The Role of Genetic on the Risk for Caries in Primary Teeth: A Scoping Review

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Abstract

Caries is the most common chronic infectious disease in children. It is caused by some correlating factors, including genetic. Genetic factor plays role in caries initiation and development. Moreover, genetic factor can affect dental enamel formation, dental morphology, salivary flow, and salivary composition.

This study aimed to review the role of genetic factor on risk for dental caries in primary teeth. We performed scoping review. Systematic literature searches were conducted using several electronic databases, such as PubMed and Google Scholar. Screening guidelines were conducted according to PRISMA Extension for Scoping Reviews (PRISMA-ScR) guidelines. Inclusion and exclusion criteria were determined based on Population, Concept, and Context (PCC) framework. A total of 12 eligible studies was included in the analysis.

We showed that genetic factor is associated with risk for dental caries in primary teeth. The genetic factor was obtained from inherited fingerprint patterns, gene polymorphism, blood types, and parental consanguinity.

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Introduction

Teeth are one of the most important organs in human body. They involved in mastication and swallowing process, speech, and have aesthetic value. Food particles on teeth contribute to brittle or decayed teeth, which can lead to impaired mastication and digestion in children.[1] Primary teeth are the first set of teeth in children, which usually begin to erupt at 6 months of age and are replaced by permanent teeth later in life. Primary teeth affect growth and development of dental arches and maintain integrity of dental arches until permanent teeth eruption.[2]

Dental caries are known as a complex chronic infectious disease given its long disease course.[3] Caries pattern in children differs from adults, depending on age and eruption sequence. Prevalence of dental caries increases with age as the most recent erupted teeth are more susceptible to caries. Dental caries in children in general is multifactorial. It is possible that several genes contribute to caries risk. Most diseases with complex pathophysiology process are affected by genetic and environment.[4,5] Blum states that general health is influenced by four factors, namely health services, environment, behavior and genetic.[6] Many previous studies said that the prevalence of caries was influenced by lifestyle, genetic factors, biogeochemical factors, climatic factors and medical factors.[7]

Genetics studies the role of heredity and genetic variation on living organisms.[8] Gene is the basic unit of heredity and located in the chromosome. Each gene responsible for certain trait or characteristic.[9] Dental enamel structure, immune response toward cariogenic bacteria, dental morphology, salivary composition, and salivary flow rate are suggested to be related with genetic factors affecting risk for caries. The gene involving in immune system is associated with enamel defects. Dental caries is more common in children with enamel defects, characterized by rough enamel surface that may affect food retention.[4,10,11]

According to studies by *University of Pittsburgh School of Dental Medicine*,

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approximately 60% cases of dental caries is caused by genetic factor. Among children, risk for dental caries may be affected by parental behavior. Pediatric dental health is indeed associated with genetic and parental behavior. Genetics play an essential role in craniofacial development, dental anomalies, and various dental diseases including caries.[12-14] Therefore, we aimed to assess the role of genetics on caries risk in primary teeth using scoping review method.

Materials and methods

Scoping review is a systematic and comprehensive method to identify studied literatures, obtained from databases, based on relevant research topics. In this study, relevant literatures were identified from electronic databases, namely PubMed and Google Scholar. Literatures were determined according to *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guideline. The concept population, concept, and context (PCC) was applied. The population was children aged 3 – 6 years. The concept was caries in primary teeth. The context was genetic factor. Inclusion criteria were original research, studies in Indonesian or English, studies were published between 2017 and 2022, and full paper could be accessed. Exclusion criteria were systematic review, meta-analysis, case report, and opinion article. We used Boolean search as follows: *"dental caries" AND "genetic factors" AND "pediatric dentistry" AND "risk factors*". PRISMA flowchart is presented in Figure 1.

Results

Literature searching was performed. A total of 355 studies from Google Scholar and 32 studies from PubMed were identified, of which 16 studies were identified as identical in both Google Scholar and PubMed. After the duplication was eliminated, there were 351 studies. Thereafter, 319 studies were excluded based on the eligibility criteria. Finally, 12 studies were included.

Data from the included study were extracted and are presented in Table 1. In this table, we showed authors names, publication years, countries, study design, sample size, and the result of the studies.

