Original Article

Consanguineous marriage as a key indicator of isolated congenital dental anomaly among South Indian population – A cross-sectional study

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Abstract

Background: Orofacial anomalies occur due to incomplete fusion of developmental lines in the head and neck region. Dental anomalies regarded as the most common orofacial anomalies either in isolated or syndromic forms arise due to genetic and environmental factors. Among genetic influences, consanguineous marriages are considered as a significant predisposition factor in the transmission of congenital defects and several autosomal recessive diseases from one generation to other with an increased risk of detrimental effects on offspring.

Aim: The present study was aimed to evaluate the prevalence and significant association between consanguinity and isolated dental anomalies with that of nonconsanguineous parents among south-Indian population.

Methodology: A total of 116 participants with and without dental anomalies in isolated form pertaining to tooth size, shape, altered morphology, number and eruption were selected followed by brief case history. Participants with a positive history of consanguinity were categorized as Group A while others were categorized under Group B.

Results: Sixty-four out of 116 participants (55.17%) showed positive consanguinity (Group A) among which 18 females (56%) and 14 males (44%) presented with isolated dental anomalies. 12 females (66.6%) and 9 males (64.2%) in Group A showed significance with first cousin ($P = 0.00204$) whereas no significance was observed in other consanguinity type ($P = 0.7287$). Nonetheless, the overall frequency of isolated dental anomalies was slightly higher in Group A than Group B that was statistically significant ($P = 0.0213$).

Conclusion: A positive correlation between dental anomalies among offspring of consanguineous marriages revealed such prevalence may be attributed to increased risk of recessive deleterious gene expression or defective allele carried to offspring.

Keywords: Consanguinity, defective allele, dental anomalies, first cousin, gene transfer, recessive disorders

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INTRODUCTION

The development of gametes, fertilization, formation of embryos and fetuses is a continuous complex process comprising of molecular, cellular and structural dynamics which involve all the naturally occurring unidirectional adaptations in the life of a human being. Understanding this complex phenomenon provides knowledge about prenatal diagnosis; treatment protocols to improve birth outcomes by preventing infant mortality; congenital birth defects; postnatal long-term complications and defining the potential to develop certain pathologies such as congenital heart disease, and even carcinogenesis.[1] The embryonic development involves the process of establishment of a primitive organ from a single cell stage over a period of 38 weeks (Approximately 266 days) that includes the preimplantation period of 1st–2nd week; the embryonic phase which involves the 3rd–8th week and the fetal period which is from 9th week till the birth.[2] Appearance and formation of germ layers namely the ectoderm, endoderm and mesoderm mark the beginning of the embryonic period around 15th–16th day that subsequently follows a series of interaction with each other by several signaling pathways as the embryo develop and contribute to the formation of all tissues and organs.[3] Proliferation of several processes and/or prominences of embryological tissues during this phase results in development of head and neck structures including skull, face and oral cavity.[4] Thus, the majority of oral and Para-oral embryological development occurs between 3rd and 8th week, and the orofacial complex structures are fully formed around 4th month. In the fetal period, all the major structures are already formed in the fetus, but they continue to grow in length and increase in weight with minimal differentiation and organogenesis.[5]

Oro-facial structures are complex anatomical structures that include hard and soft tissue components with diversifying patterns than in any other region and are more prone for developmental disturbances and anomalies caused either genetically or by acquired factors. The term "anomaly" was often used to describe the structures that are not formed regularly or those structures that appear different from their normal counterparts caused by a combination of genes or environmental factors.[6] Orofacial anomalies occur mainly due to disordered embryonic development where there is incomplete fusion of developmental lines in the orofacial region such as face, palate, tongue, lips, alveolar process including teeth, jawbones and the oral mucosa. These developmental anomalies are more likely to be seen in related parents of consanguineous marriage than unrelated parents.[7] Consanguineous marriage denotes the marriage between two individuals who are closely related family members like first/second cousins or who share a common ancestor or even closer blood relation of maternal offspring. The type of consanguineous marriage can be broadly divided as Type 1-first cousin, Type 2-second cousin and Type 3-more distant/maternal or complexly related individuals. It was widely accepted that consanguineous marriages are an important factor in the transmission of congenital defects and autosomal recessive diseases from one generation to the next with an increased risk of detrimental effects on offspring or even results in postnatal mortality.[8]

