



A Comprehensive Review of the Relationship Between Oral Health and Down Syndrome

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Abstract

Purpose of Review Individuals with Down syndrome (DS) may be more susceptible to oral disorders as a result of a combination of genetic factors, immunological disturbances, anatomical anomalies, and probable difficulties in maintaining adequate oral hygiene. Within this context, we provide a comprehensive review of the most important relationships between oral health and Down syndrome.

Recent Findings Recent investigations suggest that a diminished diversity in the oral microbiome could emerge as a critical factor affecting oral health in individuals with DS. Plausible anatomical and metabolic peculiarities inherent to DS, including alterations in salivary characteristics, the presence of obstructive sleep apnea, elevated end glycation product levels, and hypothyroidism, may exert a significant influence on the composition and dynamics of the oral microbiome. A comprehensive analysis of the evidence implies a reduced occurrence of caries in individuals with DS. Furthermore, a recent meta-analysis indicates that gingivitis (OR 1.93; 95% CI 1.09–3.41) and periodontitis (OR 3.93; 95% CI 1.81–8.53) are more frequent in people with DS and strongly associated. Oral function in DS is also affected resulting in speech, breathing and eating problems. These findings underscore the necessity to implement targeted educational and awareness programs, along with specific intervention protocols, for the younger generations of individuals with DS, their families, and caregivers.

Summary Although trisomy 21 itself does not determine a specific cause of oral diseases in DS, common oral health conditions such as gingivitis, periodontitis, and caries remain a matter of concern. The nexus between insufficient plaque control, distinctive oral characteristics, and reluctance to engage in treatment persists as noteworthy determinants. The necessity for oral health professionals to exercise patience and commitment when addressing oral care for individuals with Down syndrome is crucial.

Keywords Down syndrome · Oral health · Caries · Periodontitis · Special needs dentistry · Oral microbiome

Introduction

Down syndrome (DS) stands out as one of the most widespread chromosomal disorders. According to the World Health Organization, it has an estimated global incidence ranging from 1 in 1000 to 1 in 1100 live births [1, 2••]. While DS is connected with a variety of physical and cognitive issues, one component of health that is frequently overlooked is oral health. While individuals with DS do not

have specific oral health pathologies, they frequently exhibit a spectrum of oral health issues that tend to manifest with increased severity compared to their non-syndromic counterparts. These issues encompass dental anomalies, delayed tooth eruption, and higher predisposition to both periodontal diseases and caries. Oral health is not only important for physical health, but it also affects quality of life [3•]. Additionally, they frequently struggle with communicating skills, making oral health issues particularly relevant. Hence, poor oral health can worsen these issues, resulting in social isolation and low self-esteem [4]. Research in this area not only enhances our understanding of the syndrome's broader health implications but also aids in the development of inclusive and specialized dental care approaches for individuals with special needs. Here, we provide a comprehensive review of the most important relationships between oral health and DS.

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Definition, Craniofacial, and Oral Features of Down Syndrome

Down syndrome (DS) stands out as the most prevalent autosomal aneuploidy found in surviving newborns. This genetic anomaly arises from the complete or partial triplication of chromosome 21 and manifests in three distinct karyotypes: complete trisomy 21, mosaicism, and translocation. In individuals with DS, there is an elevated number of copies of genes located on chromosome 21. Importantly, the genes implicated in DS exhibit normal characteristics, and their gene products remain unaffected. The genetic irregularity associated with DS results in an overexpression of genes on chromosome 21, leading to increased production of gene products in cells and tissues. This overexpression, in turn, contributes to the manifestation of phenotypic abnormalities [5, 6].

Various characteristics linked to the oral cavity have been documented in DS, although their occurrence is not universal among patients or across all age groups, displaying variations based on ethnic backgrounds. Reported

alterations encompass structures such as the jaws, tongue, dental features, and muscular disorders (Table 1). These variations can impact occlusion, phonation, swallowing, and overall quality of life in diverse ways [7–9].

