placed on the anterior palate was 89.3%. However, other placement sides exhibited significantly higher success rates ranging from 90% to 91.3%. Despite these differences, chi-square testing revealed no correlation between placement sides and miniscrew success/failure rates (p>0.05).

The success rates for miniscrews with lengths of 10 mm and 8 mm were almost equal at 91.8% and 88.88%, respectively, while miniscrews with a length of 6 mm showed no failures. Chi-square testing indicated no correlation between miniscrew length and the success/failure rate of miniscrews (p>0.05).

Additionally, the success rates of patients in Group 1 and Group 2 were similar, but patients in Group 3 exhibited a success rate almost 1.4 times lower than that of patients in Groups 1 and 2. Chi-square testing revealed a statistically significant correlation between patient age and the success/failure rate of miniscrews (p< 0.05). (Tab. 2)

Table 2 Success Rates of Different Miniscrew Lengths

Miniscrew Lenght	Overall amount	Success	Failure	SD(success)	SD(Failure)	Chi-square (p-value)
10 mm	49	45 (91.8%)	4 (8.2%)	0.27 (0.29%)	0.09 (0.9%)	p>0.05
8 mm	90	80 (88.88%)	10 (11.12%)	0.32 (0.36%)	0.1 (0.95%)	
6 mm	3	3 (100%)	0	0	0	

The success rate of miniscrews placed in male patients (96%) was higher than that of those placed in female patients (87.1%). Only two miniscrews failed in male patients, while twelve failed in female patients. However, chi-square testing revealed no correlation between the gender of patients and the success/failure rate of miniscrews (p > 0.05). (Tab. 3)

Table 3: Success Rate by Age group and Gender

Patients age	Overall amount	Success	Failure	SD(success)	SD(Failure)	Chi-square (p-value)
Group 1(8-19 years)	73	68 (93.1%)	5 (6.84%)	0.25 (0.28%)	0.25 (3.72%)	P<0.05
Group 2(20-39 years)	57	52 (91.2%)	5 (8.77%)	0.28 (0.3%)	0.28 (3.29%)	
Group 3(40-60 years)	12	8 (66.7%)	4 (33.3%)	0.47 (0.7%)	0.47 (1.4%)	
Gender						
Male	49	47 (96%)	2 (4%)	0.19 (19.69%)	0.2 (20.27%)	p>0.05
Female	93	81 (87.1%)	12 (12.9%)	0.32 (32.2%)	0.11 (11.04%)	

Discussion

The stability of miniscrews is crucial for reliable anchorage and predictable orthodontic treatment outcomes. Miniscrew failure can significantly impact the initial treatment plan. Numerous studies have investigated the success/failure rates of miniscrews, yielding varied results. In our retrospective study, the success rate was found to be 91.8%, which aligns closely with the findings of some of the aforementioned studies[2,3,10,11].

We observed a relatively high success rate for interradicular placements (90-96.5%), except in the lower left quadrant. This phenomenon might be connected to the fact that the surgeon was right-handed, making left-side placement less convenient.

In some cases, bicortical fixation was achieved in the upper jaw, which can significantly increase stability[12]. Additionally, nearly half of the interradicularly placed miniscrews were utilized as indirect anchorage.

Forty-five percent (65 pieces) of all miniscrews were placed in the anterior palate, and seven of them failed. All palatally placed miniscrews were inserted without predrilling and had a length of 8 mm. Interestingly, in one patient, miniscrews placed in the anterior palate failed three times, significantly impacting the statistics. The overall success rate was 89.3%, which differs from findings reported in several studies[10,13,14].

The correlation between patient age and miniscrew survival rate has been studied by different authors[6,10,14-17].

In this study, a significant portion of all miniscrews were placed in patients under 40 years of age (91.5%). Specifically, 73 miniscrews were placed in patients aged 8-20 years, with a success rate of 93.1%, while 57 miniscrews were placed in patients aged 20-40 years, achieving a success rate of 91.2%. The number of miniscrews placed in patients over 40 years of age was considerably less (only 12 miniscrews), with a success rate of 66.7%. Interestingly, all miniscrews placed in patients over 40 years were interradicular.

We found that the difference in success rates between male and female patients was not statistically significant. These results are similar to those reported in several other studies. However, there are also studies that have suggested a correlation between patient sex and miniscrew success rate [6,18-20].

In summary, our study indicates a relatively high success rate of orthodontic miniscrews. We observed the highest success rate in the upper right quadrant and the lowest rate in the lower left quadrant. Despite examining various factors such as insertion site, miniscrew length, patient age, and sex, we found a significant correlation only between success rate and patient age. Specifically, we noted a lower success rate in patients over 40 years of age compared to those under 40. It's important to note that our study did not consider factors such as malocclusion type, growth type, or anchorage design. These findings underscore the need for further research to better understand the factors influencing miniscrew success in orthodontic treatment.

Conclusion

Orthodontic miniscrews can serve as reliable anchorage for various types of tooth movement. This retrospective study revealed that miniscrew success rate is not significantly influenced by insertion side, miniscrew length, or gender, but rather by patient age. Interradicular placement of miniscrews exhibits a success rate comparable to that of miniscrews placed in the anterior palate.

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Conflicting interest

None

Ethical Approval

Institutional Human Ethical Committee Yerevan State Medical University and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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RESEARCH ARTICLE

FORDYCE GRANULES AS A POTENTIAL CHAIRSIDE CLINICAL PREDICTOR FOR HYPERCHOLESTEROLEMIA: A CROSS-SECTIONAL STUDY

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Abstract

Background: Fordyce's granules (FGs) are ectopic sebaceous glands commonly located in the oral cavity, appearing most frequently on the buccal mucosa, vermilion border of the lips, and occasionally in the retromolar areas. Owing to its lipid content, there has been conjecture regarding a potential connection between FGs and dyslipidemia, a disorder characterized by elevated lipid levels that may be linked to ectopic lipid deposits in different tissues.

Aim: The purpose of this cross-sectional study was to ascertain whether Fordyce's granules could be used as a chair side clinical marker to identify those who are at risk for dyslipidemia.

Methods: The cross-sectional study was carried out at Saveetha Dental College and Hospitals in Chennai over the course of a year, from June 2023 to May 2024. 100 adult dental patients between the ages of 18 and 60 were examined clinically by an oral medicine specialist to determine whether Fordyce granules were present. Every participant had their blood drawn in order to determine their lipid levels. Analysis was performed on the data to determine predictors for hypercholesterolemia.

Results: Patients with detectable oral FG had a mean age of 50.2 ± 12.3 years. A mean total cholesterol of 250.3 ± 41.7 mg/dL ($p < 0.001$) and mean HDL cholesterol value of 42.0 ± 8.1 mg/dL ($p < 0.05$) were seen to be associated with presence of FG with statistical significance. The odds ratio (1.083) indicates that for every unit increase in TC, the odds of FG increase by 8.3%.

Conclusion: The presence of oral Fordyce granules may indicate increased total cholesterol predisposing individuals to hypercholesterolemia. Factors such as age, smoking, and diabetes mellitus showed no association between Fordyce granules and lipid profiles.Previously regarded as a normal anatomical variation, fordyce granules should be considered in conjunction with other risk factors to identify possible dyslipidemia.

Keywords: Cholesterol, serum, lipids, mouth, dyslipidemias

Introduction

Fordyce's granules (FGs) are ectopic sebaceous glands commonly located in the oral cavity, appearing most frequently on the buccal mucosa, vermilion border of the lips, and occasionally in the retromolar areas. They are also found on the genital mucosa, including the glans penis and labia minora. These granules, initially documented by Kölliker and later described by Fordyce, are now understood as normal anatomical variations rather than pathological findings[1,2]. Clinically, FGs are small, asymptomatic, yellowish to whitish papules that range from 0.2 to 2 mm in diameter and often remain stable throughout life. Although present in up to 80-90% of individuals, FGs become more visible after puberty and are more common in those with oily skin[3-5].

The pathogenesis of FGs remains unclear, although their lipid-rich composition is similar to typical sebaceous glands, comprising triglycerides, wax esters, and squalene, which create a lipid barrier on skin surfaces[6,7]. This lipid content has led to speculation about a possible link between FGs and dyslipidemia, a condition marked by abnormal lipid levels, which could be associated with ectopic lipid deposits in various tissues[8]. While FGs are generally harmless, recent studies have explored their potential connection with systemic lipid imbalances. For instance, findings suggest that higher FG density may correlate with hyperlipidemia, indicating that these granules could have diagnostic relevance. Either the increased fatty content of clinically undetectable glands, which makes them readily evident during the oral examination, or the de novo differentiation of cells, which results in more oral FGs, are two ways that hyperlipidemia may contribute to the development of oral FGs[9].

Despite several studies documenting the prevalence of FGs, few have examined their clinical significance. Given the role of dyslipidemia as a risk factor for cardiovascular disease, identifying visible markers such as FGs could aid in early detection and intervention. This cross-sectional study seeks to determine whether the presence of Fordyce's granules may serve as an accessible clinical marker for identifying individuals at risk for dyslipidemia.

Methods

This study was a cross-sectional study conducted between a time period of one year from June 2023 - May 2024 at Saveetha Dental College and Hospitals, Chennai. Adult dental patients aged 18-60 years who visited the OP during the given time frame, were subjected to a thorough clinical examination by an Oral Medicine specialist, to identify the presence of Fordyce granules. Patients with no previous history of lipid-altering medications or medical conditions affecting lipid metabolism who were willing to participate in the study were included. Patients with genetic lipid disorders, those on treatment for dyslipidemia at the time of examination, patients with any other oral mucosal lesion and pregnant patients were excluded from this study. Approval was obtained from the Institutional Human Ethical Committee (Reference number – IHEC/SDC/UG-1962/23/OMED/192) and informed consent was obtained from all the included patients prior to study commencement.





Figure1. Oral fordyces granules on buccal mucosa
Figure 2. Oral fordyces granules labial mucosa

Sample size calculation

Sample size was calculated considering the prevalence of FG of 5.3% and a prevalence rate of dyslipidemia of 37.5 % among adult Indian population along with a standard alpha level of 0.05[10,11]. For this study, with 90% power, a sample size of approximately 29 participants was needed to detect an association between the presence of Fordyce's granules and dyslipidemia based on the given prevalence rates. However, to ensure robust results and given the time frame of 1 year of the study, we included a larger sample size of 100 patients to account for potential variability.

Bloodsamples was collected from all participants to measure lipid levels. Blood samples were analyzed using standardized laboratory techniques. The patients were not mandatorily under overnight fasting of 12 hours at the time of collecting blood samples. This was not practical, as the included patients were those visiting a dental hospital for routine dental treatments. However, lipid profiles can often be assessed without fasting, especially for total cholesterol (TC) and HDL cholesterol, as non-fasting values tend to be comparable to fasting ones. Hence, in this case we assessed only the TC and HDL values. Patients with high TC or low HDL levels were classified as having dyslipidemia based on the following thresholds[12,13].

1. Total Cholesterol (TC):
    - Desirable: TC < 200 mg/dL
    - Borderline High: TC 200–239 mg/dL

- High: TC ≥ 240 mg/dL

2. HDL Cholesterol:
   - Low HDL (risk factor):
     - Men: HDL < 40 mg/dL
     - Women: HDL < 50 mg/dL
   - Normal HDL: HDL ≥ 40 mg/dL for men and ≥ 50 mg/dL for women
   - Protective (high HDL): HDL ≥ 60 mg/dL

Dyslipidemia is classified as present if either total cholesterol is 200 mg/dL or higher or HDL is below the thresholds specified (40 mg/dL for men, 50 mg/dL for women)[12,13].

Statistical Analysis

The collected data were entered into Microsoft Excel 2016 and analyzed using IBM SPSS Statistics for Windows, Version 29.0 (Armonk, NY: IBM Corp). Descriptive statistics, including frequency and percentage analyses, were applied to summarize categorical variables, while the mean and standard deviation (SD) were calculated for continuous variables. An independent sample t-test was conducted to assess significant differences between bivariate samples in independent groups, and the Chi-square test was used to evaluate associations in categorical data. Binary logistic regression with the enter method was applied to identify predictors of Fordyce's Granules presence. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

100 patients were included in the study which constituted 51 males and 49 females. Out of 35 patients who had FG, 35.3% (18) were males and 34.7%(17)were females(p> 0.05) **(Table 1)**.

Table 1Association between gender and presence of FG

			Fordyces Granules		Total
			Present	Absent	
DM	Yes	Count	19	24	43
		%	44.2%	55.8%	100%
	No	Count	16	41	57
		%	28.1%	71.9%	100%
Total		Count	35	65	100
		%	35%	65%	100%

Pearson Chi-Square Test, p = 0.950

The proportion of non-smokers (78%) was higher in the study population compared to that of smokers (22%).

Among the 35 patients with Fordyce's granules, only 4 reported a history of smoking, while the other 31 were non-smokers. The relationship between smoking history and presence of FG was found to be statistically insignificant in this study **(Table 2)**.

Table 2 Association between smoking history and presence of FG

			Fordyces Granules		Total
			Present	Absent	
Smoking History	Non-Smoker	Count	31	47	78
		%	39.7%	60.3%	100%
	Smoker	Count	4	18	22
		%	18.2%	81.8%	100%
Total		Count	35	65	100
		%	35%	65%	100%

Pearson Chi-Square Test, p = 0.061

19 (44.2%) patients had presence of FG and were diabetic, as well. 16 (28.1%) of the study population were not diabetic, although, had presence of FG (p>0.05) **(Table 3)**.

Table 3 Association between Diabetes Mellitus and presence of FG

			Fordyces Granules		Total
			Present	Absent	
DM	Yes	Count	19	24	43
		%	44.2%	55.8%	100%
	No	Count	16	41	57
		%	28.1%	71.9%	100%
Total		Count	35	65	100
		%	35%	65%	100%

Pearson Chi-Square Test, p = 0.094

Among the 35 patients with presence of FG, 25(71.4%) patients were found to be dyslipidemic. 40.3% of dyslipidemic patients had clinical presence of FG in their oral cavity ($p > 0.05$) **(Table 4)**.

Table 4. Association between Dyslipidemia status and presence of FG

			Fordyces Granules		Total
			Present	Absent	
Dyslipidemia	Yes	Count	25	37	62
		%	40.3%	59.7%	100%
	No	Count	10	28	38
		%	26.3%	73.7%	100%
Total		Count	35	65	100
		%	35%	65%	100%

Pearson Chi-Square Test, p = 0.154

Patients classified to be dyslipidemic had a mean age of 50.2 ± 12.3 years. A mean total cholesterol of 250.3 ± 41.7 mg/dL ($p < 0.001$) and mean HDL cholesterol value of 42.0 ± 8.1 mg/dL ($p < 0.05$) were seen to be associated with presence of FG with statistical significance **(Table 5)**.

Table 5. Interaction of Mean values of age, TC and HDL with FG

	Fordyces Granules	N	Mean	SD	P value
Age	Present	35	50.2	12.3	0.592
	Absent	65	48.9	11.4	
TC	Present	35	250.3	41.7	0.0000
	Absent	65	213.0	23.3	
HDL	Present	35	42.0	8.1	0.017
	Absent	65	45.9	7.3	

Independent Samples T Test

Results of logistic regression analysis exploring the association of Fordyce's granules with specific predictors included in the model is represented **(Table 6)**.

Table 6. Logistics Regression

		B	S.E.	Wald	df	P value	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1a	Age	-0.047	0.036	1.678	1	0.195	0.954	0.889	1.024
	Gender(1)	-0.005	0.690	0.000	1	0.994	0.995	0.258	3.844
	Smoking(1)	1.376	0.915	2.262	1	0.133	3.959	0.659	23.785
	TC	0.079	0.021	13.645	1	0.0002	1.083	1.038	1.129
	HDL	-0.017	0.066	0.070	1	0.791	0.983	0.863	1.119
	Dyslipidemia(1)	2.105	1.024	4.229	1	0.040	8.205	1.104	60.995
	DM(1)	0.513	0.897	0.327	1	0.568	1.670	0.288	9.690
	Constant	-17.687	6.425	7.557	1	0.006	0.000		

A. Variable(s) entered on step 1: Age, Gender, Smoking History, Total Cholesterol, HDL, Dyslipidemia Status, DM.

B: The regression coefficient, S.E.: Standard error of the regression coefficient, df: Degrees of freedom, Exp(B): Odds ratio

Age is not a significant predictor of FG. The odds ratio (0.954) suggests a slight negative association, but it is not statistically meaningful. Gender does not significantly impact the odds of FG. The odds ratio (0.995) indicates no meaningful change in odds based on gender. The odds ratio (3.959) suggests smokers may have higher odds, but this finding lacks statistical support. Total cholesterol is a statistically significant predictor of FG ($P < 0.05$). The odds ratio (1.083) indicates that for every unit increase in TC, the odds of FG increase by 8.3%. HDL is not a significant predictor of FG. The odds ratio (0.983) suggests a negligible negative association. Dyslipidemia is a significant predictor of the outcome ($P < 0.05$). The odds ratio (8.205) indicates that individuals classified as dyslipidemic have significantly higher odds (8.2 times) of FG. Diabetes mellitus is not a significant predictor of FG. The odds ratio (1.670) suggests a potential positive association, but it is not statistically meaningful.

DISCUSSION

Oral Fordyce granules (FGs) are frequently identified during routine dental check-ups and are regarded as normal anatomical variations[13]. However, rarely they have been suggested to be associated by hypercholesterolemia[14]. One case report of dermoid cyst in the oral cavity highlights that presence of FG in the site was the only clinical finding[15]. A study done among Middle East population reported a very high prevalence (89.7%) of detectable FGs in oral cavity[16]. Another study from Karachi reported the presence of oral FG in half (50.9%) of the included sample[17]. A study from Iraq noted that only 25% of the study population had FG in

the oral cavity[18]. A large cohort study on European population revealed a very low prevalence rate of 1.2% for oral FG[19]. This suggests a varying wide range of prevalence of FG in oral cavity reported in the literature. The current study on dental patients visiting a dental hospital observed the clinical finding of oral FG in 35 out of 100 patients documenting a prevalence rate of 35% for the same.

FG, Age and Gender

J H Olivier assessed the prevalence of FG on the prolabial and oral mucous membranes among South African population which was found to be 62.07% in adult males and 57.25% in adult females[20]. In a study by Shahzad et al., compared to female patients (37%), male patients had a higher prevalence of Fordyce's granules (57%). They found a higher frequency in patients older than 20 years. Fordyce's granules were shown to be highly prevalent in the third and fourth decades of males and the fourth and fifth decades of females[17]. In two individual studies Cawson et al., and Pindborg JJ et al., have concluded that prominence of FG increases with increase in age. Whereas, Flinck A et al, found that the number of these granules decreased with advancing age. No statistical dominance for any particular age group was reported by Gaballah KY et al[16]. In the current study it was recorded that the FG presence was associated significantly with a mean age of 50.2 years favoring the former study results.

FG and smoking status

The current study only 11.4% of individuals with FG had positive smoking history. It should be noted that the study sample constituted a majority of nonsmokers and the association obtained was statistically insignificant. In the study by Gaballah et al., The detection of FGs did not show a statistically significant difference between smokers (98.8%) and non-smokers (87.7%)[16]. On the other hand, UM Olivio et al., reported that compared to present smokers (0.9%, n = 3) or past smokers (0.7%, n = 4), non-smokers (1.5%, n = 15) had higher levels of Fordyce granules[19]. Another epidemiological study on Iranian population also revealed Forduces granules presence to be more in non-smokers (42%) than smokers (26.7%)[21]. These studies along with present study results supports the smoking can obscure the appearance of Fordyce granules. This could be an impact of thickening of the oral epithelium and increased melanin[22].

Diabetes Mellitus and FG

Fordyce granules did not show any significant relation with the diabetes mellitus in the study by Jahanbani et al[21]. A study on oral alterations in diabetics suggested that 2.3% of patients with type II DM had FG[23]. Souza MGM et al., reported that FG is common in type II DM[24]. However, the current study did not find any statistically significant association between DM and FG.

FG and Dyslipidemia

AR Diajil concluded that fordyce granules were found in one-fourth of patients with hypercholesterolemia, however the majority of cases had normal triglyceride levels, HDL, LDL, and VLDL levels. The lipid profile and these granules did not correlate, according to the chi-square test. Their study however included patients who visited a primary health centre and were subjected to serum lipid profiling after 8-12 hours overnight fasting. Also, they scored the test values as normal, borderline and high which was different from the classification criteria used for dyslipidemia in this study. Correlation analysis were performed on the data, while the present study assessed the odd's ratio values using regression analysis[18].

Gaballah KY et al also evaluated the possible interplay between FG and hypercholesterolemia. They scored the FG based on the number of spots. It was seen that among the individuals scored with 6-30 spots the number of patients with hypercholesterolemia was twice (n=76) than in those with controlled lipid levels (n=33). They pointed out that the individuals with an elevated lipid profile had higher chance of exhibiting a surge in the number of FG in the oral cavity[16].

Another study tried to explore the association between blood grouping, FGs and serum lipid profile. Their study results suggested that those with AB positive blood group had higher number of FGs and also, the individuals having the same blood group were more likely to have hypercholesterolimia[25].

The current study results are consistent with the previous, though scanty, literature which indicates a possible association between FGs and lipid profile. Dyslipidemia was found to be associated more with those in their 6th decade of life. With statistical significance, the presence of FG was linked to a mean HDL cholesterol value of 42.0 ± 8.1 mg/dL and a mean total cholesterol of 250.3 ± 41.7 mg/dL. A logistic regression analysis was applied which revealed that total cholesterol (P = 0.0002) and dyslipidemia (P = 0.040) were the significant predictors in this model in comparison with other variable such as age, gender, smoking, HDL, and diabetes that did not show a statistically significant impact. This suggested that total cholesterol and dyslipidemia play a substantial role in clinically detectable oral FGs, while other factors may require further investigation in larger or different samples.

Limitations, Advantages and Future Prospects

Not taking the triglyceride and LDL levels for the lipid profile can be taken as one of the limitations of this study. This made comparison of dyslipidemia status of patients with existing studies challenging due to the variation in the classifying criteria. Serum cholesterol can be influenced by other confounding factors such as dietary habits, family history, physical activity and alcohol consumption which were not taken into account in this analysis. In subsequent research, histochemical analysis can be done for the fordyces granules in patients with and without deranged lipid profile to further elucidate the interplay between serum cholesterol and oral FGs.

Nevertheless, the current study is unique in other aspects. Considering the studies in literature, firstly most of the related studies report epidemiological data which have studied FG as a mucosal variant or alteration in different population[20,21]. The studies which have tried to assess the possibility of FG as having an association with the systemic status is extremely limited in number.

The current study done on South Indian population stands out in its attempt to evaluate the role of FG in the lipid status of dental patients visiting a hospital for dental treatment. For applicability, in dental clinical set up, we assessed TC and HDL levels for the lipid profile without mandatory fasting. Non-fasting tests are generally sufficient for cardiovascular risk prediction, making testing more convenient for patients. However, fasting samples may still be required if initial levels are high, as non-fasting triglycerides can be significantly elevated due to recent food intake. We considered testing only TC and HDL levels as these readings do not tend to be significantly affected by in case of non-fasting. The American Heart Association and other major guidelines now accept non-fasting lipid panels in routine testing, reserving fasting measurements for more detailed assessments if initial triglyceride levels are unusually high[12,13]. Another noteworthy feature of this study is that the oral examination of included patients for the presence of FG was performed by an Oral Medicine specialist. Many general practitioners tend to not identify the granules as FGs or may ignore the finding[26].

Hence, in this study screening by a specialist ensured that cases were not missed out. Many research studies are ongoing to assess the lipid profile in dental patients for various clinical applications in dentistry[27-30].

This study which underscores a possible association of oral FGs with dyslipidemia in dental patients could indicate the potential use of oral FGs as a surrogate marker for hypercholesterolimia.

CONCLUSION

Within the confines of this cross-sectional study, the authors conclude that presence of oral fordyces granules can point towards an increase in total cholesterol and a drop in the high-density lipoprotein, thereby, resulting in a predisposition to hypercholesterolemia. Other factors like age, smoking habit and a history of diabetes mellitus were not seen to have any link with oral fordyces granules in comparison with the lipid profile.

Dentists often encounter patients with prominent fordyces granules during routine examination. The results of this study can be an add-on to the deficient literature base which emphasizes the need to consider these granules to be interconnected with the patient's lipid profile. Previously touted as a normal anatomical variation, dentists should bear in mind this possible interdependence. If a patient exhibits prominent fordyces granules along with other risk factors for dyslipidemia or cardiovascular disorders like age, obesity, smoking history, family history, stress, poor diet and lack of physical activity, then the dentist should consider evaluating the lipid profile to rule out dyslipidemia.

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Conflicting interest

None

Ethical Approval

Institutional Human Ethical Committee/Saveetha DentalCollege/Undergraduate-1962/23/Oral Medicine/192) and was conducted in accordance with theDeclaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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CASE REPORT

THE IMPACT OF IN-HOUSE SURGICAL GUIDES ON GENIOPLASTY PRECISION

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Abstract

Objective: The aspect, volume, shape, and projection of the chin contribute to a "well-balanced and harmonious" face, and good projection influences psychosocial well-being, playing a fundamental role in facial aesthetics. The aim of this paper is to discuss the importance of using surgical guides in genioplasty.

Case Series: Two patients underwent bimaxillary orthognathic surgery with genioplasty using 3D-printed guides were reported.

Case 1 involved posterior impaction and 2mm advancement genioplasty.

Case 2 addressed chin rotation, posterior impaction, and lowering without advancement. The chin's form and projection contribute to facial harmony.

Conclusion: Computer-assisted surgical simulation allows precise guide creation, making genioplasty safer and minimally invasive. Guides reduce complications and offer cost-effective benefits over traditional methods. Genioplasty with in-house 3D-printed guides shows promise in improving predictability, precision, and safety. Further research on printers, materials, sterilization, and open-access software is needed

Keywords: Genioplasty; Printing, three-dimensional; Surgery, computer-assisted; Orthognathic Surgery; Planning Techniques.

INTRODUCTION

Chin plays a fundamental role in facial aesthetics, with the lower third being an important area, even to an untrained eye. It is one of the facial structures that draws the most attention in facial aesthetics, with an impact on social and personal relationships [1]. Considering an aesthetic evaluation, an imbalance in this area in terms of shape, size, and position contributes to the overall disharmony of the face [2]. Genioplasty is a widely used surgical technique to correct chin deformities. Trauner and Obwegeser were the first surgeons to perform chin advancement osteotomy through an intraoral approach, calling it genioplasty [3]. This technique has been modified by several others to move the chin in all three dimensions of space.

High predictability cutting guides are created through preoperative three-dimensional simulation, primarily aiming to preserve critical areas such as nerves and tooth roots, and allowing for repositioning of the chin to the desired position defined in the virtual planning [4].

Alterations in the lower third of the face are sensitive to the amount of advancement or setback, as well as vertical displacement of the bony segment. Virtual genioplasty planning focuses on the horizontal and vertical movements of the segment, rather than the design of the osteotomy itself. It is important to consider the mentolabial fold in the

virtual planning for frontal and vertical displacement of the bony segment, as it has a significant effect on the cephalometric points of the soft tissue portion of the segment.

Correcting chin deformities improves facial balance and harmony, and many patients are unaware that there are ways to correct them through chin augmentation or reduction [3]. Chin aesthetic treatments should consider chin height and width, projection, and shape, and should also take into account the adjacent facial structures. Thus, the aim of this work was to report two clinical cases using virtual planning with 3D-printed cutting guides to perform a genioplasty.

Case Series

This is a retrospective single-center consecutive case series according to the recommendations from the Consensus Preferred Reporting Of CasE Series (PROCESS) guideline [5]. Two young patients were submitted to a bimaxillary orthognathic surgery and genioplasty. Some slight differences in virtual surgical planning were discussed. Both patients were submitted to CT scans, intraoral scanning (iTero), Virtual Surgical Planning through Dolphin Imaging ® 11.91 software. The surgical guides were obtained through 3D printing using an Elegoo Mars 2 Pro Teresina printer and Smart Dent - Smart 3D Print Bio Clear Guide resin. The surgeries were performed according to the simulated planning. Both genioplasties were performed with piezosurgery.

Case 1

A 28-year-old female patient underwent bimaxillary orthognathic surgery with genioplasty. The genioplasty was planned with posterior impaction and 2mm advancement, in addition to a 2mm symmetry correction (fig. 1). The decision to create a surgical guide was made due to the intraoperative challenge of accurately removing this bony slice, which could compromise facial aesthetics if not executed precisely (figs. 2 and 3). In this case, removal of adipose tissue on the muscle surface was necessary.

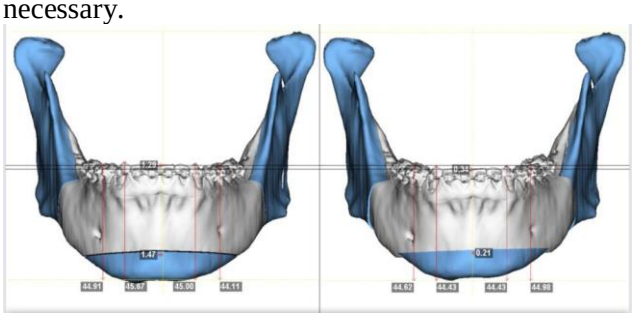


Figure 1. Pre and postoperative Virtual Surgical Planning correcting chin asymmetry.

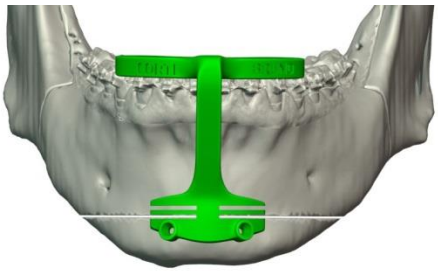


Figure 2.Genioplasty cutting guide.

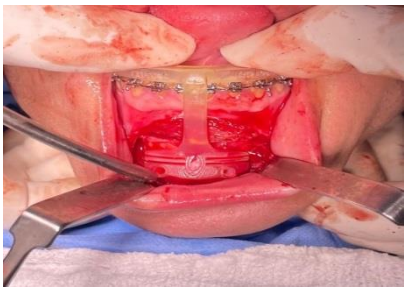


Figure 3. Genioplasty cutting guide.

Case 2

A 24-year-old male patient underwent bimaxillary orthognathic surgery with genioplasty. In this case, there was neither advancement nor setback of the chin. The difficulty in performing the surgery was associated with a clockwise rotation of the chin, a 2mm posterior impaction, and a 3mm advancement of the chin (fig. 4), something quite challenging to execute without surgical guides. A positional guide was crafted and 3D printed (fig. 5).

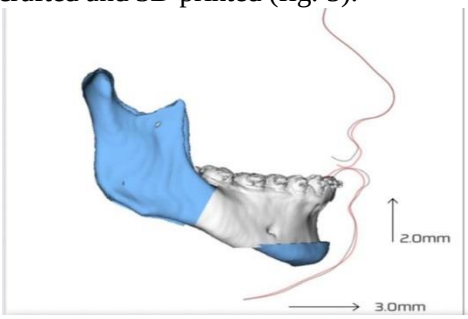


Figure 4. Profile Virtual Surgical Planning demonstrating chin impaction. A very hard to perform surgical step without aid of a cutting guide, notably in posterior region.



Figure 5.3D printed genioplasty positional and cutting guides.

Discussion

The aspect and volume of the chin are important, and their boundaries are determined by the mentolabial fold, the lip commissures, and the submental cervical fold. The shape and projection of the chin contribute to a "well-balanced and harmonious" face, and good chin projection influences psychosocial well-being.

With the rapid development of computer-assisted surgical simulation (CASS) technology, surgeons are now able to design a surgical guide in the preoperative phase through virtual planning. The printed guide is accurately transferred to the patient in the operating room exactly as planned digitally [6].

Genioplasty is a procedure that has great potential to transform facial profiles, and the technique using customized guides helps mitigate the disadvantages of the procedure, making it safe, precise, and predictable. In the past, the difficulties in performing genioplasty led to the procedure being exclusively performed in a surgical center under general anesthesia, and today it can be performed with local anesthesia on an outpatient basis with sedation [7,8].

The average duration of a genioplasty, from the first incision to the final stitches' ranges from 30 to 90 minutes. The surgeon's experience, the means used to perform the osteotomy (saw, drill, piezo), the technique used for genioplasty, and the bone movements performed should be considered. The development of 3D printing techniques and piezosurgery provided the basis for the establishment of a genioplasty technique that combines both technologies: Minimally Traumatic Guided Genioplasty. A previous study evaluated the profile with correct lip position in women and correct chin position in men, considering cephalometric measurements, and all profiles with deviations from the average obtained lower scores. These findings are important to establish a gold standard and improve awareness during the decision-making process [4,8,9].

Mental nerve injuries, paresthesia, asymmetries, and intraoperative bleeding are the main immediate complications of genioplasty. The literature agrees that operating with guides is much more comfortable as it not only promotes the protection of anatomical structures but also reduces complications. The cost-benefit ratio seems largely in favor of using 3D printing technology during genioplasty compared to traditional techniques. Some advocate for the use of chin implants due to their simplicity and predictability, although the long-term results are unpredictable and unknown in the literature [4,6–9].

The predictability of osteotomy results and osseous repositioning in the soft tissues of the chin is still controversial and requires more specific parameters to predict better results regarding the skin surface response after genioplasty. Result predictions have been made in studies using standard two-dimensional cephalometric analysis or 3D methods, where the latter is the better choice. The finite element method (FEM), already described in the literature, is a viable and accurate method for predicting changes in soft tissues during surgery [8].

The chin is a cortical bone that requires intense and risky osteotomy due to the two cortical plates and the risks and limited visibility in the region where the mental nerve emerges. Osteotomies in the chin are challenging to achieve a perfect level of symmetry, even with guides, and this challenge is greater in cases of asymmetry or secondary genioplasty. Additionally, the positioning of the osteotomized fragment is complex, as it can be placed in different positions in the three planes of space [7].

Financial costs should be considered as they vary according to the printer, the cost of printing materials, and the software used. An European study found that in a dedicated laboratory, the cost of printing a genioplasty guide does not exceed 5 euros after acquiring a 3D printer and utilizing free medical 3D software. They also indicated that the costs of genioplasty guides with external companies range from 400€ to 1000€ on average [9].

Several factors can cause the chosen cutting plan in virtual planning to not correspond exactly to the guide during surgery, including possible software and hardware errors, data loss, 3D printing issues (imprecision of the 3D printer, insufficient rendering quality, quality of the raw material), guide deformation during the process and storage, guide instability when used in the surgical procedure, and sterilization [4,6].

Although several studies have described virtual planning and surgical guides as a precise technique, it still remains a challenge. This protocol reduces the complexity of the procedure and surgical time, guarantees results, minimizes surgical and aesthetic complications, and allows the procedure to be performed with only local anesthesia and oral sedation [7–9].

The complications described in the literature are well-known complications of genioplasty; no new complications due to this new technique and no increase in complication rates have been found [9].

Future research is needed to increase the accuracy of virtual planning and surgical guides in genioplasty, with long-term evaluations, prospective study designs, and control groups. To ensure high-quality and comparable results, future researchers

should be encouraged to focus on automatic 3D analysis according to standardized and validated methods [10].

Conclusion

Performing genioplasty with a surgical guide using 3D printing technology is a promising technique that can improve predictability and precision, protect anatomical structures, reduce morbidity, and provide safer results. The type of printer and material used, as well as sterilization techniques, should be further researched. The use of open-access software should also be explored to allow more surgeons to utilize these new technologies. Lastly, prospective multicenter studies with larger samples should be conducted to definitively conclude on the benefits of this new technology and enable its routine use.

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Competing interests

Authors declare that they have no conflicts of interest to disclose.

Clinical trial number

Not applicable.

Ethical approval

This article is exempt of ethical approval since it was performed in our private practice. This study was conducted in accordance with Good Clinical Practice guidelines and the principles of the Declaration of Helsinki.

Patient consentment

The authors certify that they have obtained appropriate patient consent forms.

Authors contribution

All authors contributed equally to this manuscript. All authors participated significantly to the study design and execution, and have read, revised, and approved the final manuscript.

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RESEARCH ARTICLE

COMPARATIVE EVALUATION OF HYBRID ARCH BAR AND ERICH ARCH BAR IN THE MANAGEMENT OF MAXILLOMANDIBULAR FRACTURES

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ABSTRACT

PURPOSE: The purpose of this study was to compare operative time, effect on the gingiva, glove penetration rate and post-operative complications of the Hybrid arch bar (HAB) and Erich arch bar (EAB). **MATERIALS AND METHODS:** Patients reporting to our institution, diagnosed with maxillomandibular fractures indicated for IMF were included in the study and randomized into two groups (Group I with Hybrid arch bars and Group II with Erich arch bars). Operative time in minutes, glove penetration rate were evaluated during the placement and removal of the arch bar. Gingival health was evaluated before the placement and after removal of the arch bar and different complications encountered were evaluated during every visit. Both of the groups were compared using t test and chi-square tes

RESULTS: Of the 80 cases studied, 40 were in the Hybrid arch bar group and 40 in the Erich arch bar group. The Hybrid group had a mean age of 30.10 years, while the Erich group had a mean age of 26.10 years, with a statistically significant age difference between the groups. The Hybrid group showed a lower gingival index post-IMF compared to the Erich group (0.99 vs. 2.07), and the Hybrid arch bar required significantly less time for placement (44 minutes vs. 74 minutes) and had no glove penetrations, unlike the Erich group, which had a 40% penetration rate. Post-operative complications were also lower in the Hybrid group, with fewer cases of loose screws.

CONCLUSION: The hybrid arch bar system can be used as an alternative to traditional Erich arch bars for maxillomandibular fixation in patients with maxillomandibular fractures with no major complications. It provides quicker placement of the arch bars improving the safety of the operator and preserving the gingival health of the patient.

Keywords: Fractures, Erich Arch bar, Arch bar, Intermaxillary fixation

INTRODUCTION

Maxillofacial fractures constitute a common subset of injuries that may result in significant morbidity and disability. The administration of maxillofacial fractures constitutes a pivotal element of trauma care, necessitating the implementation of effective and efficient therapeutic modalities[1]. Maxillomandibular fixation, formerly referred to as intermaxillary fixation (IMF), is a technique employed to stabilize the maxilla and mandible in an optimal dental occlusion. The application of maxillomandibular fixation is fundamental in the management of patients who have sustained facial trauma, as well as those in need of reconstructive and orthognathic surgical interventions. It is an integral aspect of the treatment protocol for mandibular fractures, particularly in cases requiring closed reduction and the majority of open reduction and internal fixation (ORIF) procedures. The three primary objectives of maxillomandibular fixation encompass the establishment of occlusion, provision of stability, and immobilization of the jaw[2].

Various forms of arch bars have been delineated in the literature, including Sauer's arch bars, Schuchardt's arch bars, Dautrey's arch bars, Jelenko arch bars, Krupps arch bars, and Erich arch bars (EAB). Currently, Erich arch bars (Fig 1) are the most frequently utilized apparatus for achieving intermaxillary fixation due to the stability they confer. Intermaxillary fixation utilizing EAB is considered the gold standard as it facilitates superior occlusal stability in comparison to alternative methodologies[3].



Fig 1. Erich arch bars

EAB offers a proficient and adaptable approach to maxillomandibular fixation; however, its application is accompanied by certain adverse effects. Dental structures are exposed to therapeutic forces that may induce mobility or even avulsion, while additional repercussions comprise potential damage to the gingiva and a heightened risk of penetrating injuries to the surgeon due to glove perforation by wires during the application and removal of the EAB.(4) The incidence of glove penetration has been estimated at 70%.[5] Another drawback is the extended duration required for the application and removal of the arch bar. Innovations in the design of maxillofacial hardware may address the limitations associated with EABs while preserving stability and versatility. This has culminated in the development of hybrid arch bars (HAB), which feature a modified design that is bone-supported and retained by screws affixed to the maxilla and mandible[4].

The HAB is characterized as an arch bar equipped with eyelets that are anchored to the bone via self-drilling screws (Fig 2).

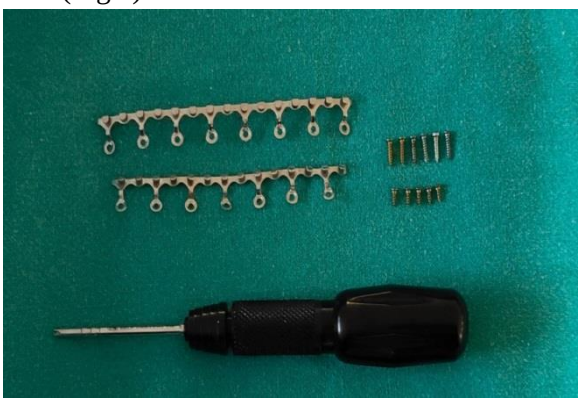


Fig 2. Hybrid arch bars

This arch bar amalgamates the benefits of bone-supported devices, such as expedited and straightforward application, alongside the advantages inherent to traditional arch bars. It has been engineered to optimize the benefits associated with arch bars, including its flexibility, capacity to function as a tension band, and the rapidity and ease of application akin to that afforded by IMF screws, while also encompassing all advantages of bone-supported maxillomandibular fixation, thereby reducing both operative time and glove penetration rates[7].Numerous studies have been conducted, partially contrasting the efficacy of EAB and HAB; however, there exists a deficiency in the literature regarding various parameters. Consequently, this study is undertaken to address this gap through a comprehensive analysis and comparison of differing parameters.

The main aim of the study was to evaluate the efficacy between the use of Hybrid arch bar and Erich arch bar

in the management of maxillomandibular fractures. The purpose of this study was to compare operative time, effect on the gingiva, glove penetration rate and post-operative complications of the Hybrid arch bar and Erich arch bar.

MATERIALS AND METHODS

To address the research purpose, a randomized clinical study was designed and implemented. The study population was composed of all the patients diagnosed with maxillomandibular fractures indicated for IMF from June 2022 through January 2024 at a single institution. To be included in the study sample, patients had to be between 18 to 65 years of age, free of any systemic diseases, indicated for IMF. Patients were excluded as study subjects if patients had communited mandibular fractures, completely edentulous patients, patients with absolute or relative contraindications to IMF, patients who need splint therapy for the stabilization of mobile teeth due to trauma. Patients were divided into two groups by randomisation.

In group I, patients underwent IMF using placement of Hybrid arch bars fitted with eyelets for self-drilling screw fixation to the maxilla and mandible (Fig 3).



Fig 3. Placement of Hybrid arch bars

In group II, patients underwent IMF using placement of Erich arch bars secured with circum-dental wires (Fig 4).



Fig 4. Placement of Erich bars

In group II, Erich arch bars were secured in place using 26-gauge round stainless steel circum-dental wires placed around the teeth.[8]

In group I, Hybrid arch bars were generally fixated using 5 2.0- and 6-mm-long self-drilling locking screws in the maxilla and 5 2.0- and 8-mm-long screws in the mandible. The number of screws placed was based on stability obtained.[9,10]

In both the groups, 26-gauge, round, stainless steel wires were used to achieve intraoperative IMF.(11) Pre-operatively patients were evaluated by using gingival index score by checking the health of marginal and interproximal tissues in the 1st visit (pre-op/diagnostic visit). Intra-operatively operative time in minutes, glove penetration rate were evaluated during the placement of the arch bar in the 2nd visit. In closed reduction, IMF was done for 4-6 weeks.[12] In open reduction cases, even though plating fixation reduces the requirement of postoperative IMF, temporary intra operative IMF was done to secure occlusion and post operatively IMF with elastics was given if required to prevent functioning problems.[13,14] Patients were recalled every week for 4 weeks 3, 4, 5 visits) for general check-up. At the end of the 4th week (6th visit), loose hardware (loosening of screws, wires), other complications were evaluated before the removal of the arch.[15] Post operatively patients were analysed for gingival index on removal of arch bar.[15] A departmental database was reviewed to identify patients who were potential candidates for the study. Patient charts were reviewed to confirm that patients met the inclusion and exclusion criteria, and then the predictor, sample, and outcome variables described were collected.

Statistical analysis

The data analysis has been performed by the statistician. The data was assessed for normality using Kolmogorov-smirnov test, and it followed a normal distribution. Hence, parametric tests were applied. The descriptive statistics such as Mean (μ), Standard Deviation (SD), minimum and maximum values, frequency and percentages have been obtained. For the categorical data such as gender, glove penetration and loose hardware, chi square was applied. Paired t test was applied to assess the means at two time interval (before and after intervention with IMF) for the measurement of gingival index and operating time in the groups separately. Further,

Independent t test was applied to assess the means of two independent groups (Hybrid arch bars & Erich arch bars) before the treatment and after the treatment separately. A p value of <0.05 was considered as statistical significance.

RESULTS

Of the 80 cases included in the study, 40 each were in the Hybrid arch bar group and Erich arch bar group respectively. Mean (SD) age in years of the patients in the Hybrid arch bar group was 30.10 (4.73) with a range of 23-40 years. In the Erich arch bar group, the mean (SD) age in years was 26.10 (7.46) with a range of 18-42 years. There was a statistical significance between the age comparison of the 2 groups [X^2= 60.00; df= 14; p = <0.001 (S)]. The total number of females in this study were 12 (15%) with 4 (10%) in Hybrid arch bar group and 8 (20.0%) in the Erich arch bar group. The total number of males in this study were 68 (85.0%) with 36 (90.0%) in Hybrid arch bar group and 32 (80.0%) in the Erich arch bar group. The results did not any statistical significance with respect to the gender [X^2= 1.56; df= 1; p = 0.21(NS)] as illustrated in Table 1.

Post-Operative complications such as loose hardware were assessed between both groups. There were no glove penetrations (0%) with the use of Hybrid arch bar, however, with the use of Erich arch bar, there were 16 (40%) glove penetrations and this was statistically significant [X^2 = 20.00; df = 01; p = <0.001 (S)] and has been illustrated in the Table 1. Table 1 also shows the results of any loose hardware. Only 4 (10.0%) loose screws were seen in the former group while the majority of the loose hardwares viz., loose screw 2 (5.0%), loose wire 10 (25.0%) and loose arch bar 2 (5.0%) were present in the latter group and this shows a statistical significance [X^2 = 14.28; df = 03; p = 0.003 (S)].Loe and Silness Gingival Index (GI) was measured pre and post operatively in both the groups using paired t test (Table2).

Table 1. Frequency and percentage distribution of gender, glove penetration and loose hardware in Hybrid arch bar and Erich arch bar groups with chi square test

	Groups		Total	Sig.
	Hybrid arch bars	Erich arch bars		
Gender				
Female	4 (10.0%)	8 (20.0%)	12 (15.0%)	X^2= 1.56
Male	36 (90.0%)	32 (80.0%)	68 (85.0%)	df= 1
Total	40 (100%)	40 (100%)	80 (100.0%)	p = 0.21 (NS)
Glove penetration				
No	40 (100%)	24 (60.0%)	64 (80.0%)	X^2 = 20.00
Yes	0 (0%)	16 (40.0%)	16 (20.0%)	df = 01
Total	40 (100%)	40 (100%)	80 (100.0%)	p = <0.001 **(S)**
Loose hardware				
None	36 (90.0%)	26 (65.0%)	62 (77.5%)	X^2 = 14.28
loose screw	4 (10.0%)	2 (5.0%)	6 (7.5%)	df = 03
Loose wire	0 (0.0%)	10 (25.0%)	10 (12.5%)	p = 0.003 **(S)**
Loose arch bar	0 (0.0%)	2 (5.0%)	2 (2.5%)	
Total	40 (100%)	40 (100%)	80 (100.0%)	

Table 2. Comparison of the gingival index and operating time during and after the IMF placement in Hybrid arch bar and Erich arch bar groups using paired t test

		Mean (SD)	SEM	95% CI		t value	Sig.
				LB	UB		
Gingival index							
Hybrid arch bars	PRE OP	1.09 (0.27)	0.04	-.12679	-.05321	-4.949	<0.001 **(S)**
	POST OP	0.99 (0.38)	0.06				
Erich arch bars	PRE OP	0.99 (0.38)	0.06	-1.20527	-.95473	-17.438	<0.001 **(S)**
	POST OP	2.07 (0.60)	0.09				
Operating time							
Hybrid arch bars	APPLICATION	44.40 (4.05)	0.64	11.069	14.531	14.958	<0.001 **(S)**
	REMOVAL	31.60 (1.93)	0.30				
Erich arch bars	APPLICATION	74.20 (5.50)	0.87	41.029	45.171	42.092	<0.001 **(S)**
	REMOVAL	31.10 (2.91)	0.46				

In the Hybrid arch bar, the mean±SD of GI before the IMF was 1.09±0.27) and after the IMF was 0.99±0.38 and this was statistical significant (p = <0.001). In the Erich arch bar, the mean±SD of GI before the IMF was 0.99±0.38 and after the IMF was 2.07±0.60 and was statistical significant (p = <0.001). The GI was also measured before the application of the IMF in both the groups and there was no statistically significant difference between then Hybrid arch bars and the Erich arch bars [p =0.183 (NS)]. However, during the removal of the arch bars, the gingival index score was lower in the Hybrid arch bars when compared to the Erich arch bars and this was statistically significant [p = <0.001 (S)]. These have been illustrated in Table-3. The operating time was measured in minutes during the application and the removal of the arch bars in both the groups (Table 2). The mean (SD) time taken to place and remove the Hybrid arch bars was 44.40 (4.05) and 31.60 (1.93) respectively and the results are statistically significant at p = <0.001. The mean (SD) time taken to place and remove the Erich arch bars was 74.20 (5.50) and 31.10 (2.91) respectively and the results are statistically significant at p = <0.001. The operating time was compared in both the groups during the application of the IMF using the independent t test. The application and removal time was lesser in the Hybrid arch bars when compared to the Erich arch bars and this was statistically significant [p = <0.001 (S)] as shown in Table-3.

Table 3. Between-group comparison of the gingival index and operating time in Hybrid arch bar and Erich arch bar groups using independent t test

Table 3		Mean (SD)	SEM	95% CI		t value	Sig.
				LB	UB		
Gingival index							
PRE OP	Hybrid arch bars	1.09 (0.27)	0.04	-0.04	0.24	1.34	0.183 (NS)
	Erich arch bars	0.99 (0.38)	0.06				
POST OP	Hybrid arch bars	1.18 (0.34)	0.05	-1.10	-0.67	-8.14	<0.001 **(S)**

	Erich arch bars	2.07 (0.60)	0.09				
Operating time							
APPLICATION	Hybrid arch bars	44.40 (4.05)	0.64	-31.95	-27.64	-27.55	<0.001 **(S)**
	Erich arch bars	74.20 (5.50)	0.87				
REMOVAL	Hybrid arch bars	31.60 (1.93)	0.30	-1.10	-0.67	-8.14	<0.001 **(S)**
	Erich arch bars	31.10 (2.91)	0.46				

Discussion

The purpose of this study was to compare operative time, effect on the gingiva, glove penetration rate and post-operative complications of the Hybrid arch bar and Erich arch bar in the treatment of maxillomandibular fractures. The specific aims of the study were to evaluate the following parameters

1) Operative time required for application and removal of the arch bar,

2) Gingival Index before the application and after the removal of the arch bar,

3) Glove penetration rate during the application and removal of the arch bar,

4) Loose hardware such as loose arch bar, wires and screws. Several techniques have been described for MMF which include direct interdental wiring, Indirect interdental wiring (eyelet or Ivy loop), Continuous or multiple-loop wiring, Embrasure wires, Ernst ligatures, Cap splints and Arch bars.[16,17] These approaches typically involve placement of wires around teeth, which can cause mucosal or dental injuries and are limited in patients with poor dentition or who are partially edentulous. There is an added risk of needle stick injury due to the hardware involved. Technological advances in the design of maxillofacial hardware may overcome the drawbacks of using EABs while maintaining stability and versatility. This led to the development of hybrid arch bar (HAB) which consists of a modified arch bar that is bone supported and is retained by the screws in the maxilla and mandible. It combines features of arch bars and bone-supported devices, potentially yielding the advantages of both.[2] In the present study, the application time required for the placement of the arch bar was significantly more in the group I when compared to the group II. In the present study there was statistically significant difference in the application time required for the placement of the arch bars similar to the studies of Chao et al,[18] . King et al,.[19] Hesham et al. [20] but the time required for the removal of the arch bar was similar in both groups with no statistically significant difference similar to the study of chao et al. The average time required for placement of arch bar in group I was 44 mins similar to study of Chao et al. [18] but was higher when compared to other studies. Increased requirement of time may also be caused due to the reason that stainless steel hybrid arch bars used in the present study when compared to titanium arch bars used in the other studies. Stainless steel has low malleability compared to titanium. Adjusting the eyelets position will be much easier when using titanium arch bars compared to stainless steel arch bars. Amount of time required for the placement and removal in either of the groups was high when compared to studies by Bouloux et al. [21]Hesham et al.[20] as the present study was an institutional study and was performed by training surgeons.

Statistically significant difference in the gingival index with lower score for group I was noted. The results coincide with the study of Hesham et al.[20] with higher gingival index in the Erich arch bar group probably due to the presence of wire around the tooth over the marginal and interdental gingiva which may inhibit the maintenance of the gingiva. Group II reported a 40% incidence of needle stick injuries and there were no glove penetrations in Hybrid arch bar group I. These findings are

consistent with previous studies by Hesham et al. (20)and King et al.[19] which also found a higher glove penetration rate with the Erich arch bar than the Hybrid arch bar.[22–25] The majority of reported wire-stick injuries occurred during wire placement, particularly during interproximal wire placement, where gloves could snag on exposed wires or improperly positioned wires in group II.[25,26]

The increased penetrations observed in the group II are attributed to the greater hardware used during its placement. Other arch bar specific complications such as mucosal over growth, root fracture of HAB and tooth mobility of EAB were also evaluated.

Our analysis revealed that anterior screws achieved mucosal coverage more rapidly and consistently than posterior screws(fig.5).



Fig 5. Mucosal over growth on Hybrid arch bar eyelets

We found that mucosal overgrowth may prolong the duration needed for arch bar removal, it does not lead to any undesirable clinical effects.[27] Proper utilization of the screw spacer instrument can mitigate the risk of mucosal migration over the screw. This instrument is positioned between the mucosa and the metal rim of the hole, lifting the metal rim away from the mucosa to prevent gingival compression and mucosal overgrowth.[27] Root fractures were assessed postoperatively using Orthopantomogram (OPG) in our study. While some patients showed root contact on OPG, (Fig 6) none exhibited symptoms of root injury or required endodontic treatment or extraction.



Fig 6. OPG showing fixation with Hybrid arch bars

No cases of tooth mobility were observed in this study in group II. This contrasts with findings from studies by Hamid et al., [27]and Hesham et al.[28] where tooth mobility was reported as a complication associated with Erich arch bars. The potential for tooth mobility in those studies may be attributed to extrusive forces applied during wire twisting around the tooth. Additionally, pre-existing tooth mobility could exacerbate this issue.[29,31] It's worth noting that in our study, we excluded patients with mobile teeth due to trauma, which may have contributed to the absence of recorded tooth mobility cases.

The advantages of the study encompass randomization, a singular institutional experience, and the assessment of multiple parameters. The constraints of the study comprise a limited sample size and potential bias stemming from the involvement of various operating surgeons. The implementation of stainless steel hybrid arch bars necessitates a distinctly different technique that requires considerable time for proficiency.[30,32] It is plausible that as experience accumulates, the duration for the placement of the hybrid system may be further diminished, consequently reducing the associated complications. A pre-operative radiographic assessment is essential to ascertain the optimal placement of screws and to appropriately adjust the hybrid arch bar. Specialized instruments explicitly designed for hybrid arch bars, including a screw holder, screwdriver, and spacer, must be utilized to facilitate the application process of stainless-steel hybrid arch bars.[33] This investigation illustrated that the hybrid arch bar system may serve as a viable alternative to traditional Erich arch bars for maxillomandibular fixation, exhibiting no significant complications. The current study aligns with the findings and outcomes of prior research that employed titanium hybrid arch bars. It indicated reduced operative time, lower rates of glove penetration, and superior gingival health with fewer complications when utilized for intermaxillary fixation. Additional investigations are warranted regarding various designs of stainless steel hybrid arch bars, which may lessen the operator's exertion to manipulate the stainless steel arch bar, thereby minimizing the risk of root injury and potentially decreasing the application time for the placement of the arch bar and the incidence of complications.

Conclusion

The hybrid arch bar system can be used as an alternative to traditional Erich arch bars for maxillomandibular fixation in patients with maxillomandibular fractures with no major

complications. It provides quicker placement of the arch bars improving the safety of the operator and preserving the gingival health of the patient.

DECLARATIONS

Ethics Approval and Consent to Participate
Not applicable.

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Conflict of Interest
The authors declare no conflict of interest

Informed consent
Informed consent was obtained from all individual participants included in the study

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CASE REPORT
CYSTIC LESIONS OF THE SALIVARY GLANDS
(Report of 3 cases)

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Abstract

At least one-third of cystic salivary gland lesions are neoplastic. Cystic lesion of the salivary gland requires only surgery, because regardless of the type and location, drug therapy is not possible with this diagnosis.. If the cystic neoplasm is localized in a hard-to-reach place and if it is localized in the parotid gland, the surgical manipulation is performed from the outside, it is removed simultaneously with the parenchyma of the salivary gland. The FNA specimens from salivary gland cystic lesions can be no informative very often, because FNA of these lesions demonstrates hypocellular mucinous material contents, possibly with inflammatory cells and also scant epithelial cells. For example, the presence of mucin and admixed lymphocytes in cyst fluid can be demonstrated both in the benign inflammatory cysts and cystic neoplasms. A definitive diagnosis of cystic neoplasms of the salivary glands is possible only through histological examination of the neoplastic tissue. Prevention of cystic neoplasms of the salivary gland consists of preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist. This article presents cases of the salivary glands cystic neoplasms, which are the clinical interest.

Keywords: salivary glands cysts; maxillofacial surgery

INTRODUCTION

Diseases of the salivary glands account for up to 5% of all dental pathologies. From 3 to 5% of all neoplasms of the maxillofacial region are neoplasms of the salivary glands, among them the tumors of the parotid gland percentage is 92%[1].

Salivary gland cysts are pathological benign lesions most often are unicystic, less often polycystic. They are grouped based on their localization and histological structure.

There are two types of salivary gland cysts: the retention type (retention cyst of the minor salivary gland, formed when saliva is retained in the excretory duct) and the type of intratissue secretion, when the duct wall is injured, the saliva flows directly into the fibrous tissue surrounding the gland[2].

They differ by place of localization.

1. Cysts of small salivary glands (buccal, labial, palatal, lingual, molar).
2. Cysts of large salivary glands.
   - sublingual salivary gland (ranula)
   - parotid salivary gland
   - submandibular salivary gland

The cysts are filled with white or yellow mucous fluid from the inside, surrounded with fibrous capsule. More than half of all cases are cysts of small salivary glands, less often large ones are affected: sublingual, parotid, submandibular[3].

Depending on the gland in which it formed, the symptoms of a salivary gland cyst can be distinguished. Salivary gland cysts themselves do not pose a danger to the patient, unlike complications that can develop in the absence of treatment. Penetration of pathogenic microorganisms into the lesion (most often, representatives of the opportunistic microflora of the oral cavity) leads to the development of an inflammatory process. In

general, the risk of malignancy is higher with smaller salivary glands than with larger salivary glands (for example, the parotid gland has a lower risk of malignancy than minor salivary glands).

In addition, a cyst can have got false or true nature. The former arise as a result of various types of soft tissue injuries, the latter - because of the occurrence of pathologies. In this case, a true cyst has an epithelial lining inside, a false cyst does not have one. Benign cystic lesions of soft tissues of the maxillofacial region do not represent a genetically homogeneous group. Cystic pathology can be caused by trauma or a tumor that compresses the channel and prevents the outflow of saliva[4]. As a result, the fluid stretches the glandular lobule or the salivary duct itself, and a cyst is formed at the site of the pathology.

Congenital types of pathology are formed because of a violation of embryonic development. Acquired cysts of the salivary glands, as a rule, are a consequence of blockage of the excretory duct. Predisposing factors are: inflammatory process (stomatitis, sialoadenitis); duct trauma; sialolithiasis (the excretory duct is blocked by a stone); lesion of a mucous plug in the duct. There are reports regarding the possible role of oncogenic viruses (Epstein-Barr, cytomegalovirus, herpes virus) in the development of salivary gland tumors[5].

As in the case of neoplasms of other localizations, the etiologic role of gene mutations, hormonal factors, adverse environmental influences (excessive ultraviolet radiation, frequent X-ray examinations of the head and neck area, previous radioactive iodine therapy for hyperthyroidism, etc.), smoking (smoking causes one type of benign tumor - Warthin's tumor) is considered. An opinion is expressed about possible alimentary risk factors (high cholesterol content in food, lack of vitamins, fresh vegetables and fruits in the diet, etc.). At least one-third of cystic salivary gland lesions are neoplastic (Warthin tumor, sebaceous adenoma, sebaceous lymphadenoma, intraductal papilloma, pleomorphic adenoma, mucoepidermoid carcinoma, acinic cell carcinoma, cystadenoma, cystadenocarcinoma, secretory carcinoma, any neoplasm (e.g., lymphoma) with cystic degeneration, metastatic carcinoma to intra-glandular node). Non-neoplastic cystic salivary gland lesions include obstructive sialadenopathy (mucus retention cyst, mucocele), lymphoepithelial cyst, sclerosing polycystic adenosis, polycystic (dysgenetic) disease, epidermoid cyst, first branchial arch anomalies, hydatid cyst. Salivary gland cysts can typically be identified by ultrasound. However, occasionally, benign or malignant tumors (e.g., lymphoma, metastases) can be misinterpreted as a simple cyst, pseudocysts can be hard to discern, and paradoxically certain cystic lesions can present as solid lesions on ultrasound [6,7]. Cysts of the salivary glands are recognized on the basis of the clinical picture, instrumental and laboratory studies. In addition, additional methods allow differential diagnosis of cystic formations with salivary gland tumors.

Fine needle aspiration (FNA) is a common diagnostic tool used in the initial evaluation of parotid masses[10,11].

Employing FNA early on in the diagnostic work-up of patients can help avoid unnecessary surgery[12].

Presents treatment 3 cases of the salivary glands cystic neoplasms, which are the clinical interest.

Case reports.

In cases 1 and 2, the patients are with a preliminary diagnosis of a neoplasm in the left postmandibular region. The complaints and clinical symptoms in both cases were the same, according to the patients, they considered themselves sick for about a year. They noticed a swelling in the postmandibular region, which gradually increased, which was not painful. They did not mention other diseases during their lifetime.

A preliminary diagnosis was made already at the stage of external examination of the patient's face and oral cavity, during which a characteristic lesion in the projection of the gland was found.

Palpation allowed to verify the absence of pain, local increase in temperature, tissue edema and other signs of the inflammatory process. In palpation the cystic lesions had a spherical shape with an elastic structure. The skin above the cyst localization site did not change color or structure. The gland affected by the cyst did not show signs of fluctuation and did not cause painful sensations, it was mobile. The lesion of the parotid salivary gland was accompanied by swelling of the tissues in the ear area, facial asymmetry. The color and appearance of the skin were not changed. The facial nerves were not involved in the tumor process. To understand the actual size of the cystic lesions, patients were sent for magnetic resonance imaging, which was performed by contrast, during which clearly defined cystic lesions were detected, and the cervical lymph nodes were not enlarged.

An examination was performed according to the A-scheme: complete blood count (blood group, coagulogram, Rh), biochemical (glucose, creatinine, total-bound-free bilirubin), albumin, chest X-ray, ECG, ultrasound, general urine examination. Based on the clinical laboratory and instrumental examinations performed, the cystic lesion diagnosis was confirmed.

Case 1.

Men, 61 years old. In the left postmandibular region revealed a 3*3*1.5 cm volumnious mass with clear borders in the left parotid salivary gland (Figure 1).



Figure 1. The patient with parotic gland cystic lesion, external view of the patient



Figure 2. a,b MRI picture of the cystic lesion in 2 projections.



Figure 2. b MRI picture of the cystic lesion in 2 projections.

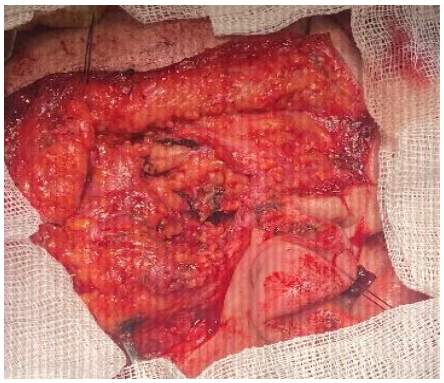


Figure 3. Intraoperative view of the exposed tumor

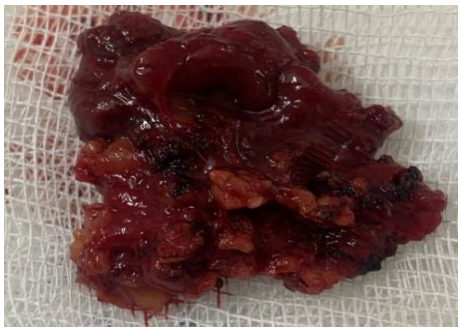


Figure 4. Removed tumor



Figure 5. View of the postsurgical wound



Figure 6. Gross appearance of the removed tumor

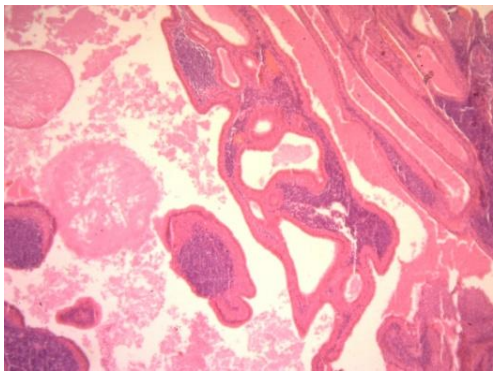


Figure 7. Microscopical picture of the removed tumor (Warthin tumor). Stained with hematoxylin-eosin, x 100.

Case 2.
Men, 69 years old. In the left postmandibular region revealed a 4.5*3*2 cm volumnious mass with clear borders in the left parotid salivary gland, (Figure 8).



Figure 8. The patient with parotic gland cystic lesion, external view of the patient

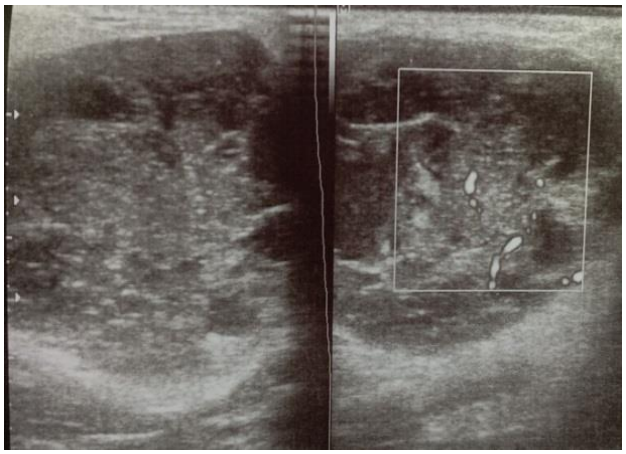


Figure 9. MRI picture of the cystic lesion

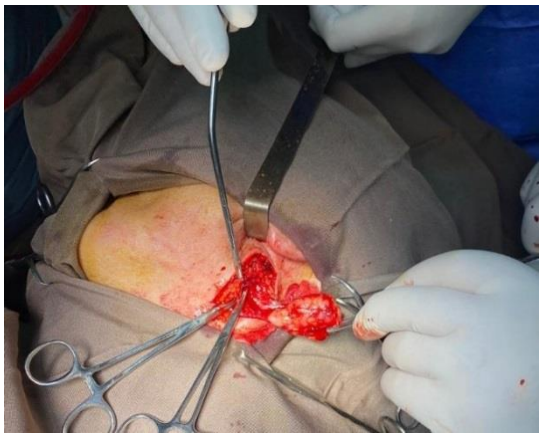


Figure 10. Intraoperative view of the exposed tumor



Figure11. Intraoperative view of the exposed tumor

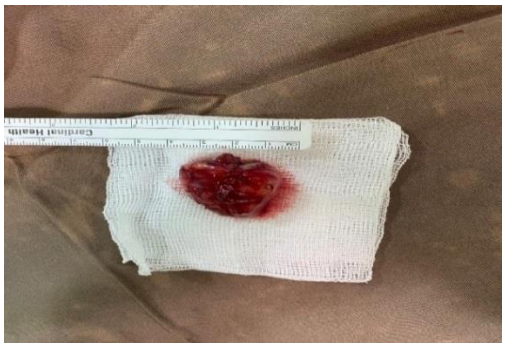


Figure 12. Removed tumor



Figure 13. View of the postsurgical wound



Figure 14. Gross appearance of the removed tumor.

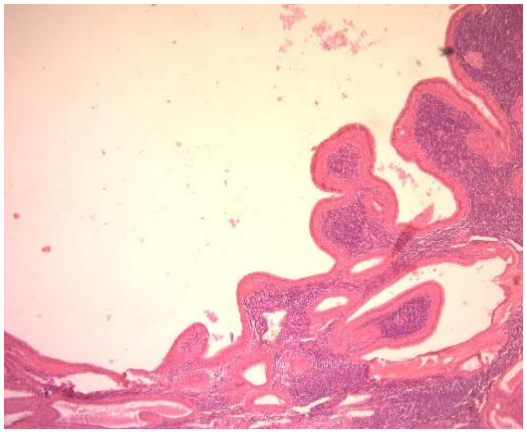


Figure 15. Microscopical picture of the removed tumor (Warthin tumor). Stained with hematoxylin-eosin, x 100.

