A REVIEW ON STREPTOCOCCUS MUTANS WITH ITS DISEASES DENTAL CARIES, DENTAL PLAQUE AND ENDOCARDITIS

Said Mohamed Daboor^{1,*}, Farheen Syed Syed Masood², Marwa Salm Al-Azab³, Elbagir Elhassan Nori⁴

¹Associate Professor of Microbiology and Head of Biomedical Sciences Department, ²Teaching Assistant of Microbiology, ^{3,4}Teaching Assistant, Al-Farabi College, Riyadh, K.S.A.

*Corresponding Author:

E-mail: daboorsaid@yahoo.com

ABSTRACT

Microorganisms present in our oral cavity which are called the human micro flora attach to our tooth surfaces and develop biofilms. In maximum organic habitats microorganisms generally prevail as multispecies biolfilms with the help of intercellular interactions and communications among them which are the main keys for their endurance. These biofilms are formed by initial attachment of bacteria to a surface, development of a multi—dimensional complex structure and detachment to progress other site. The best example of biofilm formation is dental plaque. Plaque formation can lead to dental caries and other associated diseases causing tooth loss. Many different bacteria are involved in these processes and one among them is Streptococcus mutans which is the principle and the most important agent. When these infections become severe, during the treatment the bacterium can enter the bloodstream from the oral cavity and cause endocarditis. The oral bacterium S. mutans is greatly skilled in its mechanical modes of carbohydrate absorption. It also synthesizes polysaccharides that are present in dental plaque causing caries. As dental caries is a preventable disease major distinct approaches for its prevention are: carbohydrate diet, sugar substitutes, mechanical cleaning techniques, use of fluorides, antimicrobial agents, fissure sealants, vaccines, probiotics, replacement theory and dairy products and at the same time for tooth remineralization fluorides and casein phosphopeptides are extensively employed. The aim of this review article is to put forth the general features of the bacterium S.mutans and how it is involved in certain diseases like: dental plaque, dental caries and endocarditis.

Key Words: Streptococcus mutans, Biofilm, Dental Caries, Plaque, Endocarditis

INTRODUCTION

In every individual's oral cavity there is unlimited construction of microbial biofilms which is very common because of different niches and abundant sources of nourishment in it. individual's microflora is extremely convoluted and extraordinary group of microorganisms forming various associations in the mouth thereby residing more than 700 dissimilar species[1]. Bacteria are dominant considerably the most microorganisms existing in the human oral cavity and few examples are S.sanguis, S.mitis, S.mutans, S. salivarius, L. acidophilus, L.salivarius, L. casei, Staphylococcus spp, Eubacterium spp, Neisseria spp, Actinomyces Peptostreptococcus spp, Micrococcus spp, etc. Among them Streptococci alone form the biggest association in the oral cavity^[2]. Maximum of the above mentioned species show α haemolysis, green zone around growth [3] of their colonies on blood agar^[2]. Some mircobiologists^[4] classified the genus Streptococcus into six important groups (the pyogenic group, the anginosus group, the mitis group, the salivarius group, the bovis group, and the mutans group) and this is shown by Fig. 1^[4]. S. mutans is the most prevailing species. high in rank than other streptococci [5]. S.mutans is a facultative anaerobic, Gram-positive cocci bacterium [6] which appears in chains on Gram stain Fig. 2 [7]. One feature of this organism is it develops deep

convex colonies on mitis salivarius agar. It has homofermentative property plus it is highly aciduric with the other alternative streptococci^[8]. By utilizing an enzyme glucosyl transferase S.mutans produces an extracellular polysaccharide from sucrose which causes dental caries. This extracellular substance possesses α (1-3) glucose linkage which helps in the attachment of the bacterium. Furthermore this polysaccharide aims in supplying energy during deficiency of any extraneous carbohydrate. S. mutans also generates Lipo Teichoic Acid that precisely adheres to the external enamel thus assisting the progress of colonization^[9]. It attaches to the tooth superficially, break down sugar for energy, decrease the pH, makes the surrounding acidic and this causes demineralization of the external structures of the tooth like enamel and dentine and sometimes in the lack of prior medication the mechanism advances ultimately developing dental caries [6]. Hence, S. mutans is not only the basic bacterium engaged in the development of plaque but also for the commencement of dental caries [7].