The tongue represents a distinctive feature in individuals with DS, as it may appear enlarged. However, contemporary understanding negates the notion of a genuinely enlarged tongue, characterizing it instead as a pseudo-macroglossia linked to diminished dimensions of the craniofacial bones. Notably, research has also indicated that individuals with DS may, in fact, exhibit a comparatively smaller tongue (2432 mm²) in contrast to a control group [8]. As age advances, there is a decline in both anterior and posterior tongue strength, impacting functions such as swallowing and phonation [10]. Additionally, individuals with DS exhibit a dry lingual surface attributed to the oral respiration they commonly experience [11, 12].

Esbensen (2016) reported that oral breathing and muscular hypotonia in association with sleep disorders, affecting structures such as the jaw and tongue in DS [13]. Individuals with DS may exhibit alterations in maxillary sizes, characterized by

Table 1 Craniofacial and oral features of Down syndrome

Craniofacial features

- Flat facial profile: Individuals with Down syndrome often exhibit a flatter facial profile, with a smaller nose and midface.
- The face is round, flat, and with little relief. The skull is small and the occiput flat.
- Upward slanting eyes: The eyes may slant upwards and have an epicanthic fold (a skin fold of the upper eyelid that covers the inner corner of the eye).
- Small ears: The size of the ears is often smaller in proportion to the head.
- Small mouth and protruding tongue: The mouth may be smaller in size, and individuals may have a tendency to protrude their tongue.
- Broad and short neck: The neck may appear broader and shorter in individuals with Down syndrome.
- Flat back of the head: The back of the head (occiput) may appear flat.
- Single palmar crease (simian crease): Some individuals with Down syndrome may have a single palmar crease instead of the typical three creases on the palm.
- Hypotonia (low muscle tone): Hypotonia can affect the muscles of the face, contributing to the characteristic appearance.
- Small nose with a flattened nasal bridge: The nose may be smaller, and the nasal bridge may appear flattened.
- Tendency for skeletal class III development.

It is important to note that the degree to which these features are expressed can vary among individuals and not every person with Down syndrome will exhibit all of these features.

Oral features

- Delayed tooth eruption: Children with Down syndrome may experience delayed eruption of primary and permanent teeth.
- Hypodontia and oligodontia: Some individuals may have fewer teeth than the typical number, a condition known as hypodontia. In severe cases, oligodontia (missing multiple teeth) may occur.
- Malocclusion: Malocclusion, which refers to misalignment of teeth, is common in individuals with Down syndrome. This can include issues such as crowding, overbite, underbite, and crossbite.
- Bruxism: Bruxism is the habit of grinding or clenching teeth, and it can be more prevalent in individuals with Down syndrome.
- Periodontal disease susceptibility: Individuals may be more susceptible to periodontal diseases. This susceptibility could be related to factors such as immune system function and oral hygiene challenges.
- Small or abnormal shaped teeth: Teeth in individuals with Down syndrome may be smaller in size, and the shape of the teeth may be different from those without the condition.
- Protruding tongue: This is a common facial feature in Down syndrome and can contribute to problems with speech and oral function (pseudo-macroglossia). It is thick, rough, and with many folds and may present a posterior displacement towards the pharynx (glossoptosis).
- Macroglossia, glossoptosis, and narrow upper airways are associated with obstructive sleep apnea.
- High-arched palate: A high-arched palate is a condition where the roof of the mouth is elevated. This can sometimes affect speech and contribute to orthodontic challenges.
- Oral motor challenges: Hypotonia (low muscle tone) can affect the muscles of the oral cavity, impacting oral motor skills, including speech and swallowing.

It is important to note that these features can vary among individuals, and not everyone with Down syndrome will experience all of these oral and dental characteristics.

a reduction in the middle third of the face, leading to a skeletal class III tendency. Furthermore, hypodontia is also common which can influence the correct development of the jaws [14].

