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Research Paper

Oral Microbiome: Development, Composition and Diseases

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ABSTRACT

The mouth cavity protects around 700 types of microorganisms. It harbors bacteria, fungus, viruses, and protozoa. Microbes colonize the teeth and oral mucosa of the mouth, creating a complex ecosystem. The oral microbiota begins digestion and maintains oral and systemic health. Untreated dental caries is the most frequent illness worldwide, while simple periodontitis is the sixth. Bacteria from the mouth are increasingly linked to systemic illnesses. Poor oral hygiene, dental operations, periodontitis, and improper tooth brushing can induce bacteremia, which can lead to infective endocarditis. Systemic disorders and therapies can reduce salivary flow and disrupt the oral flora, impacting dental health. Dental and medical researchers are beginning to exchange knowledge about human disease's etiology and pathogenicity and the makeup and metabolic activities of the oral microbiome.

HIGHLIGHTS

- The oral microbiota is an active and complex ecology.
- A core microbiome and a variable microbiome exist in humans.
- Oral Cavity harbours multiple microbial niches which are affected by environmental factors such as pH, oxygen levels, and nutrition availability.
- Researchers have shared their findings on the oral microbiome's role in the aetiology and pathogenesis of human illness.
- Metagenomic studies can lead to the advancement of therapeutic and diagnostic procedures, as well as create personalized dental medicine.

Keywords: Microbiomes, Oral diseases, Virome, Mycobiome

Microbiomes, microbiota, and microflora are all names for groups of microorganisms that live in our bodies. Joshua Lederberg came up with the word "microbiomes" to describe the biological community of helpful, harmful, and neutral microbes (Kilian *et al.* 2016). Scotti *et al.* (2017) found that the number of germs in our bodies is almost the same as or even higher than the number of cells. Gao *et al.* (2018) found that people have oral microbiomes in their mouths. Antony van Leeuwenhoek, a Dutchman, was the first to find out about the mouth microbiome. In 1674, he saw plaque on his own teeth and said it looked like "little living animalcules moving in a pretty way" (Patil *et al.* 2013). After this important discovery in the 1800s, biochemical subtyping, which is based on the growth of functional and cultivable microbes (Hiergeist *et al.* 2015), was developed as a culture-based method for identifying bacteria. After the 1980s, new technology came out that made it possible to get more than a trillion strings of genetic information (Ha and Devkota, 2020). Precision medicine is based on the human genome and the genomes of the bacteria, viruses, and fungi that reside in the human body (Carrasco-Ramiro *et al.* 2017). Human Microbiome Project (HMP) started in 2007 as a continuation of the Human Genome Project (HGP) with the intention of establishing 3000

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reference genomes from the oral, gastric, intestinal, urinary, and cutaneous tracts. It is the second-biggest collection of microorganisms in the body after the gut. The human core microbiome is made up of many different types of bacteria. Everyone has the same basic microbiome, but everyone's microbiome is different and can be changed based on how they live and how their bodies work. Two of the sites in your mouth where germs may survive are the hard and soft enamel of the teeth, as well as the oral mucosa (Zaura *et al.* 2014). Dewhirst *et al.* (2010) say that microbes can grow well in the hard and soft palates, lips, gingival sulcus, teeth, tongue, and cheeks. Microorganisms might be able to grow well in the mouth region and the connected nasopharyngeal areas. The average temperature of the mouth cavity is 37°C if nothing important changes and this gives bacteria a safe place to live. Also, the pH of saliva stays between 6.5-7, which is just right for most types of germs to grow and survive. Lim *et al.* (2017) reported that it also helps microbes get the nutrients they need by making sure they stay moist. One of the world's most widespread ailments, dental caries, can be prevented, due to the oral microbiome's protective effects (Petersen, 2003). Dental caries are caused by acid-forming bacteria, a carbohydrate source, and the sensitivity of the host. This leads to bacterial dysbiosis and the loss of minerals in tooth tissues (Lif Holgerson *et al.* 2015). *Streptococcus mutants*, which are a type of acid-tolerant bacteria, are thought to be a major cause of tooth caries. Mouth germs have been linked to a number of systemic diseases, like aspiration pneumonia and heart disease, as well as a number of mouth diseases, like alveolar osteitis, tonsillitis, and osteomyelitis (Aas *et al.* 2005; Duran-Pinedo *et al.* 2015).

