Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

Relation of Amelogenin Gene Polymorphisms to Dental Caries Among Iraqi Teenagers

Elaf Abdulkareem Alidan[1], Ahlam Taha Mohammed[2], Batool Hassan Al-Ghurabi[2]

1College of Dentistry, University of Ashur, Baghdad, Iraq

2College of Dentistry, University of Baghdad, Baghdad, Iraq

Abstract

Objective: To examine the relationship between dental caries and single nucleotide polymorphisms (SNPs) in AMELX gene.

Methods: This study was a comparative cross- sectional study encompassing 78 adolescents (aged 13-15 years) was conducted. All of them were examined for their oral and dental status under the WHO recommended criteria, and clinical information such as DMFT and DMFS were evaluated. Individuals whose DMFT and DMFS index lower than 2 were designated 'very low caries experience' and higher than 9 were designated 'higher caries experience'. Genomic DNA was extracted from saliva samples, and single nucleotide polymorphisms of AMELX were genotyped. Genotyping of three SNPs (rs17878486, rs5933871, rs5934997, intron) in AMELX gene was determined by direct sequencing and analyzed with SNPStats. Chi-square was used to compare allele and genotype frequencies between cases and controls.

Results: There was no significant difference between the high and low caries groups but in high caries group, it showed a deviation from Hardy-Weinberg equilibrium with a significant difference among the three genotypes (p=0.013) in rs5933871 and rs5934997, while a highly significant difference in rs17878486 for both high and low caries groups (p=0.000 and p=0.001). A highly significant and positive correlation between rs17878486 with DMFS in the control group and a positive significant correlation between rs17878486 and DMFT.

Conclusion: Although no significant difference of the investigated SNPs of AMELX between high and low caries groups, but rs17878486 had a significant and positive correlation with DMFT and DMFS which made this SNP as marker for caries susceptibility.

Keywords: AMELX, Dental Caries, Health Risk, Amelogenin, Single Nucleotide Polymorphisms.

Citation: Alidan et al. (2025) Relation of Amelogenin Gene Polymorphisms to Dental Caries Among Iraqi Teenagers. Dentistry 3000. 1:a001 doi:10.5195/d3000.2025.842
Received: February 2, 2025
Accepted: March 9, 2025
Published: May 2, 2025

Email: elaf.abdukareem@au.edu.iq.

Introduction

Dental caries is a highly prevalent infectious oral disease in humans known for its complexity, is influenced by multiple factors, including lifestyle, socioeconomic status, genetic elements, and oral environmental characteristics [1]. Despite the advancement of methods for prevention and treatment, dental caries remains a significant concern, impacting the quality of life [2,3].

Findings from prior studies have illuminated characteristics associated with processes linked to caries development, categorized into the following four groups:

1) Salivary composition and flow: Saliva contains elements that possess the capability to directly combat cariogenic bacteria. Additionally, it is abundant in calcium and phosphates, which play an active role in the re-mineralization of tooth enamel. The mechanical action of saliva flow aids in dislodging pathogens such as viruses, bacteria, and yeast from both teeth and mucosal surfaces. Moreover, saliva can aggregate microbes, facilitating their removal through swallowing before they establish firm attachment [4,5].

2) Tooth morphology: Malposition of the teeth, deep anatomical grooves, and retention regions resulting from the natural shape of the tooth structure can make brushing and fluoride penetration difficult, and are therefore thought

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

to be caries risk factors, particularly for pit and fissure caries [6].

3) Dietary and taste preferences: Diet indeed has a significant impact on oral health, including its influence on plaque formation, the presence of cariogenic microorganisms, and overall caries risk. diet can have various potential impacts. It has the potential to affect both the quantity and composition of plaque buildup and debris on teeth, as well as the presence of cariogenic microorganisms. The interplay of factors such as the cariogenic nature of specific foods (like sucrose), eating frequency, and the physical characteristics of the diet can individually or collectively influence the development of tooth decay. Conversely, taste preferences play a significant role in shaping dietary habits. People often make food choices based on their taste preferences. For instance, children tend to have a strong affinity for sweet foods while typically avoiding bitter flavours. As a result, they are more likely to consume foods that align with their favourite tastes [7,8].

