Genetics as a Tool for Oral Health Diagnosis and Disease Prevention: A Family Based Study

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ABSTRACT

To account the cumulative effects of genes on dental caries between the sexes and to assess the heritability of midline diastema, melanin pigmentation, frenal attachment and tongue tie in family trees. A descriptive study was conducted among 100 families selected conveniently from Udham Singh Nagar, Uttrakhand. Pre structured performa was drafted to record demographic data and clinical examination of dental caries, frenal attachment, melanin pigmentation, midline diastema and tongue tie. Findings was compared within the pairs: grandparents- grandchildren pair and parent-offspring pair, to access heritability.

Among grandfather-grandchildren pairs 36.76% had dental caries when compared with grandmother was 33.72%. Grandparent pairing with granddaughter had higher prevalence as compared to their pairing with grandson. Similar result was seen in parents-offspring pair. While it was vice versa in case of melanin pigmentation and no differences in its prevalence was seen in son and daughter pairs. In midline diastema, was higher in father son pair. Types of Frenal attachment was found to be statistically significant within all pairs and tongue tie was found clinically acceptable for all individuals.[1] Genetics influence should be considered, in efforts to understand the multi-factorial nature of the diseases and can act as a vital tool in the easy diagnosis and prevention of these diseases.

Keywords: Grandparents, Parents, Children, Inheritance

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INTRODUCTION

A recent mammoth body of work concerning the systematic analysis for the global burden of diseases, injuries and risk factors with regard to oral diseases for the past 25 years has indicated that there is no change in the trend of the oral disorders. On a global scale, it is reported that the age standardized prevalence of oral conditions remained relatively stable between 1990 and 2015. Indian oral disorder burden has not changed over the years. As per the manuscript, India lost 2656292.55 (1583657.57-4095978.39) Disability Adjusted Life Years (DALYs) with an annual change of about 0.3% per year. Currently in India, 1.09% (1.00–1.19) or 0.83% (0.81–0.86) of all DALYs are contributed by oral disorders while during the same period, the DALYs for all causes were-0.12. This indicates that other branches of medicine were successful in combating and reducing the DALYs while dentistry as whole has failed. Drastic changes in dental sector and increase in dental workforce in India , opening of private dental sectors, community water fluoridation, school-based programs and preventive health educational programme etc., it is logical to believe that oral disease burden should be reduced. Probably as a result of numerous preventive interventions, burden of oral diseases has not changed over the years. Apart from above mentioned factors, genetics could be one of the factor in determining health and disease in families and interplay of such factors with environmental factors Your parents may have given you more than just your eye color and your sense of humor. You might also have inherited an increased risk for dental problems [2]. Yes, dental issues can run in the family. And it's not just because you've learned bad habits from your family, or passed on oral bacteria by sharing silverware. Many oral health conditions have a hereditary basis. That means you may be at higher risk for developing certain conditions, in spite of your habits. These familial aggregations may result from shared genes, environmental exposures and similar socio-economic influences Dental caries is a multifactorial complex disease remains the most common chronic disease. Although a decline in dental caries rates in the United States and other industrialized nations was found until the mid-1980s, later reports have suggested that this decline has slowed or even reversed in the U.S. and elsewhere. This has also been supported by recent NHANES data. The etiology of dental caries involves a complex interplay of environmental and genetic factors. Epidemiological studies have tried for many years to understand fully the mechanisms of this disease, with the eventual goal of prevention. Thus, identifying the underlying genetic and environmental risk factors is a crucial step toward that goal Moreover, caries prevalence was observed to vary among different racial groups, with non-Hispanic whites having the lowest caries prevalence and severity. However, this could be partly due to different genetic factors as well. Pioneering twin studies investigating the heritability of dental caries in children have clearly supported the key role of genetics in tooth decay. Caries heritability estimates for children based on twins range from 645-85%. In recent, heritability study based on larger family's heritability of dental caries in the primary dentition was over 50%.