Development of the Oral Microbiome in Infants

Microbial colonization of the mouth is not something that is typically thought to happen until after birth. The oral microbiota of a newborn might be affected by whether they were born vaginally or by caesarean section. When a mother gives birth vaginally, her baby will pick up germs from the vaginal microbiota, whereas a baby born through a caesarean would pick up bacteria from the skin and the hospital. Infants can get germs from their mothers' oral microbiomes. The development of the human microbiome prior to birth has, however, recently become the subject of intensive study. *Streptococcus*, *Fusobacterium*, *Neisseria*, *Prevotella*, and *Porphyromonas* are just some of the oral microorganisms that have been discovered in human placentas, and they are present in the amniotic fluid of up to 70% of pregnant women. (Aagaard *et al.* 2014; Bearfield *et al.* 2002). Gomez-Arango *et al.* examined the placental microbiome's possible origin by sequencing 16S rRNA from the microbiomes of the pregnant woman's stomach, mouth, and placenta. *Prevotella*, *Streptococcus* and *Veillonella* are three prevalent taxa that were discovered in all gastrointestinal, oral, and placental samples (Gomez-Arango *et al.* 2014).

Oral bacteria from the mother's saliva and skin may affect the infant's oral microbiome, especially during nursing. Breastfeeding and formula feeding have both been found to affect the composition of an infant's oral microbiota. Beneficial bacteria, such as *Lactobacilli* and *Bifidobacteria*, can flourish in the oral cavity due to the prebiotics and probiotics that exist in breast milk. The oral microbiota goes through further transformations when a newborn first begins to consume solid meals, which normally occurs around the age of 6 months. The beginning of oral hygiene practises in newborns, such as cleaning their teeth with a toothbrush, also has an effect on the formation of the oral microbiome. Siblings, pets, and the family environment might affect newborns' oral microbiomes. Under the effect of the newborn's contact routes and immunological tolerance, the newborn is exposed to a range of microorganisms during and after birth, including bacteria, fungi, parasites, and viruses (Gomez-Arango *et al.* 2008). Microorganisms establish colonies inside the mouth cavity in a temporal and geographical sequence, and only a tiny percentage of them become permanent inhabitants (Palme *et al.* 2008). Early colonizers, including streptococci and actinomycetes, have the ability to stick on particular molecules that exist in the enamel pellicle, and now these early colonizers serve as attachment sites for other microbes, such as *Fusobacteria*, *Veillonella* and *Rothia* (Whittaker *et al.* 1996). Early colonisers seem to have an influence on later colonisers, which results in ecosystems that are more complex and stable as adults (Gronlund *et al.* 1999). It's crucial to keep in mind that every

infant's unique microbial profile is the result of a complex interplay between genetic predispositions, immunological responses, and oral hygiene practices. Understanding the dynamics of the oral microbiome in newborns and its development variables is vital for designing treatments and strategies to promote a healthy oral microbiome and avoid dental illnesses from an early age.

Composition and Diversity of the Infant Oral Microbiome

A newborn's oral microbiota evolves dramatically in the first several years. Genetics, delivery method, eating habits, oral cleanliness, and environmental exposures are only a few of the variables that might affect the composition and growth of the oral microbiome. Both a core microbiome and a variable microbiome exist in humans. The term "core microbiome" refers to the major species present in numerous sites throughout the body in a healthy state. Each person has a unique microbiome that has evolved in response to the way they live (Benn *et al.* 2017). The oral cavity's microbial ecology provides a unique habitat for the colonization of bacteria due to its high level of complexity and diversity, as well as its many different niches. This environment is ideal for bacterial growth. Gingival sulcus, tongue, cheek, hard and soft palates, floor of mouth, throat, saliva, and teeth are all examples that comprise these niches (Dewhirst *et al.* 2010; Zarco *et al.* 2010). Distinct regions in the mouth are colonized by oral bacteria because they have distinct adhesins on their surface that connect to corresponding receptors on an oral surface (Aas *et al.* 2005).