Case 3.

M, 62 years old was admitted to the maxillofacial surgery department. The patient was complaining of swelling and mild pain in the sublingual region. He considers himself ill for about 8 months. The patient's mouth opened normally. Mild swelling is observed in the left maxillolingual sulcus, the mucous membrane is slightly red, palpation is mildly painful (fig 16). Palpation in the maxillolingual sulcus area reveals a mildly painful lesion with sizes approximately 4 x 1.5 cm thick. CT of the lower jaw examination did not reveal any bone changes (fig.17). Based on the performed examinations, a neoplasm of the left maxillolingual sulcus was diagnosed. The tumor was removed under general anesthesia and sent for histological examination (fig18,19,20,21,22). The patient spent 4 days in the hospital. The surgery and the postoperative period went smoothly, without complications. During this time, the patient received antibiotics and analgetic drugs.



Figure 16. The patient with sublingual gland cystic lesion.

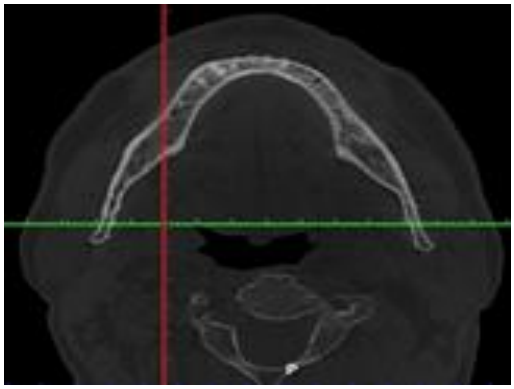


Figure 17. CT picture of the cystic lesion.



Figure18. Intraoperative view of the exposed tumor.



Figure 19. Removed tumor

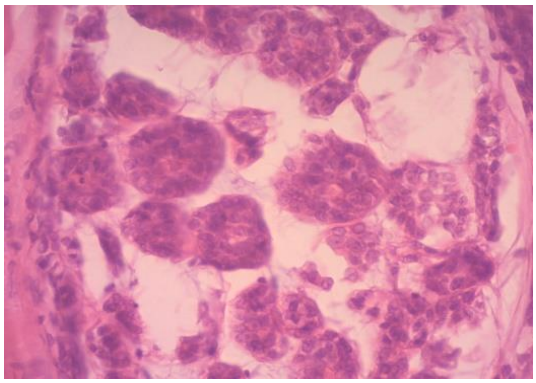


Figure 20.Microscopical pictures of the removed tumor (Sclerosing polycystic adenoma)

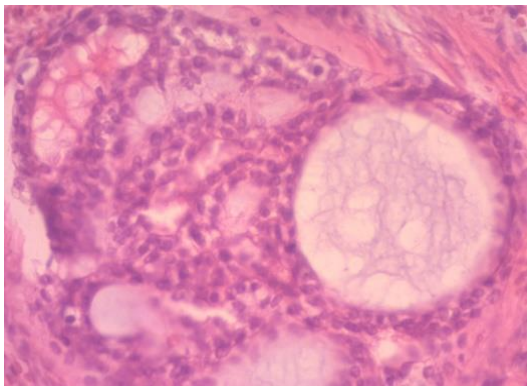


Figure 21. Stained with hematoxylin-eosin, x 100.



Figure 22.View of the postsurgical wound

Surgical operation

Both patients (cases 1 and 2) underwent surgery under general anesthesia for removing the tumor. The operation was a subtotal resection of the left parotid salivary gland with preservation of the branches of the facial nerve, followed by sending the removed lesion of the parotid salivary gland for a planned histological examination.

The surgical and postoperative course went smoothly, without complications. The patients spent 1 day in the hospital and were gone out with improvement.

In case 3 the patient surgery was planned to remove the tumor under general nasotracheal anesthesia. The patient was warned about the possible complications associated with the surgery. The tumor was removed completely with sublingual gland, which was totally replaced with the tumor. The wound healed by primary intention.

Morphological study

The materials for morphological studies were the samples of lesion tissues. According to the standard histological scheme, the pieces of the tissue were fixed in 10% neutral formalin, dehydrated and embedded in paraffin. A series of sections 4 μm in thickness were stained with hematoxylin–eosin for a general assessment of the condition of the examined tissues. Histological micropreparations were studied with a ZEISS Primo Star trinocular microscope (ZEISS Microscopy, Jena, Germany) under 100, 400- and 1000-times magnification. Microphotographs were taken with a ZEISS Axiocam ERc 5 s (Carl ZEISS Microscopy, Jena, Germany).

Results

Grossly, in the first and second cases, macroscopically, cystic neoplasms were clearly delimited and represented single, unilocular lesions filled with yellowish mucous fluid. Solid areas and multiple cysts with papillary projections are apparent on the cut surface.

Microscopically, varying proportions of papillary cystic structures lined by bilayered oncocytic epithelial cells and surrounded by a lymphoid stroma including germinal centers. Epithelial component is comprised of inner columnar and outer cuboidal cells.

Limited foci of squamous, mucous, ciliated and sebaceous cells can be present. Histopathological diagnosis: Warthin tumor of the left parotid gland.

In third case, grossly the lesion was well delimited, pale, firm, with sizes 4x1,5 cm.

Microscopically, it was circumscribed with preservation of lobular architecture, composed of irregularly distributed bilayered ducts and acini within a sclerotic stroma. Ducts range from small tubules to ectatic spaces; may contain secretory material or foamy macrophages.

Ductal cells were vacuolated, foamy, apocrine and mucous appearances.

Hyperplastic ductal epithelium is forming solid, microcystic and cribriform structures in some places. Small eosinophilic globules of basement membrane-like material was revealed in some cribriform areas. Histopathological diagnosis: Sclerosing polycystic adenoma.

Discussion

The diagnosis and treatment of cystic lesions of the salivary glands have been widely discussed in the pathology literature.

The latest World Health Organization 2017 Classification of Head and Neck Tumours includes a new chapter on tumors and tumor-like lesions of the neck and lymph nodes.[13-15]

Tumor-like lesions include a variety of cystic lesions of the parotid gland. Cystic lesions of the parotid gland can be divided into three groups: non-neoplastic cysts, benign tumors with macrocystic change, and malignant tumors with macrocystic change. It is important to distinguish these lesions from one another because treatment and patient management differ among the three groups.

Cystic lesions as a group account for about 5% of all salivary gland tumors, most are unilateral, and nearly 50% mimic benign salivary neoplasms and require surgical resection and histopathologic examination. Bilateral or multiglandular salivary gland involvement is occasionally seen, and may indicate systemic pathologic processes such as Sjogren's syndrome, cystic fibrosis, and human immunodeficiency virus (HIV).

Parotid duct cysts are part of a larger group of parotid cysts (Table 1), and represent 10% of all salivary gland cysts.Most parotid cysts are detected in the fifth to seventh decades of life, and prevalence rates are similar in men and women.[16]

Table 1

Classification of parotid cysts (modified from Pieterse[2])

I- Cystic tumours
1. Benign
   a. Warthin's tumour
   b. Pleomorphic adenoma
   c. Cystadenoma
   d. Lymphangioma
2. Malignant
   a. Low-grade mucoepidermoid carcinoma
   b. Adenoid cystic carcinoma
   c. Metastatic squamous cell carcinoma
   d. Lymphoma

II- Non-neoplastic cysts
1. Epithelial - unilocular or multilocular
   - with lymphoid tissue (may be associated with HIV infection) or without lymphoid tissue
   a. Epidermoid
   b. Epidermoid with sebaceous glands
   c. Ductal
   d. Branchial
   e. Multiple
   f. Traumatic
   g. Associated with cholesteatoma of mastoid air cells
2. Non-epithelial
   a. Tuberculosis
   b. Abscess
   c. Parasitic
   d. Gas in glassblowers and musicians
   e. Traumatic

Parotid gland cysts can be congenital or acquired. Congenital cysts are thought to result from a malformation of the embryonal duct system or from defects of the first branchial pouch and cleft.[17] Congenital parotid cysts are referred to as branchial cleft cysts or lymphoepithelial cysts.

Although they are congenital, such cysts may not manifest until adulthood. Cysts in the parotid gland represent a small percentage of benign parotid masses. They usually arise within the gland from salivary or non-salivary parotid tissue, and may be congenital or acquired. Some, however, may arise from surrounding structures.

Unless the cyst is superficial and therefore readily amenable to proper examination, it usually escapes a definite diagnosis even with the help of sialography or more sophisticated procedures. Exploration is eventually resorted to for diagnosis and treatment. That is why the surgeon should be ready to perform extensive surgery if the findings at exploration necessitate it.

One-third of cystic salivary gland lesions are neoplastic[18].

The clinical diagnosis is frequently a mass that is considered to be solid.

Salivary gland cysts can typically be identified by ultrasound.[19]

However, occasionally, benign or malignant tumors (e.g., lymphoma, metastases) can be misinterpreted as a simple cyst, pseudocysts can be hard to discern, and paradoxically certain cystic lesions can present as solid lesions on ultrasound.[20]

In such a scenario, the fluid should be aspirated and sent for cytology, which may reveal the nature and diagnosis of the swelling.

Radiologically benign cysts (e.g., mucous retention cysts, lymphoepithelial cysts, cysts of the first branchial cleft, ranulas, parotid cysts, and pseudocysts) have similar intensity on computed tomography and MRI.

Salivary gland cytopathology is one of the most challenging areas of diagnostic cytology. Salivary Gland Cytopathology will use a simplified algorithmic approach based upon differential diagnostic groups to cover practical aspects of diagnosing common as well as challenging salivary gland lesions.[21]

In order to provide a practical classification system an improve communication between cytopathologists and clinical teams, the first edition of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was released in February 2018 and further updated in July 2023 [22,23].

The MSRSGC comprises six diagnostic categories: non-diagnostic, non-neoplastic, atypia of undetermined significant (AUS), neoplasm (A. benign; B. salivary gland neoplasm of uncertain malignant potential, SUMP), suspicious for malignancy and malignancy

Table 2. illustrates how various cystic salivary gland lesions are handled according to the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).

Table 2. The Milan System for reporting salivary gland cytopathology for cystic lesions

Diagnostic category	Example of cystic salivary gland lesion
Non-diagnostic	Cystic non-mucinous fluid only
Non-neoplastic	Inflammatory cyst with amylase crystalloids
Atypia of undetermined significance	Histiocytes ± scant epithelial cells in a background of abundant mucin (cannot exclude low-grade mucoepidermoid carcinoma)
Benign neoplasm	Warthin tumor, or cystic pleomorphic adenoma
Salivary gland neoplasm of uncertain malignant potential (SUMP)	Cellular oncocytic/oncocytoid neoplasm with cystic background (differential includes Warthin tumor or oncocytic cystadenoma)
Suspicious for malignancy	Atypical cells in a mucinous background, suspicious for low-grade mucoepidermoid carcinoma
Malignant	Keratinizing squamous cell carcinoma

Acellular aspirates from cystic non-mucinous lesions are classified as nondiagnostic (cystic fluid only) while hypocellular samples with mucinous material are classified as atypia of undetermined significance (AUS). However, these two diagnostic categories should only be used after all cyst contents have been processed and examined.

The Milan System for reporting salivary gland cytopathology provides useful criteria for acellular aspirates derived from cystic non-mucinous lesions (i.e., classified as non-diagnostic) and those containing mucinous material but with only scant epithelial cells (i.e. classified as atypia of undetermined significance). Evaluation of the literature regarding salivary gland cysts is challenging given the change in terminology for several of these cystic entities.

Also, further studies are required to determine the feasibility of employing newer ancillary studies to evaluate hypocellular cyst samples.

A definitive diagnosis of cystic neoplasms of the salivary glands is possible only through histological examination of the neoplastic tissue[24,25]

Most neoplastic parotid cysts develop in benign tumours, usually Warthin's type. Any cartilage or lymphoid tissue that is detected in the walls of a parotid cyst during histopathological examination is presumed to be of branchial origin, and should alert the surgeon to the possibility of associated sinuses and fistulae.

Only a limited number of articles have reported cytopathology studies of cystic salivary gland lesions[26,27].

Nevertheless, FNA remains a useful procedure early on in the diagnostic work-up of patients with cystic salivary gland lesions since it can help reduce the number of patients requiring surgery[28-30].

The FNA specimens from salivary gland cystic lesions can be no informative very often, because FNA of these lesions demonstrates hypocellular mucinous material contents, possibly with inflammatory cells and also scant degenerated cuboidal, oncocytic or squamoid epithelial cells[31,32].

For example, the presence of mucin and admixed lymphocytes in cyst fluid can be demonstrated both in the benign inflammatory cysts associated with chronic sialadenitis, sialolithiasis with duct ectasia and in Warthin tumor moreover, the clinicians should be informed that by FNA a low-grade mucoepidermoid cannot be excluded.

The diagnostic value of FNA can be increased if, after drainage of cyst fluid, any residual solid components are also sampled. FNA may yield mucoid (mucin) or non-mucoid (e.g., serous) material[34-36]. For this reason aspirates of cystic salivary gland lesions are typically divided into "mucinous" and "non-mucinous types".

Mucin (mucicarmine-positive) may be viscous and resemble thick colloid-like material. Non-mucinous cyst contents are generally more watery, proteinaceous and may contain scattered acute and/or chronic inflammatory cells (e.g., lymphocytes, macrophages) and debris. Crystals may sometimes also be identified Some Warthin tumors can have squamous metaplasia which may contain atypical squamous cells, making it possible to misdiagnose them as squamous cell carcinoma. There may infrequently also be mucinous metaplasia, which raises the consideration of a MEC.

If FNA findings show only necrotic debris they should be reported as non-diagnostic with a comment that this finding raises the possibility of a neoplastic process. Given that aspirates with only scant epithelial cells and mucinous cyst contents may represent a low-grade MEC, they are considered to be indefinite for a neoplasm, and hence best classified as AUS. If abundant inflammatory cells are present (e.g., abscess material, granulomatous inflammation), even without an epithelial component, such cases should be interpreted as adequate and non-neoplastic.

Other salivary gland cysts that belong to this non-neoplastic category are the benign inflammatory

cysts associated with chronic sialadenitis, duct obstruction (sialolithiasis) and duct ectasia.

Ultrasound is considered a very valuable, reliable and useful method in the differential diagnosis of neoplastic lesions of the salivary glands, however, ultrasound does not allow for the correct assessment of lesions located in hard-to-reach places (for example, in the deep lobe of the parotid gland, behind the bones), and is ineffective for the differential diagnosis of small lesions[37-41].

Surgical treatment of the maxillofacial region's cystic lesions is difficult for patients to bear on a psycho-emotional level, because one of the main external criteria for the beauty of a person is the face, which, forms the first impression and creates a decent self-esteem of the individual in society[42].

Regardless of the type and location, drug therapy is impossible with this diagnosis. Cystic lesion of the salivary gland requires surgery. If the cystic neoplasm is localized in a hard-to-reach place and if localized in the parotid gland, surgical manipulation is performed extraorally, it is removed simultaneously with the parenchyma of the salivary gland, since in most cases it atrophies under the pressure of a large tumor[43-44].

However, it is necessary to try as much as possible to do this operation carefully, preserving the facial nerve. Since this is associated with the risk of damage to the facial nerve, the operation requires careful visual control, since damage to the facial nerve leads to paralysis of the facial muscles and delesion of the face for life, the development of postoperative salivary fistulas[45]. Prevention of cystic neoplasms of the salivary gland consists in preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist. Early diagnosis and initiation of appropriate therapy is of the most importance for effective treatment, as well as for long-term prognosis, especially in cancer.

Surgical treatment of salivary gland pathologies applies to all types of lesions, both neoplastic and non-neoplastic[46-50].

Prevention of cystic neoplasms of the salivary gland consists of preventing injuries and inflammations of the oral cavity, careful hygiene and regular visits to the dentist.

This article presents cases of the salivary glands cystic neoplasms, which are the clinical interest.

In the presented clinical cases, based on clinical, laboratory and instrumental studies, the diagnosis of the cyst was confirmed and surgical treatment was performed. The operation and postoperative period went smoothly, without complications.

All cystic lesions were retrospectively evaluated with respect to preoperative diagnostic examinations and histopathological confirmed diagnosis. Cystic components in surgical specimens were also evaluated histopathologically. The relationships with magnetic resonance imaging (MRI) findings and histopathological confirmed diagnosis were studied.

Our cases is consistent with previous reports that describe cystic lesions with well-defined margins and no solid components as indicative of non-neoplastic cysts on MRI. In conjunction with the typical MRI characteristics, served to reinforce the diagnosis of an epidermoid cyst rather than a cystic degeneration of a benign tumour.

This cases contributes valuable insights into the management of gland lesions and reinforces the necessity for careful diagnostic and surgical planning in cases of cystic formations.

To prevent such problems, it is important to consult a doctor, undergo the necessary diagnostics and eliminate the pathology.

Conclusion

Cystic parotid gland lesions are difficult to diagnose correctly before surgery, but the evaluation of cystic components by MRI and histopathology is helpful in differentiating between benign and malignant tumors. Surgical treatment of salivary gland cystic lesions and neoplasms may prevent further malignant transformation.

Declarations

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Literature Review

UNVEILING THE POTENTIAL OF SALIVARY EXOSOMAL BIOMARKERS IN CARDIOVASCULAR DISEASE:INSIGHTS AND FUTURE DIRECTIONS

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Abstract

Cardiovascular disease (CVD) is the primary cause of mortality world wide, necessitating innovative diagnostic approaches due to the limitations of current tools. The growing significance of salivary exosomes as biomarkers for CVD detection and treatment is explored in this narrative review. Salivary diagnostics offer a non-invasive alternative, with exosomes-small extracellular vesicles containing proteins, lipids, and nucleic acids—serving as potential indicators of cardiovascular health. The review highlights how salivary exosomes reflect the physiological states of their parent cells and can indicate systemic inflammation, oxidative stress, and endothelial dysfunction, all critical factors in CVD progression. Furthermore, it discusses specific exosomal biomarkers linked to different cardiovascular diseases such as valvular heart disease, coronary artery disease, cardiac fibrosis, arrhythmias, and heart failure. By integrating salivary exosome analysis into clinical practice, there is potential for enhanced early detection, risk stratification, and monitoring of cardiovascular diseases, ultimately paving the way for more personalized treatment strategies. This exploration underscores the transformative potential of salivary exosomes in improving cardiovascular disease management and patient outcomes.

Keywords: *Cardiovascular diseases; Exosomes; Micro RNA; Salivary biomarkers.*

INTRODUCTION

Cardiovascular disease (CVD) refers to a group of conditions affecting the heart and blood arteries, including disease of coronary artery, cardiomyopathy, congenital heart disease, arrhythmias and heart failure. CVD is the primary cause of death worldwide, accounting for 18.6 million deaths, which emphasizes the need for more sophisticated and easily available diagnostic tools.[1,2] The pathogenesis of CVD is multifactorial, involving complex interactions between genetic, environmental, and lifestyle factors.[3] Traditional risk factors include hypertension, hyperlipidemia, diabetes, smoking, and obesity, which contribute to the development of atherosclerosis and other cardiovascular conditions.[4,5] Early detection and risk stratification are crucial for implementing preventive

strategies and improving patient outcomes.[2,3]

In recent years, the field of salivary diagnostics has gained momentum as a promising approach for detecting and monitoring various diseases, including CVD.[6–8] Saliva, as a biological fluid, offers several advantages over traditional blood-based tests, such as ease of collection, non-invasive nature, and potential for frequent sampling.[6,8] Within the salivary milieu, extracellular vesicles (EVs), particularly exosomes, have emerged as potential biomarkers for CVD. Exosomes are small extracellular vesicles released by multiple cell types, including those in the cardiovascular system, and they carry a cargo of nucleic acid , lipids and proteins that represent the physiological condition of their parent cells.[9,10] The analysis of salivary exosomes offers a non-invasive method for obtaining valuable information about systemic health, including cardiovascular status. Studies have shown that specific molecular signatures within salivary exosomes can indicate the presence of cardiovascular risk factors, such as inflammation and oxidative stress, which are critical in the pathophysiology of CVD.[10,11]

The integration of salivary exosome analysis into routine clinical practice could revolutionize the approach to cardiovascular disease management. By providing insights into the molecular mechanisms underlying CVD, salivary exosomes may aid in early diagnosis, risk stratification, and monitoring of disease progression.[9,10] Furthermore, the ease of saliva collection compared to blood draws enhances patient compliance and facilitates frequent monitoring.

This review serves to highlight the importance of salivary exosomes in the context of cardiovascular disease, emphasizing their potential to transform current diagnostic practices. By exploring the biochemical composition and functional implications of salivary exosomes, we aim to contribute to the growing body of knowledge that supports their use as reliable biomarkers.

Exosomes

The word "exosomes" was initially used by Johnstone et al.,[12] and Pan et al.[13] who found exosomes in sheep reticulocytes. Exosomes are tiny extracellular vesicles that are essential for communication between the cells and are generated through a specific biogenesis process. Early-sorting endosomes (ESEs) are produced when the plasma membrane invaginates inward, which is the first step in the synthesis of exosomes.[14] These ESEs can mature into late-sorting endosomes (LSEs) and ultimately develop into multivesicular bodies (MVBs), which contain intraluminal vesicles (ILVs). The MVBs can either fuse with lysosomes for degradation or merge with the plasma membrane to release the ILVs as exosomes, typically ranging from 40 to 160 nm in diameter.[14,15] These tiny vesicles, which typically have a density of 1.10 to 1.19 g/mL, are made up of proteins, lipids, messenger RNA (mRNA), microRNA (miRNA) circular RNA (circRNA), long non-coding RNA (lncRNA), and DNA.[16,17] They are encased in a lipid bilayer. Numerous cell types, including B lymphocytes, platelets, glial cells, dendritic cells, mast cells, adipocytes, endothelial cells, smooth muscle cells, and stem cells, can create exosomes. It's interesting to note that some microbes can also produce exosomes, which increases their biological relevance.[10]

Exosomes function in intercellular communication has drawn a lot of interest, especially when it comes to disease processes. They are involved in a number of pathological and physiological processes, such as tissue healing, tumor growth, and immunological responses.[10,12,17] Exosomes help move bioactive molecules from one cell to another, changing the behavior of the receiving cell and assisting in the control of inflammation and immunological responses. Because of their ability to mirror the chemical changes in their parent cells in response to a variety of stimuli, including disease conditions, exosomes are promising candidates for biomarker identification and therapeutic applications.[10,16,17]

Exosomes and CVD

The molecular content of exosomes represent the pathological and physiological states of their parent cells, making them potential indicators of oxidative stress, endothelial dysfunction and systemic inflammation—key factors in the development and progression of CVD.[10,17] Exosomes play a crucial role in cardiovascular signal transduction, serving as effective disseminators of biological signals related to myocardial function. These nano-sized extracellular vesicles mediate local communication in the heart through crosstalk between different cell types, such as cardiac fibroblasts, endothelial cells and cardiomyocytes.[17]Exosomes secreted by these cells can influence the same cells that release them (autocrine signaling) or target other cell types (paracrine signaling). Additionally, exosomes facilitate remote communication, enabling functional crosstalk between the heart and other organs like the kidneys, brain, and bone marrow. This exchange of proteins, lipids, and nucleic acids through exosomes regulates transcription and post-transcriptional processes in target cells, contributing to the maintenance of cardiac function under normal and pathological conditions.[17]

Exosomes derived from various cardiac cell types exhibit distinct functions. Cardiomyocyte-derived exosomes regulate angiogenesis and cardiac hypertrophy through the transfer of specific miRNAs, such as miR-222, miR-143, and miR-217. Cardiac fibroblast-derived exosomes induce cardiomyocyte hypertrophy by delivering miR-21-3p and promoting the production of angiotensin II.[18,19] Endothelial cell-derived exosomes play a crucial role in regulating endothelial senescence, angiogenesis, and cardiomyocyte resistance to ischemia/reperfusion injury. These exosomes modulate various signaling pathways, including ERK1/2 MAPK and the inhibition of autophagy and glucose metabolism in cardiomyocytes. [20,21]Circulating exosomes also contribute to cardiovascular signal transduction, carrying bioactive molecules like angiotensin II receptors and miRNAs.[17] Exosomes derived from cardiomyocytes can be detected in the circulation and mediate functional crosstalk between the bone marrow and ischemic heart. These circulating exosomes regulate the number of progenitor cells and facilitate systemic responses to cardiac injury. Additionally, exosomes from patients with myocardial ischemia initiate angiogenesis through the miR-939-iNOS-NO pathway. [22]The ability of exosomes to modulate various aspects of cardiovascular pathophysiology highlights their potential as biomarkers and therapeutic targets for cardiovascular diseases.

Exosomes facilitate intercellular communication by transferring their cargo to recipient cells. This transfer can have both beneficial and detrimental effects. In the context of CVD, exosomes from injured or stressed cells may transfer harmful molecules that promote inflammation, apoptosis, and fibrosis in neighboring cells. Conversely, exosomes from healthy or therapeutic cells can carry molecules that counteract these pathological processes.

Salivary exosomes with cardiovascular disease biomarkers

Cardiovascular exosomes are extracellular vesicles formed in cardiovascular cells, such as endothelial cells and cardiomyocytes.[15] Salivary exosomes are derived primarily from salivary glands and contain a rich array of bioactive molecules. Their composition can change in response to pathological conditions, making them promising candidates for biomarker discovery.

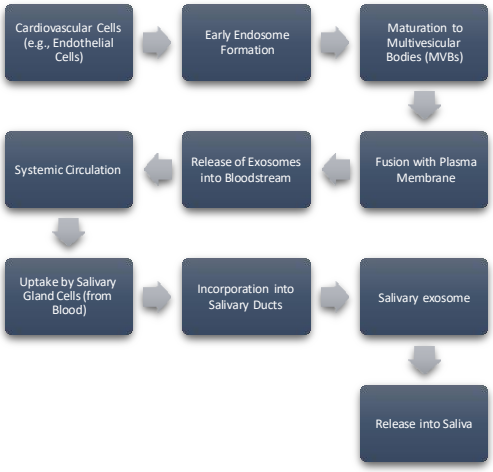


Figure1. Release of cardiovascular exosomes in saliva

Salivary exosomes, originating from cardiovascular cells, undergo a multi-step formation and transfer process. Cardiovascular cells, including cardiomyocytes and endothelial cells, first create exosomes by budding the plasma membrane inward to create early endosomes. These endosomes then develop into multivesicular bodies (MVBs) that contain intraluminal vesicles (ILVs). These MVBs then fuse with the plasma membrane, releasing ILVs as exosomes into the extracellular space.[10,11,15] The exosomes enter the bloodstream and circulate systemically. Notably, extracellular vesicles are known for their ability to traverse epithelial barriers, such as the blood-brain barrier, through a process called transcytosis.[23,24] This capability facilitates the movement of RNAs and other cargo from the blood into saliva. In the salivary glands, cardiovascular exosomes are taken up by glandular cells from the blood, incorporated into saliva, as these cells release the exosomes into the salivary ducts, thus becoming part of the saliva. As a result, salivary exosomes contain cardiovascular biomarkers that can be detected and analyzed for diagnostic purposes(Figure 1).

As we explore the potential of exosomal biomarkers, it becomes clear that their application in cardiovascular diseases is both promising and transformative. So far, we have examined the link between exosomes, cardiovascular diseases (CVD), and salivary exosomes, including their production mechanisms. Now, we will focus on the various exosomal biomarkers identified for diagnosing different cardiovascular conditions. Notably, many of these biomarkers can also be found in saliva, positioning them as promising candidates for non-invasive diagnostics. This emerging field holds significant potential for early detection and monitoring of cardiovascular diseases, enhancing our ability to provide tailored therapeutic approaches.

Coronary artery disease (CAD)

Coronary artery disease (CAD) is a significant public health issue defined by the narrowing or blockage of coronary arteries due to atherosclerosis.[25,26] Ischemic heart diseases are a group of diseases characterized by reduced blood flow to the heart due to obstruction of coronary vessels by atherosclerotic plaque formation. Hence ischemic heart diseases and coronary artery diseases are two terminologies which go hand in hand.[27] This condition can lead to various clinical manifestations, including myocardial infarction (MI), ustable angina, stable angina, and sudden cardiac death. CAD is commonly classified into acute coronary syndrome (ACS) and stable CAD (SCAD) based on the severity and clinical characteristics.

Exosomal Biomarkers in CAD Diagnosis

1. **Growth Arrest-Specific 5 (GAS5):** In the context of atherosclerosis, exosomal lncRNA GAS5 plays a regulatory role in the death of macrophages and vascular endothelial cells, indicating its potential as a CAD biomarker.[28]
2. **SOCS2-AS1:** Liang et al.[25] identified that exosomal SOCS2-AS1 levels are downregulated in CAD patients. This lncRNA may serve as a specific indicator for CAD.
3. **miR-126, miR-21, and PTEN:** Ling et al.[26] demonstrated distinct differences in the levels of these exosomal biomarkers in ACS patients compared to healthy individuals. miR-21 was found to be downregulated, while miR-126 and PTEN were upregulated, suggesting their roles as specific serum markers for ACS .
4. **miR-208a:** Bi et al.[29] reported that exosomal miR-208a levels are elevated in ACS patients, highlighting its potential as both a diagnostic and prognostic marker for ACS
5. **miR-146a:** Li et al.[30] found that the levels of exosomal miR-146a were raised in ACS patients, suggesting its utility as a novel diagnostic biomarker and its involvement in inflammatory responses . It also regulates autophagy in hypoxic cardiomyocytes, reducing apoptosis and fibrosis.[31,32]
6. **Cysteine-Rich Protein 61 (Cyr61):** Increased exosomal Cyr61 levels in plasma were linked to ACS, indicating its potential use for diagnosis and prognosis in ACS patients .[33]
7. **miR-942-5p, miR-32-5p, and miR-149-5p:** These exosomal miRNAs were found to be significantly elevated in SCAD patients, suggesting their potential as novel diagnostic and prognostic indicators.[34]
8. **miR-19a:** Research demonstrated that miR-19a can reduce oxidative stress-induced apoptosis in myocardial ischemia-reperfusion injury, making it a potential therapeutic target for CAD.[35]
9. **miR-210:** Huang et al.[36] highlighted that exosomal miR-210, upregulated by hypoxia-inducible factor 1 (HIF-1), enhances cardiac progenitor cells' tolerance to oxidative stress, suggesting its therapeutic potential for CAD.
10. **miR-133a:** This miRNA, abundant in the heart, has shown to improve cardiac function in myocardial infarction models, indicating its role as a CAD biomarker.[37]
11. **miR-25-3p:** It reduces myocardial cell apoptosis and inflammation. The miRNA promote cell survival and vascularization, which are crucial for heart recovery. Elevated levels of this miRNA in circulation can indicate ischemic stress and ongoing cardioprotection, making them potential biomarkers for early diagnosis of MI.[38]

These studies illustrate the diverse roles of exosomal biomarkers in diagnosing and managing CAD, reflecting their potential to enhance our understanding and treatment of this prevalent cardiovascular condition.

Cardiomyopathy

Cardiomyopathy is a disease that affects the heart muscle, causing it to become enlarged, thick, or rigid. This can make it harder for the heart to pump blood effectively, leading to heart failure and other complications. There are several types of cardiomyopathy, including Diabetic cardiomyopathy (DCM) , uremic cardiomyopathy (UCM), dilated, acute peripartum cardiomyopathy (PPCM)and septic. [39]

1. miR-1, miR-208, and miR-499: These are associated with myocardial injury and serve as potential diagnostic indicators for diabetic cardiomyopathy (DCM). They regulate cardiac muscle function and influence apoptosis and hypertrophy in cardiomyocytes.[39]

2. miR-19b-3p and miR-181b-5p: These influence cellular stress responses and apoptosis in cardiomyocytes, providing insights into cardiac health. They positively correlate with myocardial status, used for diagnosis and prognosis of DCM.[40]

3. miR-126 and miR-320: These enhances endothelial function and angiogenesis. Also inhibits angiogenesis and impacts cardiac function, reflecting changes in cardiac health and are increased in patients with DCM, serving as a diagnostic markers**.** [41]

4. miR-26a and miR-155: These are linked to muscle preservation and mediating cardiomyocyte pyroptosis in UCM. The miR-26a inhibits muscle wasting and improves insulin sensitivity. miR-155 regulates inflammatory responses and cell death in cardiomyocytes, influencing UCM progression.[41]

5. miR-122 and miR-29a: These are associated with mitochondrial function and cardiac parameters in obesity-related cardiomyopathy. miR-122 regulates mitochondrial protein function, impacting cardiac remodeling. miR-29a is involved in the regulation of extracellular matrix and fibrosis, combating obesity-mediated cardiac dysfunction.[42]

6. miR-30, miR-21, miR-133a, miR-29, and miR-26: These are being linked to Dialated cardiomyopathy and are associated with collagen production markers and factors that control fibrosis. They regulate the MMPs/TIMPs system involved in extracellular matrix metabolism and fibrosis.[43]

7. miR-146a: It is induced by the 16-kDa prolactin fragment (16K PRL) through NF-κB activation, leading to inhibition of angiogenesis. It promotes the release of miR-146a-enriched exosomes from endothelial cells (ECs), which can be taken up by cardiomyocytes, resulting in decreased levels of downstream factors like Notch1, Erbb4, and Irak1, thus affecting cellular mitogenesis and differentiation. Higher plasma levels of exosomal miR-146a are observed in PPCM patients. [44]

8.miR-223: Implicated in cardioprotection during sepsis, its levels are reduced in sepsis patients compared to healthy controls and in non-surviving versus surviving patients. It downregulates Sema3A and Stat3 through MSC-derived exosomes, leading to reduced macrophage inflammation and cardiomyocyte cell death.[45] Regulates pro-inflammatory markers such as IL-6, IL-1β, and ICAM-1. The decreased levels of miR-223 can result in increased expression of these inflammatory proteins, contributing to myocardial depression.[46]

Cardiac fibrosis

The pathological condition known as cardiac fibrosis is typified by an overabundance of extracellular matrix (ECM) components accumulating in the heart, mostly due to fibroblast activation. It is a medical condition that causes changes in the heart structure and compliance , which can eventually result in cardiac failure and death.[47]

1. **miR-155:** These are prevalent in exosomes generated from macrophages and, by encouraging aberrant fibroblast proliferation and differentiation, can exacerbate inflammation and cardiac fibrosis.[48]
2. **miRNA-425**: Circulating exosomal miRNA-425 was discovered by Wang et al.[49] as a new biomarker that can forecast the development of cardiac fibrosis and heart dysfunction in heart failure patients.
3. **miRNA-744**: Alongside miRNA-425, Wang et al.[49] also reported that miRNA-744 functions as a biomarker for cardiac fibrosis progression in heart failure patients.
4. **HSP70**: Yang et al.[50] discovered that HSP70 on the surface of serum exosomes is linked to cardiac fibrosis and negatively correlated with age, indicating that it may be a useful target for diagnosing myocardial fibrosis associated with aging.
5. **miR-208a:** Following myocardial infarction, it is increased in rat cardiomyocytes and transported to fibroblasts through exosomes, resulting in cardiac fibrosis and fibroblast proliferation. This pro-fibrotic effect could be reversed by a miR-208a antagonist.[50]
6. **miR-217:** Cardiomyocyte-derived miR-217 delivered by exosomes exacerbated pressure overload-induced myocardial fibrosis and cardiac dysfunction.[18]
7. **miR-92a-3p**: Liu et al.[51] discovered that miR-92a-3p in exosomes generated from endothelial cells is associated with atherogenesis, suggesting its involvement in the mechanisms of cardiovascular disease.
8. **miR-21**: Mice with myocardial infarcts showed enhanced cardiac function and less scarring when miR-21-rich exosomes were directly injected into the region. Nevertheless, the capacity of exosomes produced from heart failure patients' cardiac stromal cells to stimulate endothelial tube formation and cardiomyocyte proliferation was hampered by dysregulated miR-21-5p expression.[52,53]

9. **miR-142-3p:** By activating myofibroblasts via miR-142-3p-WNT signaling, exosomes from activated CD4+ T cells accelerated post-ischemic cardiac fibrosis.[54]
10. **HIF-1α**: Sun et al.[55] demonstrated that by encouraging the development of new blood vessels during myocardial infarction, overexpression of HIF-1α in exosomes derived from mesenchymal stem cells decreased heart fibrosis.
11. **miR-30d**: Li et al.[56] showed that negative cardiac remodeling and elevated expression of genes linked to inflammation and fibrosis are correlated with decreased expression of miR-30d in heart-derived exosomes.
12. **miR-30d:** It targets integrin α5 in fibroblasts through a paracrine mechanism, preventing fibroblast proliferation and fibrosis, and is increased in cardiomyocytes in ischemic heart failure models in rats and mice.[56]

These miRNAs have been identified as potential exosomal biomarkers that modulate fibroblast proliferation, differentiation, and cardiac fibrosis. Targeting these miRNAs in exosomes may help diminish fibrosis and ameliorate cardiac function.

Valvular heart disease (VHD)

Valvular heart disease (VHD) is associated with significant anatomical and functional abnormalities of cardiac valves, leading to conditions such as stenosis and regurgitation. Recent studies have identified specific microRNAs (miRNAs) that play crucial roles in the pathogenesis of VHD and may serve as biomarkers for diagnosis:

1. **miR-23**: Acts as a negative feedback regulator of hyaluronic acid synthase 2 (Has2), preventing excess deposition of hyaluronan in cardiac jelly, which is crucial for cardiac valve formation. Aberrant regulation of miR-23 can lead to cardiac valve defects.[57]
2. **miR-9**: Involved in the regulation of cardiomyocyte energetics and fibrosis, associated with the progression of myxomatous mitral valve disease and congestive heart failure.[58]
3. **miR-181c**: Similar to miR-9, it regulates cardiomyocyte energetics and is linked to valve disorder progression and heart failure.[58]
4. **miR-495**: Associated with mitochondrial function and involved in the regulation of fibrotic processes in valve diseases.[58]
6. **miR-599**: Also involved in cardiomyocyte energetics and linked to the pathophysiology of valvular heart disease and heart failure.[58]
7. **lncRNA HOTAIR**: Modulates calcification-related gene expression in valvular smooth muscle cells (VSMCs) during aortic valve disease, influencing the progression of calcification.[59]

Heart failure

Heart failure (HF) is a is a complex disorder characterized by the heart's inability to pump enough blood to meet the body's demands, resulting in a variety of systemic consequences. Recent research has highlighted the potential of specific microRNAs (miRNAs) as biomarkers for diagnosing HF.[60] Here are some key miRNAs associated with heart failure, along with their functions and relevant studies:

1. **CD14, SerpinG1, SerpinF2:** These are systemic vascular markers associated with the development of heart failure (HF) in patients suspected of acute HF.[61]
2. **miR-146a:** Increased levels are associated with the attenuation of inflammatory targets and provide cardioprotective effects against oxidative stress in HF patients.[62]
3. **miR-486:** Similar to miR-146a, it plays a role in mitigating inflammation and protecting against oxidative stress in HF.[62]
4. **miR-155:** Activated in response to TGF-β treatment, associated with hypertrophic responses in cardiomyocytes.[63]
5. **miR-21:** Promotes cardiac hypertrophy through paracrine signaling; regulates key pathways linked to hypertrophy and fibrosis in cardiomyocytes.[64,65]
6. **miR-21-3p (miR-21):** Acts as a paracrine mediator of cardiomyocyte hypertrophy, targeting pathways that lead to cardiac enlargement and dysfunction.[64]
7. **miR-214, miR-135b, miR-125a, miR-145-5p**: Involved in angiogenesis by upregulating or downregulating target gene expression in endothelial cells (ECs).[66–71]

CONCLUSION

To conclude, while exosomes are key components that have been extensively studied in relation to cardiovascular diseases (CVDs), it is vital to also focus on the salivary assessment of these exosomes. Salivary exosomes provide a non-invasive method for monitoring and diagnosing CVDs, carrying a diverse array of biomarkers that reflect cardiovascular health. Their ability to transport specific indicators associated with conditions such as

coronary artery disease and heart failure positions them as valuable tools for early detection and personalized treatment approaches.

Among the various contents of exosomes, microRNAs (miRNAs) are increasingly recognized for their roles in CVD. These small RNA molecules are essential for regulating gene expression and are linked to numerous cardiovascular processes. Therefore, research should emphasize the evaluation of salivary miRNAs to fully harness their potential as biomarkers. By integrating salivary miRNA analysis into clinical practice, we could significantly enhance our understanding and management of cardiovascular diseases, underscoring the need for further exploration in this promising area.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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Literature Review

THE ROLE OF CONTINUOUS MONITORING IN ONCOLOGY PATIENTS RECEIVING RADIOTHERAPY OR CHEMOTHERAPY. REVIEW

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Abstract

Background: Oral cancer is a major public health problem worldwide and the prevention of oral cancer and its associated morbidity and mortality depends on early detection. Delayed diagnosis is a major contributor to the dismal oral cancer survival rate over five years.Currently, various monitoring methods have been actively used for the purpose of active early detection of asymptomatic oral cancer.

This study provides an overview of the main concepts and principles of organizing continuous monitoring in oncology patients receiving radiotherapy or chemotherapy.

Methods: This review was reported per the PRISMA guidelines and was conducted in publications covering scientific research on diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms in Medline, Scopus, Web of science, PubMed (search 162 which finally included 75 articles).

Two review authors screened the results of the searches against inclusion criteria, extracted data and assessed risk of bias independently and in duplicate.

Results: To prevent or minimize oral complications, an appropriate oncology protocol is needed which should include early oral assessment prior to treatment. Early recognition and diagnosis can improve patient survival and reduce morbidity.

Conclusion: Continuous monitoring of patients with in primary care settings receiving radiation therapy or chemotherapy may reduce oral complications and improve the effectiveness of combination therapy. To reduce the risk of complications in the oral cavity, it is very important to pre-treat existing oral diseases, and in this aspect, the cooperation of the dentist and oncologist as one team is very important. This review will help dental practitioners manage the risks and prevent potential complications in patients with oral complications requiring dental care.

Keywords: *oral potentially malignant disorders,* Oral cancer, chemotherapy, radiation therapy, prevent complications, monitoring oral cancer

INTRODUCTION

Treatment of cancer at early stages is one of the most urgent in medicine, since the results of standard generally accepted methods often do not give the desired results [1,2] .

In the mid-1980s, when it was proven that adding chemotherapy to radiotherapy and/or surgery improves the survival of cancer patients, by means of multidisciplinary approach emerged in oncology [3].

The treatment of cancers is ideally a multidisciplinary approach involving the efforts of surgeons, radiation oncologists, chemotherapy oncologists, nutritionists, and rehabilitation as well as restorative specialists [4,5]. The location, size of the tumor, lymph node involvement, and the presence or absence of distant metastases are important factors in choosing a specific treatment option. The most common cancer treatment is oncosurgery.

When treating a localized primary tumor with en bloc surgical procedures, this technique is the most effective method [6].

Chemotherapy and radiation therapy are included in the complex methods of treatment of malignant diseases. Radiation therapy is the use of a special type of energy of electromagnetic radiation or beam

of elementary nuclear particles that can kill tumor cells or inhibit their growth and division [7].

Radiation damages both normal cells and cancer cells. Normal cells can usually recover more quickly and maintain their normal functional status than cancer cells. Some healthy cells that fall into the irradiation zone are also damaged, but most of them are able to recover [8].

Tumor cells divide faster than the healthy cells surrounding them. Therefore, radiation has a more destructive effect on them. These differences determine the effectiveness of radiation therapy for cancer. During radiotherapy, tumor cells experience a decrease in their proliferation rate due to DNA damage-induced cell cycle arrest [9].

Radiation therapy before cancer surgery (neoadjuvant therapy) is aimed at shrinking the tumor. Radiation therapy after surgery (adjuvant therapy) will kill any microscopic tumor cells that remains[10].

Often, to destroy tumor cells, radiation is carried out together with antitumor drugs (chemotherapy)[11-13].

To date, the agents found to be most effective for treating oral cancer include cisplatinum, carboplatinum, taxanes, 5-fluorouracil, methotrexate, and ifosphamide [14].

Chemotherapeutic drugs act preferentially on cells that are divided at a higher rate, causing malignant cells to be destroyed faster than normal cells at the tumor site. However, chemotherapeutic drugs will also seriously affect normal cells, causing side effects including: myelosuppression (leukopenia, thrombocytopenia, and anemia), nausea, vomiting, diarrhea, mucosal ulceration, dermatitis, and alopecia [15].

The choice of chemo-preventive drugs, dosage and duration of treatment is mainly based on the type and stage of cancer [16,17].

In most cases, a team of specialists including radiologists, dieticians, psychologists and a primary consultant jointly decide on treatment plans, dosage, duration of cycles and additional supplements.

Radiation therapy and chemotherapy like any other type of treatment, may be accompanied by general and local (in the area of tissue exposure to radiation) side effects [18,19].

These effects may be acute (short-term, occur during treatment) and chronic (develop several weeks or even years after the end of treatment). Long-term exposure to these drugs can have excessively adverse effects on the patient's physical and mental health, making it difficult to continue ongoing treatment Side effects of radiotherapy most often manifest themselves in tissues and organs that have been directly exposed to radiation. Most side effects that develop during treatment are relatively mild and are treated with medication or proper nutrition [20].

When using radiation therapy and chemotherapy, a number of complications arise in the oral cavity in the form of a number of oral diseases [21-31].

Complications after radiotherapy and chemotherapy appear 7–14 days after the start of the course and have a significant impact on the quality of life of patients[32-34].

This complication may lead to changes or interruptions in treatment, which affects cure rates. There are various factors in the etiopathogenesis of complications in the oral cavity associated with chemotherapy and radiation therapy for treatment of cancers [35-37].

Chemotherapy and radiation therapy lead to the death of basal epithelial cells, slow or stop the growth of new cells, disrupt normal tissue healing, because of the replication of basal epithelial cells is disrupted [38,39].

Among the factors, pro-inflammatory cytokines and bacterial metabolic products may also play a role, also weaken the oral immune system due to the loss of tissue immune cells. Among complications in the oral cavity during radiotherapy and cancer chemotherapy, dental caries, periodontitis, mucositis, fibrosis, oropharyngeal candidiasis, oral infections (viral, fungal, bacterial), infection caused by the herpes simplex virus - herpetic gingivostomatitis, chronic recurrent aphthous stomatitis, hypofunction of the salivary glands and xerostomia, neurosensory disorders (pain in the mucous membrane and taste dysfunction) [40-43].

Mucositis is the most common disease of the oral cavity, patients treated with chemotherapy/radiotherapy are effected up to 34%–43%.

Mucositis with clinical manifestations of varying severity, from ulceration to an inflammatory process, in which the patient has difficulty eating solid food can seriously affect the comfort and well-being of patients [44,45].

Mucositis patients are associated with an increased risk of infection, pain, decreased food intake and malnutrition, and can impact on the effectiveness of treatment[46].These complications significantly worsen the quality of life of patients. In some cases, oral mucositis is the reason for interrupting courses of antitumor therapy. Accordingly, the effectiveness of the planned and ongoing chemotherapeutic treatment is reduced. These same reasons can have a detrimental effect on the long-term results of the planned treatment as a whole.

Davit Mathevosyan. The role of continuous monitoring in oncology patients receiving radiotherapy or chemotherapy. Bulletin of Stomatology and Maxillofacial Surgery. 2025;21(2)88-98: DOI:10.58240/1829006X-2025.2-88

This review provides an overview of the main concepts and principles of organizing continuous monitoring in oncology patients receiving radiotherapy or chemotherapy.

Methods

Comprehensive Search Strategy

This review was reported per the PRISMA guidelines and was conducted in publications covering scientific research on diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms in Medline, Scopus, Web of science, PubMed (search 162 which finally included 75 articles).

Review author screened the results of the searches against inclusion criteria, extracted data and assessed risk of bias independently and in duplicate. Potentially eligible studies underwent a full-text review, and discrepancies between reviewers were resolved through discussion Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement.

Inclusion criteria:included clinical trials, considered randomized controlled trials, cross-sectional studies, case-control studies, and cohort studies in human subjects that evaluated the current literature on the oral cancer, oral squamous cell carcinoma, head and neck carcinoma, systematic screening, diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms written in English articles. There was no limitation on minimal quality, minimal sample size, or the number of patients.

Exclusion criteria were: original primary studies, due to language limitations, abstracts, letters to the editor, book chapters, case reports, conference abstracts, duplicate publications, and in vitro and in vivo animal experimental studies.

Data extraction

2 reviewers extracted data from the included studies using a standardized data extraction form. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. Discrepancies in data extraction were resolved by discussion.

Quality assessment

The effectiveness were evaluated by synthesising relevant outcome data extracted from selected studies. For prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms, screening methods that reduce cancer incidence and detect precancerous lesions. The effectiveness' program in cancer screening, is usually cancer mortality, defined as the number of deaths from the cancer.

Data synthesis

The results of this review were reported following the PRISMA guidelines. A narrative synthesis of the findings was provided.

Effect measures

Evaluating the effectiveness of a monitoring program for patients with malignant neoplasms receiving radiotherapy and chemotherapy is an important criterion.

Results of the search

Conducted a preliminary search and reviewed titles and abstracts in this review and 75 full-text articles were selected of high methodological quality. For a further description of our screening process, see the study flow diagram in figure 1.

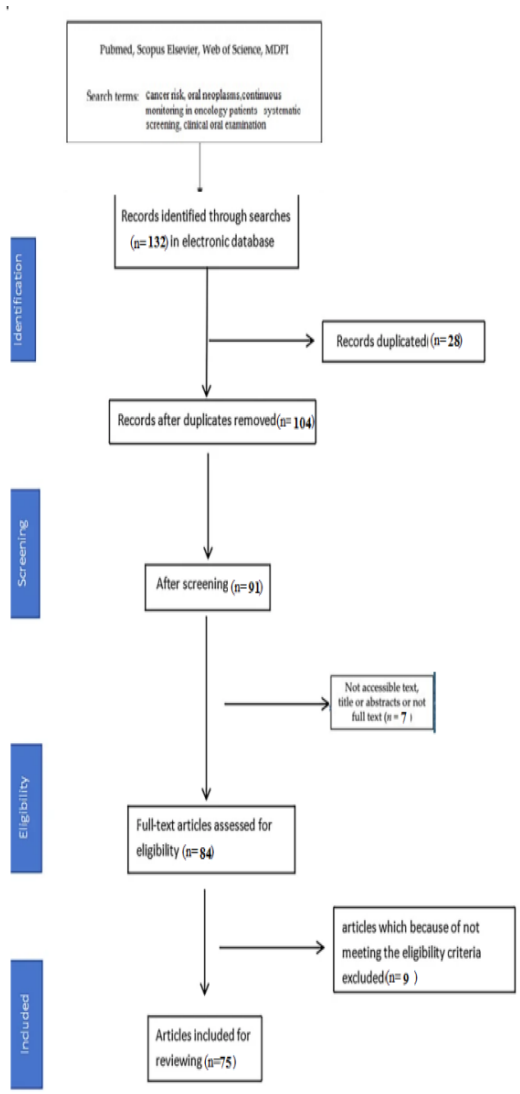


Figure 1. Diagram study flow method used the PRISMA

Risk of bias in included studies

In developing the data collection instrument, we considered. The form collects information needed to monitor the status of screening, reviewing and summarizing of each article by 2 reviewers.

Developing tables that summarize the body of evidence. The form captures detailed descriptive data about the intervention and evaluation.

Classifying other key characteristics of the intervention and assessing the quality of the study's execution. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. This information is used as a criterion for continued inclusion of the study in the body of evidence for an intervention.

Following the study design, has identifie domains rating the certainty of evidence: risk of bias, inconsistency, inconsistency, imprecision, and publication bias.

To reduce the side effects of chemotherapy and radiation therapy of the head and neck, it is necessary to develop a set of preventive measures and, when possible, use minimally invasive surgical methods such as (transoral robotic surgery, transoral laser microsurgery) [47,48].

For oral care, complication chemotherapy and radiation therapy it is recommended to use standardized oral care protocol [49-51] (figure 2).



Figure.2 Oral care protocols complication chemotherapy and radiation therapy

Treatment is symptomatic, for pain relief, topical analgesics may be useful. Although protocols for the management of patients in this category are constantly updated, however, there are no universally effective protocols for the prevention of side effects of chemotherapy and radiation therapy for cancer. To prevent complications of chemotherapy and radiation therapy and achieve optimal comprehensive oral care, the key point is the organization of oral care rooms in cancer centers and constant dynamic monitoring [52].

Many studies argue for a multidisciplinary approach to the management of these patients, cooperation of the dentist and oncologist as one team is very important [53]. The main role of the dentist during chemotherapy and radiation therapy is to minimize undesirable consequences and deliver timely treatments [54-56].

Cancer screening is indicated for all patients with cancer. The screening program for each disease is unique and includes a specific list of necessary examinations [57-59].

There are several types of tests and recommendations for cancer screening. The Cancer screening can be carried out using medical examinations, blood tests, radiological (visualizing) tests, such as computed tomography (CT) positron emission tomography and specific MRI parameters, and biomarker testing [60-63].

Recommendations for cancer screening are different for people of different ages, as well as for each organ examined separately and depend on the risk factors that exist for a given type of cancer [64].

Screening diagnostics contributes to effective treatment and maintaining the quality of life of this category of patients at a decent level. To establish a diagnosis, it is necessary to conduct a full-fledged comprehensive screening examination, which allows identifying pathological changes in the oral cavity at early stages [65](figure3).

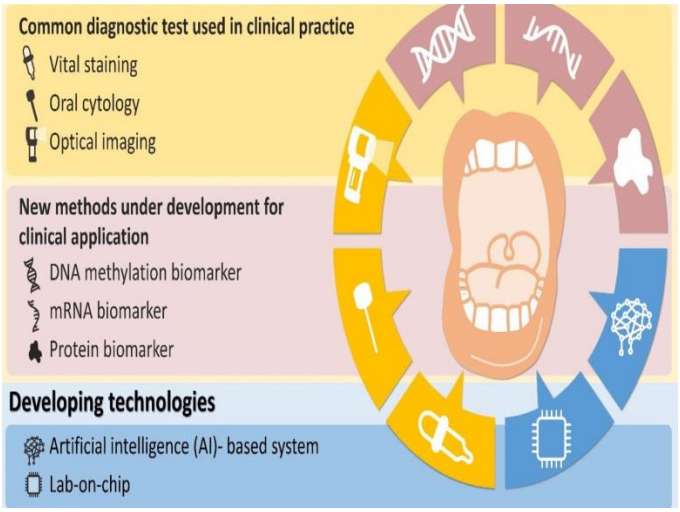


Figure 3. Examples of individual screening timing patterns

An oral/dental assessment including radiographs should be performed prior to initiating cancer therapy [66,67].

- Identify existing oral diseases and potential risk for oral diseases.

- Eliminate oral/dental infectious foci prior to initiating cancer therapy.
- Prepare the patient for expected side effects of cancer therapy.
- Establish an adequate standard of oral hygiene to address increasing challenges during cancer therapy.
- Develop a plan for maintaining oral hygiene, providing preventive care, completing oral rehabilitation, and follow-up.
- Establish appropriate multidisciplinary collaboration within the cancer center to reduce/alleviate oral symptoms and consequences before, during, and after cancer therapy.

During external examination, it is necessary to pay attention to the configuration of the face, its symmetry, skin color, palpate the lymph nodes, study the condition of the temporomandibular joint, nasolabial folds, red border of the lips and skin around the lips.

During intraoral examination, the mucous membrane of the lips, cheeks, mucous membrane of the vestibular and oral surfaces of the alveolar process of the upper and lower jaws, hard and soft palate, pharynx, all surfaces of the tongue, the floor of the oral cavity should be studied(figure 4).

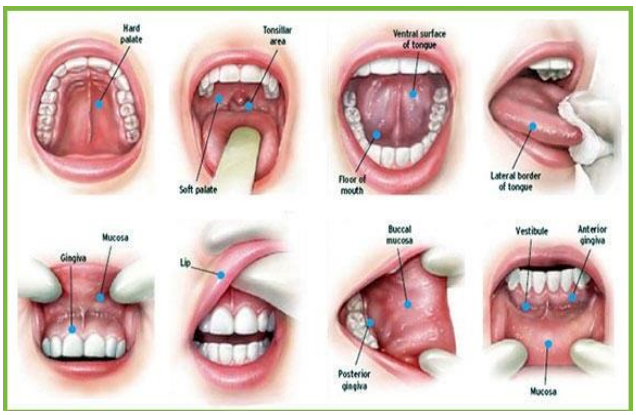


Figure.4 Oral Cancer Screening chart to check visual examination of the oral cavity (VOE)

A detailed assessment of the elements of the oral cavity lesion is carried out, which includes an assessment of the change in color, in which they could be white, red or combined, assess the change in relief, which can be smooth, convex, concave or elevated. Determine the violation of the integrity of the epithelium, localization, shape, size, depth of the lesion. Using palpation, it is possible to determine pain in comparison with the surrounding tissues, determine the area of the lesion and its contours.

Assess the condition of the periodontal tissues, determining the presence of supragingival and subgingival dental plaque, gum inflammation, the presence of periodontal pockets and gum recessions, tooth mobility, changes in the position of the teeth, the condition of the hard tissues of the teeth, dentures and dentition. Using dental radiographs, determine the foci of odontogenic infection, such as apical periodontitis.

Based on the clinical examination, according to the indications, conduct emergency care professional oral hygiene. Recommendations were given for oral care, hygiene products were selected. Monitoring should include not only clinical and instrumental examinations but also a survey [68,69].

The questionnaire should include questions regarding dental status and deterioration of quality of life due to pain, nutritional problems, communication difficulties. Patients (with the help of a dentist) should answer the proposed questions on a point scale.

1. Do you notice any tongue movement disorder/restriction?
   - none;
   - discomfort;
   - partially limited;
   - severely limited;
   - impossible.

2. Do you notice any taste disorder?
   - normal taste perception;
   - distorted taste perception in the presence of a stimulus;
   - distorted taste perception without a stimulus;
   - distorted taste perception with partial loss;
   - total absence of taste perception.

3. Do you notice any chewing disorder?
   - no difficulty;
   - discomfort;
   - partially limited;
   - severely limited;
   - impossible.

4. Do you notice any eating disorder?
   - no difficulty;
   - moderate discomfort;
   - severe discomfort;
   - limited, only liquid forms;
   - eating is impossible.
   - 5. Do you notice any speech production disorder?

- none;
- moderate discomfort during prolonged conversation;
- severe discomfort during conversation;
- limited;
- impossible.

6. Do you/your loved ones notice halitosis (bad breath)?
- no smell;
- weak, undetectable smell when speaking;
- weak, but detectable smell when speaking;
- moderately pronounced, unpleasant smell;
- strongly pronounced, intolerable smell.

7. Burning sensation in the mouth:
- absent;
- periodic, short-term;
- periodic, prolonged;
- constant, moderate intensity;
- constant, intolerable (intensity
- significantly pronounced)

8. Painful sensations in the mouth:
- absent;
- periodically occurring, short-term;
- periodically occurring, prolonged (long-term);
- constant, moderate intensity;
- constant, intolerable.

9. Xerostomia (dry mouth):
- absent;
- dry mouth appears after long conversations;
- constant dry mouth, difficulty speaking and eating;
- severe dry mouth, pain during talking and eating.

Evaluation of common side effects in patients receiving anticancer drugs should include myelosuppression, nausea, vomiting, oral complications, diarrhea, hypertension.Based on the clinical examination, according to the indications, conduct emergency care professional oral hygiene. Recommendations were given for oral care. Oral hygiene products were selected. Patients should be taught to record side effects of treatment when they occur.For safe complex antitumor treatment, patient monitoring is very important as it helps to identify toxicity and complications at an early stage, allows for quick action, prevents serious complications and possible hospitalization. To improve the quality of life for patients with malignant disease, who are receiving cancer therapy that has implications for oral comfort and function, by promoting consistent, evidence-based high standards of oral care through a co-ordinated team approach [70].

The oncology patient will require a multidisciplinary approach to achieve the best oral outcomes [71-73].

This review provided useful information evaluating prophylactic interventions for oral complications in cancer patients.

Most patients who receive a course of radiotherapy and chemotherapy in the complex treatment of cancer experience various oral complications [74,75].

In patients receiving radiotherapy or chemotherapy the pathological changes appear on the mucous membranes of oral cavity, on the skin, in the subcutaneous tissue, salivary glands and in the bone marrow of the jaw bones.. To reduce the risk of complications in the oral cavity, it is very important to pre-treat existing oral diseases, and in this aspect, the cooperation of the dentist and oncologist as one team is very important. There are different protocols for oral care, monitoring, cancer patients, in which the main focus is on prophylaxis and pain relief.

CONCLUSION

Continuous monitoring of patients with in primary care settings receiving radiation therapy or chemotherapy may reduce oral complications and improve the effectiveness of combination therapy. This review will help dental practitioners manage the risks and prevent potential complications in patients with oral complications requiring dental care.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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LITERATURE REVIEW

THE USE OF HYPNOSIS IN DENTISTRY IN ANXIOUS PATIENTS. SYSTEMATIC REVIEW OF THE LITERATURE OF THE LAST 5 YEARS

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Abstract

Background: Dental anxiety and odontophobia significantly impact patient care and oral health. These conditions stem from factors such as direct conditioning, vicarious learning, and psychological predispositions, often leading to somatic symptoms and severe avoidance behaviors. Hypnosis has emerged as an effective approach for managing dental anxiety, providing benefits such as reduced fear and pain perception, improved patient collaboration, and enhanced healing.

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Materials and Methods: This systematic review followed PRISMA guidelines and analyzed studies retrieved from PubMed, Scopus, and Cochrane databases between 2019 and 2024. Randomized controlled trials, cross-sectional studies, and comparative analyses examining hypnosis for dental anxiety and phobia were included. The Newcastle-Ottawa Scale assessed study quality and risk of bias. Data extraction focused on study design, outcomes, and patient demographics.

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Results: The search identified 75 papers, of which 56 were screened after removing duplicates. Following inclusion criteria, eight studies were analyzed. The risk of bias varied, with one high-quality study, two medium, and five low-quality studies. Evidence demonstrated hypnosis reduced anxiety, improved patient cooperation, and supported better oral health outcomes by addressing anticipatory anxiety and avoidance behaviors. **Conclusion:** Hypnosis, combined with techniques like hypnotic communication and iatrosedation, offers a non-pharmacological strategy to manage dental anxiety and phobia. These approaches establish trust, redefine negative past experiences, and personalize patient care, leading to improved dental experiences and psycho-oral health. Implementing these methods in dental practice can enhance patient well-being and treatment outcomes.

Keywords: odontophobia, dental anxiety, hypnosis, iatrosedation

INTRODUCTION

Anxiety is an adaptive emotional response to potentially threatening or dangerous situations. Dental anxiety relates to the fear, stress or dread induced before, during or after dental treatment.

Anxiety is a significant source of perioperative discomfort that affects the patient's quality of life by increasing pain perception. Inadequate management of postoperative pain is responsible for the onset of forms of anxiety and depression, generating a break between them. Preoperative anxiety and depression may therefore persist over time and well beyond the period of surgery.

Odontophobia is based on the dysregulation of the natural defenses of the individual, responsible forthe

transition from a physiological anxiety, directed towards a real danger, to a pathological anxiety, directed towards a dental treatment often totally devoid of pain. Odontophobia show severity of their physiological and psychological symptoms. Triggers of fear are the perception of the visual, olfactory, and sensory stimuli during dental treatment (sound of drill, dentist's chair). Odontophobia can be divided into Dental Anxiety, Dental Fear and Dental Phobia.

The American Psychological Association (APA) Division defines hypnosis as "a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion".

The phenomenology of hypnosis can be considered as the result of intentional introspective activity.
The good acceptance of hypnosis and the effectiveness in reducing anxiety in patients with dental phobia is reported by several authors. Positive effects of hypnosis in patients with dental phobias include reduction of fear and anxiety, prevention of avoidance behavior and the resulting lack of dental treatment, reduction of felt pain, less bleeding during tooth extractions, and better and faster wound healing.

Hypnosis is a powerful tool for the dental field because it can guarantee:

a) Effective and deep sedation and amnesia, while maintaining patient's collaboration;
b) Treatment of anxiety and dental phobia, helping the patient to overcome it, as well as for other associated anxiety disorders.

Materials and methods

Research question.

What is the effect of hypnosis for dental anxiety and dental phobia?

Protocol and registration

Following the formulation of the Research Questions, a research protocol was defined prior to the start of the review process. This protocol follows the reporting guidelines of the of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) model.

Search strategy

PubMed, Scopus and Cochrane databases were searched using "hypnosis AND dentistry" combination to retrieve the articles. The search included only articles published in English between 2019 and December 2024 with no location restrictions.

Study selection

Two observes were involved in article selection. In case of discrepancies between them, a third reviewer was consulted and consensus was sought through discussion. Articles were first imported from the databases to Excel to exclude the duplicates.

The remaining article were screened on Title and Abstract and included or excluded by the same reviewers according to inclusion criteria: randomized controlled trials, cross-sectional studies, comparative studies, validation studies and evaluation studies, reporting hypnosis effects for dental anxiety and phobia in patients of any age were searched and evaluated. (Table 1)

Table 1. General characteristics of the included studies

N	First Authors Name/Year of Publication [Reference Number]	Design	Country	Total, n	Mean age, years	Scores	Dental treatment	hypnosis type/ Study design
1	Tieri 2023	Case control	Italy	150	5-10	VAS, FLACC and Heart rate monitoring	Dental care	

2	Retrospective longitudinal study	Germany	311	5-12	Wong–Baker Scale	Dental care	Comparisonof compliance of children during dental treatments with midazolam or hypnosis techniques
3	Randomized control trial	Norway	1083	8-12	VAS, HR, and SPO 2	Extraction of tooth	Hypnosis and Progressive Muscle Relaxation in paediatric dentistry
4	Randomized clinical trial	*Iran*	66	6-10	Venham Clinical Anxiety Scale and the Venham Picture Test	Posterior primary tooth extraction	N2O/O2 inhalation and hypnosis are effective in reducing self-reported and observed anxiety and improving cooperationlevels in pediatric patients during dental extraction.

5	Erappa 2021	Randomized cross-sectional clinical trial	India	200	6-10	Pulse rate, respiratory rate and anxiety rate	Dental care	Assess and compare the efficacy of acupressure, hypnosis and audiovisual aids in reducing anxiety in children during the administration of local anesthesia
6	Moghadam 2021	Single-blind clinical trial	/	33	/	Pulse rate, respiratory rate and anxiety rate	Surgical third-molar removal, implant surgery, maxillary bone augmentation, and mucogingiva l surgery	This study aimed to investigate the impact of hypnosison relievingthe pain of injected dental infiltration anesthesia.

7	Girón 2023	Randomized controlled trial	Mexico	60	5-7	FLACC	Pulpotomy in the primary mandibularright or left first or second molar	Hypnosis to reduce anxiety andpain during dental treatment.
8	Hidoussi Sakly 2020	A Cross-SectionalStudy	Tunisia	200-300	26-60	VAS	Dental care	To assess the attitudes, experiences, training levels, and interest in future education regarding the use of hypnosis bydentists

The full text of the resulting articles was retrieved to and checked for final inclusion. The PRISMA flow chart (Figure 1) illustrates the selection process followed during this review.

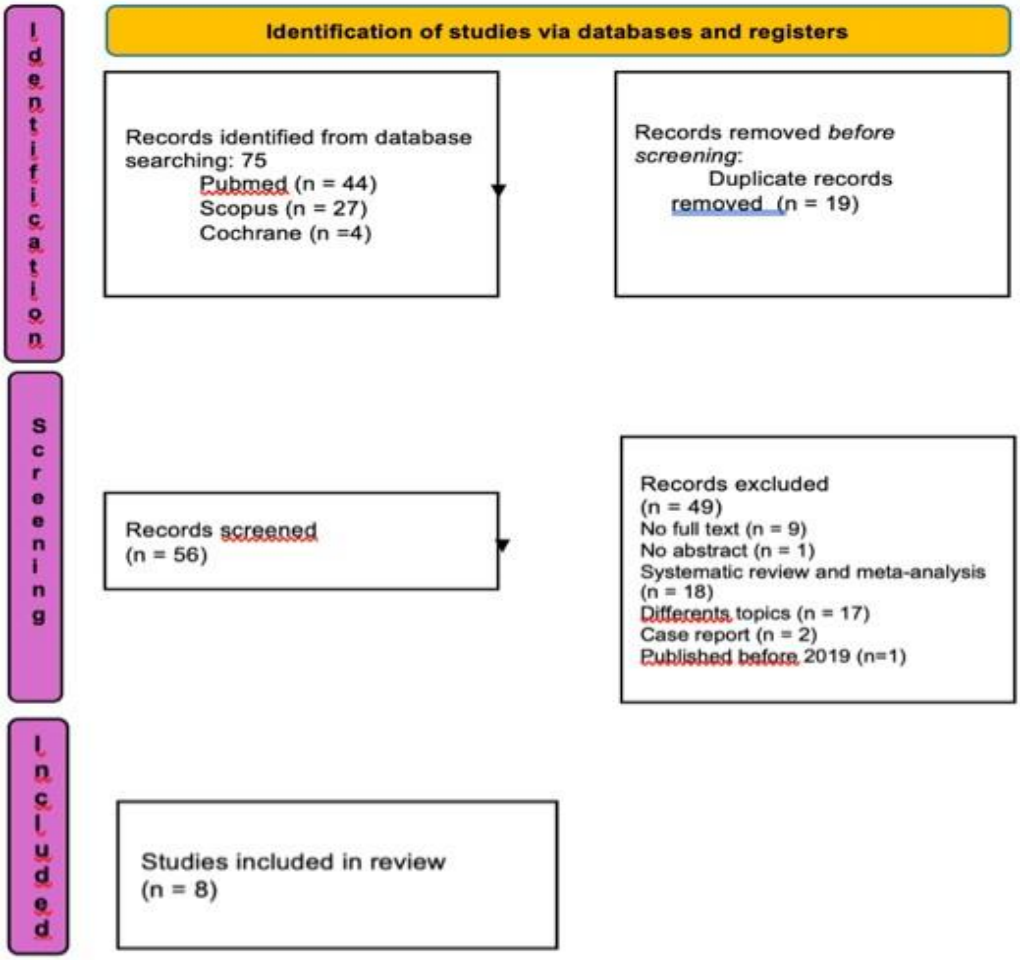


Figure 1. Summary of the search strategy employed in the qualitative analysis

Data collection and synthesis

Data extraction was made by two observers independently. For each paper, the following data were searched and recorded when available: author, year of publication, design, country, sample, mean age, scores, dental treatment and aim of the study.

