Review Article

Insights to Oral Microbiome from Birth to Infancy

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Abstract

Oral microbiome is the microbial residents found in the human oral cavity. Multiple microorganisms colonize the oral cavity and are distinctive to this niche as they have an excruciating specificity for oral colonization. Facultative anaerobes are the primary colonizers of oral surfaces. Greater microflora species diversity is present in toddlers at 18–24 months of age than at 12 months of age. The imbalance in the microbial flora can lead to oral diseases in children. Poor oral hygiene and diet have a catalytic effect in the progression of early childhood caries. To prevent the occurrence of infections caused by microorganisms in newborns, infants, and toddlers, strict hygiene measures should be adopted by the mother and the caregivers.

Keywords: Early childhood caries, microflora, oral microbiome

Introduction

Oral microbiome, oral microbiota, or oral microflora refers to the microbial environment found in the human oral cavity.[1] Joshua Lederberg, a Nobel Prize winner, introduced the term "microbiome" to describe the ecological community of symbiotic and pathogenic microorganisms. Microbiota change as the hostages, and their diversity and composition can change substantially due to the particular physiology, diet, and environmental exposure at a specific stage of host development.[2]

Facultative anaerobes such as *Streptococci* and *Actinomyces* species are the primary colonizers of oral surfaces. Multiple microorganisms colonize the oral cavity and are distinctive to this niche as they have an excruciating specificity for oral colonization. Distinct microenvironments such as the firm nonshedding surfaces of the teeth and the epithelial surfaces of the mucosal membranes in the oral cavity are excellent environmental factors for microbial colonization. For the continuation of healthy life and development of the oral cavity, resident oral microflora plays a major role and any change in its normal oral flora may lead to disease.[3]

The imbalance in the microbial flora can lead to early childhood caries (ECC) in children below the age of 6 years. It is a disease process which leads to the destruction of calcified structures of teeth. ECC is caused by multiple factors such as genetic, biochemical, socioeconomic, physical environment, and behavioral factors influencing health. The period of interaction of microorganisms with sugar present on the tooth surface plays an important role in the initiation and progression of the diseases.[4]

The diversity of the microbial flora reflects a tremendous diversity of information. Recent advance in molecular biology is broadening our understanding of bacterial diversity and interactions between species within the oral cavity. This has also helped in understanding the involvement of oral microbiome in health and disease. This review discusses about the development of oral microbiota since the birth of the child and of microbial diversity and interactions in children, especially in relation to ECC.

Microbiota in Predentate Infants

At the time of delivery, the oral cavity of human infant is considered germ-free. Immediately after delivery, the newborn is uncovered to multitude of microorganisms.[5] Bacterial

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colonization inside the oral cavity probably starts off at the primary hours or days after delivery.[6] It has been seen that 8 days after delivery, there may be vast variability in oral bacteria, and each aerobe and anaerobe may be detected inside the mouth. The Gram-positive bacterial commensal *Streptococcus salivarius* is a pioneer colonizer of the human mouth. Large populations persist at host's lifetime and this bacterial species represents as much as 98% of the overall oral microbiota to the eruption of teeth.[7]

Streptococcus (*Streptococcus epidermidis* and *S. salivarius*), *Staphylococcus* spp., and *Fusobacterium* are the most commonly discovered early colonizers in the oral cavity. The high prevalence of *Streptococcus* in the early oral cavity is due to two factors, mainly that *Streptococcus* spp. can adhere to epithelial cells, and also because of the most common bacteria present in human breast milk is *Streptococcus* spp. *S. salivarius* is also a common *Streptococcus* species discovered in the oral cavity of newborns, with the peak abundance at 3 months of age and thereafter.[8] *S. epidermidis* colonizes a newborn's oral cavity between 10 min and 8 h after birth, and its levels climbed by about 90% after 53 h of life. *Streptococcus mitis* and *Streptococcus oralis* are found in the oral cavity of newborns. Some literature claim that *Streptococcus mutans* (SM) is not found on babies' mucous membranes, while others claim that SM can be found in children as young as 2 months old and 3 months old, before tooth emergence.[7] Other bacterial species seen in the first 3 months of life are *Rothia mucilaginosa*, *Veillonella parvula* group, *Gemella haemolysans*, and *Veillonella* HB016. Between 3 and 6 months of age, the prevalence of other species expands, including members of the *Prevotella*, *Granulicatella*, and *Neisseria* genera.[9]