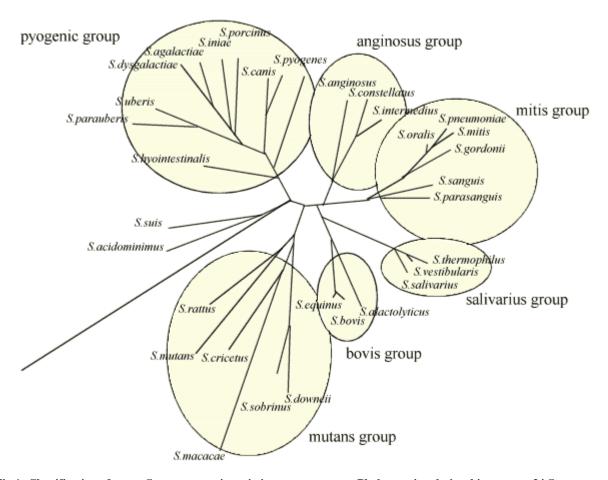


Fig 1: Classification of genus Streptococcus into six important groups, Phylogenetic relationships among 34 Streptococcus species. Adapted from "Determination of 16S rRNA Sequences of Streptococcus mitis and Streptococcus gordonii and Phylogenetic Relationships among Members of the Genus Streptococcus," by Kawamura et al, 1995, International Journal of Systematic Bacteriology, 45, p. 406. Copyright 1995, International Union of Microbiological Societies.

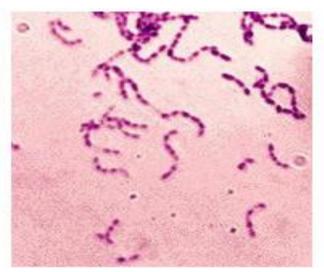


Fig 2: Gram stain image of *Streptococcus mutans*, Todar, K., 2009. *Streptococcus mutans*. Gram stain. CDC. [Figure online]. Available from: textbookofbacteriology.net/normalflora.html. [Accessed 8 April 2015]

The bacterium is non-motile, catalase negative $^{[6]}$ and happens to have four serotypes designated as c, e, f, and k, based on the chemical

composition of the serotype-specific rhamnose-glucose polymers^[10]. Mutans streptococci are a group of bacteria greatly denoted to dental plaque^[6]. The

principle dwelling places for S. mutans are mouth, pharynx, and intestine. Various essential aspects of dental caries are attachment to enamel surface, construction of acidic metabolites, ability to form glycogen reserves and capability to produce extracellular polysaccharides [11]. Dental caries is caused when any modification takes place in the oral cavity which happens to generate during additional glucose consumption which alters the homeostasis of the ecosystem to notably acidophilic bacteria those which are commonly involved in destroying the teeth [12]. Mutans streptococci are intense acid builders which generate an acidic environment and therefore constitute a danger for dent formation [11]. Dental caries is a universal chronic disease of childhood. It can actually appear in young children, soon after the eruption of first teeth, and sometimes can be serious too. In a majority of children, early childhood caries causes pain and spoils the status of wellbeing, and for few it develops into severe disease, hospitalization, and also sometimes death^[5]. Therefore dental caries is the main cause of tooth loss both in children and young adults [1].

Caries has been described as establishment of ecological association in the mouth, by engaging infectious bacteria and easily accessible sugars in drinks and food^[13]. Dental Caries may also be explained as a communicable microbiological disease of the teeth the one which ends in confined disintegration and loss of hard tissues. It is evolved from latin word which means to 'Rot or Decay' ^[9]. *S. mutans* has been stated as the leading etiological factor of dental cavities and a common dweller of dental plaque^[13]. Dental caries leads to pain, uneasiness and expensive medical care which are the fundamental aspects pertained to emphasis and bad circumstances with children and adults^[9].

These streptococci bacteria have a unique feature to colonize tooth surfaces and during fixed circumstances exist in huge mass in cariogenic biofilms and build more additional biofilms with other organisms along with various new streptococci and bacteria [1]. A biofilm is described as a mutual bacterial association which adheres to a solid (such as denture prosthesis or an intravenous catheter) or with one another protected in an extracellular polysaccharide matrix. Nearly 65% of human infections are considered to be linked for microbial biofilms. Dental plaque formed on tooth surfaces is a typical illustration of a biofilm^[14]. S. mutans is also able to acquire entry into the blood stream which leads to transient bacteremia during rigid conditions like dental procedures, oral infections, dental hygiene and eating. This bacterium which enters the blood stream then aims for infective endocarditis [15].