Key microbial taxa reported to be present in the oral microbiome of infants include *Streptococcus* sp., *Veillonella* sp., *Actinomyces* sp., *Neisseria* sp., *Rothia* sp., *Candida* sp., etc. Nevertheless, studies on a normal microbiome have only been conducted on the bacteriome, and research on the mycobiome, which is a microbiome connected to fungi, is quite limited (Zaura *et al.* 2014). Besides bacteria, the oral microbiome comprises fungi, archaea, viruses, the newly discovered potential group of ultra-small bacteria, and protozoa (Baker *et al.* 2017). According to McLean (2014), the total number of genomes that may be found in the mouth cavity is close to 1500. Oral micobiome has approximately 700 known prokaryote species, and about 54% of these species are well characterized, 14% are unnamed but culturable, and 32% are solely recognized as uncultivated species (Zhao *et al.* 2017).

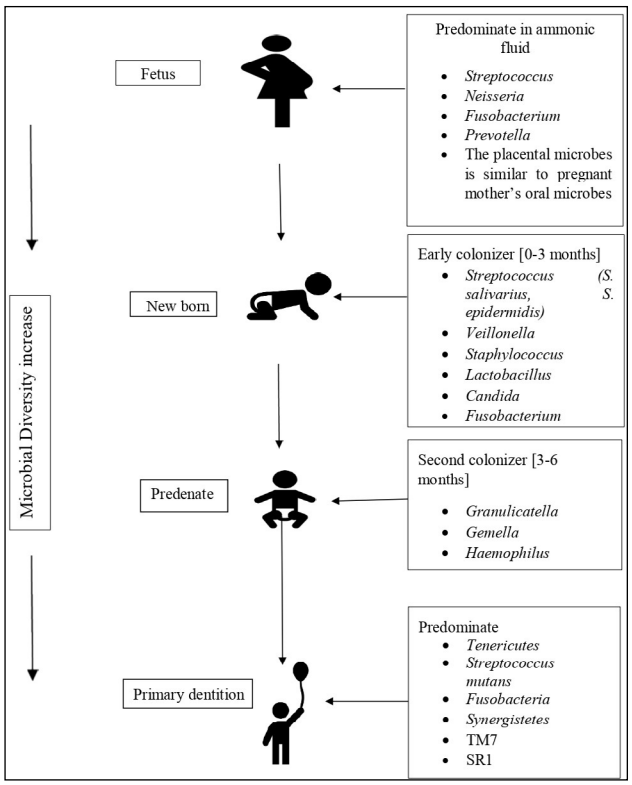

Fig. 1: Early childhood oral microbiota formation

The makeup and function of the oral microbiome may change dramatically and rapidly as the host evolves. The introduction of solid meals into an infant's diet leads to an increase in the diversity of gut microbes, particularly those responsible for breaking down complex carbohydrates (Fig. 1). It is necessary to do more study in order to get a more in-depth understanding of the microbial interactions and the functional functions of particular taxa in the oral microbiome of infants.

Oral Cavity Harboring Multiple Microbial Niches

One of the most studied microbiomes currently known is the microbiome of the oral cavity is home to 392 unique species. The different types and distributions of microorganisms in the oral cavity are affected by environmental factors such as pH, oxygen levels, and nutrition availability, which vary from one microbial niche to another. The main microbial niches within the oral cavity consist of the tongue surface, saliva, teeth surface, oral mucosa,

tonsils, gingival sulcus, periodontal pockets, cheeks, etc. These microbial niches offer a wide variety of environments in which bacteria can flourish and interact with both their hosts and other microbes. Local variables in the oral ecosystem like bacterial adhesion, surface shape, and availability or non-availability of oxygen and nutrients make up the microbiota, and this is also reflected in the presence of different microbial communities in the region (the tongue, buccal mucosa, supragingival plaque, and subgingival plaque) inside the mouth (Xu *et al.* 2015; Ren *et al.* 2017; Mason *et al.* 2018). Papillae and crypts on the dorsum of the tongue provide an ideal environment for obligate anaerobes, and the eruption of teeth provides non-shedding surface for supra- and subgingival plaque buildup which further increase microbial community buildup (Xu *et al.* 2015). In the mouth, bacteria can coaggregate with other bacteria and even cling to the teeth and oral mucosa.