Dental agenesis is frequently reported in DS, often marked by the absence of three or more teeth. Among permanent teeth, the upper lateral incisor (27%), mandibular second premolar (21%), and upper second premolar (18%) exhibit the highest prevalence of agenesis [15]. Additionally, various associated findings have been reported, including malocclusions such as anterior open bite, temporomandibular joint alterations, bruxism, and delayed tooth eruption [16].

While DS does not exhibit specific oral features, certain oral and craniofacial aspects are altered in individuals with DS. Depending on the severity of these alterations, they can have substantial implications for their oral health. To guarantee whether adult and pediatric patients receive the right care, dentists and medical care professionals should be aware of recognizing these unique traits and modifying treatment plans accordingly.

The Oral Microbiota and Microbiome in Down Syndrome

The composition of the oral microbiota has been studied in individuals with DS. Cuenca et al. (2021) stratified diverse periodontal conditions, encompassing 62 cases of DS-periodontal health, 34 cases of DS-gingivitis, and 28 cases of DS-periodontitis and studied the subgingival microbiota using q-PCR and culture-based techniques. *Tannerella forsythia* was the most prevalent species across all groups (67.9% in DS-periodontitis, 47.0% in DS-gingivitis, and 48.8% in DS-periodontal health), exhibiting significantly higher percentages in DS-periodontitis compared to DS-gingivitis and DS-periodontal health. Furthermore, the frequency detection, counts, and proportions of *Porphyromonas gingivalis*, *Prevotella intermedia*, *T. forsythia*, and *Eikenella corrodens* exhibited a progressive increase, correlating with the deterioration of periodontal status [17]. A systematic review included 26 studies of which 24 focused on determining the bacterial microbiota in DS-periodontitis, while 2 others delved into the oral fungal and oral viral composition [18••]. These results suggest that the oral bacterial composition may be similar between DS and non-syndromic individuals with periodontitis. Nevertheless, a study in children with DS (5.5 years old) without periodontal breakdown found that the subgingival microbiota at their deciduous teeth harbored important periodontal pathogens (*Aggregatibacter actinomycetemcomitans* and *T. forsythia*) that would suggest close monitoring and preventive measures in DS patients.

The microbiome, which consists of the diverse community of microorganisms (bacteria, viruses, fungi, and more) residing in different niches such as the mouth, plays a crucial role in maintaining oral health and has broader implications for

overall health. In the past decade, our understanding of the intestinal microbiome and its bidirectional interaction with the brain has significantly advanced. It is now recognized that the microbiota may exert influence on cognitive function, and conversely, cognitive function may impact the composition of the microbiota [19–21]. The microbiota-gut-brain axis assumes a pivotal role not only in the development of neurodegenerative diseases [22] but also in the context of DS, as alterations in the intestinal microbiome have been documented in individuals with this condition [20, 23]. A study identified a strong correlation between the prevalence of DS and the use of antibiotics, specifically tetracycline and beta-lactamase-resistant narrow-spectrum penicillin. This association was attributed to antibiotics that can act as disruptors of the human microbiome [24••]. Low diversity composition of gut microbiota has been found to be linked to cognitive impairment in DS. Furthermore, genera such as *Blautia* and *Citrobacter* demonstrated a negative correlation with cognitive scores [20]. In non-syndromic individuals, the development of the intestinal microbiota occurs postnatally through mother-child contact, facilitating the transmission of crucial species such as *Bifidobacterium* and *Bacteroides* [25]. In the case of DS patients, microbiota alterations have been identified even in the pregnant mother before birth. A pilot study indicated that pregnant women giving birth to infants with DS exhibited a distinct microbiome composition compared to the control group [23].

