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Caries risk and streptococcus mutans adherence mechanism in down syndrome children: A scoping review

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Abstract

Objective: The aims of this study are to examine caries risk and S. mutans adherence mechanism in DS children.

Material and Method: Original research articles published about caries risk factors and S. mutans adherence mechanism in DS children were extracted from three electronic databases such as PubMed, Science Direct, and Google Scholar. The selection process involved looking for English language articles published between 2013-2023. Data extraction was carried out through the content of the abstracts and full texts.

Results: 660 original studies were retrieved from the three databases, and 21 were extracted. Caries risk factors associated with the development of dental caries and play a role in the virulence of S. mutans by promoting biofilm formation are GTF, GBP and SAg. S. mutans adherences mechanism is controlled by two independent mechanisms: sucrose-dependent and sucrose-independent.

Conclusion: From this scoping review, we found that GTF, GBP, SAg as important factors related to dental caries in DS children by adherence mechanism.

Keywords: Child health, Dental caries, Down syndrome, Glucan binding protein, Streptococcus mutans.
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Introduction

Down syndrome (DS), caused by the presence of chromosomal abnormality HSA21 that resulting in intellectual disability and oromotor dysfunction. The World Health Organization (WHO) reported there are eight million DS cases worldwide, at the incidence of 1:1.000 or between 3.000 to 5.000 childbirths. Deterioration in the ability and motivation of children with DS needs to carry out oral care, resulting in oral health conditions are not optimally. Hypotonic motor function development resulted in a consistent reduction in symptoms when compared to typical children. The disability in this motor skill-related illness encourages the affected children to undertake preventive measures to improve their general and mental health, which eventually contributes to the rise in the prevalence of dental caries.[1]

Dental caries in DS children, which has become a topic of controversy in many studies. Based on research in one of schools for students with special needs at Bandung city Indonesia, the prevalence of caries in children aged 6 to 14 years was high 93% in this category, with a DMF-T index of 6.1. However, according to research by Hashizume et al (2017) the prevalence of caries in DS patients was 43%, lower than compared to non-DS individuals. This condition can be happened because of changes in salivary composition, including decreased flow rate, elevated viscosity, that indicates a higher risk of cariogenic biofilm formation influenced by the adherence mechanism involving GBP, GTF and SAg in DS children.[2,3]

GBP and GTF facilitates attachment of S. mutans to other microorganisms through dental biofilm formation. Dental biofilm is a microorganism bonded to the extracellular polymeric substance (EPS), protein, and nucleic acid. EPS promotes the initial attachment of S. mutans to the tooth surface, EPS play a crucial role in the adherence mechanism of S.mutans by facilitating initial attachment, promoting biofilm maturation, and enhancing the bacterium's ability to produce acids that damage teeth. EPS matrix influences architecture of the biofilm and these proteins bind to glucans, contributing to the formation of a stable and structured biofilm. The potential cariogenic biofilm may have a greater influence on the pathogenesis of dental caries in DS children.[4]

S. mutans biofilm formation is controlled by two independent mechanisms: sucrose-dependent and sucrose-independent. GBP and GTF were classified as sucrose-dependent virulence factors, whereas SAg as sucrose-independent factor which does not require sucrose for binding to the tooth surface. GTF and GBP increase bacterial colonization by acting as acid producers in response to S. mutans acidogenic ability and major pathogen of dental caries. GBP mediate the binding of glucans synthesized from sucrose by action of GTF. SAg is present in human saliva as a receptor for adherence mechanism of S. mutans which is absorbed into hydroxyapatite and simulates the tooth surface coated with pellicle.[5]

The information presented here indicates that GTF, GBP and SAg are important factors that involved in the development of dental caries and may

Table 1. Full search strategy

Databases	Keywords
PubMed	((“Caries”[MeSH Terms] OR “Caries risk”[Title/Abstract]) AND (“Streptococcus mutans”[MeSH Terms] OR “Biofilm”[Title/Abstract]) AND (“Down Syndrome”[MeSH Terms]) AND (“Glucan Binding Protein”[MeSH Terms] OR “Glucosyltransferase”[MeSH Terms] OR “Salivary Agglutinin”[Title/Abstract] OR “GBP”[Title/Abstract])).
Sci-Direct	(TS=(“caries” OR “caries risk”) AND TS=(“Streptococcus mutans”) AND TS=(“biofilm” OR “glucan binding protein” OR “glucosyltransferase” OR “salivary agglutinin” OR “GBP” OR “GTF”) AND TS=(“Down syndrome”))
Google Scholar	(TS=(“caries” OR “caries risk”) AND TS=(“Streptococcus mutans”) AND TS=(“biofilm” OR “glucan binding protein” OR “glucosyltransferase” OR “salivary agglutinin” OR “GBP” OR “GTF”) AND TS=(“Down syndrome”))

Table 2. Important factors that related to the prevalence of dental caries in DS patients.