Researchers haven't figured out what the mucin-rich layer that covers the mucosal surfaces of the mouth canal does and if this layer protects the mucosal health and may encourage or prevent microbial invasion of the mucosal surfaces. Secretory IgA, a salivary antibody, is abundant in the mucosal pellicle and inhibits bacterial adhesion to surfaces. IgA1 is the predominant secretory IgA subtype in saliva, while IgA2 is present in human milk. At its hinge region, the IgA1 chain is protected from enzymes that break down proteins. Some oral commensals as well as a few pathogens, such as *Streptococcus oralis*, *Prevotella* species, *Capnocytophaga* species, and *Neisseria meningitidis*, produce highly specific IgA1 proteases that can cleave IgA1 in the hinge region, thus neutralising the inhibitory impact of secretory IgA on their bacterial adherence. As a result, these organisms can now colonise the mucosal pellicle (Kilian *et al*. 1996). Saliva transports bacteria around the mouth and also possesses adherence-promoting components; on the contrary, it also has IgA, which inhibits bacteria from sticking and prevents bacterial colonisation. Only a few studies have examined the microbial makeup of neonates' different oral environments due to limitations such as small sample sizes, focusing on specific bacteria, or a lack of longitudinal data. Since saliva and plaque samples do not reveal all genotypes of *S. mutans* and *S. sobrinus*, preliminary findings demonstrate that saliva and plaque are not representative of the oral ecosystem.

Oral Bacterial community

The collection of bacteria that live in the mouth cavity is referred to as the oral bacterial community or the oral microbiota. This community is home to hundreds of distinct kinds of bacteria, attesting to its extraordinarily rich diversity. *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, *Actinobacteria*, and *Fusobacteria* are few of the most common bacterial phyla found in the oral microbiota. Both beneficial as well as pathogenic bacteria inhabit oral cavity. Microbial pioneers begin colonising and establishing in the mouth cavity as soon as the newborn gets exposure to the outside world via breathing, eating, and contact with carers. Before the eruption of teeth, bacteria mostly colonize mucosal surfaces. Early colonizers in the mouth cavity include a wide variety of bacteria, but the most prevalent are *Streptococcus* sp. (*Streptococcus epidermidis and Streptococcus salivarus*), *Staphylococcus*, and *Fusobacterium* (Human Microbiome Project, 2012; Dzidic *et al.* 2018). Due to *Streptococcus* sp.'s ability to cling to epithelial cells and the fact that these species are one of the predominant bacterial groups in human breast milk, there is a significant concentration of this bacterium in the early oral cavity. The most prevalent *Streptococcus* species in a newborn's oral cavity is *Streptococcus salivarius* (Human Microbiome Project, 2012) and it makes up between 10% to 15% of all *Streptococcus* species when it spreads its peak abundance at 3 months of age. In line with the eruption of teeth, *S. salivarius* richness gradually declines and peaks at 3 months of age (Hegde *et al.* 1998).

In the first few months of the life of a newborn, bacteria such as *Escherichia coli*, *Pseudomonas*, *Staphylococcus*, and the *Lactobacilli gasseri, Lactobacillus crispatus*, and *Streptococcus* spp. are commonly found in the mouth (Nelson-Filho *et al.* 2013; Gomez *et al.* 2017; Cephas *et al.* 2011). New binding sites are created with tooth eruption; however there are also ecological alterations to the oral environment. The persistence of *Streptococcus mutans* on its preferred attachment surface teeth hastens colonization during this stage. At the finish of the first year of life, the oral microbial community was dominated by *Fusobacteria*, *Synergistetes*, and *Tenericutes.* Human

Microbiome Project (2012) found that *Streptococcus* and *Veillonella* were the two most common genera in children's saliva, whereas Veillonella, *Streptococcus*, *Actinomyces*, *Selenomonas*, and *Leptotrichia* were the most common genera in plaque.