4) Enamel and dentin formation: Dental caries is an erosive process that causes tooth enamel to be lost, causing the enamel and dentin to continue to deteriorate, and finally leading to the formation of cavities within the tooth structure. The main cause of caries is enamel demineralization, while on the other hand, remineralization of enamel can act as a preventative measure against caries. As a result, a person's vulnerability to caries is greatly influenced by the genes that control how enamel and dentin are formed. Regarding how genes associated with enamel may affect the emergence of carious lesions, there are two tenable hypotheses: they may increase enamel thickness and fluoride concentration, increasing protection against caries, or they may interact with oral microorganisms like Streptococcus mutans, affecting caries vulnerability [9].

Mature tooth enamel is primarily composed of inorganic material, accounting for more than 90% of its composition. However, during its development, enamel initially contains an organic matrix, which is gradually replaced by mineral compounds. Several chemical and physiological processes, including the secretion, assembly, folding, and degradation of proteins, mineral growth, and gene expression, contribute to the formation of tooth enamel. Both the quality and quantity of enamel have a direct impact on susceptibility to dental caries. Enamel-formation genes, such as *AMBN*, *AMELX*, *TUFT1*, *KLK4*, and *ENAM*, constitute a group of genes involved in the process of odontogenesis in dentin-containing teeth [10,11]. Previous studies have explored the association between genetic variants in this gene cluster and susceptibility to dental caries, yielding varying and inconclusive results [12-14].

The most significant secretory proteins can be categorized into amelogenin and non-amelogenin proteins [15]. Amelogenins are highly conserved proteins and make up over 90% of the extracellular matrix protein content. They are believed to play a crucial role in directing the growth and organization of enamel crystals [16,17].

Non-amelogenin proteins encompass ameloblastin, enamelin, and tuftelin. Ameloblastin serves as a cell adhesion protein responsible for preserving rod integrity and regulating cell differentiation. Enamelin, in cooperation with amelogenin, plays a role in controlling elongated growth and mineral nucleation, while tuftelin is suggested to potentially act as a nucleator for enamel crystallites [16].

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

In Iraq, research has been conducted to establish connections between genetic factors with other diseases like periodontal disease and among individuals with type 2 diabetes [18,19]. However, no prior studies have been able to establish links between genes related to enamel development, such as amelogenin (*AMELX*) gene in the saliva of individuals with dental caries. As a result, the primary objective of the present study was to identify and assess individuals susceptible to dental caries, while comprehending the role of genes in the development of this condition. The study encompassed examinations aimed at determining whether variations in the amelogenin gene were linked to the occurrence of caries.

Dental caries is a highly prevalent infectious oral disease in humans known for its complexity, is influenced by multiple factors, including lifestyle, socioeconomic status, genetic elements, and oral environmental characteristics [1]. Despite the advancement of methods for prevention and treatment, dental caries remains a significant concern, impacting the quality of life [2,3].

Findings from prior studies have illuminated characteristics associated with processes linked to caries development, categorized into the following four groups:

1) Salivary composition and flow: Saliva contains elements that possess the capability to directly combat cariogenic bacteria. Additionally, it is abundant in calcium and phosphates, which play an active role in the re-mineralization of tooth enamel. The mechanical action of saliva flow aids in dislodging pathogens such as viruses, bacteria, and yeast from both teeth and mucosal surfaces. Moreover, saliva can aggregate microbes, facilitating their removal through swallowing before they establish firm attachment [4,5].

2) Tooth morphology: Malposition of the teeth, deep anatomical grooves, and retention regions resulting from the natural shape of the tooth structure can make brushing and fluoride penetration difficult, and are therefore thought to be caries risk factors, particularly for pit and fissure caries [6].

