**GUT-BRAIN-ORAL DYSBIOSIS**

Geetanjali Jadhav\*,Preetam Shah, Rahul Hegde, Anand Shigli, Pallavi Naik.

Keywords: Gut microbiota, Oral Microbiota, Dysbiosis, Immunological signalling

The bidirectional communication line connecting the stomach and the central nervous system is referred to as the gut-brain axis. Through neural, hormonal, and immunological signalling mechanisms, the gut and the brain can communicate. The control of metabolism, immunological response, and behaviour are just a few of the physiological and pathological processes that have been linked to this communication channel. The gut-brain axis' impact on dental health is one component that has gained more recognition in recent years. The gut-brain axis, specifically, may have an impact on the emergence of dental caries, a prevalent chronic illness that damages the teeth and is brought on by bacteria in dental plaque.

The gut-brain axis is a sophisticated, two-way communication mechanism that links the gut bacteria and the brain. A number of ailments, including neurological conditions and dental cavities, have been linked to this association. The potential role of the gut-brain axis in dental caries has been investigated in recent research. It is thought that the relationship between the brain and the gut bacteria may have an impact on how caries develops. For instance, some bacterial species have been associated with a higher risk of developing caries, and it has been proposed that these bacteria may be able to affect how the brain reacts to dental health.

The gut-brain axis may have a role in the onset and progression of dental caries, according to studies. There have been theories that cariogenic biofilms and caries may be related, and that the gut microbiota may have an impact on how these biofilms form. Additionally, the microbiome might be able to affect the immune and inflammatory reactions to cariogenic bacteria, which could increase the risk of developing caries.

Overall, the gut-brain axis is a crucial link between the stomach and the brain, and it may contribute to dental caries' onset and progression. According to research, the gut microbiota's makeup can affect a person's chance of acquiring dental caries. Additionally, research has revealed that psychological stress, which is known to impact the gut-brain axis, can affect dental caries risk.

Additionally, the oral cavity itself is regarded as a component of the gut-brain axis. A complex microbial population that interacts with the host immune system and lives in the mouth can have an impact on general health. Dental caries and dysbiosis, or an imbalance of the oral microbiota, are both conditions that affect the mouth.

In conclusion, the gut-brain axis affects the gut microbiota and has an impact on psychological stress, both of which contribute to the development of dental caries. Additionally, the oral cavity is thought to be a component of the gut-brain axis, and dental caries can be facilitated by oral microbiota dysbiosis.

The new born baby microbiota is quite dynamic throughout the first few years of life and experiences fast compositional changes before stabilising to resemble that of an adult and including discrete microbial communities with particular roles at certain body regions. Oral mucosal surfaces start to get colonised after birth when bacteria and fungi are introduced by a variety of routes, such as maternal transmission during childbirth, parental exposures, food, and horizontal transmission from carers and peers. With the formation of permanent teeth in children and the eruption of primary teeth in early infancy, the oral microbial community continues to develop and develops into a complex and diversified microbiome.

Early microbial uptake and the formation and development of the neonate's immunity interact in a complicated way. These prenatal interactions between the microbiota and the human host are what shape postnatal physiological development, innate and acquired immunological characteristics, and future health.

The dental cavity serves as the first point of colonisation for the oral and gut microbiota, making it a readily accessible body location for microbial community evaluation and the biological indicators used to diagnose, forecast, and monitor both oral and systemic disorders.

Recent studies indicate that changes in early oral colonisation and formation of a healthy oral microbiome may affect the evolution of both oral and systemic disorders in children, similar to documented links between microbiome and adult health. Children's tooth decay, infant weight gain, paediatric appendicitis, paediatric inflammatory bowel disease, and paediatric appendicitis are just a few of the health conditions that may have an oral microbial involvement and harbour oral microbial signatures. However, more longitudinal studies are urgently needed to provide substantial evidence on the link of causality between the oral microbiome and oral/overall health.

Oral sample collection in the form of saliva and mucosal swabs is non-invasive and so provides an ideal diagnostic medium that has tremendous potential for use as diagnostic tools for the most vulnerable groups, new born and young children. Additionally, scientists are looking into the microbiome's potential applications, with a focus on microbial manipulation. In the low-complexity microbiome of the infant stomach, microbial intervention of a single bacterial strain was shown to be beneficial in changing illness risk. Although studies on the effects of altering the oral microbiome on systemic disease have not yet been conducted, we can envision a future in which salivary diagnostic tools could be used in infancy to better understand and mould our oral and gastrointestinal systems.