Factor	Features	Relation to DS	Sources
Anatomical Features	Presence of craniofacial anomalies such as midface hypoplasia and macroglossia.	These structural differences can lead to challenges like mouth breathing and malocclusion, increasing caries risk.	Rai et al. [27]
Oral Hygiene Practices	Often compromised due to motor skill limitations and cognitive challenges	Difficulties in maintaining oral hygiene can lead to increased plaque accumulation and caries	Rai et al. [27]
Motoric Dysfunction	Impaired fine motor skills, reduced manual dexterity	Limits the ability to perform effective tooth brushing and flossing, leading to plaque buildup and caries	Subramaniam et al. [7]
Salivary composition	Often calcium and phospate reduced in some studies, potentially affecting protective functions	Lower calcium can impair remineralization of enamel, increasing caries susceptibility and imbalance phosphate can affect remineralization.	Scalioni et al. [28]
Salivary Flow	Typically increased flow rate with altered buffering capacity	May provide some protection against caries despite poor oral hygiene in DS children Potential modifications in salivary agglutinin levels or structure	Siquiera et al. [23]
Salivary Agglutinin	Potential modifications in salivary agglutinin levels or structure	Changes in this glycoprotein in DS may contribute to increased adherence of S. mutans to teeth.	Scalioni et al. [28]
Tooth Eruption	Delayed eruption and anomalies like hypodontia	Delayed eruption can result in prolonged exposure of primary teeth to cariogenic challenges	Rai et al. [27]
Dietary Habits	Potential preference for soft, carbohydrate-rich foods	Dietary preferences may increase exposure to fermentable carbohydrates, promoting caries	Scalioni et al. [28]
Oral Microbiome	Differences in microbial diversity and balance in the oral cavity	Altered microbiome may disrupt protective bacterial communities and favor growth of cariogenic organisms	Willis et al. [29]
Cariogenic Bacteria Levels	Variable levels of S. mutans; some studies report higher counts in caries-active individuals	Higher S. mutans levels are associated with increased caries risk	Hashizume et al. [2]
Glucan Binding Proteins (GBP)	More expression of GBP in S. mutans to promote adherence and biofilm formation	Higher GBP activity in DS impair S. mutans’ ability to adhere to tooth surfaces.	Fujita et al. [14]
Glucosyltransferases (GTF)	Lower GTF activity in dental plaque	Increased GTF lead to higher cariogenicity due to more extracellular polysaccharide (biofilm matrix) production.	Takashima et al. [15]

contributes to virulence factors that cause by S. mutans through biofilm formation. The aims of this study are to examine caries risk and S. mutans adherence mechanism in DS children.

Material and Methods

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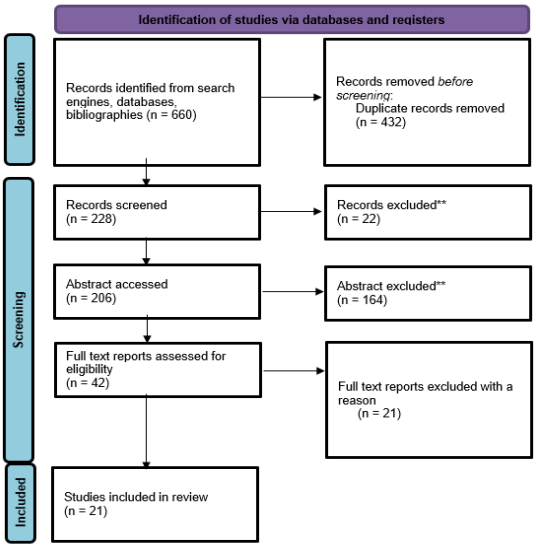

Figure 1. PRISMA flowchart describing the study selection process.

Results

Finally, all the articles with at least English abstracts indexed in the databases (n = 660) were identified and retrieved. After eliminating the duplicates, the remaining 228 articles were reviewed by titles. Furthermore, 206 articles were reviewed regarding abstracts, and 42 were retrieved from full texts to check if they met the inclusion criteria. In the end, 21 articles were included in this study figure 1.

Based on the results obtained from the included studies, We found important factors that related to the prevalence of dental caries in DS patients table 2. Most studies in this category highlighted GTF, GBP and SAg are important factors that involved in the development of dental caries and may contributes to virulence factors that cause by S. mutans through biofilm formation.