Willis et al. (2020) employed a comprehensive approach, utilizing 16S rRNA metabarcoding and high-throughput sequencing, along with culture and proteomics-based identification of fungi, to investigate the oral microbiome in individuals with DS in comparison to control samples. The initial observation revealed that DS individuals displayed lower salivary pH, and the microbiome exhibited reduced diversity. Specifically, individuals with DS demonstrated an elevated abundance of *Kingella*, *Gemella*, *Cardiobacterium*, *Staphylococcus*, *Rothia*, and *Actinobacillus*, coupled with a decreased abundance of *Alloprevotella*, *Atopobium*, and *Candidatus saccharimonas*. In the same study, the prevalence of fungi in individuals with DS was higher than controls (54% vs. 26%). Notably, *Candida parapsilosis* showed a significantly higher prevalence in DS (15.4% DS vs. 0.60% controls), as did *Candida dubliniensis* (15.4% DS vs. 1.51% controls), while the prevalence of *Candida albicans* was 30.8% in DS and 19% in controls [26]. In a recent case-control study [27], the salivary microbiome composition in children aged 1–13 years with DS was investigated using 16S DNA sequencing. The study found no statistically significant differences between the two groups in terms of diversity, except for a higher detection rate of *Candida albicans* in the mixed dentition of the DS group. Additionally, the DS group exhibited a high relative abundance of *Corynebacterium* and *Cardiobacterium* species with a low abundance of TM7. Furthermore, another study reported that Japanese children with DS do not exhibit red complex

microorganisms (*Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia*) and that gingival inflammation impacts the diversity of the oral microbiome [28]. In contrast, once periodontitis is established, the subgingival microbiome of individuals with DS exhibits a higher abundance of *Porphyromonas*, *Treponema*, *Tannerella*, and *Aggregatibacter*, along with a lower abundance of genera such as *Filifactor*, *Fretibacterium*, and *Desulfobulbus* indicating a microbial profile similar to that observed in non-syndromic individuals with periodontitis [29].

While emerging research suggests differences in the oral microbiome between DS and non-syndromic individuals, the link between these findings and oral diseases requires additional investigation and ultimately will be essential for developing strategies to maintain oral health and potentially mitigate risks to overall health in individuals with DS. In addition, it appears plausible that specific anatomical and metabolic aspects of DS, such as changes in saliva characteristics, obstructive sleep apnea, increased end glycation products, and hypothyroidism, may influence the oral microbiome and hence create a susceptible environment for oral infections. These exploratory findings, when taken together, provide a glimpse into the specific oral microbiota in DS and allow for a greater knowledge of the oral health trends in this population.

Susceptibility to Periodontal Diseases

It is widely acknowledged that people with DS are more prone to periodontal diseases. In the seventies, Saxén et al. (1977) reported that the prevalence of bone loss (>5mm) in DS participants was 69% as compared to 20% in controls [30]. Other investigations found that clinical periodontal attachment loss is increased in people with DS; however, the difference is only about 0.6 mm when compared to controls [31–33]. A recent systematic review with meta-analysis revealed that the probing depth resulted in a mean difference of 0.40 mm (95% CI 0.09–0.70) between DS and non-syndromic people, which appears clinically insignificant. Hence, clinical periodontal findings do not support a clear association between DS and the severity of periodontal destruction. In contrast, the systematic review concluded that gingivitis (OR 1.93; 95% CI 1.09–3.41) and periodontitis (OR 3.93; 95% CI 1.81–8.53) were more frequent in people with DS and strongly associated [34••]. Furthermore, the prevalence of periodontitis in individuals with DS also rises with age and several studies have encompassed younger individuals (<15 years old), where a higher prevalence of gingivitis was observed [35, 36]. While the severity of periodontitis does not appear to be significantly elevated in individuals with DS, the increased frequency of periodontitis does lend support to the association between these two conditions. However, it is important to take into

account factors such as variations in study designs and the utilization of partial periodontal indices, which may lead to an increased likelihood of overestimation.

Susceptibility of periodontitis has been studied from multiple perspectives. It has been recognized that inadequate oral hygiene plays a crucial role in predisposing individuals with DS to periodontitis [16, 37]. This susceptibility is attributed to factors such as cognitive disability, reduced manual dexterity, and a tendency to be uncooperative with treatment [38•, 39••]. Moreover, DS individuals often exhibit higher plaque indices compared to non-syndromic individuals, which can be exacerbated by dental abnormalities like peg-shaped teeth and dental crowding/malocclusion [40, 41]. Nevertheless, oral hygiene may be deemed satisfactory in individuals, typically children aged 10 years or younger, who receive assistance with toothbrushing from their parents or caregivers [42].