In order to better understand the development of the oral microbiome throughout early infancy, the mechanisms involved in oral microbial profiling, and the benefits and drawbacks of utilising the oral microbiome of children to predict future dental and systemic disorders, this review aims to gather information.

Early infancy oral microbial community establishment:

Different stages of early childhood are described using a variety of terms. In terms of medicine, an infant is considered to be a new born or neonate if they are more than 28 days old. In most cases, the term "infant" refers to young children under 1 year of age, while other definitions extend this age range to 2 years. The word "toddler" may be used instead when a youngster starts to walk between the ages of 1 and 4. Early childhood is defined as the time from birth until preschool age (about 5 or 6 years old).

Traditional wisdom holds that oral microbial colonisation occurs after birth; however, new research has highlighted the fact that the human microbiome begins to develop before birth. According to studies, up to 70% of pregnant women have germs in their amniotic fluid. Particularly, the human placenta has been found to harbour various oral microbes, including Streptococcus, Fusobacterium, Neisseria, Prevotella, and Porphyromonas. Gomez-Arango et al. used 16S rRNA sequencing to analyse the gut, oral, and placental microbiomes from pregnant women in order to determine the potential source of the placental microbiome. Prevotella, Streptococcus, and Veillonella were three shared taxa that were discovered in all intestinal, oral, and placenta samples. Surprisingly, when the microbes in the stomach and mouth cavity were examined, the placenta microbiome did not include distinct core species. The placental microbiome also mimics the pregnant oral microbiota more so than the gut microbiome, even though the placental colonisation may have many origins (oral and gut).

Under the effect of contact pathways and an infant's immunological tolerance, the newborn is exposed to a broad range of microorganisms during and after delivery, including bacteria, fungi, parasites, and viruses. Surprisingly, only a small subset of bacteria colonise the mouth cavity permanently, and this colonisation occurs in a temporal and geographical sequence. The group of earlier colonisers appears to influence the later colonisation, which results in more complicated and stable ecosystems as they mature.

bacteria in the oral cavity

The colonisation and establishment of microbial pioneers in the mouth cavity begin as soon as a baby is born and comes into touch with the outside world through breathing, eating, and interaction with carers. Mason et al. used a cross-sectional approach to examine oral mucosal swab samples from 47 newborns who were in the predentate stage. They found 178 species-level operational taxonomic units (s-OTUs) that are divided into 50 genera, with (65 18) s-OTUs in each baby. These species were mostly recognised as facultative Gram-positive bacteria, then as Gram-negative anaerobes. Mason et al. also identified the genera Streptococcus, Gemella, Granulicatella, and Veillonella as the core oral microbiota for predentate newborns. It's interesting to note that just 45% (23%–61%) of each infant's oral microbiota was made up of these core species.

Oral bacterial variety and richness develop throughout time as a baby gets older. Dzidic et al. conducted a longitudinally collected oral sample set of 90 children to evaluate the temporal evolution and maturation of the oral microbial ecology in early infancy and childhood using the sequencing of 16S rRNA gene V3-V4 hypervariable regions. From the time of birth to the age of 7, these kids were monitored. Mucosal surfaces are the main locations for bacterial colonisation prior to tooth eruption. Streptococcus, including Streptococcus epidermidis and Streptococcus salivarius, Staphylococcus spp., and Fusobacterium, are the most often seen early colonisers in the oral cavity.

The high prevalence of Streptococcus in the early oral cavity is due to two factors: (a) Streptococcus spp. can adhere to epithelial cells, and (b) they are one of the major bacterial species found in human breastmilk. The oral settlement of Streptococcus spp. is caused by direct physical contact during bread feeding and is aided by a sufficient nutrient supply in breast milk that promotes their growth. Streptococcus salivarius, which makes up 10%–15% of all Streptococcus species, is the most often seen species in the oral cavity of newborns. Its prevalence peaks at 3 months of age.