Larger families help in the clustering of several diseases within families. In fact, this clustering is often the first indication that a disease may have a genetic component. A pattern consistent with genetic factors occurs when the similarity or correlation of a trait among closely related individuals, for example, siblings, is greater than for more distant relatives and/or greater among relatives than unrelated individuals. Therefore, the present family based study was planned to assess the genetic influence on dental caries pattern, frenula attachment, melanin pigmentation, midline diatom and tongue tie.

MATERIALS and METHODS

A descriptive study was conducted with a convenient sample of 100 households comprising 454 individuals, from Sikh community, from the district Udham Singh Nagar, Uttarakhand, India, who fulfilled the following eligibility criteria. Families included should have at least 2 generations representation in same house or within same locality and biologically related with each other, who gave the written informed consent was included in the study. Handicapped and bed ridden, Individuals undergoing orthodontic treatment, patient undergone any mucogingival surgery or depigmentation and children in ugly duckling stage were excluded from the study. The study was reviewed and approved by the institutional ethics and review board of the of Kothiwal dental college and research center with Ref Before the commencement of the study, the examiner were trained in the department of Public Health Dentistry .The Kappa coefficient value for inter - examiner reliability during examination was found to be 0 .92 for D and F component/d and f component of DMFS index, 0.82 for Melanin pigmentation, 0.84 for Feral attachment, and 0.81 for Tongue tie. These values reflect a high degree of conformity in observations. A pre -structured Preformat was used to record demographic and clinical details of the variables mentioned below.

The subjects were examined by type III clinical examination in respective households for dental caries using DMFS/doffs index Midline diatom was recorded using CPI probe; Space of more than 0.5 mm was considered as midline diatom Melanin pigmentation, feral attachment and tongue tie was recorded by index. Final analysis was performed on relative pairs of: Parent - offspring pair and Grandparent-Grandchildren pair. Data was analyzed using IBM SPSS Statistics version-19. Descriptive data was expressed as numbers (%). Chi square test was used to test the association of non-parametric data between relative pairs. Statistical significance was set at a $p < 0.05$.

RESULTS

The present study was done to assess the genetic influence on Dental caries pattern, feral attachment, Melanin pigmentation, Midline diatom and Tongue tie. 100 households comprising a total of 454 individuals were enrolled in the study. Families consisting of confirmed biological relation ranged from 4-6 individuals (Table 1).

Demographic characteristics	
Sample size	454
Number of families with 3 generations	66 families
Number of families with 2 generations	34 families
Both grandparents present	38 families
Only grandfather present	11 families
Only grandmother present	17 families
Number of relative pairs	
Grandfather-grandchild	68 pairs
Grandmother-grandchild	86 pairs
Father-children	199 pairs
Mother-children	205 pairs
Siblings	50 pairs

Table 1. Demographic characteristics of the study sample

In case of Dental caries, the prevalence was higher in granddaughter pairing with grandparents, which were found to be statistically significant (p<00001), whereas in Midline diatom, the prevalence was similar in grandson and granddaughter when paired with grandfather, which was statistically non-significant.[3] The prevalence was highest in granddaughter-grandfather pair in case of melanin pigmentation, which was found to be statistically significant and the prevalence of both the frenula attachment in grandson and granddaughter was found similar when being paired with each of grandparent (Table 2).

Variables	Pairs, n (%)	Son, n (%)	Daughter, n (%)	P- value
	Father-children			
	64/199 (32.16)	35/125	29/74	<.00001

DENTAL		-28	-39.2	
	Mother-children	42/131	48/74	0.64
	42/131 (32.06)	-32.06	-64.9	
	Father-children	29/125 (23.2)	27211	0.02
	36/199			
MIDLINE	(18.9)		-9.45	
DIASTEMA	Mother-children	10/131	0 / 74	0.49
	20/205 (9.75)	-13.15	-13.5	
	Father-children	55/125	41/74	0
	96/199			
MELANIN	(48.24)	-44	-55.4	
PIGMENTATION	Mother-children 106/205 (51)	61/131	45/74	
		-46.56	-60.8	0.18
	Father-children			
MARGINAL	68/199 (34.17)	41/125	27/74	36.5
FRENAL		-32.8	-36.5	
ATTACHMENT	Mother-children	43/131	29/74	0.52
	72/205 (35.12)	-32.82	-39.2	
	Father-children	72/125	43/74	0.09
	115/199			
GINGIVAL	(57.78)	-57.6	-58.1	
ATTACHMENT	Mother-children	65/131	42/74	0
	107/205 (52.19)	-49.61	-56.8	