Liquid chlorhexidine gluconate is beneficially used as an antiplaque agent. Additionally at a greater

concentration it is also helpful as a denture disinfectant $^{[14]}$.

REVIEW METHODOLOGY

Searching for literature:

First we determined the suitable keywords that fit the research questions such as Plaque mediated diseases, Dental Caries, *Streptococcus mutans*, Biofilm and Endocarditis, then we also determined the selection criteria such as:

- 1. The articles based on the study design.
- 2. The methods used.
- 3. The main causative agent of the dental caries i.e. *Streptococcus mutans*.

However, we did not apply any exclusion criteria because we wanted the review to be comprehensive. To make the search effective & efficient, we applied the triangulation approach.

First we use Google Scholar to find articles that have been published in the various websites of the internet, then we used PubMed and OVID to access articles published in Medline, Pubmed central and OVID databases. Finally we accessed other special data bases like Embase, African Journals Online (AJOL), and Educational Media Reviews Online (EMRO) library databases.

To be able to find electronic full text articles we used Google Scholar just to compile a list of journals articles, and then we looked through the abstracts to compile a short list of articles, then we accessed these articles through Saudi Digital Library (SDL) to be able to download full text articles. We used the Health Internetwork Access to Research Initiative (HINARI) to download journals that we could not access through the SDL.

Important Properties:

Streptococcus mutans, a leading etiologic agent of human dental caries, is specifically active to develop biofilms above solid tissues of the human oral cavity [11]. Some specific strains of S. mutans also produce bacteriocins. The restriction of S. mutans bacteriocin production by oral bacteria happens to be powerful inside the biofilms [16]. It easily colonizes the oral cavity due of its capability to form biofilms on dental surfaces [15]. The construction of the oral biofilm is established through basic attachment of the bacteria, S. mutans which are the former colonizers. A film of saliva which includes albumin, glycoproteins, acidic proline-rich proteins, mucins, sialic acids, and many more compounds coat the enamel of the tooth. This salivary film is called acquired pellicle, supply receptors to the S. mutans (primary colonizers). S. mutans contribute many distinct surface adhesins, the ones which can attach to the salivary pellicles that are built on the teeth [11]. Following the first attachment by means of particular surface adhesins, oral streptococci adhere inevitably to the pellicle constituents. The progression of growth includes coaggregation coadherence of oral bacteria, and provided that uninterrupted biofilms change into a stratified, composite biofilm [17]. The major fundamental phases for the development of biofilm usually studied are (1) construction of acquired pellicle, (2) transport of microorganisms and reversible attachment, (3) primary microbial colonizers and irreversible attachment (4) coadhesion (5) formation of mature biofilm (6) separation of bacteria that can colonize different regions [17] and these stages are clearly illustrated in Fig.3^[17].

S. mutans synthesizes polysaccharides that are present in dental plaque and causes dental caries. Dental caries happens to be a disease of transmission

of bacterial metabolism by the production of acid and disintegration of mineral by penetrating inside the enamel and dentine [9]. As shown by Fig.4. [17] Dental caries is a multifactorial disease therefore developed physical, behavioral and hereditary interactions of the host, microorganism and the environment. Various components that contribute to a person's danger for caries contains: Environmental aspects like nourishment, oral hygiene, risk of fluoride, and the degree of colonization of cariogenic bacteria; and host factors being salivary discharge, salivary buffering capacity, position of teeth connected to one another, surface features of tooth enamel, and size of occlusal fissures on posterior teeth. Hereditary changes of the host factors can extend the danger for caries [17].

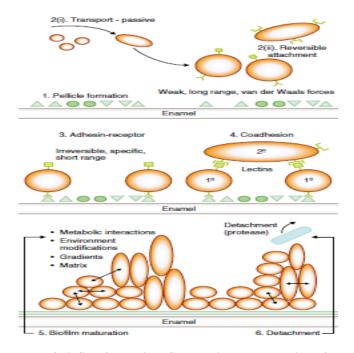


Fig 3: Fundamental stages of biofilm formation, Schematic representation of the different stages in the formation of dental plaque. Adapted from "Oral Microbiology" (p. 78), by P. D. Marsh and M. V. Martin, 2012, U.K: Printed in China. Copyright 2009 by Elsevier Limited.