Interestingly, with the advent of the first tooth, the oral environment is reformed. When compared to the predentate infants, the primary dentition's salivary microbial community exhibits significantly higher alpha diversity and equitability. When moving from the predentate to the primary dentition, a lower level of Gram-positive facultative and a higher level of Gram-negative facultative are observed. For instance, Escherichia coli, Pseudomonas, Staphylococcus, along with the lactic acid-producing bacteria such as Lactobacillus gasseri, Lactobacillus crispatus, and Streptococcus spp. are particularly widespread throughout the first few months of an infant's life, prior to tooth eruption. Along with new binding sites being created by tooth eruption, the oral environment also experiences new ecological occurrences. For instance, Streptococcus mutans speeds up colonisation at this point since teeth are their preferred adhesion surface. By the end of the first year of life, Fusobacteria, Synergistetes, Tenericutes, TM7, and SR1 have come to dominate the oral microbial community.65 Even though the majority of oral microorganisms colonise the mucosa, tongue, and teeth after tooth eruption, the proportions may vary depending on the colonisation sites. In comparison to the oral mucosa and saliva, the teeth and tongue have a higher microbial load. The variety and richness of the overall bacterial community has been steadily rising over time, along with the emergence of distinct microbial niches at various oral locations. Nearly 550 OTUs were found in the oral cavity at the end of the primary dentition, at age 7, and the Shannon diversity index was around 2.4.

A new, separate oral community is formed by the plaque microbiota during tooth eruption. According to our study's findings, regardless of caries status, the microbial composition varied significantly across saliva and plaque samples when the oral microbial community of preschool children with and without caries was compared using 16s sequencing.

Influencing factors for children's oral microbiomes

For healthy adults, a person's oral microbiome is influenced by a variety of variables, such as their age, gender, food, environment, and dietary habits. Similar to this, host and environmental variables also have an impact on how the oral microbiome develops in young children. Genetics, labour length, delivery type, usage of antibiotics throughout pregnancy and the first few months of life, feeding technique, and mother oral microbiome features are among the most extensively researched aspects. Both bacterial and fungal populations are shaped by these influencing aspects.

Genetics:

Examining how the host's genetics affects the makeup of the oral microbiome and caries phenotypes has also attracted interest. Despite the discovery of some heritable oral taxa, scientists are still divided over whether the prevalence of historically thought of as cariogenic bacteria has any heritable features. With a mean age of 7.8 years, Gomez et al. profiled the supragingival plaque microbiome from 485 dizygotic and monozygotic twins. This research team found that, regardless of caries status, the similarity of the oral microbiota increased with a shared host genotype. It's interesting to note that the most heritable oral bacteria, including P. pallens, were linked to age and sugar intake rather than caries status. P. pallens was less prevalent as children aged and as sugar consumption increased. However, the findings from Gomez et al. that some cariogenic bacteria are abundant but lack heritable traits are at odds with some other studies. Previous twin research that looked at the heredity of oral microorganisms employed array- and culture-based methods to gather microbial data. These research' findings suggested a strong genetic link between the prevalence of the cariogenic S. mutans and certain pathogenic characteristics such acid generation in dental plaque and saliva. Furthermore, it has been discovered that SNPs in host genes for ATP-binding cassettes, protein synthesis, cell division, and tumour suppression are connected to the abundances of Prevotella, Pasteurellaceae, and Leptotrichia.

Pregnancy:

A difference in oral microbiota diversity between full-term and preterm newborns was not found, despite a modest number of research comparing the oral microbiota across infants with various pregnancy lengths. For instance, Younge et al. described the oral and skin microbiota of 40 full-term infants with an average age of 1 day (0-122) and 89 preterm infants (23-36 weeks) in intensive care with an average age of 42 days (1-252) during their birth hospitalisation. Infants who were born preterm were 48% white, 50% black or african american, and 3% of other races; infants who were born full term were 51% white, 31% black or African-american, and 15% of other races. In another modest research, the oral microbiota of seven preterm newborns (25–27 weeks gestational age) was examined at three different time periods within the first five days following delivery. In the newborns' oral cavity, this study found a shift in the dominant species, from Mycoplasmataceae and Moraxellaceae in the first 36 hours of life to Staphylococcaceae and Planococcaceae by day 5.

Studies have linked the use of neonatal antibiotics with lower levels of Clostridial colonisation in newborns' guts when given over an extended period of time. Intriguingly, a research by Gomez-Arango et al. found that the use of antibiotics by the mother after delivery affects the growth of the infant's oral microbiota. The findings of this study, in which oral swabs from newborns were collected within the first three days of delivery, revealed that Streptococcaceae, Gemellaceae, and Lactobacillales predominated in neonates who had not been exposed to intrapartum antibiotics while Proteobacteria predominated in newborns who did.

