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REVIEW ARTICLE

THE INTERPLAY BETWEEN DOWN'S SYNDROME AND PERIODONTITIS: A REVIEW OF CURRENT INSIGHTS

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Periodontitis is a chronic inflammatory disease which can affect all age groups depending on the etiology either local or systemic. Most of systemic conditions cause periodontitis and one of them is downs syndrome which is also called trisomy 21. It was also observed that 90% of downs syndrome children have periodontal disease (PD) with majority in the age group of 7-10 years. Due to anatomical abnormalities or impaired learning disabilities or intra oral tissue abnormalities or neurological deficiencies, Down's syndrome patients cannot maintain their oral hygiene properly leading to progressive periodontitis. Other immunological abnormalities such as proteolytic enzyme deficiency, inflammatory cytokine deficiencies can also aggravate tissue destruction and bone resorption.

Therapeutic treatment protocols such as scaling and root planing, use of mouth washes, electric tooth brushes, regular dental checkups and non–invasive procedures such as photodynamic therapy, laser, probiotics etc. can help the patient's periodontal tissues to stay healthy. An initial search of 437 articles from PUBMED, EMBASE, Cochrane library, web of science, and google scholar was done. 22 articles were excluded records excluded due to inappropriate title and abstract. 72 articles were excluded after abstract screening and 89 full text articles were assessed. 32 articles were excluded as outcome of interest was not reported and 21 due to incorrect study design. A final of 36 articles were studied to elaborate the review on Down's syndrome and periodontitis.

***Keywords*:** Down Syndrome, Gingival Inflammation, Immune Dysfunction, Oral Health, Periodontitis

INTRODUCTION

Downs syndrome (DS) or Trisomy 21 was first discovered by Langdon-Down in 1966 and Jones in 1988 had found out that the oral environment is different in downs syndrome children as compared to normal age matched children.[1] It was also observed that 90% of downs syndrome children have periodontal disease (PD) with majority in the age group of 7-10 years. Downs syndrome is most common chromosomal separation disorder which is characterized by phenotypical variations of face, intellectual disabilities, systemic disorders and oral disorders.[2]

Genetic polymorphisms in inflammatory factors and immune deficiency are the leading causes for PD in DS patients.[3] Other factors include abnormal oro-facial morphology leading to abnormalities in tooth anatomy and gingival epithelium. Early colonization of periodontal bacteria can also lead to altered oral microbiome and eventually periodontitis in DS patients.[4]

Prevalence and severity:

A study done by Johnson and young found out that bone loss in DS patients was more than patients with same learning disabilities but without DS. The bone loss followed a horizontal pattern and mostly seen in

lower anterior segment.[5]

Another study done by Saxen et al found out that subjects with DS (69%) agedbetween 9 to 39 years had more than 5mm bone loss compared with 20% of the control group who had similar levels of plaque and calculus.[6]

Anatomical and physiological variations in Down's syndrome patients:

The anatomical features of DS patients are typically the same and have mid facial abnormality, small and low set ears, sunken eyes, flat nasal bridge, small mouth, epicanthic folds, flat occiput, up-slanting palpebral fissures. Intraoral features include decreased tooth size, abnormal crown shape, delayed eruption, missing and malformations and collapsed palate.

Table 1. Clinical manifestations in Down's syndrome patient[8]

System affected	Symptoms and manifestations in DS patients
Neurodevelopment abnormalities	Intellectual disability Delay in development Language disorders Cerebellar hypoplasia
Psychiatric	Anxiety Depression Behavioral disturbances
Neurological	Epilepsies Alzheimer's disease
Cardiovascular	Atrioventricular septal defects (Congenital heart defects)
Musculoskeletal	Short fingers Small stature Hypotonia Atlantoaxial instability
Respiratory	Respiratory tract infections Obstructive sleep apnea
Autoimmune	Thyroid disease Coeliac disease Alopecia Type I diabetes mellitus
Craniofacial	Small and low set ears Flat nasal bridge Flat occiput Small mouth Upslanting palpebral fissures Epicanthic folds
Sensory	Refractive errors, cataracts, amblyopia Conductive and sensorineural hearing loss

Etiology of periodontitis in Down's syndrome patients:

Periodontal disease in Down's syndrome patients can occur due to either local factors or general factors. Few of the anatomical variations extra orally and intra orally as well as neurological abnormalities mentioned in the above table also contribute to early periodontitis.