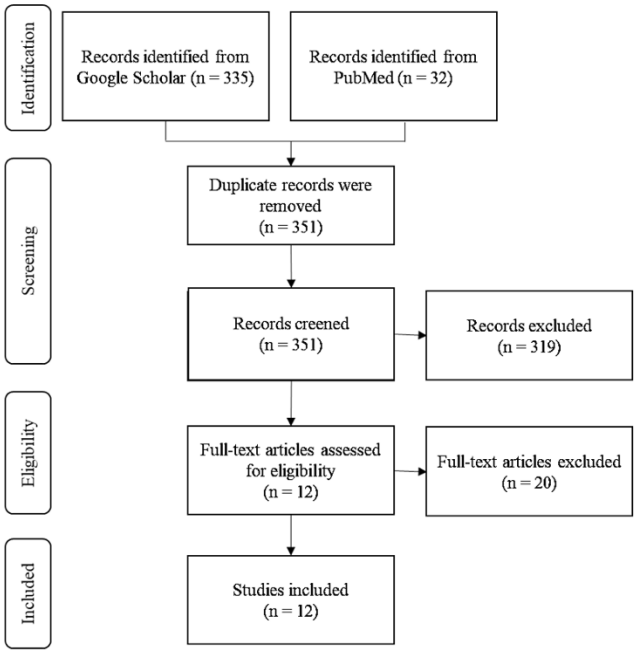

Figure 1. PRISMA flowchart diagram.

Discussion

As a result of a thin primary tooth enamel, dental caries is the most common infectious dental disease and the main cause of tooth loss in children. Several studies have reported the importance of genetic factor in dental caries.[15] According to the 12 studies included in this scoping review, genetic factors affecting dental caries include inherited fingerprint pattern, gene polymorphism, and offspring of consanguineous parents.

Fingerprint has become the best and most common approach to diagnose physiological, medical, and genetic conditions during embryogenesis.[16] In dentistry, fingerprint patterns show individual susceptibilities to periodontitis, dental caries, and various congenital anomalies. Most fingerprints consist of three patterns: *arches, whorls,* dan *loops.*[17] Asalui and Susilowati (2018) based on their research, mention that dermatoglyphic pattern has been considered as a marker for dental caries given that both epithelial cells in finger and enamel are from ectoderm and are developed in the same intrauterine period. If fetal dermal is damaged, dental anomalies may consequently occur.[18] This study was conducted by taking fingerprint patterns using ink in children with and without dental caries, respectively. A study by Matar et al (2018) showed that patients with

fingerprint pattern of whorl had higher risk for caries. Therefore, fingerprint patterns can be utilized as a genetic marker for dental caries.[19]

Polymorphism is a gene change or mutation that results in the variation of protein function without any change in protein structure. Genetic polymorphism refers to the presence of ≥2 variants of a particular DNA sequence which takes place among different individuals or populations. The most common polymorphism involves variation in single nucleotide (i.e., single nucleotide polymorphism [SNP]). Polymorphism does not have any clinical manifestation, but it affects individual susceptibility to certain disease. Polymorphism in enzyme coding gene that involves in homocysteine metabolism (such as methionine synthase [MTR] and methionine synthase reductase [MTRR]) may affect folic acid and vitamin B12 metabolism. This study was conducted by performing oral health and dental assessment to determine caries and genotype analysis extracted from buccal cell.[20,21] A study by Antunes et al (2018) in Brazil demonstrated that MTR and MTRR genes affect teeth enamel, and hence increase risk for dental caries. Similarly, previous study by Kwan et al (1998) reported a higher incidence of caries among children with low folic acid concentration.[22]

Genetic variation influencing taste preferences has been suggested as a risk factor for dental caries. Taste preferences are determined by G protein-related heterodimer coded by protein in the TAS1R gene family. In this study, dental caries was assessed clinically, and salivary sample was collected for DNA extraction. Study by Arid et al (2020) in Brazil showed that the TAS1R family played a small role in caries development. On the contrary, study by Erikson et al (2019) demonstrated that the TAS1R family affected dental caries among children in Sweden. The discrepancy between those findings might be due to difference in dietary pattern and genetic profile between the study populations.[23]