Studies have shown the rate of congenital malformations is 2.5 times higher in parents of consanguineous marriages than nonconsanguineous marriages due to the increased risk of carriers of the same deleterious gene or defective allele of offspring.[9] Several studies have also demonstrated a significant association between consanguinity and complex diseases such as genetic and chromosomal aberrations, neurological defects, mental retardation, hypertension, diabetes, gastrointestinal disorders, dental anomalies and even malignancies.[10,11] In the orofacial region, studies have shown higher incidences of craniofacial syndromes such as hereditary ectodermal dysplasia, Down syndrome; pigmented lesions like Xeroderma pigmentosum; oral defects such as cleft lip and palate among offspring of consanguineous married parents.[12] However, dental anomalies in isolated form pertaining to disturbances in teeth such as fusion, germination, supernumerary teeth, enamel hypoplasia, oligodontia and delayed eruption was not fully evaluated.[13] Hence, the present cross-sectional study was conducted among the South Indian population of consanguineously married individuals to evaluate the prevalence and significant association between consanguinity and isolated dental anomalies with that of nonconsanguineous parents.

METHODOLOGY

The present cross-sectional study was conducted among the patients visiting the outpatient department of our dental college and hospital from June 2019 to January 2021. All the patients aged between 18 and 60 years with and without dental anomalies were evaluated for their participation and were informed about the purpose of the study as well as assured that their participation was purely voluntary. The study included all the individuals of both genders more than 18 years of age who presented with isolated dental anomaly in any form pertaining to tooth size (microdontia, macrodontia), shape/altered morphology (fusion, gemination, dilacerations, taurodontism, dens invaginates, dens evaginatus, talon

cusp), number (oligodontia) and eruption (delayed, transposition) with known information of consanguineous or nonconsanguineous marriage (type) of their parents.

Individuals with congenital orofacial anomalies with dental defects, dental anomalies associated with systemic diseases or any syndromes, uncertain history on consanguinity, permanent residents/nativity other than south India, and all those unwilling to participate in the study were excluded from the study. A total of 116 participants with and without dental anomalies in isolated form pertaining to tooth size, shape or altered morphology, number and eruption were selected into this cross-sectional study based on the exclusion and inclusion criteria. A briefcase history about their demographic characteristics (age, gender, place of birth, residential address), presence of any systemic diseases and marriage particulars of their parents was recorded. Participants with a positive history of consanguinity marriage irrespective of the parents' consanguinity type such as first cousin (Type 1), second cousin (Type 2) and more distant/maternal or complexly related individuals (Type 3) were all accepted and categorized as Group A while participants of nonconsanguineous parents were categorized under Group B. A complete oral examination was performed; the type of isolated teeth anomaly was identified and documented for every single individual.

Using statistical package for the social sciences (SPSS, Version 19.0. IBM Corp., Armonk, NY). Descriptive statistics was carried out to categorize the variables such as gender, presence and absence of anomalies based on the number of observations and resulting percentages to evaluate their prevalence. Chi-square analysis was applied to test significance among and between the groups followed by paired *t*-test (two samples for means) to find interrelationship and differences between the ratios. Statistical significance level was accepted as $P < 0.05$.

RESULTS

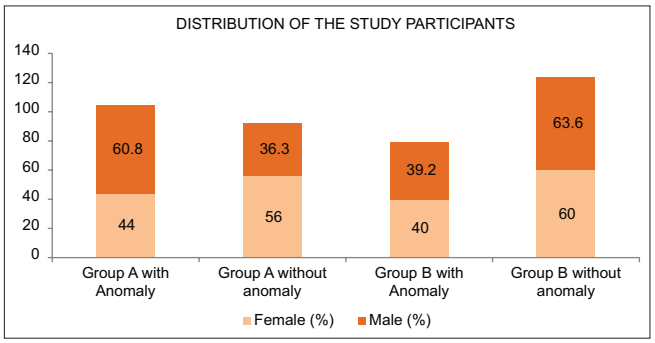
This study included a total of 116 participants ranging from 18 to 60 years of age. Sixty-four (41 Females, 23 Males) out of 116 participants (55.17%) showed positive consanguinity (Group A) comprising of 32 (50%) individuals with anomaly and 32 (50%) were presented without any anomaly. Among the 52 participants in Group B (30 Females, 22 Males), 20 (38.4%) presented with anomaly and 32 (61.5%) without any anomaly. The assessment of isolated anomaly subtypes such as tooth size, shape or altered morphology, number and eruption was not performed among each category due to unequal distribution of data since some anomalies included for consideration were not witnessed in any of the study categories and are thus not included in our observational results. However, overall frequency of isolated dental anomalies was slightly higher in the positive consanguinity (Group A), a difference that was statistically significant ($P = 0.0213$).

