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genetic contribution to early childhood caries in pre-school aged children in Iraq

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Abstract

Background: The investigation of the genetic components of human physical characteristics and disorders uses twin research. Cotwins who are monozygotic (MZ) share all of their genes, whereas dizygotic twins (DZ) typically only share half of their DNA. Therefore, one can assess the relative contributions of genetic and environmental influence to observed variances in certain features or traits by assuming that both types of twins have been sampled from the gene pool and that equivalent environmental forces have been placed upon them. Numerous oral features including dental caries appear to have a significant hereditary component, according to twin studies. contribution.

Aim of the study: The current study was aiming at exploring the prevalence rate and genetic contribution to dental caries in pre-school Iraqi children.

Patients and methods: The present study has been designed as a case control study carried out between August 2021 and November 2022 in Hilla city. Only healthy children under 6 years of age (3–6 years) in primary dentition attending the governmental and private kindergarten present at the time of the study and whose parents signed an informed consent were included. Twin children enrolled in the groups according to the similarity in the physical properties. To record personnel profile of the children, a questionnaire in Arabic language was designed by the investigator according to the guidelines of the American Academy of Pediatric Dentistry.

Results: The prevalence rate of dental caries according to the results of DMFT and DMFS was 91.1 %. There was no significant difference in rate of carries between subgroup A and subgroup B in all groups (p = 1.000). Comparison of median DMFT and DMFS scores between subgroup A and subgroup B, in all enrolled groups, revealed also no significant variation ($p > 0.05$). In terms of correlation, strongest and most significant correlation was seen in identical twin group, followed by fraternal twin group ($p < 0.00$). Furthermore, the correlations in related and unrelated children groups were weaker and not significant ($p > 0.05$).

Conclusion: The strong and significant correlation of DMFT and DMFS between subgroups in the identical twins and the less significant and less strong correlation in fraternal twins added to the lack of correlation in non-twins are strong evidence of the participation of genetic factors in dental caries at least partially in pre-school children.

Key words: Twins, genetic, dental caries, pre-school children, Iraq

Introduction

Although there is mounting evidence that heredity has a role in caries, there haven't historically been many studies tackling the issue from this angle. The interplay of host factors, microbial infection, and substrate that supports the cariogenic microbiota results in caries. The genetic processes that modulate each of these variables, such as saliva factors that affect bacterial adhesion or acidic buffer capacity, are easily proposed (1, 2). Studies with twins and models based on humans show that caries has a hereditary component. Even though the participants in the study ingested caramels four times a day in between meals and the original Vipeholm study clearly shown that increased exposure to sugar-rich foods enhanced the severity of caries, 20% of them had no caries lesions after a year. This finding implies that personal susceptibility also modifies dental experiences (3). The genetic component of dental caries has also been studied by numerous researchers (4).

Single nucleotide polymorphisms (SNPs) in certain genes are examined in order to find genetic elements that contribute to caries and how their presumed or known function relates to the condition. The last ten years have produced the majority of the data used in the genetic investigations of dental erosion. Some of the most significant candidate genes investigated to date include those involved in salivary production, immunological response, taste, and enamel development, with immune response genes being the most thoroughly investigated (5).

Given that numerous studies have found favorable correlations between caries experience and variation in enamel formation genes, it is plausible to believe that variants in enamel formation genes may be involved in the susceptibility to dental erosions. Dental caries severity and genetic diversity in the genes that create enamel are linked, according to a clinical investigation by Sovik et al (4). However, it's crucial to keep in mind that levels and frequency of acid exposure are difficult to gauge and regulate. By examining covariance between relatives with similar behavior, practice, and habits, one might simulate genetic relationships (4, 6).

The investigation of the genetic components of human physical characteristics and disorders uses twin research. Cotwins who are monozygotic (MZ) share all of their genes, whereas dizygotic twins (DZ) typically only share half of their DNA. Therefore, one can assess the relative contributions of genetic and environmental influence to observed variances in certain features or traits by assuming that both types of twins have been sampled from the gene pool and that equivalent environmental forces have been placed upon them (7).

Numerous oral features appear to have a significant hereditary component, according to twin studies (8, 9). Finn and Caldwell (10), Goodman *et al*., (11) and Horowitz *et al*., (12) showed that dental caries possess a genetic contribution. Studies on spacing of teeth and alignment by Corruccini and Potter (13) and teeth count by Townsend GC (14) and Markovic (15) revealed a greater contribution in monozygotic twins because of similar genetic design following comparison to dizygotic twins.