Table 2. Factors which cause periodontitis in Down's syndrome patient:[9]

Local factors	Systemic factors
Morphology of teeth	Inflammatory mediators and proteolytic enzymes
Composition of microbiological plaque	T-cell dysfunction
Open mouth breathing	Matrix metalloproteinases
Oral hygiene	Neutrophil dysfunction
Dietary habits	IL-110 imbalance

Local factors include:

A) Oral hygiene: Poor oral hygiene is one of the commonest causes of periodontal disease in DS patients. This might be due to poor manual dexterity and decreased fine motor skills causing improper brushing method. Most of the downs syndrome patients brush only once and are reluctant to get dental procedures done. Other causes for poor oral hygiene can be due to microdontia, macroglossia, abnormal facial formations, poor dietary habits, medications, and infections in upper respiratory tracts, compromised development in swallowing, mastication and speech.[10] Cohen et al examined 100 DS individuals and found out that oral hygiene was poor as compared to healthy individuals.[11]

B) Open mouth breathing: Open mouth breathing is common in DS patients and can be mostly due to underdevelopment of facial middle third. This can lead to hypo plastic maxilla and hypergnathic mandible causing enlarged tonsillar area and upper airway obstruction. Incompetent lips are other cause for open mouth breathing DS patients. PD can be caused in DS patients with open mouth breathing. This can be due to decreased salivary flow leading to increased bacterial growth, plaque accumulation and eventual gingival inflammation and bone loss.[12]

C) Morphology of teeth: Most of the authors have found out those teeth in downs syndrome patients are short and have fused roots.[13] According to a study done by Lamani et al, DS patients with short roots had more bone loss than with normal roots.[14]

D) Composition of Microbiological plaque: Higher levels of periodontopathic bacteria are seen in DS patients. A study done by Sakellari et al found out that DS patient with all age groups had more of periodontopathic bacteria as compared to normal individuals. Higher prevalence of Porphyromonas gingivalis, Tanerella forsythia and Actinomycetes actinocomitans was seen.[15] Another study done by Amano et al found out that periodontopathic bacteria were present in DS patients of early age of 2-4 years. The bacteria which were found to increase with age in DS patients were P gingivalis. DS patients also had a higher amounts pf herpes virus species in subgingival sites. It was found out that 26% had human cytomegalovirus, 32% had Epstein barr virus and 16% herpes simplex virus.[16]

Systemic factors include:

A) **Inflammatory mediators and proteolytic enzymes:** Host and bacteria derived proteolytic enzymes were the most important etiology for periodontal destruction in DS patients according to Liu et al.[17] Mean level of Prostaglandin E2 (PGE2) in the gingival crevicular fluid was higher in DS patients than in healthy individuals. Altered composition of microbial flora can be considered as one of the reasons for increased PGE2 levels in DS patients.[18]