3) Dietary and taste preferences: Diet indeed has a significant impact on oral health, including its influence on plaque formation, the presence of cariogenic microorganisms, and overall caries risk. diet can have various potential impacts. It has the potential to affect both the quantity and composition of plaque buildup and debris on teeth, as well as the presence of cariogenic microorganisms. The interplay of factors such as the cariogenic nature of specific foods (like sucrose), eating frequency, and the physical characteristics of the diet can individually or collectively influence the development of tooth decay. Conversely, taste preferences play a significant role in shaping dietary habits. People often make food choices based on their taste preferences. For instance, children tend to have a strong affinity for sweet foods while typically avoiding bitter flavors. As a result, they are more likely to consume foods that align with their favorite tastes [7,8].

4) Enamel and dentin formation: Dental caries is an erosive process that causes tooth enamel to be lost, causing the enamel and dentin to continue to deteriorate, and finally leading to the formation of cavities within the tooth structure. The main cause of caries is enamel demineralization, while on the other hand, remineralization of enamel can act as a preventative measure against caries. As a result, a person's vulnerability to caries is greatly influenced by the genes that control how enamel and dentin are formed. Regarding how genes associated with enamel may affect the emergence of carious

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

lesions, there are two tenable hypotheses: they may increase enamel thickness and fluoride concentration, increasing protection against caries, or they may interact with oral microorganisms like Streptococcus mutans, affecting caries vulnerability [9].

Mature tooth enamel is primarily composed of inorganic material, accounting for more than 90% of its composition. However, during its development, enamel initially contains an organic matrix, which is gradually replaced by mineral compounds. Several chemical and physiological processes, including the secretion, assembly, folding, and degradation of proteins, mineral growth, and gene expression, contribute to the formation of tooth enamel. Both the quality and quantity of enamel have a direct impact on susceptibility to dental caries. Enamel-formation genes, such as *AMBN*, *AMELX*, *TUFT1*, *KLK4*, and *ENAM*, constitute a group of genes involved in the process of odontogenesis in dentin-containing teeth [10,11]. Previous studies have explored the association between genetic variants in this gene cluster and susceptibility to dental caries, yielding varying and inconclusive results [12-14].

The most significant secretory proteins can be categorized into amelogenin and non-amelogenin proteins [15]. Amelogenins are highly conserved proteins and make up over 90% of the extracellular matrix protein content. They are believed to play a crucial role in directing the growth and organization of enamel crystals [16,17].

Non-amelogenin proteins encompass ameloblastin, enamelin, and tuftelin. Ameloblastin serves as a cell adhesion protein responsible for preserving rod integrity and regulating cell differentiation. Enamelin, in cooperation with amelogenin, plays a role in controlling elongated growth and mineral nucleation, while tuftelin is suggested to potentially act as a nucleator for enamel crystallites [16].

In Iraq, research has been conducted to establish connections between genetic factors with other diseases like periodontal disease and among individuals with type 2 diabetes [18,19]. However, no prior studies have been able to establish links between genes related to enamel development, such as amelogenin (*AMELX*) gene in the saliva of individuals with dental caries. As a result, the primary objective of the present study was to identify and assess individuals susceptible to dental caries, while comprehending the role of genes in the development of this condition. The study encompassed examinations aimed at determining whether variations in the amelogenin gene were linked to the occurrence of caries.

Material and Methods

Design and sample

In this particular, a group of 78 healthy and unrelated Iraqi adolescents were included. Among them, 39 subjects were had a high caries score with a DMFT (decayed, missing, filled teeth) value greater than 9, whereas the other group should have had a low caries score with a DMFT value less than 2 [20]. All participants had complete permanent dentition and lacked any dental anomalies. Prior to the examination, consent was obtained from the parents of the patients.