Twin research is an effective method for determining if and how much genetic variation contributes to a certain characteristic or disease. When comparing identical or monozygotic twins with dizygotic twins, it is possible to compare individuals who share 100% of their genomic DNA with those who only share 50%, presuming that both sets of twins are living in the same environment. Dental caries occur when children live with the same parents, in the same home, and follow the same dietary and oral hygiene routines as well as cultural and lifestyle norms. These findings have repeatedly indicated that heredity is responsible for a significant amount of the diversity in dental caries in communities (16). The current study was aiming at exploring the prevalence rate and genetic contribution to dental caries in pre-school Iraqi children.

Patients and methods

The present study has been designed as a case control study carried out between August 2021 and November 2022 in Hilla city. The study took a long time because of children incompliance in attending schools due to covid 19 out breaks. Only healthy children under 6 years of age (3–6 years) in primary dentition attending the governmental and private kindergarten present at the time of the study and whose parents signed an informed consent were included. Children with systemic disease or general health issue, oral habits, absent during the dental examination and/or whose parents did not consent to their participation were excluded from the study. Twin children enrolled in the groups according to the similarity in the physical properties. To record personnel profile of the children, a questionnaire in Arabic language was designed by the investigator according to the guidelines of the American Academy of Pediatric Dentistry. The questionnaire included information about; (gender, age, birth weight, type of deliver, type of feeding weather breast feeding, bottle feeding or mixed, weaning age, sweat desire and oral hygiene behaviors (start of tooth brushing, time of brushing and tooth brushing method).The investigator reviewed the questionnaires for appropriateness and children who fulfilled the inclusion criteria were examined. Clinical examination carried out with assistance of the kindergarten staff according to WHO 1987 method and by using dmft and dmfs index for recording the carious teeth.

Data were described, presented and analyzed using statistical package for social sciences (SPSS) version 16. The presentation of variables was done using standard deviation, inter-quartile range, range, median and mean in addition to count and percentage. Comparison of ratios was done using chi-square test, Yates correction or Fischer exact test according to statistical assumptions. Comparison of mean values was done using one way ANOVA and comparison of mean rank was done using Mann Whitney U test. The level of significance was considered when p value is equal to or less than 0.05.

Results

In this study and in all enrolled children, the prevalence rate of dental caries according to the results of DMFT and DMFS was 91.1 %, as presented in figure 1.

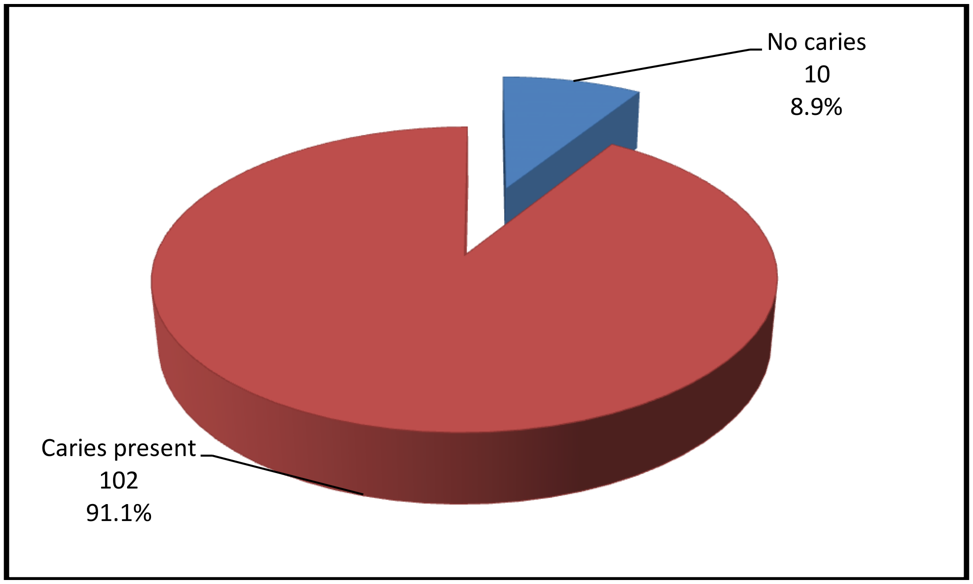

Figure 1: Pie chart showing the prevalence rate of carries among all enrolled children

Mean age and age range of children enrolled in the current study classified into twins and non-twins is shown in table 1. The means of ages were 4.64 ±0.66 years, 4.90 ±0.66 years, 4.77 ±0.90 and 4.83 ±0.65 years and ranged were 4-6, 4-6, 3-6 and 4-6 in identical twins group, fraternal twins group, related children group and unrelated children group, respectively. There was no significant difference in mean age among enrolled groups (p = 0.618). There was also no significant difference in frequencies of males and females among groups (p = 0.814).