Oral Mycobiomes

The fungus community found in the mouth is called the oral mycobiome. Research into the oral microbiome has typically focused on bacteria, but newer studies have shed light on the existence and potential significance of fungi in the oral ecology. Ascomycota along with Basidiomycota fungi both dominate the oral mycobiome. The most common oral fungi include *Candida* sp. and other species like *Saccharomyces*, *Cladosporium*, *Aspergillus* and *Cryptococcus*. Oral mycobiome fungus can create biofilms that can coexist alongside bacterial biofilms, creating complicated oral microbial interactions. Oral candidiasis can result from fungus biofilms. Oral *Candida* was more common among children born vaginally to women who were already colonized with the yeast than in those born through Caesarean section or vaginally to mothers who were not yet colonized (Al-Rusan *et al.* 2017). The rate of oral *Candida* colonization fluctuates throughout the first year according to the research's population and methods of detection, with rates of detection ranging from 40% to 82% (Kleinegger *et al.* 1996; Darwazeh, 1995; Scully *et al.* 1994). Despite being opportunistic, *Candida* was the sole fungus acknowledged for a very long time as a component of the typical oral microbial population. A metagenomic analysis of healthy human mouths revealed the presence of 74 cultivable fungal species and 11 uncultivable fungal genera. Despite the fact that 75% of the participants had isolates of the fungus Candida, other fungal groups, like *Cladosporium* (65%), *Aureobasidium* (50%), *Saccharomycetales* (50%), *Aspergillus* (35%), *Fusarium* (30%), and *Cryptococcus* (20%), were also present (Ghannoum *et al.* 2010). On the basis of a traditional culture method, it has been discovered that *Candida albicans* and *C. parapsilosis* are the *Candida* species that are most commonly found in newborns and older children (Amadio and Hahn 2011).

Oral Viromes

The word "virome" is used to describe the possible set of viruses, including both prokaryotic and eukaryotic ones, that are found in or on a human body. The oral virome is a collection of viruses existing in the oral cavity. Recent studies have begun to identify the variety and possible influence of viruses in the oral ecosystem, which previously had been largely overlooked in the oral microbiome research community. Any given person's mouth cavity contains 300–2000 different virus genotypes (Pride *et al.* 2012). Rotavirus, norovirus, HIV, hepatitis C, HSV1 and HSV2, influenza viruses and Epstein-Barr virus are commonly isolated from the oral cavity (Corstjens *et al.* 2016). Although numerous viruses are capable of infecting oral mucosal cells, only a few of them cause symptoms in humans. HSV1 and HSV2 could infect newborns, which can lead to aphthous stomatitis, orofacial herpes, and herpetic gingivostomatitis (Parras-Molto *et al.* 2014; Pinninti *et al.* 2018). The incidence of herpes simplex virus (HSV) infection in newborns is low, ranging from 1.6 to 33 cases per 100,000 live births (Mahnert *et al.* 2007). Due to the weakened and immature immune systems of newborns, HSV infection can be extremely dangerous and even fatal (Kimberlin *et al.* 2001). During early life, the Coxsackie virus and other viruses have the potential to colonise the mouth. Researchers analysed the whole virome in the saliva of 21 people and found that only a small percentage were related to eukaryotic viruses (herpesviruses and circoviruses), while the vast majority were bacteriophages (Robles-Sikisaka *et al.* 2013). Eukaryotic DNA virus samples from 102 healthy individuals in the Human Microbiome Project showed distinct viral fingerprints at different body locations. *Roseolovirus* (97%), *lymphocryptovirus* (29%), *betapapillomavirus* (21%), *mastadenovirus* (18%), and *polyomavirus* (15%) were the most common oral eukaryotic DNA viruses (Wylie *et al.* 2014).

Oral Archaea

In the realm of microbes, archaea stand apart from both bacteria and eukaryotes. Archaea are rare in the oral microbiome. *Methanobrevibacter oralis*, *Methanosarcina mazei* and *Methanobacterium curvum* are all examples of archaea that have been found in the oral cavity. Oral archaea's interactions with other microbes, especially bacteria, are unclear. Oral archaea may compete with bacteria for resources and interact metabolically. Archaea can remain

in healthy people, although it seems to be more common in people who have periodontitis (Lepp *et al.* 2004; Matarazzo *et al.* 2011). Mouth archaea research is still in its infancy, and more research is needed to understand their quantity, distribution, interactions, and possible effects on mouth health and illness.