Discussion

Relationship Between DS and Occurrence of Dental Caries

Porovic et al. (2016) stated that DS is associated with an increased incidence of dental caries. However, Subramaniam et al. (2014) reported that DS is related to a decreased incidence of dental caries, and AlSarheed M. (2015) found no difference in the occurrence of dental caries between individuals with DS and non-DS patients.[6-8]

Several factors influence the relationship between DS and increased dental caries, including deficiencies in cognitive, motor, and mental development, which affect oral hygiene behavior and require parental involvement. Common oral findings in these children include mouth breathing leading to xerostomia and hypotonic facial muscles, which increase food residue stagnation.[9,10]

Children with DS living in lower socio-economic conditions also face challenges such as uncontrolled cariogenic diets and a lack of interest, involvement, and awareness among parents regarding dental visits. Age also influences the increased occurrence of dental caries in DS patients. Porovic et al. (2016) highlighted that the longer exposure time in the oral environtment of permanent teeth compared to primary teeth results in a higher incidence of caries in permanent teeth. These factors contribute to the association between DS and increased dental caries.[6,11]

Conversely, indicators that influence the relationship between DS and decreased dental caries, as noted by Sekerchi et al. (2014), include delayed eruption of both primary and permanent teeth, reducing the exposure time of teeth to the oral environment, and congenital oligodontia, resulting in fewer teeth in the oral cavity. Differences in saliva composition also affect caries, with increased concentrations of IgA, pH, electrolytes (calcium, phosphate, chloride, sodium, and potassium), and higher salivary buffer capacity reducing caries risk by inhibiting S. mutans growth and preventing tooth demineralization. Additionally, higher socioeconomic status in families of DS patients lowers the incidence of dental caries due to increased awareness and regular dental care.[12]

S. mutans Biofilm Formation

Dental biofilm, also known as dental biofilm plaque, is a complex community of different types of bacteria. These biofilms have a three-dimensional organization in which microorganisms are arranged and surrounded by an extracellular matrix. Biofilm production begins with interactions between surface and foodborne bacteria in response to appropriate environmental stimuli.[5] Protein factors associated with the development of dental caries and play a role in the virulence of S. mutans by promoting biofilm formation are GTF, GBP and SAg. As described above, S. mutans biofilm formation is controlled by two independent mechanisms: sucrose dependent and sucrose-independent. In addition to GBPs, adhesins and other surface receptors on S. mutans facilitate its attachment to tooth surfaces, particularly in the presence of sucrose. These receptors help the bacteria adhere directly to the glucan-rich matrix or the tooth enamel itself.[13]

In the absence of sucrose, SAg leads to mediates S. mutans adhesion and bacterial aggregation. In the presence of sucrose, GTF including GTF B, GTF C, and GTF D, secreted by S. mutans use the glucose moiety of sucrose as a substrate to form

growing glucan polymers, also called exopolysaccharides. S. mutans synthesizes at least four glucan-binding proteins (GBP), including GBP A, GBP B, GBP C, and GBP D, which are thought to promote organism adhesion and biofilm formation.[14]

GBP, GTF as Sucrose-dependent mechanisms of S. mutans

S. mutans expresses GBP on its cell surface. These proteins are specifically designed to recognize and bind to the glucans produced by GTF. After glucan production, GBP on the surface of S. mutans bind to the glucan chains, anchoring the bacteria to the developing biofilm on the tooth surface. GBP as one of sucrose-dependent component promote organism adhesion and biofilm formation through bind to S. mutans. The functions of GBP are related to changes in biofilm production, cell wall strength, peptidoglycan hydrolase action, dextran-dependent accumulation, and lipase action.[15]

In the presence of sucrose, the production of glucans and the binding of S. mutans to glucans via GBP leads to the formation of a dense biofilm, which protects the bacteria from environmental stress and enhances their ability to thrive in the oral cavity. This biofilm is a major factor in the development of dental caries, as S. mutans within the biofilm can ferment carbohydrates, producing lactic acid that demineralizes tooth enamel.[16]

There are several types of GBPs, including GBP-A, GBP-B, GBP-C, and GBP-D, each playing distinct roles in adherence and biofilm formation. GBP A contains 563 amino acids and has a molecular weight of 59 kD. The carboxyl termini of GBP A and GBP D are identical to the glucan-binding domain of GTF enzymes. Additionally, GBP A requires α-1,6 bonds for adhesion. This protein promotes binding to the cell surface and appears to be involved in cariogenicity of S. mutans both in vivo and in vitro. GBP A, GBP C, and possibly GBP D are involved in optimal aggregation and formation of plaque biofilms.[17]