Table 1: Mean age, age range and gender frequency of children enrolled in the current study classified into twins and non-twins

Characteristic	Identical twins *n* = 22	Fraternal twins *n* = 30	Related children *n* = 30	Unrelated children *n* = 30	*p*
Age (years)					
Mean ±SD	4.64 ±0.66	4.90 ±0.66	4.77 ±0.90	4.83 ±0.65	0.618 O NS
Range	4 -6	4 -6	3 -6	4 -6	
Gender					
Males, *n* (%)	14	16	16	18	0.841 C NS
Females, *n* (%)	8	14	14	12	

n: number of cases; data were presented as mean ±standard deviation or count (%); **SD**: standard deviation; **O**: one way ANOVA; **C**: Chi-square test; **NS**: not significant

Comparison of rate of dental caries and median level of DMFT score between subgroup A and subgroup B in each enrolled group is shown in table 2. There was no significant difference in rate of carries between subgroup A and subgroup B in the identical twins group, 81.8 % versus 90.9 %, respectively (p = 1.000). There was also no significant difference in rate of carries between subgroup A and subgroup B in the fraternal twins group, 93.3 % versus 86.7 %, respectively (p = 1.000). In addition, there was no significant difference in rate of carries between subgroup A and subgroup B in the related children group, 93.3 % versus 86.7 %, respectively (p = 1.000). Moreover, there was no significant difference in rate of carries between subgroup A and subgroup B in the unrelated children group, 100.0 % versus 93.3 %, respectively (p = 1.000). Comparison of median DMFT score between subgroup A and

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subgroup B, in all enrolled groups, revealed also no significant variation ($p > 0.05$).

Table 2: Comparison of rate of dental caries and median level of DMFT score between subgroup A and subgroup B in each enrolled group

Group	DMFT	Subgroup A	Subgroup B	*p*
Identical twins *n* = 11	No caries, *n* (%)	2 (18.2 %)	1 (9.1 %)	1.000 Y NS
	Caries present, *n* (%)	9 (81.8 %)	10 (90.9 %)	
	Median (IQR)	2 (6)	2 (5)	1.000 M NS
Fraternal twins *n* = 15	No caries, *n* (%)	1 (6.7 %)	2 (13.3 %)	1.000 Y NS
	Caries present, *n* (%)	14 (93.3 %)	13 (86.7 %)	
	Median (IQR)	6 (5)	6 (7)	0.677 M NS
Related children *n* = 15	No caries, *n* (%)	1 (6.7 %)	2 (13.3 %)	1.000 Y NS
	Caries present, *n* (%)	14 (93.3 %)	13 (86.7 %)	
	Median (IQR)	4 (4)	6 (7)	0.416 M NS
Unrelated children *n* = 15	No caries, *n* (%)	0 (0.0 %)	1 (6.7 %)	1.000 F NS
	Caries present, *n* (%)	15 (100.0 %)	14 (93.3 %)	
	Median (IQR)	6 (6)	6 (9)	0.558 M NS

n: number of cases; data were presented as count (%) or median (IQR); **IQR**: inter-quartile range; **Y**: Yates correction; **M**: Mann Whitney U test; **F**: Fischer exact test; **NS**: not significant

Comparison of rate of concordance and correlation of DMFT between subgroup A and subgroup B in each enrolled group is shown in table 3. Concordance rate in identical twin group was 90.9 % and this was slightly lower than that seen in fraternal twins group, related children group and unrelated children group (93.3 % for all); however, in terms of correlation, strongest and most significant correlation was seen in identical twin group, followed by fraternal twin group, ($r = 0.979$; $p < 0.001$ versus $r = 635$; $p = 0.011$, respectively). Furthermore, the correlations in related and unrelated children groups were weaker and not significant ($r = 0.424$; $p = 0.116$ and $r = 0.137$; $p = 0.626$, respectively).