Table 2. Prevalence of Dental caries, Midline diastema, Melanin pigmentation and Frenal attachment in Grandparents and grandchildren pairs

The prevalence of dental caries is highest in daughter-mother pair, which was statistically non-significant. Whereas in Midline diatom, it is in Son-father pair and in Melanin pigmentation, it is highest in Daughter-mother pair, which was statistically non-significant. The prevalence of both the frenula attachment in Son and daughter was found similar when being paired with each of parent.

DISCUSSION

Present study was carried out in district of Udham Singh Nagar, India. Sample composed of Sikh community emigrated from Pakistan during partition in 1947. These families with 2-3 generations had agriculture background therefore were living in the same locality, all bound by the common relationship. So it was convenient to collect sample for our study to assess the heritability patterns with in generations of Dental caries, midline diatom, frenula attachment, pigmentation of gingiva and tongue tie.

In present study, daughter pair had higher inheritance of dental caries from parents as compared to son pair. Many Epidemiological and clinical studies, through the use of tools such as DMFT and DMFS scores, have revealed a consistent trend in caries development, with female child having higher prevalence than males. The mechanisms of any genetic contributions to the increased prevalence of caries in females versus males can be speculated to reside in the sex chromosomes, exhibiting sex-linked modes of inheritance. The Amelogenin (AMEL-X) gene resides on the p arm of the X chromosome. Its locus is Xp22.31-p22.1. This gene and its protein product contribute to enamel formation in the dentition many studies explain that in females, it is possible for this kind of variation in AMELX to occur through the mechanisms of X inactivation and mosaics. Normally, the inactivation of one X chromosome is random, with 1: 1 distribution of the two AMELX genes inherited in females on the X chromosomes (mosaics in regards to the X chromosome, since one comes from one parent and the other comes from the other parent). Another way to explain the role of AMEL-Y in caries susceptibility is to consider its production of the Amelogenin protein. AMEL-Y gene only expresses 10% of Amelogenin that is expressed by AMEL-X. However, this additional 10% is not attained by females exhibiting X inactivation. Therefore, males may be expressing a greater amount of Amelogenin, contributing to the strength of the tooth and less caries susceptibility of the host. These proposed mechanisms of AMEL-Y may be one way to explain why when exploring the role of Amelogenin on caries formation, female's exhibit greater prevalence than males.

In our study, children of parents with dental caries also had higher prevalence of dental caries. Heredity has been linked with dental

caries incidence in scientific literature for many years. One of the earliest studies was in 1946 when Kline reported on 5400 people in 1150 families of Japanese ancestry, demonstrating that the decayed, missing, filled teeth (DMF) that occurred in offspring was quantitatively related to that which had been experienced by their parents. It was found that a high DMF father and a high DMF mother produced offspring, both sons and daughters, with a high DMF rate. The authors concluded that dental caries is strongly familial based with probable genetic and sex-linked associations. Similarly, Book and Grainne selected the parents and siblings of subjects from the Vipeholm study who were highly resistant to dental caries and found they also had significantly lower caries experience than the parents and siblings of the remaining subjects. The strong influence of the role of genes/heredity was observed in these historical landmark studies which laid the foundation for further research.

In our study, we found that prevalence of dental caries was higher in mother-children pair as compared to father-children pair. As dental caries is a transmissible disease and Sultans bacterium can be transmitted both vertically and horizontally. In vertical transmission S. mutants spread mainly from mothers to their children Therefore, we can assume that these familial aggregations may be a result of shared genes as well as from environmental exposures. When the data was analyzed for pattern of inheritance of dental caries, by Pedigree analysis, it showed that if both the parents have dental caries it conferred risk of inheriting dental caries in offspring (Figure.1).