The inclusion criteria encompassed individuals aged between 13 and 15 years, who were part of the Iraqi Arab Population. They should not have had any systemic diseases or taken any medications in the preceding three weeks.

Exclusion criteria involved patients with systemic diseases, cleft lips,

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

congenital anomalies, widespread dental issues, or those who were using fixed orthodontic appliances. Participants who had received fluoride supplements or had undergone fissure sealant treatment were also excluded. Individuals falling within the DMFT range of more than 2 but less than 9 were not considered for the study.

Ethical considerations

The study was conducted in accordance with the ethical principles that had their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee of Baghdad university, college of dentistry according to the document number 366 (including the number and the date in 1/8/2021) to get this approval.

Measures

In this study, various demographic details such as age and gender, along with medical and dental histories, were recorded. Unstimulated saliva was collected, followed by an intraoral examination using disposable instruments. The evaluation of tooth decay was scored based on the criteria set by the World Health Organization [21], utilizing the "decayed missing and-filled teeth/surfaces" (DMFS/DMFT) index for permanent teeth, without the use of radiographs. The severity of dental caries was assessed according to WHO's 1976 guidelines [22].

Unstimulated saliva was gathered over a span of 5 minutes. Participants were instructed to expel saliva through a funnel into a sterilized tube that featured a scale, and this was repeated every minute, following the methodology outlined by Navazesh in 2008 [23]. After the completion of saliva collection, the samples were divided into two segments. In the case of the portion meant for determining lactoferrin concentration, it was subjected to centrifugation at 4000 revolutions per minute (rpm) for a duration of 5 minutes. This process was undertaken to segregate the mucins. Subsequently, the clear supernatant was separated using a micropipette and was then stored at approximately -80°C, as per the manufacturer's instructions (MyBioSource, U.S.A.). For the other portion of the sample intended for DNA extraction, centrifugation was performed at a speed of 12000 revolutions per minute (rpm) for a span of 3 minutes.

DNA Extraction and Quantitation: The genomic DNA was extracted from the saliva samples using the ReliaPrep™ Saliva gDNA Miniprep System protocol by Promega. To determine the concentration of the extracted DNA and assess the quality of the samples for subsequent procedures, the Quantus Fluorometer was employed.

Primer preparation, optimization and PCR amplification: The primers were provided by Macrogen Company in a lyophilized (freeze-dried) state. The DNA template was subjected to amplification using the same pair of primers, consisting of a forward primer and a reverse primer. Following the PCR (polymerase chain reaction) amplification process, agarose gel electrophoresis was utilized to verify the successful amplification. The efficacy of the PCR was entirely reliant on the quality of the extracted DNA.

PCR products were submitted for Sanger sequencing using the ABI3730XL automated DNA sequencer from Macrogen Corporation – Korea. Subsequently, the outcomes were delivered via email and

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

subsequently assessed using the Geneious software.

ELISA assay for measuring lactoferrin levels: The collected saliva samples from participants were examined for lactoferrin concentration using commercially available ELISA kits in accordance with the manufacturer's instructions (MyBioSource, U.S.A.).

Statistical analysis

This study used Computerized software statistical package for social science (SPSS version-24) was used. The variation of frequencies between groups were analyzed using Chi- square test. Hardy-Weinberg equilibrium (HWE) was used to calculate the expected common homozygotes, expected heterozygotes, expected rare homozygotes. Chi-square test was used to find out genotype deviation from HWE, and to compare the distributions of genotypes and allele frequencies in the disease and control groups. The relative risk (RR) is the real measure of association between exposure to a certain factor and having the disease or outcome. The risk associated with individual genotypes or alleles was calculated as the odds ratio (OR) with 95% confidence intervals (95% CI). Which indicate how many times more frequently a disease develops in individuals carrying the allele or genotype than in individuals lacking it.