Mode of delivery:

Some studies discovered that the delivery methods—vaginal delivery or caesarean section—influence the development of the oral microbial community in infants, which is similar to what happens to the gut microbiota in early infancy. However, the duration of the influence is still unknown. The newborn's oral, nasopharyngeal, cutaneous, and intestinal bacterial niches are all quite similar to one another just after delivery. Nevertheless, as time goes by, bacterial communities colonised on infants born vaginally resemble mothers' vaginal bacterial communities, predominantly Lactobacillus, Prevotella, Bacteroids, TM7, and Sneathia spp., whereas the bacterial profile of infants born by caesarean section resemble those present in mothers' skin, predominantly Staphylococcus, Corynebacterium, Slackia, Veillonella, and Propionibacterium spp. Early infancy's different bacterial community depending on delivery method may persist, diminish, or even have long-term consequences on the makeup, metabolism, and general health of the child's oral microbiome. These predictions still require confirmation by more carefully designed longitudinal birth studies.

Feeding modalities:

Infants who are breastfed and those who are fed formula have different oral microbiotas, which is similar to how feeding practises affect the gut microbiota. The different oral microbiomes of infants may result from the transmission of bacteria through milk,the effects of different milk components on bacterial attachment in the oral cavity,106 the different ways that bacteria use the carbohydrates in breastmilk and formula, and/or the infant's enhanced innate immunity from breast milk and its impact on early oral microorganism colonisation.

The oral microbiota of babies who were breastfed and those who were fed formula was examined and analysed by Swedish researchers. Infants who were breastfed had an oral microbiome pattern that was quite different from infants who were fed formula, and they had a reduced species richness at 4 months of age. However, interestingly enough, by the time these infants were 12 months old, the difference in oral species richness between breastfed and formula-fed infants had vanished. Contrary to species richness, some microbial community characteristics differed even after breastfeeding was stopped, suggesting that breastfeeding may have long-term effects on the oral microbiota and that this phenomenon warrants more research.

The study also investigated into how different types of formula could affect how the oral microbiome develops. Comparing experimental formula with added bovine milk fat globule membranes to conventional formula. The consumption of the experimental formula was linked to appreciable differences in taxa abundance, as evidenced, for example, by the lower level of Moraxella catarrhalis found in the experimental formula group, despite the fact that oral species richness did not differ between the experimental and standard formula groups. In addition, babies who stopped nursing before becoming 1 year old appeared to have more diverse oral flora when they were 2 years old.

The metabolism and adhesion of S. mutans may be inhibited by both human and bovine milk, according to in vitro research. Although there is some debate regarding the link between breastfeeding and caries risk because S. mutans is a well-known cause of caries, the fact that formula-fed infants have higher S. mutans levels at 12 months of age supports breastfeeding's beneficial effects in preventing dental caries. In addition to breastfeeding and bottle feeding, it has been discovered that using a dummy can increase the chance of S. mutans colonisation in an infant's mouth during the initial few months of life. A limitation that needs to be highlighted while analysing the impact of feeding practises on newborn oral microbiome is that research groups from published literatures were frequently not randomised, which may present unknown group variations connected to oral microbiota acquisition, in addition to the feeding practises. These imbalanced factors between groups, such as race, ethnicity, age, gender, health conditions, and carers' oral and general health, are confounding factors and may result in biased results, which is a common limitation for non-randomized trials.

Transmission:

Colonisation of oral mucosal surfaces starts at birth with the introduction of bacteria and fungus by a variety of pathways, including horizontal transmission from carers and peers, parental exposures, parental perineum-infant oral transmission after birthing, digit sucking, and parental exposures. Transient maternal transfer of strains coming from many sites is confirmed by strain-resolved metagenomic analysis, with the vaginal, cutaneous, oral, and gut communities all contributing to the early newborn microbiome. A few days after delivery, the skin and vaginal microbiomes' contributions have diminished, whereas the mother's gut bacteria continue to be present in the the infant's gut, most likely by oral entrance. 95% of the infant's oral microbiome was shared with the mother's microbiome by day 3 of life.