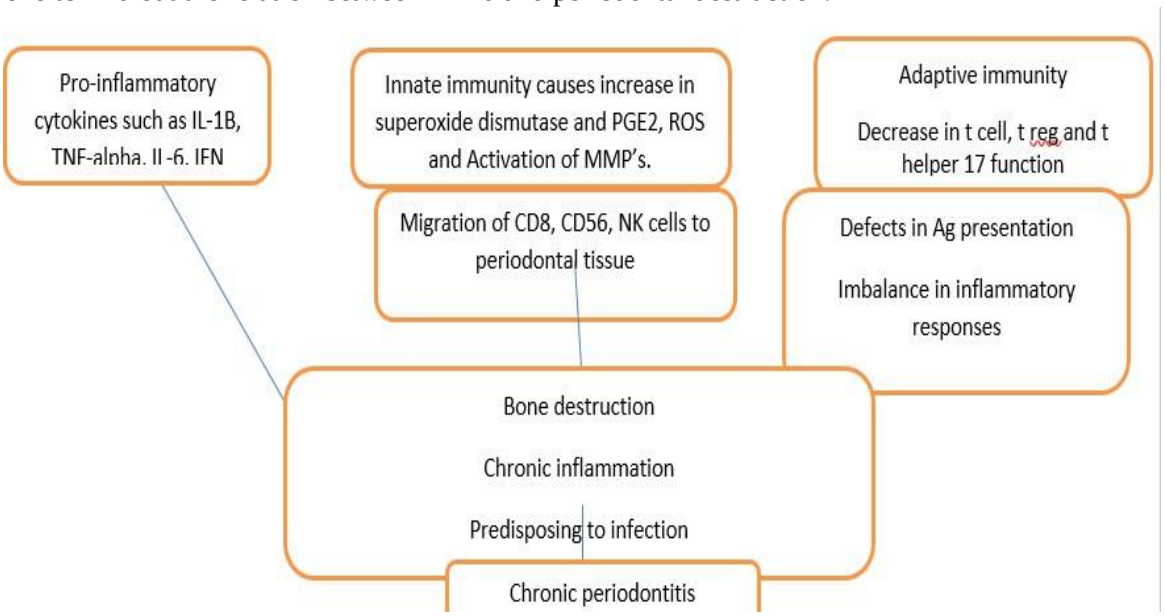
B) **T-lymphocyte dysfunction:** A study done by Cichon et al found out that Down's syndrome subjects had both qualitative and quantitative deficiency of T- lymphocytes. T-lymphocytes had decreased ability to recognize and respond to specific antigens.[19] This can probably lead to periodontitis in early stages of downs syndrome patients. Other researchers have observed that DS subjects had lesser T cell receptor bearing lymphocytes than healthy individuals with periodontitis. Low serum zinc levels in downs syndrome patients can also lead to depressed neutrophil chemotaxis and lymphocyte responsiveness. As zinc is essential mineral for synthesizing RNA and DNA, zinc supplementation in DS patients can help in improving the function of neutrophil and T-lymphocytes.[20]

C) **Neutrophil dysfunction**: Neutrophil dysfunction is the main and important etiology in progression of any periodontitis in healthy or in abnormal gingiva. Periodontitis can lead to accumulation of neutrophils in junctional epithelium, connective tissue and in gingival sulcus.[21] A study done by Izumi et al found out that DS patient had impaired neutrophil chemotaxis. In periodontitis patients, the disease progression is inversely proportional to defective neutrophil chemotaxis.[22]

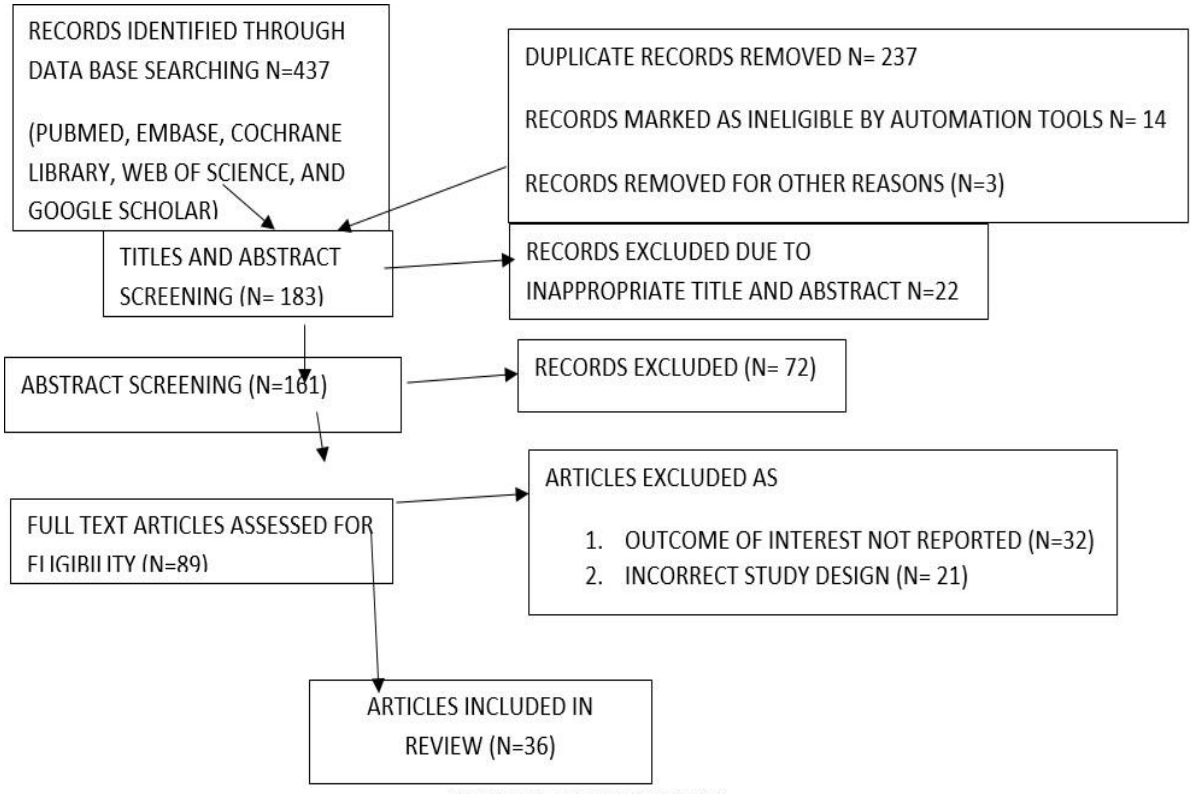
D) **Matrix metalloproteinases (MMP's)**: Matrix metalloproteinases are proteolytic enzymes which are mainly increased in inflammatory conditions causing tissue remodeling and destruction of extracellular matrix.

