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UNDERSTANDING THE IMPACT OF EARLY CHILDHOOD CARIES ON SIGNATURE ORAL MICROBIOME: INSIGHTS FROM ASIAN COHORTS

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ABSTRACT

Early Childhood Caries remains a major public health concern across Asia, influenced by complex interactions between host factors, behaviors, and the oral microbiome. This review synthesizes current research on the diversity of the oral microbiome in healthy and ECC patients among eight Asian countries, highlighting distinct regional microbial patterns and their associations with caries status. Evidence suggests, ECC is consistently linked to microbial dysbiosis, with elevated levels of acidogenic and aciduric taxa such as *Streptococcus mutans*, *Lactobacillus*, and *Candida albicans*. These three species are the most dominant species among ECC cases across Southeast Asia (India, Thailand, Indonesia) and East Asia (China, Japan). Despite these commonalities, healthy oral microbiota shows striking regional variation: *Neisseria* is abundant in Japan and Korea, *Prevotella* in Thailand, *Granulicatella* in Malaysia, *Proteobacteria* in Myanmar, and *Gracillibacteria_GN02* in India. These findings highlight that geographic, dietary, and cultural differences contribute to population-specific microbial profiles. Notably, maternal oral health, mode of delivery, and early feeding practices significantly shape the infant oral microbiome. Understanding

these dynamics offers new opportunities for microbiome-informed diagnostics, risk prediction, and personalized interventions tailored to the diverse sociocultural contexts of Asia.

Keywords: Early childhood caries, oral microbiome, microbial dysbiosis, microbiota, temporal dynamics

1. INTRODUCTION

Human microbiomes are thought to develop in a reproducible and ordered manner; however, our understanding of the complex bacterial communities that constitute the oral microbiomes of individuals across different global populations remains limited **[1]**. The oral cavity hosts a highly structured and diverse microbial ecosystem composed of over 700 bacterial species, along with fungi, viruses, and archaea. These microbial consortia colonize distinct anatomical niches—such as the teeth, tongue, buccal mucosa, and gingival sulcus—and contribute significantly to both oral and systemic health by modulating immune responses, regulating local pH, and competitively excluding pathogenic organisms **[2-4]**. This balanced ecological state, termed *eubiosis*, is essential for maintaining oral homeostasis. Disruption of this balance can lead to microbial dysbiosis, a key factor in the pathogenesis of numerous oral conditions, including early childhood caries (ECC), one of the most prevalent non-communicable diseases affecting children worldwide **[5-6]**.

ECC is defined as the presence of one or more decayed, missing, or filled tooth surfaces in any primary tooth of a child under six years of age and constitutes a significant global public health concern. The pooled prevalence of Asia was reported 52% however, its burden is severe in many parts of Asia, especially in Southeast Asian countries **[7-8]**.

Epidemiological data report ECC prevalence of approximately 50% in India, 20.6% in Japan, 50–72% in China and 40–60% in Korea, and up to 90% in parts of Southeast Asia, including Myanmar, Thailand, Malaysia, and Indonesia **[8-11]**. The condition disproportionately affects children from both rural and underserved urban communities, imposing not only a significant financial burden on households and health systems but also affecting children's nutrition, growth, speech development, academic performance, and psychosocial well-being **[12-13]**.

Historically, the microbial etiology of ECC was poorly understood due to the constraints of culture-dependent diagnostic methods. These traditional techniques captured only a limited subset of the oral microbiota,

predominantly aerobic and fast-growing organisms, while excluding the slow-growing, anaerobic, and fastidious taxa now known to play critical roles in biofilm formation and acid production **[14-15]**. The development of culture-independent molecular approaches—most notably next-generation sequencing (NGS) and 16S rRNA gene amplicon profiling—has facilitated a more comprehensive and accurate characterization of oral microbial communities in both healthy and disease states **[16-17]**.

Emerging evidence demonstrates substantial population-level differences in the composition of the oral microbiome, shaped by a confluence of genetic, dietary, cultural, environmental, and behavioral factors **[18-19]**. A study on variation in microbiota between ethnic groups of American children noted abundances of *Capnocytophaga, Prevotella, and Leptotrichia* among all groups **[20]**. Microbial alpha and beta diversity was also noted in same study **[20]**. A review article on ECC children of western countries noted "*S. mutans*, *Actinomyces, Abiotrophia, Atopobium, Bifidobacterium, Lactobacillus, Olsenella, Pseudoramibacter, Scardovia, Selenomonas,* and *Veillonella"* are the most common types of oral microbiota **[21]**. In contrast, consolidated data on oral microbiota in Asian populations affected by ECC are not yet compiled.