Health implications:

In healthy people, the oral microbiome maintains its stability throughout time despite being exposed to a range of host and environmental stressors. A number of oral and systemic disorders are linked to the unique oral microbial flora. Changes in the oral microbiota's characteristics may offer correlative insight and projection into the onset, progression, and recurrence of human diseases, even though the majority of these studies are cross-sectional or case-control designed, with small sample sets, making it impossible to establish a causal relationship between the oral microbiome and diseases. Here, we focused even more on children's health and outlined research that have made significant contributions to our understanding of the oral microbial indicators of children's oral and systemic health.

Early Childhood Caries:

With over 1.8 billion new cases every year worldwide, ECC remains the most prevalent chronic childhood illness despite being entirely avoidable. Poly-bacterial tooth infections are related to the microbial aetiology of ECC. S. mutans is typically blamed for causing ECC because of its acidogenicity, aciduricity, and capacity to produce extracellular glucans. S. mutans was found in the infants' oral cavities in the early stages of infancy, even before teeth began to erupt, but at extremely low levels. The amount of S. mutans increased with the advent of teeth, and it was noticeably greater in children with ECC.

It's significant to note that during the Neolithic and Mediaeval centuries, the makeup of oral bacteria remained mostly unchanged, according to a recent investigation of calcified tooth plaque. With the industrial revolution came a large increase in the production of processed wheat and sugar, which led to the dominance of cariogenic bacteria (such as S. mutans). It has been shown that employing S. mutans to predict ECC risk has a high degree of prediction accuracy in well-designed longitudinal studies. Fontana et al. observed that infants with more than 105 colony-forming units per mL salivary S. mutans at the baseline were at increased risk for developing ECC. They prospectively monitored a group of 329 US children ((26 6) months old) for 1 year. In a 2-year prospective study, Piva et al.141 assessed a sample of 163 Brazilian toddlers (ages 3–4) and discovered increased S mutans counts and caries progression.

The oral microbiota of children with active caries has been characterised in various studies, and additional species linked to the condition have been found. These species include S. salivarius, S. sobrinus, S. parasanguinis, S. wiggsiae, S. exigua, L. salivarius, Parascardovai denticolens, Porphyromonas, Actinomyces, and Veillonella. With a mean age of 23.6 months, Gross et al. sequenced plaque samples from 36 children with severe ECC (S-ECC) and 36 children without caries (CF) and tracked how the microbiota changed as S-ECC developed. They verified that many infants with S-ECC, but not all of them, had S. mutans as the dominating species. Children with S-ECC also exhibited higher levels of S. salivarius, S. sobrinus, and S. parasanguinis among other species. Children with no or low levels of S. mutans had elevated levels of these species, indicating that these species were performing alternate pathogenic roles. Targeting species other than S. mutans may be a potential strategy for ECC and S-ECC. Veillonella, rather than S. mutans or other species that produce acid, was found to be a predictor of future caries in children who had no prior history of tooth decay.The prevalence of Veillonella is closely proportional to the total number of species that produce acid. The primary explanation for the phenotype is that Veillonella is recognised for metabolising lactate, which is a byproduct of Streptococcus species' catabolism of carbohydrates, many of which are linked to caries.

Streptococcus mitis group, Neisseria, and S. sanguinis were a few of the specific taxa whose abundance decreased with the development of caries and progression of caries stages; community diversity was also decreased in caries-affected children compared to healthy controls.

Oral-Systemic Dysbiosis:

Obesity:

The oral microbiota may be crucial and act as a gauge of a baby's growth. According to a recent study, when compared to the gut microbiome, the mouth microbiome has a stronger bacterial profile for predicting early infancy weight growth. In this study, the scientists collected information on baby fast weight growth as well as gut and oral microbiota of 226 young infants at seven different time intervals throughout the first two years of life using 16S rRNA sequencing. In particular, information on an infant's weight and length was gathered in order to spot those who were gaining weight quickly and to create development curves using cutting-edge functional data analysis methods.

Celiac disease:

When a genetically vulnerable person consumes gluten from wheat, rye, and their cross-related types, CD, a chronic immune-mediated enteropathy, damages the small intestine mucosa.Paediatric CD is thought to affect between 1/100 and 1/400 children. Diarrhoea, failure to thrive, and abdominal bloating in early newborns in the months after gluten introduction are the hallmarks of CD symptoms in children. Francavilla et al. looked at the metabolome and salivary microbiota of 13 CD kids on gluten-free diets (T-CD) and their healthy counterparts (HC). Their findings imply that CD is linked to oral microbiota dysbiosis, which may result in oral metabolome. The number of total cultivable anaerobes in the saliva of T-CD and HC children varied considerably (P 0.05). Compared to healthy controls, children with T-CD had a less varied salivary microbiome and higher concentrations of Rothia, Porphyromonas endodontalis, Gemellaceae, Prevotella nanceiensis, S. sanguinis, and Lachnospiraceae.Actinobacteria, Actinomyces spp., Atopobium spp., and Corynebacterium durum were less prevalent in children with T-CD. The relative abundances of these taxa are associated with greater concentrations of organic volatile substances in the saliva of afflicted children, such as ethyl-acetate, nonanal, and 2-hexanone.