Single Nucleotide Polymorphisms (SNPs), including enamelin (ENAM), matrix metallopeptidase-20 (MMP20), TAS2R38, lactotransferrin (LTF), are genes associated with enamel formation, taste preference, immune response. These SNPs are associated with caries risk in children. Study by AlMarshad et al (2021) in Saudi Arabia showed that MMP20 was the most predominant gene in the risk for caries. Matrix metallopeptidase (MMP) is a gene family involved in extracellular matrix degradation before mineralization. In addition, MMP20 gene affects enamel formation. Study by Borilova Linhartova et al (2020) indicated the evidence of association between MMP20 gene and severity of caries in primary teeth in The Czech Republic was lacking. According to a study by Abbasoglu et al (2015), there was no association between MMP20 variant and early childhood caries (ECC) among Turkish children. Taken this together, it is possible that MMP20 gene has different effect on dental caries, depending on demography, ethnicity, and other backgrounds in the population.[24]

The cause of dental caries is complex interaction between gene and environment.[2] As a biological macromolecule in nucleus, vitamin D receptor (VDR) gene acts to modulate biological function of vitamin D main metabolites. These metabolites play an essential role in teeth formation, particularly in enamel and dentin calcification. Vitamin D is important to maintain equilibrium between phosphate and calcium ions, which is crucial in protecting and upholding dental structure. In this study, visual examination was performed, and DNA sample from buccal epithelial cells was extracted.[25]

Study by Kong et al (2017) in China reported a gene from VDR family, namely Bsml, contains a genotype that may increase risk for caries in primary teeth.[26]On the other hand, study by Qin et al (2019) in China found no association between caries risk in primary teeth with any variants from VDR family. These findings indicate that association between gene polymorphism and dental caries may vary, depending on geographical area, ethnicity, baseline teeth assessment, and research methodology used.[27]

The role of SNPs was evaluated by investigating the association of caries and amelogenin x (AMELX), ameloblastin (AMBN), tuftelin-1 (TUFT1), and kallikrein 4 (KLK4). In this study, visual assessment was performed, and DNA sample was collected from buccal swab. A study by Gerreth et al (2017) in Poland indicates SNPs in AMELX, AMBN, TUFT1, KLK4 as risk factors for dental caries in children. Amelogenin, ameloblastin, and tuffelin are main components of dental enamel. They regulate their formation and degrade enamel protein. On the other hand, kallikrein can modify protein function and interrupt enamel mineralization. Genetic change

in enamel gene may influence enamel microhardness. Therefore, there is a strong association between these gene variants with dental caries in children.[28]

Gene polymorphism in enamel formation, including dentin sialophosphoprotein (DSPP), runt-related transcription factor 2 (RUNX2), kallikrein 4 (KLK4), is associated with caries development. In this study, dental and oral health was assessed to evaluate caries by calculating CEFT index. Moreover, salivary sample from buccal was collected. A study by Sanhueza et al (2021) in Chile found an association of dental caries in young children with DSPP and RUNX2 genes, but not with KLK4. DSPP is an essential protein in enamel formation. RUNX2 regulates differentiation of osteoblasts, which are responsible for matrix secretion and mineralization. To achieve good mineralization, adequate differentiation and quantities of odontoblasts are required.[29]

Polymorphism in enamel formation gene (MMP) may contribute to change in enamel structure. Consequently, enamel porosity and mineral composition may be reduced. In this study, intraoral examination was performed clinically. Salivary sample was extracted as DNA genome. A study by Dindaroglu et al (2021) in Turkey showed that genetic variant in collagenase-3 (MMP13) gene was associated with increased risk for caries. MMP-13 may affect caries development through activating other proteases involved in dental caries. Other studies found an increase in MMP13 expression along with the spread dentin sialophosphoprotein (DSPP), runt-related transcription factor 2 (RUNX2), kallikrein 4 (KLK4ing of dentin caries.[30]

Genetical difference in tasting ability can affect eating behavior and nutritional intake. In this study, intraoral examination was performed, and salivary sample for DNA extraction was collected. A study by Kilic et al (2022) in Turkey showed TAS1R2 gene contributes to caries susceptibility. TAS1R2 is gene associated with sweet taste receptor, a taste that children like. Carbohydrate consumption is associated with caries, and it may be affected by genetic code associated with taste perception.[31]

Blood group is an inherited genetic character. Some studies have investigated the association between blood group and systemic diseases, such as cancer, diabetes mellitus, skin diseases, genetic diseases, and dental caries. The phenotype association between blood group and dental caries (based on DMFT or DEFT score) might be due to secretion of blood group component in saliva (i.e., ABO blood group antigen is not only presence in red blood cells, but also in other body fluids including saliva.[31] Blood group component secreted in saliva contributes to accumulation of microorganisms in oral cavity.[32-34]