Table 3: Comparison of rate of concordance and correlation of DMFT between subgroup A and subgroup B in each enrolled group

Group	Concordance		Correlation	
	Concordance rate	**Discordance rate**	***r***	***p***
Identical twins *n* = 11	90.9	9.1	0.979	< 0.001 ***
Fraternal twins *n* = 15	93.3	6.7	0.635	0.011 *
Related children *n* = 15	93.3	6.7	0.424	0.116 NS

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Unrelated children *n* = 15	93.3	6.7	0.137	0.626 NS

n: number of cases; **NS**: not significant; *: significant at $p \leq 0.05$; ***: significant at $p \leq 0.001$

Comparison of rate of dental caries and median level of DMFS score between subgroup A and subgroup B in each enrolled group is shown in table 4. There was no significant difference in rate of carries between subgroup A and subgroup B in the identical twins group, 81.8 % versus 90.9 %, respectively (p = 1.000). There was also no significant difference in rate of carries between subgroup A and subgroup B in the fraternal twins group, 93.3 % versus 86.7 %, respectively (p = 1.000). In addition, there was no significant difference in rate of carries between subgroup A and subgroup B in the related children group, 93.3 % versus 86.7 %, respectively (p = 1.000). Moreover, there was no significant difference in rate of carries between subgroup A and subgroup B in the unrelated children group, 100.0 % versus 93.3 %, respectively (p = 1.000). Comparison of median DMFS score between subgroup A and subgroup B, in all enrolled groups, revealed also no significant variation (p > 0.05).

Table 4: Comparison of rate of dental caries and median level of DMFS score between subgroup A and subgroup B in each enrolled group

Group	**DMFS**	**Subgroup A**	**Subgroup B**	***p***
Identical twins *n* = 11	No caries, *n* (%)	2 (18.2 %)	1 (9.1 %)	1.000 Y NS
	Caries present, *n* (%)	9 (81.8 %)	10 (90.9 %)	
	Median (IQR)	2 (9)	2 (7)	0.894 M NS
Fraternal twins *n* = 15	No caries, *n* (%)	1 (6.7 %)	2 (13.3 %)	1.000 Y NS
	Caries present, *n* (%)	14 (93.3 %)	13 (86.7 %)	
	Median (IQR)	9 (11)	8 (12)	0.647 M NS
Related children *n* = 15	No caries, *n* (%)	1 (6.7 %)	2 (13.3 %)	1.000 Y NS
	Caries present, *n* (%)	14 (93.3 %)	13 (86.7 %)	
	Median (IQR)	5 (8)	6 (12)	0.632 M NS
Unrelated children *n* = 15	No caries, *n* (%)	0 (0.0 %)	1 (6.7 %)	1.000 F NS
	Caries present, *n* (%)	15 (100.0 %)	14 (93.3 %)	
	Median (IQR)	8 (7)	6 (14)	0.901 M NS

n: number of cases; data were presented as count (%) or median (IQR); **IQR**: inter-quartile range; **Y**: Yates correction; **M**: Mann Whitney U test; **F**: Fischer exact test; **NS**: not significant

Comparison of rate of concordance and correlation of DMFS between subgroup A and subgroup B in each enrolled group is shown in table 5. Concordance rate in identical twin group was 90.9 % and this was slightly lower than that seen in fraternal twins group, related children group and unrelated children group (93.3 % for all); however, in terms of correlation, strongest and most significant correlation was seen in identical twin group, followed by fraternal twin group, (r = 0.974; p <0.001 versus r = 588; p = 0.021, respectively). Furthermore, the correlations in related and unrelated children groups were weaker and not significant (r = 0.405; p =0.134 and r = 0.357; p = 0.192, respectively).

Table 5: Comparison of rate of concordance and correlation of DMFS between subgroup A and subgroup B in each enrolled group

Group	Concordance		Correlation	
	Concordance rate	Discordance rate	*r*	*p*
Identical twins *n* = 11	90.9	9.1	0.974	< 0.001 ***
Fraternal twins *n* = 15	93.3	6.7	0.588	0.021 *
Related children *n* = 15	93.3	6.7	0.405	0.134
Unrelated children *n* = 15	93.3	6.7	0.357	0.192

n: number of cases; **NS**: not significant; *: significant at $p \leq 0.05$; ***: significant at $p \leq 0.001$

Discussion

Dental carries has been attributed in the majority of literatures to acquired environmental factors such as sugar and acid action and lack of oral hygiene (4, 6); however, the observation of familial and genetic evidence in associations with dental caries has been raised in a lot of published articles worldwide; however, the exact genetic predisposition appears to be multifactorial and acts in synergism with environmental factors to produce its final adverse outcome. One of the best suggested genetic models to assess the association between diseases and genetic predisposition is to study such disorders in twins and non-twins. Previous authors have assessed such associations with respect to dental carries in various regions of the world and on different ethnic groups (8-10) and in our study we aimed to evaluate such association on a sample of Iraqi children.