Risk of bias of the included studies

The risk of bias assessment was conducted by the Newcastle-Ottawa Scale (NOS). Data extrapolated from the selected papers was divided into three sections: selection, comparability and outcome. Eachsection was analized by the official coding manual's questions. The NOS ranges from 0 (lowest) to 9 (highest), and studies with scores≥6 are considered high quality (Table 2).

Table 2. Quality of the studies

Author and year	Selection (maximum 4 stars)				Comparability (maximum2 stars)	Outcome (maximum 3 stars)		
	Rapresentativeness of the sample	Non-exposed	Ascertainment ofthe exposure	Outcome of interest was not present at start of the study	Comparability of cohorts	Assessment of outcome	Same method of ascertainment for cases and controls	Non-responserate
Tieri 2023	A*	C	B*	B	B*	A*	A*	C
Rienhoff 2022	B*	C	B*	A*	A*	A*	A*	B*
Sabherwal 2020	A*	A*	B	B	A*	B*	/	C
Motallebi 2024	B*	A*	B	A*	B*	B*	A*	C
Erapp a 2021	B*	C	A*	B	A*	B*	A*	B*

Mogha dam 2021	B*	C	A*	B	A*	C	A*	B*
Girón 2023	B*	C	A*	A*	A*	A*	A*	B*
Hidoussi Sakly 2020	C	C	B*	A*	/	D	B	B*
Authorand year	Selection (maximum 4 stars)				Comparability (maximum2stars)	Outcome (maximum 3 stars)		

	Rapresentativeness of the sample	Non-exposed	Ascertainment of the exposure	Outcome of interest was not present atstart of the study	Comparability of cohorts	Assessment of outcome	Same method of ascertainment for cases and controls	Non-responserate
Tieri 2023	A*	C	B*	B	B*	A*	A*	C
Rienhoff 2022	B*	C	B*	A*	A*	A*	A*	B*

Mogha dam 2021	B*	C	A*	B	A*	C	A*	B*
Girón 2023	B*	C	A*	A*	A*	A*	A*	B*
Hidoussi Sakly 2020	C	C	B*	A*	/	D	B	B*
Author and year	Selection (maximum 4 stars)				Comparability (maximum 2 stars)	Outcome (maximum 3 stars)		

	Rapresentativeness of the sample	Non-exposed	Ascertainment of the exposure	Outcome of interest was not present atstart of thestudy	Comparability of cohorts	Assessment of outcome	Same method of ascertainment for cases and controls	Non-response rate
Tieri 2023	A*	C	B*	B	B*	A*	A*	C
Rienhoff 2022	B*	C	B*	A*	A*	A*	A*	B*

Sabherwal2020	A*	A*	B	B	A*	B*	/	C
Motallebi 2024	B*	A*	B	A*	B*	B*	A*	C
Erapp a 2021	B*	C	A*	B	A*	B*	A*	B*

Moghadam 2021	B*	C	A*	B	A*	C	A*	B*
Girón 2023	B*	C	A*	A*	A*	A*	A*	B*
Hidoussi Sakly 2020	C	C	B*	A*	/	D	B	B*
	Selection (maximum 4 stars)				Comparability (maximum 2stars)	Outcome (maximum 3 stars)		
Author and year	Rapresentativeness of the sample	Non-exposed	Ascertainment of the exposure	Outcome of interest was not present at start of the study	Comparability of cohorts	Assessment of outcome	Same method of ascertainment for cases and controls	Non-response rate

Results

The search strategy identified 75 papers in the three databases; 56 were selected after removing duplicates. A total of 48 articles were excluded for inclusion criteria. The systematic reviews and meta-analyses were excluded but they were read (Figure 1).

Risk of bias

Based on NOS 1 study was scored as high level, 2 study was scored as medium and 5 was scored aslow level of bias.

Discussion

Dental phobia is a universally widespread and frequent phenomenon, although not always known, and underestimated by the dentist.

Recent epidemiological research suggests that its prevalence values are between 6-15% of the world's adult population. Significant differences are found between the various countries, mainly related to the socio-cultural status, which play an important role in the etiology and development of the problem. In western civilization, 3 to 5% of the adult population have a form of dental phobia, whileup to 30% report a moderate level of anxiety towards dental treatment. The female sex is most interested, with a male ratio: female approximately 1 to 2.

Knowing the causes of odontophobia allows to prevent the onset and progression if the phenomenonwas already present.

The odontophobia depends essentially on three factors that act independently of each other or combine increasing severity. These factors are:

- Direct packaging;
- Vicarious learning;
- General psychological state.

Direct conditioning is an unpleasant personal experience in the past. This experience represents a more or less intense pain at an early age in the dental practice. 50-60% of odontophobic people recognize this traumatic experience as the origin of their disorder.

The vicarious learning, typical of the childhood, is expressed through observation, identification and indirect suggestion of behavioral models. In fact, the odontophobiac patients come from families whose members have suffered adverse dental experiences characterized by hostile attitudes or fear towards the dentist.

As a child grows up, he records and irreversibly associates the ideas of pain and fear with the dentist, transforming them into an anxiety or phobic syndrome that will manifest itself in adulthood.

These first two factors are included in a model of odontophobia called "exogenous" in relation to the source of the disorder, ie situations or information external to the individual. The age range between 3 and 14 years is a critical period for the beginning of this typology, as it was observed an increased vulnerability to negative or particularly traumatic experiences.

The typology classified as "endogenous" finds a causal source within the subject, that is to say, its own psycho-pathological profile. Endogenous odontophobia is the expression of an organic disorder, and depends on the individual's vulnerability to anxiety disorders. This form of odontophobia is accompanied by a general state of high anxiety, intense multiple fears, mood disorders and stress.

Several studies have revealed the existence of an association between odontophobia and various types of phobic anxiety (agoraphobia, claustrophobia, social anxiety and panic attacks), nonspecific anxiety (tension, nervousness, difficulty in resting), paranoia (paranoid thoughts and ideas, suspicion, centrality, disappointment and loss of autonomy), obsessive-compulsive disorders and, more generally, psychological problems or psychiatric disorders. In this type of person, odontophobia tends to develop at a later age and its symptoms can be significantly more severe than those caused by an exogenous disorder.

The somatic component of the patient with dental anxiety is represented by a wide spectrum of symptoms on the neurovegetative system. Typically found is:

- Increased respiratory rate with dyspnea and tachypnea;
- Muscle tension, especially in the head, neck and back;
- Heart rate and palpitations accelerated;
- Tremors;
- Hypersensitisation, especially in the palms of the hands;
- Vasodilation.

These signs are perfectly recognizable by the dentist when he is about to treat an anxious patient. When affected by this symptomatology, the patient immediately stops treatment in panic, screamingand shaking on the chair, making it difficult to regain control and continue the treatment.

In the most serious patient, violent reactions can occur, with even aggressive attempts to escape.
The emotional component is fundamental in the patient's response to the phobic stimulus: the odontophobic patient subjectively lives the experience as an "existential threat". It is possible to distinguish two dimensions:

- "threat of breach" means the fear of being a victim of unforeseeable and tragic events such asunbearable pain, damage, permanent injury, scarring or mutilation due to operator errors. In this case,the patient is terrified at the thought of dental treatment
- the "loss of autonomy and independence", that is, the feeling of losing complete control overthe situation being experienced, the perception of being weak, vulnerable and defenceless. In general,the feeling of panic comes from being completely powerless towards the dentist.

Among the negative thoughts that afflict the patient we find the fear of being considered weak and infantile. It is therefore essential to predict and erase these thoughts in order to contain the patient's reaction during the course of treatment.

It is good to remember the phenomenon of anticipatory anxiety; when the patient feels safe from possible contacts with the phobic stimulus, odontophobia is asymptomatic. When the possibility of dental treatment becomes closer in time, the patient becomes persistently anxious. The days precedingthe dental visit are therefore characterized by a state of apprehension, with symptoms in the cognitivesphere and vigilance, insomnia and difficulty in falling asleep and physical ailments. As the appointment becomes imminent, anxiety becomes so intense and unbearable that in the most serious cases it leads to avoidance behavior. This situation can persist despite the presence of acute pain symptoms, as this is always lower than the extent of the phobia perceived by the patient. Dental problems are thus postponed and appointments postponed for many years.

The worst consequence of dental phobia is its impact on oral health and, in a direct way, on the quality of life associated with it. Numerous studies have been published to show that patients suffering from odontophobia represent a significant portion of the population for public health: this is due to phobiic patient avoidance behaviors that if prolonged, can lead to dental problems and serious general health issues such as facial osteomyelitis, intracranial extensions of periapical abscesses, sinusitis, sepsis, mediastinitis, fever, septicaemia, pneumonia and urinary tract infections.

Hypnotic communication

Hypnosis is based on the concept of communication. Hypnotic communication is a conscious communication technique that guides the patient in the perception of himself and the experience he is experiencing using the action of words at neuro- physiological level building reaction between the operator and the patient. To implement hypnotic communication is essential to establish a relationship of trust between doctor and patient, without it everything would be futile. To facilitate the establishment of such a relationship it is necessary to understand the cultural background of the subject in front of you, using a clear terminology that especially creates empathy and not discomfort.

Hypnotic communication, by making use of the conscious use of the tool of the word, can be used even without a change in the state of consciousness to lead to a state of trance.

The dentist manages good hypnotic communication with patients using the right communication channel.

The human species is characterized by its ability to build instruments, of which the main one is language; normally used to communicate thoughts and feelings given by the combination of sounds, Gestures, symbols written by our social structure. In literature, therefore, reference is made to the three main communication channels:

- Visual;
- Auditory;
- Kinesthetic.

Statistically, visual subjects represent 40% of the population. Auditory subjects represent about 20% of the population. Cinestesia represents about 40% of the population. It is therefore essential in any pre-talk to be able to recognize the preferred communication channel of the patient so that you can improve the establishment of a relationship.

A very useful technique is the "mirroring" in which the operator using the same predicates of the patient, repeat the same words of the interlocutor, trying to understand what systems of representation uses by checking if the language is of visual type, auditory or kinesthetic.

Finally, it is effective to use implicit commands with the aim of communicating directly with the unconscious mind; for example: "I am curious to know if you will learn to relax and get comfortable in the chair within a short time".

In hypnotic communication it is therefore essential to work on the convictions of the interlocutor, since these can have a potentiating or limiting action. For this reason, phrases like "I go to the dentistand feel sick" must be effectively changed by the dentist into "I go to the dentist and I'll be fine".

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This method allows the dentist to obtain the necessary information to meet the needs and concerns ofthe patient, being able to reassure them about their fears so that they can plan the best possible treatment plan.

The main purpose of this methodology is to create a basis for establishing a relationship and creating a relationship of trust between doctor and patient.

Conclusions

Anxiety before the patient undergoes dental treatment is very common.

The dentist must create an empathic and trusting bond with the patient by modifying his or her previous experiences.

The therapy must be personalized for each patient according to the case assessments, in relation to the experience and skills of the dental practitioner, the age, the degree of collaboration and anxiety of the patient.

The ability to know how to highlight the right communication channel of the patient, giving importance to the pre-clinical talk paying attention to past experiences and the possibility of creating a new and different experience for the relationship of trust between dentist and patient.

Using iatrosedation and hypnotic communication, allows to improve both for the dentist and for the patient experience, eliminating old negative preconceptions and improving the quality of life of the patient understood as psycho-oral health.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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Literature Review

NUTRIGENOMICS -AN ENIGMA TO PERIODONTAL DISEASES

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Abstract

Background: Nutrigenomics is used to learn about how genes and diet together may affect an individual's health and risk of developing diseases and also to prevent and treat disease. It also helps in the interaction between nutrients with the genome at the molecular level to get insight into the role of nutrients that may affects or influences health. Periodontitis results from imbalance between host and microbial response which results in improper functioning of periodontal tissues. Although there are several novel techniques to readdress and restore the function of periodontal structures, Nutrition can act as an anti-inflammatory component and can decrease the incidence of systemic conditions such as cardiovascular diseases, diabetes mellitus, rheumatoid arthritis, and Crohn's disease which are known to be associated with periodontal diseases. Nutrigenomics is an area of nutrition and periodontics which is involved with the influence of diet and its components on the genome, proteome, and metabolites.

Materials and methods: This review was reported per the PRISMA guidelines. PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 15 articles were included for full text. This article reviews nutritional impact and impact of nutrigenomics on periodontitis.

Keywords: *Nutrigenomics, Periodontitis, Nutrition*

INTRODUCTION

Periodontitis is an inflammatory condition which is caused by particular microorganisms or their groups involving episodic, progressive loss of the dento-gingival complex and the periodontal ligament resulting in exfoliation of teeth in susceptible patients.[1] It is the 2nd most common disease globally, after dental caries with a prevalence of 30-50% with mild forms of the population in United states, but only about 10% have periodontitis in severe forms.[2] Nutrigenomics is an emerging field of science dealing with the mutual-relationships between dietary components and human genome through the use of metabolomics, transcriptomics, epigenomics

and proteomics.[3]

This field is extensively related with the impact of nutrients on genome, proteomes (total proteins in body), and metabolites (Total metabolites in the body).[4] Dietary products that decrease or eliminate the undesirable effects of pro-inflammatory genetic variations may represent excellent preventive agents for periodontal diseases that enhance and benefit large sections of the population.

Pathophysiology of periodontal diseases is complex and involves various pathways. Susceptibility to periodontitis involves the reciprocity between local, bacterial, genetic, nutritional, environmental factors. For example, loss of tooth has been associated with changes in diet preferences and nutrient deficiency.[2] Common dietary agents act either directly or in an indirect way to modify gene structure and expression, on the human genome. Degree of gene expression can be modified by nutrition which can alter the physiologic and diseased processes during lifetime through environmental (Epigenetic) influence mechanisms that are critical for gene expression. Investigating the inter-relation between dietary components and alveolar bone loss is essential to thoroughly understand the probable role of nutritional adjustments in preventing and treating periodontal disease.[3,4] Understanding the patho-physiology behind attachment apparatus destruction, protective role of dietary components and the beginning of novel genomic functional measurement tools have increased the attention in researching the correlation between periodontal disease and nutrition. This review was reported per the PRISMA guidelines (fig.1).

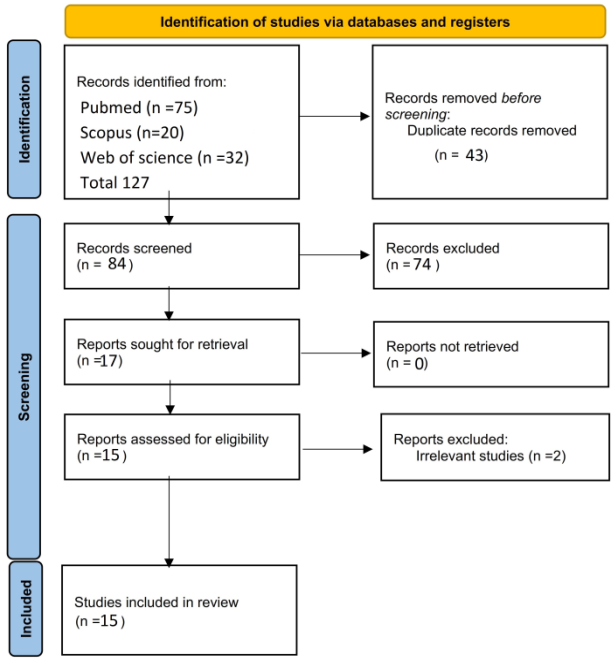


Figure 1. Prisma flow chart

PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 15 articles were included for full text.

History of Nutrigenomics and its Introduction

- First nutrigenomics company was launched In 1997.
- Term "Nutrigenomics": 2001 from Pelegrin (2001).
- Human Genome Project was launched on April 14th, 2003, which had the complete sequencing of Human Genome. This project had marked the beginning of new revolution in biological and medical sciences which was named as "OMICS" revolution.

The 'omics" revolution

- 2004: European Nutrigenomics organization NuGo was born and continued till 2014.
- In 2007, Nestle research center collaborated with the (KCGIF) Kluyver Centre for genomics of industrial fermentation, Netherland.
- In 2008, US Berkley scientist forecasted human genome tests within 5 years for $100.

"OMICS" Technology

It includes

Genomics: It focusses on resolving inter genome variations. It is the study of genome that involves an approach to gene mapping, sequencing, and analysis present in the genome.

Proteomics: It helps in expression of protein structure and physiology. This helps to differentiate the sum of proteins in a genetic (biologic) sample at the functional level. The sample can be from cell, organ, tissue or biofluid.

Metabolomics: Scientific study that involves quantitative analysis of metabolites. It also measures the level of substances (other than DNA, RNA, or protein) present in a sample.

Transcriptomics: This involves study m-RNA expression levels. It describes the approach in which m-RNA expression is evaluated in a sample using either oligonucleotide or cDNA microarray technology.

Goals of Nutrigenomics

1. Identify transcription factors which are sensors for nutrient recognition and the target genes for the interpretation of the signaling pathways associated with representation of main Dietary signals.

2. Cell and tissue specific gene representation (expression) signatures measurement and validation; Metabolic outcomes of specific micro-nutrients and macro-nutrients are also measured.
3. Regulatory pathways associated with various nutrients and Pathway interaction prior to inflammatory stress.
4. To recognize the process of dysregulation of metabolic pathways that lead to diet related diseases.
5. Detection of risk factors (Genotypes) to attain improvement of diet related systemic conditions such as myocardial infarction, diabetes, and hypertension.
5. Development of biomarkers (early metabolic dysregulation and susceptibility) using nutritional systems biology.

Practical Applications of Nutrigenomics [3,5,6]

1. Nutrients which can modify the genes and particular proteins which are expressed differentially in wellbeing and illness are identified.
2. Specific nutrients that influence proteins, genes and metabolites and are known to be advantageous or detrimental are identified.
   - ✓ To detect the variation by dietary fats associated with CVD's (cardiovascular diseases).
   - ✓ To detect that are altered by ω-3 fatty acids.

3. Nutrient-gene interactions can be identified.

Secret behind the concept of Nutrigenomics

The plaque biofilm initiates mechanisms uncovering Nutritional Modulation of Periodontitis. Tissue destruction is a result of abnormal inflammatory immune response represented by hyper inflammation.[5]

This inflammation fails to exterminate the causative pathogens and generates the continued release of pro-inflammatory mediators, reactive oxygen species (ROS), neutrophil proteolytic enzymes which terminate the tooth attachment apparatus. [6]

Many studies have found out that macro and micronutrients regulate the inflammatory process and can modify the pro-inflammatory and anti-inflammatory cascades, influencing one's own inflammatory status.

Besides providing energy and co factors for body functioning, nutrient's play a very important role in acting as a molecular signal which can modulate molecular gene and protein expression leading to alteration of inflammation.[7]

Oxidative stress and its role

Oxidative stress is caused by diet-induced hyperlipidemia leading to down streaming of inflammation.

The basis for pro-inflammatory adipokines include the hepatocytes which form lipoproteins which are converted to FFA (free fatty acids) and taken up by adipocytes. In oxidative stress, a process known as lipid peroxidation arises where low-density lipoproteins are oxidized (oxLDL) and bind to "toll-like receptors" (TLR-2/4) which are a group of PRR'S (pattern recognition receptors) on membranes of inflammatory cells, triggering Nuclear Factor - kappa β activation (fig.2). [5,6,7]

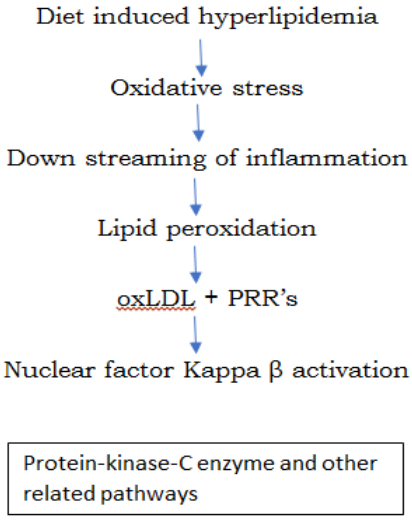


Figure 2. Oxidative stress and its role in Periodontitis

It has also been reported that Periodontitis patients have higher levels of serum n-6 PUFA, suggesting that a discrepancy between ω-6 and 3 fatty acids may lead to susceptibility to peridontitis.[6]

Role of Nutrients in inflammation reduction

Evidence suggests that periodontitis is associated to some extent with reduced serum micronutrient levels which may include insufficient diet, lifestyle factors like smoking. Genetic factors also impact on some of the metabolic and physiological processes such as bioavailability, absorption, distribution, and synthesis of micronutrients.

- Macro and micro-nutrients can modulate pro- and anti-inflammatory cascades in the body and can reduce the inflammatory pathway.
- Restriction in Sugars and fats can decrease the levels of oxidative stress.
- Reductions in simple sugars, saturated fats and refined carbohydrates reduce activation of a diverse range of pathways thereby reducing oxidative stress.
- Foods's rich in antioxidants such as green leafy vegetables such as broccoli, spinach, Amaranthus etc., all types of berries (Blueberries, blackberries, strawberries, cranberries) etc. red beans, green tea, turmeric, dark chocolate (>70% cocoa) are rich in key antioxidant micronutrients and would help reduce oxidative stress.

- Diets which include nuts, olive and fish oils having antioxidant properties can help in slowing down digestion resulting in less evident increase in blood glucose levels.

Micro-Nutrients

As suggested by Vander Velden in 2011, nutrition is crucial in addressing the balance between human microbe interactions because it is implicated in several inflammatory conditions.[8]

Nutrients	Function
vitamins A, C, E and selenium, copper, zinc, Antioxidants	Participate in Immune and inflammatory responses, maintain epithelial cell structure and integrity.
Selenium	Help to decrease the harmful lipids such as LDL and phospholipid hydroperoxides to safe products.
Vitamin C	Powerful free radical scavengers
Vitamin E	Stabilizes membrane structure, terminates free radical chain reaction, Mitigatory effects on inflammation and collagen breakdown.
Vitamin D	Influences the action of monocytes, macrophages and dendritic cells which express the vitamin D receptor (VDR)
ω-3 fatty acids Eg: n-3 PUFA	Increase the tissue concentration of n-3 fatty acids such as eico-sapentaenoic acid, docosahexaenoic acid and down-regulate inflammation directly inhibiting bone loss
Isabgol extract	Effective antibiotic and weak inflammatory effect [9]

Pomeogranate

Polyphenolic flavonoid content is the primary functional value of pomegranate in oral health.[9]

Pomegranate juice: The hydro-alcoholic extract in pomegranate juice, showed to decrease the Colony Forming Unit CFU/ per ml's of dental plaque by 84%. It was found to inhibit (PG) Prostaglandins (E2), human salivary α-amylase, cytokine Interleukin-8, nitric oxide, α- glucosidase function and found to decrease enzyme aspartate aminotransferase activity in saliva.[10]

Garciania magostana

Researchers demonstrated an inverse relationship between antioxidant depletion locally in the periodontium and within the plasma and periodontitis.[11]

Garcinia mangostana seeds are reported to be a rich source of vitamin C. Component delivery in the form of a biodegradable chip, gel, or ointment with antimicrobial or antibacterial activity is provided to treat periodontitis against periodontal pathogens. On contacting gingival fluid, the component forms a liquid crystal structure to provide a sustained release dosage and releases active ingredients progressively. [12]

Morinda citrifolia

Gingival inflammation was significantly improved by the effect of Morinda citrifolia L. fruit juice by its anti-inflammatory effects. Good oral hygiene maintenance along with the fruit juice had significant influence on gingivitis and periodontitis. [12]

Animal studies (Rodents) have shown that zinc deficiency has been associated with increased plaque and higher gingival index measurements and finally increased vulnerability to periodontal disease progression. One study investigated the potential role of zinc (micronutrient essential mineral), a zinc transporter gene and nutrigenomics tool for assessing role of nutrition in the risk of developing type 2 diabetes and in developing associated periodontal diseases. [13]

A locus for genetic susceptibility to diabetes and alveolar bone loss comprising a single nucleotide polymorphism (C/T; rs13266634) (non-synonymous) in a β cell-specific zinc-transporter gene has been identified through genome wide association study.[14]

Insulin storage and release is controlled by this SLC30A8, a zinc transporter gene which is coding for ZnT8. The recommendations of the 2011 EWP (European Workshop on Periodontology) suggested that the dental clinicians should consider including diet of fish oils, fiber, fruits, and vegetables and reduce refined sugar levels as part of a alveolar bone and tooth loss prevention and treatment regime with a note on general health benefits [13,14]

Nutrigenomics in Future

Nutrigenomics provides a scientific basis for better outcomes in periodontal treatment through dietary means. It aims to focus on the inter relationship between nutrition with genome and addresses the terms like genotype, phenotype diet interactions on periodontal health. Future personalized diet modifications or designed individual diets will revolutionize the future of food industry. The concept of nutrigenomics for the prevention or management of periodontal diseases seems promising.

Conclusion

Periodontitis is a destructive disease. Nutrigenomics is the mixture of nutrition and gene modification through structured diet. A much comprehensive understanding of nutritional gene interactions and their impact on physical characteristics of gene is required to identify and plan strategies for dietary intervention. During last decades, enhanced understanding of tools to assess and structure the

status of nutrition, has developed along with the importance of assessing nutritional intake.

The current evidence on the inter-relationship between nutrition and alveolar bone loss, tooth mobility, gum diseases is mostly questionable and further studies with large sample size are to be conducted to prove the effect of nutrition on periodontal diseases.

DECLARATIONS

Conflicts of interest and financial disclosures

None declared

Ethical approval

Not applicable

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Literature Review

PROGRESSIVE MUSCLE RELAXATION THERAPY TO RELIEVE DENTAL ANXIETY

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Abstract

Background: Dental anxiety is complex phenomenon which is associated with the thought of visiting the dentist for therapeutic or care. It may be either physical, mental or social anxiety. The most common causes of anxiety in dental patients is fear of injections, fear of choking or gagging and fear of blood. It can be shown as fear, anxiety, phobia, stress, shivering, sweating, crying during or before dental treatment. Sympathetic nervous system is activated during dental anxiety and there is provoke of fight or flight response. This causes changes in various physiological activities such as reduction in pain threshold, increase in treatment complications, post- treatment pain, late healing. Identifying anxiety in dental patient is the first and foremost step in determining the type of treatment and schedule of appointments. Progressive muscle relaxation is one such technique a where muscles and body are allowed to relax after they are tensed.

Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 73 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 34 articles were included for full text. This review aims at detailing progressive muscle relaxation technique, a non-pharmacological, economical approach to relieve dental anxiety.

Keywords: *Dental Anxiety, Progressive muscle relaxation therapy, Non-Pharmacological*

INTRODUCTION

Dental anxiety is complex phenomenon which is associated with the thought of visiting the dentist for therapeutic or care. It may be either physical, mental or social anxiety. It can be shown as fear, anxiety, phobia, stress, shivering, sweating, crying during or before dental treatment.[1] This dental anxiety is shown to delay or cancel appointments and can even cause behavioral issues leading to stressful and unpleasant experience for practitioner and the patient. These consequences of dental anxiety can further cause pain, poor dental health complicating the treatment. The most common causes of anxiety in dental patients is fear of injections, fear of choking or gagging and fear of blood.[2]

Agras et al in a study has found out that dental anxiety is one of the top ten causes of anxiety in general public.[3] A Canadian survey found out that 5.5 % of respondents were very afraid or terrified" of dental visits whereas 9.8% were somewhat afraid.[4] Studies have shown that dental anxiety in adult patients is 20 % with 5-7% having high anxiety. A study done by Santuchi et al has reported that patients with periodontal problems had higher dental anxiety due to their inflamed gingiva and bleeding gums.[5] As already mentioned earlier that etiology of dental anxiety is usually not single and is

multifactorial, no monotherapy for this anxiety is not promising.

Sympathetic nervous system is activated during dental anxiety and there is provoke of fight or flight response.This causes changes in various physiological activities such as reduction in pain threshold, increase in treatment complications, post-treatment pain, late healing. Evoking physical, emotional, behavioral and cognitive responses can make treatment more challenging and stressful to dentists.[6]

Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 73 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 34 articles were included for full text (fig.1).

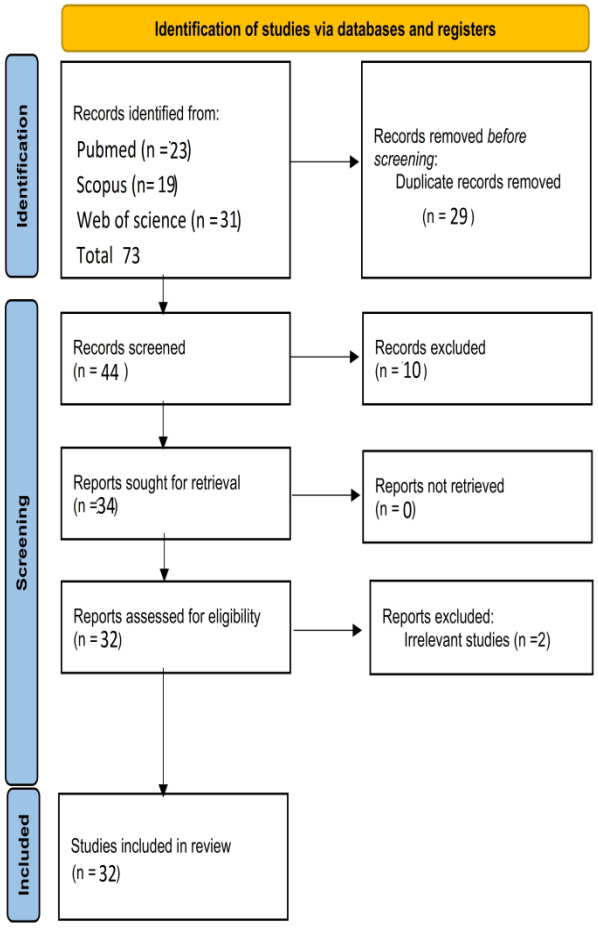


Figure 1. Prisma flow chart

This review aims at detailing progressive muscle relaxation technique, a non-pharmacological, economical approach to relieve dental anxiety.

Types of dental anxiety

Four types of dental anxiety have been identified and is shown below in table format. Please have a look.[7]

Table1.Types of dental anxiety and management strategies

SNO	Type of dental anxiety	Characteristics
1.	**Fearful of specific stimuli**	These can be easily identified and the stimuli include injections, pain associated with dental treatment, sound, smell or sight of drill/ handpiece. Management includes, relaxation strategies and gradual systematic desensitization.
2.	**Fearful of medical catastrophe**	These individuals are afraid that treatment may cause medical emergency. They complain of allergy due to latex or anesthesia, shortness of breath, palpitations etc. management includes medical history, gradual exposure to dental treatment etc.
3.	**Generalized dental anxiety**	These individuals have generalized anxiety and its difficult to identify one aspect. Relaxation strategies can help and gradual exposure can also help the patient to gain a sense of mastery.
4.	**Distrustful of dental personnel**	They complain that the treatment procedure was not under their control i.e., the dentist just pulled out a tooth without his/her notice. These patients should be clearly explained before starting a procedure.

The major disadvantage of dental anxiety is it affects proper dental treatment by delaying the appointments and increased pain after treatment causing delay in recovery. This anxiety is associated with avoidance of dental care and oral health, postponement of dental treatment leading to mental anxiety and decreased quality of life.[8]

Therefore, to improve the quality of life and provide a better dental treatment with lesser appointments, reducing anxiety during dental procedures is a must. This requires proper evaluation by identifying the source and level of anxiety.[9] Anxiety can be triggered

by clinic ambience, interaction with receptionist and even while scheduling the appointments. Anxiety in a dental patient can be identified by psychophysiological responses such as muscle tightness, restlessness, clearing the throat, stiff posture, holding things tightly, hands unsteady, sweating of palms, forehead, frequent urination etc. In children, behavioral and emotional responses include panicky, hyperactivity, nervousness, sitting on the edge of the chair, leaning forward, inattentiveness, excessive worrying, poor memory, getting tongue tangled etc. Once a dentist or clinician identifies these responses, he/she should attempt to reduce the anxiety by anxiolysis, later start the treatment.[10]

Anxiolysis is a procedure which helps in decreasing the anxiety by different techniques either pharmacological or non-pharmacological. American dental association has made it mandatory to use anxiolytic methods in patients with dental anxiety. During ancient times, plants such as papaver and somniferum were used to reduce anxiety. Other methods included incubation which is physiological healing process through sleep. To induce sedation and anesthesia, ancients used Aleppo sponge which is a combination of mandragora, cannabis, hyoscyams, opium, black night shade.[11]

Now a days, pharmacological methods are being used to reduce dental anxiety by inhalation or injective sedatives with benzodiazepines, nitrous oxide and general anesthesia, but the risk of side effects, higher cost and need for trained personnel have limited their use. The major side effects with sedatives include increased time of absorption, gastro-intestinal disorders, respiratory depression, nausea, vomiting and allergic reactions.[12] Therefore, drug free methods have been implemented in reducing the dental anxiety or before the treatment. Anxiolysis through pharmacological methods will not affect respiratory and cardiac functions while putting the patient respond to verbal instructions. Cognition and coordination are impaired slightly.

Psychotherapeutic techniques or Non-pharmacological methods are easy and don not have any side effects. These techniques include physical restraints, behavior modification techniques, communication and rapport building and cognitive behavior therapy. Other techniques to manage dental fear and anxiety include tell and do, audio analgesia or white noise, systematic desensitization, hypnosis, biofeedback and progressive muscle relaxation. These are conservative and non-invasive.[13]

Progressive muscle therapy in dental practice

Let us discuss more about progressive muscle relaxation therapy practiced during dental anxiety. Progressive muscle relaxation technique is a systematic technique to relax the muscles and body which was developed several decades ago. This procedure was successful in managing variety of anxiety disorders and in managing dental anxiety.[14] Dental anxiety is usually stimulated by psychological and physiological response and thereby activate sympathetic nervous system. Muscle relaxation therapies help in reducing this activity of sympathetic nervous system. This in turn helps in lowering the heart rate, respiratory rate and blood pressure. This technique also regulates central and peripheral nervous system and eventually reduces stress, anxiety, depression leading to improved quality of life.[15]

The other process by which progressive muscle relaxation technique decreases dental anxiety is based on basic principle of physiology of muscle. When is muscle is tensed, releasing tension causes relaxation of muscle. Once the muscle is relaxed it does not return to pre-tension state, but becomes more relaxed when it is allowed to rest. Here, the patient is asked to focus on specific voluntary muscles by tensing them later relaxing. As the process of tensing and relaxing progresses, other physiological responses also gradually and naturally become slow. These responses include breathing which becomes slower and deeper, blood pressure and heart rate decreases, vasodilation in small capillaries of extremities resulting in subjective calmness and ease. The patient is trained for progressive muscle relaxation technique to practice at home for 1-2 weeks later used in clinics.[16]

Bernstein and Borkovec were the first to describe the procedure of progressive muscle relaxation technique this was used in many other studies.[17] Conrad A and Roth WT in their studies found out that progressive muscle relaxation techniques can help in decreasing generalized anxiety states and panic disorders.[18] Isa MR et al conducted a study among prostate cancer patients who were suffering from anxiety and depression. They recorded the anxiety using Depression Anxiety Stress Scale-21. The results showed significant improvement in anxiety levels in progressive muscle relaxation group.[19] Progressive muscle relaxation technique has thought to even reduce blood pressure, heart rate thereby reducing triglyceride levels, and total cholesterol as in a study conducted by Chaudari et al.[20]

Sabherwal et al in 2021 conducted a study on 60 children who were aged between 8-12 years and undergoing primary tooth extraction. He measures anxiety by Visual Facial Anxiety scale, partial pressure of oxygen, heart rate, blood pressure and pain using Wong-baker faces pain scale were recorded pre/post-operatively. The children were randomly allocated to hypnotic group and progressive muscle relaxation technique group. He

found out that both hypnotic therapy and progressive muscle relaxation therapy were equally effective for managing pain and anxiety in pediatric dental patients.[21]

The technique of Progressive muscle relaxation

Though there is limited literature in dentistry for managing dental anxiety, its technique and advantages make dental practitioners force to use progressive muscle relaxation to provide better treatment. Berggren et al in 2000 conducted a study on 112 patients with dental anxiety and evaluated the effect of progressive muscle relaxation technique. There was significant reduction in dental anxiety in progressive muscle relaxation technique group compared to cognitive therapy group.[22]

Park et al in 2019 conducted a study on dental anxiety patients and found out that progressive muscle relaxation therapy helped in reducing anxiety, depression, pulse rate and depression in patients undergoing periodontal surgery.[23] Miller et al in 1978 conducted a study on dental anxiety patients in which he recorded anxiety using dental anxiety scale. They found out that group receiving progressive muscle relaxation technique had less anxiety levels compared to corresponding control group.[24] Similarly, lamb et al in 1980 also found out effectiveness of progressive muscle relaxation technique and reported that there was significant decrease in anxiety levels even in next dental appointment. Progressive Muscle Relaxation can decrease neuromuscular tension and help in alleviating anxiety during or before dental procedures.[25]

Jacobson's technique of progressive muscle relaxation:[26]

Another technique by Jacobson is also being used in dentistry to reduce dental anxiety. In this technique the patient is stimulated to reach a state of whole-body deep relaxation through voluntary and conscious tensing as well as relaxing of specific muscle groups. Individual muscle parts are tensed in specific order initially for 5-7 seconds, they are held for brief time and then released for 20 seconds. In this technique, there is continuous reduction in tension in individual muscle groups. Muscle parts which are tensed include toes, knees, heels, shoulders, elbows and facial muscles. 15-20 minutes of time is given to the patient to practice the relaxation technique. Repeated use of this technique helps in making the patient sensitive to the body and to feel even the slightest tension in order to know where to relax. This technique helps in successful management of dental anxiety.

For example, the patient coming for a dental treatment will be asked to

STEP 1: Sit comfortably or Lie down in supine and comfortable position with minimal distractions.

STEP 2: The patient is also asked to clench teeth and lips, held briefly and let go. Finally, the patient is asked to express how the muscles felt after exercise.

STEP 3: Press the tongue briefly to roof of the mouth and hold it for few seconds and let it drop loosely. Let the eyes screw them up a little, hold and let go.

STEP 4: Similarly frown the forehead a little, hold and let go.

STEP 5: Ask the patient to take deep breath through nose, held for few seconds and then breath out.

STEP 6: To pull toes near knees, gently pull shoulders towards ears, press elbows and upper arms towards body, gently clench hands, push head forward slightly, held briefly and let it go.

STEP 7: tense the muscles of stomach and chest, hips, buttocks

These all steps are held for 5 seconds and released slowly for 10 seconds. During the release the patient should experience the sense of relaxation.

Here, each muscle is tensed to 75% of full tension approximately, held for 5-10 seconds, and then relaxed for about 10 seconds focusing on tension and relaxation of specific muscles.

Note: The person performing this technique should be cautious not to tense the points which are in physical pain while taking slow, deep breaths throughout the exercise.[27]

Progressive muscle relaxation technique for children

In this technique, the child is asked to close his or her eyes and breath in and out i.e., inhale and exhale 5 times. This is followed by tensing and relaxing target muscle groups from tip to toe sequentially. This can include tighten and then relax the jaw, shoulders, stomach, chewing. Starching arms high above the ceiling and relaxing. Child is advised to imagine walking on the sand, squeezing toes and then relaxing. This technique is based on Karasu et al, 2009.[28]

Other combination techniques for progressive muscle relaxation include:

1. *Music therapy:* Music therapy is age old technique to relax the muscles and simultaneously anxiety. It helps in producing physiological arousal such as blood pressure, pulse rate, galvanic skin response and temperature resulting in simultaneous drop in psychological measures of anxiety. Progressive muscle relaxation technique is

combined with music therapy to relieve dental anxiety.[29] Stoudenmire found out in his research that listening to music and muscle relaxation were equally effective and reduced anxiety. Combination of both found to be even more effective.[30] A study done by Lahmann et al in 2008 found out that muscle relaxation technique was safe, effective and economically sound non-pharmacological approach in short term reduction of dental anxiety when compared to music distraction.[31]

2. *Deep breathing/Meditation:* Progressive relaxation technique is combined with deep breathing or meditation when a patient is called for a dental appointment. She/he is advised to meditate for 2 weeks prior to treatment along with practicing progressive muscle relaxation.[32]

Conclusion

In order to improve oral health and an individual's general well-being, it is essential to identify and eliminate dental anxiety and phobia as these conditions can have detrimental effects on a person's quality of life. Excellent dental care is one of the fundamental principles in treating a patient with dental problems. Communication with patient can help in identifying the source of anxiety and fear while enabling to categorize the patient into mild, moderate and severe. Several methods can be employed to reduce the fear or anxiety gradually and help the patient to slowly get through while improving quality of life.

Patients who are under stress can benefit from therapy interventions that involve relaxation techniques. Progressive muscle relaxation technique is one such method to reduce the fear or anxiety slowly and gradually. In progressive muscle relaxation, the muscles and body are tensed and gradually relaxed leading to decrease in stress and anxiety. Clinician can employ this technique to manage patients with anxiety as this method is easy, economical and doesn't require high equipment for employing.

DECLARATIONS

Conflicts of interest and financial disclosures

None declared

Ethical approval

Not applicable

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CASE REPORT

SPONTANEOUS EXPULSION OF A LARGE SUBMANDIBULAR SIALOLITH FOLLOWING FAILED SURGICAL ATTEMPT: A CASE REPORT

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Abstract

Sialolithiasis, a common pathology of the submandibular salivary gland. While small, accessible stones respond well to conservative treatment like ductal milking and palliative care, larger or deeply embedded stones require surgical intervention. Here, we report a unique outcome in a 24-year-old woman presenting with a year-long history of progressive right sublingual swelling. Imaging confirmed a large sialolith obstructing Wharton's duct. An initial surgical attempt to access the stone was unsuccessful due to its deep positioning and associated inflammation, leading the surgical team to close the site without further manipulation. Surprisingly, within a week, the patient returned to the clinic holding the stone in her hand, after manually expelling the stone herself, experiencing complete symptom relief. This case highlights that minimal manipulation can sometimes achieve outcomes beyond conventional surgical intervention. It also illustrates the importance of patient education and cautious postoperative management, and how patient engagement can achieve more favorable outcomes.

Keywords: submandibular salivary gland, *large submandibular sialolith*, surgical intervention

INTRODUCTION

Sialolithiasis is the second most common salivary gland disorder after sialadenitis, with the submandibular glands being most frequently affected. This predisposition is attributed to the gland's long and tortuous duct, the flow of saliva against gravity, and the unique characteristics of submandibular saliva, which is mucous, highly alkaline, and rich in calcium and phosphate.[1] The typical clinical symptoms of sialolithiasis include swelling and pain, especially during meals. Diagnosis is usually straightforward due to these clinical symptoms, and stones can often be palpated above the mylohyoid muscle insertion. However, imaging is essential for therapeutic planning.[2] Most sialoliths have sufficient calcium content to be visualized on conventional dental radiographs, particularly occlusal and panoramic views.[3] Advanced imaging techniques such as computed tomography (CT), ultrasound, sialography, and magnetic resonance imaging may be required in more challenging cases.

Patients presenting with symptoms of sialolithiasis and confirmed stones should be initially managed with hydration and antibiotics if infection is present, followed by definitive treatment. Treatment options include stone removal or, in some cases, gland excision depending on the stone's location and gland

condition. Sialoliths located anterior to a line drawn between the first mandibular molars are often visible on occlusal radiographs. They can be approached intraorally for removal if spontaneous passage does not occur with adequate hydration and sialagogue therapy. For intraoral removal, the duct is cannulated, the stone is localized, and a ligature is placed distal to the stone before the duct is opened. After stone removal, sialodochoplasty is performed to create a new opening in the floor of the mouth or to transpose the ductal opening distally, ensuring unobstructed future salivary flow. Stones located more proximally (posterior to the mylohyoid muscle) often necessitate gland excision, particularly when recurrent obstructions have led to significant parenchymal destruction.[4]

Management approaches range from conservative to surgical. Non-invasive measures include patient hydration, sialagogue prescriptions, and gland massage, all of which promote salivation and facilitate calculus expulsion. Minimally invasive techniques involve using lacrimal probes and dilators to open the duct orifice, allowing manipulation of the stone forward for removal. The surgical approach, used for stones in the distal third of Wharton's duct, involves a longitudinal incision directly onto the stone for extraction, especially for submandibular calculi.[5]

Case Report

A 24-year-old female, with no significant medical history, presented to the maxillofacial surgery clinic at Jordan University Hospital in 2024, complaining of a gradually increasing swelling in the right sublingual region over the past year. The swelling was intermittent, occurring particularly during meals, and was associated with moderate discomfort but no systemic symptoms such as fever or dry mouth.

On clinical examination, the patient was found to have a firm, tender swelling in the right sublingual area, corresponding to the floor of the mouth. The intraoral examination revealed a palpable mass along the course of Wharton's duct, with the overlying mucosa appearing normal and intact. There were no signs of erythema, pus discharge, or ulceration.

The patient was subsequently referred for imaging. A CT scan of the submandibular region revealed a large, well-defined hyperechoic structure within Wharton's duct, measuring approximately 0.6 cm in diameter, consistent with a salivary gland stone (sialolith), as shown in (figure 1).

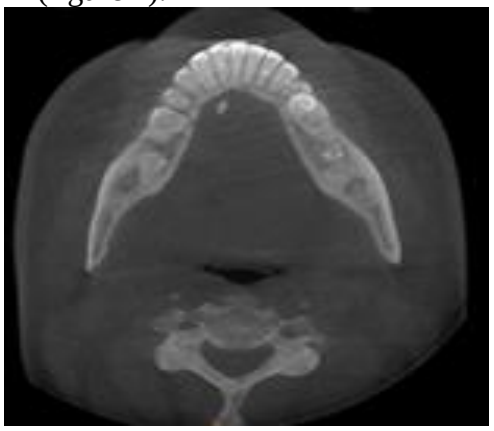


Figure 1. Axial thin high resolution CT scan showing a 0.6cm sialolith

The stone was located deep within the duct, close to the gland, and appeared to be causing a partial obstruction.

Given the size and location of the stone, it was determined that conservative measures, such as ductal milking or sialagogues, would be unlikely to succeed. The decision was made to proceed with surgical removal of the stone to alleviate the patient's symptoms and prevent further complications. The surgical procedure was performed under sedation, with the surgical team opting for an intraoral approach to access Wharton's duct. During the surgery, careful dissection was performed along the duct to expose the stone. A silk suture was applied distal to the expected stone location to prevent its proximal mobilization. However, the stone was found to be deeply embedded within the duct, surrounded by significant inflammation and fibrotic tissue. Despite multiple attempts to distally mobilize the stone, its position made it inaccessible without risking damage to surrounding structures, including the sublingual gland and the nearby neurovascular bundle.

The surgical team decided to limit intervention, recognizing the potential risks of over-manipulation. The site was thoroughly irrigated, and the incision was closed. The duct wall was sutured to the floor of the mouth to make the duct more patent. Post-operative care instructions were given, including pain

management, the use of antibiotics to prevent infection, and maintaining optimal oral hygiene. The patient was advised to follow up in the clinic the following week for assessment. Remarkably, when she returned, she was holding the stone in her hand, as shown in (figure 2).



Figure 2. The stone in patients hand

She reported feeling the stone move closer to the opening of Wharton's duct later that week. By applying gentle pressure intraorally, she was able to manually expel the stone herself, providing immediate relief from the swelling and discomfort.

The expelled stone measured approximately 0.6 cm in diameter, consistent with the imaging findings. Following its expulsion, the patient reported complete resolution of symptoms, and physical examination confirmed the absence of residual swelling or tenderness. The surgical site had healed well, and no further intervention was required. The patient provided informed consent to the publication of this case.

DISCUSSION

Sialolithiasis is a common condition, particularly affecting the submandibular gland due to the anatomical characteristics of Wharton's duct, which predisposes it to stone formation. Most cases of sialolithiasis are successfully managed with conservative approaches, such as hydration, sialagogues, and ductal milking, especially when the stones are small and accessible. However, larger, or more deeply embedded stones often require surgical intervention. The case presented here involves a large submandibular stone that was initially deemed surgically inaccessible but was later expelled manually by the patient, offering a unique perspective on the management of sialolithiasis.

The standard surgical approaches for removing submandibular stones, as reported in the literature, include intraoral sialolithotomy and, in some cases, external approaches, particularly when the stones are large or located close to the gland. Studies have shown that while intraoral approaches are successful, they can be challenging when the stones are deeply embedded or surrounded by significant inflammation, as was the case here. For instance, in a 2019 case study by Pachisia et al., intraoral sialolithotomy was successful in 85% of cases. However, complications such as ductal stenosis and stone fragmentation were noted, particularly with larger stones.[6]

This case aligns with these findings, highlighting the difficulties associated with surgically accessing deeply located stones. However, it differs in its outcome. While traditional approaches would consider secondary surgery or more invasive techniques, this case demonstrates that, in certain situations, spontaneous expulsion of the stone is possible, even after an unsuccessful surgical attempt. This corresponds with reports in the literature suggesting that non-invasive management should be pursued whenever feasible, particularly in cases where surgical risks outweigh the benefits.

The patient's ability to manually expel the stone herself is particularly noteworthy. There are no reports in the literature of patients managing to expel stones spontaneously. Our case report emphasizes the role of patient awareness and education in managing sialolithiasis. It reinforces the importance of involving patients in their care and educating them about potential signs of stone movement, which can lead to non-surgical resolution.

Furthermore, this case underlines the importance of a cautious approach during surgery, as excessive manipulation could increase the risk of complications such as infection, ductal injury, or lingual nerve damage. The decision to avoid further manipulation was validated by the subsequent spontaneous expulsion of the stone, resulting in a positive outcome without additional invasive procedures.

In conclusion, this case contributes to the existing body of literature by highlighting an unconventional outcome in the management of sialolithiasis. It suggests that, in certain cases,

patient involvement and conservative post-operative management may lead to successful outcomes, even after initial surgical failure. This emphasizes the need for a flexible approach to the management of sialolithiasis, tailored to the individual patient's situation.

Conclusion

This case report presents an atypical yet notable outcome in the management of sialolithiasis. A patient with a large, surgically inaccessible submandibular gland stone successfully expelled the calculus spontaneously, underscoring the potential efficacy of patient-centered, non-invasive approaches. This case emphasizes the importance of patient education and empowerment, as informed patients may actively contribute to their own treatment in unexpected ways. While surgical intervention remains the standard of care for large or inaccessible salivary gland stones, this case serves as a reminder that a comprehensive treatment plan should always consider individualized patient care and conservative management options.

DECLARATIONS

Competing Interest

The author declares that he has no competing Interest. None of the authors have relevant financial relations with a commercial interest.

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Consent for publication

Patients were informed verbally and in writing about the study and gave written informed consent.

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Literature Review

EXPLORING THE INTERSECTION OF PROSTATITIS AND PERIODONTITIS

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Abstract

Background: Periodontitis which is an immune-inflammatory condition which can either be caused by systemic disease or can cause a systemic disease. The complex association between prostatitis and periodontitis involves immunological, microbiological, and systemic health factors. Interestingly, studies have shown a positive relation between patients with poor oral hygiene and prostatitis. Therefore, it is important to get regular dental checkups to evaluate periodontal health. Here, in this review we will dive to know about link between periodontitis and prostatitis as well as their bidirectional relation.
Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.
Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 22 articles were included.
Conclusion: Periodontitis has a very strong relation with prostatitis. Most of research has found out to have a positive association between both of them. Having thorough knowledge all systemic diseases is very important for today's clinicians since these diseases negatively impact the progression of periodontitis and vice versa. Positive association can be established with further larger studies.

Keywords: Periodontitis, Prostatitis, Oral hygiene, Stress.

INTRODUCTION

Periodontitis which is the most common oral immune inflammatory condition was once thought to be caused only by inevitable consequence of aging.[1] Many factors cause periodontitis which include local factors such as poor oral hygiene, abnormal tooth position, dislodged restorations, smoking, stress etc.[2] Similarly, various systemic diseases also cause periodontitis or periodontitis can indirectly cause systemic diseases. These include diabetes, hypertension, renal diseases, liver diseases, obesity, metabolic syndrome, rheumatoid arthritis. Respiratory diseases, cognitive impairment, prostatitis etc.[3]

As the research progressed, many authors have found out that periodontitis was not caused only by aging but has various risk factors and indicators. This discovery of risk components has led to new concept of linking systemic health, conditions and diseases to periodontal health. One of the important systemic disease which has a potential link with periodontitis is prostatitis.[4] Let us discuss about prostatitis in detail and its relation with periodontitis.

Prostatitis is basically inflammation of prostate gland which accounts for about 50% of Indian men by the

age of 60. Prostatitis clinically manifests as painful penis and testicles which leads to pain during micturition, difficulty in emptying the bladder, increased urination frequency, pain in penis increases during ejaculation, with associated fever and chills.[5]

The main etiology of prostate infection has been employed to gram negative bacteria such as Escherichia coli and Klebsiella species.[6] Other mechanism which is thought to be a causative factor for prostate infection id role of immune system which is mediated by proinflammatory cytokines, such as interleukin (IL)-1b and tumor necrosis factor-α (TNF-α). This involvement of pro-inflammatory mediators in prostatic inflammation significantly contributes to increased serum Prostate-specific antigen (PSA) levels.[7]

Prostate-specific antigen (PSA), a glycoprotein is a biological or tumor marker which is produced mainly by the epithelial acinar cells of the prostate gland. This is secreted into the lumen of prostate gland, and then passes through the prostatic ducts into the semen. It mainly helps in diagnosis of benign prostatic hyperplasia, prostate cancer. In contrast to individuals with a PSA volume, those with a PSA level below 4.0 ng/ml are considered normal, and those with a level over 0.35 ng/ml/year have a comparatively increased chance of death from prostate cancer.[8]

The National Institutes of Health classified prostatitis into four clinical categories:

Table 1. Classification of clinical categories of prostatitis[7]

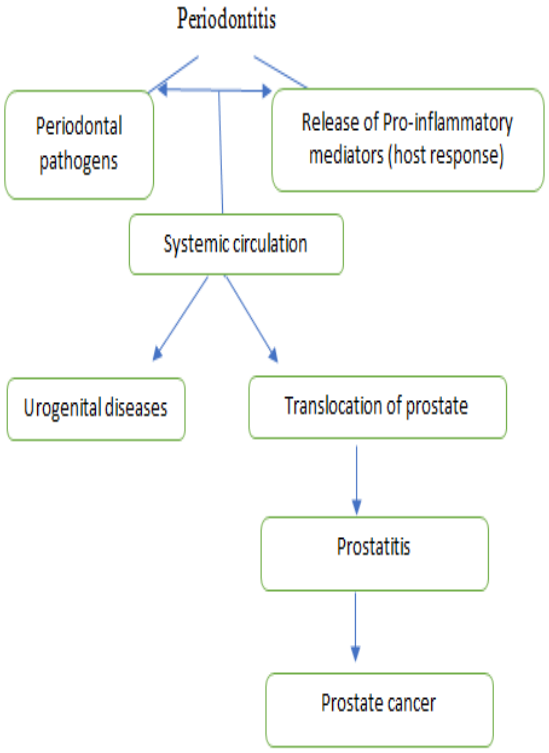
Category	*Prostatitis*
Category I	Acute bacterial prostatitis;
Category II	Chronic bacterial prostatitis;
CategoryIII a	Inflammatory chronic pelvic pain syndrome
CategoryIII b	Non- inflammatory chronic pelvic pain syndrome
Category IV	Asymptomatic inflammatory prostatitis

Unveiling the link between Prostatitis and periodontitis

Men with periodontal disease have been found to release significantly more prostate-specific antigen.[9] Periodontitis can cause immune inflammatory condition in the body leading to release of pro-inflammatory mediators in turn causing urogenital diseases and translocation of prostate. This translocation can cause prostatitis and finally may lead to prostate cancer.[10]

According to research, PSA values are greater in men with prostatitis and periodontal disease than in individuals without these conditions.

Pathophysiology of periodontitis causing prostatitis



Flow chart 1. Periodontitis and Prostatitis[10]

Other mechanisms of periodontitis causing prostatitis

According to available data, periodontal disease increases the host's inflammatory burden by elevating C-reactive protein and proinflammatory cytokines such Tumor Necrosis Factor-a, interleukin 1, 6. It has also been reported that males with prostatitis had higher serum levels of TNF-a and IL-1 than do healthy people. Thus, by boosting the inflammatory response in the prostate and disseminating cytokines that exacerbate pre-existing inflammation of the gland, periodontitis may indirectly contribute to prostate gland inflammation.[11]

These pro-inflammatory mediators can be released from periodontal tissues as well. This might result in a persistent inflammatory weakness that could trigger the emergence of systemic illnesses. A bacterial prostatitis may be explained by the potential inflammatory effect of cytokines.[12]

Another explanation is that inflammatory reactions degrade the prostate glandular epithelium, which increases PSA leakage into the blood.[13]

The third explanation is that prostate gland enlargement can lead to inflammatory reactions

which can increase the production of PSA. This increase in PSA can cause seepage into the bloodstream. Another distant, non-prostatic source of PSA, such as the periodontium, can also result in elevated blood PSA levels. Research is required to ascertain whether serum PSA levels, the impact of inflammatory mediators on the prostate gland, and the integrity of the prostate epithelium are impacted by non-prostatic PSA sources.[4]

Materials and methods: PubMed, Scopus, Web of Science, Google scholar was searched using pre-specified search strategy. Narrative and systematic reviews are included for the data synthesis.

Results: Extensive literature search was carried out using pre-defined search strategy was carried out. A total of 48 titles were screened rigorously by two independent evaluators and after duplicate exclusion, removal of irrelevant titles, 22 articles were included.

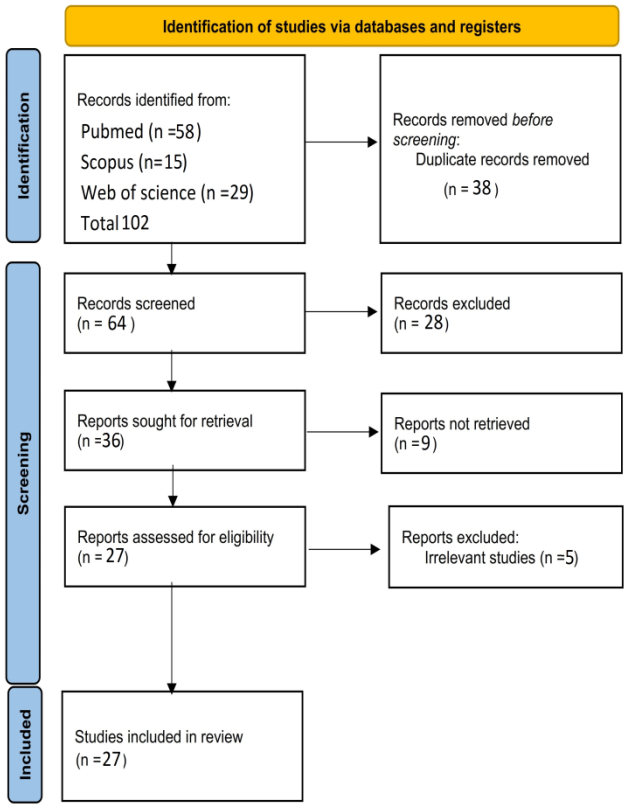


Figure 1. Prisma flow chart

Literature review

Fu et al in 2020 conducted a study on 5510 patients with chronic periodontitis and found out in this National Health Insurance Research Database cohort study that patients with periodontitis had 4.6-fold high risk of developing prostatitis than control group i.e., without periodontitis.[14]

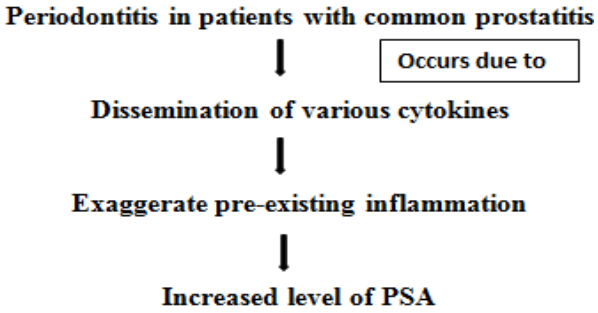
Two recent studies done by Lee et al and Corbella et al found out positive correlation between periodontitis and prostatitis and prostate cancer.[15,16]

Inflammatory burden in periodontitis and prostatitis

PSA levels in periodontitis and prostatitis patients:

Now having a better insight of etiopathogenesis of periodontitis and prostatitis, we know that there might be a connection between these two conditions, which may show up as higher blood PSA levels.

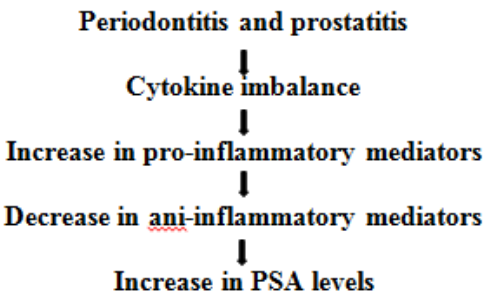
Patients with common prostatitis may have elevated PSA levels due to periodontitis, which most likely happens as a result of the spread of several cytokines that might exacerbate pre-existing inflammation. Joshi et al. in 2010 found that PSA levels were lower in little or mild periodontitis then in those with moderate to severe periodontitis which shows clear association of periodontitis and prostatitis.[4]



Flow chart 2 Periodontitis causing increase in PSA levels in prostatitis patients[4]

Hypothesis II

Gram-negative bacteria have been proposed as the causative agents of category I and II prostatitis as well as periodontitis. However, the bacterial cause of types III and IV prostatitis has not yet been determined. Both periodontitis and prostatitis have been linked to cytokine imbalance, with increased proinflammatory and reduced anti-inflammatory cytokines.[11,12]



Flow chart 3. How does PSA levels increase in both periodontitis and prostatitis?

Hypothesis III

Lastly, a different theory suggests that a localized rise in PSA levels-which may even take place in the periodontium-causes the prostate glands inflammatory reaction.

The production of PSA in the tissues of the periodontium would suggest that pro-inflammatory mediators are altered systemically, indicating a dysfunction of these mediators.[17]

Assessment of PSA levels

Important tool in interpreting increased PSA values (PSA density) is the measurement of prostatic size. Variations linked to prostate gland enlargement may be revealed by interpreting increased PSA values and density. However, only a small portion of the gland is represented by prostate needle biopsy specimens.[18]

According to Kandirali and colleagues, there is a positive link between serum PSA levels and the degree and severity of prostate inflammation in biopsy specimens.[19] This is supported by the higher PSA levels observed in individuals with moderate/severe prostatitis. This similar conclusion was also supported by Hasui et al who suggested that the elevated blood PSA was caused by a disruption in the prostate gland's epithelial integrity rather than a direct rise in PSA production.[20]

In a study to evaluate the changes in serum PSA and inflammatory cytokine levels like CRP and IL-1β following nonsurgical periodontal treatment in men with chronic periodontitis, Alwithanani et al. found that the periodontal treatment reduced PSA values and improved prostate symptom scores in men with chronic periodontitis.[21]

Ramanaryana B et al in 2019 conducted a study on 100 chronic periodontitis patients and found out a positive correlation between PSA levels and CAL, PD scores indicating mutual dependency between both.[9]

Serum PSA levels were found to be directly correlated with prostate volume by Morote et al., but not with the degree or kind of inflammatory infiltration.

Given this uncertainty, it's likely that the rise in PSA levels could be caused by a different non-prostatic source of PSA, like the periodontium, which is comparable to the PSA produced by the female breast.[22]

Recommendations for budding dentists and hygienists

Since we know oral health is gateway to many systemic diseases, dentists should include prostatitis has a regular health checkup condition to avoid complications such as prostate cancer. Dentists can conduct a regular checkups for risk of periodontitis and can educate the patients for the connecting systemic diseases.

As there is 4.6-fold higher risk pf prostatitis in periodontitis patients, these patients should be evaluated for further management.

Conclusion

Having thorough knowledge all systemic diseases is very important for today's clinicians since these diseases negatively impact the progression of periodontitis and vice versa.

This knowledge can help in all diagnostic and therapeutic procedures.

Since prostatitis prevalence is increasing, the association between prostatitis and periodontitis should be established with further studies which can characterize the importance of periodontal pathogens on bacterial prostatitis.

DECLARATIONS

Conflicts of interest and financial disclosures

None declared

Ethical approval

Not applicable

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RESEARCH ARTICLE

ASSOCIATION OF ABO BLOOD GROUPS IN ORAL POTENTIALLY MALIGNANT DISORDERS AND ORAL SQUAMOUS CELL CARCINOMA

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Abstract

Background: The objective of this study was to evaluate the correlation between ABO blood group types and oral potentially malignant disorders and oral squamous cell carcinoma. According to the earlier study findings (based on available literature), an individual's susceptibility to certain cancers, such as oral squamous cell carcinoma is influenced by ABO blood type. As one third of oral squamous cell carcinomas develop from potentially malignant disorders it is imperative to identify the association between ABO blood group and these lesions.

Materials and Methods: The study was conducted in the Department of Oral Medicine and Radiology in collaboration with Department of Oral Pathology at Malla Reddy Institute of Dental Sciences, Hyderabad on 158 clinically diagnosed potentially malignant disorders and oral squamous cell carcinoma patients. Out of which 122 were males and 36 were females. Patients' ABO blood types were ascertained using the rapid slide agglutination test.

Results: The Chi square test was used to determine the statistical relationship between ABO blood types and the risk of oral cavity malignancies. In this study Incidence of Squamous cell carcinoma found to be more in A+ve blood group, Oral Submucous fibrosis more in B+ve blood group, Oral leukoplakia more in B+ve and Oral lichen planus more in O+ve blood group. A statistically significant association was observed.

Conclusion:According to this study, the A+ve blood group had a higher incidence of squamous cell carcinoma, the B+ve blood group had a higher incidence of oral submucous fibrosis, the B+ve blood group had a higher incidence of oral leukoplakia, and the O+ve blood group had a higher incidence of oral lichen planus.

Keywords: **ABO blood groups, Oral squamous cell carcinoma, Oral potentially malignant disorders**

INTRODUCTION

Oral cancer has been impacting humans for a long time. In the developed countries, after heart diseases Cancer is the second leading cause of death. In developing countries cancer is the third leading cause of death.

3 % of malignancies recorded worldwide are oral cavity cancers. In men it accounts for 6 th most common cancer and in women it is 12 th most common cause[1].

There are no reliable histological markers to predict possible malignant transformation, however up to one-third of oral potentially malignant illnesses will eventually progress to oral squamous cell carcinoma over a period of ten years.

In 2005, the WHO recommended the term "Oral Potentially Malignant Disorders" (OPMDs), which encompasses both premalignant lesions and conditions[2]. In India the prevalence of OPMDs is more because of rampant practice of deleterious habits. OPMDS have much better treatment modalities and prognosis when compared to Oral Cancer.

Oral Leukoplakia, Erythroplakia and Oral submucous Fibrosis are the major OPMDs.

The high frequency of OPMD s and OSCC in India is generally ascribed to cultural, geographic, socioeconomic, and other lifestyle factors. Very little research has been done to investigate the genetic connections between the most common OPMDs. Blood types play a vital part in the immunogenetic system. Most of the human cancers are derived from epithelial cells and ABO antigens are found on the surface of RBCs and epithelial cells. An alteration in blood group antigens is a key factor in many human cancers[3].

ABO groups are the most sensitive blood grouping system to create out of all the genetically driven blood grouping systems. The ABO group genes, which are linked to the 9q34.2 region-a location where genetic changes are frequently seen in numerous cancers—encode the antigen that causes tumors. The expression of blood group antigens may be impacted by a genetic mutation in a tumor.

Changes in cellular mobility and interactions between tumor cells and distant organ endothelial cells can result from the presence or lack of these antigens. Numerous cancers have been linked to A or B epitope deficiencies[4].

