GENETICS AS A TOOL FOR ORAL HEALTH DIAGNOSIS AND DISEASE PREVENTION: A FAMILY BASED STUDY

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Abstract

Objectives:
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.
Materials and methods: 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.
Results: 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 & 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
Conclusion: 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

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 (−0.16–−0.09).11 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 programmeetc, 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 factorin determining health and disease in families and interplay of such factors with environmental factors[3]

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. 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.[1]

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 (NHANES surveillance summaries on oral health, 2005). 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.[4]

Moreover, caries prevalence was observed to vary among different racial groups, with non Hispanic whites having the lowest caries prevalence and severity (NHANES, 2005). However, this could be partly due to different genetic factors as well. Pioneering twin studies investigating the heritability (i.e., proportion of variation due to genes) 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 64–85%. In recent, heritability study based on larger families, heritability of dental caries in the primary dentition was over 50% [4.]

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 [2].

Therefore, the present family based study was planned to assess the genetic influence on dental caries pattern, frenal attachment, melanin pigmentation, midline diastema and tongue tie.

Methodology

A descriptive study was conducted with a convenient sample of 100 households comprising 454 individuals, from Sikh community, from the district Udham Singh Nagar, Uttrakhand, 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 centre with Ref No.KDRC/ IERB/ 11/2016/06

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 Frenal attachment, and 0.81 for Tongue tie. These values reflect a high degree of conformity in observations.A pre -structured Proforma 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/dmfs index Midline diastema was recorded using CPI probe; space of more than 0.5 mm was considered as midline diastema . Melanin pigmentation, Frenal attachment and tongue tie was recorded by index given by Takashi et al, Plecek Mirkoand Kotlow' sclassification .Final analysis was performed on relative pairs of: Parent – offspring pair and Grandparent – Grandchildren pair.

Statistical methods:

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, Frenal attachment, Melanin pigmentation, Midline diastema 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)

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 diastema, the prevalence was similar in grandson and granddaughter when paired with grandfather, which was statistically non-significant. 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 frenal attachment in grandson and granddaughter was found similar when being paired with each of grandparent. (Table 2)

Variables	Pairs, n (%)	Grandson, n %)	Granddaughter, n (%)	P- value
DENTAL CARIES	Grandfather-grandchildren 25/68 (36.76)	5/38 (13.15)	20/30 (66.66)	<.00001
	Grandmother-grandchildren 29/86 (33.72)	7/48 (14.58)	22/38 (57.9)	<.00001
MIDLINE DIASTEMA	Grandfather-grandchildren 16/68 (23.52)	9/38 (23.62)	7/30 (23.33)	.338352
	Grandmother-grandchildren 7/86 (8.1)	2/48 (4.16)	5/ 38 (13.51)	1
MELANIN PIGMENTATION	Grandfather-grandchildren 26/68 (38.23)	11/38 (28.94)	15/30 (50)	.3828
	Grandmother-grandchildren 21/86 (24.41)	19/48 (39.5%)	2/38 (5.26)	.112
	Grandmother-grandchildren 107/205 (52.19)	65/131 (49.61)	42/74 (56.75)	.0001

MARGINAL FRENAL ATTACHMENT	Grandfather-grandchildren 96/199 (48.24)	55/125 (44)	41/74 (55.4)	36.48
	Grandmother-grandchildren 72/205 (35.12)	43/131 (32.82)	29/74 (39.18)	.5168
GINGIVAL FRENAL ATTACHMENT	Grandfather-grandchildren 115/199 (57.78)	72/125 (57.6)	43/74 (58.10)	.088

·Tongue tie: No relevant cases detected

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 diastema, 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 frenal attachment in Son and daughter was found similar when being paired with each of parent. (Table 3)

Variables	Pairs, n (%)	Son, n (%)	Daughter, n (%)	P- value
DENTAL CARIES	Father-children 64/199 (32.16)			
		35/125 (28)	29/74 (39.18)	<.00001
	Mother-children 42/131 (32.06)	42/131 (32.06)	48/74 (64.86)	.639
MIDLINE DIASTEMA	Father-children 36/199 (18.9)	29/125 (23.2)	7/74 (9.45)	.022
	Mother-children 20/205 (9.75)	10/131 (13.15)	0 / 74 (13.51)	.4917
MELANIN PIGMENTATION	Father-children 96/199 (48.24)	55/125 (44)	41/74 (55.4)	.003
	Mother-children 106/205 (51)	61/131 (46.56)	45/74 (60.81)	.1792
MARGINAL FRENAL ATTACHMENT	Father-children 68/199 (34.17)	41/125 (32.8)	27/74 (36.48)	36.48
	Mother- children 72/205 (35.12)	43/131 (32.82)	29/74 (39.18)	.5168
GINGIVAL FRENAL ATTACHMENT	Father-children 115/199 (57.78)	72/125 (57.6)	43/74 (58.10)	.088
	Mother-children 107/205 (52.19)	65/131 (49.61)	42/74 (56.75)	.0001

·Tongue tie: No relevant cases detected

Table 3: Prevalence of Dental caries, Midline diastema, Melanin pigmentation and Frenal attachment in Parents and Children

Discussion

Present study was carried out in district ofUdham 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 diastema, frenal 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. 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 mosaicism. 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 (mosaicism 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, females exhibit greater prevalence than males[16]

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 Klien 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 Grahnen 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[4,5] . 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 S.mutans bacterium can be transmitted both vertically andhorizontally. In vertical transmission S. mutans 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)

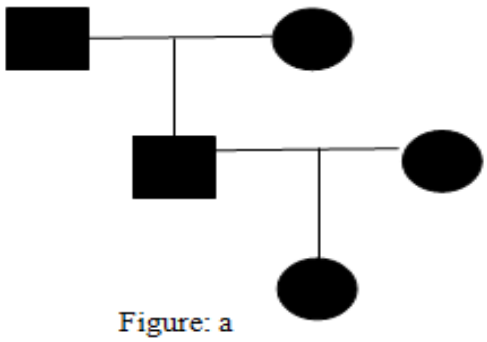

Figure: a

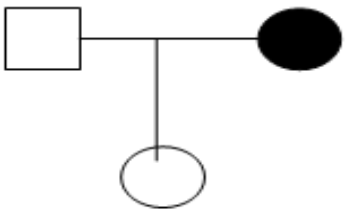

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Fig 1: Pedigree of families showing most repeated patterns of dental caries (Shaded symbol represents a family member reported to be affected).