Infant oral cavity is also colonized by fungal species, specifically *Candida*. The other most abundant and prevalent fungal species in the newborn oral cavity are *Cladosporium velox, Cladosporium parapsilosis, Cladosporium tropicalis, Saccharomyces Cerevisiae, Cladosporium orthopsilosis, Cladosporium albicans,* and *C. tropicalis*. Viruses have also been discovered in the oral cavity, and their presence is primarily regarded as pathogenic. HSV1 and HSV2, which cause herpetic gingivostomatitis, orofacial herpes, and aphthous stomatitis, can infect newborns.

Due to the impaired and immature immune systems of newborns, HSV infection can be exceedingly serious and even fatal. The coxsackievirus is another virus that can invade the oral cavity during early development.[8] Figure 1 shows the factors associated with the development of oral microbiome in early childhood.

Changes in Microbiota during Eruption of Teeth

The eruption of primary teeth produces two additional niches for bacterial colonization: a supragingival habitat made up of a nonshedding enamel tooth surface and a subgingival habitat made up of an abiotic tooth surface, junctional epithelium, and gingival sulcus epithelial lining.[10] Oral bacterial diversity is substantially higher in the primary dentition than in the predentate stage.[11] Anaerobic niches also occur in the oral cavity during primary dentition. At 18 and 24 months, toddler's microbiota species diversity is greater than at 12 months. *Capnocytophaga*, *Neisseria*, *Streptococcus*, *Kingella*, and *Leptotrichia* were the most common species in 12 month old; at 18 and 24 months of age, *Capnocytophaga* abundance ratios continued to decline, while *Burkholderia* and *Stenotrophomonas* ratios increased, and *Enterobacteriaceae*, in particular, became a dominant genus. Despite these changes, *Streptococcus, Neisseria*, and *Leptotrichia* were consistently shown to be the leading genera in toddlers aged 12–24 months.[5]

During the teething period, the microflora colonization in a toddler's oral cavity is a dynamic and continuous process involving certain core species that remain dominant, with different species gathering and colonizing around the core species at different ages to eventually reach microbial balance through a series of complex processes such as symbiosis, competition, and inhibition. As the number of teeth erupted increased from 18 to 24 months, the proportion of Gram-negative bacilli such as *Selenomonas* and *Prevotella* decreased, but Gram-negative cocci such as *Streptococcus* and *Burkholderiales* increased. The microbial composition and structure of 24-month-old toddlers were more similar to those of 3–5 years old with deciduous dentition. In toddlers, *Streptococcus* and *Neisseria* are early and important constituents of the oral microbiota. *Actinomyces* are early colonizing microorganisms in the oral cavity that have been linked to the development of dental caries in infants and the creation of early plaques.[12] Caufield *et al*. discovered a "window of infectivity" in which babies acquired *Mutans Streptococci* (MS) from their mother hosts in 1993. This "window" began at 19 months and lasted to 31, with a mean of 26 months. The prevalence of MS increased from 0% to 82% throughout this time span. Caufield theorized that the presence of nondesquamated hard surfaces, such as newly erupted teeth, was directly related to the discontinuous nature of the first MS acquisition.[13] The age maturation of phylum *Actinobacteria* in the oral cavity may be linked to the replacement of deciduous

Table 1: Virulence factors of *Streptococcus mutans* that contribute to their cariogenicity

Property	Description
Acid production	Ability to produce organic acids, mainly lactic acid
Sugar transportation	Ability to metabolize sucrose to form insoluble polysaccharides, which helps in colonization persistence on tooth surfaces
Aciduricity	Ability to tolerate environmental stresses such as low pH, which is considered a toxic environment for other bacterial species in the mouth
IPS production	Ability to use IPS to continue producing acids in the absence of dietary sugars
EPS production	Contributes to the biofilm matrix, localizes acidic fermentation products, and consolidates cell attachment