Oral parasites

Parasites like protozoa, helminthes, and arthropods may live in the mouth. Parasites in the oral cavity are rare, but they can affect oral health. Recent investigations have indicated that protozoa are more abundant in the mouth cavity than previously thought, and their global prevalence, however, may range anywhere from 4% to 53%, depending on geographic region. The most prevalent oral parasites are the protozoa *Entamoeba gingivalis* and *Trichomonas tenax*, which are typically commensal, non-pathogenic microbes. These protozoa can be seen in children and adolescents who lack caries, despite their oral colonization being linked to poor dental hygiene and low socioeconomic position. The protozoa colonize at a higher pace in children between the ages of 11 and 19 than in younger children as they get older. Protozoa, however, are significantly more common in adults, especially in those who have periodontal disease. Periodontal pockets and tooth plaque harbour *Trichomonas tenax*, which causes bad breath and gum problems. Though both protozoa may coexist, *E. gingivalis* colonises faster than *T. tenax* with age. (Ghabanchi *et al.* 2010; Dahlén, 2009; Vrablic *et al.* 1991). Helminths such as *Ascaris lumbricoides* (roundworm) and *Enterobius vermicularis* (pinworm) can move to the mouth, producing coughing, throat discomfort, and oral blockage. *Pediculus humanus capitis* and *Sarcoptes scabiei* are two arthopods that can cause problems in the mouth, especially in newborns and toddlers.

Functional Roles of Oral Microorganisms

Bacteria in the mouth help initiate digestion by converting complex carbohydrates into more easily absorbed sugars. They aid in digestion by producing enzymes like amylase, which break down carbohydrates in meals. Microbial communities in the human body play crucial roles in digestion, energy production, mucosal and immune system development, fat and calorie storage and management, metabolic control, and the elimination of harmful substances from the body (Kilian *et al.* 2016). Plaque on teeth is caused by bacteria in the mouth, and this biofilm protects microorganisms and harbours diseases. Microbiota physiology and ecology have a close connection to host physiology and ecology. The microbiome has an important influence on how a disease grows or is promoted (Mark *et al.* 2016). Oral bacteria can convert salivary nitrates into nitrites, and these nitrites are further converted into nitric oxide (NO) inside the stomach. Nitric oxide possesses antibacterial activity and blood flow-regulating effects. Commensal oral bacteria compete for nutrition and produce antimicrobials to prevent pathogen development. Microbial antagonism keeps dental health and dangerous germs in check. Commensal bacteria may increase the effectiveness of immunotherapy with checkpoint inhibitors. Tumour growth was suppressed by *Bifidobacterium* treatment in a manner comparable to that of PD-L1-specific antibody therapy. When PD-L1-specific antibody therapy was combined with oral *Bifidobacterium* administration, tumour development was significantly slowed (Sivan *et al.* 2015). Bacteriocins produced by *Streptococcus dentisani* conceal the production of bacteria that are responsible for caries. (Lo´pez *et al.* 2017). *S. mutans* and *S. salivarius* produce antimicrobial peptides as well as bacteriocins, which kill other bacteria in the mouth (Sintim and Gursoy, 2016). *Streptococcus mutans* inside the mouth can ferment carbohydrates from food into acids and further dissolve the protective layer of enamel on your teeth, causing cavities.s

Human Oral Microbiome Database (HOMD)

In-depth information on the microorganisms that reside in people's mouths may be found in the Human Oral Microbiome Database (HOMD). The HOMD promotes research into oral microbiology and wellness as well as disease. Academics, doctors, and students will use a single oral microbiota resource. The database describes the mouth's microbial community's taxonomy, genetic sequences, metabolic pathways, and more. Compare data from healthy people and those with oral problems to study oral conditions. HMP's (Human Microbiomes Project) primary goal was to generate 1000 microbial reference genomes;

around 300 of them were from oral microorganisms. The HOMD is the first public database dedicated solely to the oral cavity, providing researchers with extensive information on multiple species of the oral microbiome (Peterson *et al.* 2009). The HOMD database and web-based interface were developed by the National Institute of Dental and Craniofacial Research's Foundation for the Oral Microbiome and Metagenome and are structured according to taxonomic classifications established from 16S rRNA sequencing data (Chen *et al.* 2010; Dewhirst *et al.* 2010). The specified oral species and taxa that were identified using 16S rRNA sequencing were placed in their appropriate and individual human oral taxon (HOT) numbers that were assigned to them. The genetic, bibliographic, clinical, and phenotypic data of each taxon are all linked by the HOT.