On analysis of the prevalence among female population, it was observed 18 (44%) out of 41 females in Group A and 12 (40%) out of 30 in Group B showed anomaly whereas 23 (56%) and 18 (60%) of Group A and B presented without any anomaly respectively with no statistical significance between both the groups ($P = 0.742288$). In male population, it was observed 14 (60.8%) out of 23 in Group A and 8 (36.3%) out of 22 in Group B showed anomaly whereas 9 (39.2%) and 14 (63.6%) of Group A and B presented without any anomaly respectively with no statistical significance between both the groups ($P = 0.10019$) [Graph 1].

In addition, the frequency according to consanguinity type was 21 out of 32 for Type 1 (First cousin) (65.6%) and 11 out of 32 (34.4%) for Type 3. None of the participants observed were identified under Type 2. Of the total 32 participants with isolated dental anomaly, 12 out of 18 females (66.6%) and 9 out of 14 males (64.2%) in Group A belong to first cousin consanguinity showed significance ($P = 0.00204$) whereas no significance was observed in 6 female (33.3%) and 5 male (35.8%) from maternal consanguinity ($P = 0.728$). Table 1 shows the summary of data distribution in terms of several parameters (Group, Gender, subtypes for groups) observed in the study and their significant level. Statistical significance level was accepted as $P < 0.05$.

DISCUSSION

Over the years, primary health care providers and clinical genetics specialists consider that consanguineous marriage leads to increased genetic homogeneity of



Graph 1: Graph showing the frequency distribution of dental anomalies among female and male population

Table 1: Distribution of all participants based on group and subtypes for groups, *n* (%) and the statistical analysis

Group	Subtypes of groups	Gender	Anomaly present, *n* (%)	Anomaly absent, *n* (%)	χ^2	*P*	Overall *P* value
Group A	Type 1	Female	12 (66.6)	18 (78.2)	6.071	0.00204*	0.0213*
		Male	9 (64.2)	6 (66.7)			
	Type 3	Female	6 (33.3)	5 (21.7)	0.1202	0.72879	
		Male	5 (35.8)	3 (33.3)			
Group B	Female	-	12 (40)	18 (60)	0.0709	0.79001	
	Male	-	8 (36.3)	14 (63.6)			

*$P<0.05$, statistically significant. Group A: Consanguineous marriage, Group B: Nonconsanguineous marriage, Type 1: First cousin, Type 3: Maternal related, χ^2: Chi-square test

hereditary-related (in-bred) individuals triggering adverse impact in terms of increased genetic risks/negative effects to the offspring as a result of homozygosity of detrimental genes as opposed to the potential social and economic benefits. The highest consanguineous marriages are reported in North Africa and Western Asian countries (20%–50%) that are usually related to several factors such as low socioeconomic status, cultural practices, social norms, illiteracy and population resident of rural areas.[14] In the recent years, the practice of consanguineous marriage has been drastically declined in countries such as the United States, Western Europe and in parts of Asia and Africa however despite risk association in many parts of the middle-east nations, and in Indian subcontinent, it is still followed owing to belief on strong family bonds, customs, cultural practices, the integrity of a specific group of population, low socioeconomic status, illiteracy and rural habitation.[15]

In the present study, 52 out of 116 (44.8%) participants presented with at least one isolated developmental dental anomaly among which 32 (61.5%) were offspring of consanguineous marriage parents and 20 were from nonconsanguineous type. Studies by Guttal *et al*.,[16] Patil *et al*.,[17] Deolia *et al*.[18] and Bandaru *et al*.[19] among Indian population also showed isolated forms are more common than syndromic-associated dental anomalies. The reason behind this dissimilarity of reported isolated anomalies may be associated with differences in population group, sample size considerations, examination methods, inclusion and exclusion criteria, not taking into account of environmental or local factors such as medications, systemic diseases associated, vaccination against rubella or varicella acquired by the mother at the time of pregnancy/delivery and even ancestral alterations between the studied population.

