Saliva: The Unsung Hero in Early Childhood Caries

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Introduction:

Early childhood caries is an exaggerated and aggressive form of dental caries and is also one of the most prevalent biofilm dependent infectious diseases in the world. [1] If left untreated, it can cause rapid and extensive cavitation in the teeth. Beltrami identified this pattern of caries and described it as *'les dents noire de tout-petits'* which is translated as 'black teeth of the very young'. The term ECC was devised by Davies in 1998 and was preceded by terms such as nursing bottle caries, infant and early childhood decay, etc.

Statistics around the world have demonstrated widely varied caries prevalence in children ranging from 3% to 85%. In India, numerous studies have reported an overall prevalence of 44% with a tendency towards lower prevalence in urban areas than rural. [2] ECC has a complex and multifactorial etiology and has been attributed to various environmental, behavioural, socioeconomic and biological factors.[3] However, the biology of ECC can be altered by various other endogenous and exogenous factors such as immaturity of the host defence systems, salivary characteristics, feeding patterns and the pattern of oral hygiene care in early childhood. [4]

Saliva is a complex secretion of the salivary glands which maintains the integrity of the oral tissues. From a dentist's perspective, moisture control is of utmost importance and hours are spent eliminating this fluid from the site of operation. Yet, this secretion provides a new horizon in the fields of minimal intervention and preventive dentistry. The etiopathogenesis of ECC suggests that the flow, dilution, pH, buffering, and remineralizing capacity of saliva are factors that may regulate the progression and regression of the caries process.

Hence, saliva poses as a promising tool in manipulating the initiation and progression of caries in children. Various caries risk assessment

models have been proposed with salivary analysis as a main component.

SALIVA IN ECC

As saliva plays an important role in the oral health, any changes in the quantity or quality of saliva may affect the overall health status of the mouth.

FUNCTION	SALIVA DERIVED COMPOENENTS
Remineralization	Proline-Rich Glycoproteins, Statherins, Calcium, Phosphate, Fluoride, Mucins
Acid Buffering	Bicarbonate, Phosphate, Carbonic Anyhydrate, Sialin, Basic Alkaline Proteins, Urease
Digestion	Amylase, Lipase, Gamma Protease, DNAase, RNAase
Lubrication (viscoelasticity)	Mucins, Proline-Rich Glycoproteins
Aggregation and clearance of microorganisms	Mucins, Lactoferrin, Immunoglobulin S, Proline-Rich Glycoproteins, Statherin, Lysosome
Antibacterial agents	Mucins, Lysosome (muramidase), Lactoferrin ,Lactoperoxidase, Histatins, Cystatins, Agglutinin, Defensins, Cathelicidin, Proline-Rich Glycoprotein
Antifungal and antiviral agents	Iimmunoglobulins (primarily A), Mucins and Histatins
Bolus formation	Mucins
Taste	Mucins, Zinc

COMPONENTS OF SALIVA AND THEIR ROLE IN EARLY CHILDHOOD CARIES

1. Salivary Flow Rate

"Salivary clearance" or "oral clearance capacity" is the flushing and neutralizing action of saliva and it is considered to be one of the most important functions of saliva.[5]In general, higher the flow rate, faster is the clearance[6] and higher is the buffering capacity.[7] A reduction of oral defense systems causing severe caries and mucosal inflammations may be seen in the event of a reduced flow rate.[8] In early childhood caries night feeding practices is considered to be one of the major contributors for ECC as reduced nocturnal salivary flow further reduces the oral clearance. This in turn results in higher levels of lactose in the resting saliva and dental plaque for longer durations than what would be expected during the day. The stimulated salivary flow rate varies from 1 to 3 ml/minute. It is considered to be a potential risk factor whenever it is lower than 0.3ml/min. However, in his study, El-kwatehy et al, could not correlate the salivary flow rate to the development of caries.[9] This was in contrast to the works of Papas et al who found a strong correlation between salivary flow rates and caries development.[10]

2. Buffering Capacity Of Saliva and pH

The saliva has three major buffer systems: the bicarbonate, the phosphate and the protein buffer systems. A combination of the salivary buffering capacity and the salivary pH level help in neutralising the acidic environment. El-kwatehey et al in 2016 found a significant reduction salivary pH in ECC affected children and associated it to larger and faster quantities of acids that are produced in these children.[9] Bagherian and Asadikaram et al in 2012 conducted a study in which it was observed that the buffering capacity of saliva in the caries – free group was significantly higher than in the ECC group.[4]

Srivastava et al found a significant decrease in salivary pH after half and one hour following the consumption of probiotic curd.[11] Sultan et al used natural chewable products like tulsi, sesame seeds, fennel seeds and coconut based chewing gums to assess the change in plaque pH. Maximum increase was found with fennel seeds followed by tulsi, further reinforcing the use of these natural products in the prevention of caries.[12]

3. Saliva as a Medium of S. Mutans Transmission

It has been established over the years that the mother is the primary source of infection for children who carry S.mutans strains and saliva is the main tool for the transfer of such strains. Berkowitz et al reported that mothers with high salivary S.mutans count exceeding 105 colony forming units (CFU) were about nine times more likely to pass the causative bacteria on to their children than mothers with low salivary S.mutans count.[13] Salivary levels of mutans streptococci at $\geq 10^6$ colony-forming units/mL of saliva and/or lactobacilli at $\geq 10^5$ colony-forming units/mL of saliva place an individual at high risk for caries development.