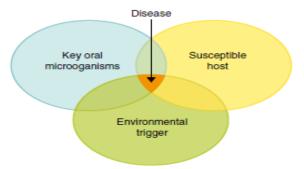


Fig.4: Factors that cause Dental Caries, The inter-relationships that lead to oral disease. Adapted from "Oral Microbiology" (p. 4), by P. D. Marsh and M. V. Martin, 2012, U.K: Printed in China. Copyright 2009 by Elsevier Limited.

Transmission:

Dental caries is observed as a transmissible disease. There is a severe action of enamel demineralization and remineralization that happens due to activity of organic acids formed by microbial associations inside the dental plaque [9]. S. mutans, which is said to be the beginner for the destruction process of nearly all dental caries, also spreads the diseases both horizontally and vertically between humans. Thus, dental caries is perhaps discussed as the utmost universal and contagious diseases prevailing in the world [12]. Nearly all the diseases of the world of children are dominated by dental caries and this leaves an important oral health issue globally considering both children and adults^[9]. Microbiological tests towards human dental plaque dates back to 1924 and the pioneer microbiologist who found these oral streptococci was Clarke^[18]. Later Keyes identified a specific organism from the streptococci group, which was later identified as S. mutans. His contributions brought forth the virulence and contagious characters of dental caries [18].

Pathogenesis and Diseases:

The relationship of oral bacteria in the pathogenesis of cardiovascular diseases currently gained the center of consideration in enormous subjects. The bacterial composition in cardiovascular tissues was found to be markedly distinct from that in dental plaque, with only a limited number of species, including *S. mutans*, in the cardiovascular regions shown to have possibly originated from the oral cavity ^[19]. *S. mutans*, a pathogen of dental caries is known to be associated with bacteremia and infective endocarditis ^[10]. In some diseases, a very important role played is the ability of bacteria to form multi-dimensional complex structure known as biofilm. The most common disease of the oral cavity, known as dental caries, is a top leader ^[20].

The most important virulent features of S. mutans for infections were: (i) capability of the bacteria to yield enormous amounts of organic acids from carbohydrate metabolism; (ii) the potency of the bacteria to reside at lower pH; and (iii) the excellency to synthesise extracellular glucan homopolymers using sucrose and all these characters perform the acts like early adherence, colonization and build up of biofilms on tooth surfaces [21]. The sugars play an etiological part in dental caries is identified a millennium before. But today it is completely known that sugar is a selected substrate for the cariogenic bacteria, the one that exists in dental plaque especially the mutans streptococci, furthermore the acid by- products of the metabolic actions cause of the enamel [22].

Laboratory Diagnosis:

For the identification of S. mutans diseases like dental caries and dental plaque the swab samples from the infected tooth and saliva from the mouth are collected [6]. The testing samples were obtained from patients showing indications and problems of dental caries from various hospitals and clinics. Swabbing is done before beginning the antibiotics to the patients in a clean and common saline solution in tubes. The swabs were then transferred to the laboratory for further procedures. Culturing of samples, isolation, detection and labeling the type of identified isolates were performed by means of suitable methods [23]. S. mutans were recognized on selective media, mitissalivarius agar, MacConkey agar, mitis-salivariusbacitracin agar [24] by examining their colonial characteristics. It is a slow procedure. For this reason, immunological and biochemical tests has been presently carried out for the isolation of bacterial colonies. However, a polymerase chain reaction (PCR), a new procedure which is easy, fast and shows clear identification of mutans streptococci species is further been established [25]. Nested PCR is able to identify S. mutans very quickly and directly in human saliva. This achievement is proved to be very valuable to analyze and explain the role played by the streptococcal species in the etiology of dental caries

Management of the Diseases:

1. **Treatment:**

Even though the treatment for Early Childhood Caries is mainly direct, it is essential for the young children to chiefly give common anesthesia for dental procedures because of age, behavior and difficulty of treatment. The better and acceptable method of treatment for Early Childhood Caries and many more dental diseases is to fill every cavity on a case-by-case means and make effort to enlighten adults regarding appropriate oral hygiene and nutritional habits [12]. Biofilms are inter mutual makeup of microorganisms protected in an exopolymeric covering that build upon both organic and inorganic surfaces and have been linked with a wide range of endless infections that show unsatisfactory actions against common antibiotic chemotherapy [27]. The microorganisms which are present in biofilm seem to be highly susceptible to antibiotics and are profusely engaged in health hazards, causing acute and chronic infections and spoiling the implanted prosthetic instruments [28]. This oral bacteria (S. mutans) developing inside biofilm like dental plaque exhibit a considerable decrease susceptibility antibiotics to antimicrobial agents over other things that are employed in mouth toothpastes and mouthwashes. More antimicrobial agents can be given effectively along mouth rinses, and the most powerful agent prior to this is chlorhexidine. This agent has shown confirmed antibacterial, antiviral and antifungal activity, and is considered to have antiplaque activity too [17].