This review aims to synthesize the current understanding of the oral microbiome's role in ECC pathogenesis, with a particular focus on studies conducted in diverse Asian populations. We highlight key pathogenic taxa that distinguish ECC-associated microbiomes from those of healthy children. This review can help clinicians and researchers identify future diagnostic and therapeutic strategies tailored to specific microbial risk profiles.

2. Temporal dynamics in oral microbiome succession

The oral cavity is home to the second-most-diverse microbiome in the human body. This community contributes to both oral and systemic health **[22]**. Childhood is considered crucial in establishing the future oral microbiota**.** The oral microbiome in children undergoes a dynamic, multi-phase process shaped by maternal transmission, delivery mode, feeding practices, environmental exposure, and distinct cultural, dietary, and genetic factors, resulting in unique patterns of microbial acquisition and community structures essential for understanding population-specific trajectories that predispose children to ECC **[23-24]**. Initial microbial colonization of the infant's oral

cavity begins primarily through vertical transmission from the mother, particularly during birth and early infancy, as well as through horizontal transmission via feeding practices and close physical contact **[25, 26]**. It can progress from a simple community at birth to a more mature, stable, and adult-like microbiota by around 3 to 5 years of age. The microbial diversity begins to increase rapidly as infants are exposed to environmental factors such as feeding (breast milk or formula), contact with caregivers, and introduction to solid foods **[27-28]**. Infants born by cesarean section show an initially altered microbial profile compared to vaginally delivered infants, but this difference tends to diminish with age. The detection rates of many main constituent bacteria, including *Neisseria, Haemophilus*, and *Fusobacterium*, increase markedly between 6 and 18 months **[22, 29]**. The oral microbial community undergoes significant compositional shifts, with increasing alpha diversity (species richness and evenness) and complexity as the infant's diet diversifies and teeth begin to erupt **[30]**. By 18 months, the oral microbiome has already started to resemble that of adults in terms of bacterial composition, although it remains partially immature **[29]**. Later Childhood Development and Stabilization (18 Months to 5 Years). From 18 months to around 3 years, the oral microbiome continues to diversify and stabilize. The weighted UniFrac distance analysis shows that by 36 months, children's oral microbiota are within the range of adult individual variation, indicating substantial maturation **[22, 29]**.

Studies conducted in Chinese populations have revealed that the mother's oral health influences the composition of the infant's oral microbiome. It is speculated that mothers with higher levels of *S. mutans* transfer to their children at birth **[30]**. The mode of delivery significantly affects the initial acquisition of microbes; cesarean-delivered Asian infants demonstrated different patterns of delayed colonization and diversity compared to vaginally delivered infants **[31]**. The protective effect of healthy oral microbes is often counteracted by the early introduction of cariogenic weaning foods, such as sweetened rice porridge and fruit-based preparations in India and other Asian countries. These foods are commonly introduced between 4–6 months of age in many Asian cultures, creating conditions conducive to *S. mutans* acquisition during what is typically referred to as the "window of infectivity **[32-34]**. Longitudinal data found that the oral microbiome of children at 5 years remains distinct from that of their mothers, suggesting

that full maturation to an adult-like state may occur later in childhood or adolescence **[35, 36]**.

3. Signature oral microbiome profiles of children with ECC in various Asian regions

High-throughput molecular technologies, including microarray assays, real-time PCR, and next-generation sequencing, have identified a diverse range of microorganisms implicated in ECC pathogenesis. Several machine-learning modelling are also predicting the onset of dental caries in recent years **[37-39]**. A study from the USA reported *Rothia, Streptococcus* and *Veillonella* as important discriminatory biomarkers of risk for ECC onset **[37]**. The present review identified studies across China, Thailand, India, Japan, Myanmar, Indonesia, Malaysia, and other Southeast Asian countries that feature similarity and differences in patterns of microbial dysbiosis relating to ECC **(Table 1)**. The most prevalent microbiota forming the healthy microbial community in China include *Streptococcus salivarius, S. pneumoniae, Neisseria lactamica, Veillonella*, and *Prevotella* species, while *Alternaria alternata* and *Bipolaris sorokiniana* were most prominent mycobiomes, which maintain a stable population throughout early childhood development **[40-44]**. Longitudinal studies of Han and Uyghur preschool children in China have demonstrated that the species richness and diversity in saliva decline with the progression of ECC **[41]**. ECC children consistently had higher numbers of isolates with *S. mutans, Lactobacillus, Veillonella, Prevotella, Candida albicans* showed relatively higher abundance in ECC teeth of children **[45]**. Healthy teeth of those patients were noted to contain *Actinomyces, Bifidobacterium,* and *Abiotrophia* **[40]**.