Other lines of research indicate that plaque is not the only issue and that the DS underlying systemic disorders may have a significant impact on susceptibility to periodontal diseases. Khocht et al. (2012) found that the percentage of monocytes actively involved in phagocytosis (whole blood samples) was significantly less in DS than that for controls and was associated with a slightly greater periodontal attachment loss (0.5 mm) [43]. Furthermore, studies have found increased oxidative burst activity in DS patients' peripheral monocytes, granulocytes, and saliva, which may lead to inflammation of periodontal tissues and consequent loss of periodontal attachment [44, 45].

Research involving gingival biopsies and gingival crevicular fluid (GCF) from individuals with DS who have periodontitis suggests an alteration in immunoregulation. The findings indicate a more pronounced inflammatory cell infiltrate, which almost completely occupies the connective tissue, and an increased frequency of HLA Class II expression on both inflammatory cells and keratinocytes in the oral gingival epithelium. Additionally, there is an elevated CD4⁺/CD8⁺ T lymphocyte ratio, along with higher counts of CD4 T lymphocytes and monocytes/macrophages, indicative of a more active and destructive lesion. Analysis of GCF reveals elevated concentrations of cytokines associated with Th1, Th2, and Th17 responses, as well as increased levels of matrix metalloproteinases (MMP-2, MMP-8, and MMP-9) and prostaglandin E2 [46–50]. In recent years, genotyping and bioinformatic research have unveiled significant signaling pathways, such as the phosphatidylinositol 3-kinase (PI3K-Akt) pathway, which regulates cell proliferation and the inflammatory response. This pathway has also been found to be altered in individuals with DS who have periodontitis [51, 52].

In summary, research indicates that while gingivitis and periodontitis are considerable oral complications in DS patients, the underlying mechanisms are still debatable.

However, the implementation of preventive measures, such as oral health programs for parents and caregivers, along with the early initiation of periodontal treatment and maintenance, has been shown to significantly enhance periodontal outcomes in individuals with DS [53••].

Susceptibility to Caries

Studies on the association between DS and caries have produced contrasting results. However, a recent systematic review determined that the incidence of caries in children and adolescents with DS was lower compared to control groups (49.9% vs. 63.4%) [54•]. But the certainty of this evidence is low since factors such as the type of affected dentition, caries index used, age, and geographic location significantly affect the results. Moreover, analyzed studies have low certainty of evidence and present issues such as small sample sizes, absence of a suitable control group, broad age ranges among participants, and even a deficiency in statistical analysis [54•, 55, 56]. These findings highlight the difficulty in controlling all pertinent variables that could potentially influence the results, making it challenging to draw definitive conclusions.

Possible explanations for the observed low incidence of caries in individuals with DS include the presence of diastemas, delayed tooth eruption and simpler tooth morphology, featuring fewer evident pits, and fissures. Some DS individuals also experience bruxism which smoothens the occlusal surfaces leading to enhanced self-cleaning and less biofilm retentive surfaces [57, 58]. Additionally, some studies suggest that individuals with DS exhibit elevated levels of salivary immunoglobulin A (sIgA), which inhibits the adhesion of bacteria responsible for dental caries to the tooth surface. This mechanism not only neutralizes extracellular enzymes involved in the caries process but also plays a crucial role in minimizing caries-related factors in individuals with DS [59]. In addition, research suggests that DS children exhibit reduced genotypic diversity and lower counts of *Streptococcus mutans*, resulting in decreased acidogenicity [60]. But despite the presence of observable traits seemingly associated with a lower incidence of caries, some studies imply that individuals with DS might still be more susceptible to dental caries. In terms of oral health, DS patients are thought to be at a disadvantage when compared to non-syndromic individuals. As a result, an early program of preventative measures is suggested that focuses on dental cleanliness, anti-plaque agents, and oral hygiene instructions not only for DS patients but also that include parents and caregivers [61].