Many studies have found out that ds patients have higher levels of MMP's than healthy individuals. These MMP's include MMP-2, MMP-3, MMP-8, and MMP-9. These are increased in periodontium following inflammation and help in transmigration of inflammatory cells. Gingival crevicular fluid and saliva samples of DS patients had more of MMP'S showing periodontal inflammatory changes.[23]

E) **Interleukin-10 (IL-10) imbalance:** Anti-inflammatory cytokines such as IL-10 help in inhibiting the induction of pro-inflammatory cytokines such as IL-6, tumor necrosis factor- α (TNF- α) and IL-12. In periodontitis, the levels of IL-10 are decreased in GCF leading to increased destruction of periodontal structures. Very few studies have reported the levels of IL-0 in DS patients and increased periodontal destruction. Further studies should be done to find out the relation between IL-10 and periodontal destruction.[24]



Flow chart: Immune function in Downs syndrome leading to periodontitis



PRISMA FLOW CHART

Role of microbiota in destruction of periodontal structures:

It is found out that DS patients had increase in certain species such as Propionibacterium acnes, Streptococcus gordonii, Selenomonas noxia, Streptococcus constellatus, Streptococcus mitis, Streptococcus oralis, and Treponema socranskii. P.acnes which is common bacteria found in human skin was also found in some DS patients who have a habit of thumb and finger sucking. These bacteria are responsible for apical periodontal infections.[25]

Some bacteria will help in initial plaque development and aid in formation of a biofilm helping bacteria to attach to the tooth surface. These bacteria include S. gordonii, S. mitis, and S. oralis. The age of DS patients also is important for colonization of bacteria. Some bacteria such as eikenella corodens, Peptostreptococcus micros, and Prevotella nigrescens are mostly found in young Downs syndrome patients. Pubertal age groups have majority of red complex bacteria which are mostly responsible for the progression of periodontitis be impaired immune response, altered electrolyte concentration and combination of low salivary flow.[26]

Therapeutic approaches to periodontitis in Downs syndrome patients:

Downs syndrome patients usually do not cooperate to dental procedures and show reluctance towards dental checkup. Due to learning disabilities, DS patient's do not sit in the dental chair for longer time. As periodontal surgical procedures take long time, these are not advised to DS patients. Non-surgical therapeutic options can help in decreasing the severity of periodontitis and these methods have gained importance in management of downs syndrome patients.[27]

Various non-surgical approaches include:

1. **Oral hygiene education:** DS patients can be educated about oral hygiene practices such as brushing technique, frequency and duration, flossing, interdental cleaning methods. They should be encouraged for regular dental checkups. Due to lack or decrease in manual dexterity, DS patients can be given electric tooth brushes in their regular oral hygiene practice.[28]
2. **Scaling and root planning:** this is a non-surgical procedure to remove any plaque and calculus on the tooth structure. Since DS patients are apprehensive and do not cooperate for electric scaling, these procedures should be encouraged with manual scaling techniques by dental professionals.[28]

1. **Mouth washes with anti-bacterial effects:** Mouth washes can be encouraged once a while for DS patients but not for long term use. These can reduce bacterial count and inflammation of gingiva.
2. **Systemic and local antibiotics:** Severe inflammation and periodontitis can cause bad breath, mobility of teeth, and recession of gums in downs syndrome patients and can affect the overall mastication ability in turn leading to indigestion. Therefore, one of the non-surgical approaches which can reduce the bacterial count, inflammation and can improve the gingival health is administration of local or systemic antibiotics. Local drug delivery is the best and safe option for downs syndrome patients and can effectively treat periodontitis without any side effects. Local drug delivery agents can be antibiotics, anti-viral or herbal agents and can be delivered in the form of fibers, gels, strips or nano particles in the subgingival pockets.[30]
3. **Photodynamic therapy**: This is an effective non-surgical and non-invasive approach to decrease inflammation, bacterial count, through a low level led or laser light. This can promote reattachment of gum tissue by reducing periodontopathic bacteria. This method can help in reducing the levels of pro-inflammatory cytokines such as IL-1, TNF-alpha, and IL-6 while modulating the immune system and reduce tissue destruction.[31] Novaes et al in 2012 had found out that photodynamic therapy was effective in reducing aggreagatibacter actinomyceticomitans, taneralla forsythia, porphyromonas gingivalis and Treponema denticola in 10 patients.[32] Silva et al in 2022 had used photodynamic theapry on 8 DS patients and found a reduction in bleeding on probing.[33]

6. Probiotics, prebiotics and symbiotics: Use of probiotics and prebiotics which are non-digestible substances and symbiotics which consist of both probiotics and prebiotics are beneficial for restoring the microbial environment, modulating the immune system without any side effects. Lactobacillus, Streptococcus and Bifidobacterium species are the most common probiotics used for periodontitis. Lactobacilli and streptococcus are effective against P gingivalis, P intermedia and A. actinomycitocomitans. Lactobacillus strains help in reducing the inflammation by decreasing the expression of IL-8 in gingival epithelial cells.[34] Baddouri et al in 2024 had found out beneficial effects of L. reuteri ATCC PTA 5289, L. reuteri DSM 17938 in 62 chronic periodontitis patients by improving clinical measurements.[35]

7. LANAP: Laser assisted new attachment procedures can also done on DS patients with severe periodontitis and with pocket probing depth of 5-6 mm. each quadrant can be planned on single visit so that the patient doesn't lose his/her patience and can cooperate well with the treatment.[36]

It is necessary to conduct specialized research to evaluate the effects and possible adverse effects of these adjunctive treatments because of the unique conditions of these DS patients, which include immune system deficiencies, oral and orofacial abnormalities, and a particular makeup of the oral bacterial community.[3,4] Additionally, the advancement of clinical understanding is thought to benefit from the need for systematic studies and meta-analyses to enable a thorough review of these treatment approaches as well as informed decision-making regarding their use in the treatment of PDs in people with DS.

CONCLUSION AND FUTURE PERSPECTIVES:

In this review we have delved into the most important factors such as relationship of PD and DS patients, predisposing factors for periodontitis in DS patients, how host immune responses and enzymes cause periodontitis in DS patients and therapeutic options. Periodontitis in DS can be multifactorial involving both intra oral factors such as oral hygiene, tooth morphology, mouth breathing habit and extra oral factors such as learning disabilities, anatomical and neurological abnormalities. More research on adjunctive non-surgical treatments for DS patients can help in managing periodontitis at early stage. Tailored procedures can benefit this vulnerable population and can help maintain their oral hygiene

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Competing and conflicting interests

The authors declare no competing interests or conflicts of interest related to this work.

Informed consent

Not applicable.

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