In India, studies using molecular techniques such as next-generation sequencing and PCR have identified a diverse microbial community dominated by *S. mutans*, TM7, *Lactobacillus*, *Candida albicans* and*, C. dubliniensis* in severe childhood caries teeth. However, all studies reported *S. mutans* is mainly accounted for caries **[35, 46-48]**. Indian children with ECC also exhibit enrichment of *Bacteroidetes, Fusobacteria*, *S. oralis*, *S. noxia*, *Prevotella saccharolytica, Campylobacter gracilis, Pseudomonas, Absconditabacteria* SR1 and *Neisseria oralis,* on ECC-affected and adjacent teeth, suggesting a dysbiotic shift. Cross-kingdom fungal-bacterial biofilms involving *C. albicans* are also prominent, appeared in 50% of Indian studies included **[35, 46-49]**. *Gracillibacteria_GN02* was noted to be a unique species in caries free population, suggesting region-specific microbial signatures and highlighting the influence of

geography, diet, and lifestyle on oral microbiota composition **[35, 48]**.

Table 1: Oral microbiome of healthy and ECC patients in Asian populations

Country/Region	Dominant taxa in Caries-free	Dominant taxa in healthy teeth of ECC patients	Dominant ECC-Associated Taxa
China [40-45]	***Actinomyces, Bifidobacterium,* and *Abiotrophia***	***Streptococcus salivarius, S. pneumoniae, Neisseria lactamica, Veillonella*, *Prevotella*, *Alternaria alternata* and *Bipolaris sorokiniana***	***S. mutans, Lactobacillus, Veillonella, Prevotella, Candida albicans***
India [35, 46-49]	***Gracillibacteria_GN02***	***Bacteroidetes, Fusobacteria*, *S. oralis*, *S. noxia*, *Prevotella saccharolytica, Campylobacter gracilis, Pseudomonas Absconditabacteria* SR1 and *Neisseria oralis***	***S. mutans*, *Saccharibacteria* TM7, *Lactobacillus*, *Prevotella saccharolytica, Campylobacter gracilis, Pseudomonas, Neisseria oralis, Candida albicans* and, *C. dubliniensis***
Indonesia [50]	**-**	**-**	***S. mutans, S. sanguinis* and *C. albicans***
Thailand [51-53]	***Prevotella nanceiensis*, *Leptotrichia* sp. HMT 215, *Prevotella melaninogenica*, and *Campylobacter concisus***	**-**	***Lactobacillus* spp., *S. mutans***
Japan [27, 54-57]	***Neisseria*, *Haemophilus*, *Fusobacterium, Streptococcus, Rothia, and Gemella***	***S. sobrinus***	***Lactobacillus salivarius*, *S. mutans* and *S. sobrinus* while *S. sobrinus,***
Korea [58, 59]	***Neisseria oralis, Lautropia, and Leptotrichia***	**-**	***Scardovia wiggsiae* and *Leptotrichia wadei, Granulicatella, Streptococcus, Bulleidia*, and *Staphylococcus***
Myanmar [60]	***Proteobacteria***	**-**	***Firmicutes* and *Bacteroides***
Malaysia [61]	***Granulicatella***	**-**	***Vibrio, Haemophilus,* and *Aggregatibacter***

The dominance of *S. mutans* and *C. albicans* was also noted in Indonesia. They also reported a positive correlation between the occurrence of *S. sanguinis* with *S. mutans* in the ECC group **[49, 50]**. Data from Thailand reveal a distinct microbial profile in children with severe ECC, who had increased salivary *Lactobacillus* counts and *S. mutans* proportion, suggesting a community shift toward acid-tolerant organisms **[51, 52]**. The relative abundance of *Prevotella nanceiensis*, *Leptotrichia* sp. HMT 215, *Prevotella melaninogenica*, and *Campylobacter concisus* were noted among caries-free children **[52, 53]**.