Salivary Agglutinin (SAg) as Sucrose-independent adhesion of S. mutans

Saliva refers to a clear, weak substance consisting of secretions from the major salivary glands (i.e.,submandibular, parotid, and sublingual) and secretions from various salivary glands. Minor salivary glands are distributed throughout the oral mucosa and divided into labial, buccal, palatal, lingual, and retromolar glands. Saliva secretion is a two-step process in the acinar cells secrete a watery plasma-like fluid in the first step, which is modified during transmission through the waterproof ductal cell system. The autonomic nervous system regulates saliva secretion through a signal transduction system that links receptor stimulation with ion transport mechanisms and protein secretion. Saliva secreted from the salivary glands provides "moisture" essential for bacterial growth.[18]

SAg also called gb340 is present in human saliva and regulates the accumulation of S. mutans via the P protein. Interaction between S. mutans and SAg mediates sucrose-independent adhesion and promotes bacterial accumulation on tooth surfaces. This antigen binds directly to salivary follicles and mediates bacterial adhesion even in the absence of sucrose. SAg also plays a role in bacterial aggregation. By binding to S. mutans and other bacteria, SAg can promote bacterial clumping, which can either facilitate the formation of biofilms or, conversely, help clear the bacteria through swallowing if the aggregates are large enough.[19]

Expression GBP, GTF and SAg in DS Children

Trisomy in DS children sufferers leads to facial anomalies, malocclusion and oromotor dysfunction that manifests in salivary gland secretion. As a result, there are changes in salivary composition and immune response in DS children that affect the microbial environment of the oral cavity. Children with DS exhibit an altered cellular immune response characterized by differences in the activation and function of immune cells such as B cells and T cells. This can lead to a decreased ability to produce adequate immunological responses to infections or vaccinations compared to typically developing peers. Compromised immune system may be associated with increase of sensitivity to periodontal disease due to functional defects of cellular polymorphonuclear leukocyte (PMN) and monocyte found.[21]

DS children often exhibit a lower salivary flow rate, leading to a dry mouth and related oral health challenges. In contrast, typical children generally maintain a normal salivary flow, which supports effective oral hygiene. The effectiveness of GBP in promoting adherence and biofilm formation may be particularly pronounced in these children due to potential alterations in salivary flow and composition, which can influence the availability of substrates for glucan production and the overall microbial balance. Consequently, the robust adherence mechanism mediated by GBP can contribute to an increased risk of dental caries in DS children.[20,21]

According to a study of Culp et al (2021), the flow rate in children with DS was significantly lower than typically children. The increased activity of SAA (a glycoprotein that makes up the salivary pellicle) in DS children plays an important role in the colonisation and metabolism of S. mutans, which causes dental plaque formation and caries. Although

amylase itself is not a direct cause of caries, its activity may contribute to the formation of an environment that favors the formation of dental plaque and caries.[22]

SAA is a component of acquired enamel pellicle and as an adhesion of bacteria to the tooth surface, where this molecule binds to streptococcus bacteria. The amount is about 40-50% of the total salivary protein. Monea's research (2018), shows that SAA greatly affects the occurrence of caries, based on the data collected, a person with a high caries risk has more SAA levels than a person with a low caries.[23]

Study of Siquiera (2015), shows differences in saliva composition and flow can affect the condition of SAg. Low salivary flow can increase the activity of SAg, thereby impacting on their role in bacterial aggregation and attachment. Increases of SAg in DS children support the function that increase adherence, facilitate S. mutans colonisation and contribute to a higher risk of dental caries.[24]

In DS children, there may be an increased consumption of fermentable carbohydrates providing more substrates for GTF activity. This can enhance glucan production and subsequently increase the adhesive capabilities of S. mutans, further contributing to the formation of cariogenic biofilms.[25]

The combined effect of GBP, GTF and SAg significantly impacts the adherence mechanism of S. mutans in DS children. GBP and GTF work synergistically: GTF synthesizes the glucans from dietary sugars, and GBP binds these glucans, securing the bacteria to the tooth surface. Meanwhile, salivary agglutinin can either promote bacterial clearance or enhance their adhesion, depending on the oral environment. In DS children, the unique salivary and immune profiles often favor conditions that enhance bacterial adherence and biofilm formation. This interplay of mechanisms results in a higher susceptibility to dental caries, necessitating specialized dental care and preventive strategies to manage oral health effectively in these children.[26,27]

Conclusion

The adherence mechanisms of S. mutans, particularly involving GBP, GTF, and SAg play a significant role in promoting cariogenic biofilm formation. GBP, GTF and SAg levels increase with higher DMFT levels in DS children. Based on data collected, it was found that GTF, GBP and SAg are related to caries risk factors in DS children by adherence mechanism.

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Conflict of Interest

The authors report no conflict of interest.

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