The study was conducted by collecting blood sample and oral health screening. A study by Govindaraju et al (2018) in India showed a significant association between blood group and dental caries in children. Blood group AB had a higher risk for ECC, whereas blood group O had a lower risk. A lower prevalence of ECC in particular blood group may be due to increase of antibody concentrations to kill bacteria. Hence, blood group is considered as potential indicator for ECC development.[35]

Consanguineous marriage has been reported to be associated with genetic disorders and some other diseases, including dental caries, in their offspring. In this study, clinical assessment for caries was performed and parents were interviewed comprehensively. A study by Khan et al (2020) in India demonstrated a higher DEFT score among offspring from consanguineous parents. A study in Najran found that genetic contributes to high prevalence of caries in area where consanguineous marriage is common. A study in Saudi Arabia, a country where consanguineous marriage is likely, indicated that consanguinity can be a genetic component that can cause high caries prevalence.[36]

Genetic has been studied intensively, and recent studies have reported the potential contribution of genetic on the risk for dental caries. Some studies also showed significant genetic profile difference between offspring from consanguineous parents and offspring from non-consanguineous parents. Although consanguineous marriage is common, its effect on oral diseases needs to be investigated further.[37]

Conclusions

Based on the results of the analysis that has been carried out, this study shows that genetic factor can increase the risk for dental caries in primary teeth. Genetic factor includes

inherited fingerprint pattern, gene polymorphism, blood groups, and offspring from consanguineous marriage. Genetic influences enamel structure formation. The risk for caries differs by geographical area, ethnicity, and population demographics.

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Declaration of Interest

The authors declare that there is no conflict of interest

No	Author and year	Country	Study design	Sample size	Genetic factors	Results
1.	Matar, 2018	Egypt	*Case control*	60	Fingerprint pattern in children	Most fingerprint patterns in children without caries had loops, while fingerprint patterns in children with caries were dominated by whorls. Fingerprint patterns were considered as a genetic marker for dental caries.
2.	Antunes et al,2017	Brazil	*Cross-sectional*	488	MTR and MTRR gene expression	MTR and MTRR expressions, which involve in folic acid and vitamin B12 metabolism, could influence enamel development. Hence, it may increase risk for caries.
3.	Arid et al, 2020	Brazil	*Cross-sectional*	525	TAS1R family	TAS1R family played a small role in caries development among children.
4.	AlMarshad et al, 2021	Saudi Arabia	*Case control*	360	*Single Nucleotide Polymorphisms* (SNPs) on various genes	MMP20 gene might affect risk for dental caries development.
5.	Kong et al, 2017	China	*Case control*	380	VDR gene family	Bsml polymorphism of the VDR gene was associated with increased risk for dental caries in primary teeth.
6.	Qin et al, 2019	China	*Case control*	549	*Single Nucleotide Polymorphisms* (SNPs) on vitamin D receptor (VDR) genes	No VDR gene variant was associated with dental caries in primary teeth.
7.	Gerreth et al, 2017	Poland	*Case control*	262	*Single Nucleotide Polymorphisms* (SNPs) on various genes	SNPs on AMELX, AMBN, TUFT1, KLK4 genes were suggested to be risk factor for pediatric dental caries.
8.	Sanhueza et al, 2021	Chile	*Cross-sectional*	125	Polymorphism in the DSPP, RUNX2, and KLK4 genes	DSPP and RUNX2 genes were associated with incidence of dental caries among young children. KLK4 gene was not associated with increased likelihood for dental caries.
9.	Dindaroglu et al, 2021	Turkey	*Cross-sectional*	200	Polymorphism in the MMP13 and MMP20 genes	Genetic variant in MMP13 gene increased caries risk.
10.	Kilic et al, 2022	Turkey	*Cross-sectional*	178	Polymorphism in TAS1R2 gene	TAS1R2 gene increased susceptibility for dental caries.
11.	Govindaraju et al, 2018	India	*Cross-sectional*	500	Blood group in children	There was a significant association between blood types and dental caries in children. Blood type is considered as an inherited genetic material.
12.	Khan et al, 2020	India	*Cross-sectional*	2000	Offspring from parents with consanguinity (incest)	DEST score was higher in children born from parents with consanguinity. Parental consanguinity was considered as a risk factor for dental caries in young children.

Table 1. Data extraction.

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