A similar trend was observed in Japan, where ECC children exhibit elevated *Lactobacillus salivarius*, *S. mutans* and *S. sobrinus* while *S. sobrinus,* concentrations. Studies also reported a high

co-colonization rate of *S. sobrinus* (60–80%) with *S. mutans*, indicating a synergistic effect in biofilm formation and acid production **[54-57]**. *Neisseria*, *Haemophilus*, *Fusobacterium, Streptococcus, Rothia, and Gemella* were reported in healthy counterparts **[27]**. In Korea, *Scardovia wiggsiae* and *Leptotrichia wadei* were present in children with severe ECC, and *Granulicatella, Streptococcus, Bulleidia*, and *Staphylococcus* were identified as key microbial markers. Studies also reported that *Neisseria oralis, Lautropia, and Leptotrichia* were abundant in the non-caries samples **[58, 59]**. Limited data from Myanmar suggest *Proteobacteria* were abundant in caries-free children, in contrast, *Firmicutes* and *Bacteroides* were abundant in children with dental caries **[60]**. Malaysian severe ECC children were found to harbor higher levels of *Vibrio, Haemophilus,* and *Aggregatibacter*, while caries-free samples were rich in *Granulicatella* **[61]**.

Studies from different countries indicate that every healthy child has a vast oral microbiome. The progression of ECC is frequently associated with a shift in the microbial equilibrium of the oral cavity **[62]**. Among eight countries explored, certain bacterial taxa remain ubiquitous, and the proportional abundance and specific strain prevalence vary by population and geography. Across Asia, ECC children consistently exhibit a vast microbial diversity and higher prevalence of acidogenic species, suggesting microbial dysbiosis. High abundance of *S. mutans* among ECC patients is reported from three Southeast Asian countries: India, Thailand, Indonesia and two Eastern Asia countries: China and Japan. *Lactobacillus* and *Candida* species were reported as second and third most abundant species among these Asian countries. The present review also noted that healthy microbiota of different countries are rich with unique species, such as *Neisseria* is prominent in Japan and Korea; however, *Prevotella* is common in Thailand, *Granulicatella* in Malaysia, *Proteobacteria* in Myanmar and *Gracillibacteria*_GN02 in India. Although, Early childhood caries (ECC)-associated dysbiosis is characterized by an increased presence of acidogenic and aciduric microbiota, the variations in the composition of a healthy oral microbiome across populations confirm that those microbes are strong geographical signatures. This uniqueness is influenced by regional dietary habits, exposure to local microbial reservoirs, climatic conditions, hygiene practices, and ethnicity **[62-65]**.

Host-related characteristics—such as genetic background, immune system variability, and salivary composition also play crucial roles in

shaping the oral microbiome. Differences in innate immunity, mucosal barrier integrity, and the secretion of antimicrobial peptides contribute to individual variations in microbial colonization and stability **[64-68]**.

Urbanization further impacts microbial diversity. For example, studies from Indonesia show that children living in urban areas tend to exhibit greater microbial richness and diversity than their rural counterparts, likely due to variations in hygiene, diet, and environmental exposures. Diet, particularly the consumption of fermentable carbohydrates and refined sugars, is a well-established factor influencing oral microbiota. Diets high in fiber and low in sugar are typically associated with more diverse and stable microbial communities **[69-70]**. The consequences of untreated ECC go beyond oral health. It can lead to nutritional deficiencies that may adversely affect brain development in young children **[71]**. Therefore, implementing comprehensive early childhood health programs aimed at preventing ECC is vital for promoting both oral and cognitive health in early life.

4. CONCLUSION

In Asia, ECC is a significant public health issue characterized by microbial dysbiosis in children below six years. Regional differences in healthy oral microbiomes were noted due to variation in genetic, environmental, and cultural aspects. However, *S. mutans*, *Lactobacillus* species, and *Candida* species are noted as the main culprits of early childhood caries. Mapping of population-specific microbial signatures through this study will enable the implementation of precision medicine approaches, such as microbiome-oriented diagnostics and therapeutics, transforming pediatric dental care in diverse Asian populations toward culturally informed, personalized prevention strategies.

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