Following the discovery by Arid and Bentall (1953) that blood group "A" was linked to stomach cancer, other investigators have looked at the possible correlation between blood groups and a number of illnesses[5]. The purpose of the current study was to evaluate the association between the incidence of oral squamous cell carcinoma (OSCC) and potentially malignant disorders (OPMDs) and ABO and Rh blood types.

MATERIALS AND METHODS

Study population: The current study was conducted at Malla Reddy Institute of Dental Sciences, Hyderabad after obtaining institutional ethical committee approval. An informed consent has been taken from all the participants.

According to the world health organization guidelines for diagnosing oral mucosal lesions[3], 30 leukoplakia, 57 Oral Submucous Fibrosis, 28 oral lichen planus, 43 oral squamous cell carcinoma subjects were selected for the study.

Detailed case history was taken from all the subjects and Blood group was determined using a blood group kit with the Rapid Slide agglutination test by the department of oral pathology. To minimize inter-examiner variability, calibration was done. After carefully washing their mouths with water, the patients were inspected under an incandescent light source. Lesion characteristics, anatomical position, extent, possible etiological or associated factors, dental status, and habits like alcohol and tobacco use were evaluated throughout the examination. Furthermore, in cases requiring additional evaluation, biopsies were conducted to obtain a definitive diagnosis. Estimation of blood group was done using blood group kit which contained antiserum A, antiserum B and antiserum D. The blood group was determined based on the presence of agglutination.

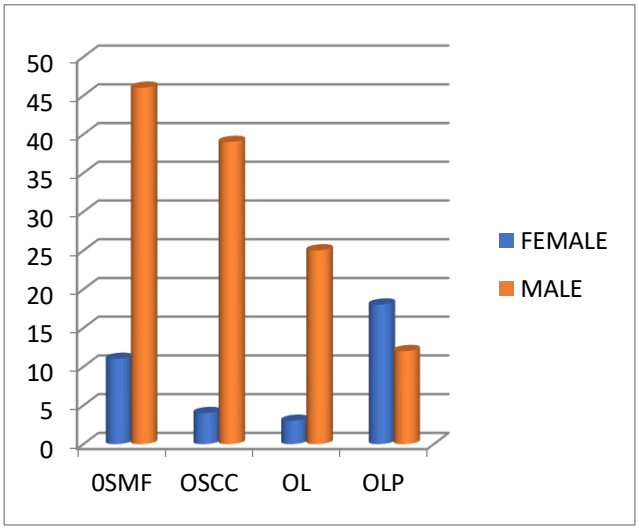
Results

Data was analyzed using SPSS software version. Descriptive statistics to summarize the data and chi square test were done to find the association between ABO Rh blood group and oral potentially malignant disorders. A total of 158 patients with oral potentially malignant disorders and oral squamous cell carcinoma were recorded during the study period of 2 years.

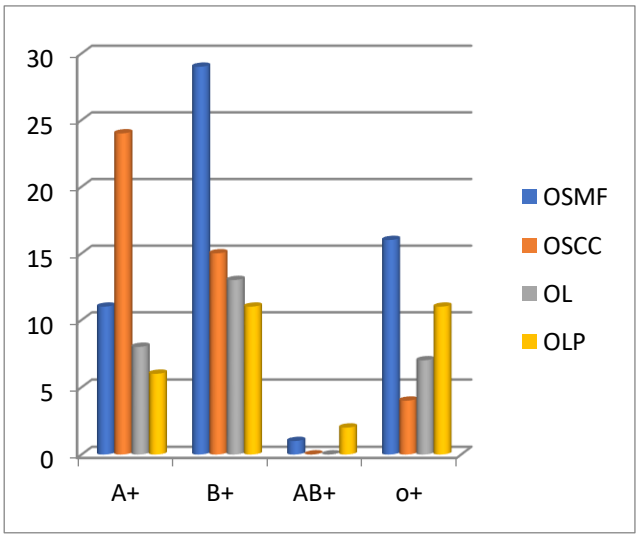
Out of which 122 (77.21%) were males and 36 (22.78%) were females (Graph 1). Number of females

was more in oral lichen planus than males. Number of males was more in oral sub mucous fibrosis, oral leukoplakia and oral squamous cell carcinoma.

57 out of 158 were diagnosed with oral submucous fibrosis, 43out of 158 were diagnosed with oral squamous cell carcinoma, 28 out of 158 were diagnosed with oral leukoplakia and 30 out of 158 were diagnosed with oral lichen planus (Graph 2).



Graph 1. Gender distribution among different potentially malignant disorders and squamous cell carcinoma



Graph 2. Distribution of A, B, AB, O blood groups in different potentially malignant disorders and squamous cell carcinoma

29 (50.9%) patients with blood group B+ found out of 57 patients of OSMF which is statistically significant. 23(53.5%) patients with blood group A+ were detected out of 43 OSCC cases which is statically significant. 13(46.4%) patients with blood group B+ detected out of 28 oral leukoplakia patients. 11(36.7%) patients with blood group O+ were detected out of 30 OLP cases which is statically significant.(Table1, 2).

Table 1. shows the prevalence of Squamous cell carcinoma and other Potentially malignant disorders

			Squamous cell carcinoma	Potentially malignant disorders			Total
				Oral submucous fibrosis	Oral leukoplakia	Oral Lichen Planus	
Blood groups	A +VE	Count	23	10	7	5	45
		% of Total	14.6%	6.3%	4.4%	3.2%	28.5%
	B +VE	Count	15	29	13	10	67
		% of Total	9.5%	18.4%	8.2%	6.3%	42.4%
	AB +VE	Count	0	1	0	1	2
		% of Total	0.0%	0.6%	0.0%	0.6%	1.3%
	O +VE	Count	4	16	7	11	38
		% of Total	2.5%	10.1%	4.4%	7.0%	24.1%
	A-VE	Count	1	1	1	1	4
		% of Total	0.6%	0.6%	0.6%	0.6%	2.5%
	B-VE	Count	0	0	0	1	1
		% of Total	0.0%	0.0%	0.0%	0.6%	0.6%
	AB-VE	Count	0	0	0	1	1
		% of Total	0.0%	0.0%	0.0%	0.6%	0.6%
Total		Count	43	57	28	30	158
		% of Total	27.2%	36.1%	17.7%	19.0%	100.0%

Table 2. The association between different blood groups and squamous cell carcinoma and other potentially malignant disorders Chi-Square Tests

	Value	df	Sig. (2-sided)
Pearson Chi-Square	32.812[a]	18	.018
No of Cases	158		

P<0.05 statistically significant

In this study, incidence of Oral Submucous fibrosis was more in B+ve blood group, Squamous cell carcinoma more in A+ve blood group, Oral leukoplakia in B+ve and Oral lichen planus more in O+ve blood group. A significant association was observed. All the associations were statistically significant with the p value at (0.018 which is less than 0.05)

The incidence and fatality rates of oral cancer have dramatically grown during the last few decades. Approximately 270,000 new cases of oral cavity cancer are reported worldwide each year, accounting for around 3% of all cancers [1]. Since Arid and Bentall's discovery in 1953 of a link between stomach cancer and blood group "A," numerous studies have explored the potential relationship between blood groups and various diseases. People with blood group A were 1.46 times more likely to acquire oral cancer than people with other blood groups, according to a study done on 235 patients with the disease[5]. Similarly, in the current study, the prevalence of oral squamous cell carcinoma is higher in individuals with blood group A+ve.

In the present study the incidence of OSMF increased between the age groups of 20-40,which is similar to the study conducted by Srivastava R et al for 2 years duration in 2016[6]. This could be linked to the enhanced social interactions and economic independence that people enjoy at this age in a quickly expanding country like India. During this stage, individuals may engage in many dangerous behaviours such as chewing betel nut, gutkha, pan masala, smoking, and alcohol consumption—either for stress relief, as a fashion trend, or due to peer pressure.

E Dabelsteen et al showed an increased incidence of numerous types of carcinomas in patients with blood groups A and B[7]. Similar to the findings in the studies mentioned above, the present study suggests that certain blood groups may have a higher likelihood of developing premalignancies that could subsequently progress into malignancies. Blood group antigens are found not just on the surface of red blood cells, but also on epithelial cells in many tissues, including the oral mucosa.

The downregulation of glycosyltransferases involved in the production of A and B antigens has been linked to tumor growth[8].

The ABO blood group genes are found on the 9q chromosome, which is known to be a hotspot for genetic mutations in many cancers[9]. More than 80% of instances there was a reduction in the expression of A and B antigens in oral squamous cell carcinoma. These results were also reported in potentially malignant disorders with epithelial dysplasia[10]. The Thomsen-Friedenreich (T) antigen, a tumor marker, is expressed on many malignant cells but is repressed in normal cells. The Tn antigen, a precursor to the T antigen, is not inhibited as cells become malignant. There is also a structural similarity between these two antigens and antigen A[11]. Due to this structural similarity, individuals with blood group A exhibit a lower immunologic response to T and Tn antigens. This reduced immune recognition may allow cancer cells to evade detection and bypass the immune system, facilitating tumor progression[12].

Cancer patients with blood group A exhibit a consistent suppression of Tn antigens, regardless of age, cancer stage, or tumor morphology, along with lower levels of anti-B isohemagglutinins. This phenomenon may help explain the poorer outcomes observed in many cancers among individuals with blood group A, as their immune response is less effective in recognizing and combating tumor cells[11]

When a cancer cell loses blood group antigens, it loses its cohesiveness, gaining the ability to circulate throughout the body. In addition, these cells often lose the expression of several cell adhesion proteins, such as integrins, which normally express A-like antigens on their receptors and regulate cell movement. This loss of adhesion molecules facilitates tumor spread and metastasis[13].

In a study conducted by Bhateja s reported that prevalence of oral leukoplakia was high in blood group A but in the present study high prevalence of oral leukoplakia is found in blood group B[14].

People with blood group A were more prone to the mucosal phenotype of lichen planus (LP), according to a 2016 study by Shahidi-Dadras M. However, the O blood group has a higher prevalence of lichenplanus in the current study[15].

Gopal Reddy V K conducted a study on the association of OSMF and ABO blood grouping revealed that people with blood group A were at higher risk of developing OSMF in comparison to others in contrary to this the present study showed high prevalence rate in individuals with blood group B[16].

Very few studies conducted on the association of ABO blood grouping and premalignant lesions and conditions, they have failed to provide a unifying and testable hypothesis. It can just be the outcome of a person's lifestyle, environment, diet, tobacco, smoking, and alcohol use, as well as population history. When predicting cancer risk factors, variables such as blood group distribution by race and ethnicity are important. The current study provides some insight into the patterns of oral precancer incidence. The current study highlights the need of considering blood group type in conjunction with other risk factors for oral squamous cell carcinoma and other potentially malignant illnesses.

Conclusion:

The study highlights a noteworthy correlation between ABO blood groups and the risk of developing oral cancer and other potentially

malignant oral conditions. Individuals with blood group A appear to be at a higher risk of oral cancers, likely due to their lower immunologic response to tumor-associated antigens such as T and Tn. Additionally, this study observed a correlation between blood group B and conditions like oral sub mucous fibrosis and lichen planus, diverging from some previous studies. The loss or reduction of A and B antigens in cancer cells
suggests a potential mechanism by which tumor cells enhance their mobility and metastatic potential, due to the loss of cell adhesion properties. While this association may be influenced by lifestyle, environmental factors, and genetic predisposition, blood group analysis could be considered as part of a broader risk assessment for oral precancerous and cancerous conditions, especially when combined with other known risk factors.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

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CASE REPORT

A CUSTOMIZED 3D-PRINTED TITANIUM IMPLANT FOR ANTERIOR MANDIBULAR RECONSTRUCTION: A CASE REPORT

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Abstract

The advent of patient-specific implants (PSIs) in oral and maxillofacial surgery marks a significant milestone in the field, promising enhanced precision, functionality, and aesthetic outcomes of the patient. PSIs are custom-designed to match an individual patient's anatomy, offering a tailored approach to complex surgical procedures. This case report looks at how custom-designed implants made with cutting-edge 3D printing technologies changed the life of a patient with a large ameloblastoma of the follicular and plexiform type in anterior mandibular region. We made the implants to fit the patient's specific anatomy and physiological needs. We used a 3D computed tomography scan to identify and diagnose this abnormal growth, and obtained DICOM detailed imaging and then performed a successful intraorally surgical procedure for simultaneous resection and rebuilding, utilizing a custom-made 3D-printed implant for the patient. This case report exemplifies how patient-specific implants when tailored to a patient's unique anatomy, can significantly enhance the quality of care in oral and maxillofacial surgery, offering substantial benefits in both complex tumor resection and reconstruction.

Keywords: patient specific implant (PSI), 3D CT, periosteal pouch technique, mandibular reconstruction, ameloblastoma, 3D Printing

INTRODUCTION

Ameloblastoma is the most common noncancerous tumor in the maxillofacial region, accounting for approximately 1% of all cysts and tumors in that area.[6] Typically, this tumor is painless and exhibits modest but aggressive growth in a localized region. It stimulates the growth of the cortical bone or causes the lingual or buccal cortical plate to rupture, enabling it to penetrate the soft tissues permanently.[1] The ages of 20 to 40 have the highest incidence rate of this condition, but it can occur in any age group, with an equal predilection for both men and women (1:1). On a standard OPG, these tumors may appear as solitary or multiple well-defined radiolucent areas, exhibiting a distinct pattern resembling a honeycomb, soap bubble, or tennis racket. Compared to other kinds of tumors, ameloblastoma is more likely to demonstrate the proliferation of buccal and lingual cortical plates.[2]Although a conventional OPG is sufficient for moderate lesions in the mandibular area, CT and MRI are required for extensive lesions to accurately evaluate the extent of the lesion. Enucleation, curettage, or resection are the surgical treatments that surgeons select for ameloblastoma, contingent upon the tumor's size, location, and form. The risk of recurrence ranges from 17.7% for en-bloc resection

to 34.7% for conservative treatment. To avoid recurrence, we prioritized performing segmental resections with a healthy bone safety margin.

Case Report

A 28-year-old female patient presented with a primary concern of swelling in lower front tooth area during the last two years that has progressively grown in size to its current dimensions without causing any symptoms. A visual examination from outside the mouth revealed widespread swelling in the chin area, measuring about 5 cm by 6 cm and spreading upwards from the lower lip to the lower edge of the jawbone. The skin covering the front part of the lower jaw showed no abnormal swelling. There is a single, clearly marked swelling in the lower jaw that stretches from tooth 44 to tooth 32. The swelling crosses the midline, leading to the loss of the mouth's normal contour. The mucosa covering the area was unremarkable, displaying a typical coloration, smooth texture, and glossy appearance. We observed Grade I movement in teeth 41, 42, and 44 and concluded that they were nonvital. Upon palpation, the swelling exhibited a firm consistency and was devoid of tenderness. The clinical examination results and the historical information led to a tentative diagnosis of ameloblastoma. The buccal and lingual cortical plates were growing on a CT scan, and thick septae separated several regions of radiolucency between teeth 44 and 32. A panoramic radiograph revealed an extensive and well-defined multilocular radiolucency in the jaw, spanning from tooth 44 to tooth 32. There is no root resorption, an enlarged periodontal ligament space, and a diminished lamina dura. CT imaging revealed a well-defined, multi-chambered growth with damaging alterations and weakening of the outer layer. The lesion underwent an incisional biopsy, and the histological investigation revealed the presence of lengthy interconnected cables. Columnar or cuboidal ameloblast-like cells surrounded the larger sheets of these cords, while loosely organized epithelial cells covered them. Several discrete tumor islands compose the supporting stroma. The islands consist of a layer of cuboidal or columnar cells, with nuclei that are often polarized and located along the margins. The core regions of follicles exhibited stellate reticulum-like cells. Histopathological examination indicated the presence of both follicular and plexiform ameloblastomas. We performed a complete intraoral marginal resection, a surgical procedure that involved the removal of a section of the mandible from tooth 45 to tooth 33. During the procedure, we preserved the periosteum by forming a pouch along the defect location for bone formation in the future. We then used CT and 3D printing to create a patient-specific titanium implant to reconstruct the anterior mandible. We placed the PSI in the periosteal pouch in a strategic location to facilitate new bone growth in the future. We rectified the PSI using screws, ensuring a seamless postoperative period. Six months after the surgical procedure, we proceeded to affix the crowns to the PSI. We successfully rehabilitated the patient's appearance and ability to do tasks. We observed no problems or recurrences during the patient's five-year follow-up.

Pre-operative pictures



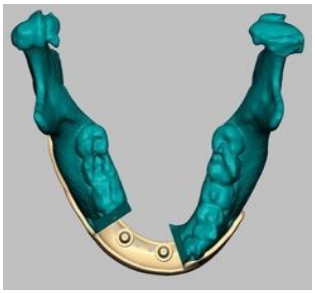
Figure 1. Preoperative frontal view





Figure 2**.** Preoperative intraoral view
Figure 3. Preoperative mandibular occlusal view

Patients specific implant design pictures



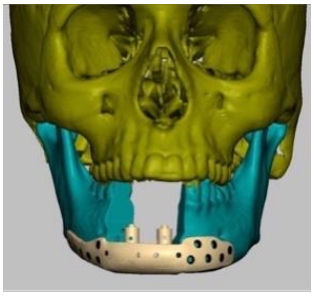
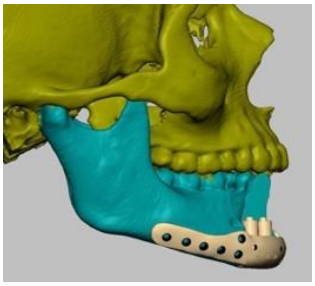


Figure 4. Mandibular occlusal view (virtual planning)
Figure 5. Frontal view (virtual planning)



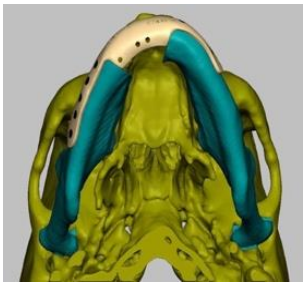


Figure 6. Lateral view (virtual planning)
Figure 7. Worm's view (virtual planning

Intra operative pictures




Figure 8. Intraoperative - anterior mandible
Figure 9. Full thickness mucoperiosteal flap elevation




Figure 10. Exposure of lesion
Figure 11 resection of lesion

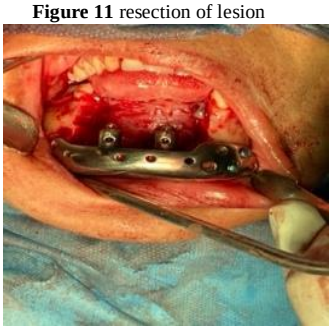


Figure 12. Placement and fixation of psi

Post-operative photos



Figure 13. Preoperative frontal view

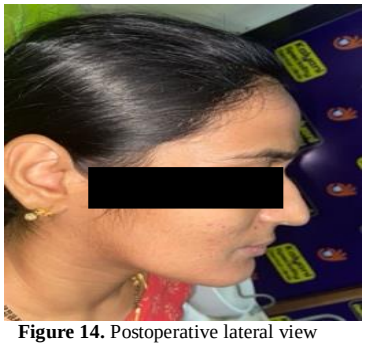


Figure 14. Postoperative lateral view




Figure 15. Postoperative intraoral view
Figure 16. Fabricated prosthesis

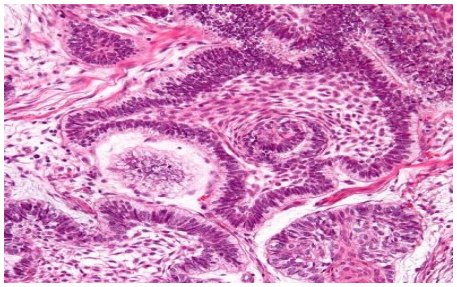


Figure 17. Histopathological picture

Follow up pictures



Figure 18. Preoperative opg

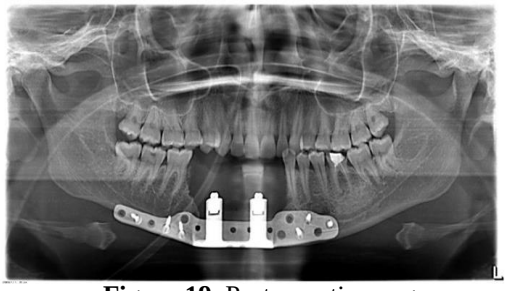


Figure 19. Postoperative opg

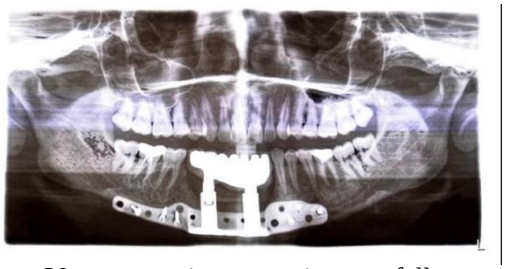


Figure 20 postoperative opg – six years follow up

Discussion

Ameloblastoma is a non-cancerous tumor that originates from the outer layer of tooth cells. The tumor has the ability to cause significant damage by eroding bone and spreading to other tissues. This growth can lead to facial asymmetry, tooth movement, jaw misalignment, and disease-induced fractures. Upon examination, the patient exhibited a substantial and rigid mass in the lower mandibular anterior region. This mass resulted in asymmetrical facial characteristics, teeth that are not firmly attached, and the expansion of both the outer and inner layers of the jawbone. [3]Ameloblastoma originates from the cellular components of epithelial tissue and dental structures at various stages of development. Although the exact origin of ameloblastoma is still uncertain, studies have shown a connection between this condition and abnormal gene regulation throughout the process of tooth formation. Ameloblastomas occur with similar frequency in both genders.[8] About 70% of ameloblastomas are found in the molar ramus region of the jaw. Another 10–15% are found near an undeveloped tooth, and the last 10% are in the mandibular anterior region.[4] The current case had an ameloblastoma in the anterior mandibular region, but no unerupted teeth were visible. We classify ameloblastomas as either extraosseous or intraosseous. Benign tumors, known as peripheral ameloblastomas, slowly develop and connect to the gums or the inner surface of the teeth without affecting the underlying bone.[7] They can either be flat or have projecting stems. We classify six types of jaw ameloblastomas: unicystic, desmoplastic, mixed cystic, and solid forms. The coexistence of cystic and solid forms has a heightened degree of aggressiveness and is susceptible to recurrence. The histopathological variants include the follicular and plexiform types, followed by the acanthomatous and granular cell types. Desmoplastic, basal cell, clear cell, keratoameloblastoma, and papiliferous ameloblastoma are less common variants.[5] We describe ameloblastoma as a painless, gradually developing, solid tumor, and in our specific case, it was similarly painless and exhibited firm swelling. The onset of symptoms occurred around two years after the patient's first presentation. Additional clinical symptoms of the disease include pain or numbness in the affected region. On x-rays, ameloblastoma appears as a radiolucent lesion with a single- or multiple-lens appearance.[9] It may cause the cortical plate to grow, or it may not. Conservative treatment options include enucleation and curettage, marginalization, or radical surgery, which may involve excision with or without continuity defects. We suggest doing a marginal resection that extends about 1.5–2 cm beyond the radiological limit affecting the mandible. This ensures the complete removal of all microcysts and daughter cysts. In this case, upon histological investigation, the material exhibited a follicular and plexiform form, leading to a clearing margin of 1.5 cm. Rebuilding significant mandibular lesions may involve various techniques, including microvascular surgery. The free fibula flap has become a gold standard for mandibular reconstruction due to its unique anatomical and functional characteristics and fibula provides a long segment of bone that can be used to reconstruct extensive mandibular defects, whether resulting from trauma, infection, tumor resection, or congenital anomalies. Its length and strength allow for reconstruction of nearly the entire mandible if needed.[10-13] We performed a segmental resection to treat the tumor, which was extensive in the mandible, and reconstructed it with a patient-specific implant, maintaining the patient's aesthetic appearance without requiring a donor site.

Conclusion

The surgical treatment technique seems to have the most impact on the likelihood of a recurrence of the disease. Typically, professionals advise a yearly check-up for at least a decade. Multiple writers have suggested implementing an annual follow-up for five years. We have monitored the patient for five years and have seen no recurrence. The utilization of patient-specific implants (PSIs) in the treatment of mandible tumors represents a transformative advancement in oral and maxillofacial surgery. By leveraging cutting-edge 3D printing technology and meticulous preoperative planning, PSIs offer unparalleled customization, ensuring a precise fit and optimal functional and aesthetic outcome. Clinical evidence shows that PSIs greatly improve the reconstruction of mandibular defects. This means that patients recover faster and with less pain after surgery, and their oral functions and facial symmetry are restored more effectively than with traditional methods.

DECLARATIONS

Conflicts of interest and financial disclosures

No conflicts of interest

Ethical approval Consent to participate

The study was approved by the Hospital Ethical Committee

Consent to participate

A written informed consent was obtained from the individual for the publication process.

Data availability

The data is available upon the considerable request to the corresponding author

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BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
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RESEARCH ARTICLE

KNOWLEDGE, AWARENESS AND ATTITUDE OF PRE PRACTITIONERS, INTERNS, POST GRADUATES AND DENTAL EDUCATORS TOWARDS THE DIGITALIZATION OF OPD IN DENTAL SCHOOLS - A MULTI CENTRIC QUESTIONNAIRE BASED STUDY

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Abstract

Background: Digitalization in dental outpatient departments (OPDs) has the potential to significantly improve dental education and patient care. However, research on the awareness, proficiency, and attitudes towards digital tools among dental students and educators is limited. This study examines the impact of digitalization in dental OPDs, focusing on how factors such as gender, educational status, and college affiliation influence perceptions and familiarity with digital tools.

Materials and Methods: This cross-sectional study involved dental students and educators from various dental colleges of the newly formed state of Andhra Pradesh. Data was collected through structured questionnaires assessing awareness, proficiency, and attitudes toward digitalization in OPDs. Statistical analysis, including Chi-Square tests, were conducted to explore associations between educational status, gender, and perceptions of digital tools. The sample included final BDS students, interns, postgraduates, and dental educators.

Results: The findings indicated that 91.3% of participants were aware of digitalization, and 52.0% had received training in digital tools. Educational status was significantly associated with proficiency, with postgraduates and educators showing higher expertise in using digital tools. Gender differences were evident, with females more likely to view digitalization positively, especially in terms of enhancing patient care and follow-up. Moreover, significant differences were observed across the colleges regarding the extent of digital tool training, indicating variability in institutional approaches to digital education.

Conclusion: The study underscores the importance of integrating digital tools in dental education and practice. It reveals the need for targeted digital training programs that consider educational status, gender, and institutional factors. The results suggest that dental schools should standardize digital education to ensure all students and educators are adequately prepared for the evolving digital landscape in dentistry.

Keywords: Digitalization, Dental Education, Outpatient Departments, Gender Differences, Training, Awareness, Perceptions

Rupa Chandini Dabbiru. Suresh Kumar Pakki, Venkata Ramani Chintada et al. Knowledge, awareness and attitude of pre practitioners, interns, post graduates and dental educators towards the digitalization of OPD in dental schools -a multi centric questionnaire based study. ***Bulletin of Stomatology and Maxillofacial Surgery*****. 2025;21(2).146-155:doi 10.58240/1829006X-2025.2-146**

INTRODUCTION

Digitalization offers a wide array of technologies that helps to optimize dental care. These tools can facilitate better communication between dental practitioners and patients, enhance treatment planning and collaboration among healthcare providers, and improve the patient experience. However, the successful adoption and implementation of these technologies depend significantly on the awareness, familiarity, and proficiency of dental students and educators.

As digital tools become an integral part of dental institutions, understanding the perceptions and attitudes of dental students towards these changes becomes crucial for effective curriculum design and training initiatives.

Digitalization encompasses a wide range of technologies, including electronic health records (EHRs), tele dentistry, digital imaging, and appointment scheduling systems, all of which aim to improve the efficiency and quality of dental care. As the dental profession increasingly utilises digital tools such as electronic health records (EHRs), digital imaging, tele dentistry, and automated appointment scheduling, it is essential to assess how these innovations are perceived by those who will be utilizing them in their future careers. Therefore, evaluating their awareness, attitudes, and benefits of digitalization is essential for informing educational strategies and training programs.

This study aims to explore the perceptions of dental students across various dental institutions, regarding the impact of digitalization on critical aspects of dental education and practice. The research focuses on several key areas, including communication, efficiency, collaborative practices, accessibility of dental care, administrative effectiveness, and the scope for ongoing improvements in digitalization practices.

By examining these perceptions, this study aims to identify potential barriers to the effective integration of digital technologies, highlight areas where educational strategies may need to be adjusted, and discover opportunities to enhance student readiness for a technology-driven healthcare environment.

As new generations of dental practitioners enter the field, they must be equipped not only with clinical skills but also with the technological competencies which will help them to survive in a digital world. Consequently, this study will explore critical questions such as:

What are the current levels of awareness and familiarity with digital tools among dental students? How do perceptions of digitalization vary across different demographic groups, including gender and educational status?

What benefits and challenges are associated with the integration of digital technologies in dental OPDs?

By addressing these questions, the study aims to contribute valuable insights into the integration of digitalization of OPD in dental education, ultimately having a more effective and innovative approach to dental care.

This study aims to assess the awareness and perceptions of dental stakeholders (Final BDS students, interns, postgraduates, and dental educators) regarding the digitalization of outpatient departments (OPDs) in dental education using a structured questionnaire.

Objectives

- To evaluate awareness of digitalization in OPDs among dental students and educators.
- To investigate attitudes towards the benefits and challenges of digitalization in treatment efficacy, communication, collaboration, and patient experience.
- To assess familiarity and proficiency with digital tools, including training experiences.
- To explore gender and educational status differences in perceptions of digitalization in OPDs.

METHODS

- This cross-sectional survey assessed dental students' perceptions of the digitalization of outpatient departments

(OPDs) in various dental colleges of the newly formed state of Andhra Pradesh. The study targeted 400 participants, including final BDS students, interns, postgraduates, and dental educators, to provide reliable insights into the digitalization perceptions in dental education. The Institutional Ethical Committee approval was obtained for the study.

- Data was collected using a structured online questionnaire, which comprised 20 questions, including demographic information (age, gender, educational status, awareness of digitalization in OPDs, training experiences, and attitudes toward its benefits and challenges. The questionnaire was distributed via email and WhatsApp in Google Form format for ease of access and completion.
- The questionnaire was divided into three sections: demographic details (Q1-3), knowledge-based questions (Q4-10), and awareness (Q11-20). A pilot study involving 20 dental students was conducted to test the validity and reliability of the questionnaire. Feedback from the pilot study led to adjustments in question clarity and format. The final version was validated by subject matter experts to ensure it accurately measured the intended concepts.
- Reliability analysis revealed a Cronbach's alpha score of 0.8, confirming internal consistency. Participants had two weeks to complete the online survey. Data was then tabulated and analyzed using SPSS software. Descriptive statistics were employed to summarize demographic characteristics and responses. Chi-square tests examined associations between categorical variables, particularly gender and educational status, with a significance level set at $p < 0.05$.

RESULTS

The study had a predominance of female participants, with 68.0% (282 respondents) being female and 32.0% (133 respondents) being male (figure 1).

The study participants were evenly distributed across different categories, with 25.3% (105 respondents) being postgraduates, 25.1% (104 respondents) final-year BDS students, 24.8% (103 respondents) interns, and 24.8%(103 respondents) dental educators(fig. 2).

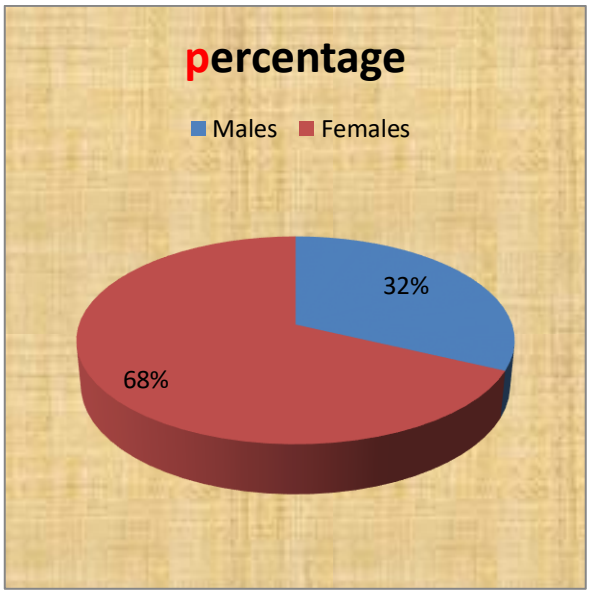


Figure 1 - Gender Distribution

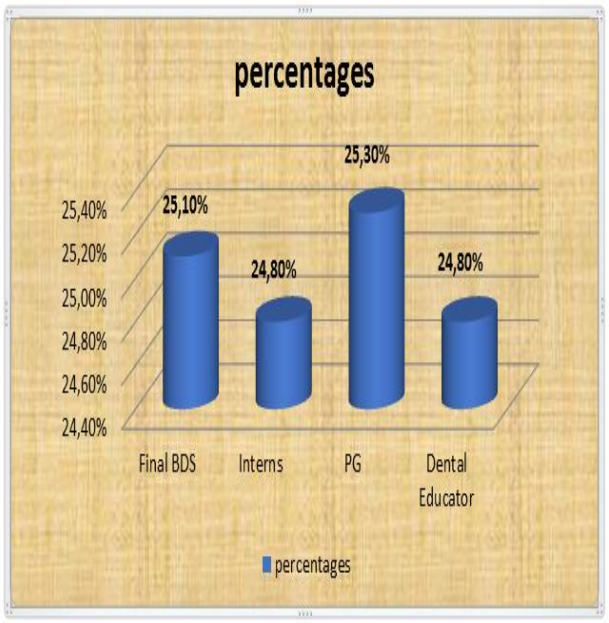


Figure 2 - Educational status

Table 1 – shows the participants knowledge and awareness regarding digitalization of OPD

Question	Strongly Disagree	Disagree	Natural	Agree	Strongly Disagree
Digitalization has the potential to improve efficacy and accuracy in the dental OPD	0 (0%)	0 (0%)	49(11.8%)	208 (50.1%)	158 (38.1%)
Digitalization of OPDs in dental schools will decrease time required for treatment planning	1(2%)	28(6.7%)	79(19%)	200 (48.2%)	107 (25.8%)
Digitalization of OPDs in dental school will enhance patient communication and education through the use of digital platforms	0(0%)	11(2.7%)	63(15.2%)	229 (55.2%)	112 (27%)
Use of of Digital systems in OPDs will facilitate better collaboration among dental students and faculty	0(0%)	3(0.7%)	78(18.8%)	217 (52.3%)	117 (28.2%)
Digitalization of OPDs leads to reduction in administrative errors in patient records	4(1%)	13 (3.1%)	75 (18.1%)	199 (48%)	124 (29.9%)
Digitalization of OPDs in dental schools provide more personalized treatment options for patients	0(0%)	13(3.1%)	67 (16.1%)	236 (56.9%)	99(23.9%)
Digitalization of OPDs will encourage more efficient appointment scheduling for patients	0(0%)	2 (0.5%)	46 (11.1%)	236 (56.9%)	131 (31.6%)
Question	Significantly improves	Somewhat improves	No effect	Somewhat worsens	Significantly worsens
Digitalization of OPDs will impact the accessibility of dental care for patients	180 (43.4%)	181 (43.6%)	53(12.8%)	1(0.2%)	0(0%)
Digitalization of OPDs in dental school affects the overall patient experience	165 (39.8%)	201 (48.4%)	48 (11.6%)	1 (0.2%)	0 (0%)
Question	Very important	Important	Neutral	Not Important	Not sure
How important is it for dental student to be well versed in using digitalization of OPD for their future prospects/career?	173 (41.7%)	199 (48%)	38 (9.2%)	1(0.2%)	4(1%)

Rupa Chandini Dabbiru. Suresh Kumar Pakki, Venkata Ramani Chintada et al. Knowledge, awareness and attitude of pre practitioners, interns, post graduates and dental educators towards the digitalization of OPD in dental schools -a multi centric questionnaire based study. *Bulletin of Stomatology and Maxillofacial Surgery*. 2025;21(2).146-155:doi 10.58240/1829006X-2025.2-146

Table 2 shows perceptions and insights on digitalization of OPD

Question	Yes	No
Awareness of digitalization of OPD used in dental colleges	379 (91.3%)	36 (8.7%)
Received any training or orientation on using digital tools in Dental OPD	216 (52%)	199 (48%)
Increase in digitalization of OPD might reduce direct patient interaction	218 (52.6%)	197 (47.4%)
Digitalization of OPD helps in patient follow up protocol which in turn benefits the patient	401 (96.6%)	14 (3.4%)
Digitalization Of OPD has to be kept uniform in all dental schools across India	336 (80.9%)	79 (19.1%)
Do you think digitalization of OPD can be further improved	378 (91%)	37 (9%)

The study on digitalization in dental OPDs highlights strong support for its benefits. A majority of participants (68%) were female, with representation across educational levels, including final BDS students, interns, postgraduates, and dental educators.

Awareness of digitalization was high (91.3%), and while 52% had training, many reported feeling familiar (56.1%) or proficient (33.3%) in using digital tools.

Participants expressed confidence in the positive impacts of digitalization, with 88.2% believing it enhances treatment efficacy and 96.6% acknowledging its role in patient follow-up.

Concerns about reduced patient interaction were raised by 41.7%, emphasizing the need for balance.

Despite this, 89.7% agreed that proficiency in digital skills is crucial for future careers. Many felt that digital tools foster collaboration (80.5%) and reduce administrative errors (77.9%).

Digitalization was also seen as beneficial for personalized treatment (80.8%) and improving accessibility to dental care (87.0%).

Additionally, 88.5% believed digital tools would improve appointment scheduling, and 88.2% felt it would enhance the patient experience. The majority (82.7%) recognized opportunities for further improvement in digital practices.

Overall,

these findings demonstrate a strong endorsement of digital tools in dental education and practice, along with a willingness to embrace ongoing advancements.

Also, the study revealed several significant insights regarding gender, educational status, and college affiliation in the context of digitalization of outpatient departments (OPDs) in dental education.

Table 3 shows statistical significanc observed among different parameters

Question	Gender Chi-square value (p-value)	Educational status Chi-square value (p-value)	College Chi-square value (p-value)
Digitalization has the potential to improve efficacy and accuracy in dental OPD	1.931(0.38)	3.3(0.770)	7.338 (0.291)
Digitalization of OPDs in dental school will decrease time required for treatment planning	15.829(0.003)*	20.608(0.056)*	15.171 (0.232)
Digitalization of OPDs in dental school will enhance patient communication and education through the use of digital platforms	6.043(0.110)	33.743(0.00)*	31.556(0.000)*
Digital systems in OPDs will facilitate better collaboration among dental students and faculty	10.842(0.013)*	32.962(0.00)*	26.189(0.002)*
Digitalization of OPDs leads to reduction in administrative errors	4.589(0.33)	20.203(0.063)	50.055(0.000)*
Digitalization of OPDs in dental schools will provide more personalized treatment	7.8(0.05)*	24.498(0.004)*	25.657(0.002)*
Digitalization of OPDs will encourage more efficient appointment scheduling for patients	9.106(0.02)*	13.658(0.135)	19.515(0.021)*
Digitalization of OPDs will impact the accessibility of dental care for patients	9.478(0.02)*	11.673(0.232)	25.432(0.003)*
Digitalization of OPDs in dental school affects the overall patient experience	11.038(0.012)*	18.368(0.031)*	30.750(0.000)*
How important is it for dental student to be well versed in using digitalization of OPD for their future prospects/career?	5.793(0.2)	22.507(0.032)*	28.671(0.004)*
Level of familiarity with digitalization used in dental OPD	4.062(0.131)	46.68 (0.00)*	5.552(0.475)*
Awareness of Digitalization of OPD used in dental colleges	0.04(0.84)	15.27 (0.002)*	11.498(0.009)*
Received any training or orientation on using digital tools in Dental OPD	2.036(0.154)	9.12 (0.028)*	29.829(0.000)*
Increase in digitalization of OPD might reduce direct patient interaction	5.970 (0.051)*	9.036(0.172)	11.180(0.083)

Digitalization of OPD helps in patient follow up protocol which in turn benefits the patient	0.77(0.378)	12.240(0.007)*	0.865(0.834)
Digitalization Of OPD has to be kept uniform in all dental schools across India	4.110(0.128)	8.769(0.187)	6.86(0.33)
Digitalization of OPD can be further improved	0.50(0.776)	6.275(0.393)	10.345(0.111)

*Pearsons chi-square test, p <0.05 (S)**

Gender: Chi-Square test results indicate significant gender-based differences in perceptions of digitalization's impact on treatment planning, collaboration, and patient communication. Males tend to show a slightly stronger agreement with the benefits of digital tools in reducing treatment planning time, fostering collaboration, and providing personalized treatment options. However, both genders generally agree that digitalization enhances the accessibility of dental care and improves patient experiences. Notably, males are more inclined towards seeing the effectiveness of digital tools in providing personalized treatment, while females express stronger consensus on their benefits for patient communication and follow-up.

Educational Status: There is a significant relationship between educational status and awareness, familiarity, and perceptions of digitalization. The p-value of 0.002 indicates that different educational levels—final BDS students, interns, postgraduates, and dental educators—show varying awareness levels of digital tools in OPDs. Higher educational status correlates with greater familiarity and proficiency in using these digital tools, with postgraduates and educators being more confident in utilizing digital systems. Perceptions of digitalization's impact on patient care, collaboration, and treatment personalization also differ by educational status, with higher educational levels recognizing its benefits more strongly. The study suggests that digital skills training should be tailored according to the educational level to ensure effective adoption across all stages.

College Affiliation: College affiliation also plays a critical role in shaping perceptions of digitalization. Significant differences were found in awareness and training experiences regarding digital tools across different colleges. The p-value of 0.002 suggests that some colleges are more proactive in training students on digital tools in OPDs. College affiliation further influences students' attitudes towards digital skills in dental practice, with some institutions emphasizing the importance of digital tools more than others. Additionally, students from colleges with strong digitalization programs tend to view digitalization more favourably, especially in terms of improving patient care, accessibility, and appointment scheduling efficiency.

Gender, educational status, and college affiliation significantly influence dental students' and educators' perceptions of the digitalization of OPDs. These findings highlight the need for targeted interventions and strategies that consider these demographic factors to enhance the integration of digital tools in dental education and practice.

Discussion

This study highlights the transformative role of digitalization in dental education and practice, reflecting broader trends in healthcare technology. A high level of awareness (91.3%) and familiarity with digital tools among participants aligns with global adoption patterns, as noted by Hall et al[1] (2023). The reported training levels (52%) underscore efforts to integrate technology into curricula, supported by recommendations from organizations like the American Dental Education Association.

The perceived benefits of digitalization—such as enhanced treatment efficacy (88.2%) and improved patient follow-up (96.6%)—echo findings from Avhad et al[2](2022), who emphasized how digital tools optimize clinical workflows and outcomes. Additionally, the recognition of improved accessibility (87.0%) and personalized treatment options (80.8%) is consistent with Nayakar et al [3] (2022) conclusion that digital systems reduce healthcare disparities and facilitate tailored interventions.

Concerns about reduced patient interaction (41.7%) reflect a critical issue in the digitalization discourse. Similar concerns were raised by Hall et al[1] (2023), who stressed the importance of maintaining patient- centered care amid technological reliance. Balancing digital tools with personal engagement is crucial, as noted in this study's findings.

The belief that proficiency in digital skills is essential for future careers (89.7%) aligns with Favaretto et al[6](2020), who identified digital competence as key in modern healthcare. Consensus on the benefits of digital systems for collaboration (80.5%) and reducing administrative errors (77.9%) mirrors Sharab et al[4](2022) observations in other healthcare disciplines.

Participants' advocacy for further improvements (82.7%) supports the need for continuous innovation, as suggested by Gross et al[7] (2019), who called for addressing challenges such as system usability and training gaps. Dental education can benefit from expanding digital training access while fostering a culture that embraces change. Chi-Square test results revealed significant associations between gender and various perceptions of digitalization in outpatient departments (OPDs). These findings suggest that demographic factors influence attitudes toward digital tools in dental education and practice. The relationship between gender and the belief in digitalization's benefits for treatment planning time ($p = 0.003$) implies that gender may shape perceptions of technological efficiencies, consistent with Tulasi et al[5] (2022).

The association between gender and perceptions of digitalization's role in collaboration ($p = 0.013$) highlights the importance of considering diverse perspectives in creating collaborative environments. Males showed slightly stronger agreement, while overall agreement across genders emphasizes digitalization's potential for fostering teamwork. These findings Sharab et al[4] (2022), who observed demographic differences in embracing collaborative tools.

Pearson Chi-Square results ($p = 0.050$) highlighted gender differences in attitudes toward personalized treatment options enabled by digitalization. Males were more favourable toward significant improvements, while females exhibited stronger consensus on the benefits, reinforcing Hall et al [1] (2023), who emphasized the need for tailored digital initiatives.

The study also found a significant relationship between gender and perceptions of digitalization's impact on accessibility and appointment scheduling efficiency. While females expressed higher agreement, males were more inclined to report significant improvements. This suggests differing expectations or experiences with digital systems, reflecting Favaretto et al[6] (2020) on gender-specific preferences in system design.

These gender-based differences emphasize the need for dental schools to consider diverse perspectives when implementing digital strategies. Addressing gender-specific concerns and leveraging shared views will create a more inclusive environment for digital adoption. Future research should explore barriers and preferences to refine these strategies, as recommended by Gross et al[7] (2019).

The Chi-Square results revealed significant associations between educational status and various aspects of awareness, proficiency, and perceptions of digitalization in OPDs. This underscores the influence of educational background on attitudes toward digital tools. The significant relationship between educational status and awareness ($p = 0.002$) suggests that training and exposure influence understanding of digital systems, as supported by Avhad et al[2] (2022).

The strong association between educational status and familiarity with digitalization ($p < 0.001$) emphasizes the importance of integrating digital competencies into curricula.

Postgraduates and dental educators showed higher familiarity, consistent with Tulasi et al[5] (2022), who identified postgraduate training as crucial for developing technical skills. This calls for targeted training programs to address gaps at the undergraduate and internship levels.

Differences in perceptions of digitalization's impact on career advancement further highlight the influence of educational status. Dental educators and postgraduates were more likely to emphasize the importance of digital skills, in line with Vander et al[6] (2018), who found that career stage influences attitudes toward technology adoption. Tailoring interventions to support lifelong learning in digital skills is essential.

The association between educational status and perceptions of digitalization's benefits for patient follow-up and communication ($p < 0.05$) reflects varying levels of exposure to digital tools in practice. Postgraduates and educators, more involved in patient care, recognized these benefits more strongly, as noted by Nayakar et al[3] (2022). Integrating real-world applications into undergraduate training could address this gap.

Finally, the study found strong associations between educational status and perceptions of personalized treatment options and overall patient experience ($p = 0.004$). Educators and postgraduates were more likely to value these benefits, reflecting a deeper understanding of patient-centered care. Hall et al[1] (2023) emphasized aligning digital systems with clinical goals to maximize impact.

This study underscores the need to tailor digitalization strategies to address the diverse perspectives of individuals at different educational levels. Targeted training programs can ensure that all stakeholders are equipped to effectively adopt digital technologies. Future research should focus on identifying barriers to adoption at each educational stage and developing interventions to overcome them.

Conclusion

The study emphasizes the pivotal role of digitalization in dental OPDs, highlighting the impact of demographic, educational, and institutional factors. Awareness and proficiency with digital tools varied by educational level, with postgraduates and educators showing higher competency. Gender differences were noted in perceptions of digital tools' benefits. The study stresses the need for targeted training, standardized curricula, and balanced approaches to ensure digital integration enhances patient care and operational efficiency.

DECLARATIONS

Conflicts of interest and financial disclosures

No conflict **of interest** and there was no external source of funding for the research in question.

Ethical approval

Study was approved by Institutional Research Review Board, GITAM Dental College and Review Board, GITAM Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

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RESEARCH ARTICLE

PREVALENCE OF TEMPOROMANDIBULAR JOINT-TMJ DISORDERS IN A SAMPLE OF THE LEBANESE POPULATION

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Abstract

Objective: The aim of this study was to evaluate the prevalence of temporomandibular joint (TMJ) disorders in a sample of the Lebanese population.
Materials and Methods: This study analyzed data of TMJ disorder rates and their links to age and sex from 689 patients referred to a private dental clinic in Beirut, Lebanon, from 2012 to 2017.
Results: The overall prevalence was 17.8%, with disc displacement with reduction (DDR) most common (10.2%), followed by myalgia (6.4%) and disc displacement without reduction (DDwR) (1.2%). Prevalence peaked in the 46–60 age group (27.5%) and showed no significant gender difference.
Conclusion: This study highlights a significant prevalence of TMJ disorders among Lebanese dental patients, particularly in older age groups, underscoring the need for targeted interventions, early diagnosis, and tailored treatment strategies to improve patient care and inform future research.

Keywords: Temporomandibular Joint, disorder, prevalence, disc displacement, myalgia.

Introduction

The temporomandibular joint (TMJ) disorder pertains to a group of conditions where there is pain in the TMJ or the tissues around it, limitations in the functional movement of the mandible, or clicking sensations in the TMJ when it is in motion.[1] Pain in this area can arise from internal joint-related conditions, surrounding structures, or a combination of both factors. Possible causes of the pain include degenerative joint disease, inflammatory issues affecting the TMJ, disc displacement, and trauma.[2]
A 2021 systematic review and meta-analysis revealed that the worldwide prevalence of TMJ disorders, representing a significant oral health concern, is approximately 31% among the adult and elderly population.[3]
Because of the remarkable prevalence of this condition, it becomes essential to precisely diagnose it. In order to diagnose TMJ disorders, a healthcare professional usually conducts a comprehensive medical history review, a thorough physical examination, and may also employ imaging tests. The diagnosis relies on the patient's reported symptoms and the findings from the physical examination.[4]
A spectrum of treatment options is available for TMJ disorders, often starting with conservative, non-invasive approaches such as physical therapy, medications including analgesics or muscle relaxants, occlusal adjustments, and intraoral splints. If necessary, interventions such as trigger point injections, electrostimulation, and surgical procedures may be considered.[5,6]

The most suitable treatment plan must be individualized, considering the underlying etiology of the disorder, symptom severity, patient preferences, and the potential risks and benefits of each approach. This study aims to determine the prevalence of TMJ disorders among patients seeking care at a private dental practice in Lebanon. Guided by this goal, we sought to answer the following research question: What is the prevalence of TMJ disorders among patients seeking dental care at a private practice in Lebanon, and is there an association between age, sex, and TMJ disorders prevalence in this population?

The findings of this study can be used to guide decisions regarding the allocation of resources within the practice (e.g., specialized equipment, staff training). Furthermore, it establishes a baseline for future research, allowing healthcare professionals to track changes in TMJ disorders prevalence over time within different patient groups and assess the effectiveness of prevention and treatment strategies. Notably, this research addresses a significant gap in the literature, as only one previous study[7] had explored TMJ disorders prevalence in Lebanon. Using a comprehensive dataset from patients' diagnostic records, this study explores the potential correlations between demographic factors and the presence of different TMJ disorder groups.

Materials and Methods

Study Design

This observational study utilized a retrospective analysis of data collected from patients at a private dental practice in Mount Lebanon Governorate, Lebanon, between 2012 and 2017. The reporting of this study was guided by the Standards for Reporting Qualitative Research (SRQR) guidelines.[8]

Inclusion/Exclusion Criteria

Inclusion Criteria:

- Lebanese adults
- Males and Females

Exclusion Criteria:

- Non-Lebanese adults
- Individuals with missing age or sex data
- Patients presenting with subluxation or hyperlaxity

Data Collection and Management

Patients who first presented to the clinic between 2012 and 2017 underwent TMJ screening as part of their initial clinical evaluation. All patients provided informed consent for their anonymized data to be used in future research. All diagnoses were made by a single specialist with advanced training in occlusion and TMJ disorders, ensuring consistency of the examination. Medical and dental students, under the supervision of the research team, assisted with data entry, transferring information from clinical records into a standardized format using a pre-defined data entry protocol. This protocol included procedures for ensuring data accuracy, such as double-entry verification. Data was managed and analyzed using Microsoft Excel (Microsoft Corporation, USA) and Statistical Package for the Social Sciences (SPSS) software (IBM, 2014).

Variables

- Outcome Variable: Presence of TMJ disorders (Yes/No) based on diagnosis.
- Predictor Variables:
  - Age (continuous and grouped)
  - Sex (Male, Female)
  - TMJ disorders Subtypes:
    - Myalgia of head and neck (Yes/No)
    - Disc Displacement with Reduction (DDR) (Yes/No)
    - Disc Displacement without Reduction (DDwR) (Yes/No)

Statistical Analysis

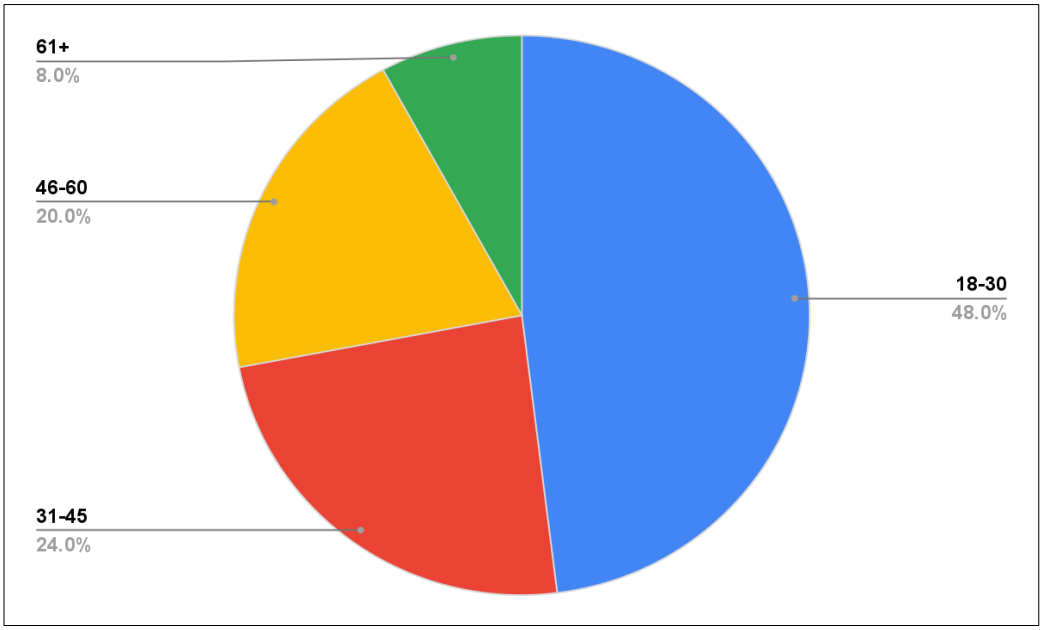
Data cleaning procedures were performed prior to analysis to identify and correct any errors in data entry. These procedures included checks for outliers, missing values, and inconsistencies. Descriptive statistics (frequencies, percentages, means, and standard deviations) were used to summarize sample characteristics and prevalence rates. Chi-square tests assessed the association between TMJ disorders and categorical variables (age group, sex, subtypes). A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

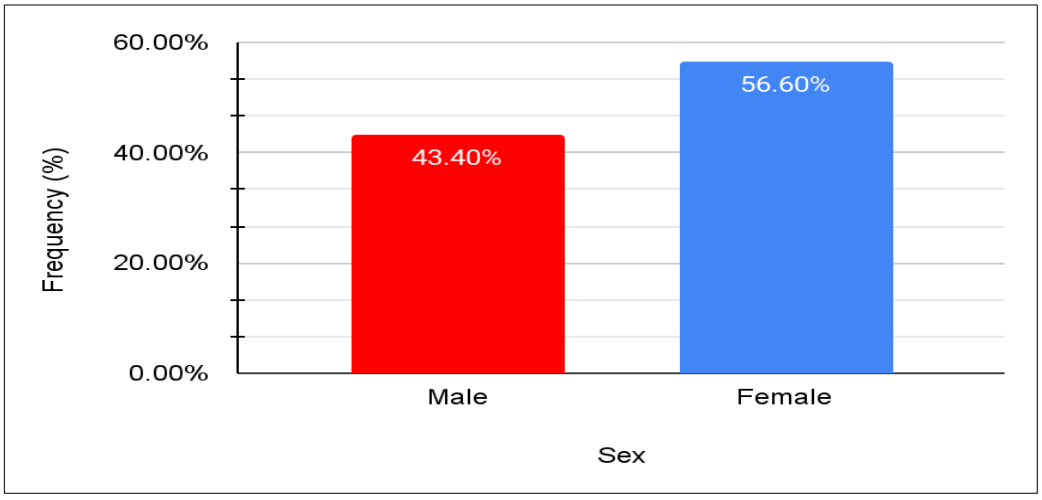
Sample Characteristics

The study sample consisted of 689 individuals. The mean age of participants in our study was 39.47 years.

The distribution of age and sex is presented in Graphs1and 2.



Graph 1. Distribution of participants in different age groups



Graph 2. Gender distribution of participants

Prevalence of TMJ disorders

The overall prevalence of TMJ disorders in this sample was 17.8%. Disc displacement with reduction (DDR) was the most common (10.2%), followed by myalgia (6.4%), and disc displacement without reduction (DDwR) (1.2%).

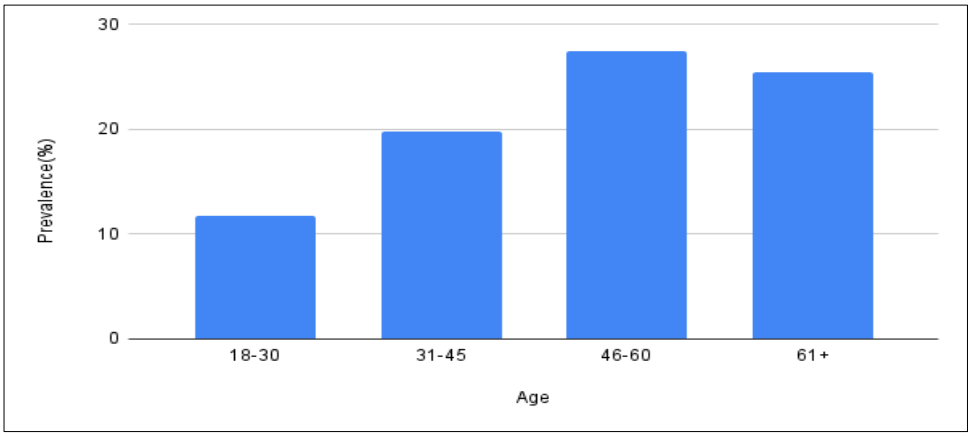
TMJ Disorders Prevalence by Age Group and Sex

The prevalence of TMJ disorders varied across age groups and by sex.

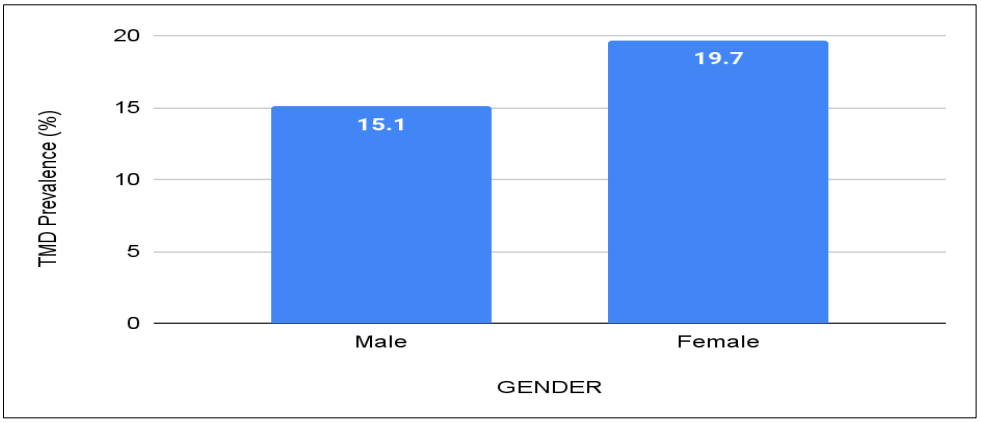
As shown in Graph 3, the prevalence of TMD was 11.7% among individuals aged 18-30, increasing to 19.8% in the 31-45 age group and peaking at 27.5% among those aged 46-60. The prevalence slightly decreased to 25.5% in the 61+ age group, suggesting that TMD is more common in middle-aged and older adults. A chi-square test confirmed a statistically significant association between age group and TMD prevalence ($p = 0.007$).

Older age groups (46-60 and 61+) demonstrated significantly higher prevalence rates compared to younger age groups. Regarding sex, 19.7% of females and 15.1% of males presented with TMD (Graph 4).

A chi-square test showed no significant association between sex and TMD prevalence ($p=0.067$).



Graph 3. TMJ disorders prevalence in different age group



Graph 4 TMJ disorders prevalence according to gender

TMJ disorders Subtype Prevalence by Granular Age Group

TMJ disorders subtype prevalence by granular age group is summarized in Table 1

Table 1: Prevalence of TMJ disorder subtypes across age groups (in percentages)

Age Group	Myalgia (%)	DDR (%)	DDwR (%)
18-27	6.1	3.0	0.0
28-37	7.4	5.9	0.0
38-47	11.6	11.6	0.8
48-57	13.7	12.0	2.6
58-67	12.5	12.5	2.8
68+	8.7	17.4	2.2

Both myalgia and DDR showed a general trend of increasing prevalence with age. While DDwR remained relatively uncommon, it also exhibited a slight increase in older age groups.

Discussion

The prevalence of TMJ disorders represents a significant global oral health burden. Our study contributes to this growing body of research by investigating the prevalence of TMJ disorders among the Lebanese population. Valesan et al. conducted a meta-analysis on different populations, suggesting a prevalence of 30% among adults.[3]

Consistent with previous reports from different countries, our findings revealed a high prevalence of TMJ disorders in Lebanon, with 17.8% of participants meeting the diagnostic criteria. This aligns with studies by Progiante et al.[9]
in Brazil (32.7%), Loster et al.[10]in Poland (18% in 18-year-olds), and Guerrero et al.[11]
in Chile (49.6% in adults). These changes can be attributed to the heterogeneity in diagnosis criteria as well as the variability in many areas, including cultural and other factors, among the different groups evaluated. Notably, this prevalence is slightly lower than that reported by Kmeid et al. in their Lebanese study (19.7%), which could be attributed to differences in sample characteristics, diagnostic criteria, or study methodologies.[7]
Furthermore, the strengths of our study include the large sample size of 689 participants based on clinical examination ensuring robust statistical power and representativeness. Regarding Kmeid et al.,[7] their study involved 459 respondents who completed a survey, which is thought to be more subjective and susceptible to biases according to Berman.[12] Additionally, the rigorous data collection process, involving specialized medical professionals and supervised data entry, ensured the accuracy and quality of the data.

This current study demonstrated a statistically significant correlation between advancing age and increased TMJ disorders prevalence, emphasizing the need for age-specific clinical approaches.

Furthermore, we observed a higher prevalence among females (19.7%) compared to males (15.1%), which corresponds with the findings of Al-Khotani et al. [13] in Saudi Arabia (59.6% females vs. 40.4% males in children/adolescents) and De Melo Júnior et al. [14] in Brazil (68.7% females vs. 31.3% males in adolescents). This gender disparity in TMJ disorder prevalence is well-documented in the literature and may be attributed to hormonal factors and psychosocial influences. Al Khotani et al. demonstrated, along with previous research, that TMJ disorders onset typically occurs after age 12, suggesting that puberty and associated hormonal changes may contribute to the higher prevalence of TMJ disorders in older age groups.[13]
These physiological transformations could potentially explain the observed increase in temporomandibular disorder symptoms with advancing age.

However, while females (19.7%) had a slightly higher prevalence of TMJ disorders than males (15.1%) in the sample, this difference was not statistically significant.

Regarding the specific subtypes of TMJ disorders, this study found that DDR was the most common (10.2%), followed by myalgia (6.4%), and DDwR (1.2%). These results are comparable to the findings of Aravena et al. in Chile, who reported prevalence rates of 39%, 8.5%, and 6.5% for myalgia, DDR, and DDwR, respectively. [15]
Bertoli et al. also observed a high prevalence of myalgia (10.3%) among Brazilian adolescents.[16]
Examining the prevalence of these subtypes across different age groups revealed that both myalgia and DDR exhibited an increasing trend with age: specifically, for each one-year increase in age, the odds of having TMJ disorderS increased by 4.5%. This suggests that older individuals may be more susceptible to developing these specific TMJ disorder subtypes, potentially due to age-related degenerative changes in the TMJ or surrounding tissues. While DDwR remained relatively uncommon, it also showed a slight increase in older age groups.

These findings contribute to the growing body of literature on TMJ disorders and highlight the need for targeted interventions to address this significant health issue in Lebanon. Future research should aim to replicate and expand upon these findings, explore underlying mechanisms and risk factors, and evaluate the efficacy of various treatment modalities for improving patient outcomes and quality of life.

The retrospective nature of this study design limits our ability to draw causal inferences. Prospective, longitudinal studies are essential in assessing other risk factors such as jaw injuries and genetics and in enhancing the quality of care. This approach could be crucial for better diagnosis through early detection, preventative strategy development, and individualized treatment plans.

This study was limited to a single private practice, which limits the generalizability of the findings, as the patient population at this private practice may not be fully representative of the broader Lebanese population in terms of socioeconomic status, access to care, or other demographic factors. Further research involving a more diverse sample drawn from multiple clinics or a community-based setting would enhance the generalizability of these findings.

Conclusion

This study provides valuable insights into the prevalence and risk factors of TMJ disorders among the Lebanese population, serving as a foundation for further research, raising awareness and informing clinical efforts to improve the diagnosis, treatment, prognosis, and overall management of these conditions.

Declarations

Conflicts of interest and financial disclosures

The authors declare that they have no conflicts of interest, and there was no external source of funding for this research.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

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RESEARCH ARTICLE

EFFECT OF TETRADIUM RUTICARPUM AND ITS BIOACTIVE COMPOUNDS ON INTRINSIC APOPTOTIC SIGNALLING IN ORAL SQUAMOUS CELL CARCINOMA (OSCC) CELLS IN VITRO: ROLE OF WNT/β-CATENIN PATHWAYS

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Abstract

Background: A major global health concern, oral cancer is becoming more common due to a combination of environmental and hereditary factors. Oral cancer is primarily caused by dysregulation of the Wnt/β-catenin signaling pathway, which promotes cell proliferation and inhibits apoptosis. As such, it is an important target for therapeutic intervention. *Tetradium ruticarpum* extracts may be able to modulate the Wnt/β-catenin pathway to restore apoptotic mechanisms and stop the growth of tumors.

Materials and method: The DPPH radical scavenging assay was used to measure antioxidant activity, while the albumin denaturation inhibition method was used to measure anti-inflammatory qualities. In a CO_2 incubator, human oral cancer KB cells were grown in DMEM containing medium supplemented with 10% FBS and 1% antibiotics. Using the MTT and trypan blue tests, cytotoxicity was investigated. Using Real-Time PCR, the gene expression of apoptotic markers was examined. To investigate compound-protein interactions, molecular docking studies were carried out using PyRx and Biovia Discovery Studio. One-way ANOVA was used to evaluate the data ($p<0.05$).

Results: Results of Preliminary biochemical analysis showed that rutaecarpine significantly improved DPPH radical scavenging activity and inhibited albumin denaturation suggesting the strong antioxidant and anti-inflammatory potential ($p<0.001$). Treatment of rutaecarpine to oral cancer cells (KB) resulted in dose-dependent antiproliferative activity in both 20 and 40µM concentrations ($p<0.002$). Futher, gene expression anlaysis by q-RT-PCR registered the compound's ability to inhibit the over expression of Wnt/Beta catenin signaling molecules (β-catenin, Bcl-2 and Wnt mRNA). Molecular docking anlyais also authenticated the results of cell line model by showing the strong binding intercations with the target molecules (β-catenin, Bcl-2 and Wnt).

Conclusion: The potential of rutaecarpine as an anticancer treatment is highlighted in this work by its capacity to inhibit inflammatory processes, decrease cell viability, and modify apoptotic and wnt/ β-catenin signaling pathways in human oral cancer cells. Future research is made possible by its molecular docking and antioxidant results, which further support its therapeutic promise against oral cancer.