IPS: Intracellular polysaccharide, EPS: Extracellular polysaccharide

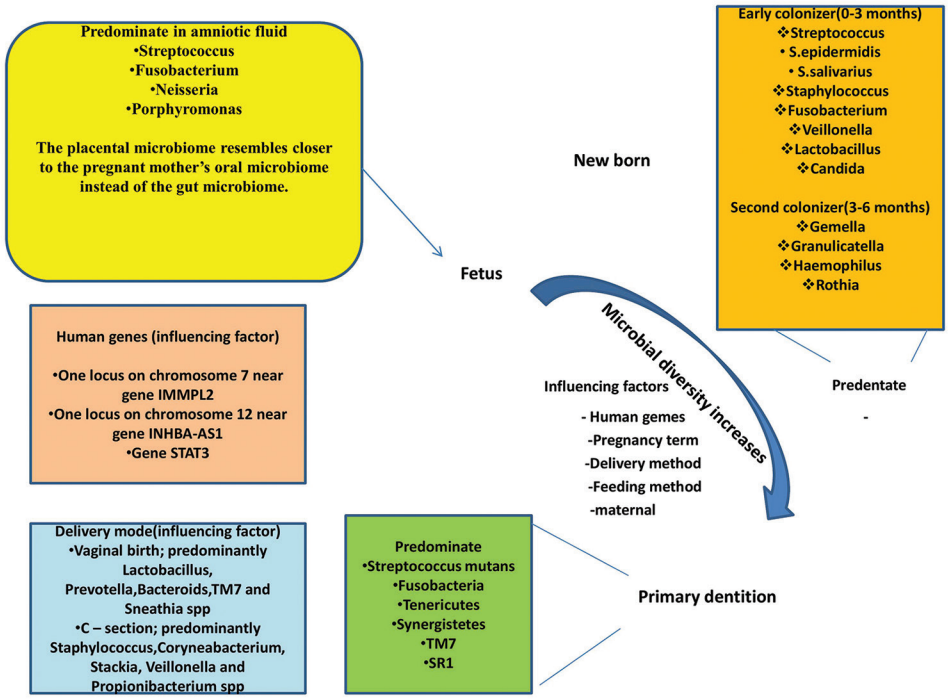

Figure 1: Factors associated with oral microbiome development in early childhood.

teeth with permanent teeth in mixed dentition.[14] Table 1 shows the virulence factors of SM that contribute to their cariogenicity.

Microbes in Early Childhood Caries

ECC affects up to 70% of children in some countries, and the oral microbiome plays a key role in many dental illnesses. The ECC is a disease that can be passed from person to person. The most well-known causative agents are SM and *Streptococcus sobrinus*. *Lactobacilli* also play a role in the course of caries but not in its initiation. According to the literature, SM can be transmitted in two ways: vertically and horizontally. Vertical transmission occurs between caregiver and child (i.e., mother or father to child), whereas neonatal variables may enhance the risk of SM acquisition in horizontal transmission. When an infant is born through cesarean section, SM is transmitted earlier than when the baby is born naturally. Between SM colonization and caries lesion onset and progression, about 13–16 months is required.[15] Other ECC contributors include *Bifidobacterium, Veillonella, Granulicatella, Scardovia, Fusobacterium, Prevotella*, and *Actinomyces*. *Scardovia* sp. has been isolated from dentinal caries in these microorganisms and has previously been linked to the progression of deep caries in severe-ECC (S-ECC). Other *Scardovia* or *Scardovia*-like species, such as *S. sobrinus*, *Streptococcus intermedius*, many *Lactobacillus* species, *Rothia dentocariosa*, and *Scardovia inopinata*, which are genetically related to *Scardovia wiggsiae*, have been linked to dental caries.[16] Gram-negative bacteria have also been found in deep dentinal caries in ECC-affected teeth, as well as deep pulpal infections in primary teeth. *Firmicutes* and *Actinobacteria* were discovered to dominate the microbiota of exposed essential pulp chambers of carious deciduous teeth.[17]