Srivastava et al found significant reductions in S.mutans counts after consumption of probiotic curd.[11] However, Montalto et al did not find any significant reductions in the S.mutans counts.[14]

Currently, numerous herbal products have been used. Mishra et al found a decrease in bacterial count and plaque accumulation after using a mouth rinse containing triphala. He also suggested the use of other plant products like, Quercus infectora and tulsi for the same.[15] In a study done at Nitte University, it was found that herbal green tea and coffee were effective in preventing the formation of plaque and it was comparable to CHX (Unpublished).[16] In another study, a neem with honey and cocoa with honey mouthwashes showed anti-plaque, anti-inflammatory and anti-microbial properties comparable to CHX (Unpublished).[17] However, Shapiro et al compared 12 different mouth rinses and inferred that the herbal rinses were less effective than CHX.[18]

4. Saliva and Pellicle Formation

The pellicle is defined as the acellular layer of adsorbed salivary proteins and other macromolecules on the dental enamel surface approximately 10 micrometers thick. The pellicle allows for the subsequent adhesion of micro-organisms, which in turn form dental plaque.[19]Though the pellicle serves as the initial substratum for undesirable plaque formation, the molecular surface characteristics of pellicle could actually exhibit beneficial effects by facilitating a selective adsorption of harmless bacteria and thereby minimizing the development of oral disease.

5. Antimicrobial Effect of Saliva:

Saliva forms a major defense mechanism of the body and harbours a wide array of antimicrobial components. The peroxidases in saliva have been reported to reduce the incidence of caries. Thus, their addition to dentifrices and mouth washes has been attempted and has proven to be effective as an antiplaque agent thus preventing dental caries. The Nitric oxide in saliva results in auto inhibition of cariogenic bacteria and hence is a good antimicrobial agent. Hedge et al found a low incidence of early childhood caries in children with high salivary Nitric Oxide levels. [20]The most abundant immunoglobulin in saliva is the dimeric secretory lgA. De Farias et al , Almoudi et al and Bagherian et al found a positive association between the salivary IgA levels and the presence of ECC.[4;21;22] However, Parkash et al found a low salivary IgA level in children with caries.[23] Consumption of probiotics with dairy products (milk, cheese, yogurt and ice-cream) used as vehicles help in stimulating the production of sIgA thereby reducing dental caries. Lactoferrin is an iron-binding protein in saliva that has the ability to sequester iron from the oral environment. As Iron is essential for bacterial metabolism, this protein inhibits Mutans

streptococci growth by an iron-independent mechanism. Lysozyme is an antimicrobial enzyme that acts by disrupting the bacterial cell wall leading to their destruction. Salivary mucins are glycoproteins that promote clearance of bacteria from the oral cavity by masking the bacterial surface adhesion molecules and inhibiting bacterial colonization of the mucosa and exposed tooth structures. Salivary antioxidants on the other hand reduce the oxidative stress that results in the development of various inflammatory oral lesions and dental caries. Biomarkers for oxidative damage that are found in saliva are 8-hydroxy-desoxguanosine (8-Hodgkins) and Malondialdehyde (MAD). Enzymatic antioxidants include glutathione peroxidase (GPx) and superoxide dismutase (SOD) while the non- enzymatic antioxidant systems include uric acid (UA) and glutathione (GSH). Da Silva et al in 2015 found a decrease in oxidative damage in saliva of children with severe early childhood caries and attributed it to the increase in the enzymatic and non-enzymatic antioxidant systems.[24] Kumar and Pandey et al in 2011 also found an increase in the total antioxidant capacity of saliva in severe early childhood caries.[25] However, Tulunoglu et al and Preethi et al, in their respective studies, found no significant increase in the salivary antioxidant level in children with early childhood caries .[26;27]

Salivary α-defensin forms a part of the antimicrobial innate immunity. Numerous studies have shown a significant increase in α-defensin levels in children with caries.[28;29] However in an isolated study, Toomarian et al found no difference in their levels in childhood caries and caries free preschool children.[30]

6. Homeostasis of Inorganic Components

Saliva is supersaturated with calcium and phosphate with respect to hydroxyapatite. Several salivary proteins bind hydroxyapatite and aid in the maintenance of the supersaturated state of saliva. Contrasting studies are available regarding the calcium and phosphate ion concentrations in caries risk and caries free individuals. In a study done by Hegde et al in 2014, an increase in Calcium and Phosphate was seen in saliva of caries free and E-CC children after administration of milk, cheese and tooth mousse. However, Tooth Mousse showed higher bioavailability of calcium and phosphate.[31] Contrasting studies have been seen in relation to the salivary protein content as a risk marker in early childhood caries. Roa et al did not find any significant difference in the salivary total protein levels in children with caries.[32] However, Dodwad et al reported that the total proteins were significantly higher in caries active children in comparison to those without caries.[33]

DISCUSSION

Early Childhood Caries (ECC) involves a complex host- diet-microbe interaction that initiates with the formation of a biofilm on teeth. This biofilm matrix plays a key role in the pathogenesis of dental caries, particularly when conditions (dietary sugar, feeding habits, etc.) are favourable to the development of ECC. Saliva is an important biological fluid that contains various microbial and host biological components that can be used for caries risk assessment. The collection of saliva forms a non-invasive, safe and inexpensive method and thus, can be used for caries risk assessment tests. This helps in the development of a caries profile for such children.

The proposed salivary caries profile is as follows:

1. Decreased salivary flow rate
2. Decreased buffering capacity and pH
3. Decreased calcium, phosphate ions and protein levels

4. Increased S.mutans counts

Even though these properties of saliva have been associated with the incidence of ECC, it is important to remember that other environmental factors such as, feeding habits, fluoride exposure and pattern of oral hygiene care are also important in the dental caries process and may affect some of the salivary characteristics as well.

Thus, to summarize, the enhanced knowledge about the pathogenesis of ECC and technological advancements point towards newer horizons in research. Hence further studies are required to understand the effects of saliva and its components on ECC.

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