In the present study, the prevalence rate of carries in all enrolled children was relatively high (91.1 %). Youssefi and Afroughi (17) reported a prevalence rate of dental carries in children of up to 89.9 % in school age children. Although, the rate in our study is approximately similar to that of Youssefi and Afroughi (17), the age range in our study is younger since we limited our research to preschool children. The frequency has been estimated to be as high as 70% in less developed nations and among disadvantaged groups in wealthier nations (18, 19). Some Middle Eastern nations, like Palestine (76%) and the United Arab Emirates (83%), have a high prevalence of ECC (20, 21). Inconsistent prevalence of ECC was seen in some nations' national surveys, including Greece (36%), Brazil (45.8%), India (51.9%), and Israel (64.7%). (22-25). Ismail and Sohn (26) conducted a systematic review and discovered that the prevalence ranged from 2.1% in Sweden to 85.5% in children from rural China. Additionally, the prevalence of ECC varies significantly by a number of characteristics, including race, culture, and ethnicity; socioeconomic position; way of life; dietary habits; and oral hygiene practices; as well as by a number of factors that vary from nation to country and from area to area (27).

The most important point in this study is that the correlation of DMFT and DMFS between subgroups within the identical twin group was the strongest and the most significant when compare to the rest of groups enrolled. In addition, we observed significant correlation of these dental parameters showed significant correlation within fraternal twins group, but the level of strength was lower than that of identical twins and these observations are in support of a genetic role at least partially in the causation of dental caries. This evidence becomes more string when our observation of the lack of significant correlation of DMFT and DMFS between subgroups within related non-twins and unrelated twins. Similar results of such correlation has been observed in the study of Kuppan *et al* (28) on dental caries in identical and fraternal twins, there was significant correlation in DMFS between subgroups and the concordance rate comparison revealed no significant difference between identical and non-identical twins in close similarity to our study.

Dental caries twin studies have demonstrated the importance of both hereditary and environmental variables (29, 30, 31). Caries resistance or susceptibility may result from a combination of environmental, phenotypic, and genotypic factors (32). The percentage of variation in a phenotype that may be traced to individual genetic variations is known as the heritability estimate (33). Other investigations that demonstrated that MZ twins had higher dental caries similarity corroborated this observation (30, 31). According to these research, the MZ twins displayed a higher correlation than the DZ twins. 82 pairs of twins between the ages of 6 and 12 were investigated by Liu et al. for various dental features (34). Significant differences in caries incidence were seen between the MZ and DZ groups, and the heritability was 24.47%. In a study of 314 twin pairs between the ages of 1.5 and 8, Bretz et al. discovered that the heritability estimates were highest at 1.5 years of age (29). Additionally, Ooi et al. examined the prevalence of dental caries in 84 twins between the ages of 4 and 6 and discovered that 18% of the DZ twin pairs had dental caries, as opposed to 3% of the MZ twin couples (35). Dental caries have a high concordance rate in monozygotic and dizygotic twins, according to a Chinese study by Gao (36).

Dental caries have a heritability of 40% to 60%, and earlier studies have shown that heredity plays a significant influence in the development of the condition (37, 38, 39). A significant genome-wide association study of dental caries revealed a possible genetic component to the disease's causation (40). Children with dental caries had two frequent polymorphisms in the genes for the sweet taste receptor (TAS1R2) and glucose transporter (GLUT2) analyzed. This information suggested that certain genetic variations in the GLUT2 and TAS1R2 genes may have an impact on the chance of developing dental caries (41). According to Zhang et al analysis of the plaque microbiota in twin kids with divergent caries manifestations, twins typically have similar microbial compositions. They came to the conclusion that environmental variables predominantly control the microbial makeup of dental plaque and the development of caries, while genetic factors primarily affect an individual's susceptibility to dental caries (42).

Conclusion

The strong and significant correlation of DMFT and DMFS between subgroups in the identical twins and the less significant and less strong correlation in fraternal twins added to the lack of correlation in non-twins are strong evidence of the participation of genetic factors in dental caries at least partially in pre-school children.

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