Results

Genetic Analysis of AMELX SNPs
Agarose Gel Electrophoresis of PCR Products

Three SNPs were detected in *AMELX* gene according to primer design located at rs5933871, rs5934997 and rs17878486 which located in the second intron.

Genotype and Allele Frequency Analysis

Analysis by Hardy-Weinberg equilibrium for study groups were done for the three SNPs (rs5933871, rs5934997 and rs17878486) to compare the three genotypes in each study groups.

The comparisons of genotypes and allele frequencies computed for *AMELX* SNPs are shown in Tables 1 and 2. For all SNPs, it showed that no significant difference between the high and low caries groups but in high caries group, it showed a deviation from Hardy-Weinberg equilibrium with a significant difference among the three genotypes (p=0.013) in rs5933871 and rs5934997, while a highly significant difference in rs17878486 for both high and low caries groups (p=0.000 and p=0.001).

There was a larger frequency of the major TT homozygote in rs5933871 and rs5934997, while the minor CC homozygote showed a higher odd ratio OR and relative risk RR with no discernible difference between them (OR = 1.8, RR=1.31, p=0.346; OR = 2.16, RR=1.83, p=0.225) respectively. While rs17878486 the major TT was higher in study group compared with control with high OR and RR but no significant difference (OR = 1.58, RR=1.10, p=0.701) These findings point to the CC and TT genotype as possible high-risk variations for the research group's experience with caries.

The genetic analysis for *AMELX* Gene SNPs in the present study revealed allele frequency for three SNPs in study groups as shown in table (3-12, 13, 14). For rs5933871 and rs5934997 there was a high frequency of allele T in low caries group than high caries group in contrast to rs17878486 which allele T had a high frequency in high caries group. While the frequency of C allele was higher in high caries group in rs5933871 and rs5934997 (41.0% and 41.0%) respectively than that in low caries group (37.1% and 33.3%), on the other hand the low caries group in rs17878486 showed higher allele C (33.3%) than that in high caries group (14.1%). However, the

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

difference in allele frequency between groups in three SNPs were non-significant at p-value >0.5. While there is a deviation from Hardy-Weinberg equilibrium in allele frequency in high caries groups which was significant in for rs5933871 and rs5934997. While in low and high caries group of rs17878486, the difference in allele frequency was a high significant difference (p=0.000).

Discussion

It is important to remember that *AMELX* gene is essential for the development of healthy enamel and any abnormalities in this gene are mostly to blame for congenital diseases such amelogenesis imperfecta and mineralization problems. As a result, some scientists have hypothesized that genetic variants may contribute to structural alterations in enamel, which may result in greater mineral loss, bacterial colonization, or the production of biofilms [9]. Mammalian *AMELX* was previously identified as a potential candidate for carrying mutations that could increase a person's susceptibility to caries by evolutionary analysis of *AMELX* and genetic investigations utilizing SNP markers [9-24].

The study investigated SNPs in the *AMELX* gene for their potential association with dental caries and assessed the role of amelogenin and its deficiency in affecting enamel formation and caries development; unfortunately, our study did not produce any significant results between study and control groups but there was a significant difference among the three genotypes in each study groups.

Despite numerous studies strongly suggesting a link between enamel formation genes and caries susceptibility, discrepancies in results persist, particularly in relation to the age, gender, and ethnicity of the individuals studied [25]. In our investigation, none of the studied SNPs showed an association with the risk of dental caries, which aligns with the findings of Ergoz et al. in 2014 [13], but contradicts the findings of Jeremias et al. in 2013 [26] and Gerreth et al. in 2017 [14], who reported an association between the *AMELX* rs17878486 polymorphism and susceptibility to dental caries. Additionally, Kang et al. in 2011 [27] discovered significant relationships between the rs5933871 and rs5934997 SNPs and caries susceptibility, particularly in the group receiving water fluoridation.