Keywords: Apoptosis, Beta-catenin, Cytotoxicity, Gene Expression, Molecular Docking, Oral Cancer, Protein Denaturation, Rutaecarpine

INTRODUCTION

The intricate relationship between natural compounds and cancer biology has garnered significant attention in recent decades, particularly within the context of oral cancer.[1] The exploration of various phytochemicals has highlighted their potential in modulating apoptotic pathways, thereby

offering a therapeutic avenue to combat malignant growth. Among these, Tetradium ruticarpum, a plant renowned for its rich bioactive compound profile, presents a compelling case for further investigation. This study aims to dissect the effects of Tetradium ruticarpum extracts on apoptotic signalling mechanisms in oral cancer cells, specifically focusing on the Wnt/β-catenin pathway.[2] Given the pathway's critical role in cellular proliferation and survival, understanding its modulation through natural compounds may illuminate new strategies for therapeutic intervention. As the global burden of cancer continues to rise, this research contributes to the growing body of evidence supporting the role of natural products in cancer treatment and prevention.[3]

Oral cancer, marked by the malignant transformation of epithelial cells, often results from a combination of genetic predispositions and environmental factors, including tobacco use and excessive alcohol consumption.[4] At the cellular level, tumours manifest via dysregulation of oncogenic and tumour suppressor pathways, with the Wnt/β-catenin signalling cascade emerging as a significant player in promoting cell proliferation while inhibiting apoptotic mechanisms.[5] This disruption in apoptosis not only contributes to unchecked cellular growth but also enhances resistance to conventional therapies, emphasising the necessity for targeted treatments that re-establish normal apoptotic processes.[6] By exploring the modulation of Wnt/β-catenin signalling, researchers aim to devise novel strategies that restore the balance between cell survival and death, ultimately improving patient outcomes in oral cancer therapy.[7]

Characterised by its rich phytochemical composition, Tetradium ruticarpum has emerged as a subject of interest in the realm of cancer research.[8] This plant is noted for its diverse array of bioactive compounds, including flavonoids, alkaloids, and phenolic acids, each contributing to its purported anti-cancer properties.[9] The synergistic effects of these compounds may enhance their potential in modulating cellular pathways involved in apoptosis and tumour suppression.[10] Preliminary studies indicate that these phytochemicals can impact key molecular targets linked to Wnt/β-catenin signalling, a critical pathway implicated in oral cancer progression and metastasis.[11] By disrupting this pathway, Tetradium ruticarpum may induce apoptotic signalling in cancer cells, thereby inhibiting their proliferation and promoting cell death.

In exploring the multifaceted intricacies of the Wnt/beta-catenin signalling pathway, it becomes apparent that its dysregulation plays a pivotal role in the pathogenesis of oral cancer.[12] This pathway, crucial for cell proliferation and differentiation, is often aberrantly activated in cancerous tissues, leading to increased cell survival and proliferation while inhibiting apoptosis. Specifically, the accumulation of beta-catenin in the nucleus promotes the transcription of genes associated with oncogenesis, thereby contributing to the aggressive nature of oral tumours.[13] Given the significance of this signalling cascade, therapeutic strategies targeting Wnt/beta-catenin components could potentially enhance treatment efficacy and patient outcomes.[14] The influence of bioactive compounds derived from Tetradium ruticarpum in modulating this pathway opens exciting avenues for research, particularly in their ability to restore appropriate signalling dynamics and facilitate apoptotic processes in oral cancer cells, challenging the status quo of current therapeutic modalities. The intricate interplay between Wnt signalling and beta-catenin activation plays a pivotal role in cellular processes, particularly apoptosis. Activation of the Wnt pathway leads to the stabilisation and accumulation of beta-catenin in the cytoplasm, allowing its translocation into the nucleus.[15] Once within the nucleus, beta-catenin collaborates with transcription factors, such as TCF/LEF, to initiate the expression of target genes that promote cell proliferation and inhibit apoptotic signalling.[16] This dysregulation is especially pronounced in various types of cancer, where aberrant Wnt/beta-catenin signalling can confer a survival advantage to tumour cells, thereby impairing apoptosis and facilitating tumour progression.[5] Understanding these mechanisms is crucial for uncovering novel therapeutic strategies aimed at reinstating apoptotic pathways in cancerous tissues. Moreover, targeted interventions that disrupt Wnt signalling could potentially exacerbate apoptosis in oral cancer cells, paving the way for innovative treatments involving natural compounds like Tetradium ruticarpum.

Antioxidant activity (2, 2-Diphenyl-1-picrylhydrazyl (DPPH) Free Radical Scavenging Activity): Scavenging of DPPH radicals was measured according to the standard method. An aqueous solution of DPPH (1.0 ml) was added to 1mg/ml pyrogallol solution at different concentrations (100, 200, 300, 400 µg/ml). The reaction mixture

was incubated at 37 °C for 50 min and the absorbance was taken at 517 nm. For the DPPH assay, different standard concentrations (100, 200, 300, 400µg/ml, respectively) were taken. The scavenging activity of the DPPH radical was expressed in terms of percentage inhibition ability using the following formula: (Control OD—Sample OD/Control OD).

Anti-inflammatory activity albumin denaturation inhibition: It was followed by an Albumin denaturation inhibition assay according to Osman et al. 2016.[17] Positive standards ibuprofen and diclofenac prepared as 0.1 percent each which is 1.0 mg/ml with plat drug. Each reaction vessel contained 1000 µl of the test compound, 1400 µl of PBS, and 200 µl of egg albumin. Distilled water was used instead of the compound as a negative control. Finally, the mixtures were further heated after a 15-min incubation at 37 °C, for 5 min at 70 °C. The previously described absorbance was read after cooling. The percentage of inhibition of protein denaturation was subsequently calculated using the formula below.



Figure 1. Reagents of Antioxidant and Anti-inflammatory activity

Cell Culture: The Human oral cancer cells, KB, were obtained from NCCS, Pune. The cells will be maintained by serial passaging in culture in a CO2 incubator having 10% FBS, 1% penicillin and streptomycin antibiotics mix, and DMEM media obtained from Himedia.

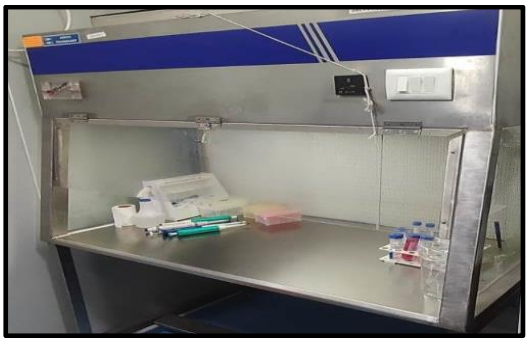


Figure 2. Cell culture hood



Figure 3. T25 Cell Culture Flask

Cell viability by MTT: This study further explored the cytocompatibility of the natural compound on KB cell lines using the MTT and trypan blue assays.[18]

Associatively, the 1×10^4 population was seeded and followed by overnight incubation. After the overnight incubation period, the MTT reagent was added and dissolved using DMSO, and the reading at 590 nm was determined.

Gene expression by Real Time-PCR: KB cells at a density of 5×10^6 cells per well were seeded into a 6-well plate. On the morning of the next day, after about night-long incubation, RNA was extracted using Total SYBR Green RNA isolation reagent, TRIR by Abgene, UK. Extracted RNA concentration was measured in micrograms (µg) by spectrometric quantification. Further, 2 µg of total RNA was subjected to reverse transcription for the conversion into cDNA following the protocol mentioned in Jayaraman et al. (2024).[19]

For mRNA expression analysis by Real-Time PCR, a reaction mixture was made using Takara SyBr green master mix and custom-designed forward and reverse primers on FOXM1.

For target gene expression, the thermal cycling consisted of an activation initial stage of 5 minutes at 95 °C, followed by 30 to the two-step cycling procedure, in which each cycle consists

of denaturation for five seconds at 95 °C and then combined annealing and extension of 8 seconds at the temperature of the specific primer that ranged from 56 to 65 °C. Target gene expression primer set.

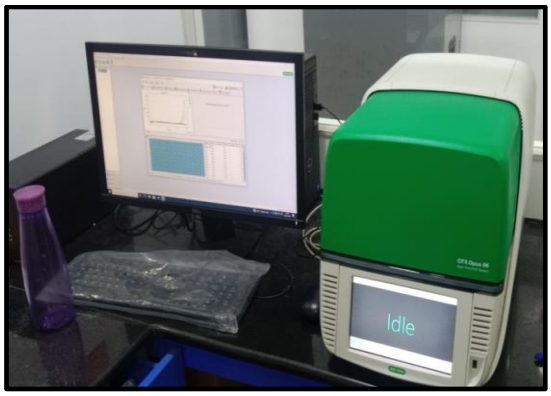


Figure 4. Real Time-PCR



Figure 5. Total RNA isolation Reagents

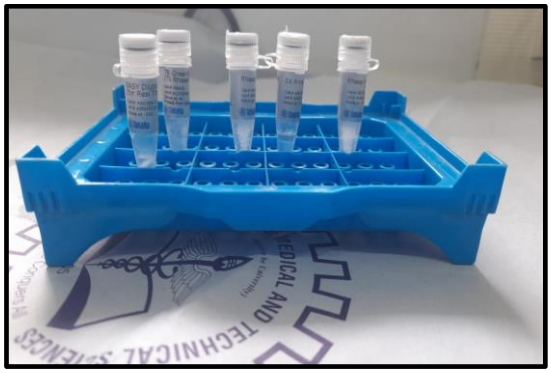


Figure 6. cDNA synthesis kit and Real-Time PCR Master Mix

Molecular docking analysis: Molecular docking studies will be done to explore the possible interaction of active compounds with target proteins. The protein structures were downloaded from the Protein Data Bank. The inhibitory potential was one of the firm bases for establishing a criterion for selecting the compounds to be docked. The chemical structures of compounds were taken from PubChem, a chemical database. Molecular docking simulations were carried out with molecular docking software like PyRx, incorporating a grid-based procedure. 2D and 3D visualisations were performed on PyRx and Biovia Discovery Studio.

Statistical Analysis

Results are expressed as means ± SEM from three different and independent experiments performed in triplicate. One-way ANOVA will be conducted, with significance considered at $p<0.05$.

RESULTS

Gene expression analysis: mRNA expression of apoptotic molecules

The beta-catenin mRNA expression levels of treatments are shown in a bar graph Fig 7). When compared to the control group, beta catenin-mRNA levels dramatically rise at a concentration of 20 µM. Nevertheless, the levels fall considerably below the 20 µM and control groups at 40 µM. This points to a biphasic response in which beta-catenin is upregulated at lower treatment concentrations (20 µM), potentially enhancing cell survival or proliferation. On the other hand, beta-catenin is downregulated at a higher concentration (40 µM), which may help cause apoptosis or decrease proliferation.

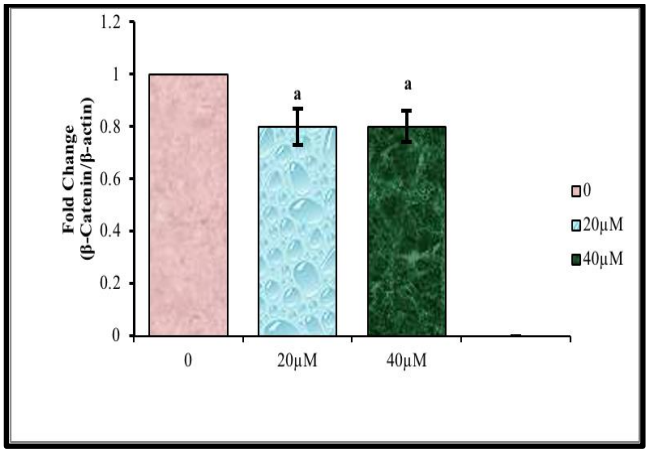


Figure 7. Beta-catenin mRNA expression levels in cells treated with 20 µM and 40 µM dosages of rutaecarpine

Fathima Shirin, Vishnu Priya Veeraraghavan, Selvaraj Jayaraman. Effect of tetradium ruticarpum and its bioactive compounds on intrinsic apoptotic signalling in oral squamous cell carcinoma (OSCC) cells in vitro:Role of WNT/BETA catenin signalling. *Bulletin of Stomatology and Maxillofacial Surgery*. 2025;21(2).163-173: doi:10.58240/1829006X-2025.2-163

The pattern of Bcl-2-mRNA expression is comparable to that of beta-catenin. Increased expression is indicated by the significantly greater Bcl-2-mRNA levels at 20 μM compared to the control. Bcl-2-mRNA levels fall below control levels at 40 μM. One anti-apoptotic protein is called Bcl-2. A rise in expression at 20 μM implies that cell survival may be enhanced by the therapy at this dose. The decrease at 40 μM suggests that there may be a pro-apoptotic effect, which would intensify cell death processes (Fig 8).

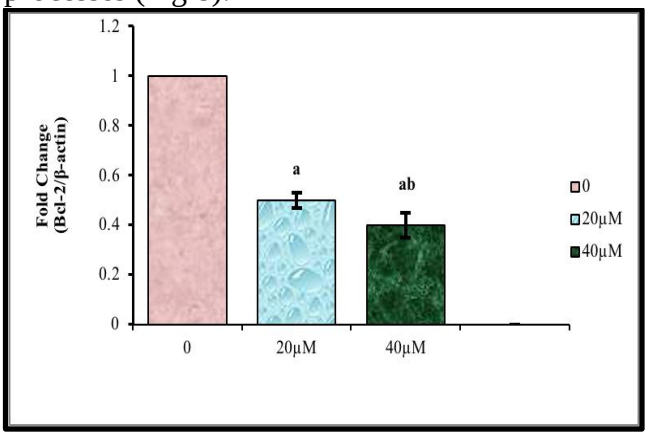


Figure 8. Bcl-2 mRNA relative expression levels in cells treated with 20 μM and 40 μM Rutaecarpine concentrations.

The control group had the greatest levels of Wnt mRNA, which subsequently decreased dramatically when treated with 20 μM and 40 μM. The survival and multiplication of cells depend on Wnt signalling. Because Wnt mRNA expression is lower at both treatment dosages, the treatment may inhibit Wnt signalling, which would lead to a decrease in cell proliferation and an increase in apoptosis (Fig 9).

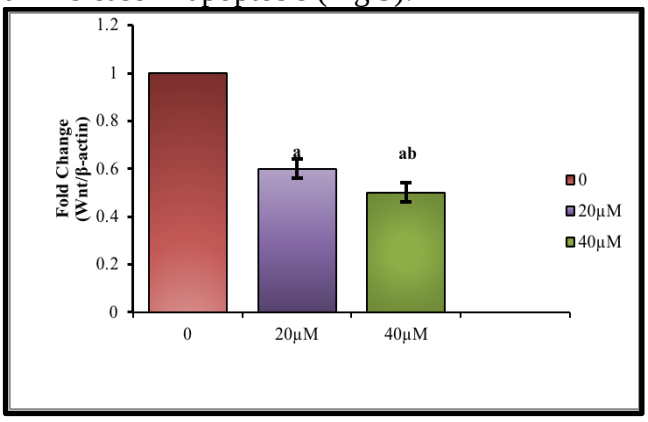
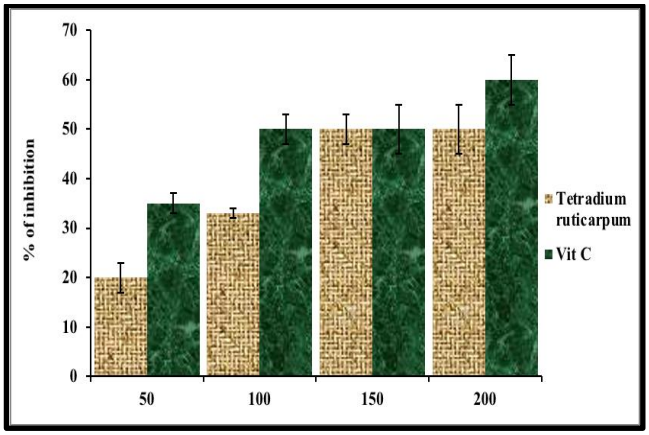


Figure 9. Differential Wnt mRNA expression levels in cells treated with 20 μM and 40 μM rutaecarpine

In vitro biochemical analysis: The bar graph shows that as treatment concentrations rise from 50 to 200 μg/mL, DPPH radical scavenging activity increases as well. The DPPH assay quantifies a substance's ability to function as an antioxidant. The medication appears to have strong antioxidant qualities, according to the results, and these properties get stronger with concentration. The capacity to scavenge free radicals can shield cells from the damaging effects of oxidation (Fig 10).



The protein denaturation inhibition increases concentration-dependently from 50 to 400 μg/mL of the therapy, as seen in the bar graph. Inflammatory processes are linked to protein denaturation.

Greater inhibition at higher treatment concentrations suggests that the compound has strong anti-inflammatory qualities, as it prevents protein denaturation, which lowers inflammation (Fig 11).

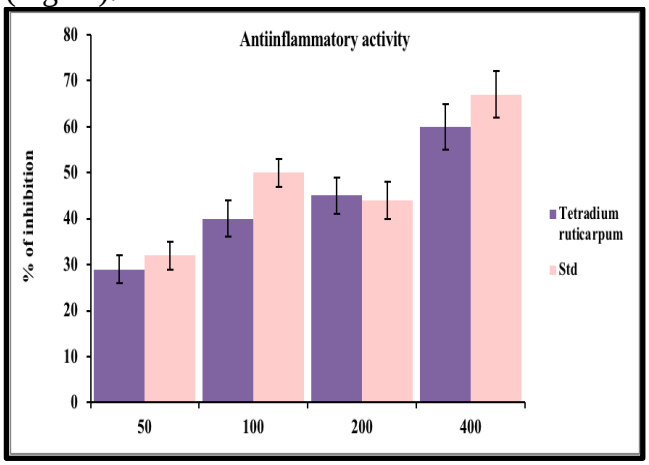


Figure 11. Rutaecarpine's effect on the prevention of protein denaturation at different doses (50-400 μg/mL).

Cell viability: As can be seen from the pictures

and bar graph, cell viability dramatically drops under 20 μM and 40 μM treatments, with the drop being more pronounced at 40 μM. The treatment's cytotoxic effects are indicated by decreased cell viability at increasing concentrations. Cell viability starts to decline at 20 μM and gets even more obvious at 40 μM, indicating that the treatment causes dose-dependent cell death (Fig 12).

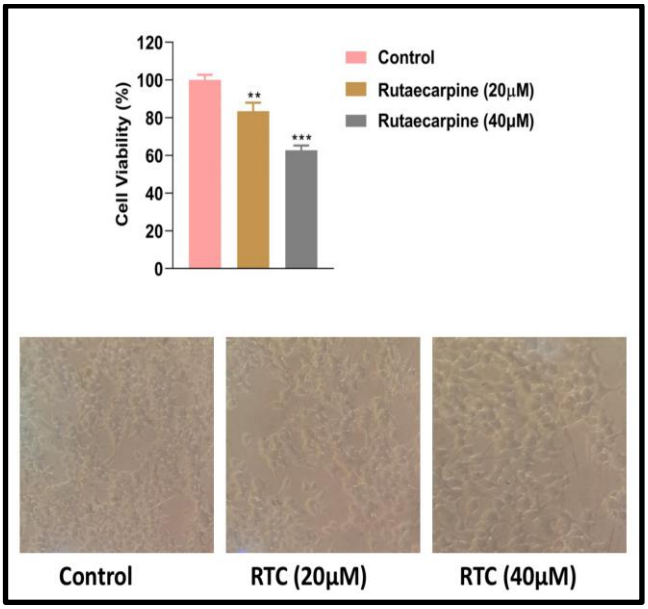


Figure 12. Cell viability assay for cells treated with and without rutaecarpine (20 μM and 40 μM). Cell morphology is represented by images, and cell viability is expressed as a percentage of control in a bar graph.

Molecular docking analysis; interaction of Rutaecarpine with apoptotic signalling molecule: Rutaecarpine's contact sites and binding energies with Wnt, Bcl2, and β Catenin proteins are displayed in the docking images and data table for Wnt-Rutaecarpine, Bcl2-Rutaecarpine, and β Catenin-Rutaecarpine.

According to molecular docking studies, rutaecarpine can attach to important apoptotic signalling molecules. These proteins' functions may be modulated by this binding, impacting apoptotic pathways.

Binding to β Catenin and Wnt, for instance, may disrupt their functions in cell survival and prolife (Fig 13-15).

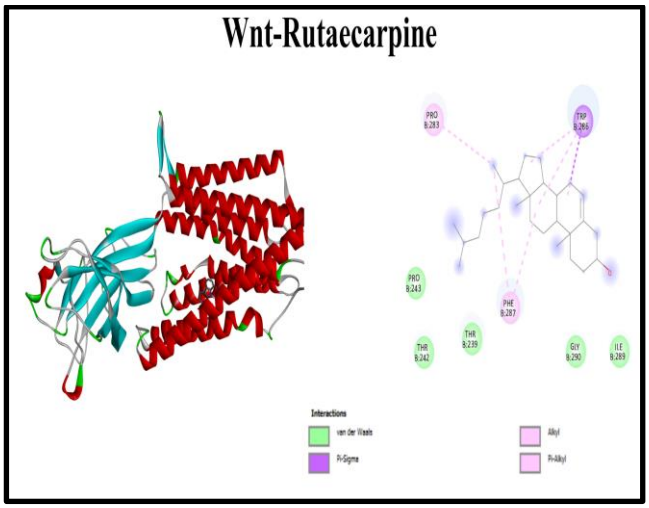


Figure 13. Rutaecarpine and Wnt protein interaction depicted in a molecular docking model.

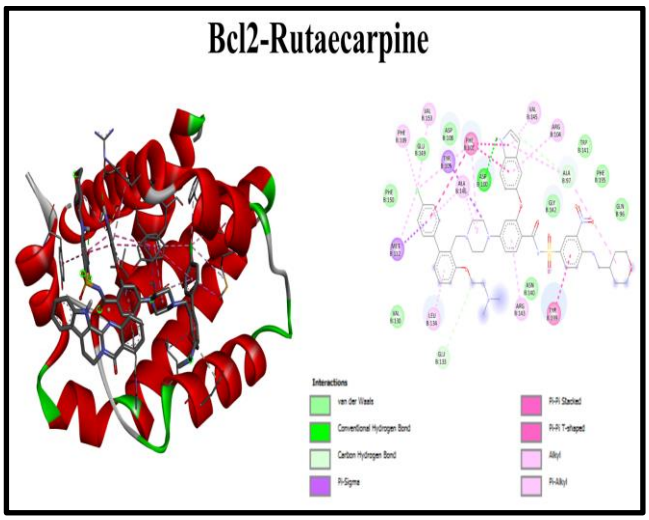


Figure 14. Molecular docking showing rutaecarpine's binding to the Bcl2 protein.

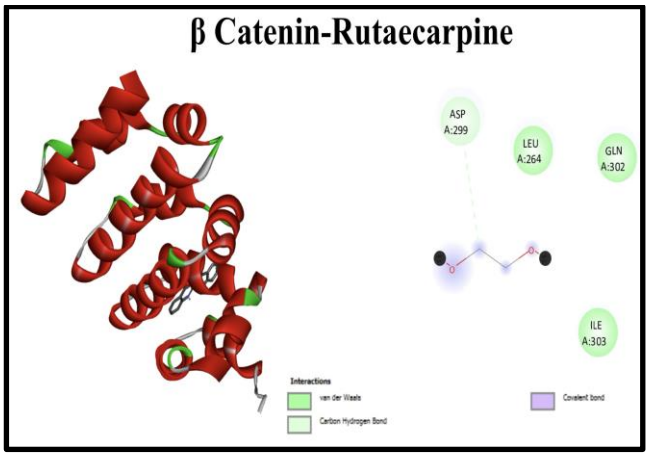


Figure 15. The visualisation of Rutaecarpine binding to β Catenin via molecular docking.

S.No	Ligand	Target	Binding energy (kcal/mol)
1	Rutaecarpine	Bcl2	-6.3
2		β cateni	-8.0
3		Wnt	-9.4

Table 1: Rutaecarpine's binding affinities with apoptotic signalling molecules, which show how well each target protein interacts with Rutaecarpine.

Amplification plots showing gene expression analysis: The alterations in gene expression levels over cycles for various treatments are shown in the amplification graphs. The changes seen in the bar graphs for the gene expression analysis are confirmed by the amplification plots. They offer a quantitative real-time measurement of mRNA levels, verifying if certain genes are upregulated or downregulated in response to the therapies. Plots demonstrating the efficiency and amount of changes in gene expression support the patterns in mRNA levels of beta-catenin, Bcl-2, and Wnt (Fig 16).

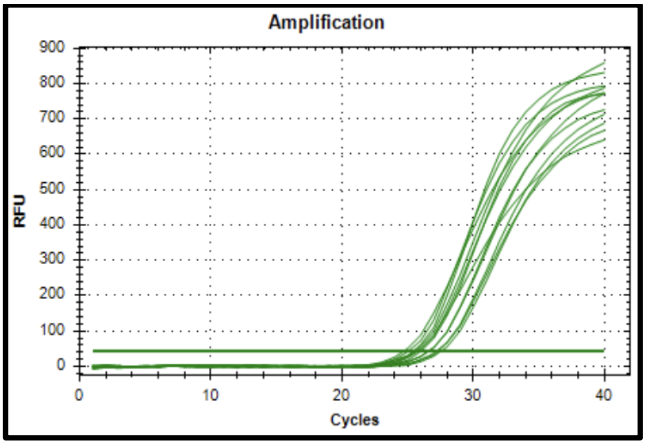


Fig 16: Amplification plots showing the levels of gene expression of apoptotic markers (Bcl-2, Wnt, and beta-catenin) in response to treatment with rutaecarpine. The information shows the relative expression of mRNA during amplification cycles.

DISCUSSION

Oral squamous cell carcinoma (OSCC) is the most prevalent form of oral cancer, representing over 90% of cases. It exhibits varying degrees of histological differentiation and is characterized by its high potential for invasion and metastasis.[20-22] Current treatment strategies primarily involve a combination of surgery, chemotherapy, and radiotherapy. However, these approaches often fail to significantly improve long-term survival rates and are frequently associated with severe side effects.[20-22] As a result, there is growing interest in exploring therapeutic agents derived from medicinal plants, which are believed to offer fewer or no adverse effects. Among the various signaling pathways implicated in oral carcinogenesis, the Wnt/beta-catenin pathway stands out as a key contributor to the development and progression of OSCC. This pathway plays a critical role in regulating cell proliferation, differentiation, and invasion in oral tissues, making it an important target for potential therapeutic strategies.

The beta-catenin mRNA expression levels in relation to treatments are shown in a bar graph. When compared to the control group, β-catenin-mRNA levels dramatically downregulated at a concentration of 20 and40 μM. This biphasic response, where beta-catenin is upregulated at lower treatment concentrations and downregulated at higher concentrations, has been observed in other studies examining the effects of natural compounds on Wnt/β-catenin signalling in cancer cells.[23] The upregulation at lower doses may enhance cell survival or proliferation, while the downregulation at higher doses may help cause apoptosis or decrease proliferation, as reported in previous research. [24]

The pattern of Bcl-2-mRNA expression observed in this study is comparable to previous reports on the effects of Rutaecarpine's and its bioactive compounds on Bcl-2 expression in other cancer cell types.[25] The significantly low Bcl-2-mRNA levels at 20 μM compared to the control suggest that the compound treatment induces apoptosis in oral cancer cells indicating that potential pro-apoptotic effect at the higher concentration, which could intensify cell death processes.[26, 27] This is consistent with previous research demonstrating that inhibition of Wnt

signalling can lead to reduced cell proliferation and increased apoptosis in cancer cells.[25] The survival and multiplication of cells depend on Wnt signalling. Because Wnt mRNA expression is lower at both treatment dosages, the treatment may inhibit Wnt signalling, which would lead to a decrease in cell proliferation and an increase in apoptosis.[28, 29, 30-32]

The protein denaturation inhibition increased concentration independently from 50 to 400 μg/mL of the therapy, as seen in the bar graph. This finding is consistent with previous studies demonstrating the anti-inflammatory properties of *Tetradium ruticarpum* and its bioactive compounds. Inflammatory processes are linked to protein denaturation, and the greater inhibition of protein denaturation at higher treatment concentrations suggests that the compound has strong anti-inflammatory qualities, as it prevents protein denaturation, which lowers inflammation.[30]

The bar graph shows that as the treatment concentrations of Tetradium ruticarpum extract rise from 50 to 200 μg/mL, the DPPH radical scavenging activity increases as well. The DPPH assay is a common method to quantify a substance's ability to function as an antioxidant. Consistent with previous studies on the antioxidant properties of *Tetradium ruticarpum* and its bioactive compounds,[29,31] the results indicate that the extract has strong antioxidant qualities, and these properties become more pronounced with increasing concentration. The capacity to scavenge free radicals can shield cells from the damaging effects of oxidation, which is an important mechanism in the potential anticancer effects of this traditional Chinese medicinal herb.[30, 32]

The observed concentration-dependent decrease in cell viability is consistent with previous reports on the anticancer effects of *Tetradium ruticarpum* and its bioactive compounds in various cancer cell lines. Consistent with these prior studies, the current results show that cell viability dramatically drops under 20 μM and 40 μM treatments, with the effect being more pronounced at the higher 40 μM concentration. This concentration-dependent cytotoxicity is indicative of the treatment's ability to induce cell death, as evidenced by the declining cell viability starting at 20 μM and becoming even more obvious at 40 μM.[33] The molecular docking analysis revealed that rutaecarpine can bind to key apoptotic signalling molecules such as Wnt, Bcl2, and β Catenin, consistent with previous studies on the compound's interactions with these proteins.[34] The specific contact sites and binding energies for these interactions are shown in the docking images and data table. This binding may modulate the functions of these proteins, thereby impacting apoptotic pathways, as reported in prior investigations.[35] For instance, the binding of rutaecarpine to β Catenin and Wnt could potentially disrupt their roles in cell survival and proliferation, while its binding to Bcl2 may suppress the protein's anti-apoptotic activity and encourage cell death, similar to findings from earlier studies. The alterations in gene expression levels over cycles for various treatments are shown in the amplification graphs. The changes seen in the bar graphs for the gene expression analysis are confirmed by the amplification plots. They offer a quantitative real-time measurement of mRNA levels, verifying if certain genes are upregulated or downregulated in response to the therapies.[36, 37] Plots demonstrating the efficiency and number of changes in gene expression support the patterns in mRNA levels of beta-catenin, Bcl-2, and Wnt, consistent with previous studies on the effects of *Tetradium ruticarpum* and its bioactive compounds on apoptotic signalling pathways.[38]

CONCLUSION

In conclusion, this study demonstrates the potent anticancer effects of Tetradium ruticarpum and its bioactive compound rutaecarpine against oral squamous cell carcinoma cells. The findings suggest that rutaecarpine induces apoptosis in oral cancer cells by modulating the Wnt/β-catenin signalling pathway. Rutaecarpine exhibits a biphasic effect, initially enhancing pro-survival signalling at lower concentrations, but at higher doses, it downregulates key apoptotic regulators to trigger cell death. These results warrant further investigation of Tetradium ruticarpum and rutaecarpine as a potential therapeutic strategy for the treatment of oral squamous cell carcinoma.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance

with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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CASE SERIES

HUMAN PAPILLOMAVIRUS –RELATED ORAL LESIONS IN KUWAIT – CLINICAL CASE SERIES

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Abstract

Human papillomaviruses (HPV) are known to be a causative agent for a number of papillary lesions. The variants HPV-16 and HPV-18 have been linked with cervical, oropharyngeal, and lung cancers. HPV is also responsible for HPV-related oral lesions (HPVOL), which can clinically manifest as squamous papilloma, verruca vulgaris, condyloma acuminatum, and multifocal epithelial hyperplasia.

This review paper presents cases of benign oral manifestations of HPV infections in patients attending oral medicine clinics in Kuwait. We present a case series of human papillomavirus-related oral lesions (HPVOL) presented to our oral medicine clinics, with emphasis on the possible risk factors for its increased incidence.

Known risk factors for the development of an HPV infection have been highlighted with emphasis on changing sexual practices, smoking, alcohol consumption, and poor oral hygiene in the EMENA region. While the prevalence of oral HPV in men and women aged between 14 and 69 years is around 7%, unsafe sex practice was scored the lowest in Kuwait. Further, there tends to be a higher prevalence of HPV oral infection with smoking and alcohol intake, and both can act synergistically in the presence of an oral HPV infection, further increasing the oncogenic potential of HPVOL. Poor oral hygiene is also a known factor in HPVOL.

The role of dental practitioners is to raise awareness of the risk of developing HPV and the preventive measures to reduce that risk. These include engaging in safe sexual practices, smoking cessation, and improving oral hygiene. Incorporating the HPV vaccine into the national immunization scheme could contribute to increase in vaccine uptake and hence better population immunity. The recognition of the clinical presentations of HPVOL as presented herein, facilitates dentists' diagnostic skills and aids in making appropriate referrals.

Keywords: Human papillomavirus (HPV), HPV-related oral lesions (HPVOL), HPV vaccine

INTRODUCTION

Human papillomaviruses (HPV) are recognized as causative agents for a group of clinically presenting papillary lesions. Specifically, high-risk HPV types such as HPV-16 and HPV-18 have been linked with cervical, oropharyngeal, and lung cancers.[1] HPV is also responsible for HPV-related oral lesions (HPVOL), such as squamous papilloma (α group) and verruca vulgaris (β group), as it targets the squamous epithelium of mucous membranes.[2] The molecular basis of HPV carcinogenesis involves the integration of viral DNA into the host genome, which leads to genomic instability and ultimately progression to malignancy.[3-5]

The most common route of infection is sexual transmission, including oral sex, or through saliva via mouth-to-mouth contact. Oral sex is one of the major risk factors for HPV infection.

Alternative routes of transmission, including non-sexual ones, have also been reported. However, a main issue with HPV infection is the high percentage of asymptomatic cases, allowing unintentional transmission.[6] HPVOL can manifest in various clinical forms, such as squamous papilloma, verruca vulgaris, condyloma acuminatum, and multifocal epithelial hyperplasia. Although the clinical features of these entities vary, common features include the

presence of newly noticed mucosal abnormality, a burning sensation in the mouth, and the presence of verrucous or papillary lesions around the lips, tongue, and inner sides of the cheeks and lips.[7] Additionally, HPV presence has also been depicted across a spectrum from benign lesions to potentially malignant lesions, being more prevalent among more advanced cases.[8,9] This suggests that dentists play a critical role in the early detection and monitoring of HPVOL through thorough history taking and clinical examination at routine visits.

Although HPV is a known causative agent of oral lesions globally, evidence investigating HPVOL in Kuwait is severely lacking.

Herein, we present a case series of HPVOL attending the Oral Medicine Clinic, with emphasis on the possible risk factors for its increased incidence within the Kuwaiti population.

Case Series

The most common entity of all HPVOL is squamous papilloma (SP). This entity usually manifests as a small cauliflower-like lesion with a white granular or papillomatous surface (Figure 1).



Figure 1. Cauliflower-like lesion with a white granular or papillomatous surface at the junction of hard and soft palate.

Some lesions, however, may appear larger (Figure 2 and 3). They are usually solitary but multiple lesions may occur in the same patient.



Figure 2. Large squamous papilloma involving the hard palate.



Figure 3. Large squamous papilloma involving the hard palate.

SP commonly involves the soft and hard palate, but other sites may be affected such as the tongue (Figure 4), and labial or lip mucosa (Figure 5).



Figure 4. Squamous papilloma involving the dorsum surface of the tongue in a female.



Figure 5: Cauliflower-like lesion involving the upper labial/lip mucosa consistent with squamous papilloma.

Verruca vulgaris (VV) is another entity induced by HPV. They clinically present as asymptomatic, small exophytic growths with finger-like projections, often clinically indistinguishable from SP (Figure 6). The The soft palate and tongue are common sites of involvement (Figures 6 and 7). It is increasingly being detected in females (Figures 8 and 9).



Figure 6. Verruca vulgaris involving the right lateral tongue.



Figure 7. Verruca vulgaris involving the junction of hard and soft palate.



Figure 8. Verruca vulgaris involving the tongue in a young female.



Figure 9. Verruca vulgaris involving the tongue in a young female.

Condyloma acuminatum is rare in the oral cavity, however common in the anogenital region. Oral condyloma is therefore likely in patients whose sexual partners are affected with genital condyloma. In the oral cavity, lesions clinically appear as soft, pink nodules that coalesce into cauliflower-like growths (Figure 10). They tend to be larger in size compared to other HPVOL.



Figure 10. Oral condyloma appearing clinically as soft, pink nodules that coalesce into cauliflower-like growths.

Multifocal epithelial hyperplasia is another uncommon entity of HPVOL. They are clinically characterized by multiple asymptomatic papulonodular lesions. The clinical presentation usually reveals multiple well-demarcated papules with papillomatous surfaces (Figure 11). The gingiva is a common site of involvement (Figure 11).



Figure 11. Multiple papulonodular involving the gingiva consistent with multifocal epithelial hyperplasia.

Risk factors

Several risk factors have been linked to an increased incidence of HPVOL. This considerable increase is explained by changes in sex behavior and the increased practice of oral sex. HPVOL was observed more frequently among male gender than their female counterparts. A recent meta-analysis found that all types of oral HPV are higher in cases where

men have sex with men than with females (12.2% versus 2.9%).[10] Although unsafe sex is recognized as a risk factor for HPVOL, Kuwait has recorded one of the lowest global age-standardized mortality rates (ASMR) and age-standardized DAILY rates (ASDR) attributable to unsafe sex practices.[11] Moreover, HPVOL has been reported to be more prevalent among current smokers and alcohol drinkers.[12] Prior evidence conducted a study investigating prevalence of smoking in the region, it was found that around 34.4% of participants were current smokers, and smoking was most prevalent among young age groups (≤ 20 years).[13] This highlight smoking as a major risk factor for HPVOL in the Kuwaiti population, suggesting that dentists can significantly contribute to mitigating HPVOL incidence through smoking cessation and reducing alcohol consumption.

Poor oral hygiene can increase the susceptibility to HPV infection. Gingivitis and periodontitis have been identified as potential routes for HPV infection.[14] Furthermore, a higher infection rate was observed among denture users, indicating that injuries to oral mucosa, resulting from mechanical stimulation of dentures coupled with poor denture hygiene may contribute to HPV infection.[10,14] Other risk factors such as oral and facial piercings, have been implicated in infectious diseases such as hepatitis B, and hepatitis C and human immunodeficiency virus (HIV), yet their role in HPVOL remains an area of ongoing investigation.[15]

The HPV vaccine is a well-established method to mitigate the risk of HPV and HPVOL. A recent report has reported higher willingness to accept vaccine in the region if vaccine was offered free-of charge versus when payment is required (69.8% versus 23.1%).[6] However, hesitancy towards the HPV vaccine included factors such as a lack of confidence in the vaccine, and complacency regarding the risks of HPV disease. Nevertheless, the findings of this study cannot be generalized as it only included university students and excluded male participants from the study.[6]

Discussion

This case series illustrated cases of benign oral manifestations of HPV infections in patients attending an oral medicine and pathology clinics in Kuwait. These include squamous papilloma, verruca vulgaris, condyloma acuminatum and multifocal epithelial hyperplasia, which are most commonly caused by low-risk HPV subtypes 6,11,2 and 4.[16]

A review of the literature reported 481 cases of squamous papilloma of which 50% were HPV positive, and 284 cases of oral condylomas of which 75% were HPV positive.[17]

Prevalence

Little to no data regarding the prevalence of HPVOL in the Kuwaiti population is present in the literature. With regards to genital HPV infections, a single study was found which investigated the prevalence of HPV infections in 3011 women with normal cervical cytology attending a gynecology clinic in Kuwait.[18] Of all women, 2.4% tested positive for the presence of HPV DNA, of which 71.8% were infected with low-risk HPV subtypes and 32.3% were infected with high-risk HPV subtypes.[18] No oral examination was undertaken to look for concomitant oral HPV infection in the Kuwaiti women. A US-based study identified the prevalence of oral HPV in men and women between ages of 14 and 69 at 7.3%, and at 1.1% for HPV 16, with higher rates in men than women.[19] Evidence regarding the concordance of genital and oral HPV is conflicted in the literature. A study found that the risk of subclinical oral HPV is higher in both women with cervical HPV as well as their male partners.[20] Men with a genital HPV infection were found to be four times more likely to present with an oral HPV infection.[21] However, another study found no higher risk of oral HPV in female participants with cervical HPV.[22] Studies investigating the prevalence of HPV in the Extended Middle East and North Africa (EMENA) region have focused mainly on cervical HPV rather than oral HPV. Review of the literature concluded that the overall prevalence of HPV infections in the region is lower than those estimated from western countries.[23] It has been hypothesized that the comparatively lower prevalence could be due to the fact that socially accepted sexual behaviors in the region are more conservative.[24]

Modes of HPV transmission

To predict the trends of HPV prevalence in any given population, the risks of transmission need to be examined. The mode of transmission of HPV can be horizontal; through sexual intercourse, including oral sex, or through saliva via mouth-to-mouth contact.[16] HPV may also be transmitted vertically from an infected mother to her offspring at birth.[17] As with other sexually transmitted diseases, engaging in sexual intercourse earlier in life and with a higher number of sexual partners increases the risk of transmission.[19] Some studies have attributed an increase in risk of oral HPV infection to an increase in the frequency of oral sex.[16] Other studies have contested this claim, stating that it is mouth-to-mouth transmission via saliva, rather than oral sex, that poses a significant risk of infection between partners.[17] A study that followed up Finnish couples over a seven-year period found that a change in marital status and frequency of sexual intercourse

had an impact on the incidence of genital HPV in men, while the number of sexual partners had an impact on the incidence of oral HPV infections.[24] This supports the claim that having a stable monogamous relationship can reduce the risk of both oral and genital HPV infections.[24] The data on the average number of sexual partners and average age of initiation of sexual activity in the Kuwaiti population is not currently available. Although low, the rising trend in sexually transmitted diseases (STDs), including HPV, in the EMENA region has been attributed to changes in sexual behavior of young people.[9] These include engaging in premarital sex, oral and anal sex, and unprotected sex.[25] In areas where the practice of temporary marriage is socially legitimatized, the probability of having multiple partners is higher.[25] Further contributing to this trend is a lack of sexual and reproductive health services in the region, as well as the social stigma associated with STDs acting as a barrier to treatment seeking behavior and disease notification.[25]

A group of patients whose diagnosis maybe be missed and hence may contribute to an increased risk of transmission in the population, are those who have not yet had sexual intercourse. Although rare, the risk of an HPV infection in a child with an HPV positive mother is higher when compared to children with an HPV negative mother.[17]

A population group in which the prevalence of HPV is found to be higher than the general population are those who are current users or have a history of injectable drug use.[26] Among this group, those who were HIV positive and had a lower CD4 count were reported to be at an increased risk of oral HPV infection, compared to HIV positive patients with a higher CD4 count, indicating that HIV induced immunosuppression may increase patients ' vulnerability to oral HPV.[26]

HPV Vaccination

With the introduction of HPV vaccines, HPV infections have become largely preventable. Evidence showing an increase in HPV antibodies in saliva following HPV vaccination, may indicate the role of the vaccine in protecting against oral HPV infections.[17] The effectiveness of the vaccine in reducing the risk of transmission on a population level relies on the reach of the program and the resultant herd immunity.[17] Global coverage of eligible females is reported at 17%.[27] Although the vaccine is available in Kuwait, it has not yet been incorporated into the national immunization scheme. A study which interviewed female schoolteachers in Kuwait found that 88% were unaware of the availability of an HPV vaccine, and of those that were aware, 83% were unvaccinated.[28] Beyond the lack of a nationwide government endorsed vaccination scheme, the barriers to uptake of HPV vaccination in Kuwait seem to include lack of public awareness of the impact of the disease and the effectiveness of the vaccine as a protective measure.[28,29] This highlights the importance of social awareness campaigns to promote the uptake of the vaccine. Additionally, disseminating information regarding the risks of transmission, including those associated with sexual behavior, can help encourage protective sexual practices. It is important for those at risk of infection to be aware of the need for regular review at a dental clinic as oral HPV infections can be subclinical.[16] This could potentially help increase early detection, thus limiting the spread of infection. Dental professionals have a role in educating their patients on how to reduce their risk of oral HPV infections and how to protect others from infection.

High-risk HPV types

It is important to note that high risk HPV subtypes 16 and 18 can result in oral lesions with potential for malignant change.[16] In a systemic review conducted by Kreimer et al, 23.5% out of 2,642 oral squamous carcinoma cases and 35.6% of 969 oropharyngeal carcinoma tested positive for HPV.[29] Smokers tend to have a higher incidence of oral HPV infection with an increased risk of persistence.[17,19] Furthermore, tobacco use and alcohol intake are both risk factors for the development of oral cancers and may act synergistically in the presence of an oral HPV infection, further increasing the oncogenic potential of the HPVOL.[30]

Conclusion

This review paper presented cases of benign oral manifestations of HPV infections in patients attending oral medicine clinics in Kuwait. Further data is required to develop a better understanding of the prevalence and impact of HPVOL as well as the trends of transmission within the Kuwaiti population. Known risk factors for the development of an HPV infection have been highlighted with emphasis on changing sexual practices, smoking, alcohol consumption, and poor oral hygiene in the EMENA region. The role of dental practitioners is to raise awareness of the risk of developing HPV and the preventive measures to reduce that risk. These include engaging in safe sexual practices, smoking cessation, and improving oral hygiene. Incorporating the HPV vaccine into the national immunization scheme could contribute to increase in vaccine uptake and hence better population immunity. The recognition of the clinical presentations of HPVOL as presented herein, facilitates dentists 'diagnostic skills and aids in making appropriate referrals.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The authors declare to have conducted their research in accordance with the World Medical Association Declaration of Helsinki.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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REVIEW ARTICLE

COMPLICATIONS IN ENDOSCOPIC SINUS SURGERY:A NARRATIVE REVIEW

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ABSTRACT

Endoscopic sinus surgery has become a widely used technique in the treatment of chronic sinus disease, but it is sometimes accompanied by various complications, especially when used by less experienced surgeons. The risk of injury is closely related to the anatomical features, the degree and severity of the disease, the results of previous operations, and the experience of the surgeon.

The aim of this literature review is to analyze the complications associated with endoscopic sinus surgery; searches were conducted in various scientific databases, including PubMed, EMBASE, Europe PMC, PubMed, Medline, Scientific Information Database (SID) and Google Scholar. Of the total 126 entries, 32 were reviewed. The complication rate associated with endoscopic sinus surgery is not high, and improvements in surgical technology and experience may reduce its side effects. Knowledge of anatomy, good preparation, and meticulous surgical technique are essential. Early recognition and proper management of complications of endoscopic sinus surgery is extremely important to minimize and prevent disability. To minimize the risk of developing these complications, it is necessary to take into account possible anatomical variations in the structure of the paranasal sinuses and orbit, which should be identified using computed tomography at the preoperative stage. To successfully perform endoscopic sinus surgery, the surgeon must be appropriately qualified in the diagnosis and management of potential complications during surgery.

Keywords: chronic sinus diseas, endoscopic sinus surgery (ESS), complication

INTRODUCTION

Diseases of the mucous membrane of the nasal cavity and paranasal sinuses consistently have a high proportion among all diseases of the ENT organs and are one of the most pressing problems in modern otolaryngology.

Among all sinusitis, inflammatory diseases of the maxillary sinuses make up the largest number, which is due to their prevalence, tendency to chronic recurrent courses and insufficiency of traditional treatment methods. Chronic inflammation of the sinus cavity is estimated to occur in more than 15% of adults, and treatment procedures are diverse.[1]

Normally, the sinuses provide voice resonance, humidify and warm the inhaled air, participate in the sense of smell, serve as a heat insulator and provide mucus secretion.

Long-term bacterial, fungal infection, anatomical changes in the nasal cavity (deformation of the nasal septum, proliferation of the mucous membrane of the nasal concussion), allergies, dental diseases can lead to the development of sinusitis (inflammation of the paranasal sinuses).

In cases where medical therapies are ineffective, sinus surgery will be recommended to improve the symptoms associated with the disease.

The problem of surgical treatment of diseases of the maxillary sinuses is far from being finally solved.

Over the past few years, the choice of surgical intervention method on the maxillary sinus in purulent and polypous sinusitis, as well as in cysts, has variedv from the Caldwell-Luc operation with removal of the entire mucous membrane to various methods of "micro maxillary sinusotomy".[2,3]

The Caldwell-Luc operation provides the most complete access to all parts of the maxillary sinus. At the same time, this operation involves fairly large trauma to the anterior and medial walls of the sinus. It can be noted that, despite the complete removal of pathologically altered tissues from the sinus cavity, recovery of patients after such surgical intervention does not always occur.[4,5]

Endoscopic sinus surgery is an effective and safe surgical technique that has revolutionized the surgical treatment of diseases of the nasal cavity and paranasal sinuses.[6-8]

With the endoscopic endonasal approach, the natural opening of the sinus is expanded, thereby providing drainage, but this technology does not always allow for a complete examination of the sinus and careful removal of a cyst, polyps or foreign body.[9] ESS can be performed either with or without image guided navigation (IGN). The main aim of sinus surgery is to allow the surgeon to get access to different areas of the nose and nasal sinuses. This may be in order to remove diseased tissue or get a biopsy to help make decisions about further management.

Indications Endoscopic sinus surgery

- Isolated sphenoid sinus disease, e.g.,
- Aspergillosis
- Purulent bacterial infection
- Inverted papilloma
- Mucocele
- Biopsy of skull base lesions

Surgical Technique

The sphenoid ostium can be found at the level of the superior turbinate. It is often necessary to lateralize the middle and superior turbinate in order to visualize it If visibility is poor because of polyps or bleeding, the sphenoid sinus can safely be approached by staying close to the septum in the midline and palpating with the straight sucker up the posterior wall of the sphenoid At 1-1.5 cm above the posterior choana, the bone of the anterior wall of the sphenoid sinus is thin and it can be punctured by applying moderate pressure with a straight sucker It is advisable not to open the sphenoid ostium downward to a level lower than half the total height of the sinus, as a branch of the sphenopalatine artery runs along its anterior wall and if cut this can bleed briskly. Occasionally, the intersinus septum of the sphenoid is so oblique that one side can be very small. Because of its highly variable anatomy and closely related vital structures, it has many potential complications of endoscopic sinus surgery.

The aim of this literature review is to analyze the complications associated with endoscopic sinus surgery; searches were conducted in various scientific databases, including PubMed, EMBASE, Europe PMC, PubMed, Medline, Scientific Information Database (SID) and Google Scholar. Of the total 126 entries, 32 were reviewed.

According to research conducted by the European Rhinological Society (ERS), complications are classified according to severity into minor and major complications.[10]

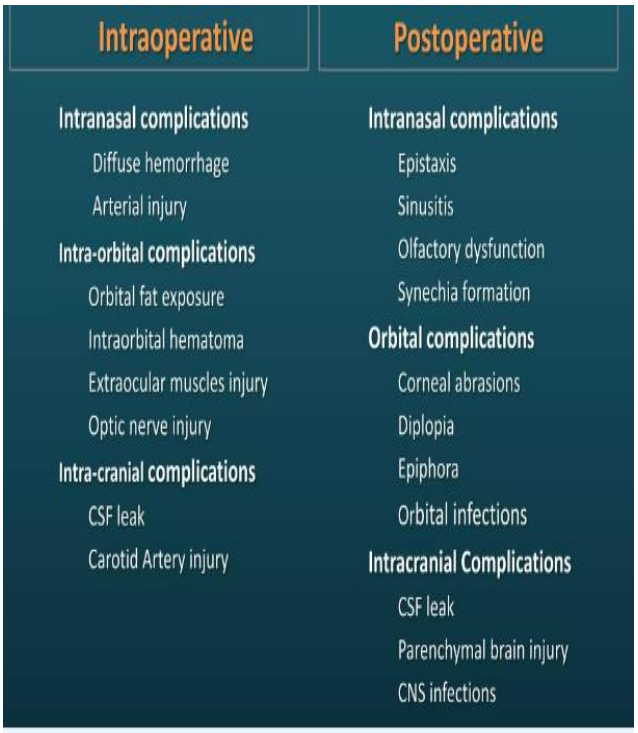
Minor complications and Major complications.[11-14]



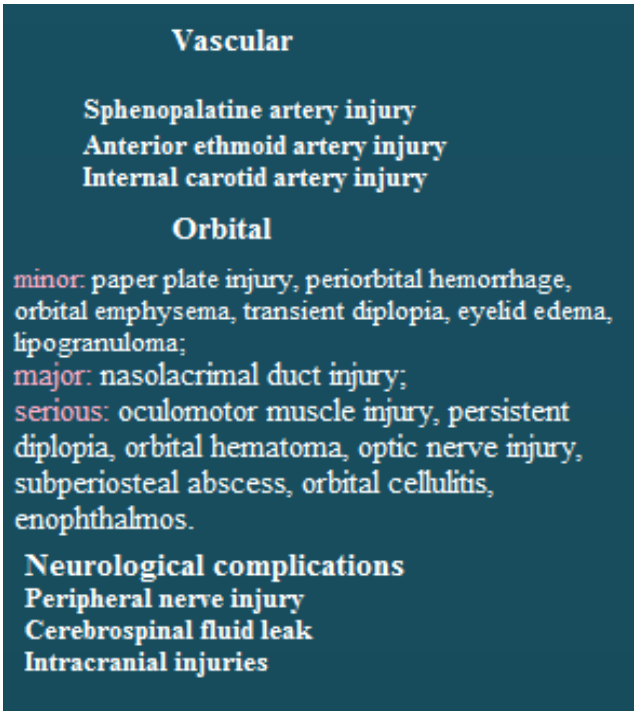
Complications of endoscopic sinus surgery can be intraoperative and postoperative.[15,16]

Stankiewicz (1987) reported an initial 5% major complication rate for his initial 90 endoscopic procedures which reduced to 0.5% for the subsequent.[17]

Intraoperative and postoperative complications of endoscopic sinus surgery



Complications of ESS can be classified according to anatomical location. These include vascular, neurological, ophthalmological, other.[18-20]



The risk of complications during endoscopic sinus surgery (ESS) is always present, and it is necessary to minimize the risks through careful preoperative preparation, careful surgical technique, and diligent postoperative care.

Iatrogenic Factors

- Absence of computed tomography (CT) scan in operating room at time of surgery; considered grounds for malpractice
- Calibration errors with image guidance
- Loss of visualization and poor surgical field
- Failure to identify complications in a timely manner

Patients most at risk for complications include those with revision surgery, extensive disease, skull base anatomic or radiologic variations or dehiscences related to disease or previous surgery, and the use of powered instrumentation.

They are intended to be used with some common sense and to facilitate communication with patients and other physicians.

Complications resulting from damage to blood vessels, including the anterior or posterior ethmoid, sphenopalatine, or internal carotid arteries, are considered major if the hemorrhage affects cerebral circulation or causes a significant drop in hemoglobin levels or requires red blood cell transfusion.

Small amounts of postoperative bleeding that do not require transfusion may be considered minor, as may facial edema, hyposmia, hypoesthesia of the infraorbital nerve or teeth, synechiae, myospherulosis, atrophic rhinitis, and osteitis.[21]

Anterior ethmoid artery injury

Bleeding from the anterior artery can cause significant intraoperative bleeding, resulting in a rapidly expanding orbital hematoma. To prevent artery transection, the important technical point is to pass the microdebride blade from posterior to anterior, with the tip near the base of the skull, and remove the tip at an angle tangent to the base of the skull.

Injury to the branch of the sphenopalatine artery

The sphenopalatine artery is a frequent source of arterial bleeding during ESS. It is usually transected if the anterior sphenoid face is removed superiorly rather than inferiorly, starting from the natural branch, with a downward-pointing instrument. At the end of the operation, it is recommended that the proximal and distal ends of the transected posterior nasal artery be electrocauterized when a large sphenoidotomy is performed.

Due to the proximity of the main stem of the

sphenopalatine artery and the presence of feeder branches, such as the posterior lateral nasal artery and the inferior rhizomatous branch, the posterior fontanelle area of the maxillary sinus is at risk of significant bleeding during antrostomy enlargement.

Internal carotid artery injury

The internal carotid artery can be injured when attempting to remove the sinus septum, and sharp bone fragments can injure the internal carotid artery.

Ophthalmic complications of endoscopic sinus surgery

The ophthalmic complications could be classified as: minor-included injury to the lamina papyracea, major - injury to the lacrimal duct and finally serious - as retroorbital hemorrhage, injury to the optic nerve or any reduction of vision or blindness and injury of orbital muscle.[22-24]

Orbital hematoma could developed as arterial injury (anterior or posterior ethmoid artery) or venous hemorrhage results from entry of the orbit through the lamina papyracea.The hemorrhage can result in visual loss from optic nerve or retinal ischemia. This situation demanded very fast identification and urgent treatment. If the risk is low (low ocular pressure and vision is not compromised) medical treatment is adequate. The optic nerve is commonly dehiscent in the sphenoid sinus or posterior ethmoid. The injury may be indirect (vascular) or direct (mechanical). Direct muscle transection is mostly seen with powered instrumentation surgery. The device extracts tissue very rapidly with very low tactile feedback to the surgeon about the removable material.

The major complications are seen in 0.01-2.25% and some of them can be serious, leading to permanent dysfunction. The incidence of serious complications does not exceed 1%.

Ocular complications can vary in severity from minor, such as localized hematomas, to extremely dangerous, such as damage to the optic nerve leading to complete blindness.[25-27]

Ophthalmic complications of endoscopic sinus surgery are rare but can be potentially dangerous.

Clinical manifestations of orbital injuries can vary from pain and diplopia to complete blindness. The management of these patients with pathology close to the orbit could be associated with serious injuries, leading to permanent dysfunction. It was proved that the extent of the surgery also influenced the rate of complications.

Neurological complications

Complications involving the cranial vault include cerebrospinal fluid (CSF) leakage, tension pneumocephalus, meningitis, abscess, intracranial hemorrhage, direct brain injury, and encephalocele formation.

Cerebrospinal fluid leak

When there is an abundance of inflamed tissue and bleeding around the site of injury, CSF leak may resemble a sudden onset of rapid venous bleeding without any noticeable "washout." If unrecognized or untreated, CSF leak may lead to postoperative pneumocephalus, tension pneumocephalus, meningitis, encephalitis, or epidural or subdural abscess.

Early intraoperative recognition and repair of a CSF leak is important in minimizing the likelihood of serious or long-term sequelae.

Intracranial injuries

Intracranial injuries are extremely rare.The severity of the injury depends on several variables, such as the size and shape of the instrument involved, the type of instrument (electrocautery, electrocautery, cold steel), the depth of penetration, the time between penetration of the skull base and recognition of the complication by the operating surgeon, and the anatomical structures damaged. Depending on the structures affected, the consequences of intracranial injury can include persistent headache, neurological deficits, intracranial hemorrhage, and intracranial infection. Meningoencephalocele can occur in the late postoperative period. Fortunately, these are extremely rare events.

Early postoperative complications may include infection, bleeding, or adhesions; they may occur immediately after surgery up to 2 weeks after surgery. Late complications may include the formation of a mucocele or mucopyocele and may occur many years after the procedure. It should be noted that all of the above classifications are artificial and subject to interpretation. They are intended to be used with some common sense and to facilitate communication with patients and other physicians.

Early signs of orbital hematoma include: a sharp decrease in visual acuity, preseptal edema, bruising, exophthalmos, and increased intraocular pressure. This complication threatens the development of blindness due to compression of the optic nerve in the retrobulbar space and requires immediate treatment.[25-27]

Direct damage to the optic nerve is also quite rare and is mainly associated with mechanical trauma to the nerve with a shaver-microdebrider.[28]

Damage to the extraocular muscles can occur if there is an existing or intraoperative violation of the integrity of the paper plate, and it can lead to the development of diplopia due to muscle entrapment by bone fragments, their direct damage, as well as secondary damage due to nerve trauma.[29]

To prevent intraoperative complications it is recommended to: [30-36]

- identify the contour preoperatively, the presence of infraorbital or supraorbital structures, and their thickness using CT data;
- since the anterior ethmoidal artery is a critical structure, the location of which helps to avoid intraoperative bleeding, a CT image showing a bony protrusion at the junction of the medial rectus and superior oblique muscles is a useful landmark for determining the location of this artery;
- identifying the sphenoethmoid cells (Onodi cells) before performing ECP will help prevent damage to the optic nerve and internal carotid artery;
- the optic nerve and carotid artery form a depression in the lateral wall of the sphenoid sinus. It can be unilateral or bilateral. Some of these depressions have a dehiscence (a gap in the bony canal), which puts the optic nerve and carotid artery at risk. Preoperative axial tomography will help to avoid iatrogenic complications;
- general anesthesia and controlled hypotension will minimize intraoperative blood loss;
- topical decongestants, prothrombotic agents, and bipolar cautery should be available intraoperatively;
- assess the thickness of the periorbital fat pad and the periorbita if the integrity of the paper plate is compromised. If the periosteum of the eye is intact and there is no evidence of orbital trauma, the surgical intervention can be continued. If the periosteum of the eye is damaged and the orbital fat pad is exposed, intraocular pressure should be measured. The presence of periorbital fat or orbital periosteum (periorbita) in the surgical field can be confirmed by gentle balloting of the eye and endoscopic observation;
- avoid blind cautery to prevent injury to the extraocular muscles and optic nerve. Bipolar cautery is effective in situations where bleeding is not associated with the orbit itself;
- keep the patient's eyes open during endoscopic surgery. If there is any evidence of swelling, bruising, or afferent pupillary defect, the operation should be stopped immediately;
- do not use nasal packing over the exposed orbital apex to avoid pressure on the optic nerve.

To minimize the risk of complications, a thorough examination of the patient is necessary at the preoperative stage.

Based on the data of computed tomography of the paranasal sinuses and, in some cases, magnetic resonance imaging, it is necessary to take into account in advance possible anatomical variants of the structure of the paranasal sinuses and orbit.

DECLARATIONS

Conflict of interest and Financial Disclosures

The authors declare no conflicts of interest related to this study and no source of external funding.

Ethical approval

The authors declare to have conducted their research in accordance with the World Medical Association Declaration of Helsinki.

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REVIEW ARTICLE

THE USE OF ZIRCONIUM DIOXIDE IN DENTISTRY AND ORAL IMPLANTOLOGY:NARRATIVE REVIEW

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Abstract

Background: Currently, in dentistry, great importance is attached not only to the functional effectiveness of treatment, but also to the aesthetic appearance. Currently, due to the growing need for alternative materials, there is an interest in the creation of biomaterials with special physicochemical properties and high biocompatibility. Zirconium dioxide has been clinically proven to be a successful restorative material for many different indications, zirconia restorations, veneers and implant-supported structures are in great demand.
The objective of this narrative review was to evaluate the properties, applications and prospects of zirconia dental materials to identify their potential:
Methodology: The sources for literature analysis were the existing literature (Google Scholar, Medline, Scopus, Web Of Sciences, PubMed) that presented the scope of zirconia applications in dentistry, including the main keywords zirconium dioxid, dental zirconia, biocompatibility, mechanical and chemical properties, esthetic properties, zirconia in dentistry and oral implantology, ceramic implants.
Results: Conducted a preliminary search and reviewed 168 titles and abstracts in this review and 64 full-text articles were selected of high methodological quality. The review was conducted according to the PRISMA guidelines. This literature review presents the current knowledge and scientific data on the use of zirconia in dentistry, assessing its advantages and disadvantages when used in various constructions, as well as possible future advances and innovative approaches to improve performance.
Conclusion: The conducted literature review made it possible to identify a number of advantages of modern technologies in orthopedic dentistry using zirconium dioxide (ZrO2), which improves the quality of orthopedic dental care for the population in terms of safety and reliability. This review will allow dentists to have a better understanding of zirconia-based dental structures, which will allow them to take a differentiated approach and make the right choice in different clinical situations, ensuring high functional efficiency and aesthetic appeal.

Keywords: zirconium dioxide, dental zirconia, biocompatibility, mechanical and chemical properties, esthetic properties, zirconia in dentistry and oral implantology, ceramic implants

INTRODUCTION

A modern task in the field of dental materials science is the introduction and use of materials that provide esthetics, functionality and biocompatibility in dental restoration. Companies engaged in the production of dental materials are intensively working on new strategies aimed at further improving the microstructural characteristics of these materials, as well as introducing new production technologies.
In the last decade, zirconia-based dental materials have found wide application in various branches of dentistry due to their important properties such as high flexural strength, biofunctionality, biocompatibility and esthetics.[1]
Due to their opacity, zirconia frameworks are usually covered with ceramic veneers, which provide a more natural appearance but are prone to breakage. As an alternative, veneered zirconia restorations are becoming more widely used today.
Zirconium is a metal chemical element with the symbol Zr and atomic number 40.[2] Zirconia (ZrO2) is a crystalline oxide of zirconium. Zirconium dioxide is in the family of full ceramics, more specifically, the oxide ceramics, also classified as

technical ceramics. Oxide ceramics are polycrystalline materials that are composed of oxides that do not degrade during sintering.It is not found as a pure oxide in nature, but it is mined as a silicate mineral called zirconium (ZrSiO4 gray-white, durable transition metal similar to titanium (fig.1). Zirconium is obtained by chemical processing from a mineral raw material - zirconium sand, partially stabilized with yttrium, from which zirconium blanks are formed mechanically.



Figure.1 Zircon is a soft silver metal

Zirconium dioxide (ZrO2), sometimes called zirconia. German chemist Martin Heinrich Klaproth (1743-1817) discovered the element zirconium in 1789, analyzed a zircon and separated zirconium in the form of its 'earth' zirconia, which is the oxide ZrO2. Klaproth first named the new element Zirkonerde (zircon earth, or zirconia). English chemist Sir Humphry Davy (1778-1829) suggested the name zirconium in the early 1800s. Klaproth failed to isolate the pure metal itself. In 1824, the element was isolated when the Swedish chemist Jöns Berzelius heated potassium hexafluorozirconate (K2ZrF6) with potassium metal and obtained some zirconium as a black powder that was 93% zirconium, but he could not purify it further. It was not until almost one hundred years later that high-purity zirconium could be made. This delayed progress in studying the element. The element zirconium is named after the mineral in which it was discovered, zircon.[3]

The word "zircon" was probably derived from the Persian word zargun, which means"gold-like" or "golden-colored." Some zircon crystals have a gold color.

The main sources of zirconium are zirconate (ZrO2-SiO2, ZrSiO4) and baddelyite (ZrO2), and most of the material used is chemically extracted from these two minerals. Zirconium dioxide (ZrO2) resulting from baddelyite, which is also known as zirconia.[4,5] The resulting reagent powder is mixed with additives. A distinction is made between agglomeration additives, which especially affect the sintering characteristics and the characteristics of the finished ceramics, and auxiliary materials, which facilitate shaping. Accordingly, zirconium dioxide blanks are manufactured using various methods. The spatial arrangement of atoms in zirconia is characterized by different crystallographic structures, which are characterized by certain geometrics and have three basic volumetric parameters: monoclinic, tetragonal and cubic (Fig. 1а,б,в).[6]

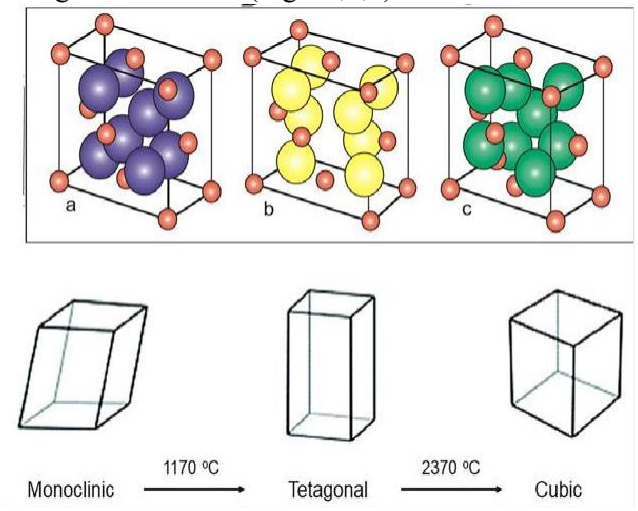


Figure 2. Crystal structure of monoclic (a), tetragonal (b) and (c) cubic zirconia

It exists in nature in three different crystal configurations at different temperatures. Pure zirconium has a monoclinic structure at room temperature, which is stable up to 1170°C. Between this temperature and 2370°C, tetragonal zirconium dioxide is formed, while cubic zirconium dioxide is formed at a temperature higher than 2370°C. Then cooling, the tetragonal form transforms back to the monoclinic form.[7]

Transformation from tetragonal to monoclinic phase can be used to improve the mechanical properties of zirconium, especially its strength. The mechanism involved in this is known as a catalytic converter. To stabilize zirconium, yttrium oxide (Y2O3), calcium oxide (CaO), or magnesium oxide (MgO) are added to it, which allows it to maintain its weld shape at room temperature after annealing. Addition of various amounts of stabilizers can lead to obtaining exceptional properties, such as high bending and tensile strength, high hardness, excellent chemical resistance and good conductivity. Zirconium in the form of pure oxide is not found in nature. Besides zircon, zirconium occurs in over 140 other minerals, including baddeleyite and eudialyte. Its most natural form, with a monoclinic crystal structure, is a rare mineral. Baddelites are the main sources of the material and require a significant amount of processing to obtain zirconium.[8]

Today, zirconia in dentistry is commonly used as a modified yttria (Y2O3) tetragonal zirconium polycrystal (Y-TZP) because it has great mechanical properties. The addition of yttria improves the physical properties of zirconium. Zirconia-based dental materials mainly consist of two components: i.e., framework (Yttria Stabilized Tetragonal Zirconia Polycrystal 3Y-TZP).

- Based on the yttria content, zirconia is classified into three main groups:
- The first group is strong, 3 mole % Y-TZP (mostly tetragonal)
- The second group is more translucent, 4 mole % Y-TZP
- The third group is more translucent, 5 mole % Y-TZP with reduced mechanical properties:

Processing of zirconium includes separation and removal of unwanted materials and impurities - silica from zircon and oxides of iron and titanium from baddeleyite (fig. 3).