Communication disorders:

Autism spectrum disorder (ASD) is characterised by varying degrees of social communication and interaction difficulties and constrained repetitive behaviour. All racial, ethnic, and socioeconomic groups experience ASD, though boys are more likely to experience it.The frequency is 1 in 88 children, according to the Centre for Disease Control and the Autism and Developmental Disabilities Monitoring Network in the USA. Given that the cause of ASD is still unknown, it is crucial to identify affected children early and administer the proper treatments. ASD is linked to a number of oropharyngeal anomalies, such as altered salivary transcriptomes, taste and texture aversions, speech apraxia, and buccal sensory sensitivity. ASD has been linked to changes in the gut microbiota, which were thought to affect behaviour through the "microbial-gut-brain axis".

Hicks et al. identified changes in the salivary microbiome of 348 preschool children between the ages of 2 and 6 using shotgun meta-transcriptomic data to find oral microbiome variations in children with ASD. Three developmental profiles were used to categorise these kids: children with ASD, children with nonautistic developmental delay (DD), and kids who are normally developing (TD). Three distinguished microbial ratios between ASD and DD (76.5% accuracy), five distinguished microbial ratios between ASD and TD children (79.5% accuracy), and three distinguished microbial ratios between ASD children with and without gastrointestinal disturbance (85.7% accuracy) were discovered by this research group.

In specifically, Ramlibacter tataouinensis TTB310 with an FDR of 0.001, Mucilaginibacter sp. PAMC 26640 with an FDR of 0.001, Bacteroides vulgatus with an FDR of 0.05, and Gemmata sp. SH-PL17 with an FDR of 0.05 showed lower abundance of four taxa in ASD children. Additionally, when the taxonomic abudance between ASD and DD children was examined, two taxa—Brucella and Enterococcus faecalis OG1RF—were enhanced in children with ASD while one taxa was decreased. The findings of the study suggest that the oropharynx may also be affected by disturbance of the gut microbiota in ASD. Future systematic evaluation of children's oral microbiomes may be developed as a non-invasive and potentially accurate diagnostic method to identify ASD and gauge the condition of the disorder's advancement.

Gastrointestinal disorders:

IBD, a chronic inflammatory illness of the gastrointestinal tract, is most likely brought on by a faulty immune response to the microbiota and other environmental factors in genetically predisposed people. Inflammation of the oral mucosa is frequently observed in IBD patients, especially those with Crohn's disease (CD). In all, oral pathology is seen in 0.5%–80% of adult CD patients.42% of new CD diagnosis in kids involved oral symptoms. Docktor et al. studied the oral microbiome in 114 children with CD, 114 children with ulcerative colitis (UC), and 114 children who were healthy controls. They found that the alpha diversity of the oral bacterial community was generally lower in children with CD compared to healthy controls. The general variability of children with UC did not, however differ from healthy individuals.

Several important taxa, including Fusobacteria and Firmicutes, were noticeably reduced in the tongue samples taken from the CD children compared to healthy children. Researchers discovered a drop in Fusobacteria in the UC children's tongue samples as compared to the control group, but an enrichment in Spirochaetes, Synergistetes, and Bacteroidetes. Between CD/UC patients and their healthy controls, there were no significant differences in any particular phylum from the buccal mucosa samples. Studies investigating the gut microbiome echoed the reduction of Fusobacteria and Firmicutes in CD children. Given the frequency of oral disease in CD and the simplicity of oral mucosal collection, Docktor et al. suggested that next research may examine the possibility of employing the oral microbiota as a diagnostic and predictive tool in pediatric gastrointestinal disorders.