The microbial composition of the tooth surface varies depending on the location. These microorganisms produce a cariogenic biofilm by interacting with one another in a dynamic and concerted polymicrobial synergy, within which the population alters as caries progresses from early onset (initial demineralization) to deeper lesions with dentin exposure.[18] Some of the bacteria detected in the ECC plaque do not fit the traditional cariogenic profile of being acid tolerant but not acidogenic or even acid-sensitive. It is important to figure out whether they are just bystanders or actively involved in cariogenesis. For example, weak or nonacidogenic but proteolytic Gram-negative bacteria such as *Prevotella* species have been found in dental plaque of children with S-ECC and have been linked to caries advancement into the dentin, which requires proteolysis of proteins denatured by acidic species (Chalmers *et al*., 2015). *Veillonella* species, meantime, are frequently seen in S-ECC lesions and are thought to be involved in the rapid progression of lesions deep into dentine. Although *Veillonella* are not acidogenic, they use lactate produced by various acidogenic species as a carbon source, which may help cariogenic species develop and survive.[19] Major species associated with ECC are shown in Table 2.

Microbial Mitigation Measures

ECC is a serious health risk that affects a child's physical and psychological well-being. Severe caries is caused by oral microbiome dysbiosis and the establishment of a favorable

Table 2: Major species associated with early childhood caries

Phylum/genus	Early childhood caries
Firmicutes	
Streptococcus	*Streptococcus mutans*
	Streptococcus sobrinus
	Streptococcus cristatus
	Streptococcus gordonii
	Streptococcus intermedius
	Streptococcus parasanguinis
	Streptococcus salivarius
Granulicatella	*Granulicatella elegans*
Lactobacillus	*Lactobacillus fermentum*
	Lactobacillus gasseri
	Lactobacillus oris
	Lactobacillus paracasei
	Lactobacillus salivarius
Pseudoramibacter	*Pseudoramibacter alactolyticus*
Dialister	*Dialister invisus*
Enterococcus	*Enterococcus faecalis*
Veillonella	*Veillonella atypica*
	Veillonella parvula
	Veillonella sp.
Actinobacteria	
Actinomyces	*Actinomyces gerencseriae*
	Actinomyces israelii
	Actinomyces timonensis
Atopobium	*Atopobium genomo* sp. C1
Propionibacterium	*Propionebacterium* FMAS
Bifidobacterium	*Bifidobacterium dentium*
	Bifidobacterium sp.
Parascardovia	*Parascardovia denticolens*
Scardovia	*Scardovia wiggsiae*
Bacteroidetes	
Prevotella	*Prevotella* sp.

cariogenic habitat. Poor oral hygiene and generalist treatment procedures cannot completely eliminate caries-causing bacteria, which can lead to persistence and recurrence.[20] Prenatal education for expectant parents should be the first step, followed by perinatal education for the mother. ECC in infants can be reduced or delayed with proper dental therapy and oral hygiene procedures during pregnancy. Parents should also be advised to maintain good dental hygiene during the prenatal and postnatal periods. Parents and caregivers should be educated about the etiology and prevention of ECC. Nurses can also conduct out preventative activities for newborns, toddlers, and their families, as well as provide counseling and support to children with ECC. The use of probiotics in the form of chewable tablets or supplements has also been shown to help decrease caries in children. However, its ability to avoid ECC is currently being researched.[21]

Conclusion

The oral microbiome is a self-contained ecosystem that keeps health in check. Pathogens can develop and cause disease when there are specific imbalances in this state of homeostasis. The number of bacterial species found in infants' oral cavity grew over time. To avoid diseases caused by germs, the mother and nursing staff should practice strong hygiene precautions. Understanding how the oral microbiome grows and behaves throughout time in healthy and sick newborns should be the focus of research. This will help to identify children who are at the greatest risk of disease and create interventions at important moments in the disease's development and progression.

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Conflicts of interest

There are no conflicts of interest.