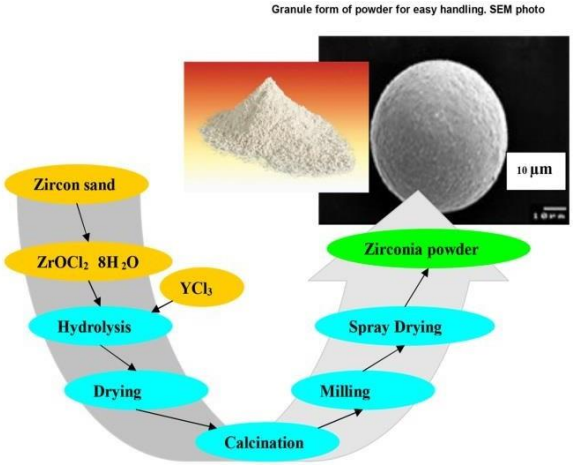


Figure 3. Production of Zirconia powder

The refined zircon is then purified into pure zirconia. There are several routes to the extraction of zirconia from zircon including:

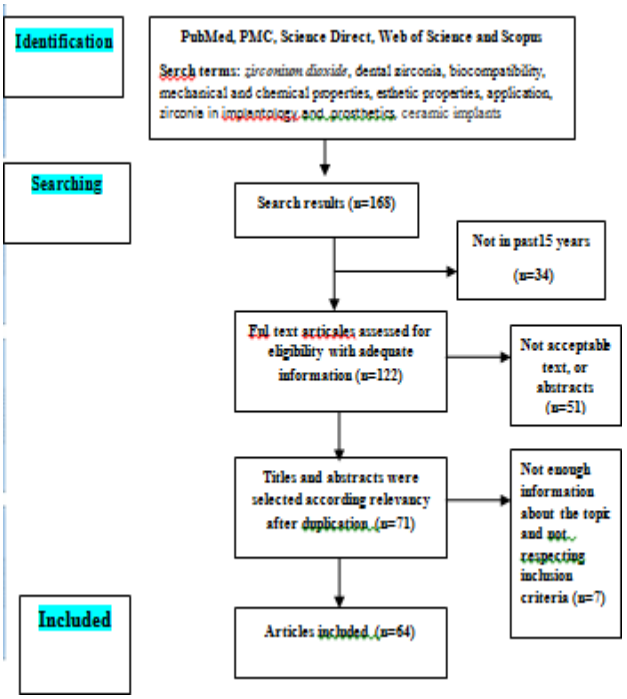
- Chlorination;
- Alkaline oxide decomposition;
- Limestone alloy;
- Plasma dissociation.

Methodology

The sources for analysis were the existing literature (Google Scholar, Medline, Scopus, Web Of Sciences, PubMed) that presented the scope of zirconia applications in dentistry, including the main keywords: Zirconium dioxide (ZrO2), zirconia, biocompatibility, mechanical and chemical properties, esthetic properties, application", zirconia in dentistry and oral implantology.

Results:Conducted a preliminary search and reviewed 168 titles and abstracts in this review and 64 full-text articles were selected of high methodological quality. Review was conducted according to the PRISMA guidelines (table 1).

Table1. PRISMA flow chart



Properties of zirconia

Physical properties

From a physicochemical point of view, zirconia is a metal oxide with ceramic properties, characterized by polymorphism and allotropy.ZrO2 is a heterogenous, highly-resistant, characterized by favorable mechanical properties: [9,10]

- Toughness: 5–10 MPa√m;
- Flexural strength: 500–1200 MPa;
- Young's modulus: 210 GPa;
- Compressive strength = 2.000mpa1/2 ;
- Fracture toughness = 8-10mpa·m;
- High fracture resistance;
- Wear of opposing dentition (mono).

Dental zirconia is resistant to acid erosive attacks in the mouth. It has extremely low thermal conductivity and the thermal expansion coefficient is $10 \times 10 - 6/°C$. Monolithic zirconia crowns with a thickness of 0.5 mm exhibit sufficient fracture resistance to withstand piercing loads in the molar region.[11,12]

Zirconium ore is purified to obtain zirconium powder. Metal oxides are added: yttrium to stabilize the tetragonal phase of zirconium, aluminum to prevent water corrosion, and hafnium oxide to reduce pore formation and color components.[13-15]

Due to saliva, temperature & stress, zirconia may transform more aggressively to monoclinic phase with micro-crack formation. This mechanical property degradation in zirconia is known as " aging".

This can cause:

- Increase in water penetration;
- Crack propagation;
- Surface deterioration;
- Phase destabilization;
- Decreased resistance to load.

The aging process depends on porosity, residual stresses, grain size, and the content of the stabilizer (Y2O3).

Chemical properties(figure):[16]

Low thermal & electronic conductivity;

High ionic conductivity;

Opaque; Chemically inert;

Corrosion resistant.



Figure 4. Typical properties exhibited by zirconia that are commonly utilized

Biological properties

Zirconia is a biocompatible biomaterial that does not cause mutations in the cellular genome.[16,17]

Zirconia has shown less bacterial adhesion and less biofilm formation compared to titanium.[18,19] The material is a hypoallergenic polycrystalline ceramic that combines perfectly with tooth tissues.[20-22] Since there is no metal in the crown, there is no need to hide its edge under the gum, thereby injuring it. Also, thanks to the absence of metal, there is no staining of gums by oxidation products.In addition to being very biocompatible, zirconia is entirely non-toxic. It also has excellent bone adherence, cell proliferation and metabolism, and a reasonable hemolytic rate. When contrasted with titanium implants, ZrO2 implants demonstrated comparable levels of biocompatibility and osseointegration.

Because of more than 15 years of global experience of using zirconium dioxide in dentistry, not a single case of allergic reactions to this material has been recorded. This also includes longer experience of using zirconium dioxide in other areas of medicine, which also shows the highest degree of biocompatibility.

Zirconium oxide is especially suitable for patients with intolerance to certain materials and metals. In terms of biocompatibility, this type of metal-free restoration is ideal.

The advantages are as follows:

- Harmless composition (no silicon oxide), very low solubility, high stability in relation to acids.
- Smooth surface that prevents plaque accumulation.
- Absolute bioinertness in relation to other materials in the oral cavity.
- High thermal insulation properties, allowing you to fully enjoy the intake of cold or hot food or drinks.

Bioinert surface helps in rapid proliferation of gingival fibroblasts over the implant surface and formation of a strong mucosal barrier(figure 5):

- Less bacterial plaque;
- Healthier mucosa;
- Better soft tissue adaptation.



Figure 5. Zirconia Biological application

Absence of galvanoza

For most patients who follow the hygiene recommendations of dentists, zirconium dioxide crowns last for decades, while maintaining their original shape and color throughout the entire period of operation.

Optical properties

Zirconia is an optically opaque material and is less aesthetically appealing than glass ceramics. The transparency of the structure and color rendering ensure that the prosthesis is invisible in the oral cavity. In order to improve its aesthetic properties, translucent zirconia has been synthesized, which is characterized by the presence of 30–35% cubic crystals. However, the strength of translucent zirconia with better optical properties is reduced

compared to tetragonal, with flexural strength values ranging from 500 to 900 MPa, and it is more prone to aging. Translucent zirconia is preferred in the anterior regions for the preparation of restorations . As an alternative to highly opaque tetragonal zirconia, manufacturers have recently begun to offer cubic phase zirconia. Although this phase has better esthetics due to its higher light transmission, the phase transformation effect is lost, making the material mechanically weaker (400 – 800 MPa).[23]

Coloring Effect

Coloring monolithic Zirconia restorations can be accomplished by either utilizing pre-colored blocks or immersing or brushing white Zir restorations in coloring solutions. Metal oxide solutions such as ferric chloride, manganese chloride, cerium acetate, cerium chloride, bismuth chloride, terbium (III) chloride, chromium (III) chloride, manganese (II) sulfate, and others are used to make coloring liquids. Pre-coloring includes integrating metal oxides such as.[24,25]

Due to the excellent light transmittance of zirconium dioxide, the ability to paint it in colors that match the shade of the patient's teeth, dentures are highly aesthetic, close to the natural color of the teeth. The light shade of the material eliminates the presence of dark edges, typical for any metal structure. The only condition is the right design. The larger the distance between the abutments, the taller and wider the connectors should be. However, in light of the stability of this material, sound dental principles should be adhered to.

Manufacturing procedures

When manufacturing a zirconium dioxide framework, the computer modeling and hardware milling technique (CAD/CAM technology) is used, which achieves exceptional manufacturing precision. First, a zirconium framework is manufactured (according to the color of the tooth), then a ceramic mass is applied to the zirconium framework.

New technologies are currently advancing, but to date zirconia is produced using CAD-CAM milling according to two different manufacturing techniques: Soft machining and hard machining.[26]

Literature data are still conflicting as to which technique is the best, as the choice is mainly driven by operator preference according to the shape, volume and complexity of the prosthetic geometry.[27]

Soft machining is based on milling pre-dispersed zirconia blanks, which are prepared by cold isostatic pressing of a mixture of zirconia powder, stabilizing oxides and binders. Soft machining requires precise matching of CAD dimensions and material shrinkage to avoid dimensional inaccuracies. Hard machining is based on milling fully sintered zirconia blanks, which are usually produced by hot isostatic pressing (HIP) at 1400°-1500°C. Immediately after hard machining, zirconia frameworks may undergo a certain amount of monoclinic transformation phase due to mechanical stress, work piece contact and overheating, sintering) significantly affect the mechanical properties and stability of zirconia.28. To obtain the appropriate color of the restorations, specific metal oxides can be used in the zirconia powder mixture. The coloring process does not affect the mechanical properties of tetragonal zirconia, while there is still no clarity regarding translucent cubic crystals.[29-31]

Use of Zirconium dioxide in dentistry

The use of zirconia in dentistry and medicine has rapidly increased over the last decade due to its advantageous physical, esthetic, biological, and corrosion characteristics. Zirconia began to be used in dentistry in the 1990s, first for root canal posts, then for prosthetics, an alternative to metal-ceramic dental restorations. It is the first choice today in cases with high aesthetic requirements.[32-34] Zirconia is used in oral and maxillofacial surgery, in prosthodontics and in implant dentistry(figure 6).

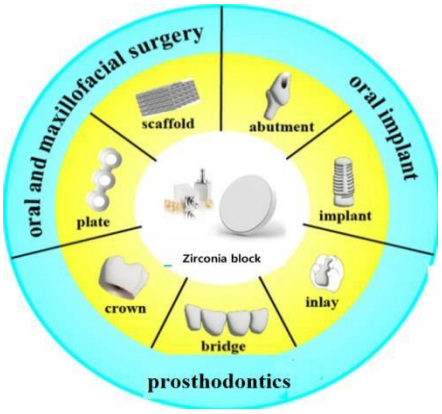


Figure 6. Use of Zirconia in oral and maxillofacial surgery, in prosthodontics and in implant dentistry

Zirconia is an excellent solution for restoring the function and esthetics of teeth. The use of zirconium dioxide in dentistry has improved the quality and esthetics of prosthetic structures. This material, together with all the technological subtleties of the manufacture of prostheses, meets the requirements of patients, doctors and society for orthopedic structures today. Zirconium dioxide has been clinically proven to be a successful restorative material for many different indications. For example, zirconia has demonstrated excellent clinical results in the fabrication of crowns in both anterior and posterior teeth. Zirconia crowns are visually almost impossible to distinguish from adjacent, real teeth. They have a color and transparency as close as possible to natural tooth enamel.

In prostheteic dentistry, zirconium dioxide is used to

produce almost all types of restorations(figure7):

- Bridge prostheses,
- Single crowns.



Figure 7. Single crowns, bridge prostheses

Zirconium oxide restorations allow for more gentle grinding of teeth. Due to the exceptional strength properties of zirconium oxide, the thickness of the framework and facing ceramics can be less than that of all-ceramic restorations. Thus, your dentist ensures that more healthy tissue is preserved during prosthetics.

If esthetics are not critical, the monolithic reconstruction method is preferred due to fewer technical complications (no risk of ceramic chipping).

Aesthetic comparison of zirconia ceramics and metal ceramics

ICE zirconium dioxide frameworks are transparent, and thus aesthetically superior to opaque metal frameworks.

One of the main advantages of zirconium crowns is their appearance, which is as close as possible to natural teeth.

For esthetic purposes, the framework has to be veneered with feldspathic ceramic. A more natural looking appearance and depth effect can also be achieved by staining and glazing the zirconia framework.[35] Zirconia is an excellent solution for restoring the function and esthetics of teeth. Zirconia can also be used as a framework for full arch prosthetics. Although the results of this reconstruction method seem promising, it should be noted that there is limited long-term documentation available at present. In general, zirconia can be used to fabricate a monolithic structure or as a framework for a two-layer structure. In the dental laboratory, zirconia is usually milled from a block of pre-crystallized material using CAD/CAM technology and then sintered at high temperatures.

The most important technological aspect of the use of zirconium dioxide is the use of CAD / CAM systems, which also contributes to their further improvement and development.

Before sintering, it is advisable to polish the blank to achieve a smooth surface relief. When working with monolithic restorations, glaze should only be applied to the axial surfaces, not to the occlusal area. This is because the glaze layer wears off after approximately 6 months of use, leaving potentially unpolished zirconia exposed. To avoid jeopardizing the opposing dentition, it is preferable to have an optimally polished occlusal surface of the zirconia structure, minimizing wear. If zirconia is used as a framework, it is essential to select a veneering ceramic that is compatible with the coefficient of thermal expansion (CTE) of zirconia, which compensates for the lower heating and cooling rates.

When an adhesive bond to zirconia is required, acid etching cannot be used to pre-treat the material, as there is no silicon matrix available. Therefore, to achieve an optimal chemical bond to zirconia, the surface should be sandblasted (with a silica coating) with alumina particles of approximately 30 µm. When using larger grain sizes, sandblasting can lead to micro cracks, which reduces mechanical stability. After sandblasting, a bonding agent containing the molecule 10-MDP (10-methacryloyloxy-decyl-dihydrogen phosphate) must be applied to the bonding surface. Ideally, a cement that also contains the molecule 10-MDP is selected to achieve optimal adhesive properties.

In dentistry, Zirconium dioxide is used in the form of ceramic blocks, which are produced by a series of compression molding processes.[36-38]

Sintered dental zirconia has a whiteness and translucency that very much resembles a natural tooth. A minimum area of 9 mm² should be available to connectors and framework wall thickness should not be less than 0.5 mm. Copings or frameworks must be anatomically shaped to ensure even layer thicknesses of veneering ceramic. Insufficient support for the veneering ceramic on the coping or bridge framework can trigger so-called chipping fractures. There's no limit to the span of a zirconia bridge or to the number of pontics.[39,40]

A modern modified material based on zirconium dioxide, Prettau Zirkon ("Prettau zircon") fully meets the high requirements for strength. Areas of occlusal-chewing contact and functional areas are completely made of this material. An exception is the vestibular surface of the frontal teeth, except for the cutting edge; it is lined with ceramic masses. Prettau Zirkon has high strength, which provides resistance to abrasive wear, guarantees the absence of chipped bumps and cutting edges. As for classic bridge-like prostheses made of solid ceramics, the probability of such damage is extremely high.

Advantages of zirconium dioxide crowns

The strength of the construction allows them to create bridge-like prostheses that are large. Possibility of fitting on vital teeth. Therefore, the

thickness of the preparation is minimal compared to other techniques. The wall of the crown frame does not exceed 0.3-0.6 mm, therefore depulpization of the tooth is not required in most cases, the pulp of the tooth is not damaged as a result of preparation.[41,42]

Disadvantages of zirconium dioxide crowns

Cracks and chips may be caused by failure to follow the recommendations for wearing dentures, or by a mistake by the dentist, who did not take into account the presence of contraindications for installing a zirconium denture. High cost, which consists of a complex manufacturing technology, mandatory use of computer equipment, high quality of the finished structure and a long service life of the denture.[43-46]

Frequent reasons for fractures Zirconia

1. Non-compliance with coping or framework wall thickness (min. 0.5 mm).
2. Connecting cross-sections are too small (9 mm² three sections, 12 mm² four sections).
3. Dry grinding the densely sintered framework, use of coarse diamonds, excessive rpms and/or exerting excessive pressure.

Facing ceramic fractures and delaminations are:

1. Insufficient support for the facing ceramic by the coping or bridge framework.
2. Copings or frameworks that are not anatomically shaped.
3. Uneven thickness of facing layers.
4. Non-compliance with the returning procedure.
5. Use of conventional ceramic heating and cooling rates.

Cementation

Based on the physicochemical properties of zirconia, glass-ionomer and hybrid cements (i.e., resin-modified glass). Ionomer cements) can be considered a good choice for cementation.[47] Use of zirconia dental implants in implant dentistry

Until recently, the only material for implants was medical titanium. Implants made of this metal and its alloys have proven themselves well, but, unfortunately, were not suitable for people with allergies to some metals. Sometimes patients refuse titanium implants for aesthetic reasons. Dentists offered an alternative to the titanium implant - a zirconium implant. Although the first ceramic implant designs appeared in the late 80s of the last century, they have become widespread in the last 10-15 years. In the USA, their use was approved only in 2011 and in Europe - a little earlier, in 2005.

In the last few years, the zirconia dental implant has emerged as an alternative for titanium implant due to its potential to osseointegrate.[48] Some studies have reported that zirconia has more biocompatibility as compared to titanium, as the latter produces corrosion products at the implant site, its naturally white color also makes it a great choice for Patients(table2).[49-51]

Table 2. Comparison of Zirconia and Metal Ceramic Crowns

Characteristics	Zirconium dioxide crowns	Metal ceramic crowns
Possibility of prosthetics without nerve removal	+	-
Minimal tooth grinding	+	-
Color selection at the level of the prosthesis framework	+	-
Excellent aesthetics (complete illusion of a real tooth, no grey metallic shade)	+	-
Any length of the structure	+	+
Computer precision design and manufacturing	+	-
Complete absence of metal (no metallic taste in the mouth)	+	-
Absence of dark border near the gum	+	-
No negative reaction to heat and cold in teeth	+	-
Low risk of developing caries under crowns and periodontal disease	+	-
Resistance to deformation	+	+
Light weight construction	+	-

According to published literature, the prevalence of titanium allergy in dental implant patients is estimated to be quite low (0.6%), which makes ceramic implants a suitable option for patients with metal allergies as they are hypoallergenic. Zirconium dioxide (ZrO2) demonstrates excellent biomechanical properties, such as high fracture toughness and flexural strength, and also ensures successful osseointegration. In vivo study, zirconia showed significantly lesser adhesion of bacteria than titanium.[52,53]

Advantages of Zirconia Dental Implants

1. Zirconia dental implants are hypoallergenic;
2. Zirconia is corrosion resistant;
3. Zirconia implants are very strong;
4. Bone integration;
5. Zirconia helps with plaque buildup;
7. Faster healing time;
8. Aesthetic advantage.

Zirconium dioxide implants are white, they do not show through the gums, which is especially important if you need to restore the front teeth. With gum recession (volume reduction), the gray strip of the titanium pin becomes visible. In such cases, the ceramic pin blends organically with the crown.

A global survey by the European Society of Ceramic Implantology (ESCI) 2021 on the operation of ceramic implants confirmed the advantages of zirconium dioxide in terms of biocompatibility and weak connection with inflammation. Ceramic implants made of zirconia represent a significant complement to titanium implants and thus an expansion of the treatment spectrum in dental implantology.

The ESCI Scientific Advisory Board states, based on the conclusions above, that the two-piece zirconia implant concept is appropriate for clinical application.[54]

– The two-piece zirconia implant concept offers advantages over the one-piece concept regarding prosthetic flexibility and clinical indications.

– Two-piece zirconia implants can resist clinical masticatory forces.

– Fracture resistance and mechanical stability of two-piece zirconia implants may vary as a function of different manufacturing processes, material properties, implant geometries and prosthetic connection concepts.

Ceramic dental implants were initially produced as monoblocks, but two-stage implants are now also produced. However, no conclusion regarding the application of two-piece ceramic implant systems can be drawn based on the existing data. Regardless of whether one-piece or two-piece implants are being placed, this drilling speed starts at approximately 800 rpm for the first drillings and decreases to 400 rpm for the last drillings. The prosthetics of a single-sided implant are almost completely identical to the prosthetics of natural teeth. In the case of two-piece implants, the procedures are identical, as for two-piece titanium implants: open or closed tray.



Figure 8. One--piece zirconia

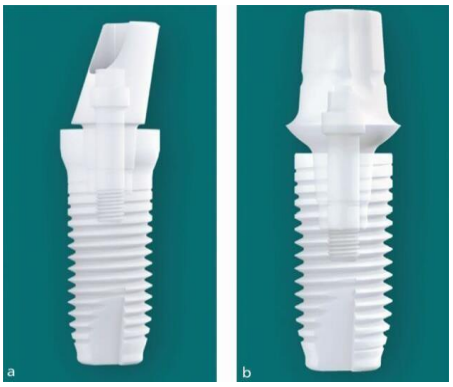


Figure 9 The two-piece zirconia

One- and two-piece zirconia implants demonstrate the same level of osseointegration and biological integrity(figure 8,9). In addition to zirconium implants, it is also recommended to use metal-free components - an abutment and a crown. When installing a zirconium abutment, the tooth will have a natural transparency and white tint, whereas when using a metal abutment, a dark metal rod may be visually visible inside the tooth(figure 10,11).[55-59]

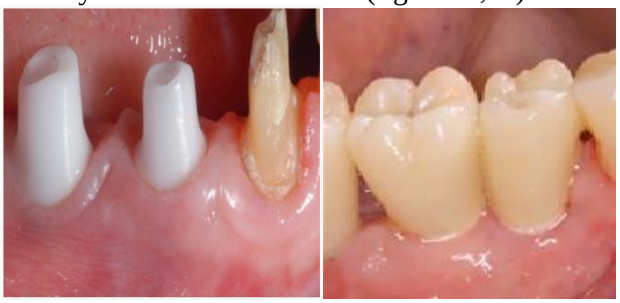


Figure10. Zirconium abutment, **Figure 11.**Zirconium crown (photo professor Curd Bollen)

A zirconium crown is also transparent and white, whereas metal ceramics have a number of disadvantages, which include a metal rim that shines through the gum, oxidation of the metal, an unnatural color of the tooth, gum recession and a change in its color due to interaction with the metal(figure12-16). [60-61]



Figure 12. Full-Arch UJ Zirconium abutment(photo professor Curd Bollen)



Figure 12. Full-Arch UJ Zirconium until fixation(photo professor Curd Bollen)

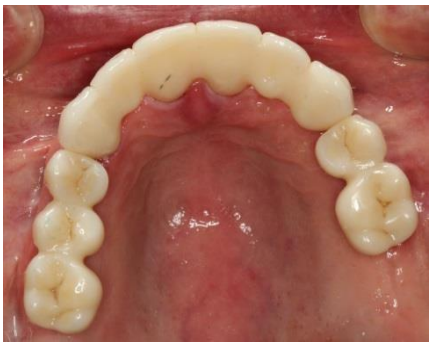


Figure 14. Full-Arch UJ Zirconium fixed in the oral cavity image from the palatal side (photo professor Curd Bollen)



Figure 15. Full-Arch UJ Zirconium fixed in the oral cavity, image from the vestibular side (photo professor Curd Bollen)

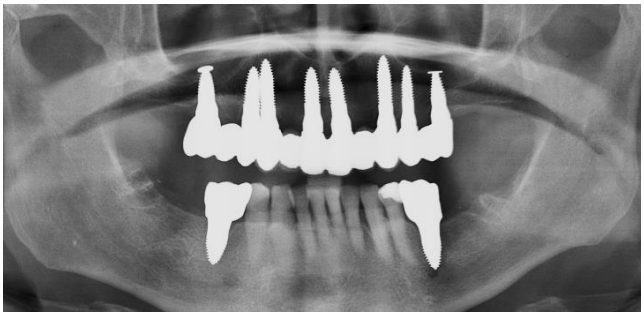
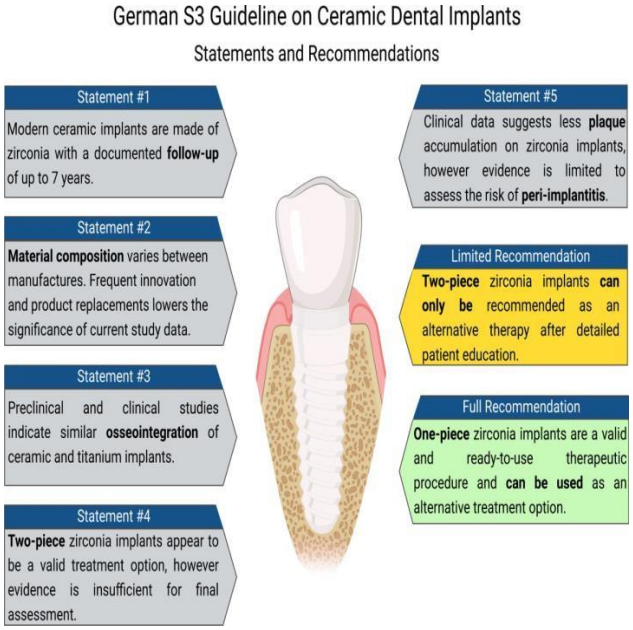


Figure 16. Full-Arch UJ Zirconium,OPG after fixation(foto professor Curd Bollen)

In the presence of an allergy to metal, zirconium prevents all the negative effects of metal ceramics, such as a metallic taste in the mouth, a galvanic effect, irritation of the mucous membrane, etc.

German Implantology Society (DGI) together with the German society for Dental and Oral Medicine (DGZMK) has developed a new S3 guideline for the use of zirconia dental implants according to the current evidence.[62]



Zirconia and titanium implants demonstrate similar soft and hard tissue integration capabilities. Titanium, however, tends to show accelerated initial osseointegration compared to zirconia.

Studies of recent implantations (3 years) show that the degree of osseointegration of ceramic implants is the same as that of titanium (95% and higher). However, numerous publications confirm that such a percentage of survival for titanium remains after 10 years. There is no data on ceramic pins from 10 years ago. It is difficult to predict what will happen to them after such a period, since long-term observations have not been conducted. According to the scientific literature, there is less peri-implantitis around ceramics than with titanium implants.[63,64]

Zirconium and materials that include, have promising indicators of strength and biocompatibility with living tissues in comparison with other materials for use in surgery. However, the use of ZrO2 is a new issue, so more in vivo experiments are needed to make widespread use of zirconium in surgery possible. This material requires special processing techniques that all laboratories must master, as it is fundamentally different from the classically employed metallic framework materials

The data on the use of modern zirconia-based ceramic implants has significantly improved in recent years. However, more long-term clinical studies are required to assess the use of dental ceramic implants more reliably.

CONCLUSION

The conducted literature review made it possible to identify a number of advantages of modern technologies in orthopedic dentistry using zirconium dioxide (ZrO2), which improves the quality of orthopedic dental care for the population in terms of safety and reliability.

This review will allow dentists to have a better understanding of zirconia-based dental structures, which will allow them to take a differentiated approach and make the right choice in different clinical situations, ensuring high functional efficiency and aesthetic appeal.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

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REVIEW ARTICALE

BIO-CHEMICAL PROPERTIES OF CURCUMIN AND CURCUMIN ANALOGUE-2 AND CURCUMIN ANALOGUE-2 IN THE TREATMENT OF PERIODONTAL DISEASE·A NARRATIVE REVIEW

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Abstract

Periodontitis is an inflammatory disease which affects both soft and hard tissues. Many treatment options have been employed to treat periodontitis out of which scaling and root planing are the standard procedures to initially reduce inflammation and improve tissue conditions. Although, scaling and root planing can reduce the inflammation, other agents or adjuncts should be used which can decrease the inflammation systemically or locally in an effective manner without side effects of using antibiotics. One of the traditional herbs used in Chinese and Indian ayurveda is Curcumin. Curcumin is known for its anti-inflammatory antioxidant and anti-microbial effect. As Curcumin is less stable with less bio-availabilty, there is need for formulation of Curcumin analogues which are long lasting, highly stable and also have high bioavailability. Curcumin analogue -2 is known to have high anti-inflammatory, anti-microbial and antioxidant effect which can combat with periodonto-pathogenic bacteria and the inflammation due to periodontal supporting tissues. Therefore, this review focuses on bio-chemical properties of Curcumin and its formulated Curcumin analogue -2 and mechanism of Curcumin analogue -2 in the treatment of periodontitis.

Keywords: Curcumin, Curcumin analogue-2, Periodontitis

INTRODUCTION

Periodontitis is a chronic inflammatory disease which is primarily caused by the by anaerobic gram negative bacteria such as red complex microorganism Porphyromonas gingivalis, Prevotella intermedia, Tanerella forsythia and others in the microbial plaque[1] that results in breakdown of periodontal connective tissue and further leading to bone loss. The host inflammatory reaction as a response to bacterial attack is mediated by release of inflammatory mediators such as interleukin-1 (IL-1),

IL-6 as well as tumor necrosis factors, prostagalndins-2, anti-collagenases like Matrix metalloproteinases.[2] Addressing the removal of etiological factors, results in elimination of the disease or arrest the progression of the disease. The conventional approach, scaling and root planing sometimes fall short in achieving the goals of periodontal therapy either because of presence of tissue penetrative bacteria or because of exaggerated host inflammatory response. This lead to emergence of local drug delivery agents which penetrates deeply in to the tissues at low concentrations and also reduces the need of the systemic antibiotics and its potential adverse effects like developing antibiotic resistance. There are many local drug delivery agents in the treatment of periodontitis which are mostly antibiotics and there are few natural herbs which have proven their efficacy in the treatment of periodontitis. One of such potential agents is the curcumin. For centuries, its been used as a culinary spice, food preservative, and as a natural yellow food colouring substance. Traditional medicinal systems like Indian Ayurveda and Chinese herbs have relied heavily on turmeric (golden spice) which is a bioactive polyphenol extract that has anti-inflammatory[3], anti-oxidant[4], wound healing[5] anti-microbial and analgesic properties. Throughout the history, it has been used primarily as an herbal remedy for a range of liver, gastrointestinal, and pulmonary conditions. It is also used as a cosmetic agent for skin care in Asia, Europe, and America.[6] According to epidemiological research, people who regularly consume turmeric may be able to reduce their risk of developing cancer by 10–50%.[7] It has also been used as a treatment for enhancing delayed healing and has demonstrated a number of additional therapeutic effects in both in vitro and in vivo model systems.

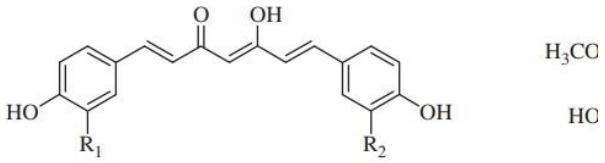
This coloring compound (curcumin 1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-hepta diene-3,5-dione; 2), a natural dietary ingredient which is derived from the perennial herb Curcuma longa L[8] was first isolated in 1815, first crystallized in 1870, and Lampe et al. clarified its chemical structure in 1910.[9] Though it possess wide range of medicinal properties, Curcumin is unstable with less bioavailability[10] and weakly soluble in water, but it dissolves readily in organic solvents like ethanol, methanol, acetone, and dimethyl sulfoxide.[11] Clinical application is still limited due to its poor absorption and requires high doses for its therapeutical actions. Due to these reasons, synthesis of novel Chemically Modified Curcumins (CMC's) with improved zinc binding have been discovered and are replacing the use of original curcumin in clinical studies.[12] These Chemically Modified Curcumins or analogs have well defined chemical composition and enhanced pharmacological properties with low toxicity and potential inhibitory activity for Matrix metallo proteinases (MMP's) and cytokines.

Therefore, Curcumin analogs with high stability and more bio-availabilty have been discovered to act as a therapeutic potential against periodontal disease. This review focuses mainly on Curcumin and it's analogues.

Structure of Curcumin

Curcumin has many functional groups and is a simple symmetrical β-diketone. It is (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6- heptadiene-3,5-dione. Two α, β-unsaturated carbonyl groups link the two aromatic rings that contain phenolic groups. According to Nelson and Pandey, the chemical formula of curcumin is $C_{21}H_{20}O_6$, and the molecular weight is 368.38 g/mole.[13,14]

In acidic and neutral pH, curcumin is not soluble in water. In the solid phase and in acidic solutions, these carbonyl groups produce a diketone moiety that occurs in keto-enolic tautomeric forms, where an energetically more stable enol-form is present. In mild alkaline conditions, curcumin readily deprotonatesto produce the enolate moiety. Curcumin's quick metabolism is thought to be facilitated by these simple tautomeric reactions.[15] Curcumin though is naturally available and advantageous; it also has few disadvantages such as instability, enolization, fast metabolism and poor bioavailability. These factors are few reasons why curcumin is less likely to be used in medical field and this led to the development of curcuminoids or curcumin analogues with enhanced properties and better bioavailability. This can be achieved by modifying the methylene group and b-diketone moiety in the structure of curcumin. Elimination of alpha hydrogen molecules can prevent enolization of curcumin.[16]



1.Curcumin (Cur-A): $R_1=R_2=OCH_3$
2.Demethoxycurcumin (Cur-B) : $R_1=H$,$R_2=OCH_3$
3.Bisdemethoxycurcumin (Cur-C): $R_1=R_2=H$

Figure1. Structure of curcumin

Curcumin analogues

Ohtsu et al. through his various experiments has synthesized a number of Curcumin analogues. Curcumin analogs are synthetically prepared by changing a molecule in the structure of curcumin. They are characterized as pleiotropic agents.[17]

They have only one target and have both anti-inflammatory and anti-proliferative properties. Analogues of Curcumin inhibit a wide range of proteins, enzymes, and molecular targets linked to inflammation and proliferation. Better anti-proliferative and anti-inflammatory properties are obtained by combining a number of Curcumin analogues with functional groups.[14]

Synthesis of curcumin analogue-2

Curcumin analogues are generally synthesized by certain reactions such as aldol condensation, or simple condensation or azide-alkyne cyclo addition. In aldol condensation, sodium hydroxide is used as catalyst and ethanol is used as solvent. Halogenated Curcumin analogues are synthesized using condensation process whereas triazoled curcumin analogues from aromatic aldehydes are synthesized using azide –alkyne cyclo addition.

According to Mazumder et al in 1997[18] and Roughley & whiting in 1973[19], Curcumin and its analogues (1–7) were synthesized by condensation of 2,4-pentanedione with two equivalents of substituted benzaldehyde based on the available methods.

The usual procedure was to dissolve 2,4-pentanedione (1.0 g, 0.01 mol) and boron oxide (0.49 g, 0.007 mol) in 10 ml of EtOAc, stir for 0.5 hours at 40 °C, then add the corresponding benzaldehyde (0.02 mol) and tributyl borate (4.6 g, 0.02 mol) and stir for another 0.5 hours. After that, n-butylamine (1 ml) was added drop wise over the course of 30 minutes in 10 ml of EtOAc. To finish the reaction, the mixture was left to stand overnight at 40 C after being stirred for an additional four hours. After hydrolyzing the mixture with HCl (0.4 N, 15 ml), the aqueous layer was extracted three times using EtOAc. [20,21]

After being cleaned with water, the combined organic layers were dried on top of Na2SO4. Pure 1–4 and 7 were obtained by recrystallizing the leftover paste from EtOH and purifying it using column chromatography (silica gel, cyclohexane–EtOAc) after the solvent was removed under low pressure.[22]

Curcumin analog 2 in Periodontitis

Curcumin analogs have more stability and high bioavailability. The production of many inflammatory mediators that contribute to the pathophysiology of several inflammatory illnesses depends on NF-κB activation. It makes host modification treatments for chronic inflammatory diseases a top target for this pathway. Activated fibroblasts, monocytes, and macrophages release pro-inflammatory cytokines such IL-1β and TNF-α, which are important in the pathophysiology of periodontitis. The direct degradation of connective tissues in chronic inflammatory illnesses is mostly caused by catabolic enzymes like MMPs, which are produced in response to the release of these cytokines. Prostaglandins and leukotrienes are examples of lipid mediators of inflammation that are produced when IL-1β and TNF-α activate other inflammatory mediators like cycloxygenase-2 and 5-lipoxygenase.[2,10]

Curcumin analogue-2 has found to reduce the excessive levels of IL-1β to B normal levels. It has also been associated with marked inhibition of both p38 MAPK and NF-κB signaling. This inhibition of p38 MAPK and NF-κB signaling reduces the synthesis of pro-inflammatory cytokines, such as IL-6, TNF-α, and prostaglandin E2 and causing reduction in periodontal inflammation. These actions eventually reduce pocket depth and help in gaining attachment.

It also significantly lowers the inflammation caused by cellular infiltration. It lowers the quantity of TRAP-positive multinucleated cells (osteoclasts) and bone resorption[10] there by mediating the inflammatory response of periodontitis.

Differences between Curcumin and Curcumin analogue-2

The below table helps us to differentiate curcumin and curcumin analogs

Table1.Difference between Curcumin and Curcumin analogues-2

Characteristic	Curcumin	Curcumin analogue -2
Bioavailability	Less	High
Solubility	High	Low
Stability	Low	High
Toxicity	High	Low
Inhibitory effect to MMPS	Low	High
Dosage required to act on humans and animals	High	Low
Fat metabolism	High	Low
Enolization	Present	Absent

Since pro MMPs can be activated by proteases like trypsin and other substances like Reactive Oxygen Species, curcumin analog -22 inhibitions of these factors may offer, at least partially, extra mechanisms for minimizing tissue breakdown.

Since Curcumin analogues have better advantages than curcumin, there is need for utilization of Curcumin analogues in management of periodontitis and other medical fields.[23]

CONCLUSION

Several modern Curcumin analogues provide improved absorption, increased potency, slowed metabolism, and delayed elimination to help with poor bioavailability. Multifunctional nano-platforms, including liposomes, NPs, nano-carriers and nano-arrays, micelles, 3D printing, and other intriguing new formulations, offer improved curcumin targeting, resistance to the metabolic process, and longer circulation times to increase therapeutic efficacy.

Improving the solubility and stability and bio-availability in Curcumin analogues can help in improving the therapeutic applications of Curcumin. Advanced researches and formulations can help in utilizing Curcumin analogues in medicinal fields.

DECLARATIONS

Conflicts of interest and financial disclosures

No conflict of interest and there was no external source of funding for the research in question.

Ethical approval

Study was approved by Institutional Research Review Board

Source of funding

The work was not funded.

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REVIEW ARTICLE

ROLE OF HERBAL SUPPLEMENTS IN MANAGING THE SYMPTOMS ASSOCIATED WITH ORAL POTENTIALLY MALGINATE DISORDERS AND ORAL CANCER: SCOPING REVIEW OF THE RECENT ADVANCES

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ABSTRACT

Oral premalignant conditions and oral cancers collectively pose a major health challenge worldwide. Various treatment modalities including antioxidants, corticosteroids and immunomodulators have been used for management of oral Premalignant conditions, in particular the ones which are symptomatic such as Oral Submucous Fibrosis and Erosive Lichenplanus. Surgery, radiation, and chemotherapy-alone or in combination are still the mainstay treatment for Oral cancer. In recent times many herbal supplements have been tried in management of these lesions with an array of reported effectiveness and there remains a conundrum regarding their actual role. The researchers behind this scoping review set out to find out how well herbal supplements worked in treating oral cancer and other possible malignant illnesses.

Keywords: oral cancer, oral premalignant disorder, alternative therapy, herbal

INTRODUCTION

Herbal supplements are botanical products widely utilised for the therapy of various ailments, particularly in the Indian subcontinent. Recent research has focused on the scientific data on their therapeutic benefits.[1] Extensive study is currently being conducted on the therapeutic properties of these plants. There is optimism that these medicinal herbs may assist with several ailments, including diabetes, allergies, and cancer. A diet high in fruits and vegetables is thought to lower the risk of developing cancer.[2–3] Some authors have also studied their unique properties such as simulation of osteoblasts and inhibition of osteoclasts.[4]

The pathophysiology of oral premalignant conditions and oral cancers indicates that specific plant derivatives may elicit nutritional and antioxidant responses.[5–6] Recent studies have focused on herbal supplements such as Curcumin, Aloe Vera, Anthocyanins, Asparagus, Green Tea, Vitamin C, and Lycopene, examining their potential in reducing symptoms linked to specific oral premalignant illnesses.[7–9] The purpose of this scoping review is to assess how herbal supplements may be used to treat mouth cancer and other potentially cancerous disorders.

MATERIALS AND METHODS

Protocol and Registration

We found studies evaluating the effectiveness of herbal supplements in treating oral cancer and premalignant diseases by using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria.

Focused Question

The main emphasis was on the function of herbal supplements as a method of treatment for oral premalignant diseases and oral cancer.

Eligibility Criteria

The study included original research articles that

detailed randomised controlled trials evaluating the effectiveness of herbal supplements in the management of cancer and oral precancer. Only articles with complete text available at no cost were included. No in-vitro or animal research, reviews or recommendations, technical reports, case reports, conference presentations, non-original publications, retrospective or longitudinal investigations, or reviews or suggestions exist. Publications in languages other than English were also excluded.

Literature Search strategy

We searched for novel randomised controlled clinical trials published from 2017 to 2022 in electronic databases such as Scopus and PubMed (Medline). Titles, abstracts, and keywords were searched via a combination of MeSH terms. They incorporated "Curcumin" OR "Aloe Vera" OR "Anthocyanins" OR "Asparagus" OR "Green Tea" OR "Vitamin C" OR "Lycopene" OR "Cannabinoids" OR "Soya Bean Derivative" OR "Cranberries" AND "Oral Premalignant Disorders" OR "Oral Pre-Cancer" OR "Oral Cancer." The writers meticulously examined the selected research titles and abstracts. Finally, the complete text of each piece was examined for inclusion.

Data extraction

The two writers independently retrieved the following facts from the source: author names, year and location of the study, aims, study design, subject count, mean age of subjects, herbal supplement, distribution mechanism, oral premalignant disease and cancer kind, therapy type, and primary results. A pre-established data gathering form facilitated their entry. Prior to the inclusion of the study in the review, any discrepancies were deliberated and ultimately reconciled by consensus.

***Risk of bias in individual* studies**

We examined the full-text papers for evidence of bias, sound design, and accurate reporting utilising an assessment method for cross-sectional studies (AXIS). The tool's twenty questions provided three response options: yes, no, and don't know, with each affirmative answer yielding a one-point gain. Every individual study was assigned a score ranging from 0 to 20. The studies were categorised into three groups based on ratings: Good (>15), satisfactory (10–15), and poor (<10).[10]

RESULTS

Study selection

We employed the PRISMA criterion to identify the appropriate studies. Refer to Figure 1. The initial search produced approximately 264 documents; 50 were later discarded due to excessive similarity. Subsequently, additional research were generated by meticulously examining the titles and abstracts of 214 articles. The removal of 205 papers resulted from a comprehensive review of their whole contents. This study comprises the whole texts of nine original investigations.

Study Characteristics

The first table summarises the main features of the first research publications. There were 9 Randomized control clinical trials . Among them 6 are parallel group prospective designs.[11,13,16–19] Three studies do not have their randomizations or study designs mentioned.[12,14,15] The total number of subjects involved in these studies ranged from 25 to 120[15,18] with the number of males being more than females.[11-19] Their ages varied from 27.8 to 65 years on average.[12,16]

Clinical Parameters estimated

The clinical parameters that were recorded were Intensity of burning sensation by Visual Analog scale[12–15,18], Interincisal Mouth Opening with Digital Vernier Calliper[12–15,18], Tongue protrusion with scale[14,18] ,Cheek flexibility[19], Oral Health status with Oral Assessment Guide[16], REU score.[11] Pain assessment by Numerical rating scale[19], Their levels were shown to be associated with how well herbal medicines worked as a therapy.[11-19]

Type of Oral Premalignant Disorders and Oral Cancer

The oral premalignant disorders included in various studies are Oral Submucous Fibrosis[12–15,18,19], Oral Lichen Planus[11]. Our evaluations also included individuals with oral mucositis receiving treatment for head and neck cancer.[16–18]

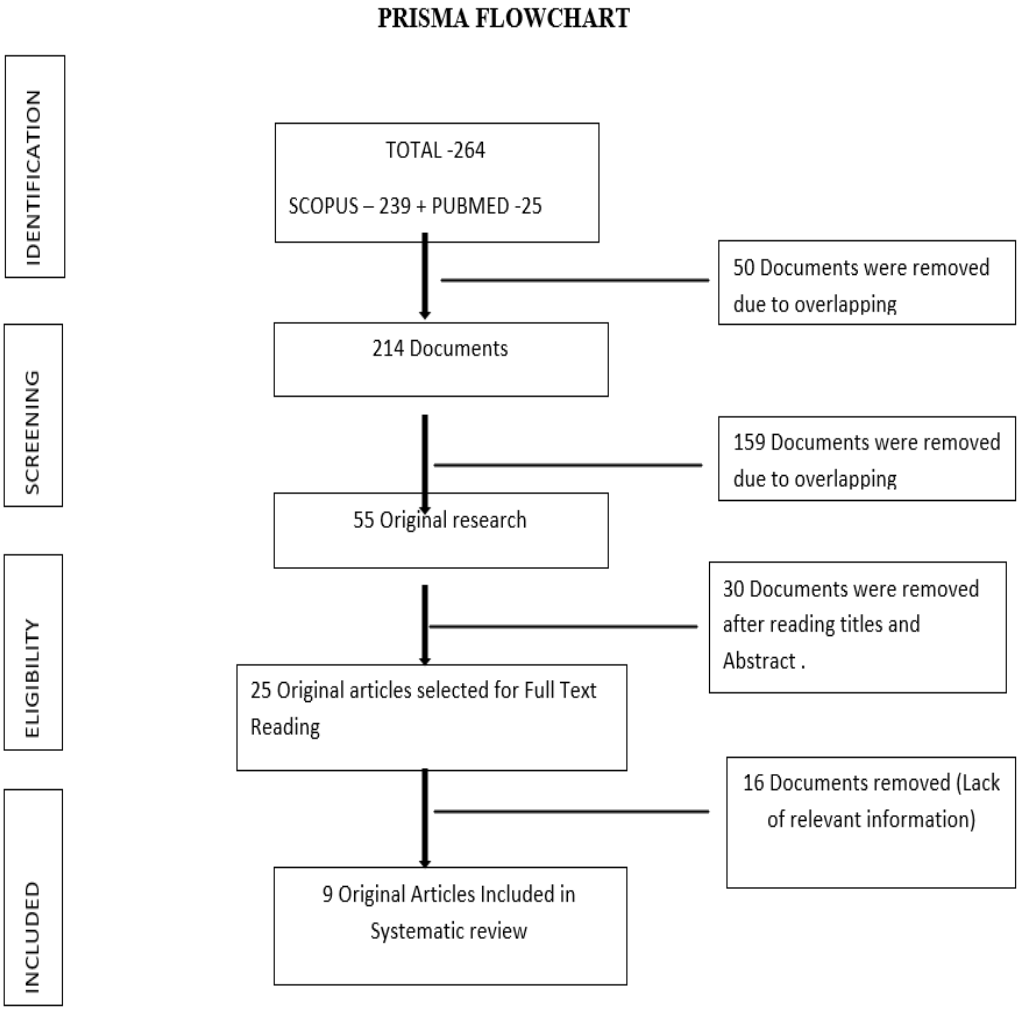
Herbal Supplements

The most common Herbal supplement used as therapeutics was Curcumin[11–15,17–19] followed by Aloe vera.[13,15] There has been little research on green tea's potential as a therapy for oral cancer.[16]

The preferred route of administration for curcumin was Gel[11–13,15] and commercially available Curcumin Capsules.[17–19]

There was a novel formulation of Bio enhanced Curcumin capsule named BCM-95®[17] for treatment of Cancer therapy induced oral mucositis. Very few studies have evaluated curcumin lozenges

(TurmNova®) as a chemoprotective agent.[14] Curcumin Gel with steroidal intralesional injection and triamcinolone acetonide rinse are two popular combination therapy.[11,12,14,15,19]



Main Outcomes

Herbal supplements, including curcumin and aloe vera, were frequently assessed for their efficacy. They demonstrated a robust correlation with clinical indicators such as the intensity of burning sensation, the inter-dental spacing, the protrusion of the tongue, and the condition of oral health over around nine trials.[11–15,17–19] Table 1 summarizes the details of the articles viewed.

Table 1. Salient Features of Therapeutic effects of Herbal Supplements on Oral Premalignant Disorders

Author Year	Aims and objectives	Herbal Supplement	Route and Dosage of Administration	Oral Cancer condition	Results and Conclusion
Mahin Bakhshi et al 2020[11]	To assess the effect of combined use of 1% nanomicelle curcumin gel and 0.1% triamcinolone acetonide mouth rinse in comparison with 0.1% triamcinolone alone for	Curcumin	1% nanomicelle curcumin gel	Oral Lichen Planus	1. use of 1% nanomicelle curcumin gel plus 0.1% triamcinolone mouth rinse was significantly more effective 2. decreased severity of clinical symptoms,

	treatment of Oral Lichen Planus				enhanced the rate of improvement 3. lower dosage is an advantage
Ashish B Lanjekar et al 2020[12]	To ascertain the efficacy of topical curcumin gel with triamcinolone and hyaluronidase mucoadhesive semisolid gel individually or in combination in the treatment of OSMF.	Curcumin	Mucoadhesive semisolid gel of curcumin	**Oral Submucous Fibrosis**	1.therapeutic effect in patients diagnosed with OSMF 2. fibrinolytic and anti-inflammatory action which helps to reduce burning sensation , improvement of colour of mucosa
Ashwini Nerkar et al 2021[13]	To compare the efficacy of Curcumin gel with Aloe Vera gel when both the gel are supplemented along with oral physiotherapy in the management of OSMF	Curcumin Aloe vera	Gel (Curenext oral gel) Aloe Vera gel (aloe gel 100%)	**Oral Submucous Fibrosis**	1.Burning sensation score improved in Aloe Vera group 2. difference in the potency of Aloe Vera and Curcumin anti-inflammatory properties
Rahul Srivastava 2021[14]	To compare the efficacy of TurmNova® lozenges and its active ingredient "curcumin" as a low-cost, safe, and non-invasive chemo preventive agent with intralesional corticosteroids (with hyaluronidase) in the management of OSMF	Curcumin	Curcumin lozenges (TurmNova®)	**Oral Submucous Fibrosis**	1. Innovative delivery system of lozenge results in a higher level of plasma curcumin level with 100 mg dose and prevents its biotransformation and its inactivation by the liver enzymes. 2. inhibiting the AKT/MTOR pathway with curcumin may also be useful as an oral chemo-preventive agent
Ankita Bohra 2021[15]	a comparative analysis of the combination of Ayurvedic therapy and combined efficacy of Steroidal intralesional injections along with antioxidant supplements.	Kali Haldi (Curcuma caesia roxib) Aloe Vera	Gel	**Oral Submucous Fibrosis**	1. Kali Haldi and Aloe vera act synergistically against oxidative free radical species in OSMF patients.
Yen-Chi Liao RN 2021[16]	To evaluate the effectiveness of green tea mouthwash for improving the oral health status in oral cancer patients undergoing cancer treatment.	Green tea	5% green tea mouthwash (100 ml)	Cancer therapy induced oral mucositis	1. Improved the oral health status from T4 to T6 in patients with oral cancer who were undergoing cancer treatment. 2. simple, natural, effective, and safe

					intervention on pharmacological treatment option for protecting the oral mucosa.
Tej Prakash Soni 2021[17]	To evaluate the efficacy of Bio-enhanced turmeric formulation in reducing the severity of oral mucositis in patients receiving adjuvant concurrent chemoradiotherapy for oral cavity cancer.	Curcumin	Capsules BCM-95®	Cancer therapy induced oral mucositis	1.incidence of grade 3 oral mucositis, dysphagia, and oral pain was significantly lower in patients receiving BTF 2. Better patient treatment compliance and fewer interruptions
Seyed Javad Kia 2021[18]	to investigate the effective- ness of capsules containing curcumin nanomicelles in patients undergoing chemotherapy with or without head and neck radiotherapy who have also developed oral mucositis.	Curcumin	Nanomicelle Curcumin capsules (80 mg)	Cancer therapy induced oral mucositis	1.Capsules of curcumin nanomicelles are more effective in chemotherapy induced OM rather than head and neck radiotherapy related OM .
Sagar Adhikari et al 2022[19]	To assess the efficacy of curcumin in combination with intralesional dexamethasone with hyaluronidase in the treatment of OSF	Curcumin	Curcumin extract (Capsule Adcumin®) Randomized, double-blind, 12-weeks parallel-design clinical trial	**Oral Submucous Fibrosis**	1. combination with intralesional dexamethasone with hyaluronidase is efficacious in the treatment of OSF in terms of improvement in interincisal mouth opening, cheek flexibility and tongue protrusion

DISCUSSION

Recent research shows an increase in the utilization of herbal supplements as treatments for oral cancer symptoms alongside premalignant conditions. The recent scoping study revealed the most commonly used herbal supplements in the past several years:

Curcumin

Turmeric under its botanical name "Curcuma longa" serves as a natural remedy throughout Ayurveda, Unani, and Siddha medicine for multiple medical conditions. Various studies demonstrate that curcumin exhibits cellular protective qualities such as reducing inflammation while possessing both antioxidant functionalities and anticancer properties. Two trials looked at topical curcumin gel and mouthwash with 0.1% triamcinolone acetonide for the treatment of oral lichen planus (OLP) and oral submucous fibrosis.[10,12]

Oral lichen planus (OLP) treatment alternatives were assessed using a 0.1% triamcinolone acetonide mouthwash and 1% nanomicelle curcumin gel. The nanocurcumin treatment achieved superior results than placebo therapy as revealed through the REU scoring at each follow-up check point. A small number of patients had entirely healed lesions, according to trial data, but these results were far more prevalent in the nanocurcumin group than in the placebo group.[10] The treatment regimen that Ashish B. Lanjekar chose as optimal included 1% Curcumin Mucoadhesive Gel and 1% Hyaluronidase Mucoadhesive Gel lead by 0.1% Triamcinol The dual

application of 1% Curcumin Mucoadhesive Gel with 1% Hyaluronidase Mucoadhesive Gel and 0.1% Triamcinolone Acetonide Buccal Paste produced substantial improvements in mucosal colour change (0.68 ± 0.47, p = 0.000) and delivered the most effective mean outcome (4.05 mm).[12]

The effectiveness of a mixture of two intralesional corticosteroids (two millilitres of dexamethasone at 4 mg/mL plus 1500 international units of hyaluronidase) and curcumin lozenges (TurmNova®) in treating cancer was assessed in individuals suffering from oral submucous fibrosis.[14] After three months of follow-up, the group that received curcumin in conjunction with corticosteroids showed substantial improvements in tongue protrusion (mean ± S.D of 3.00 ± 0.14), as well as considerable improvements in mouth opening (p < 0.001). Participants in the intervention got a once-daily dosage of curcumin via capsuled Adcumin® four times throughout the course of six weeks, whereas those who received a placebo were given a comparable schedule of translucent Placebo capsules within the same time frame. The results of the study were consistent with those of a previous study that used the same treatment approach. Each experimental group received intralesional treatment with Hyaluronidase (Hynidase®) and a solution containing 4 mg/ml dexamethasone. The average interincisal mouth opening in the Curcumin Group increased by 8.71±1.26 mm while the Placebo Group maintained stable values between their first visit and 12-week follow-up.[19]

The above studies indicate that Curcumin, especially in combination therapy; may prove to have excellent results in alleviating the symptoms associated with Oral Pre malignant Disorders.

Rarely has curcumin been studied for its ability to alleviate oral mucositis in chemo patients, whether they are undergoing radiation to the head and neck or not. The efficacy of an original bio-enhanced turmeric capsule formulation (BCM-95®) was assessed using metrics such the degree of dysphagia, mouth pain, and oral mucositis. After 6 weeks of therapy, grade 2 mucositis was found in 75% of arm A (1 g daily) and 80% of arm B (1.5 g daily) participants. Both Group A and Group B reported reduced discomfort and less acute pain at the end of the sixth week of therapy.[17] Another study looked at the efficacy of oral mucositis caused by head and neck cancer using Nanomicelle Curcumin capsules (80 mg) as a medication delivery strategy. Twenty-five people took part in the trial by taking two 80 milligrams nanomicelle curcumin capsules with their meals every day. The study group's OM was considerably better than the control group's from the first week (P = 0.010) to the fourth week (P = 0.022) and the seventh week (P < 0.001). The control group's incremental gradient was greater than that of the study group. At weeks four (P = 0.009) and seven (P = 0.012), patients receiving head and neck radiation therapy in addition to chemotherapy had significantly less severe oral mucositis than those in the control group.[18] More studies are needed to establish if curcumin is effective in cancer therapy lesions.

Aloe Vera

Recent medical data shows that aloe vera provides therapy for relieving the symptoms associated with oral submucous fibrosis. The plant contains beta carotene and iron together with zinc selenium and the antioxidant vitamins A C and E. New research examined how oral physiotherapy measures up with topical gels containing curcumin and Aloe Vera for treating OSMF. Compared to Group A, which used curcumin, patient evaluations of burning sensations rose more significantly in Group B, which used aloe vera. An applied p-value must remain under 0.05 for valid results.[13] Research compared how Aloe Vera gel treated alone can perform versus Curcumin gel treatment when combined with oral physiotherapy for OSMF management. Patient administration of a Kali Haldi 2 milligram mixture with Aloe vera gel 2 milligrams was required thrice daily during three months of treatment. A considerable improvement in average burning sensation VAS scores reduction from 47.6 + 1.02 at baseline to 75.9 was observed. The non-steroid group showed no statistically relevant differences in either cheek elasticity measurements or mouth opening improvement against steroid group tests. This research locates pure Aloe Vera gel as an effective remediation method for managing OSMF specifically. Their applications in symptoms related to various oral premalignant illnesses and post-treatment require extensive evaluation

Green Tea

Green tea remains popular worldwide because of its polyphenol antioxidants and specifically the antioxidants catechin and epigallocatechin-3-gallate.[20] According to clinical studies by Cabrera et al. (2006)[21], Min et al. (2014)[22], and Musial et al.

(2020)[23], polyphenols have potent physiological roles that include antibacterial, anti-inflammatory, and anticancer protection as well as antioxidant protection. In order to ascertain if green tea mouthwash would help patients with oral cancer after surgery and getting chemotherapy or radiation treatment, the researchers carried out a prospective, single-blind, randomised, controlled experiment in Chia-Yi, Taiwan. T_0 assessment showed no significant statistical differences in how control and intervention groups matched regarding their age, gender, cancer site, tumour stage, tumour type and treatment approach. The intervention group's oral health status score was 9.3 ± 3.5 (p=.008) lower than the control group's at the 6-month follow-up time point. At time point 5, the intervention group's oral health status score was 2.97 points lower than the control group's (SE: 0.68, p<.001). The oral health status score at T6 was 2.93 points (SE: 0.68, p<.001) higher than the control group at T_0.[16]

A major hurdle in the routine usage of herbal supplements is the lack of scientific evidence despite their widely known and used curative properties traditionally, especially in the Indian subcontinents. According to our review, the above herbal supplements, by the virtue of their anti-inflammatory and other medicinal effects; have been studied broadly but still there is still scope for more randomized controlled trials to assess their efficacy.

CONCLUSION

This scoping review indicated that herbal supplements like curcumin, Aloe vera and green tea have been found to be fairly effective in managing Oral Premalignant disorders and symptoms associated with oral cancer as per studies done recently. However, their role has largely been studied as adjunct therapy and there is lack of well-planned

clinical trials to study this.

Limitations: The scoping review design of this research meant that it could only provide a high-level summary of the available data rather than a thorough evaluation. We had taken the time frame to be five years only so as to focus on the recently reported herbal supplements rather than revisiting the ones already discussed and established in literature such as lycopene.

Declarations

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

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ORIGINAL ARTICLE

A CROSS SECTIONAL STUDY ON MALGINATE TRANSFORMATION OF ARECA NUT CHEWING SYNDROME

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Abstract

Background: Oral Submucous Fibrosis (OSMF) is a chronic and progressive condition with a significant potential for malignant transformation, primarily affecting populations in South and Southeast Asia. The condition is closely linked to habitual areca nut consumption, tobacco use, and nutritional imbalances. Characterized by excessive fibroelastic deposition, OSMF leads to restricted oral opening, mucosal stiffness, and an increased susceptibility to developing Oral Squamous Cell Carcinoma (OSCC). While the causative factors of OSMF are well established, the precise biological mechanisms driving its malignant progression remain insufficiently understood. Given its widespread prevalence in India, there is a critical need for further research to identify key risk factors contributing to the transformation of OSMF into OSCC, enabling early diagnosis and targeted therapeutic interventions.

Objective: The study aims to assess the malignant transformation of OSMF into OSCC, identify risk factors influencing this progression, and analyze the demographic, clinical, and histopathological characteristics of affected individuals.

Materials and Methods: This study analyzed OSCC cases, focusing on malignant transformation from OSMF. Patient data were categorized based on demographics, clinical features, and pathology. Cases with concurrent oral lesions, incomplete records, or other malignancies were excluded. Statistical analysis using SPSS (version 23) was performed to assess significant correlations among clinical parameters. Statistical analysis was performed using t-test and chi-square test in SPSS software to assess associations between variables.

Results: This cross-sectional study analysed 119 OSCC patients**,** identifying 13% malignant transformation from OSMF. Pan chewing (55.9%) was the most common habit. 53.3% exhibited nodal involvement**.** Organism presence (*Pseudomonas aeruginosa, Streptococcus epididymis*) significantly correlated with OSCC (p=0.00). Gender, habits, and age showed no significant impact on tumour grading (p>0.05).

Conclusion: The findings reinforce the malignant potential of OSMF and highlight the critical role of early detection and intervention. Areca nut and tobacco consumption significantly contribute to disease progression. Future research should focus on molecular and genetic factors influencing malignant transformation to develop targeted preventive strategies.

Keywords: Areca nut, Malignancy, Oral squamous cell carcinoma, Oral submucous fibrosis

INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a chronic, progressive, and potentially malignant disorder predominantly affecting individuals in South and Southeast Asia[1]. It is characterized by fibroelastic changes leading to stiffness of the oral mucosa, trismus, and an increased risk of malignant transformation into Oral Squamous Cell Carcinoma (OSCC)[2]. Despite its well-documented association with areca nut chewing, tobacco use, and nutritional deficiencies, the precise mechanisms underlying its progression to malignancy remain inadequately explored India has the highest global burden of Oral Submucous Fibrosis (OSMF), primarily due to the widespread consumption of areca nut (betel quid) and tobacco products[3]. The estimated prevalence of OSMF in the general population ranges between 0.2% and 6.3%, with significant variations based on geographic location, socioeconomic status, and cultural habits. The condition is particularly prevalent in states like Maharashtra, Gujarat, Andhra Pradesh, Tamil Nadu, and Uttar Pradesh, where areca nut chewing were deeply ingrained as social customs[4]. The malignant transformation rate (MTR) of OSMF in India has been reported to be 7-13%, which was higher than the global average of 5.5%[5]. This increased risk was attributed to multiple factors, including early onset of areca nut use, prolonged duration of exposure, and the presence of additional carcinogenic agents such as tobacco and alcohol[6]. Studies have indicated that OSMF patients who consume gutkha (a commercial areca nut and tobacco mixture) are at a significantly higher risk of developing Oral Squamous Cell Carcinoma (OSCC) compared to those who chew areca nut alone[7].

The incidence was notably higher in males, particularly those aged between 30 and 50 years, who exhibit a greater predisposition to malignant transformation. Several etiological factors contribute to this transformation, including areca nut and tobacco consumption, where arecoline—an alkaloid in areca nut—induces fibroblast dysfunction, increased collagen deposition, and oxidative stress, facilitating carcinogenesis[8]. Nutritional deficiencies, especially iron, zinc, and vitamin A, B-complex, and C, further impair epithelial repair mechanisms, making the oral mucosa more vulnerable to dysplasia. Genetic and epigenetic alterations, such as mutations in tumour suppressor genes like p53 and aberrant methylation patterns, have also been implicated. Additionally, elevated serum levels of trace elements like copper and zinc have been linked to increased malignant transformation rates due to their role in oxidative stress and tumour progression[9].

Previous studies on OSMF have faced several limitations, including the lack of standardized diagnostic criteria, which has led to inconsistencies in clinical staging and histopathological grading. Many studies have been confined to hospital-based cohorts, limiting their generalizability, and most fail to incorporate long-term follow-up data, making it difficult to establish precise malignant transformation rates. The study aimed to analyse the demographic, clinical, and pathological characteristics of OSCC cases while specifically identifying those that underwent malignant transformation from OSMF.

MATERIALS AND METHODS

The present study included patient data of individuals previously diagnosed with OSCC between May 2023 and December 2024 at Saveetha Dental College and Hospitals, Chennai.

Inclusion and Exclusion Criteria

Patients with a confirmed diagnosis of OSCC were included, while those presenting with concurrent oral mucosal lesions, incomplete medical records, OSMF associated with other malignant jaw lesions, or recurrent OSCC cases were excluded. Additionally, patients with other premalignant lesions were also omitted from the study to maintain data homogeneity.

Data Collection and Categorization

A total of 119 OSCC cases were identified, and relevant patient details were retrieved from the Diagnostic Imaging Accreditation Scheme (DIAS) database. The collected data were systematically categorized based on age, gender, oral habits, chief complaints, histopathological diagnosis, tumour grading, staging, and the primary site of involvement. From this dataset, cases of malignant transformation from OSMF to OSCC were filtered and analysed separately. Furthermore, a subset of patients exhibiting microbial growth associated with OSCC was also considered for evaluation.

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Statistical Analysis

The compiled data were subjected to statistical analysis using SPSS software (version 23). Chi-square test and t- test were employed to determine statistical significance across different variables, ensuring a comprehensive assessment of the correlations between clinical parameters and OSCC progression.

RESULTS

Out of 119 patients diagnosed as OSCC 13 patients came with the chief complaint of burning sensation, limited mouth opening and ulceration and had gutka and pan habits past 20 years with mucosa and tongue as a primary site of origin of tumour. Their diagnoses include epithelial dysplasia, invasive oral squamous cell carcinoma from oral submucous fibrosis, and superficially invasive oral squamous cell carcinoma associated with advanced oral squamous cell carcinoma. Of these, one has been diagnosed as moderately differentiated and the other twelve as well differentiated (Figure 1).

The gender distribution showed a clear male predominance, with 83% of the population being male and only 15.2% female. This suggests that OSMF and its progression to OSCC may be more prevalent among men, likely due to higher exposure to risk factors such as tobacco and betel nut consumption.

Regarding lifestyle habits, 55.9% of the population reported chewing pan, making it the most common habit. Tobacco consumption was also significant, with 11.8% of individuals using tobacco products, while 3.38% of the population were Bedi users, and another 3.38% consumed betel nuts. Other habits, such as alcohol consumption and smoking (1.69%), gutkha chewing (1.58%), and smoking alone (1.67%), were present in smaller proportions. Additionally, a small percentage (3.38%) reported engaging in a combination of pan, smoking, and alcohol consumption, indicating potential multiple risk factors contributing to disease progression. These findings highlight the strong association between oral habits, especially pan, tobacco, and betel nut consumption, with the development and progression of OSMF.

Tumour grading analysis indicates that 74.6% of cases were classified as well-differentiated, while 22% were moderately differentiated, and a small percentage (1.52%) were poorly differentiated. The presence of 13% of cases where OSMF turned into OSCC revealed the malignant potential of the disease. This suggests that although many cases remain in well-differentiated stages, a notable proportion progresses to more severe forms, emphasizing the need for early intervention.

The data on nodal involvement shows that 53.3% of cases exhibited nodal metastasis, indicating that more than half of the patients had some degree of lymph node involvement and none of the cases showed metastasis. This highlights the aggressive nature of OSCC in a substantial portion of the population, further emphasizing the importance of early diagnosis and monitoring of disease progression.

Lastly, the presence of organism growth was detected in 18.3% of the cases, suggesting that infections might play a role in disease pathology or could be secondary infections due to compromised oral health. The role of microbial factors in the progression of OSMF and OSCC needs further investigation, but their presence in a significant portion of patients suggests an area for further clinical research.

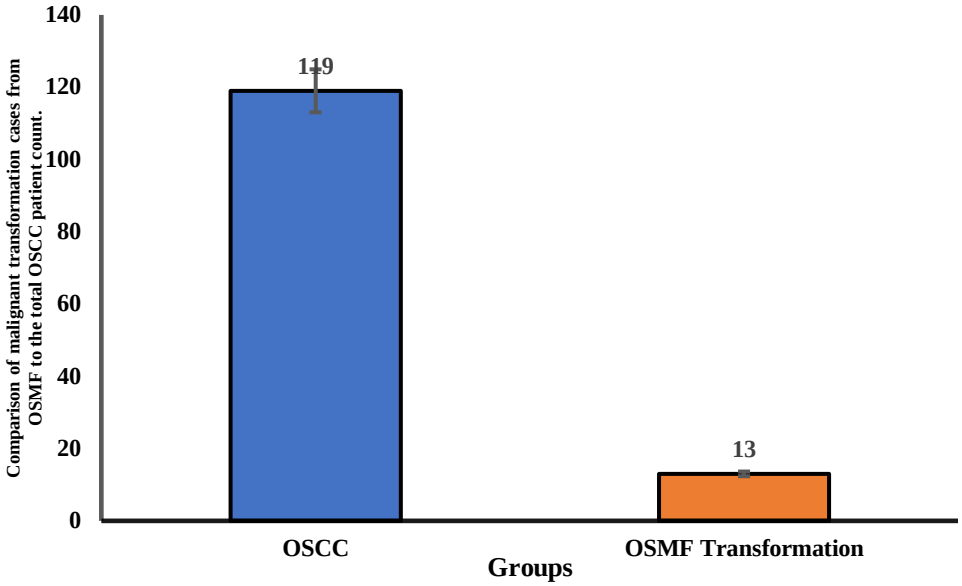


Figure 1. The bar chart compares the number of OSCC cases with malignant transformation from OSMF cases.