One possible explanation for our divergent findings may lie in the heterogeneity of our sample with respect to geographic origins. It's interesting to note that other studies [9-24] that identified *AMELX* as a candidate gene for caries susceptibility used genetic techniques on more homogeneous populations. Therefore, it is conceivable that random genetic alterations could have emerged in people with a genetically restricted background, increasing susceptibility to caries.

However, Patir and colleagues' 2008 study [9], which involved the sequencing of *AMELX* in 70 children from the Turkish community, does not support this gene as a candidate for caries susceptibility. Additionally, *AMELX* has not been identified as a target gene in genome-wide association studies carried out on bigger and more diverse populations [20-28-29], which is consistent with the findings of this investigation.

The *AMELX* rs17878486 polymorphism's T allele and TT genotypes were discovered to be linked to an elevated risk in the study group as compared to the control group. It's essential to remain open to the possibility that other genes related to enamel may harbor mutations that increase an individual's susceptibility to caries [20].

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

In a different part of the research which looked for patients who had no previous history of tooth decay or tooth decay less than 2 teeth to test the theory that *AMELX* mutations would increase resistance to caries. However, this theory was not supported by our examination of the genetic polymorphisms found in this investigation; *AMELX* SNPs were not discovered to be connected to caries prevention. This result is consistent with a previous work [30] that sequenced the variable *AMELX* area in a varied human population and found no evidence of genetic variations.

Conclusion

Given these results, none of the studied SNPs showed an association with the risk of dental caries. It's critical to keep an open mind about the possibility that mutations in other enamel-related genes could make a person more vulnerable to dental cavities.

Conflicts of interest

The authors declare no competing interest.

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

Table 1. Genotype and allele frequency comparisons calculated for *AMELX* gene SNPs.

rs5933871 (T > C) **Genotype frequency**		**Study groups**		**OR**	**CI**	**RR**	**χ2**	***P*-value**
		High caries n=39	**Low caries n=39**					
Homozygous	TT	18 (46.1%)	17 (43.5%)	1.11	(0.45-2.70)	1.06	0.028	0.865
Heterozygous	TC	10 (25.6%)	15 (38.4%)	0.9	(0.21-1.44)	0.94	1.00	0.317
Homozygous	CC	11 (28.2%)	7 (17.9%)	1.8	(0.61-5.26)	1.31	0.889	0.346
HWE χ^2		8.619	1.216					
P-value		0.013*	0.544					
rs5934997 (T > C)								
Homozygous	TT	18 (46.1%)	19 (48.7%)	0.9	(0.37-2.19)	0.95	0.027	0.869
Heterozygous	TC	10 (25.6%)	14 (35.9%)	1.11	(0.23-1.62)	1.06	0.667	0.414
Homozygous	CC	11 (28.2%)	6 (15.3%)	2.16	(0.70-6.58)	1.83	1.47	0.225
HWE χ^2		8.619	1.442					
P-value		0.013*	0.486					
rs17878486 (T > C)								
Homozygous	TT	32 (82.0%)	29 (74.3%)	1.58	(0.53-4.68)	1.10	0.147	0.701
Heterozygous	TC	3 (7.69%)	5 (12.8%)	0.63	(0.12-2.55)	0.91	0.5	0.479
Homozygous	CC	4 (10.2%)	5 (12.8%)	0.78	(0.19-3.14)	0.80	0.111	0.738
HWE χ^2		18.166	13.452					
P-value		0.000*	0.001*					

Abbreviations: OR Odds ratio, CI Confidence interval; RR relative risk; χ2 chai- square; P- value probability value; HWE Hardy-Weinberg equilibrium; NS non-significant, * significant.

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

Table 2. Allele frequency comparisons calculated of *AMELX* gene SNPs.