Gardiner discusses the etiology of the persisting midline diastema 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" (Taylor JE.,1939) similar results were found in our study. Grandfather-grandchildren pair had higher midline diastema prevalence as compared to grandmother-grandchildren pair. Higher prevalence was also seen in father-son pair.

In 1995, Muller et al. studied the mode of inheritance by drawing [15] pedigree charts. The proband always had a parent also positive for the trait. Eight of the probands inherited the trait from the father and other seven inherited from the mother, indicating complete penetrance of the gene.[15]

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 diastema to follow an autosomal dominant with full penetrance similar results were found in our study, when the data was analyzed by Pedigree analysis, that proband always had a parent also positive for the trait (Figure: 2)

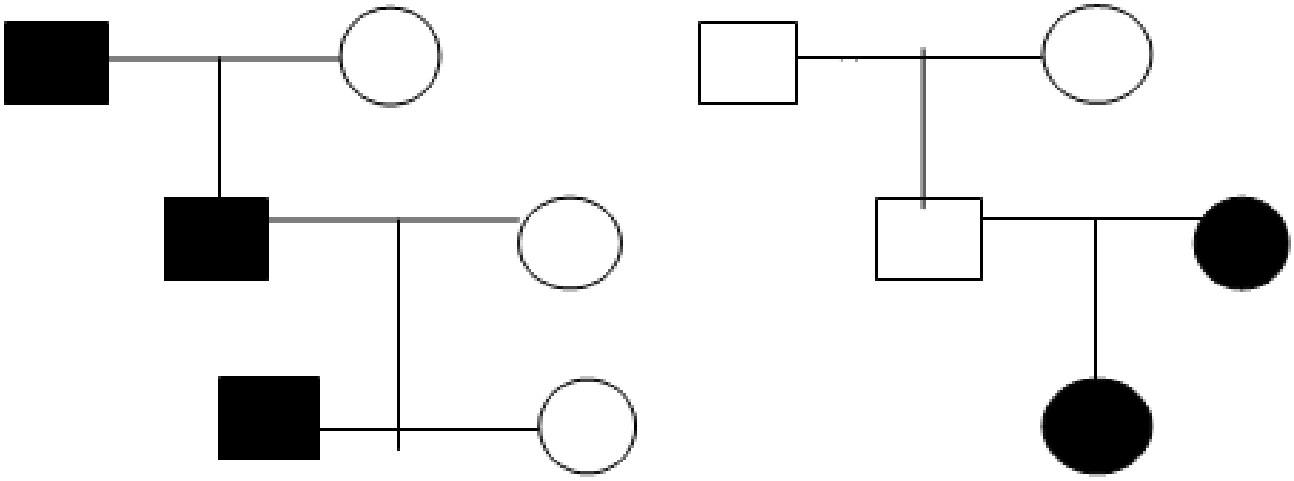

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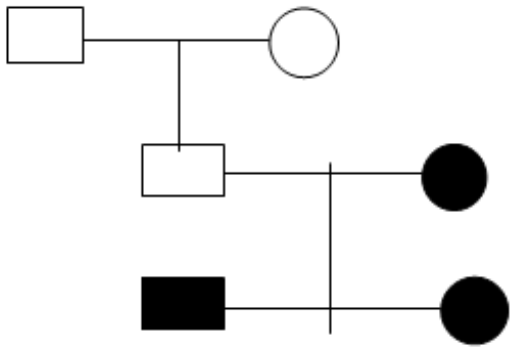
Fig 2: Pedigree of families showing most repeated patterns of Midline diastema (Shaded symbol represents a family member to be affected).

Study done by Gass JR et al on 30 extended families in Cleveland, USA, suggested a possible genetic basis for maxillary midline diastema and a greater role of environmental factors.

Melanosis universalis hereditaria, universal acquired melanosis, 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 [7]. 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 recognised, mainly: autosomal dominant autosomal recessive with germ-line mosaicism [20]. 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 probands with melanin pigmentation had a parent also positive for the trait (Figure:3).[9]



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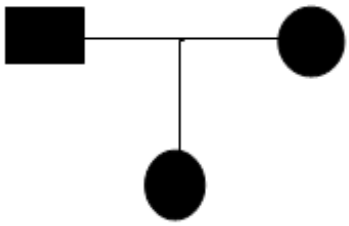

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Fig 3: Pedigree of families showing most repeated patterns of Melanin pigmentation (shaded symbol represents a family member to be affected).

In 1979, Durnmet included genetic as one of the etiological factor for melanin deposists and the diversity of range of pigmentation depends on geographical location and genetics.[16]

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 frenal attachments in majority of cases, that showed the inheritance of marginal and gingival frenal 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 heterogenous. Secondly, age differences among sample size (different age people may subject to different exposure variables that were time dependent).

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.

Conflicts of Interest: None of conflicts present

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