The literature highlights that caries is a multifactorial disease that can be influenced by socioeconomic disparities. Therefore, considering these variables is crucial when comparing DS individuals with non-syndromic individuals. Differences in diet and oral hygiene standards among these

groups can also contribute to variations in caries experiences [62]. The significance of oral hygiene appears to be pivotal in preventing dental caries in children with DS. An increase in disease experience is observed in the DS group when brushing occurs less than twice a day. This suggests that home care and health behaviors play a crucial role in determining disease experience [58]. Although the pooled evidence suggests a lower caries incidence in DS individuals, this finding should not undermine the importance of preventive oral health programs for special care patients and caregivers.

Oral Function in Down Syndrome

It is crucial to emphasize the scarcity of scientific literature dedicated to the study of oral complications in adults with DS and to avoid generalizing findings obtained from adolescent and pediatric populations [63]. Recognized risks include the heightened likelihood of developing multiple clinical comorbidities that necessitate continuous medical care, such as congenital heart disease, thyroid dysfunction, obstructive sleep apnea, dysphagia, chronic respiratory infections, and gastroesophageal reflux disease [16, 63]. Moreover, specific anatomical characteristics of DS can complicate optimal oral function [64]. For instance, an ogival palate coupled with reduced mandibular development may contribute to lingual protrusion and macroglossia, impede lip occlusion, and elevate the risk of anterior open bite and swallowing problems. Labial and lingual hypotonia, hindering proper sucking, saliva, and food bolus management, has also been reported [63]. Dental agenesis, supernumerary teeth, delayed dentition eruption, bruxism, and type III malocclusion are common dentition features; labial and tongue fissures may lead to secondary oral infections; all these features may directly affect healthy oral function in DS individuals [64•, 65].

A protruding tongue can lead to issues with speech and oral function, potentially moving posteriorly into the pharynx (glossoptosis), thereby contributing to obstructive sleep apnea. The repercussions of sleep disruption caused by sleep apnea are highly significant, particularly in terms of neurocognitive and cardiovascular effects. This, in turn, can result in a diminished life expectancy and quality of life within this population [66]. Early interventions in the oral cavity that influence jaw growth and tongue position may play a crucial role in mitigating the severity of sleep apnea.

Pharyngeal hypotonicity, where weakened muscle strength increases the risk of aspiration before and after swallowing, even leading to death by choking, is a significant concern [63]. Altered sensory perception causing intolerance to certain foods is also reported in DS individuals. These orofacial alterations may generate feeding and swallowing difficulties due to intermaxillary discrepancy hindering the stabilization of the mandible and hyoid bone, as well as poor control and

mobilization of the food bolus [63], which can lead to serious health problems, favoring constipation, dysfunctional eating habits, obesity, and adversely impacting the quality of life.

These findings underscore the necessity to implement targeted educational and awareness programs, along with specific intervention protocols, for the younger generations of individuals with DS, their families, and caregivers. Emphasizing the significance of early interventions to maintain oral health is crucial, given that disease manifest in childhood and persist throughout life. These interventions should aim to compensate for difficulties in oral functions to the extent permitted by the anatomical characteristics unique to individuals with DS. Practical guidance for oral care, both for individuals with DS and their caregivers, is available in the recommendations provided by The National Institute of Dental and Craniofacial Research. (<https://www.nidcr.nih.gov/sites/default/files/2017-09/practical-oral-care-down-syndrome.pdf>; <https://www.nidcr.nih.gov/sites/default/files/2017-09/dental-care-every-day-caregiver.pdf>).

Conclusions

Although trisomy 21 itself does not determine a specific cause of oral diseases in Down syndrome, common oral health conditions such as gingivitis, periodontitis, and caries remain a matter of concern. The nexus between insufficient plaque control, distinctive oral characteristics, and reluctance to engage in treatment persists as noteworthy determinants. This underscores the necessity for oral health professionals to exercise patience and commitment when addressing oral care for individuals with Down syndrome.

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