Allele frequency **rs5933871 (T> C)**	**High caries n=39**	**Low caries n=39**	**χ2**	***P*-value**
T	46 (58.9%)	49(62.8 %)	0.242	0.622
C	32 (41.0%)	29 (37.1%)		
HWE P-value	0.003*	0.27		
rs5934997 (T > C)				
T	46 (58.9%)	52(66.6 %)	0.988	0.32
C	32 (41.0%)	26 (33.3%)		
HWE P-value	0.003*	0.229		
rs17878486 (T > C)				
T	67 (85.9%)	63(80.7 %)	0.738	0.39
C	11 (14.1%)	15 (33.3%)		
HWE P-value	0.000*	0.000*		

Abbreviations: χ2 chai- square; P- value probability value; HWE Hardy-Weinberg equilibrium; * significant.

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

References

1. Al-Zahraa JJ, Aldhaher ZA. Evaluation of mutans streptococci concerning oral health in the saliva of pregnant women. Revis Bionatura 2023;8 (2) 81. http://dx.doi.org/10.21931/RB/2023.08.02.81

2. Mohammed H A, Sahi N M, Ahmed R T, Al-Rubaye A F.Antimicrobial Activity of Some Nanoparticles Synthesized by Laser Ablation Technique Against Some Bacteria Isolated From Oral Cavity. MJB. 2022;19 (4), pp. 601-608.

3. Ali R A, Radeef S M, Mohammed N B, Diab B S. Oral Health Related Quality of Life among Dental Implant Patients in Relation to Temporomandibular Joint Function. MJB. 2022; 19 (4), pp. 609-614.

4. Stookey GK. The effect of saliva on dental caries. J Am Dent Assoc. 2008; 139 (Suppl):11S–17S. [PubMed: 18595200].

5. Aziz A, Taha, A. The Salivary Inflammatory Biomarkers (Interleukin-6, C-Reactive Protein) in Relation with Caries-Experience among a Group of 12-Year-Old Obese Boys. J Bagh Coll Dentistry 2016; 28: 138-142. 10.12816/0024723.

6. Guzman-Armstrong S. Rampant caries. J Sch Nurs. 2005; 21:272–278. [PubMed: 16262438].

7. Wendell S, Wang X, Brown M, Cooper ME, DeSensi RS, Weyant RJ, et al. Taste genes associated with dental caries. J Dent Res. 2010 Nov;89(11):1198-202. https://doi.org/10.1177/0022034510381502

8. Juma'a Z, Fadhil R, Abdul-Hussain Y. Correlation between caries related microorganisms in the dental plaque and saliva with dental caries level in the upper and lower jaws in 5-9 years old children in baghdad city. J Bagh Coll Dentistry 2016; 28(3):132-136.

9. Patir A, Seymen F, Yildirim M, Deeley K, Cooper ME, Marazita ML, Vieira AR. Enamel formation genes are associated with high caries experience in turkish children. Caries Res. 2008; 42:394– 400. [PubMed: 18781068].

10. Pang, L., Zhi, Q., Zhuang, P., Yu, L., Tao, Y., Lin, H. Variation in enamel formation genes influences enamel demineralization in vitro in a streptococcus mutans biofilm model. Front. Physiol. 2017; 8, 851.

11. Shungin D, Haworth S, Divaris K, Agler CS, Kamatani Y, Keun Lee M, Grinde K, Hindy G, Alaraudanjoki V, Pesonen P, Teumer A, Holtfreter B, Sakaue S, Hirata J, Yu,Y-H, Ridker P. M, Giulianini F, Chasman DI, Magnusson PKE, Sudo T, Okada Y, Völker U, Kocher T, Anttonen V, Laitala M-L, Orho-Melander M, Sofer T, Shaffer JR, Vieira A, Marazita ML, Kubo M, Furuichi Y, North KE, Offenbacher S, Ingelsson E, Franks PW, Timpson NJ, Johansson I. Genome-wide analysis of dental caries and periodontitis combining clinical and self-reported data. Nature Communications 2019; 10 (1): 2773.

12. Olszowski T, Adler G, Janiszewska-Olszowska J, Safranow K, Kaczmarczyk M: MBL2 , MASP2 , AMELX , and ENAM gene polymorphisms and dental caries in Polish children. Oral Dis 2012;18:389–395.