The analysis indicates that a large proportion of the population engages in high-risk habits, with pan and tobacco consumption being particularly prevalent. The progression of OSMF to OSCC in 13% of cases, along with 53.3% nodal involvement, demonstrates the severity of the condition. The presence of bacterial or fungal growth in 18.3% of cases may suggest an added complication in disease management. These findings emphasize the critical need for public awareness, early screening, and lifestyle modifications to reduce the burden of OSMF and its transformation into OSCC (Figure2).

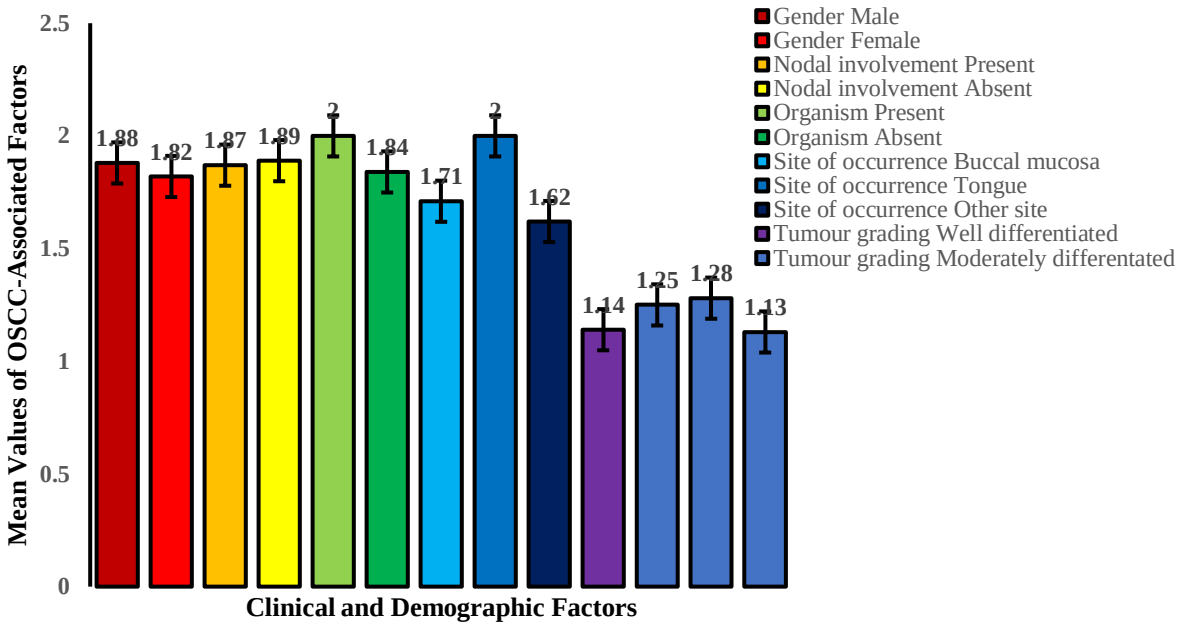


Figure 2. The bar chart presents the mean values of different factors associated with oral squamous cell carcinoma (OSCC). The factors are color-coded and categorized based on gender, nodal involvement, presence of an organism, site of occurrence, tumor grading, and habits.

Table 1. The table presents statistical comparisons (t-test) of a measured parameter across different categorical groups, including Gender, Nodal Involvement, and Organism Presence.

Clinical and Demographic Factors		N	Mean	Standard Deviation	Standard Error	Significance
Gender	Male	100	1.88	0.326	0.032	0.83
	Female	18	1.82	0.30	0.076	
Nodal involvement	Present	80	1.87	0.332	0.37	0.536
	Absent	38	1.89	0.311	0.50	
Organism	Present	26	2.0	0.00	0.00	0.00*
	Absent	92	1.84	1.84	0.037	
Site of Occurrence	Buccal mucosa	54	1.71	0.72	0.031	0.04
	Tongue	18	2	0.94	0.07	
	Other site	47	1.65	0.66	0.53	

* statistically significant ($p<0.05$)

The study analysed the effects of gender, nodal involvement, and organism presence on a measured parameter. The results showed that gender (male vs. female) had no effect, as both had the same mean value (1.88) and a high p-value (0.83), and the difference was not significant. Similarly, nodal involvement (present vs absent) also had no significant impact, with very close mean values (1.87 vs. 1.89) and a p-value of 0.536. However, the presence of an organism had a significant effect, with a higher mean value (2.0 vs. 1.84) and a p-value of 0.00, indicating a strong relationship. The low standard deviation (0.00) in the organism-present group suggests consistent results. Overall, gender and nodal involvement do not influence the measured parameter, but the presence of an organism significantly affects it (Table 1). Organism observed were predominantly *Psedomonas aeruginosa and Streptococccus epididymis.*

Table 2. Table represents the results of the **Pearson chi-square test, which examines the association between tumour grading, habits and gender**.

	Tumour grading						
Clinical and Demographic factors		**Well differentiated**	**Moderately differentiated**	**Total**	**Value**	**df**	**Significance**
Habits	Yes	76	26	100	1.868	1	0.172
	No	16	2	18			
Gender	Male	76	24	100	0.27	1	0.870
	Female	14	4	18			

The study examined whether habits (such as smoking or alcohol use) and gender have any effect on tumour grading. The results showed that there was no significant association between habits and tumour differentiation ($p = 0.172$) or between gender and tumour differentiation ($p = 0.870$). Although more people with habits had moderately differentiated tumours compared to those without habits, the difference was not statistically significant. Similarly, tumour differentiation was almost the same between males and females, meaning gender does not play a major role.These findings suggest that habits and gender do not significantly influence grading of tumour(Table 2).

Table 3. The results of a Pearson chi-square test, analysing the relationship between age groups and the progression of OSMF to OSCC.

		OSMF to OSCC	Reported as OSCC	Total	Value	df	Significance
Age	<30years	2	2	4	7.24	2	0.27
	30-50years	8	48	56			
	>50years	4	54	58			

The study analysed whether age affects the progression of oral submucous fibrosis (OSMF) to oral squamous cell carcinoma (OSCC)**.** The results showed no significant association between age and disease progression (p = 0.27). Although more cases of OSMF progressing to OSCC were seen in the 30-50 years group (8 cases) compared to <30 years (2 cases) and >50 years (4 cases) groups, this difference was not statistically significant**.** The majority of OSCC cases were in the >50 years group (54 cases)**,** likely due to longer exposure to risk factors rather than age itself being a direct cause (Table 3). These findings suggest that age alone does not play a major role in OSCC development**,** and other factors duration of tobacco use, betel nut chewing, and genetic predisposition may have a stronger influence.

DISCUSSION

The present cross-sectional study analysed the malignant transformation of OSMF to OSCC by evaluating clinical and demographic factors. The findings revealed that 13% of the OSCC cases showed malignant transformation from OSMF, with a notable male predominance of 83% and significant association with pan chewers of 55.9%. The primary site of tumour origin was the buccal mucosa and tongue, were Well-differentiated squamous cell carcinoma was the most common histological type. The malignant transformation rate (MTR) of OSMF observed in the present study was 13% aligned with the previously reported range of 7-13% in India, which is significantly above the global average of 5.5%[10]. Study by Ranganathan et al. (2004) reported similar MTRs, emphasizing the role of early-onset areca nut consumption and prolonged exposure to carcinogenic agents such as tobacco and alcohol in increasing malignancy risk[11].

The observed male predominance in this study was consistent with earlier findings, which attribute higher OSMF prevalence in males to cultural and behavioural factors, including greater exposure to areca nut and tobacco products[12]. A study by Pandiar et al. (2019) reported a similar gender distribution, with males accounting for nearly 80% of OSMF cases progressing to OSCC[13]. However, studies from other regions have reported a more balanced gender distribution, suggesting potential genetic and hormonal influences in disease progression[14]. Pan chewing emerged as the most common habit of about 55.9% among OSMF patients in the present study, in agreement with research by Hazarey et al. (2007), which highlighted the strong correlation between betel quid chewing and OSCC risk[15]. Additionally, the present study found that gutkha users had a significantly higher incidence of OSCC, corroborating findings by Gunjal et al. (2020), who reported a 4.2 times higher risk of OSCC in gutkha consumers compared to those using areca nut alone[16].

The predominance of well-differentiated OSCC cases of 74.6%) in this study was consistent with earlier studies by Arakeri et al. (2014), which suggested that OSMF-related OSCCs tend to exhibit better differentiation than tobacco-induced OSCC[17]. The buccal mucosa and tongue being the primary sites of tumour occurrence align with previous reports, further supporting the hypothesis that localized carcinogenic exposure plays a crucial role in site-specific malignancy development[18]. More than half of the patients (53.3%) in this study exhibited nodal involvement, comparable to the findings of Krishna Rao et al. (2016), who reported nodal metastasis in 50-60% of OSMF-derived OSCC cases[19]. The presence of microbial growth in 18.3% of cases suggests a potential role of secondary infections in OSCC pathogenesis. Previous studies have highlighted the involvement of bacterial species such as *Pseudomonas aeruginosa and Streptococcus epidermidis* in oral carcinogenesis, indicating a

possible link between chronic inflammation and malignant transformation[20].

While this study provides valuable insights into the malignant transformation of OSMF, certain limitations must be acknowledged. The cross-sectional design restricts the ability to establish a direct causal relationship between risk factors and OSCC development. Additionally, a larger sample size and multi-center data collection would enhance the generalizability of findings. Future research should focus on identifying molecular biomarkers for early detection and investigating the role of microbiome alterations in OSMF progression to OSCC.

CONCLUSION

The present study corroborates previous literature findings on OSMF malignant transformation, reaffirming the high-risk association with areca nut and tobacco habits, male predominance, and significant nodal involvement. The consistency of results with past studies revealed the necessity for early intervention, public awareness programs, and stringent regulations on areca nut products to mitigate the disease burden. Future studies with larger sample sizes and long-term follow-ups are essential to further elucidate the molecular mechanisms underlying OSMF progression to OSCC.

DECLARATIONS

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Conflict of Interest
The author declares that there were no conflicts of interests in the present study.

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REVIEW ARTICLE

IMPACT OF CHRONIC KIDNEY DISEASE ON NUTRITION AND ORAL DISEASES

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ABSTRACT

Background and Aim: A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. CKD like any other systemic disease is known to directly or indirectly affect the oral tissues. This condition can also affect the disease process and therapy in some patients. Nutrition plays a very important role in modifying the oral health in CKD patients. Therefore, it is important for the clinicians to recommend a regular dental checkup and also refer the patients to nutritionists for tailored diet plan in CKD and end stage renal disease patients who are under hemodialytic therapy. Here, in this review we will dive deep to explore how nutrition in chronic renal disease patients effects oral mucosa and tissues.
Materials and methods: PubMed, Scopus, Web of Science, Google scholar were searched using pre-specified search strategy. Narrative and systematic reviews were included for the data synthesis.The results of this review were reported following the PRISMA guidelines. A narrative synthesis of the findings was provided.
Results: Extensive literature search was carried out using pre-defined search strategy. A total of 125 titles were screened rigorously by two independent evaluators and after duplicate exclusion (58), removal of irrelevant titles (5) and other exclusions, 32 articles were included in total for review preparation.
Conclusion: Oral diseases have a very strong relation with chronic kidney disease. Most of research has found out to have a positive association between both of them. Having thorough knowledge on all systemic diseases is very important for budding clinicians since these diseases negatively impact the progression of oral diseases and vice versa. Positive association can be established with further research and larger sample size studies.

Keywords: Chronic Kidney Diseases, Oral diseases, Nutrition, Systemic health

INTRODUCTION

A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. As oral cavity is a point of exit and entry for external sources, it has an importance in depicting one's own systemic health.[1]

As we all know that few oral conditions and systemic health are interrelated, there is a high chance of changes in the oral cavity such as inflammation, bone loss, lesions on buccal mucosa and cheeks, ulcers, when a person is affected with a systemic condition.[2] Oral diseases are also known to be vital diseases which can affect the mechanical and functional aspect of oral cavity, quality of life and overall health. Though there are several systemic conditions which are related to oral diseases, chronic kidney disease (CKD) is one of the conditions which is directly related to major signs and symptoms in oral cavity.[3]

CKD or chronic renal disease (CRD), according to the National Kidney Foundation (NKF), is kidney impairment that lasts for three months or more and is accompanied by structural or functional abnormalities of the kidney, either with or without a decline in glomerular filtration rate (GFR).[4]

CKD like any other systemic disease is known to directly or indirectly affect the oral tissues. This condition can also affect the disease process and renal therapy in some patients. Few of the oral conditions which are frequently affected in chronic kidney disease patients include white and red patches, periodontitis, mucositis, oral candidiasis, pale mucosa or pigmented mucosa, burning sensations on cheeks and lips as well as changes in salivary composition. [5]

Clinical and radiological alterations in the oral cavity are linked to chronic kidney disease. Loss of lamina dura and radiolucent lesions in the maxilla and mandible are among the radiographic alterations. Clinical results in individuals with chronic kidney disease are similar to those reported for oral lesions in systemic illness.[6] Untreated oral lesions in CKD can lead to a high graft rejection rate (in kidney transplant patients) and an increase in systemic inflammatory load, which exacerbates the underlying systemic illness.[7] Nutrition or diet also play a major role in maintaining overall systemic health and oral health in CKD patients. CKD patients cannot maintain salts and minerals in the body properly and therefore need a proper diet to balance these salts and minerals. Calcium and vitamin D deficiency is most common in CKD patients and may lead to TMJ dysfunctions and renal osteodystrophy's.[8] There is a need for dentists to know in and out about CKD, its complications, diet modifications and how does diet improve overall health and oral health in CKD patients. Therefore, this review focuses on the nutritional therapy in CKD patients and its effect on oral cavity.

MATERIALS AND METHODS

PubMed, Scopus, Web of Science, Google scholar were searched using pre-specified search strategy. Narrative and systematic reviews were included for the data synthesis. The results of this review were reported following the PRISMA guidelines (figure 1). A narrative synthesis of the findings was provided.

RESULTS

Extensive literature search was carried out using pre-defined search strategy. A total of 125 titles were screened rigorously by two independent evaluators and after duplicate exclusion (58), removal of irrelevant titles (5) and other exclusions, 32 articles were included in total for review preparation.

Effect of Nutrition in CKD patients and their associated Oral diseases

Oral diseases are most common in CKD patients with abnormal blood urea levels. Let us discuss nutrition in CKD patients and its effect on oral cavity.

Medical nutrition therapy in CKD patients can help in delaying progression of the disease thereby improving the quality of life as well as oral health. Through elevated insulin resistance, chronic inflammation in CKD patients can cause protein catabolism, which can seriously harm a person's nutritional condition. Hyperkalemia, hyperphosphatemia, anorexia, and muscle and fat wasting are all possible symptoms of chronic kidney disease (CKD).[9,10] Hemodialysis patients are more prone to malnutrition and can be due to inadequate caloric and protein intake which is protein energy wasting and typical CKD related comorbidities such as uremic gastritis, depression, metabolic acidosis and uremic gastritis.[11] This can lead to hypo vitaminosis C, D and B. Vitamin C deficiency can also due to non-consumption of fresh fruits and vegetables. Vitamin C can help in maintaining oral and gingival health by regulating physiological blood vessel activity. It also favors animal and vegetable iron absorption. It interferes with the healing processes of wounds and aids in the development and maintenance of bone and connective tissues.[12]

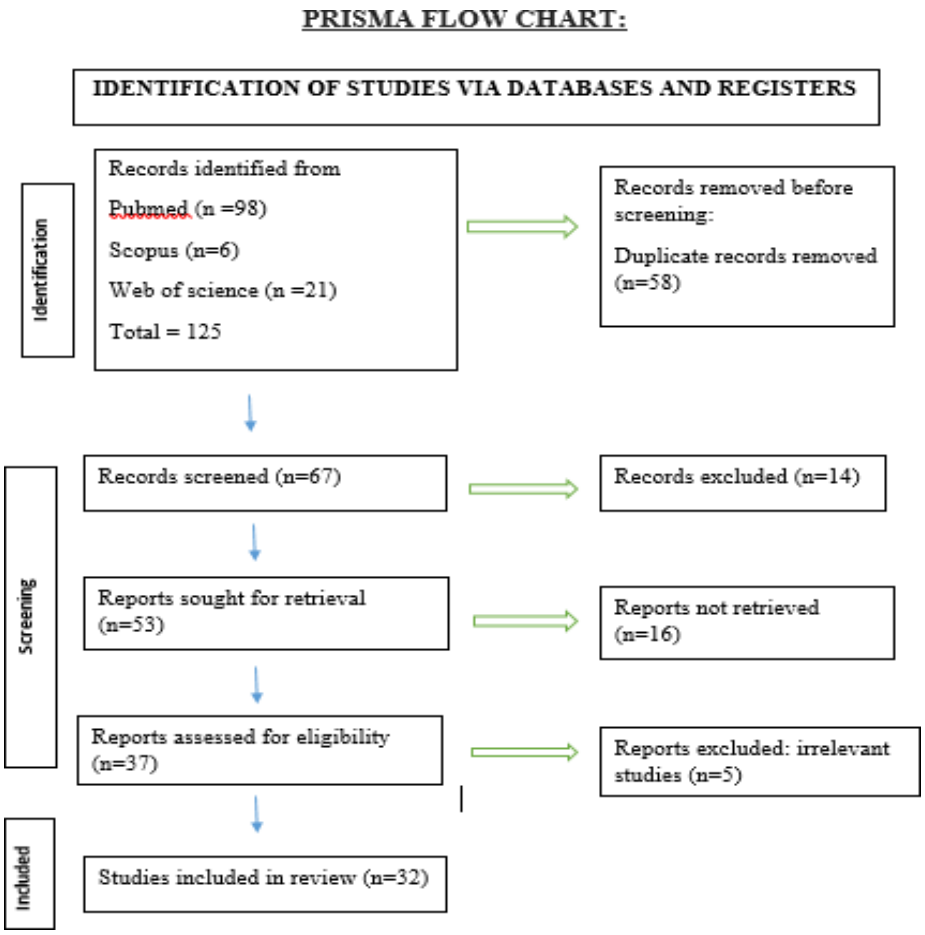


Figure 1. Diagram study flow method used the PRISMA

Etiology for vitamin deficiency in CKD patients under hemodialysis:[13]

VITAMIN C	B GROUP VITAMINS	VITAMIN D
• Dietary restrictions • Removal during Hemodialysis treatment • Gastro intestinal symptoms	• Poly pharmacy • Dietary restrictions • Removal during HD treatment • Uremic gastropathy	• Decrease activity of 1 α hydroxylase • Increased vitamin D inactivation • Decreased sun exposure • Unbalanced diet

Uremic Stomatitis

Uremic stomatitis is one of the most common condition in CKD patients due to vitamin deficiency. Here, the patient may have erythema-pultaceous, ulcerative, hemorrhagic, and hyperkeratotic forms. Untreated uremic patients also have a condition called "uremic frost" where urea crystals appear on epithelial surfaces of oral cavity after evaporation of saliva.[14]

Uremia can also cause oral ulcers/ stomatitis, bad odor, metallic taste leading to high salivary phosphate, high salivary urea, xerostomia and renal osteodystrophy.[15] These in turn cause dental caries, masticatory problems,[16] ill-fitting dentures and temporo-mandibular joint problems. The process of CKD leading to oral diseases in explained in the figure 2 below. Please have a look.

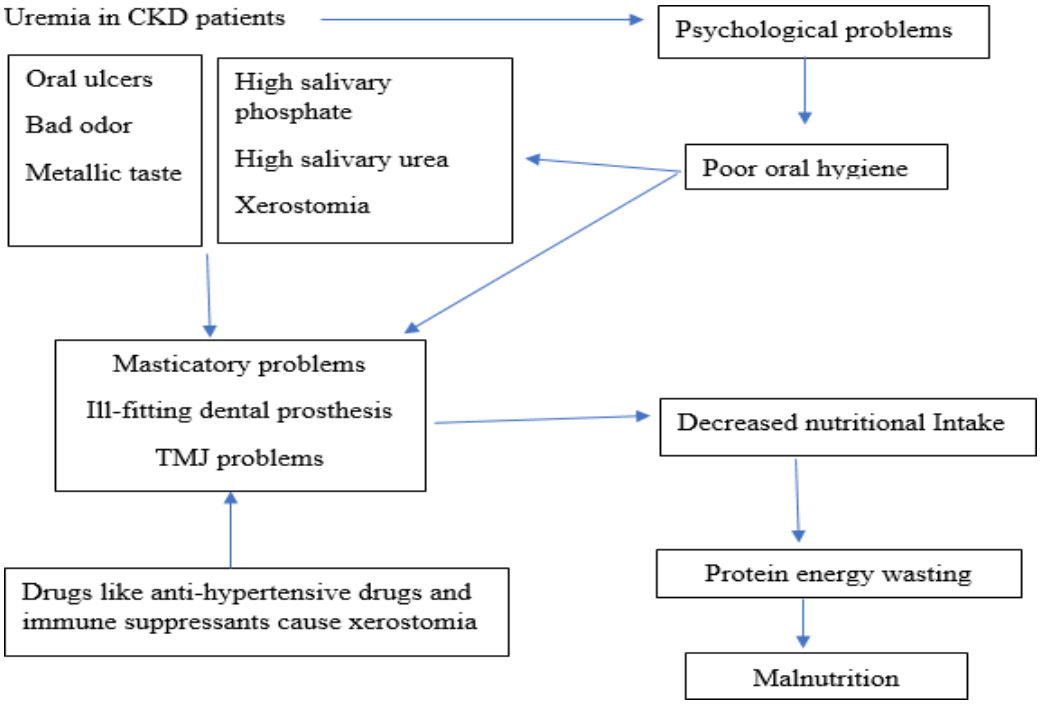


Figure 2. Flow chart **.** CKD and Oral diseases

A study from the Netherlands reported similar values for the majority of dental features, whereas a study from Spain revealed that HD patients had significantly greater plaque and calculus indices and decreased salivary secretions when compared to healthy controls.[17]

End Stage Renal Disease (ESRD)

CKD patients are more prone to ESRD. End stage renal disease patient who is under hemodialysis treatment can have malnutrition, hypovitaminosis C, B, D; low grade inflammation, metabolic acidosis, oxidative stress (figure 3). These can consequently lead to decreased bone turn over, periodontal disease, decreased salivary secretion, decreased healing process and oral microbiota alteration.[18] Proctor et al in 2005 found out that most of the CKD patients had metallic taste due to excessive usage of medication.[19]

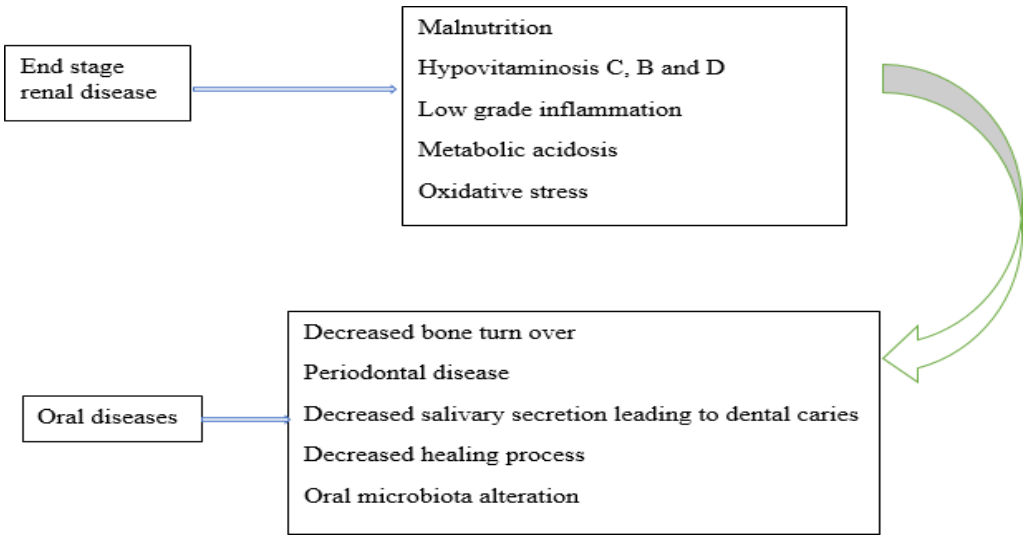


Figure 3. Link between ESRD and Oral diseases in Adults

Let us see nutritional deficiencies in CKD patients and their effects:[20]

Deficient nutrition	Effect on oral structures
Protein malnutrition	Salivary gland dysfunction
Vitamin B1	Angular cheilitis Cracked red lips
Vitamin B2	Glossitis
Vitamin B3	Uremic stomatitis or gingival ulcerations
Vitamin B6	Periodontitis Anemia, sore tongue Burning sensation in the oral cavity
Vitamin B12	Angular cheilitis Bad breath or Halitosis Alveolar bone loss Erythematous and bleeding gingivitis Oral ulceration Periodontal fiber detachment
Vitamin C	Impaired wound healing Incomplete collagen formation Periodontal disease
Vitamin D and calcium	Alveolar bone loss and gingival inflammation Renal osteo dystrophy TMJ dysfunction
Iron	Angular cheilitis Burning mouth syndrome Angular cheilitis Uremic stomatitis and ulcerations

Micronutrient deficiency in CKD and Oral diseases

Deficiencies in iron, folic acid are associated with oral candida infections. Chronic atrophic candidiasis, chronic mucocutaneous candidiasis, angular stomatitis and atrophic glossitis are seen in iron deficiency patients. CKD patients are more prone to iron deficiency.[21] This iron deficiency leads to depletion of enzyme levels, impaired host deficiencies, reduction in epithelial thickness, decreased hemoglobin levels leading to insufficient oxygen to oral mucosa. This insufficient oxygen supply causes epithelial atrophy leading to overgrowth of candida in CKD patients.[22]

Calcium and Vitamin D

CKD patients are more to renal osteo dystrophy and temporomandibular joint dysfunctions due to calcium deficiency. Numerous body processes depend on calcium, an electrolyte and multivalent cation. It is vital for bone development, blood cell production, and the proper operation of the digestive, circulatory, and muscular systems.[23] Calcium exchange in the bones, reabsorption in the kidney, and absorption in the gut all tightly control calcium equilibrium.

As chronic kidney disease (CKD) worsens, the serum calcium level falls because the kidneys play a crucial role in maintaining calcium homeostasis. Reduced calcium levels can result in secondary hyperparathyroidism, which causes metabolic bone disorders, whereas excess calcium can produce extraosseous calcification, which increases mortality and causes cardiovascular disease.[24]

A number of parameters, such as mineral controlling hormones, renal function, bone turnover, the use of vitamin D analogs, and calcium consumption via supplements, must be considered in order to maintain a balanced blood calcium level in patients with chronic kidney disease (CKD). The dialysate's calcium content and the dialysis mode are two further variables that need to be considered for patients who need maintenance dialysis. Because each patient's calcium balance is affected by different circumstances, it might be difficult to provide appropriate dietary calcium.[23]

The deficiency of calcium can be managed by

incorporating a daily intake of dietary calcium of 800 to 1,000 mg/day. Similarly, vitamin D can be taken in the form of supplements and can also be achieved by increasing the degree of sunlight exposure. There are no safe guidelines recommended for vitamin D supplements in CKD patients. Dental practitioners should refer the patient to a nephrologist for consent before commencement of any dental procedure.[25]

Phosphorous, CKD and Oral diseases

Phosphorus is an essential nutrient which helps in maintaining homeostasis in body. It also helps in acid-base balance, bone growth, mineralization and regulation of energy. Resistance to parathyroid hormone and fibroblast growth factor may result in hyperphosphatemia, or high blood phosphate levels, as chronic kidney disease (CKD) worsens. Here, phosphorus excretion is halted causing increase in phosphate levels in blood.[26]

This hyperphosphatemia can lead to inflammation of tissues eventually leading to gingivitis and periodontitis. Dietary phosphorous has an inverse relationship with salivary IL-4 concentration and a direct relationship with salivary IL-1β concentration. Dentists can recommend low phosphate diet by consulting the concerned nephrologist to decrease the level of inflammation in gingival tissues. They can also educate patient to consume low phosphate diet.[27]

CKD and Periodontal disease

It has been discovered that CKD patients had higher prevalence's of oral keystone bacteria linked to periodontitis, such as Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola, Aggregatibacter actinomycetemcomitans, and Actinomyces dentalis, than the general population.[28] Another mechanism is that changes in the microenvironment brought on by CKD also have a permissive effect, impairing both innate and adaptive immunity. In CKD, the diminished antigen presentation skills of dendritic cells and macrophages lead to decreased cytokine production, impaired neutrophil phagocytic capabilities, and decreased monocyte stimulation effectiveness (figure 4).
This can lead to periodontal disease in CKD patients.[29]

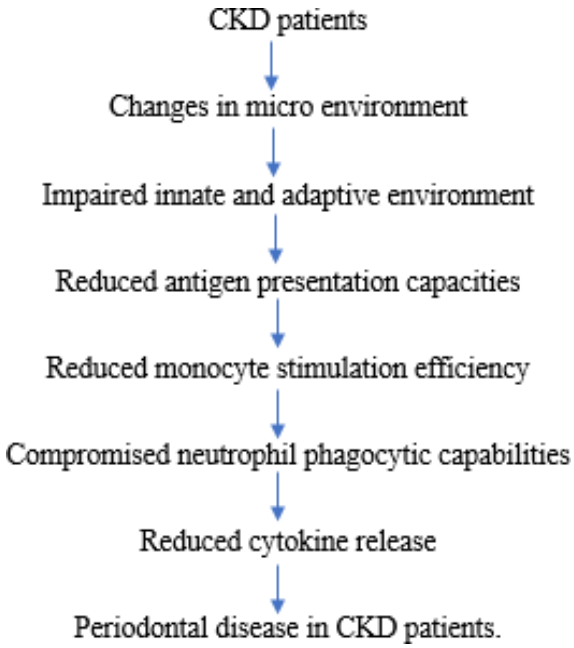


Figure 4. Flow chart CKD and Periodontal Disease

Antigen-presenting cell malfunction and decreased toll like receptors expression or activity can also lead to decreased immune function causing periodontal infections. Basic scaling and root planning can help in reducing micro-organisms and inflammation to some extent in CKD patients.[30]

Oral and Cutaneous hyper pigmentation

The inability of the kidney to eliminate excess beta melanocyte stimulating hormone (b-MSH), which builds up and stimulates melanocytes in the basal layer of the oral epithelium, causes oral and cutaneous hyperpigmentation in renal patients. Orthodox drugs prescribed for CKD patients such as antimalarials (quinacrine, chloroquine, hydroxychloroquine) can cause oral hyperpigmentation.[22]

Psychological issues in CKD patients

Uremia is most common in CKD patients which can lead to psychological problems. These psychological issues can consequently can decreased nutrition intake leading to abnormal oral conditions. Similarly, due to the usage of anti-hypertensive drugs and immune suppressants, patients with CKD have xerostomia and taste disturbances. Psychological problems can also lead to poor oral hygiene leading to increased dental caries.[18,21,22]

Poor Oral hygiene

Poor oral hygiene is the major cause of periodontal diseases which can increase gingival inflammation, bone loss and eventually tooth loss. This tooth loss in turn effects the masticatory function and digestion in CKD patients leading to poor nutritional intake and protein energy wasting.[29]

Recommendations for Clinicians, Practitioners and Hygienists

Since we know oral illness is gateway for many systemic illnesses such as CKD, dentists should recommend kidney profile has a regular investigation to rule out any renal abnormalities. These investigations include serum creatinine, glomerular filtration rate and other blood investigations. Dentists can conduct a regular checkup for risk of oral diseases and can educate the patients for blood investigations.

Thorough history of nutrition intake in CKD patients is also essential to rule out any deficiencies or protein energy wasting. Nutritional deficiencies are the major etiologies for oral diseases in CKD patients.[31,32] Patients should be referred to nutritionists for tailored diet plan so that oral diseases can be controlled to a certain extent.

CONCLUSION

A healthy oral cavity is an integrated sign of a healthy systemic health. Oral cavity is also known to be a powerful tool in diagnosing overall systemic health. Systemic diseases are always in close relationship with oral diseases. There is an overwhelming

CKD is one of them where nutrition in these patients effect the oral tissues and epithelium. Having thorough knowledge on CKD and ESRD patients as well as their diet can help the clinicians to diagnose the oral condition precisely and manage accordingly. This knowledge can also help in diagnostic and therapeutic procedures even in hemodialytic and end stage renal patients.

Since CKD is a common global condition, its association with oral diseases should be studied in detail to aid for betterment in management. Further studies to identify the association of CKD and oral conditions should be done to provide awareness in budding practitioners and patients.

DECLARATIONS

Conflicts of interest and financial disclosures

The authors declare no conflict of interest

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Consent Not

Applicable

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ORIGINAL ARTICLE

GENOMIC AND TRANSCRIPTOMIC ALTERATIONS IN THE ELN GENE NETWORK AND THEIR ASSOCIATION WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA

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Abstract

Background: Head and neck squamous cell carcinoma (HNSCC) are a common form of cancer that arises in the mucosal surfaces of various anatomical locations, including the larynx, oral cavity, and nasal cavity. The *ELN* gene plays a crucial role in elastin synthesis, a protein responsible for maintaining the elasticity of skin, blood vessels, and ligaments, thereby preventing cell senescence. Genetic alterations in the *ELN* gene family may contribute to the development and progression of HNSCC.
Objectives: This study aims to investigate the alterations in the *ELN* gene family and their potential association with HNSCC.
Materials and Methods: Computational analyses were performed using publicly available databases, including UALCAN, cBioPortal, and STRING, to identify genetic changes in HNSCC patients. The study focused on mutations (missense and truncating), gene amplification, and deep deletions within the *ELN* gene family.
Results: The analysis revealed a high frequency of alterations in *ELN* family member 11, occurring in 5% of HNSCC patients. Additionally, a significant variation in *ELN* gene expression was observed between normal samples and different cancer grades. Kaplan-Meier survival analysis indicated an insignificant difference for the *MFAP2* gene but a significant difference for the *FN1* gene between normal and primary tumour groups in HNSCC.
Conclusion: These findings suggest a potential link between *ELN* gene alterations and HNSCC, emphasizing the necessity for further experimental validation to confirm these preliminary observations and elucidate the underlying mechanisms.

Keywords: **Elastin, ELN gene, computational analysis, Gene expression, Squamous cell carcinoma**

INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) from the mucosal surfaces of the oral cavity, nasal passages, pharynx, and larynx and was one of the most aggressive malignancies. Patients with HNSCC continue to have a dismal prognosis despite improvements in therapies and diagnostic methods; the five-year survival rate was often only 50%. This outcome is often attributed to late-stage diagnosis, high rates of recurrence, and the complex molecular heterogeneity of the disease[2]. Consequently, there is a need to better understand the molecular underpinnings of HNSCC to develop more effective diagnostic, prognostic, and therapeutic strategies[3].

One promising area of research for understanding the complexities of HNSCC involved the study of genomic and transcriptomic changes. Genomic alterations refer to changes in the DNA sequence, such as mutations, amplifications, and deletions, while transcriptomic alterations pertain to changes in gene expression levels[4]. Together, these alterations can significantly impact cellular function and contribute to cancer development and progression. Among the myriad of genes implicated in cancer, the *ELN* gene network, which encodes for proteins essential in maintaining tissue elasticity, has garnered attention for its potential role in HNSCC[5].

Tropoelastin, the precursor to elastin, a crucial extracellular matrix protein that give tissues like skin, blood vessels, and ligaments their elastic qualities, which is encoded by the *ELN* gene. Elastin provides resilience and flexibility, allowing tissues to stretch and recoil[6]. In addition to its structural role, elastin also participates in various cellular processes, including cell signaling, proliferation, and migration. Alterations in the *ELN* gene or its regulatory network can disrupt these functions, potentially contributing to tumorigenesis[7].

Recent data points to a potential role for the *ELN* gene network in the etiology of HNSCC. Studies have identified various genomic alterations in the *ELN* gene, such as amplifications, deletions, and point mutations, which could affect the normal function of elastin and its associated pathways. Moreover, transcriptomic analyses have revealed differential expression patterns of *ELN* and related genes in Colorectal cancer tissues compared to normal tissues. These findings hint at a complex interplay between the *ELN* gene network and the molecular mechanisms driving Colorectal cancer[8]. To elucidate the role of the *ELN* gene network in HNSCC, it is crucial to integrate genomic and transcriptomic data. This integrated approach allows for a comprehensive understanding of how alterations at the DNA level translate into changes in gene expression and, subsequently, cellular behavior. By using sequencing technologies and advanced bioinformatics tools, researchers can map the genomic and transcriptomic changes in the *ELN* gene network, find important driver mutations, and discover potential treatment targets[9].

Additionally, understanding the importance of *ELN* gene changes in predicting HNSCC outcomes is crucial. Prognostic biomarkers can help classify patients by their risk of recurrence or disease progression, allowing for more personalized treatment plans[10]. Previous studies have suggested that alterations in gene network may correlate with clinical outcomes in HNSCC patients[11,12]. For instance, differential expression of *ELN* has been associated with varying survival rates, indicating its potential as a prognostic marker[13]. In addition to its prognostic value, the *ELN* gene network may also offer novel therapeutic opportunities. Targeting specific genomic alterations or modulating the expression of key genes within this network could pave the way for innovative treatments. For example, drugs that restore normal elastin function or inhibit pathways disrupted by *ELN* alterations could prove beneficial in managing HNSCC[14]. The objective of this study was to examine changes in the *ELN* gene network's transcriptome and genome and how they relate to HNSCC.

MATERIALS AND METHODS

Sample data set

An online tool designed for gathering, examining, and deciphering genetic data is the cBioPortal database. It provides information on genetic changes in diverse samples and genes as well as comprehensive patient descriptions from a range of cohorts. There are 530 cases of head and neck squamous cell carcinoma in the Cancer Genome Atlas (TCGA) Firehose Legacy dataset, of which 504 samples have data on copy number modification and sequencing. For every sample, the database contains the entire profile of the genes that have been deleted, amplified, and modified.

Mukundh Subramanian Seetharaman, Priyadharshini Ranganathan, Vijayashree Jayaseelan Priyadharsini. Genomic and Transcriptomic Alterations in the ELN Gene Network and Their Association with Head and Neck Squamous Cell Carcinoma. Bulletin of Stomatology and Maxillofacial Surgery.2025;21(2).230-238 DOI: 10.58240/1829006X-2025.2-230

Analysis of Oncoprint data

Every chosen gene frequency distribution was covered in depth by the Oncoprint data, which also includes information on the type of variation, modifications to the amino acids that code for proteins, gene amplifications, deletions, insertions, frameshifts, and splice site alterations. This data provides a baseline for monitoring mutations or variations, gene expression, and patient survival based on the changed genes using a variety of computational methods[15].

Analysis of the protein-protein interaction network

A database of anticipated and known protein-protein interactions which may involve functional or structural relationships called the STRING database. These relationships are the result of information compiled from several main databases and computer forecasts. Highest frequency alteration of genes within the entire family was selected for further analysis, focusing on gene expression and survival curves[16].

Analysis of gene expression and survival

Analysis of the *ELN* gene, its expression profile and tumour grading were performed similar to the previous study by Tharany et al., in 2021 using the UALCAN database. Using the Comprehensive Perl Archive Network (CPAN) module in a PERL script, the Kaplan-Meier survival analysis was carried out and the correlation of survival between groups was calculated with the p-value[17].

RESULTS

Protein protein interaction analysis

The primary connections of *ELN* with genes like these are disclosed by the protein interaction network such as *LOX, MFAP4, FBN1, MFAP2, FN1, VTN, DCN, BGN, GLB1, and FBLN5*, which play key roles in various biological processes. A p-value, which indicates the significant difference between the normal and HNSCC sample groups, was used to illustrate the expression score. The examination of functional enrichment revealed 45 edges and 11 nodes. A PPI (Protein-Protein Interaction) enrichment value of 3.04 x 10^{-13} indicated a string statistical significance. This value indicates the connections between proteins in the network and the biological interactions (Figure 1).

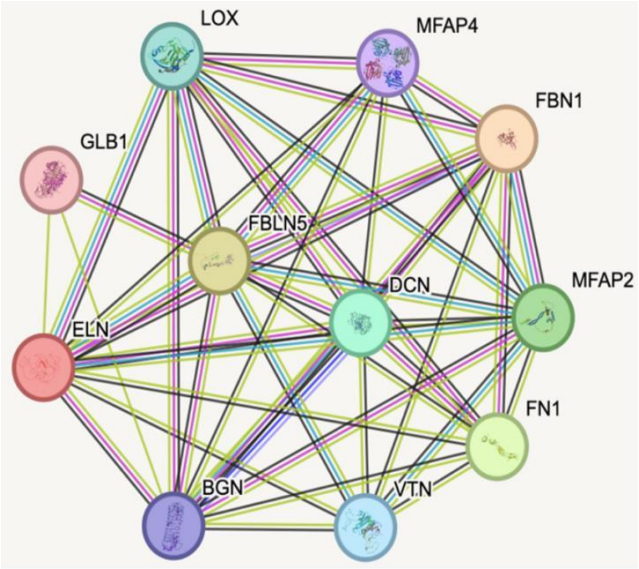


Figure 1. Protein interaction network of *ELN* gene in Homo sapiens (STRING version 12.0)

Analysis of Oncoprint data

Eleven genes had changes identified by the oncoprint data analysis, with *FN1* (5%) having the greatest frequency of Deep deletion, truncating and missense mutation (Figure 2) (Table 1). This was followed by *ELN FBLN5, BGN, FBN1* with 2-4% alteration.

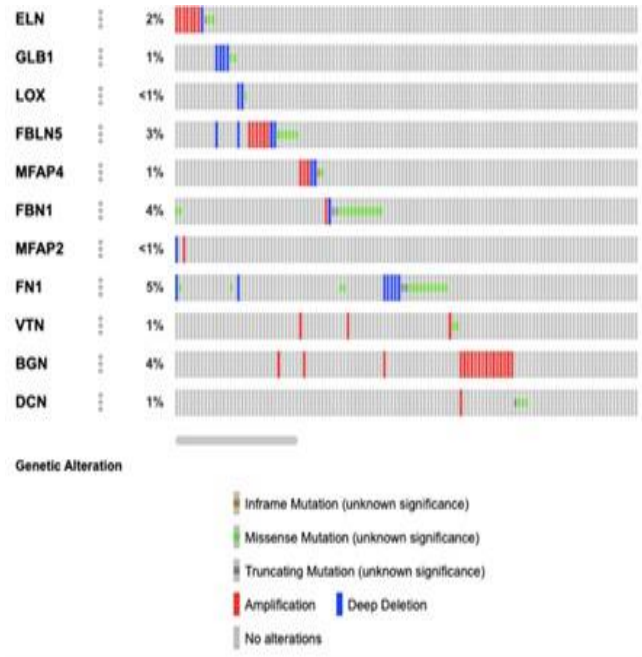


Figure 2. Oncoprint data demonstrating the alterations in the *ELN* gene network

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Table 1. The ELN gene interaction network's genetic changes

Gene	Protein encoded	Frequency of alteration (%)	Type of alteration
ELN	Elastin	2	Gene amplification, Deep deletion, inframe and missense mutation
GLB1	Beta-galactosidase	1	Deep deletion, missense mutation
LOX	Protein-lysine 6-oxidase	<1	Deep deletion, missense mutation
FBLN5	Fibulin-5	3	Deep deletion, missense mutation
MFAP4	Microfibril-associated glycoprotein 4	1	Deep deletion, inframe and missense mutations, and gene amplification
FBN1	Fibrillin-1	4	Missense mutation, truncating, deep deletion, and gene amplification
MFAP2	Microfibrillar-associated protein 2	<1	Gene amplification, Deep deletion
FN1	Fibronectin	5	Missense mutation, truncating, and deep deletion
VTN	Vitronectin V10 subunit	1	Gene amplification, missense mutation
BGN	Biglycan	4	Gene amplification
DCN	Decorin	1	Gene amplification, truncating and missense mutation

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Analysis of the protein-protein interaction network

The primary connections of *ELN* with genes like these are disclosed by the protein interaction network such as *GLB-1, LOX, FBLN 5, MFAP 4, FBN 1, MFAP 2, FN1, VTN, BGN, DCN*. The *MFAP2* and *FN1* genes demonstrated <1% and 5% gross alterations, respectively. Strong evidence was found between the *MFAP2* gene amplification and the gene expression profile, suggesting that primary tissues had higher *MFAP2* expression than normal tissues (p-value =1.62 x 10^{-12}). A p-value, which indicates the significant difference between the normal and HNSCC sample groups, is used to illustrate the expression score (Table 2). An examination of functional enrichment revealed a network with 55 edges and 11 nodes. This indicates that these proteins exhibit a higher degree of interaction among themselves, suggesting that they form a biologically interconnected group. These interactions point to a potential collective functional role or involvement in related biological processes, emphasizing the significance of their co-occurrence within the same biological pathway or system.

Table 2. Gene expression profile and survival of genes included in the ELN gene network

Gene	Gross alteration	Gene expression profile	P value
ELN	Gene amplification, Deep deletion	Insignificant	5.25 x 10^{-1}
GLB1	Deep deletion	Upregulated	1.14 x 10^{-7}
LOX	Deep deletion	Upregulated	2.68 x 10^{-12}
FBLN5	Deep deletion	Insignificant	1.03 x 10^{-1}
MFAP4	Gene amplification, Deep deletion	Downregulated	1.12 x 10^{-2}
FBN1	Gene amplification, Deep deletion	Insignificant	4.06 x 10^{-1}
MFAP2	Gene amplification, Deep deletion	Upregulated	1.62 x 10^{-12}
FN1	Deep deletion	Upregulated	1.62 x 10^{-12}
VTN	Gene amplification	Insignificant	8.83 x 10^{-1}
BGN	Gene amplification	Upregulated	1.62 x 10^{-12}
DCN	Gene amplification	Insignificant	4.41 x 10^{-1}

Gene expression and survival analysis

Significant alterations in gene expression were seen in six out of ten genes within the *ELN* gene network (p-value < 0.05). Of these, there were notable variations in the survival rates of HNSCC patients for two main genes (Figure 1). The HNSCC group's *MFAP2* gene expression profile showed a substantial increase when compared to the normal group (p-value = 1.62 x 10^{-12}).

In patients with HNSCC, low/medium and high *MFAP2* expression showed statistically significant differences in survival outcomes, according to Kaplan-Meier survival analysis (p-value = 0.031), with high *MFAP2* expression associated with poorer prognosis (Figure 3).

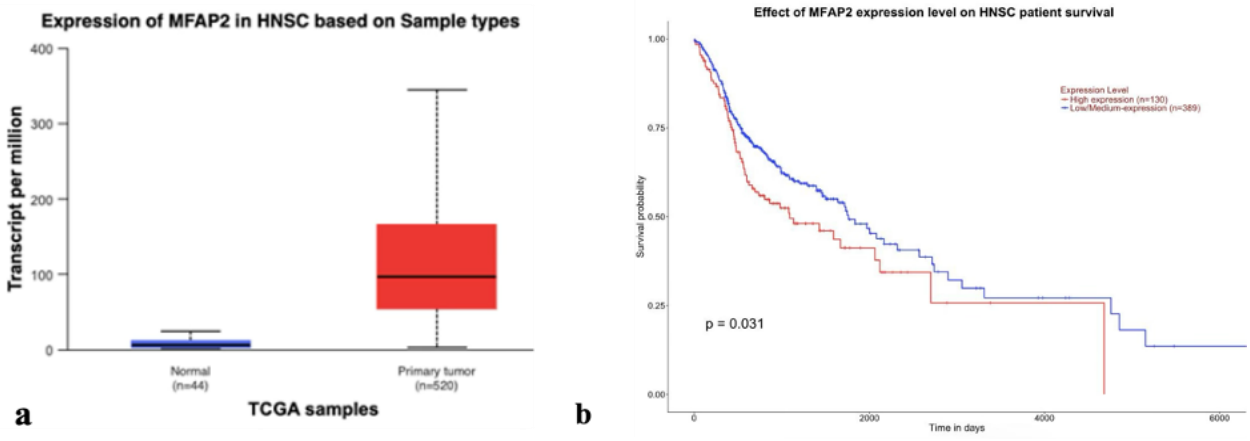


Figure 3. (a) The *MFAP2* gene expression profile. The HNSCC group had a substantial upregulation of the *MFAP2* gene in comparison to the normal (p-value = 1.62 x 10^{-12}), (b) The Kaplan-Meier Analysis of survival in the low/medium and high expression of *MFAP2* gene in HNSCC groups (p-value = 0.031). Patients presenting with high expression of *MFAP2* demonstrated a poor prognosis.

With p-values of 1.62 x 10^{-12} for *MFAP2* and *FN1*, the gene expression profiles of both genes between normal and primary tumor samples showed significant changes. There was a notable variation in the probability of survival according to the expression levels of *MFAP2* and *FN1*, even if the current finding does not support sex predilection of these genes with HNSCC. *MFAP2 and FN1* presented with significant survival probabilities of p = 0.031 and p = 0.051 respectively. (p-value less than 0.05 was considered to be significant) (Figure 3).

Comparing the HNSCC group to the normal group, the gene expression profile of *FN1* also revealed a notable increase (p-value = 1.62 x 10^{-12}). The analysis showed a near significance in survival outcomes between low/medium and high *FN1* expression in HNSCC patients (p-value = 0.051), with high *FN1* expression tending to be associated with a poorer prognosis (Figure 4).

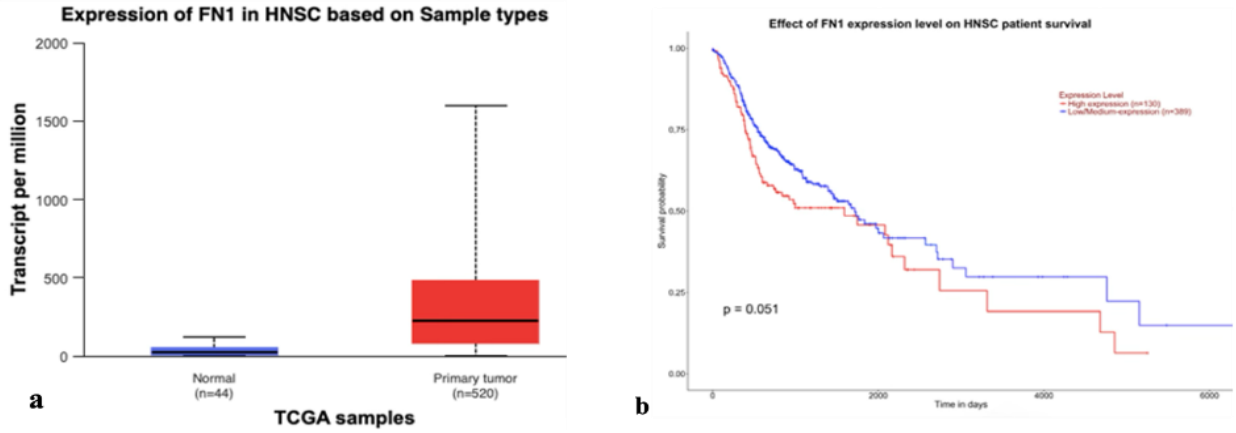


Figure 4. (a) *FN1* gene expression profile. When comparing the HNSCC group to the normal group, it was discovered that the *FN1* gene was substantially elevated (p-value = 1.62 x 10^{-12}), (b) Kaplan-Meier Survival analysis between various expression level of *MFAP2* gene in HNSCC groups (p-value = 0.051). Patients presenting with high expression of *MFAP2* demonstrated a poor prognosis.

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DISCUSSION

Our findings provide new insights into the molecular mechanisms underlying HNSCC and highlight the prognostic significance of specific gene alterations. Our analysis revealed that *ELN* interacts with several key genes, including *LOX*, *MFAP4*, *FBN1*, *MFAP2*, *FN1*, *VTN*, *DCN*, *BGN*, *GLB1*, *and FBLN5*. These genes are involved in various biological processes critical for maintaining tissue elasticity and integrity. It is possible that these proteins interact more frequently among themselves, indicating a physiologically linked group, based on the significant PPI enrichment p-value (3.04×10^{-13}). This aligns with previous studies by Halsey et al. (2023) and Ozsvar et al. (2021), which emphasized the importance of elastin and its associated proteins in cellular processes and tissue structure[6,7]. This finding suggests that the mechanisms driving *ELN* gene alterations may have broader implications beyond HNSCC, supporting the notion of shared pathways in different cancer types. Eleven genes had substantial changes found in our Oncoprint data study, with *FN1* having the highest prevalence of missense, truncating, and deep deletion mutations (5%).

The examination of the gene expression profile showed that the genes *FN1* and *MFAP2* were substantially increased in HNSCC tissues as opposed to normal tissues. A Kaplan-Meier survival study revealed that patients with HNSCC who expressed high levels of *MFAP2* had a worse prognosis (p-value = 0.031), corroborating previous studies by Guo et al. (2021) and Zhou et al. (2022)[13,18]. Similarly, high *FN1* expression tended to correlate with poorer survival outcomes (p-value = 0.051), although this result was near significant. These findings suggest that *MFAP2* and *FN1* could serve as prognostic biomarkers for HNSCC, aiding in the stratification of patients based on their risk of recurrence or disease progression. Our research contributes to the knowledge regarding the molecular causes of HNSCC. Previous research by Kleszcz et al., 2023 has highlighted the complexity and heterogeneity of HNSCC at the molecular level[3]. Our findings align with these studies, emphasizing the need for a comprehensive understanding of genomic and transcriptomic alterations in developing effective diagnostic, prognostic, and therapeutic strategies. Moreover, our identification of specific gene alterations in the *ELN* gene network, such as those in *MFAP2* and *FN1*, aligns with the work of Farah (2021) and Wang et al. (2022), who analysed the role of these genes in maintaining tissue structure and function[4,19]. Our study also highlights the potential of targeting these alterations for therapeutic purposes, supporting the therapeutic implications discussed by Eberly et al. (2024)[10].

Research should focus on longitudinal studies to monitor the temporal changes in the *ELN* gene network and their correlation with disease progression, treatment response, and recurrence in HNSCC patients. This work provides important new information on the possible connection between HNSCC and changes in the *ELN* gene. However, these findings need to be confirmed through experimental validation, highlighting the necessity for further research to establish the biological significance and clinical relevance of these genetic changes.

CONCLUSION

Our research offers fresh perspectives on the transcriptomic and genomic changes in the *ELN* gene network and how they relate to HNSCC. Key driver mutations and putative prognostic biomarkers, like *FN1* and *MFAP2*, have been found, which highlights the significance of these genes in the pathophysiology of HNSCC. Future research should focus on validating and exploring targeted therapies that restore normal *ELN* function or inhibit disrupted pathways. This integrated approach holds the potential to improve the clinical management of HNSCC, ultimately leading to better patient outcomes.

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DECLARATIONS

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Conflict of interest
All the authors declare that there was no conflict of interest in the present study

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RESEARCH ARTICLE

IN VITRO STUDY ON THE SYNTHESIS AND CHARACTERIZATION OF ERBIUM-DOPED HYDROXYAPATITE/BIOGLASS-POLYVINYL ALCOHOL SCAFFOLD FOR PERIODONTAL BONE REGENERATION

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Abstract

Background:Periodontal disease leads to alveolar bone loss, necessitating bone grafting for regeneration. Traditional grafts, including autografts and allografts, have limitations such as donor site morbidity and immune rejection. Bone tissue engineering (BTE) offers an alternative approach using biocompatible scaffolds. This study investigates the potential of an erbium-doped hydroxyapatite (HA)-bioglass-polyvinyl alcohol (PVA) composite scaffold for bone regeneration.

Materials and Methods: The study synthesized an erbium-doped HA, bioglass, and PVA composite scaffold. The scaffold was characterized morphologically using Fourier Transform Infrared Spectroscopy (FTIR) and Scanning Electron Microscopy (SEM). Biological evaluations included hemostatic behavior, anti-inflammatory response, and biocompatibility assessments using an MTT assay and live/dead cell analysis.

Results: FTIR confirmed the structural integrity of the scaffold with characteristic peaks of HA, bioglass, and PVA. SEM revealed a porous, flower-like morphology, promoting cell attachment and nutrient exchange. Hemostatic analysis demonstrated enhanced clot formation, with SEM micrographs showing aggregated RBCs on the scaffold surface, indicating strong hemostatic efficiency.Anti-inflammatory studies indicated a dose-dependent effect, with the scaffold exhibiting significant protein denaturation inhibition at 50 µg. MTT and live/dead assays confirmed high biocompatibility, with over 90% cell viability across tested concentrations.

Conclusion: The erbium-doped HA/bioglass-PVA scaffold demonstrated excellent biocompatibility, hemostatic potential, and anti-inflammatory properties. These findings suggest its suitability for periodontal bone regeneration. Further in vivo studies are required to validate its clinical applicability.

Keywords: **Rare earth element, Periodontal Regeneration, Erbium, Scaffold, Bioglass**

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INTRODUCTION

Periodontal disease, a chronic inflammatory condition affecting the supporting structures of the teeth, ranks among the most prevalent oral health problems worldwide.[1] Characterized by the progressive destruction of the periodontal ligament and alveolar bone, it ultimately leads to tooth mobility and potential tooth loss if left untreated.[1] A significant consequence of periodontal disease, is the formation of bone defects. Insufficient alveolar bone necessitates bone grafting or augmentation procedures to provide adequate support for the tooth to restore proper function and aesthetics.[2]

Traditional bone grafting methods, primarily relying on autografts harvested from the patient's own body, have long been considered the gold standard.[3]Autografts possess inherent osteogenic potential, containing viable bone cells that can directly contribute to new bone formation.[3] However, the limitations associated with autografts are significant. Donor site morbidity, including pain, infection, and prolonged healing time, is a major drawback. Furthermore, the availability of autogenous bone is limited, particularly in cases of extensive bone loss.[4] Allografts, derived from cadaveric bone, and xenografts, sourced from animals, offer alternative options but carry the risk of disease transmission and immune rejection, respectively.[5] These limitations have spurred intense research and development in the field of bone tissue engineering (BTE), aiming to create biocompatible and osteoinductive substitutes for traditional bone grafts.[6]

BTE has emerged as a multidisciplinary field that seeks to regenerate damaged bone tissue by combining osteogenic cells, biocompatible scaffolds, appropriate vascularization, and controlled culture conditions to mimic natural bone regeneration.[7] This approach leverages biochemical and physical stimuli to promote bone ingrowth, restore physiological function, and facilitate healing at the defect site. The core of BTE lies in the utilization of 3D scaffolds that serve as temporary templates for tissue regeneration.[7]

An ideal bone scaffold should fulfill several essential design requirements: (1) biocompatibility, ensuring cells can attach, proliferate, and function without triggering toxicity or immune reactions;(2) biodegradability, allowing the scaffold to break down gradually as it is replaced by newly formed bone; (3) mechanical stability, providing adequate strength to support physiological loads during the healing period;(4)structural design, incorporating appropriate porosity and pore size to enable cell migration, nutrient diffusion, and vascularization; (5) stabilizability, ensuring that the scaffold remains free from contaminants while preserving its bioactivity; and (6) controlled release of bioactive compounds, enabling the gradual delivery of growth factors or therapeutic agents to enhance bone regeneration.

Numerous materials have been explored for the fabrication of bone scaffolds, each with its own strengths and weaknesses. Ceramic scaffolds, particularly those based on calcium phosphate materials such as hydroxyapatite (HA) and tricalcium phosphate (TCP), are widely utilized due to their biocompatibility and resemblance to the mineral composition of bone.[11]

HA, with its chemical similarity to the mineral component of bone has exceptional biocompatibility and osteoconductivity that makes it an ideal choice for promoting bone apposition. Their bioactivity allows for direct bonding with native bone tissue, making them a preferred choice in BTE applications. Moreover, bioactive glasses, capable of bonding to bone and stimulating bone cell activity, have garnered increasing attention in bone tissue engineering.[13] These glasses release bioactive ions such as silicon, calcium, and phosphate upon implantation, that promote osteoblast differentiation and angiogenesis, accelerating bone formation.[13] In the periodontal environment, bioglass can effectively stimulate the recruitment and differentiation of bone-forming cells from the adjacent alveolar bone, accelerating the healing process and promoting periodontal tissue regeneration.[14] However, their intrinsic brittleness and low fracture toughness pose significant challenges, particularly in load-bearing applications where mechanical stability is critical.

To improve the mechanical properties of ceramic scaffolds**,** composite scaffolds, which integrate ceramics with polymers or other biomaterials, have been developed. By combining the osteoconductive properties of ceramics with the flexibility and degradability of polymers, these scaffolds offer improved mechanical strength and controlled degradation. Polyvinyl alcohol (PVA), a water-

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soluble, non-toxic, biocompatible, and biodegradable polymer, is frequently incorporated into HA-based scaffolds to improve their flexibility and processability.[12] PVA's ability to form hydrogels allows for efficient cell encapsulation and nutrient diffusion, creating a conducive microenvironment for tissue growth.[12] PVA's biocompatibility and biodegradability ensure that it does not interfere with the bone regeneration. Despite these advantages, polymer-based composites still fall short in load-bearing capacity, often necessitating additional reinforcement.

Hybrid scaffolds that integrate ceramics, polymers, and metals offer a promising approach to overcoming the limitations of individual materials. By combining the osteoconductive properties of HA and bioactive glass with the flexibility of polymers and the mechanical strength of metals, these composite scaffolds provide a multifunctional solution for bone regeneration

The incorporation of erbium (Er) is a key innovation of this study. Erbium is a rare earth metal that has demonstrated potential for stimulating osteogenesis. Known for its unique physicochemical properties, erbium offers several advantages when incorporated into ceramic-polymer-metal composites for bone regeneration. Its biocompatibility, antimicrobial effects, and role in enhancing osteogenesis make it a promising candidate for improving scaffold performance. Moreover, erbium has been shown to promote cell proliferation and differentiation in vitro.[15] The rationale for doping the HA-bioglass-PVA scaffold with erbium is to further enhance its osteoinductive properties and improve the mechanical properties of scaffolds.

This study takes a novel approach by exploring a composite scaffold composed of HA, bioglass, and PVA, further enhanced by the incorporation of erbium (Er). The rationale behind this specific combination of materials lies in their complementary properties, aimed at overcoming the limitations of each individual component and creating a synergistic effect that promotes enhanced bone regeneration.

MATERIALS AND METHODS

The study protocol approval was obtained from the Scientific Review Board (SRB) of Saveetha Dental College and Hospitals(SRB/SDC/PERIO-2302-24-428).

Materials

PVA(Polyvinylalcohol-341584-25G)and Cetyltriammonium bromide (Hexadecyltrimethylammonium bromide CTAB H5882-100G) were purchased from Sigma-Aldrich® US, Merck. Calcium nitrate $Ca(NO_3)_2$, Erbium chloride $ErCl_3$, Diammonium hydrogen phosphate $(NH_4)_2HPO_4$, Acetone C_3H_6O, Ethanol C_2H_5OH, Tetraethyl orthosilicate (TeOS) $Si(OC_2H_5)_4$, Phosphorus pentoxide P_2O_5, Calcium oxide CaO, Sodium oxide Na_2O, Ammonia solution $–NH_4OH$ and Tris-HCl buffer $C_4H_{11}NO_3·HCl$ used were of analytical grade.

Preparation of Erbium-Doped Hydroxyapatite (HA)

The synthesis of erbium-doped hydroxyapatite (Er-HA) begins with the dissolution of 2.1 g of cetyl triammonium bromide (CTAB), a surfactant that helps control particle morphology, in an aqueous solution. Next, 0.099 mol of calcium nitrate($Ca(NO_3)_2$), a calcium source, and 0.01 g of erbium chloride (ErCl), the dopant, are introduced into the solution. To facilitate the formation of hydroxyapatite, 0.67 g of diammonium hydrogen phosphate($(NH_4)_2(HPO_4)$) is added, ensuring a controlled Ca/P ratio. The reaction mixture is maintained at 90°C under reflux conditions overnight, promoting homogeneity and allowing complete reaction. The resultant precipitate is thoroughly washed with acetone and ethanol to remove impurities and excess reactants, yielding purified erbium-doped HA nanoparticles.

Preparation of Erbium-Doped Bioglass

For the synthesis of erbium-doped bio glass, 2 g of cetyl triammonium bromide (CTAB) is dissolved in a solvent mixture of 55 ml of water and 45 ml of ethanol. The solution is stirred for 2 hours to ensure complete dissolution of CTAB, which aids in the formation of a mesoporous structure in the bio glass. The bio glass composition consists of TeOs (0.45% silica diatomaceous), 6% phosphorus pentoxide (P_2O_5), 22.5% calcium oxide (CaO), 24.5% sodium oxide (Na_2O), and 2% erbium. To maintain uniformity in composition, tetraethyl orthosilicate (TeOs) and phosphorus pentoxide (P_2O_5) are incrementally added every 30 minutes over the course of the reaction. This step ensures controlled

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deposition and incorporation of these components into the bio glass matrix.

Preparation of PVA Scaffold

The fabrication of the polyvinyl alcohol (PVA) scaffold begins by adding 3 mL of ammonia solution to a precursor mixture to initiate the precipitation process. The mixture is allowed to react overnight, ensuring thorough gelation and the formation of a uniform polymeric network. The precipitate is then sintered and subjected to washing at 40°C for 3 hours to remove residual byproducts and improve material purity. After this treatment, a 10% PVA solution is incorporated into the scaffold .

Lyophilization (Freeze-Drying) Process

In the final step, the prepared materials are combined to create a composite scaffold. A mixture containing 1% erbium-doped HA, 1% erbium-doped bio glass, and 10% PVA solution is homogenized to achieve a uniform distribution of all components. This mixture is then subjected to lyophilization (freeze-drying) using a lyophilizer (Lyoxl Pilot range **,** LSI).

MORPHOLOGICAL CHARACTERIZATION

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed on erbium-Doped HA/Bioglass-PVA Scaffold to characterize the chemical changes. The spectra were recorded in the range of 4000-1000 cm^{-1} using Bruker's Alpha II FTIR Spectrometer [Thermo Scientific Nicolet 6700]. The obtained spectra were analysed to identify any functional group changes present in the scaffold.

Scanning Electron Microscopy (SEM) Analysis

The surface morphology of the Erbium-Doped HA/Bioglass-PVA Scaffolds was examined using SEM. The samples were sputter coated with gold and then observed under a Scanning Electron Microscope [ZEISS Gemini SEM] at an accelerating voltage of 1kV. The obtained images were analysed to visualize the morphology of the scaffold.

BIOLOGICAL CHARACTERIZATION

Hemostatic Behavior Analysis

The hemostatic potential of the scaffold was evaluated by analyzing its blood clotting efficiency and interaction with blood components. To assess clot formation time, 100 µL of fresh human blood was applied directly onto the scaffold surface, and the clotting time was measured under controlled conditions at 37°C.

For a detailed investigation of scaffold-blood interactions, Scanning Electron Microscopy (SEM) was employed. The scaffold was immersed in fresh human blood to observe red blood cell (RBC) adhesion, platelet aggregation, and fibrin network formation. To preserve cellular morphology, the samples were fixed using 2.5% glutaraldehyde and incubated at 37°C. Following incubation, excess blood was removed with phosphate-buffered saline (PBS), and the samples underwent sequential dehydration using graded ethanol solutions (30%, 50%, 70%, 90%, and 100%) before being vacuum-dried.

To enhance conductivity, the dried samples were coated with a thin layer of gold and examined under SEM, focusing on RBC adhesion, platelet aggregation, and fibrin deposition, which contribute to clot formation and overall hemostatic performance.

Anti-inflammatory Analysis

The anti-inflammatory potential of the prepared erbium-doped HA/Bioglass-PVA scaffold, different concentrations (25% and 50%) were added to a 2% bovine serum albumin (BSA) solution. The prepared solutions were then adjusted to a final volume of 2 mL using Tris-HCl buffer. The samples were incubated at room temperature for 30 minutes, followed by heating in a water bath at 75°C for 10 minutes. After heating, the samples were allowed to cool for 20 minutes. Their optical density was then measured using a UV-Visible spectrophotometer at 660 nm to assess the scaffold's anti-inflammatory properties and was compared with untreated sample(Control). The anti-inflammatory potential was calculated using a standard formula,

BIOCOMPATIBILITY TEST

MTT Assay

Human gingival fibroblast Cells were divided into

96-well microplates as much as 100 µl with density 3-5x10 to which different concentrations of the scaffold (12.5µg/ml, 25µg/ml,50µg/ml, 75µg/ml, and 100 µg/ml) were added and incubated for 24 hours at 37°C to evaluate the cytotoxicity. They were compared with untreated culture. After adding 25 µl of MTT solution, a microplate reader was used to measure the absorbance at 570 nm. The data was statistically analysed using One-way ANOVA with Tukey's multiple comparisons.