Higher frequency of these anomalies was seen in consanguineous type (61.5%) in our study compared to the previous studies by Tayebi *et al*.,[7] Bağcı *et al*.,[8] Khan,[11] Lakshmayya *et al*.,[12] Shokry and Alenazy,[20] Alsoleihat and Khraisat,[21] Packyanathan and Preetha,[22] and Kanaan *et al*.[23] in their respective population-based studies. It was proposed that the effect of consanguineous marriage on the development of higher variants of isolated dental anomalies had been attributed to increase in the presence of two identical alleles of a particular gene associated with subsequent failure of resistance to environmental factors associated.[8] However, the exact role of genetic or molecular dynamics in incidence of homozygous mutation, frequency of chromosomal aberrations, increased expression of identical allele associated with consanguineous marriage has not yet been fully established in the previous literature. Pedigree analysis studies with genetic expression analysis using methods like *In situ*-hybridization expression technique,[24] whole-exome sequencing[25] focusing on the influence of molecular pattern on dental evolution correlated with morphological variations can help in characterization of these isolated anomalies. Although in this study individuals with syndromes or known congenital diseases were excluded to eliminate the possibility of congenital anomalies arising from these syndrome associated etiology, it should not be underestimated that studies have also shown many syndromes such as Haim-Munk[26] and Papillon–Lefèvre syndromes,[27] Ehler-Danlos syndrome,[28] Chediak–Higashi syndrome[29] presenting with oral manifestations are closely related to consanguineous marriage.

In addition, the frequency according to consanguinity type was 21 out of 32 for Type 1 (First cousin) (65.6%) and 11 out of 32 (34.4%) for type 3. This observation was in agreement with other studies by Tayebi *et al*.,[7] Khan,[11] Barbour and Salameh,[30] Nath *et al*.[31] Thus, it can be claimed that children of first-cousin consanguineous marriage have an increased frequency and overall risk of being affected genetically or present with any form of isolated dental anomaly as compared to the other type and nonconsanguineous marriages. In accordance with this, we also observed first cousin marriages are more common than other types of consanguineous marriages. Bağcı *et al*.,[8] Khan[11] and Hamamy[13] put forward that this specific pattern of increased rates of marriages between first cousins among the south Indian population can be related to customs, civilization, religious belief, philosophy, cultural practices and geographical

location. Conventionally, two different hypotheses namely competition over companions and property/assets have been shown to initiate both sex-biased investment and sex-biased dispersal patterns were put forward[32] however several other factors such as cultural norms, taboos, preferences of having powerful elder-generation partners, living close with their grandparents, Joint family norms like family bonds, secure and safety that enforces family harmony were believed to play a predominant role. In the present study, children and participants <18 years of age, the family members of the study participants including their parents, siblings and individuals presented without dental anomaly who had isolated dental anomaly in the past that was treated for esthetics and other restorative purposes were not taken into consideration among both the consanguineous marriage and nonconsanguineous marriage group that may have influenced that actual prevalence ratio of occurrence of these isolated congenital anomalies among south Indian population.

CONCLUSION

Consanguineous marriages are the key determinants in the prevalence of several craniofacial abnormalities with an increased risk for congenital orofacial, dental malformations and autosomal recessive disorders due to higher expression of recessive deleterious gene or defective allele carried to the offspring with some increased consequential postnatal mortality in the progenies of first-cousin marriages. Within the limitations of the study, we observed a significant correlation between isolated dental anomalies among offspring of consanguineous marriages to the first cousin and to that of other consanguinity types with slight higher frequency than offspring of nonconsanguineous marriages. In countries like India where traditional beliefs especially at the rural areas are relatively high, increasing public awareness toward hostile effects of consanguinity by health care service providers associated with regulatory guidelines for screening consanguineous partners and their offspring are obligatory to ensure a better quality of life.

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Conflicts of interest

There are no conflicts of interest.

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