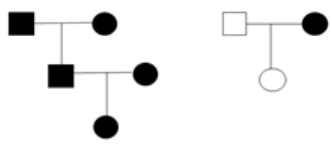

Figure 1: Pedigree of families showing most repeated patterns of dental caries (Shaded symbol represents a family member reported to be affected).

Gardiner discusses the etiology of the persisting midline diatom and noted that there is “almost no limitation concerning contributing factors. Undoubtedly, hereditary causes are found high up the list and we have all seen parents and offspring with this feature” similar results were found in our study. Grandfather-grandchildren pair had higher midline diatom prevalence as compared to grandmother-grandchildren pair. Higher prevalence was also seen in father-son pair.

Studied the mode of inheritance by drawing 15 pedigree charts. The probed always had a parent also positive for the trait. Eight of the propends inherited the trait from the father and other seven inherited from the mother, indicating complete penetrance of the gene. In 6 pedigrees, the trait was transmitted from father to daughter. Transmission was from father to son in 2 and from mother to daughter in 4. The mother transmitted the trait to the son in only 3 pedigrees excluding X lined recessive inheritance. These findings demonstrate that the transmission of median diatom to follow an autosomal dominant with full penetrance similar results were found in our study, when the data was analyzed by Pedigree analysis, that probed always had a parent also positive for the trait (Figure: 2).

Figure 2: Pedigree of families showing most repeated patterns of Midline diatom (Shaded symbol represents a family member to be affected).

Melanesia universalis hereditary, universal acquired Melanesia and familial universal are just some of the other terms coined by various authors to describe patients with a generalized diffuse hypermelanosis without systemic symptoms, but often with a familial pattern[4]. This condition has been described mostly in blacks, Hispanics, and oriental individuals, with both the sexes being affected

equally. Mode of inheritance is still debated upon since a number of inheritance patterns are recognized, mainly: autosomal dominant. Though such cases have been previously reported in dermatology, no such case has been reported in dental literature even though there are significant oral findings in these patients.

Gingival hyper-pigmentation also known as racial gingival pigmentation is accepted to be a genetic trait similarly in our present study, we found parents and their successive generations with melanin pigmentation of gingiva. When the data was analyzed by Pedigree analysis it also showed that that propends with melanin pigmentation had a parent also positive for the trait. In 1979, Durned included genetic as one of the etiological factor for melanin deposits and the diversity of range of pigmentation depends on geographical location and genetics.

Tongue-tie appears as a sole anomaly, though it is sometimes accompanied by other congenital anomalies such as cleft palate. As it has a hereditary nature, it occurs more commonly in male children and has been suggested to be related to the X-chromosome. The exact pathological mechanism of ankyloglossia remains unclear, and its conclusively hereditary nature has yet to be elucidated, though numerous relevant studies have been performed. But in our sample, we found that all the individuals had clinically acceptable, normal range of free tongue = > 16 mm. No indeed tongue tie case was not diagnosed in our sample, so on the basis of our findings we cannot conclude that tongue-tie shows inheritance pattern or not . But previous literature reports that tongue tie has a hereditary nature.

In our sample, we found marginal and gingival frenula attachments in majority of cases, that showed the inheritance of marginal and gingival frenula attachment was around 35% and 55% respectively from parents to their offspring's through the clinical examination across the three generations in a family. There are few limitations in our study, firstly, we took homogenous sample that might have some effect on results when sample were heterogeneous.[5] Secondly, age differences among sample size (different age people may subject to different exposure variables that were time dependent).

CONCLUSION

Lastly we can conclude that, these diseases/conditions have some correlations of inheritance. The pedigree analysis of genetic inheritance thus gives a valuable insight into genetic epidemiology and leads to better understanding of the pattern of occurrence of diseases. This study is one of the few attempts at defining the genes implicated in oral disease process, and lead to improved understanding and prevention of the factors leading to the disease.

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