Common Diseases Associated with Oral Microbiome

The healthy tooth microbiome is a biofilm community that produces ammonia from arginine or urea to balance acid production from carbohydrate ingestion. A biofilm can develop dysbiosis, which is characterized by a change in the composition of the bacteria, when the consumption of carbohydrates in an excessive and regular basis surpasses the buffering capacity of a healthy microbiome. Host structures, microbiological characteristics, and environmental processes are the three basic factors that contribute to the development of the disease. Microbiology variables consist of dental plaque acidogenicity, pH buffering bacteria, and infectious microbes; host structural factors involve the immune system, genetics that predispose enamel structure, and salivary composition and buffering effect; and environmental mechanisms include dietary sugars, fluoride, oral hygiene habits, and personal factors influenced by socioeconomic status and lifestyle choices. People of all ages and in all parts of the world are susceptible to developing dental caries and periodontal disease. Thus, understanding the causes of sickness would enable innovative treatments and prevention.

Gingivitis and Periodontal disease

Inflammatory conditions of the gums (gingiva) and the bone and periodontal ligament that support the teeth comprise a category known as periodontal disease. Periodontitis causes gum inflammation and infection, destroying the periodontal ligament and bone that hold together the teeth. Loose teeth, foul breath, and bite abnormalities are common symptoms of periodontitis, and if untreated, they might cause tooth loss. On the other hand, gingival health describes the condition of the gums when they are devoid of inflammation and disease. Gingivitis is characterized by the development of red, swollen, and bleeding gums. Poor oral hygiene and other factors like genetic susceptibility, smoking, hormonal changes, drugs, and systemic disorders like diabetes can cause periodontitis. The development of subgingival plaque, which alters the microbiome, is another contributor to periodontal disease. *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Tannerella forsythia*, *Eikenella corredens*, and *Treponema denticola* are the primary pathogens that are responsible for periodontitis. Regular dental cleanings and better at-home oral hygiene are typically sufficient to treat gingivitis and bring it under control. Periodontitis may require antibiotics, periodontal surgery, or scaling and root planing (deep cleaning). The severity of periodontitis, the intricacy of antimicrobial treatment, and the lack of information regarding microbial linkages make it difficult to treat. Once pockets form, periodontitis is irreversible. Antibiotics cannot reach disease-causing bacteria in pockets. In addition, periodontal infections might develop resistance to treatment when they adopt virulent characteristics, including encapsulation. Plaque-hiding infections are 1,000 times more resistant to antimicrobials than airborne pathogens. Even if pathogens are targeted, oral mucous membranes contain bacterial reserves that can recolonize treated regions.

Dental Caries

Tooth decay, often known as dental caries, affects a large percentage of the global population. Demineralization by acid-producing bacteria, especially *Streptococcus mutans*, leads to localised loss of the tooth's hard tissues like enamel, dentin, and cementum. Oral discomfort and tooth loss are its main effects. As supragingival biofilm builds up on teeth, colonies of bacteria that produce acid proliferate and contribute to the formation of plaque. These sneaky infections ferment dietary

carbohydrates, producing acidic chemicals that destroy tooth enamel or roots. Low pH helps disperse calcium, phosphate, and carbonate from teeth, which protect enamel against pathogens. Although a distinct microbiome that suggests dental caries has not yet been established, *S. mutans*, *Streptococcus sobrinus*, and *Lactobacillus acidophilus* are the most prevalent bacteria that cause dental caries (Table 1). Brushing and flossing twice a day with fluoride toothpaste removes plaque and germs and builds tooth enamel. Oral cleanliness, a healthy diet, and fluoride can prevent dental cavities.