Live/Dead Cell Assay

The biocompatibility of the prepared erbium-doped HA/Bioglass-PVA scaffold up treated human gingival fibroblast cells and the control group (untreated culture) was evaluated by morphological assessment using Phase contrast microscopy .

RESULT

MORPHOLOGICAL CHARACTERIZATION

FTIR analysis

The FTIR spectrum (Figure 1,2) of the erbium-doped HA/Bioglass-PVA scaffold exhibits characteristic absorption peaks corresponding to functional groups from hydroxyapatite (HA), bioglass, and PVA, confirming the scaffold's structural integrity. The broad peak at 3289 cm^{-1} indicates O-H stretching, confirming the presence of hydroxyl (-OH) groups and hydration in the scaffold. The absorption band between 3000–2900 cm^{-1} corresponds to C-H stretching vibrations, primarily from PVA. A distinct peak at 1660 cm^{-1} is attributed to C-O stretching, suggesting the presence of organic acetate residues. The CH_2 bending vibrations observed at 1420 cm^{-1} contribute to the organic framework of PVA, while the peak at 1327 cm^{-1} corresponds to OH rocking and CH wagging, indicating polymeric network interactions. The strong absorption band at 1065 cm^{-1} represents C-O and OH stretching vibrations, further confirming the structural integrity of the scaffold. The presence of hydroxyapatite is validated by characteristic phosphate group (PO_4^{3-}) peaks at 1012, 710, and 536 cm^{-1}, indicating effective HA formation. Additionally, a peak at 909 cm^{-1} corresponds to CH_2 rocking vibrations, contributing to the scaffold's stability, while the band at 836 cm^{-1} represents C=C stretching, further supporting polymeric interactions. These spectral features collectively confirm the successful incorporation of HA, bioglass, and PVA into the scaffold, ensuring its suitability for bone tissue engineering.

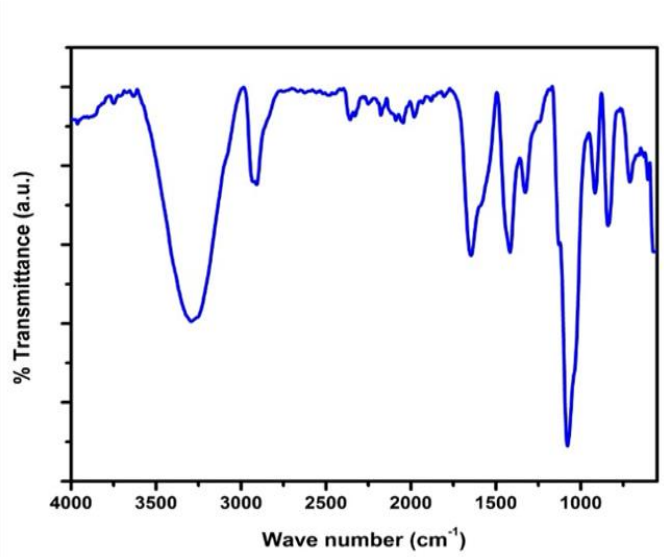


Figure 1. FTIR spectra of Erbium-doped HA/Bioglass-PVA scaffold

Wave number (cm^{-1})	Interpretation
3289	stretching O-H
3000-2900	C-H from alkyl groups
1660	C-O from acetate group
1420	CH2 bending
1327	δ (OH), rocking with CH wagging
1065	stretching of C—O and bending of OH
1012	Phosphate group
909	CH_2 rocking
836	C—C stretching
710	Phosphate group
536	Phosphate group

Figure 2. FTIR Peak Interpretation for Erbium-Doped HA/Bioglass-PVA Scaffold

SEM Analysis

The SEM analysis of the erbium-doped HA/Bioglass-PVA scaffold reveals a distinct flower-like morphology (Figure 3) with a highly porous and interconnected structure, essential for promoting cell adhesion, proliferation, and nutrient exchange.. The observed flower-like formation indicates successful incorporation of hydroxyapatite and bioglass within the PVA matrix, ensuring mechanical stability and

biomimetic properties. Additionally, the presence of micropores and nanostructured features supports the scaffold's potential for bone tissue regeneration, making it a promising material for applications in bone grafting and periodontal repair.



Figure 3. SEM analysis of erbium-doped HA/Bioglass-PVA scaffold under 500X magnification

BIOLOGICAL CHARACTERIZATION

Hemostatic Behaviour Using SEM Analysis

The SEM analysis of the erbium-doped HA/Bioglass-PVA scaffold revealed significant blood cell adhesion and interaction. The micrographs (Figure 4) displayed aggregated red blood cells (RBCs) on the scaffold surface, demonstrating its effectiveness in promoting blood clotting. The presence of platelet clusters and fibrin networks further confirmed its hemostatic potential.

The blood clotting time (BCT) for the scaffold was recorded at 4 minutes 35 seconds, significantly shorter than the average human blood clotting time of 7 minutes 10 seconds. This reduction indicates that the scaffold enhances coagulation efficiency and accelerates hemostasis.

Additionally, the rough and porous nature of the scaffold facilitated rapid blood absorption, promoting clot stabilization. The uniform dispersion of blood cells across the scaffold suggests strong scaffold-blood interactions, which play a crucial role in improving hemorrhage control and tissue regeneration.

The SEM analysis of the hemostatic behaviour of the erbium-doped HA/Bioglass-PVA scaffold reveals notable blood cell adhesion and interaction. The micrograph (Figure 4) shows aggregated red blood cells (RBCs) on the scaffold surface, indicating its effectiveness in promoting blood clotting which was found to be 4 mins 35 secs while the normal range of human blood clotting time has proven to be on an average of 7 mins 10 secs . The uniform dispersion of cells suggests strong scaffold-blood interactions, which play a crucial role in accelerating hemostasis. Additionally, the rough and porous nature of the scaffold enhances blood absorption and clot stabilization, highlighting its potential for hemorrhage control and tissue regeneration.

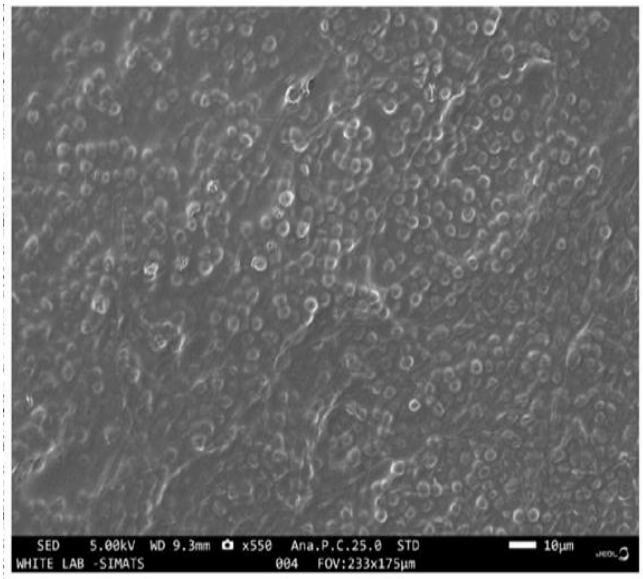


Figure 4. SEM analysis of the hemostatic behaviour of the erbium-doped HA/Bioglass-PVA scaffold under 550X magnification

Anti-inflammatory Analysis

The anti-inflammatory analysis of the Erbium-doped HA/Bioglass-PVA scaffold shows a dose-dependent effect, with the control group exhibiting the highest anti-inflammatory response (100%). At 25 µg, the scaffold significantly reduces anti-inflammatory activity to approximately 25%, increasing the scaffold weight to 50 µg results in a moderate recovery (around 50%), indicating improved but not fully restored anti-inflammatory properties (Figure

5). These findings suggest that scaffold exhibits a positive correlation with its anti-inflammatory potential and increasing concentration.

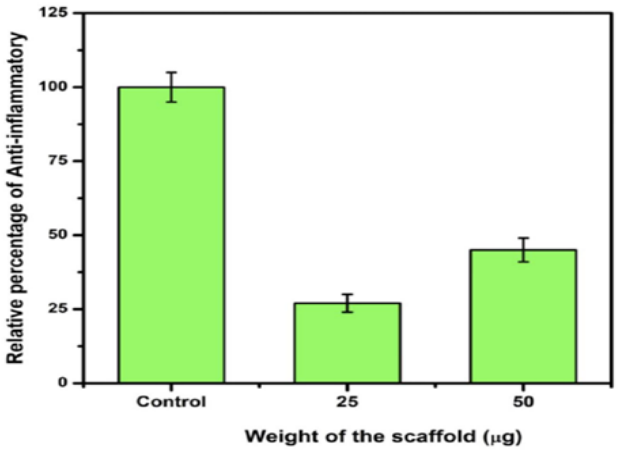


Figure 5. The bar graph represents the anti-inflammatory response of an Erbium-doped HA/Bioglass-PVA scaffold at different weights (25 µg and 50 µg) compared to a control group.

BIOCOMPATIBILITY TEST

MTT Assay

The MTT assay results indicate high cell viability across all tested concentrations (12.5–100 µg) of the PVA scaffold, comparable to the control group. At each concentration, the PVA scaffold (blue bars) maintains cell viability above 90%, with no significant cytotoxic effects observed (Figure 6). The slight variations between the scaffold and control groups are minimal, suggesting that the PVA scaffold supports cell proliferation and does not induce toxicity. These findings confirm the biocompatibility of the PVA scaffold, making it a promising material for bone tissue engineering.

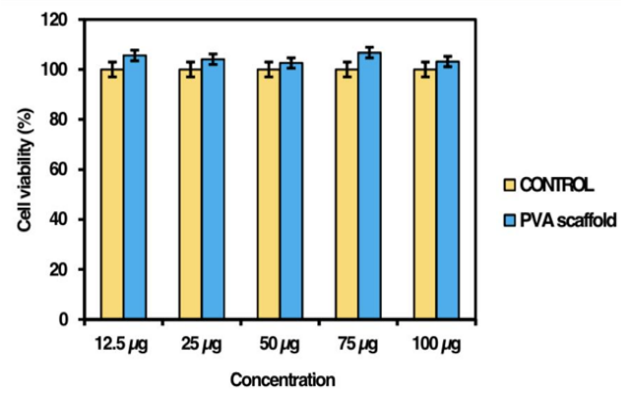


Figure 6. The bar graph represents the Biocompatibility of an Erbium-doped HA/Bioglass-PVA scaffold at different concentrations compared to control group.

Live and Dead cell assay

The live and dead cell assay image (Figure 7) of the Erbium-doped HA/Bioglass-PVA scaffold using Phase contrast microscopy shows a high density of adherent cells with an elongated and spindle-like morphology, indicating good cell viability and proliferation. The absence of significant dead cells suggests minimal cytotoxic effects, further supporting the biocompatibility of the scaffold.

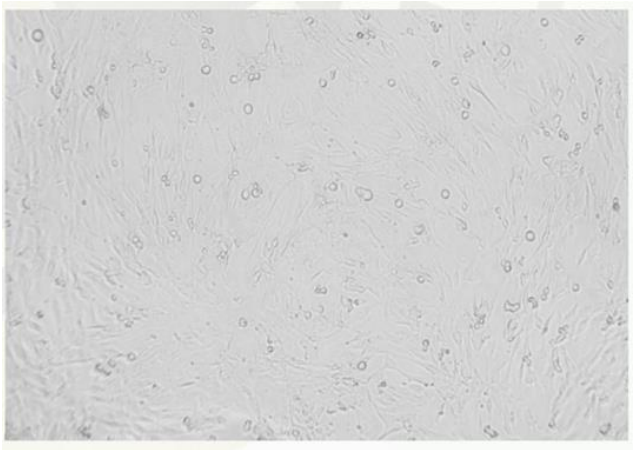


Figure 7. Live and dead cell assay of the Erbium-doped HA/Bioglass-PVA scaffold using Phase contrast microscopy

DISCUSSION

This study comprehensively examined the structural, chemical, and biological properties of Erbium-doped Hydroxyapatite (HA)-Bioglass-Polyvinyl Alcohol (PVA) scaffolds, with a primary focus on their cytocompatibility and potential application in bone tissue engineering. Fourier-transform infrared spectroscopy (FTIR) confirmed the presence of characteristic functional groups, such as hydroxyl stretching at 3289 cm^{-1} and phosphate group absorption at 536 cm^{-1}, which verified the successful integration of HA and Bioglass within the polymeric matrix. Scanning Electron Microscopy (SEM) revealed a distinct flower-like morphology, indicative of an increased surface area that enhances cellular interactions and adhesion. The consistency between our FTIR results and standard HA

crystalline structures suggests that the addition of Erbium does not disrupt the scaffold's structural integrity, reinforcing its potential for bone regeneration applications. The scaffold's hemostatic behavior and anti-inflammatory effects were assessed using SEM and bovine serum albumin (BSA) denaturation assays, respectively. Hemostatic scaffolds play a crucial role in tissue engineering by facilitating blood clotting and promoting wound healing. Prior studies, such as that of Rahman M S .,[16] have demonstrated that bioactive glass materials enhance platelet adhesion, leading to fibrin clot formation—a vital step in wound healing. Similarly, in this study, SEM analysis of the Erbium-doped HA/Bioglass-PVA scaffold revealed substantial platelet aggregation and fibrin network formation, highlighting its strong hemostatic potential. These findings correlate with the work of Lee J et al.,[17] who reported that platelet-rich plasma (PRP)-incorporated HA scaffolds significantly improved bone regeneration by stimulating the release of growth factors. Furthermore, in comparison to conventional hydroxyapatite-based scaffolds studied by Fendi et al.,[18] which primarily support osteogenesis but exhibit limited hemostatic properties, the incorporation of Bioglass and Erbium doping in the present scaffold formulation significantly improved clot formation and cellular adhesion.

The scaffold's anti-inflammatory potential was assessed using a BSA denaturation assay, a well-established method for determining protein denaturation inhibition—an essential marker of inflammation. The current study demonstrated that the Erbium-doped HA/Bioglass-PVA scaffold effectively inhibited protein denaturation, particularly at a 50% concentration, indicating significant anti-inflammatory potential. This observation aligns with research by Rahaman et al.,[16] which highlighted the intrinsic anti-inflammatory nature of Bioglass-based materials due to the controlled release of bioactive ions such as Si^{4+}, Ca^{2+}, and PO_4^{3-}, which modulate macrophage activity. The present study supports these findings while also demonstrating that Erbium doping further amplifies these effects, likely due to its established anti-inflammatory and antibacterial properties.

Comparisons with existing literature indicate that Erbium-doped Bioglass scaffolds exhibit superior hemostatic and anti-inflammatory characteristics compared to conventional biomaterials. For instance, Tian Y et al.,[19] examined chitosan-based hemostatic scaffolds, which, although effective in clot formation, lacked osteoconductive properties necessary for bone integration. Similarly, Ndlovu SP et al.,[20] explored gelatin-based scaffolds, which, despite their bioactivity and wound dressing ability , were prone to rapid degradation, thereby limiting their long-term functionality in bone regeneration. By contrast, the Erbium-doped HA/Bioglass-PVA scaffold in this study demonstrated a balanced combination of clot formation, cellular adhesion, and controlled degradation, making it an ideal candidate for bone tissue engineering applications.

A further comparison with Sr- and Co-doped bioactive glass scaffolds studied by Kermani F et al.,[21] revealed that these materials enhance osteogenesis and angiogenesis through ionic dissolution, akin to the effects observed in the current Erbium-doped scaffold. However, while strontium-based scaffolds are primarily designed to stimulate osteoinductive responses, Erbium-doped scaffolds, as demonstrated by Sepahvandi A et al.,[22] offer additional benefits such as photoluminescence, which could facilitate bio-imaging and real-time monitoring of scaffold integration in vivo. Although this study did not investigate the photoluminescent properties of the Erbium-doped HA/Bioglass-PVA scaffold, future research could explore this aspect to further expand its potential biomedical applications.

Additionally, titanium-based scaffolds, widely regarded as a gold standard in bone tissue engineering due to their mechanical strength and osseointegration capabilities , yet Topuz M et al.,[23] showed that they lack inherent bioactivity and require surface modifications to enhance cellular responses. In contrast, the Erbium-doped HA/Bioglass-PVA scaffold demonstrated in this study offers a combination of bioactivity and structural stability within a polymeric matrix, providing a significant advantage over traditional metal implants.

The biocompatibility of the scaffold was confirmed through MTT assays and live/dead cell staining, both of which demonstrated excellent cytocompatibility. These results are consistent with prior studies on composite scaffolds by Oryan et al.,[24] such as gelatin/nano-hydroxyapatite with Bioglass and strontium (G/nHAp/BG/Sr), which have also shown

enhanced biocompatibility. Furthermore, Mohan AS et al.,[25] reported that Sr-doped boron-based bioactive glass scaffolds minimized cytotoxicity while promoting controlled ion release, supporting the notion that metal-doped bioactive glasses can improve scaffold functionality while maintaining biocompatibility.

Despite the promising findings, previous research has highlighted that some metal-doped bioactive glass materials may induce mild cytotoxicity at higher concentrations. For instance , Awais M et al.,[26] observed that selenium-, silver-, and zinc-doped HA scaffolds exhibited strong antibacterial properties but induced cytotoxic effects at elevated doses. In contrast, the current study confirmed that the Erbium-doped HA/Bioglass-PVA scaffold maintains high cell viability across all tested concentrations, underscoring its superior biocompatibility with minimal adverse effects.

Overall, this study contributes to the field of bone tissue engineering by validating the cytocompatibility, hemostatic efficiency, and anti-inflammatory potential of the Erbium-doped HA/Bioglass-PVA scaffold. By integrating these findings with existing literature, it is evident that this scaffold exhibits superior multifunctional properties compared to conventional biomaterials. However, further investigations, including in vivo studies, mechanical testing, and antibacterial assessments, are necessary to fully establish its clinical relevance and therapeutic potential.

CONCLUSION

The synthesized Erbium-doped HA/Bioglass-PVA scaffold exhibited excellent biocompatibility and structural stability, making it a promising candidate for periodontal bone regeneration. Its non-cytotoxic nature supports cell adhesion and proliferation. Further in vivo studies are needed to confirm its efficacy and potential clinical applications in regenerative dentistry.

DECLARATIONS

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Conflict of Interest

All the authors declare that there was no conflict of interest in the present study

Ethical Approval

Not Applicable

Informed Consent

Not Applicable

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Dr.Maria Sharon V: Formal analysis, Investigation, Data curation, Writing - original draft, Visualization Dr.**Nidhita Suresh:** Conceptualization, Methodology, Validation, Writing - review & editing, Supervision. Dr.**Kaarthikeyan Gurumoorthy** - Conceptualization, Methodology, Validation, Writing - review & editing, Supervision. **Dr.Chitra Shivalingam-** Methodology, Validation, Writing - review & editing, Supervision

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RESEARCH ARTICLE

ATTITUDE TOWARDS LEARNING COMMUNICATION SKILLS AMONG DENTAL INTERNS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The primary objective was to assess the attitudes of dental interns in Kerala towards communication skills acquisition using the Dental Communication Skills Attitude Scale (DCSAS) questionnaire. The additional objective was to determine the association between age, gender, prior academic accomplishment, self-evaluation of communication abilities, and respondents' attitudes towards developing them.

Methods and materials: A structured proforma in Google Forms collected demographic data, and self-assessed communication skill levels of dental interns of Kerala. The validated DCSAS questionnaire to assess students' perspectives and willingness to learn communication skills during their professional course.

Results: The study participants had an average age of 22.94±0.93 years. In all four DCSAS sections, students' mean attitude scores for developing communication skills were statistically significant for most factors. Age was strongly correlated with average positive and negative attitudes towards learning communication skills. Positive attitude was highest in first-class students. Students with moderate communication skills had the greatest mean positive attitude score. Students who identified as poor communicators had the highest mean total negative attitude score, whereas those who identified as good communicators had the lowest.

Conclusion: The average positive attitude of dental interns towards communication skills development was related to gender, age, academic performance, and self-assessed communication ability. Higher self-assessment in communication skills, academic success, and older age were the main factors related to the study sample's negative attitude.

Keywords: Academic performance, Attitude scale, Dental interns, Learning

INTRODUCTION

Communication among healthcare providers is a fundamental aspect of the patient-clinician interaction. The acquisition of communication skills is essential in medical and dental schooling, as these fundamental abilities significantly enhance multiple facets of the healthcare process, such as performing thorough examinations, achieving accurate diagnoses, developing comprehensive plans, and delivering appropriate treatments.[1,2] Effective patient communications is essential for fostering confidence, enhancing rapport and cooperation, and decreasing ambiguities. An optimal atmosphere is to be established for conversation with a varied array of individuals, encompassing various interests, traits, and cultures.[3,4]

Evidence indicates that patients infer a clinician's technical proficiency and expertise from their communication skills. It also guarantees superior and ethical clinical practice, enhancing healthcare professionals' diagnostic proficiency and decision-making capabilities, while also fostering the satisfaction of healthcare users.[5] Dental students are

typically open to acquiring communication skills, and their recognition of the importance of these capabilities can be greatly enhanced by training. In recent years, the necessity of communication skills in the school of dentistry has garnered significant attention from academicians.[6,7]

The perspective of dental students about communication skills training may serve as a significant marker for the value they assign to such training, potentially impacting their communication behaviours in clinical environments.[8]

The efficacy of a communication skills instruction course could be enhanced with a deeper comprehension of students' ideas and attitudes towards relationships between doctors and patients. Competence in communication, team-building, and global awareness has grown into a fundamental component of the dental curriculum in India. To date, the literature lacks reports on assessments or training of communication skills in undergraduate dental courses in India.[9] A training program can assist students in overcoming challenges related to organizing oral examinations, acquiring precise data from patients, and understanding patients' perspectives of their oral health concerns. An individual's attitude and motivation can significantly impact their behaviour, rendering communication a learned skill. Investigating the attitudes of dental students is essential, as it may assist dental instructors in developing effective strategies to guide students in acquiring communication skills, enhancing their abilities, and preventing negative attitudes from obstructing the effective delivery of training programs.[10]

Numerous research on dentistry students' attitudes towards learning communication skills in Western contexts are available in the scholarly literature, however, few have been conducted in Indian contexts.[7] The primary objective of the study was to evaluate the attitudes of dental interns in Kerala regarding the acquisition of communication skills, utilizing the Dental Communication Skills Attitude Scale (DCSAS) questionnaire. The second objective was to ascertain the relationship between age, gender, prior academic success, and self-evaluation of communication skills and the attitudes of the respondents towards developing communication skills.

MATERIALS AND METHODS

This is a census-type survey in which all interns from dental colleges (both government and private) in the state of Kerala in 2024 were prompted to participate. The study was approved by the Institutional Ethics Committee, Government Dental College, Thiruvananthapuram, Kerala with IEC Approval No. DCT/IEC/SS/24/19 dated 05/09/2024. The interns who consented to take part were enrolled after being informed of the study objectives through a participant information form. To optimize the response rate, a representative from each institution was appointed, and contact details for all participants were gathered, with periodic notifications and personal outreach conducted periodically. A minimum of 80% of the 1200 interns across all colleges were ensured to respond.

Data were gathered through Google Forms utilizing a structured proforma that included sections for recording demographic information (age, gender, college name, and final-year BDS academic performance), self-assessed communication skill levels, and the validated pretested DCSAS questionnaire to gather data on students' perspectives and their willingness to learn communication skills during their professional course. The DCSAS questionnaire comprised 24 items addressing both positive and negative attitudes. Responses were evaluated using a 5-point Likert scale ranging from strongly disagree to strongly agree, with higher scores reflecting a more positive or negative perspective. The range of positive attitude scores for each individual was from one to 65. Scores less than or equal to 32 indicate a low positive attitude, while scores greater than or equal to 33 indicate a high positive attitude. The range of negative attitude scores for each individual was between one and 55. Scores below or equal to 29 indicate a low level of negative attitude, while scores more than or equal to 30 indicate a high level of negative attitude. The DCSAS comprises four sections: learning, importance, quality, and success, featuring 13 positively phrased items and 11 negatively phrased items.

The learning section encompassed ten items, all of which represented positive attitudes. This element encompasses both utilitarian and ethical dimensions of the dental profession. The learning attitude score varies between 10 and 50. The importance section consisted of six items, all of which addressed negative attitudes. This component signifies the intricacy of communication and the challenge of attaining proficiency. The attitude score of the importance section is between 6 and 30. The quality section consisted of four items, two reflecting a positive attitude and two reflecting a negative

attitude. This component encompasses assertions regarding the acquisition of effective communication skills and positions the significance of communication on par with other competencies and knowledge in dentistry. The learning attitude score of the quality section varies from 4 to 20. The success section comprised four elements: three negative attitudes and one positive with the attitude score ranging between four and 20. The element includes assertions regarding the process and the beneficial impacts of communication skills on achieving success in dental school.[11]

Statistical analysis

The data were analyzed utilizing the Statistical Package for Social Sciences (SPSS Inc., SPSS for Windows, Version 26.0, Chicago, IL, USA) at a 5% significance level. The data were evaluated by applying descriptive analysis, Chi-square test, unpaired t-test, and ANOVA.

RESULTS

The average age of the study respondents was 22.94±0.93 years. The survey had an 83.83% response rate (n=1006). A female preponderance comprised 72.5% of the group. Participants were between the ages of 21 and 26, with 73.5% unravelling within the 23.1 and 25 age spectrums. Participants in the study were posed two questions for self-evaluation on their roles as students and communicators. Approximately 48.41% of the students identified as first-class students. Approximately 30.91% of individuals classified themselves as second-class students, 19.78% as pass-class students, and merely 0.89% as distinction students. Among the interns, 24.25% self-assessed to be excellent communicators, 41.05% as good, 33.10% as moderate, and barely 1.59% as poor communicators (Table 1).

Table 1. Demographic profile of the study participants

Sociodemographic variables	Total N (%)	Males N (%)	Females N (%)	λ^2	p-value
Age (Years)[+]	22.94±0.93	22.98±0.92	22.89±0.94	1.36	0.17
Sector of the college					
Government	222 (22.1)	61 (22)	161 (22.1)	0.02	0.89
Private	784 (77.9)	216 (78)	568 (77.9)		
Total	1006 (100)	277 (100)	729 (100)		
Past academic performance					
Distinction	9 (0.89)	6 (2.16)	3 (0.41)	0.66	0.88
First class	487 (48.41)	134 (48.38)	353 (48.42)		
Second class	311 (30.91)	80 (28.88)	231 (31.69)		
Pass	199 (19.78)	57 (20.58)	142 (19.48)		
Total	1006 (100)	277 (100)	729 (100)		
Self-perceived communication skill					
Excellent	244 (24.25)	82 (29.6)	162 (22.22)	11.32	0.010**
Good	413 (41.05)	119 (42.96)	294 (40.33)		
Moderate	333 (33.1)	72 (25.99)	261 (35.8)		
Poor	16 (1.59)	4 (1.44)	12 (1.65)		
Total	1006 (100)	277 (100)	729 (100)		

[+]t-test; **highly significant; p>0.05-statistically insignificant

According to Figure 1, 36.48% (n=367) and 43.94% (n=442) of students believed that communication is crucial for dental academia and professional practice, respectively. Conversely, 41.95% (n=422) and 38.87% (n=391) of students believed that it was not significant for either of these reasons respectively. Furthermore, 21.57% (n=217) and 17.20% (n=173) of students were unaware of the significance of communication in educational institutions and clinical settings, respectively. The data analysis about students' attitudes towards developing communication skills across each of the four sections of DCSAS revealed that the mean attitude scores were statistically significant for most of the variables examined. The mean attitude scores of students regarding the learning aspect of DCSAS were statistically insignificant for gender (p=0.3), college sector (p=0.58), and self-reported communication skills (p=0.37) (Table 2).

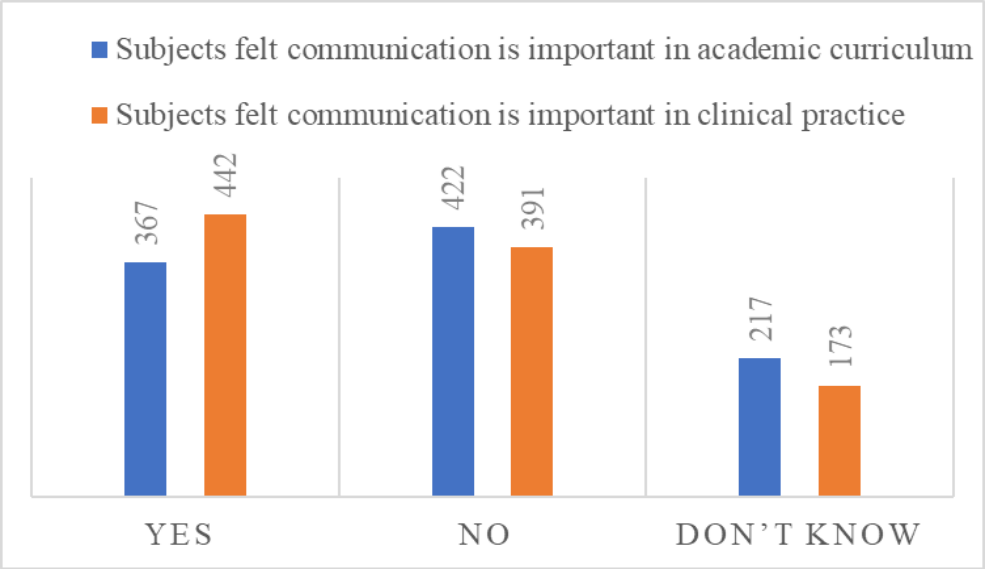


Figure 1. Distribution of responses based on opinions regarding the importance of learning communication skill

Table 2. Distribution of the means of attitude score in the four DCSAS factors concerning the variables under study

Variables under study	Learning	Importance	Quality	Success
Gender				
Male	40.71±4.88	25.85±3.47	17.53±1.42	15.73±2.42
Female	40.39±4.16	24.97±3.36	17.04±1.61	14.8±2.49
t-test	1.04	3.68	4.45	5.33
p-value	0.30	0.0002*	<0.0001*	<0.0001*
Age (Years)				
21.0-23.0 (n=174)	41.15±4.12	26.17±2.26	14.29±2.69	13.08±3.95
23.1-25.0 (n=739)	41.18±4.36	25.18±2.65	15.09±3.07	14.16±3.97
>25 (n=93)	40.0±4.28	25.23±2.44	15.14±2.18	14.0±3.98
ANOVA	3.13	10.59	5.43	5.22
p-value	0.044*	0.001*	0.005*	0.006*
Academic performance				
Distinction	43.82±3.23	23.43±4.6	14.91±2.56	16.58±1.08
First class	42.38±3.17	21.27±4.36	13.74±2.47	16.46±1.23
Second class	40.07±3.48	21.31±3.28	13.25±1.25	14.49±1.1
Pass	35.62±3.02	20.25±2.13	13.39±1.09	14.18±1.18
ANOVA	209.14	5.40	5.98	266.52
p-value	0.0001*	0.001*	0.0001*	0.0001*
Self-reported communication skills				
Excellent	44.28±2.26	23.83±3.8	16.11±1.47	17±1.08
Good	44.17±2.85	23.57±3.57	15.75±1.87	16.37±1.5
Moderate	44.01±2.3	22.8±3.6	13.08±1.98	12.49±2.35
Poor	43.37±2.14	21.23±3.14	12.35±1.68	11.21±2.87
ANOVA	1.05	6.29	187.97	427.52
p-value	0.37	0.0001*	0.0001*	0.0001*

*significant; p>0.05-statistically insignificant

The overall mean score for positive attitude was greater in females (53.41±4.80) than in males (52.74±4.73), with a statistically significant difference (p=0.047). Conversely, the total mean score for negative attitude was nearly identical between males (27.62±5.17) and females (27.76±4.79), with statistically insignificant differences observed. Age was determined to have a strong relationship with the average positive and negative attitudes towards acquiring communication skills. As age advanced, positive attitude scores increased, indicating that older interns exhibited more positive attitudes towards the acquisition of communication skills compared to their younger counterparts. Concurrently, with advancing age, there is a propensity for a diminished negative attitude towards acquiring communication skills (Table 3).

Table 3. Comparison of mean attitude scores based on gender, age, and college sector

Variables	Mean positive attitude score	Mean negative attitude score
Gender		
Male	52.74±4.73	27.62±5.17
Female	53.41±4.80	27.76±4.79
t-test	-1.99	-0.41
p-value	0.047*	0.69
Age (Years)		
21.0-23.0 (n=174)	44.29±3.91	29.08±3.86
23.1-25.0 (n=739)	46.67±3.78	28.71±4.28
>25 (n=93)	50.41±3.24	26.07±4.64
t-test	80.85	17.74
p-value	0.001**	0.001**

*significant; p>0.05-statistically insignificant

The highest mean total positive attitude was observed in students who classified themselves as first-class (52.73±4.43), while the least mean total positive attitude was noted in students who identified as pass-class (47.77±3.39). The variations in academic performance and the positive attitude towards the acquisition of communication skills were statistically significant (p=0.000). The highest mean total negative attitude was observed in students who classified themselves as pass-class students (29.66±3.97), whilst the lowest mean total negative attitude was noted in students who identified as distinction students (25.28±4.07). The mean total score for first-class and second-class students was 25.28±4.07 and 27.41±4.46 respectively. According to academic achievement, there was a statistically significant difference in the negative attitude score (Table 4).

Table 4. Comparison of mean attitude scores based on academic performance, and self-reported communication skill

Academic performance	Mean positive attitude score	Mean negative attitude score
Distinction	51.84±4.17	22.07±5.3
First class	52.73±4.43	25.28±4.07
Second class	51.22±3.48	27.41±4.46
Pass	47.77±3.39	29.66±3.97
ANOVA	68.35	58.37
p-value	0.0001*	0.0001*
Self-reported communication skill		
Excellent	51.46±4.83	27.44±3.27
Good	52.84±4.11	28.12±3.7
Moderate	53.7±4.31	29.91±3.63
Poor	48.32±3.79	38.84±5.47
ANOVA	17.97	69.85
p-value	0.0001*	0.0001*

*significant; p>0.05-statistically insignificant

The highest mean total positive attitude score was reported in students identifying as moderate communicators (53.7±4.31), whereas the lowest mean total positive attitude score was recorded in students identifying as poor communicators (48.32±3.79). The average total positive attitude score for good communicators was (52.84±4.11), whereas for excellent communicators it was (51.46±4.83). These variations were statistically significant (p=0.000). The highest mean total negative attitude score was recorded in students who self-identified as poor communicators (38.84±5.47), whilst the lowest mean total negative attitude score was noted in students who considered themselves excellent communicators (27.44±3.27). The average overall negative attitude score for good communicators was (28.12±3.7), while for moderate communicators it was (29.91±3.63). These variations were statistically significant (p=0.0001) (Table 4).

DISCUSSION

The current study employed the modified 24-item DCSAS scale owing to its robust internal consistency in evaluating attitudes towards acquiring communication skills. All responses were assessed using a five-point Likert scale, with 1 representing "strongly disagree" and 5 indicating "strongly agree." A noteworthy response rate of 83.83% was achieved, in contrast to 70.59% at Alexandria University and 82.65% at Pharos University, as reported by Atteya et al.[12] Additionally, response rates of 94.4% were noted at the University of Malaya, 83.3% at the University of Kebangsaan Malaysia,[13] and 88% at Dunedin University in New Zealand.[6] Consequently, this suggests that the survey findings may accurately reflect the intern population of Kerala.

In line with a related study conducted among Pharos interns,[12] it became apparent that age significantly influenced both positive and negative scores among the sample group.[11] As age advanced, the positive attitude ratings spiked indicating that older interns exhibited positive attitudes towards the acquisition of communication skills than their younger counterparts. The most likely cause for this observation is that senior interns may have employed their communication skills in diverse contexts beyond their academic background, including prior training experiences. Consequently, they began to acknowledge the significance, pertinence, and ramifications of effective communication abilities. This aligns with other earlier studies.[12,14-17] However, this contrasts with the results of Nor et al.[13] and Rees and Sheard,[19] who observed that younger students were more predisposed to acquiring communication skills, attributing this phenomenon to their lesser experience in interacting with unfamiliar individuals.

The current study revealed substantial gender disparities in positive attitude scores among dental students, whereas no significant differences were observed in negative attitude scores. These findings refute previous research on dental students in Bangalore,[8] and medical trainees in Sri Lanka,[20] Nepal,[17] and Iran,[21] where no significant differences were detected. The current study found a highly significant relationship between positive attitude scores and gender, consistent with findings reported among Pharos interns.[11] Female interns exhibited superior positive attitude scores in comparison to their male counterparts. This conclusion aligns with the prior studies by Nor et al.,[12] Rees and Sheard,[17] and Wright et al.,[22] who similarly reported this pattern. The mastery of communication may be more innate to females, and as a student, she is bound to value the science of dentist-patient communication more significantly.[10] Nevertheless, a study conducted in Nepal with a cohort of medical residents revealed no significant correlation between gender and positive views towards the acquisition of communication skills.[16] In the current study, the mean score for positive attitude was elevated, while the negative attitude score lowered, indicating optimistic attitudes towards communication abilities, consistent with earlier findings.[13,24] A notable disparity in positive attitudes was seen between males and females, although the mean negative attitude scores exhibited no significant difference across genders. However, earlier research by Ramesh et al.[8] revealed that male students had a more positive attitude than female students, whereas Atteya et al.,[12] reported that female students had a more positive attitude.

Students exhibiting subpar academic achievement demonstrated a more negative attitude towards communication skills, aligning with a previous study.[24] In a comparable manner, interns who indicated deficient communication abilities exhibited a markedly more negative attitude than those who reported proficient communication skills. The results align with several research indicating that students who self-assess their communication skills as proficient exhibit a more favourable attitude towards communication compared to those who perceive themselves as poor communicators.[8,12,13,23,24]

Conversely, Yavagal et al.[25] revealed that distinction students exhibited a markedly more negative attitude than first-class students. Further, Richa et al.[24] indicated that a negative score was directly associated with self-reported inadequate communication abilities.

Communication skills are acquired during dental education, which can be enhanced by integrating student perspectives and requirements into curriculum creation. Although students acknowledge the importance of communication skills, the curriculum does not assign any instructional hours for this subject. Therefore, incorporating communicational challenges into the dental curriculum from the perspectives of the dentist, dental student, and patient will facilitate the enhancement of communication skills among dentists. Dental students need to receive education in skill-based communication training grounded in the latest research. This approach will enhance dental students' preparedness for clinical practice, enabling them to manage patient anxiety, identify ethical dilemmas, and recognize critical psychological variables that contribute to more precise diagnosis and treatment, ultimately improving patient satisfaction and safety.[6]

It should be noted that as this study was cross-sectional, causality cannot be established. The self-reported questionnaire included inquiries on the students' attitudes, perhaps resulting in social desirability bias. A positive attitude score among dental students about the acquisition of communication skills reveals their recognition of the significance of these abilities in dental practice. Moreover, a dental student who has assimilated positive values related to communication skills training is likely to exhibit behaviours aligned with those values, including actively listening to patients, articulating treatments in comprehensible terms, and addressing the physical, psychological, and social needs of patients. Nonetheless, the low negative attitude scores in the present study cannot be overlooked, as they may undermine the significance of the "Communication Skill Training" component in the undergraduate dental curriculum.

CONCLUSION

The learning factor of DCSAS was determined to be statistically insignificant concerning gender, and self-reported communication skills. The importance, quality, and success components of DCSAS were statistically significant for all variables examined. The overall average positive attitude of dental interns about the acquisition of communication skills was related to gender, age, academic performance, and self-assessed communication abilities. The negative attitude of the study sample was primarily associated with advanced age, academic achievement, and elevated self-assessment in communication skills. Interns who assessed their communication abilities as good demonstrated markedly higher positive attitudes than those who evaluated their communication skills as deficient. Interns who indicated deficient communication abilities exhibited markedly higher negative attitudes compared to those who claimed optimistic communication skills.

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Competing and conflicting Interests

The authors declare no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee, Government Dental College, Thiruvananthapuram, Kerala with IEC Approval No. DCT/IEC/SS/24/19 dated 05/09/2024.

Informed consent

The interns who consented to take part were enrolled after being informed of the study objectives through a participant information form.

Type you

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REVIEW ARTICLE

INSIGHTS INTO COMMUNICATION IN DENTAL EDUCATION AND PRACTICE: A NARRATIVE REVIEW

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ABSTRACT

Background: Effective communication increases dental patients' satisfaction and improves treatment results. Despite its importance in dental curricula, there is often a gap between the theoretical aspects of communication skills and the practical application in real-world dental settings.
This research aims to explore the key components of effective dentist-patient communication and address teaching, learning, and assessment of communication skills within undergraduate dental education with a specific focus on the Armenian context.
Materials and Methods: Literary research was conducted across internet bibliographic open-access sources. The narrative review included 91 publications, comprising 67 full-text articles, 3 reports, 13 monographs and books, 5 guidelines, 3 legal acts. Databases such as Medline, Scopus, Web of Sciences, PubMed, ScienceDirect, ResearchGate and others were used. This paper presents the key findings of a literature review encompassing publications on communication skills in the field of dentistry and dental education, without constraints on publication dates. In preliminary search 142 titles and abstracts were screened and 91 publications were selected based on their high methodological quality and in alignment with the authors' conceptual approaches.
Results: In dental practice, communication is equally critical, reflecting the personal values and interpersonal skills of dental professionals. Many dental professionals underestimate the challenges of maintaining clear communication in a demanding health care system. Communication can take various forms. In modern dental education, various methods are used to train communication skills, including lectures, role-playing, small group teaching simulated patient interactions, clinical observation, real patient interviews, virtual patients and virtual reality-based trainings, use of videos, chairside teaching and feedback sessions. Traditional assessment tools may not capture the full scope of a student's communication skills. An assessment system should be designed to comprehensively evaluate the students' ability to integrate and apply their knowledge, skills and attitudes in real-world clinical settings, reflecting their readiness for professional practice.
Conclusions: There is no ideal method for training communication skills in undergraduate dental education. Combining the most effective teaching, learning and assessment approaches can help to design a structured communication skills curriculum. Students' communication competencies should be assessed through real-life scenarios with the use of structured frameworks and check-lists to ensure their readiness for professional practice.

Keywords: communication skills, dentist-patient communication, undergraduate dental education, dental curriculum, qualifications framework

'The single biggest problem in communication is the illusion that it has taken place.' - George Bernard Shaw

INTRODUCTION

Communication is a cornerstone of meaningful human interaction, enabling the exchange of ideas, emotions and information through various media, such as language, gestures, symbols and technology. Given the high prevalence and preventable nature of major oral diseases, proactive measures, such as educating patients on oral hygiene, encouraging regular check-ups and promoting strong communication skills amongst oral health professionals, can help prevent these conditions before they become a burden on the healthcare system[1,2,3].

Effective management of oral diseases relies on clear communication, which increases patient satisfaction, reduces fear and lowers the likelihood of malpractice claims. Ultimately, this facilitates accurate diagnoses and optimal treatment[4,5]. According to the World Medical Association Declaration of Lisbon on the Rights of the Patient, involving patients in their healthcare decisions is an inalienable right[6]. Such participation not only respects patient autonomy, but also fosters trust, improves adherence to treatment and enhances overall satisfaction with care[7,8].

In dental settings, communication failures may result in patient dissatisfaction and even harm[8,9,10]. In dental clinics, where the communication dynamic is often dentist-centred, patients assume a more passive role due to the physical constraints. These factors can hinder effective communication, making it challenging to convey important clinical information and address patients' concerns[11,12]. Therefore, it is essential for dental professionals to possess strong communication and interpersonal skills that foster patient engagement and facilitate clear, empathetic exchanges.

Organisations like the Association for Dental Education in Europe (ADEE) and the American Dental Education Association (ADEA) emphasise the importance of communication skills in dental education and stress the need for their development and assessment to ensure effective patient care[13,14]. Despite the recognition of the importance of communication skills training in dental curricula, there is often a gap between the theoretical knowledge and the practical application of communication competences in real-world dental settings[15].

This research aims to explore the key components of effective dentist-patient communication and address the teaching, learning and assessment of communication skills within undergraduate dental education with specific focus on the Armenian context.

MATERIALS AND METHODS

The narrative review included 91 publications, comprising 67 full-text articles, 3 reports, 13 monographs and books, 5 guidelines, 3 legal acts. Databases such as Medline, Scopus, Web of Sciences, PubMed, ScienceDirect, ResearchGate and others were used. Literary research was conducted across internet bibliographic open-access sources using the following keywords: 'communication skills', 'dentist-patient communication', 'undergraduate dental education', 'dental curriculum', 'qualifications framework'. This paper presents the key findings of a literature review encompassing published articles, reports, standards, guidelines, regulations and legal acts on communication skills in dentistry and dental education, without constraints on publication dates. In preliminary search 142 titles and abstracts were screened and 91 publications were selected based on their high methodological quality and in alignment with the authors' conceptual approaches.

RESULTS AND DISCUSSION

Communication in Dental Context

There are notable differences between dental and medical counselling[16]. Medical consultations typically involve interviewing the patient, conducting diagnostic tests, presenting a diagnosis, prescribing treatments, reviewing progress and providing advice. These sessions are primarily diagnostic and advisory, with actual treatment often occurring in separate appointments or procedures[12,16]. Effective communication is not an innate ability but a clinical skill that requires dedicated learning, regular practice, reflection and continuous improvement to prevent misunderstandings and enhance patient care.

In dental practice, communication is equally critical, reflecting the personal values and interpersonal skills of dental professionals[17]. Many dental professionals underestimate the challenges of maintaining clear communication in a demanding healthcare environment. Therefore, it is essential for dentists and other dental care professionals to be mindful of their communication with patients and colleagues, whether intentional or inadvertent, in both spoken and written forms. Dental consultations, on the other hand, often involve hands-on treatment right from the initial visit. Dentists commonly perform procedures such as cleanings, fillings or extractions during the consultation itself. This approach adds complexity and stress for both the dentist and the patient[12]. Additionally, since dental treatment involves working directly in the patient's mouth and using various instruments, it can heighten patient anxiety and trigger gag reflex often sometimes worsened by vomiting phobia[18]. Hence,

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unclear explanations of treatment plans may result in patients misunderstanding procedures, leading to anxiety, reduced adherence, or even refusal of treatment. To address this, dentists are supposed to possess strong communication skills to provide emotional support, alleviate anxiety and ensure a positive patient experience.

Effective Communication in Dental Consultations: Forms and Key Components

Communication can be best defined as the transmission of a message from a sender to a receiver in an understandable manner[19]. Communication can take various forms, including verbal and non-verbal, and para-verbal (the tone, pitch and pacing)[20]. Verbal communication involves the use of words to convey a message; it can be either oral or written. Communication starts with the sender and ends with the receiver and is made up of four key components: encoding, medium of transmission, decoding and feedback[19,21,22]. The sender is the person who initiates the conversation.

Encoding: The sender converts the message into symbols, such as words, pictures, or gestures. In dental consultation, the dentist formulates a message, such as explaining a diagnosis, treatment plan or oral hygiene instructions[19,21]. He/she may use medical terminology, visual aids or simplified explanations to convey the message[3]. The patient may also encode a message while describing symptoms, asking questions or expressing concerns.

Medium of Transmission: The dentist communicates with the patient through various media, including face-to-face conversations, written instructions. The encoded message is transmitted through a chosen medium, such as spoken words, written text, digital communication (e.g. emails, patient portals), visual aids (e.g. dental X-rays, diagrams) or body language[19,21]. When explaining the necessity of a specific treatment, dentists can enhance patient understanding and expectations by incorporating visual aids or using 3D imaging to illustrate the desired outcomes[23].

Decoding: The receiver (either the patient or the dentist) interprets and translates the encoded message back into a form that they can understand[19,21,24]. The patient interprets the dentist's message. This involves understanding the diagnosis, treatment options and instructions. Effective decoding depends on the patient's background knowledge, language proficiency and cognitive abilities[19,21,24]. Whereas, the dentist decodes the patient's verbal and non-verbal messages to understand their concerns, symptoms and preferences[19,21,24].

Feedback: The receiver (either the patient or the dentist) responds to the message, providing the sender with confirmation that the message has been understood, misunderstood, or requires further clarification. Oral communication, in particular, includes an immediate feedback mechanism, as both the speaker and listener engage in the simultaneous exchange of messages. This allows for prompt feedback, making it an efficient form of communication. When doubts or uncertainties arise, clarifications can be made directly[19,21]. To provide effective feedback, one must first develop strong listening skills, facilitating a clear transmission of ideas from the sender. This involves giving listener's full attention to the speaker, understanding the message, and avoiding judgments. Reflecting and paraphrasing what have been heard demonstrates engagement, while repeating key information ensures accurate understanding[25,26]. During the encounter, the dentist should start the conversation with an open-ended question and ask one question at a time. Active listening prior to responding is critical to maintaining focus and avoiding possible distractions, which is essential for clear communication and is highly valued in both professional and personal interactions[27]. Employing a patient-centred approach by actively listening to the patient's concerns can help ensure that patients feel heard and understood. The patient provides feedback by asking questions, expressing understanding or confusion, and showing their willingness to proceed with the treatment[22]. The dentist receives this feedback and may adjust their communication to ensure the patient fully understands. This might include re-explaining concepts, providing additional information or addressing any concerns[22].

Transmitted information from sender to receiver can lead to communication failures. According to *The Mathematical Theory of Communication* by C.E. Shannon, three levels of communication problems are: identified technical problems, semantic problems and effectiveness problems[28]. This theory can be applicable to the dental communication context as well:

Technical Problems: These involve the accuracy and efficiency with which symbols (words, images, sounds) are transmitted from the sender to the receiver[3] and address the question of how accurately the message can be transmitted. Issues at this level are concerned with the mechanics of signal transmission, including problems such as noise interference and those which can distort communication. An example could be the dentist's speech being muffled by a mask, leading to the patient's mishearing.

Semantic Problems: These concern the meaning and interpretation of the message. They address how precisely the transmitted symbols convey the intended meaning. This level deals with the relationship between the symbols and their meanings, emphasising the need for the receiver to understand the message as the sender intended[25,3]. Semantic problems arise when the meaning of the message is misinterpreted. For instance, when the dentist tells the patient, 'Your bite is misaligned', the patient might think, 'What does "bite" mean? Is that my jaw or my teeth?'. Words like 'bite' may have different meanings in various linguistic contexts. E.g. A patient misunderstanding the term 'bite' as referring to either the jaw or teeth may cause confusion during treatment.

Another example is a narrow interpretation of 'oral hygiene' as just brushing, while missing broader implications like flossing or professional cleaning.

Effectiveness Problems: These involve the impact of the message on the receiver. They address how effectively the received meaning affects the listeners' behaviour and whether the desired response or behaviour is achieved[28,19,3]. When the dentist says, 'Take an over-the-counter analgesic (NSAID) if you feel pain after the procedure', the unclear advice on a specific medicine leads to uncertainty about which painkiller to use.

Impact of Body Language and other Cues in Dentistry

Nonverbal communication is the process of conveying information without using words. There are different aspects of non-verbal communication. It includes a variety of signals and cues, such as body language, facial expressions, eye contact, gestures, posture, tone of voice, etc.[3,20]. Each of these elements plays a crucial role in how the messages are conveyed and interpreted, especially in contexts like healthcare, where empathy and understanding are essential. Nonverbal communication can reinforce or contradict what is being said verbally and often conveys emotions and attitudes more powerfully than words[3]. Nonverbal communication is essential for building trust, easing patient anxiety, and ensuring understanding between dental professionals and patients[20]. Research shows that nonverbal communication can manifest in several forms; this shapes how people interact[20,29].

Facial expressions: Smiles and frowns communicate our emotional states and reactions, making it easier for patients to feel at ease[30,20].

Eye contact: Proper eye contact demonstrates attentiveness and sincerity. This is essential in showing patients that their concerns are being actively listened to[31,3]. Maintaining appropriate eye contact when explaining a procedure builds trust, especially with anxious patients.

Body language and posture: Sitting or standing often reflects the communicator's openness and level of attentiveness[32,20]. Body language shows how engaged the dentist is in listening to the patient's questions and concerns. A dentist noticing a patient's body language might pause to ask if they have any concerns, thus showing attentiveness and care.

Paralinguistic signs: The tone, pitch and volume of speech can dramatically influence the emotional undertones of a conversation, adding depth and emotion to verbal communication. A calm and empathetic tone can reassure patients[3,29,33].

Proxemics: The physical distance from a patient affects their comfort level. Too little personal space can be intrusive, while too much can seem distant or disengaged[34,34,29]. During a dentist-patient encounter, the dentist should be mindful that different nations have different culturally determined perceptions of appropriate social distance[35].

Gestures: Gestures are not just movements, but symbols that express a full range of meanings which are different from spoken language[36]. Movements such as hand gestures or nods help to emphasise points, demonstrate attentiveness and convey understanding. They show patients that their concerns are being heard and considered[36,29].

Haptics (physical contact, touch): Haptics involves the use of touch to communicate. This can include handshakes, hugs, pats on the back, or any other form of physical contact. Touch can convey a variety of messages, from comfort and reassurance to aggression and dominance. Simple gestures like a reassuring hand on a patient's arm can ease their nervousness.

Appearance: A professional appearance influences first impressions and helps to establish trust. The dentist's attire, grooming and overall presentation can set a positive tone for the interaction[37,38].

By observing these nonverbal cues, a dentist can gain valuable insights into a patient's emotional state, comfort level and level of understanding. For example, a patient's body language might indicate anxiety or confusion, allowing the dentist to adjust his/her approach to ensure that the patient feels heard and valued.

Observing and responding to nonverbal cues such as body language, tone and gestures fosters deeper connections. However, it is not entirely accurate to define nonverbal communication as merely anything other than words. Nonverbal and

verbal behaviour impact the thought and language processes of a sender to the receiver, as well as the interpretations made by the receiver. To fully understand the conveyed thoughts, both verbal and nonverbal channels must be considered together, as they are most effective when they complement each other.

Language and Cultural Barriers in Dentistry

Demographic shifts have been significant in recent years, driven by factors such as immigration and global developments[39]. Dentists must communicate effectively with individuals from various racial, ethnic, linguistic, socioeconomic and cultural backgrounds, taking into account the impact of cultural and ethnic differences[35]. Language barriers pose significant challenges, especially when non-native speaker patients interact with native speaker healthcare professionals[40]. Limited language proficiency (LLP) can negatively affect a patient's experience. It is often a primary cause of miscommunication and misunderstandings, potentially leading to patient harm. Miscommunication due to language barriers can significantly compromise patients' safety. For example, a study by Divi et al. (2007) found that LLP patients were more likely to experience adverse events that result from communication errors compared to English-proficient patients[3,41]. These errors can range from incorrect diagnoses and inappropriate treatments to medication use mistakes, all of which pose serious risks to patients' health. It can increase risk of medical errors, increase healthcare costs and have an emotional and psychological impact on patients[4].

In the field of dentistry these issues are magnified, with studies showing that up to one-half of dental providers reported patients' inability to follow recommended oral health practices, including patients' lack of understanding of oral health information due to language and cultural barriers[43,10]. Addressing language and cultural differences in dental care not only enhances patient understanding, but also contributes to the health outcome[3,40].

This underscores the need for cultural sensitivity training to ensure that all patients, regardless of language proficiency or cultural background, can access and understand their health information[35].

Dentistry has always been a highly specialised field with a variety of specific professional terms. Hence, excessive use of dental terms will add to the complexity of dentist-patient communication. Dentists can use the 'tell-show-do method' during the encounter for patients to easily understand key health concepts[44]. Using charts or videos to explain procedures while language barriers arise could be a supportive tool for dentists. Dentists can ensure effective communication by explaining the procedure in layman terms by visually showing patents what is going to be done.

Teaching, Learning and Assessment of Communication Skills in Dental Education

Communication skills are not innate and can and should be learnt as part of an ongoing process. They should be taught at all the levels of dental education: undergraduate, post-graduate and continuous professional learning. Learning these skills can be challenging because they are often seen as intrinsic to a learner's personality, cognitive functioning and social experiences. Various social theories reveal that teaching and learning interpersonal communication between dentists and patients can be influenced by individual personality traits, situational contexts and environmental factors[15,45].

In modern dental education, various methods are used to train communication skills, including lectures, role-playing, small group teaching simulated patient interactions, clinical observation, real patient interviews, virtual patients and virtual reality-based trainings, use of videos, bedside (chairside) teaching and feedback sessions[15,46-52]. The implementation of targeted training with simulated patient feedback significantly increases clinical communication skills[49,53]. In contemporary dental education, teaching and learning occur across various environments, including lecture theatres, seminar rooms, phantom head suites and restorative dental education clinics (DECs), where students gain practical experience treating patients[54]. Additionally, students in many dental schools and hospitals attend general dental service clinics.

Role-playing is an interactive teaching technique that enables students to engage with realistic scenarios through interaction, allowing them to assume the role of themselves or another individual in a specific context[55]. Role-play as an educational method is grounded on Kolb's experiential learning theory involving four interconnected learning environments: feeling, thinking, watching and doing[56]. This method fosters active learning, allowing students to practise communication and problem-solving skills in a simulated environment[55].

Peer-assisted learning is a teaching method in which students teach their less-experienced peers. It is found to be a useful, enhancing learning experience which builds confidence and develops

communication skills[57,58,59]. Recording interactions between students and voluntary patients can be helpful. Students can review video recordings of their interactions to assess their body language, tone, word choice and overall performance. This method promotes self-awareness and encourages improvement.

Additionally, students can receive feedback from both instructors and peers as a formative assessment. A video- and feedback-based approach to teaching has been shown to enhance communication skills in dental students[60].

Problem-based learning (PBL) is a student-centred teaching-learning method which uses complex, real-world problems as a context for students to develop their critical thinking and problem-solving skills. PBL gives students the opportunity to master inter-personal and professional communication skills[61]. PBL, along with lectures, videos, role-play, patient interview and simulated patients, is found to be effective in developing active listening, establishing rapport, empathy, gathering information, cultural sensitivity and professionalism amongst students[52].

Sir William Osler, a pioneer of bedside learning in medicine, highlighted the value of hands-on teaching[62]. Bedside (chairside) teaching is a teaching method which involves a real patient to provide students with the experience to associate existing knowledge with new applications. Chairside teaching is as significant for dental students as bedside teaching is for medical students. Despite its importance, it is often under-recognised and under-reported as a teaching and learning method[54]. These chairside opportunities reinforce academic knowledge and build upon the foundations established in formal teaching environments, such as timetabled lectures and tutorials[63]. However, because chairside teaching is typically unscheduled, it depends heavily on the availability and engagement of dedicated teaching staff[54,63].

Traditional lecture-based teaching approaches limit students' learning and create difficulties in assessing practical communication skills[52]. Experiential learning methods, such as role-playing and simulation with standardised patients, are more effective in learning communication skills than traditional lecture-based approaches with assessment by written examination[12,56].

Assessment is an essential component in teaching clinical courses in dental undergraduate training to ensure patient safety. Assessment ensures that students undertake clinical procedures that they have been trained for[64,65]. In 1990, Miller proposed the Model for Clinical Competency Assessment. It is now widely used for assessing clinical competence in medical and dental education[66,12]. The model is structured as a hierarchy with four levels, representing the progression from basic knowledge to real-world application. At the lowest level of the pyramid is knowledge (student knows). It is followed by competence (student knows how to use the knowledge); then comes performance (student shows how to apply the knowledge) and action (student implements the knowledge)[66]. The level of credibility of the competency increases in a hierarchical manner, mounting closer to actual working conditions. Assessment of mental function refers to knowledge and the application of knowledge ('knows' and 'knows how to do'), gradually moving from the 'understand' level of Bloom's taxonomy to the higher 'analyse' and 'evaluate' levels[67]. Common methods of assessment, such as multiple-choice questions target the lower levels of the pyramid. Thus, this pyramid model assumes that actual practice is a much better reflection of routine performance than assessments done under academic testing, which would also be the long-term goal of a longitudinal curricular programme in communication skills training[7].

Students' assessment takes many forms, depending on the assessment aim. A summative assessment is a formal assessment of a student's work which documents the student's mastery of the required learning outcomes[68]. It is usually conducted at the end of a course or a programme and is graded[68,69,70]. Formative assessment is usually an ongoing classroom assessment which takes place throughout the course to support learning and improvement[68]. It provides feedback on each student's performance and helps the instructor continually to make necessary adjustments during instruction[71]. Formative and summative assessment methods are diverse and should be carefully selected, justified and approved in alignment with the fundamental principles of the university's grading system. These methods must adhere to relevant university policies and procedures and be clearly detailed for each course. Assessment criteria should be transparent to students and should accurately reflect their performance. A study found that integrating formative with summative assessment methods improved communication skills instruction[72]. Clinical competencies, including communication skills, can be effectively evaluated using structured checklists and guidelines[48]. The literature on structural checklists and guidelines for healthcare professionals consistently emphasises the core principle of promoting patient-centred communication during consultations[73]. These approaches have been adapted for dentist-patient

interactions, with several studies demonstrating the effectiveness of such models in training healthcare professionals[7,74]. Specific communication techniques, strategies or frameworks are being used for training communication courses and the Calgary-Cambridge Model is mentioned more often[53]. The Calgary-Cambridge Model is a structured framework developed by Kurtz and Silverman to enhance communication in healthcare settings[75]. The model outlines a five-step process: initiating the session, gathering information, conducting a physical examination, providing explanation and planning, and closing the session. Unlike traditional methods, this model integrates verbal communication with the physical examination, highlighting the interdependence of information gathering and communication[74]. The Calgary-Cambridge Model has been extensively translated and implemented for teaching communication skills in specialised settings across both undergraduate and postgraduate education levels. It has also been adapted for dental communication training[52,7,74].

The innovative 360-degree appraisal (360-degree assessment, multi-source feedback) is a workplace-based student assessment in a clinical setting that involves different groups of people associated with that particular dental clinic[76]. This comprehensive assessment tool collects feedback from diverse sources, such as peers, instructors, patients, administrative staff and the student himself/herself, to provide a holistic evaluation of students' communication competencies[77,78]. Several assessors observe and evaluate the student according to pre-defined criteria, with special attention to empathy, clarity and active listening, while remaining anonymous[79,60]. This appraisal method not only identifies strengths and weaknesses in verbal and non-verbal communication, but also helps students develop self-awareness and address areas for improvement through structured feedback. Studies have highlighted that multi-source feedback promotes professional conduct, teamwork and self-directed learning by encouraging students to reflect on their interpersonal behaviours and adjust them to meet professional standards[80]. Integrating 360-degree assessments into dental curricula, educators can ensure that graduates are better equipped to navigate the complexities of patient care and interdisciplinary collaboration effectively.

Traditional assessment methods lack structured guidelines for evaluating communication skills, and the criteria used for assessment are often unclear to students, leading to evaluator errors. A rubric within the field of education is known as a coherent set of criteria and descriptions of the levels of performance for these criteria; it is a working guide for students and teachers[81,82]. Rubrics are often given to individuals prior to assessment (in this case students) so that they know how the task will be assessed[83,81]. Clear learning objectives and assessment criteria are supportive because they provide students with a clear understanding of what they are expected to learn and how they will be assessed. Additionally, it assists assessors in ensuring transparent and fair grading.

The Objective Structured Clinical Examination (OSCE), first introduced by Harden, is a widely used assessment model designed to evaluate medical students' clinical skills and competencies in undergraduate education. It can also serve as an effective tool for teaching communication skills to dental students, as well as assessing their competency in various areas of dental education, including communication skills[48,73,46]. From various formats of assessment, OSCE is mentioned more often in the literature.

Considering the development of artificial intelligence (AI), including its potential to enhance communication skills among medical professionals, AI-driven tools are being used to simulate patient interactions, enabling students to practise and refine their communication strategies in a risk-free environment[84,85]. By engaging with AI-powered virtual patients, learners can develop essential skills, such as empathy, active listening and clear articulation of medical concepts. Furthermore, these tools provide immediate, personalised feedback on both verbal and non-verbal communication, enabling students to identify areas for improvement and track their progress over time.

Thus, the effectiveness of discussed innovative assessment methods can be complex. Traditional assessment tools may not capture the full scope of a student's communication skills, particularly in non-verbal and interpersonal interactions. To address this, new assessment frameworks need to be developed in order to account for the diverse range of skills required for effective communication in dental practice. By overcoming these challenges through strategic planning, investment in resources, and faculty development, dental schools can create a more dynamic and effective learning environment. Moreover, fostering interdisciplinary collaboration amongst faculty members (dental, medical, and communication experts) can enrich the curriculum and provide students with a broader perspective on the development of communication competences. Most importantly, as outlined in the UK General Dental Council Standards for Education, students' assessment must be reliable and valid; the chosen assessment method must appropriately demonstrate

the achievement of learning outcomes[60]. It is essential that when selecting or combining certain assessment methods for evaluating clinical competency and communication skills, educators do not view the assessment solely as a means of validating students' knowledge for a specific programme or module learning outcome. Instead, assessments should be designed to comprehensively evaluate the students' ability to integrate and apply their knowledge, skills and attitudes in real-world clinical settings, reflecting their readiness for professional practice.

Communication Skills Training Standards within Undergraduate Dentistry Curriculum

The special importance of teaching communication skills in the undergraduate dental curriculum is widely recognised[13,14,75]. The ADEE highlights the significance of non-technical skills, including communication and situation awareness, in ensuring patient safety. Similarly, the ADEA outlines competencies for new general dentists, emphasising the necessity for graduates to apply appropriate interpersonal and communication skills[13,14]. ADEE and the DentEd Thematic Network (TNP) are among the leading organisations which have consistently played a key role in shaping dental education in Europe[86]. *The Graduating European Dentist* is the latest update of ADEE's European Profile and Competence of the European Dentist. While maintaining the style, format and approach of previous editions, this version significantly advances European dental education[87]. *The Graduating European Dentist Curriculum* provides a contemporary approach reflecting best academic practice for European undergraduate dental education system. It consists of five domains: I: Professionalism, II: Safe and Effective Clinical Practice, III: Patient-Centred Care IV: Dentistry and Society, V: Research[87]. Team-work and communication competencies are integral programme learning outcomes in all domains except for domain IV: Dentistry and Society. *The Graduating European Dentist* underscores the emphasis on a holistic and practical approach to preparing graduates for evolving societal and professional needs. While some dental schools integrate communication training throughout the curriculum, others offer standalone courses or modules. Several dental education experts advocate for longitudinal teaching, which involves integrating communication skills training consistently throughout the entire dental curriculum, aligning it with students' clinical development and increasing in complexity as they progress[88].

Undergraduate Dentistry programmes in Armenia are regulated by a number of Laws, as well as the Sectoral Qualifications Framework for 'Medicine' (SQF-M) in the RA[89,90]. Graduates should meet the standards under the 7th level of Armenian National Qualifications Framework (ANQF) and the SQF-M of the Republic of Armenia. The SQF-M outlines the knowledge and competencies of dental graduates. The SQF-M specifies detailed competencies that dental graduates must achieve, including technical skills, ethical standards and professional behaviour. Communication skills are integral to these competencies, facilitating effective patient management, ethical decision-making and teamwork. Qualification holders shall possess thorough, systematised and in-depth specialised knowledge, demonstrate skills, competences and behavioural practices to pursue postgraduate education and undergo professional development training sessions in health specialties.

Despite the recognised importance of communication skills training in the Armenian dental education system, as in many other countries, it has often been disregarded. Many dental school curricula rely primarily on a didactic, one-time course, offering minimal opportunities for students to actively develop these essential skills[12].

The undergraduate study of dentistry in the Republic of Armenia is a five-year integrated academic programme leading to the award of 'Doctor of Stomatology'[91]. After the enforcement of the Sectoral Qualifications Framework for 'Medicine' (SQF-M) of the Republic of Armenia, Armenian higher medical educational institutions followed the implementation of new standards. Firstly, the desk review of Programme Learning outcomes vs SQF-M was conducted by university curriculum developers. A comparison of the SQF-M and the YSMU Undergraduate Dental Programme Learning outcomes revealed a gap in terms of communication and interpersonal competences. While some courses within the humanities block included communication-related topics, these did not comprehensively address the nuances of communication in dentistry. Communication and interpersonal skills training did take place across different courses at various stages of the programme, resulting in a fragmented approach. To address these gaps, the Dentistry Programme Learning Outcomes have been refined and a new modularised curriculum has been developed in order to place greater emphasis on teaching and learning professionalism and clinical skills. These competences are now longitudinally included in the dentistry Curriculum. Additionally, a standalone course specifically dedicated to communication skills in dentistry has been designed.

CONCLUSION

Effective communication in dentistry is a multi-faceted process involving harmonised communication cues. By mastering communication competences, dental professionals can build rapport, reduce patient anxiety and enhance patient care to achieve the most effective dentist-patient interaction. To address these needs, it is essential that a standalone module specifically focused on communication in dentistry along with integrating communication competences be integrated throughout the clinical modules within undergraduate dental curriculum. Dental programme learning outcomes should include clear and empathetic communication. Cultural sensitivity training is equally essential to equip students with the skills to deliver high-quality care to patients from diverse linguistic, ethnic and cultural backgrounds.

There is not one best method for training communication skills in undergraduate dental education. Instead, combining the most effective teaching and learning approaches can help design a structured communication skills curriculum with content appropriately aligned to different levels of dental studies. Dental students' communication competencies should be formally and comprehensively assessed through real-life scenarios with the use of structured frameworks and check-lists to ensure their readiness for professional practice.

DECLARATIONS

Conflict of interest

The authors declare that there are no conflicts of interest related to the design, conduct, or publication of this study.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

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