References

1. Deo PN, Deshmukh R. Oral microbiome: Unveiling the fundamentals. J Oral Maxillofac Pathol 2019;23:122-8.
2. Teng F, Yang F, Huang S, Bo C, Xu ZZ, Amir A, *et al.* Prediction of early childhood caries via spatial-temporal variations of oral microbiota. Cell Host Microbe 2015;18:296-306.
3. Soumya Y. A review on the human oral microflora. RRJDS 2016;4:22.
4. Ramli MZ, Azmi NS. Oral microbiome in children with caries: A systematic review. Mater Sci Forum 2020;981:271-9.
5. Dzidic M, Collado MC, Abrahamsson T, Artacho A, Stensson M, Jenmalm MC, *et al.* Oral microbiome development during childhood: An ecological succession influenced by postnatal factors and associated with tooth decay. ISME J 2018;12:2292-306.
6. Rosenblatt R, Steinberg D, Mankuta D, Zini A. Acquired oral microflora of newborns during the first 48 hours of life. J Clin Pediatr Dent 2015;39:442-6.
7. Nelson-Filho P, Borba IG, Mesquita KS, Silva RA, Queiroz AM, Silva LA. Dynamics of microbial colonization of the oral cavity in newborns. Braz Dent J 2013;24:415-9.
8. Xiao J, Fiscella KA, Gill SR. Oral microbiome: Possible harbinger for children's health. Int J Oral Sci 2020;12:12.
9. Sulyanto RM, Thompson ZA, Beall CJ, Leys EJ, Griffen AL. The predominant oral microbiota is acquired early in an organized pattern. Sci Rep 2019;9:10550.
10. Mason MR, Chambers S, Dabdoub SM, Thikkurissy S, Kumar PS. Characterizing oral microbial communities across dentition states and colonization niches. Microbiome 2018;6:67.
11. Kageyama S, Asakawa M, Takeshita T, Ihara Y, Kanno S, Hara T, *et al.* Transition of bacterial diversity and composition in tongue microbiota during the first two years of life. mSphere 2019;4:e00187-19.
12. Li F, Tao D, Feng X, Wong MC, Lu H. Establishment and development of oral microflora in 12-24 month-old toddlers monitored by high-throughput sequencing. Front Cell Infect Microbiol 2018;8:422.
13. Caufield PW, Cutter GR, Dasanayake AP. Initial acquisition of mutans streptococci by infants : Evidence for a discrete window of infectivity. J Dent Res 1993;72:37-45.
14. Shi W, Tian J, Xu H, Zhou Q, Qin M. Distinctions and associations between the microbiota of saliva and supragingival plaque of permanent and deciduous teeth. PLoS One 2018;13:e0200337.
15. Alazmah A. Early childhood caries: A review. J Contemp Dent Pract 2017;18:732-7.
16. Kressirer CA, Smith DJ, King WF, Dobeck JM, Starr JR, Tanner AC. *Scardovia wiggsiae* and its potential role as a caries pathogen. J Oral Biosci 2017;59:135-41.
17. Hurley E, Barrett MP, Kinirons M, Whelton H, Ryan CA, Stanton C, *et al.* Comparison of the salivary and dentinal microbiome of children with severe-early childhood caries to the salivary microbiome of caries-free children. BMC Oral Health 2019;19:13.
18. Lamont RJ, Koo H, Hajishengallis G. The oral microbiota: Dynamic communities and host interactions. Nat Rev Microbiol 2018;16:745-59.

19. Hajishengallis E, Parsaei Y, Klein MI, Koo H. Advances in the microbial etiology and pathogenesis of early childhood caries. Mol Oral Microbiol 2017;32:24-34.
20. Kalpana B, Prabhu P, Bhat AH, Senthilkumar A, Arun RP, Asokan S, *et al.* Bacterial diversity and functional analysis of severe early childhood caries and recurrence in India. Sci Rep 2020;10:21248.
21. Anil S, Anand PS. Early childhood caries: Prevalence, risk factors, and prevention. Front Pediatr 2017;5:157.