2. **Prevention:**

It is important to develop the state of living so as to avoid biofilm- induced caries because tooth loss in both children and adults has become an economic stress globally ^[1]. Epidemiological tests showed that the percentage of dental caries can be limited favorably by enhancing the attribution of oral hygiene ^[29]. Oral care, certainly, starts by following oral hygiene. This will clear away the bacteria and fermentable materials from mouth. The constant flow of saliva also cuts down the cariogenic bacteria on the tooth ^[18]. Extensive approaches have been made for the prevention of caries like:

- i. **Mechanical cleansing techniques** [14]: Regular brushing and flossing of teeth benefit the humans [18] to prevent dental caries [6].
- ii. **Fluorides:** Presence of fluoride in house-hold water resources ^[14], gels or fluoridated tooth paste prevents caries ^[30].
- iii. **Diet:** Stopping or decreasing between meal usage of carbohydrates is greatly helpful ^[14].
- iv. **Sugar substitutes:** Using xylitol, sorbitol, lycasin (the artificial sweeteners) [14] which acts as anticariogenic substances are adopted to moderately alter the sugar in diet [6].
- v. **Fissure sealants:** These prevent caries in pits and fissures by removing stagnation regions and obstructing potential ways of infections [14]
- vi. **Antimicrobial agents:** Using Chlorhexidine and Sodium hypochlorite in mouth washes which holds antibacterial property for cleaning of mouth. Usage of high sensitive antibiotics like vancomycin, penicillin and erythromycin has also shown extensive results ^[6].
- vii. **Passive Immunization** [9]: Locally using monoclonal antibodies against antigens of mutans streptococci prohibit recolonization by the organisms [14].
- viii. **Replacement theory:** Involving colonization of teeth by either less virulence mutants of *S. mutans* or with plaque bacteria which are harmless and which are highly competitive than wild-type *S. mutans* strains [17].
- ix. **Probiotics:** Few Lactobacilli are examined as possible oral probiotic strains. Probiotic bacteria are employed to inhibit the oral bacteria which are involved in dental diseases [17]
- x. **Dairy products (milk and milk products):** Cheese has been proved to raise salivary flow rates and to promptly promote plaque pH shifts trailing to wash off sucrose [17].

Amidst many caries-preventive approaches, that comprise increase of knowledge in oral health, chemical and mechanical regulation of dental biofilms, the application of fluorides has confirmed to be greatly productive clinically according to a considerable number of clinical tests, literature studies and more newly group examinations explaining the strength of Fluoride in controlling dental caries in tests concerning the application of rinses, gels, varnishes and dentifrices [30].

For the remineralization of the tooth agents like fluoride, casein phoshopeptide, novamin and hydroxyapatite are used [9]. Fluoride ions help remineralization of early carious lesions in enamel and dentine [14]. Milk proteins and casein products adhere on to the tooth surface, as replacement for albumin in the enamel pellicle, and decrease the attachment of S.mutans; they can also remove calcium phosphate and improve remineralization. Kappa-casein can restrict glucosyltransferase adsorption into the pellicle and decrease the activity of the enzyme, so that glucan construction is restrained. Milk can change the enamel pellicle structure in vivo, generating a different globular structure [17]. These recent advancements have increased the confidence of more new cariespreventive procedures for the future [14].

CONCLUSION

The unrestricted construction of microbial biofilms is a natural phenomenon which happens in every individual's oral cavity. The effects of this are severe dental caries, dental plaque and endocarditis caused by *S. mutans*, which shows serious impacts on the human's health. So, in order to be secured from these troublesome infections it is required to take necessary precautions like brushing twice a day, reduction in sucrose rich foods, regular mouth washing and flossing. This bacterium is also transferrable in the same individual in certain cases of the infection causing dreadful diseases. It also gets transmitted from one person to another to spread the infection. So, counseling is very important to every individual about this bacterium and its diseases.

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