13. Ergoz, N., Seymen, F., Gencay, K., et al. Genetic variation in Ameloblastin is associated with caries in asthmatic children. Eur. Arch. Paediatr. Dent. 2014; 15 (3), 211–216.

14. Gerreth K, Zaorska K, Zabel M, Borysewicz-Lewicka M, Nowicki M. Chosen single nucleotide polymorphisms (SNPs) of enamel formation genes and dental caries in a population of polish children. Adv Clin Exp Med. 2017;26: 899–905.

15. Yoshizaki K, Yamada Y. Gene evolution and functions of extracellular matrix proteins in teeth. Orthod Waves. 2013;72:1–10.

16. Moradian-Oldak J. Protein mediated enamel mineralization. Front Biosci. 2012;17:1996–2023.

17. Gallon V, Chen L, Yang X, Moradian-Oldak J. Localization and quantitative co-localization

Dentistry 3000
Vol 13 No 1 (2025) DOI 10.5195/d3000.2025.842

of enamelin with amelogenin. J Struct Biol. 2013;183:239–249.

18. Mohammed AK, MI Nader, BH Al-Ghurabi. Genotyping of HLA ClassI and II Molecules in Type 2 Diabetic Iraqi Patients. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)2014; 13 (4 III.): 44-48.

19. Fadhil R, HM Akram, A Najah, SS Gul. Association of matrix metalloproteinase-1-1607 1G/2G single nucleotide polymorphism genotypes with periodontitis in Iraqi population. Braz Dent Sci 2022; 25 (3): e3283

20. Vieira AR, Marazita ML, Goldstein-McHenry T. Genome-wide scan finds suggestive caries loci. J Dent Res 2008; 87:435–439.

21. World health organization. Oral Health Surveys Basic Methods 5th Edition, 2013.

22. Muhlemann HR. Oral epidemiology-caries. In: Zeitschriften-Verlag B, Quintessenze D. Introduction to oral preventive medicine; 1976. pp. 73-100.

23. Navazesh M, Kumar S. Measuring salivary flow: Challenges and opportunities. JADA 2008; 139(2):35S-40S.

24. Deeley K, Letra A, Rose EK, Brandon CA, Resick JM, Marazita ML, Vieira AR: Possible association of amelogenin to high caries experience in a Guatemalan-Mayan population. Caries Res 2008;42:8–13.

25. Wang X, Willing MC, Marazita ML, Wendell S, Warren JJ, Broffitt B, Smith B, Busch T, Lidral C, Levy SM: Genetic and environmental factors associated with dental caries in children: the Iowa Fluoride Study. Caries Res 2012b;46: 177–184.

26. Jeremias F, Koruyucu M, Küchler EC, Bayram M, Tuna EB, Deeley K, Pierri RA, Souza JF, Fragelli CM, Paschoal MA, Gencay K, Seymen F, Caminaga RM, dos Santos-Pinto L, Vieira AR. Genes expressed in dental enamel development are associated with molar-incisor hypomineralization. Arch Oral Biol. 2013; 58:1434–42.

27. Kang SW, Yoon I, Lee HW, et al. Association between AMELX polymorphisms and dental caries in Koreans. Oral Dis 2011;17:399–406.

28. Shaffer JR, Wang X, Feingold E, Lee M, Begum F, Weeks DE, et al. Genome-wide association scan for childhood caries implicates novel genes. J Dent Res. 2011; 90:1457-1462.

29. Shaffer JR, Feingold E, Wang X, Lee M, Cuenco KT, Weeks DE, et al. GWAS of dental caries patterns in the permanent dentition. J Dent Res. 2013; 92:38-44.

30. Richard B, Delgado S, Gorry P, Sire JY. A study of polymorphism in human AMELX. Arch Oral Biol.2007; 52:1026-1031.