Table 1: Main microbial species associated with dental caries in early childhood

Genus	Early Childhood Caries
Firmicutes	
Granulicatella	*G. elegans*
Streptococcus	*S. mutans*
	S. gordonii
	S. sobrinus
	S. cristatus
	S. parasanguinis
	S. salivarius
	S. intermedius
Lactobacillus	*L. oris*
	L. paracasei
	L. salivarius
Pseudoramibacter	*P. alactolyticus*
Veillonella	*V. atypica*
	V. parvula
Dialister	*D. invisus*
Enterococcus	*E. faecalis*
Bacteroidetes	
Prevotella	*Prevotella sp.*
Actinomyces	
Actinobacteria	*A. gerencseriae*
	A. israelii
Bifidobacterium	*B. dentium*
Propionibacterium	*Propionebacterium FMAS*
Scardovia	*S. wiggsiae*

Oral Cancer

Oral cancer affects about 300,000 individuals annually worldwide, making it the sixth most frequent disease in the world. Lips, tongue, gums, inner lining of cheeks, roof or floor of mouth, and throat are all potential sites for oral cancer due to the wide variety of cells that line these areas. Tobacco and alcohol use, human papillomavirus types 16 and 18, excessive sun exposure without protection, and poor dental hygiene are all common risk factors for oral cancer. Researchers are working on finding out if oral cancer and the activity of the oral microbiota have some sort of relationship with one another. Oral bacterial cells have been shown to influence mouth cancer-causing and cancer-promoting signalling pathways, according to research conducted at the Gill Lab at the University of Rochester Medical Centre. Oral cancer can be diagnosed with a biopsy, and its stage or location may be assessed using other imaging tests such X-rays, CT scans, MRIs, and PET scans. Oral cancer treatment may involve one or more of the following treatments like surgery; radiation therapy; chemotherapy; targeted therapy; or a combination of these methods. Several species of pathogenic oral microbes have a predisposition to increase salivary levels of carcinogenic acetaldehyde by metabolising ethanol and cigarette smoke. Saliva can absorb carcinogenic chemicals, putting the oral cavity at risk of mutation via DNA damage. When the oral mucosa becomes inflamed due to exposure to toxins, pathogenic agents are released to aid in the formation of tumors (Teles *et al.* 2020).

Oral Microbiome Related with General Diseases

The oral microbiome has been linked to a wide range of systemic illnesses and disorders, and this is further supported by research findings. Imbalances in the oral community can lead to the onset or worsening of systemic disorders. The oral microbiome has been related to a variety of general disorders, including cardiovascular disease, diabetes, respiratory infections, rheumatoid arthritis, premature birth, and low birth weight in newborns (Matsha *et al.* 2020; Beck *et al.* 2005; Gomes-Filho *et al.* 2010). Chronic inflammatory periodontal diseases, one of the most frequent chronic infections, may cause cardiovascular disease such atherosclerosis, myocardial infarction, and stroke. Bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycoplasma pneumoniae* colonise the oropharynx and cause community-acquired pneumonia. An opportunistic bacteria that has been linked to endocarditis is *Streptococcus gordonii*, which was one of the first organisms to

colonise the oral environment (Boonanantanasarn *et al*. 2011). Diabetes and periodontal disease are tightly connected with each other. The periodontal disease microorganism *Porphyromonas gingivalis* produces a lipopolysaccharide (LPS) that damages insulin-regulating cytokine proteins and even compromises blood sugar regulation. Cavities, thrush, fungus recurrence, burning mouth syndrome, and malfunctioning salivary glands are all oral complications that can arise from diabetes.

CONCLUSION

The development of a beneficial host-microbiota connection depends heavily on the host's ability to acquire and maintain a balanced microbiota. Understanding the importance of the oral microbiota emphasises the need for frequent brushing, flossing, and dental checkups to keep oral disease away. Teeth eruption, dental hygiene, sugar consumption, antibiotic exposure, maternal smoking, and carer oral health impact baby and child oral microbiome development. Longitudinal research on different oral niches is needed since newborns' oral cavities have been less sampled than adults'. Research that will be done in the future on the microbiome and the metagenome is certain to lead to the advancement of therapeutic and diagnostic procedures, including the creation of personalized medicine and personalized dental medicine.

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