Sleep hygiene:

Obstructive sleep apnea syndrome (OSAS) is a sleeping breathing condition characterised by recurring episodes of full or partial upper airway blockage that disrupt nocturnal ventilation and change regular sleep patterns. Children of all ages, including babies, are affected by OSAS, which has a peak incidence between the ages of 3 and 6 years old. Paediatric OSAS prevalence has been calculated to be around 3%. Several cross-sectional studies have found links between oral illnesses and OSAS in the adult population, but no study has found any links in the paediatric population.

Using 16S rRNA gene sequencing, Xu et al. conducted a case-control research to evaluate the makeup of the oral microbiome in 30 children with OSAS and 30 healthy peers. According to their findings, paediatric OSAS had a substantially different oral microbiota makeup from the healthy controls. Thermus, Pseudomonas, Lautropia, and Achromobacter were more prevalent in the OSAS patients than in the healthy control group, although Veillonella, Prevotella, Mogibacterium, Campylobacter, and Butyrivibrio were. Along with examining the oral microbiome, this research team also examined the urine metabolome of the study participants and found a correlation between certain oral microbial alterations and urinary metabolite perturbations in children with OSAS. However, longitudinally planned cohort studies are necessary to examine the additional causal link. The fact that there is now a wealth of evidence indicating that OSAS linked to obesity is particularly frequent in youngsters is another cause for worry.165 It is unclear if the imbalanced oral microbiota found in children with and without OSAS is a result of obesity or a nutritional imbalance that caused obesity.

Limiting factors:

The gateway to the stomach is the mouth. Its microbial ecology is a potential marker for the disease, if not a risk factor. The identification of microbial pathogens linked to oral and systemic disorders (such as dental caries, periodontal disease, autoimmune diseases, diabetes, and malignancies) has been made easier because to recent developments in salivary biomarker diagnostics and oral microbiome analysis. The oral microbiota has demonstrated its relevance and potential to be surrogates of gut microbiota, which might give equal dialogistic power with better management, despite the fact that the relationship between gut microbiota and general health has received more emphasis.

Dental sampling is more socially and psychologically acceptable for patients and healthcare professionals than gut microbiome sampling. Because oral samples are noninvasive and simple to handle, they constitute the ideal diagnostic medium for vulnerable groups like newborns and young children. As such, oral samples show tremendous promise for usage as diagnostic tools.

The following pose significant obstacles to establishing links between the oral microbiota and children's disorders despite the above-mentioned disease-diagnostic promises:

The currently available evidence from the majority of the oral microbiome studies are cross-sectional or case–control designed with a small sample size, which makes it impossible to establish causative associations between oral microbial community and diseases. For example, with the exception of the well-established association established between S. mutans and ECC from various of existing studies across case–control and prospective studies. studies that examined the oral microbiome of children with systemic diseases including pediatric autism, irritable bowel syndrome, CDs are lack of power to imply causal relationships between the oral microbiome and the diseases due to the limitation of the study design. Thus, it is not clear whether the change in oral microbial community is a predictor of future disease, or a result of systemic disorders.

Since studies on the oral microbiome have primarily concentrated on the bacterial community and have not addressed the important roles played by the microbial members of the oral microbial community, such as fungi and viruses, in oral health and disease, future research should take into consideration examining the interaction between various kingdoms.

Current research on the paediatric microbiome is focused only on 16S rRNA amplicon sequencing and is thus restricted to evaluating the taxonomic diversity and makeup of the microbiome. To determine the molecular underpinnings of these interactions and to identify specific metabolic or pathogenicity pathways as potential therapeutic targets, a thorough metabolomic investigation of microbiota activities that contribute to host-microbiome interactions within the oral environment is required.

Studies on the oral microbiome in individuals in good health show that inter-social group variance occurs along with variations related to region, race, and ethnicity. The effects of ethnic diversity on the early-infancy oral microbiome development, however, have not been thoroughly researched.

Conclusion:

In conclusion, this is a very fruitful area of scientific inquiry because of the complex interactions between the oral microbiome and microbiomes that were colonised at other body parts in early infancy, host immune factors, and health. These interactions suggest complex bidirectional, non-linear interactions that make causality difficult to tease apart. Future research into disease-specific microbial biomarkers and their integration into sensitive, focused, quick to give results, and affordable for widespread use diagnostic and preventative programmes are necessary for the use of oral microbiome to promote human health. The children's oral microbiome may take front stage in the future of precision medicine and personalised medicine with the complementarity of human genomes, proteomics, transcriptomics, and metabolomics.