The present community based study entitled “A comparative study to assess Oro – Dental Variations and Oral Health Status in children born out of Consanguineous and Non – Consanguineous marriages” was conducted in Aligarh city (Municipal Corporation); Uttar Pradesh, India.

The study population included a total of 2000 children aged 6 – 9 years and their parents (1600 Non – Consanguineous and 400 Consanguineous) living in 1597 households. The following were the aims of the study:-

1. To assess the various oral and dental developmental defects (non - syndromic supernumerary teeth, cleft lip – palate, fusion, hypoplastic/hypocalcemic defects etc) in children born out of consanguineous and non – consanguineous marriages and its association with their parents.
2. To assess the dental parameters (molar relationship, incisor relationship, spacing, crowding etc.) in children born out of consanguineous and non- consanguineous marriages and its association with their parents.
3. To assess the dental caries status (DMFT/deft index) in children born out of consanguineous and non- consanguineous marriages.
4. To record the history of risk factors associated with dental caries in children.
5. To find out the Coefficient of Inbreeding (F) for the study population.

The main reported consequence of Relation or Consanguineous marriage is the higher risk of transfer of Autosomal Recessive Disorders from one generation to the next, as it is difficult to find a partner who carries the same disorder unless they are related.\(^{127,28}\). 12.5% of genes are common between the first cousins, it is most likely that 6.25% genes are transferred to their children\(^{29,30}\).

Consanguinity in a way is responsible for alteration of genotypic frequencies; hence influences the structure and formation of a population\(^{31}\). Thus, offspring’s of first cousin
DISCUSSION

Consanguineous marriage have an overall risk of 1 in 20 of being affected or malformed as compared to 1 in 40 in the general population.

In the present study, Muslims showed a higher frequency of consanguinity. This result agrees with studies conducted in Lebanon\textsuperscript{15} and Pondicherry (India)\textsuperscript{69}. Within different religions, there are varied perceptions regarding consanguinity. Like in Christianity, consanguineous marriages have been banned. Special permission has to be taken for first cousin marriage from the Roman Catholic Church and the Protestants allow marriages up to and including first cousins only.

In Muslims, uncle – niece union is prohibited. According to Akrami SM and Osati Z\textsuperscript{17} and Saadat M\textsuperscript{18, 19}, the relationship of consanguinity with religion is limited; especially in the Muslim religion, where a Hadith (recorded pronouncements) of Prophet Mohammad (PBUH) quotes that “Do not marry cousins, as the offsprings may be disabled at birth”, hence altogether discouraging such marriages. However, the Prophet did marry his daughter to his first cousin. Thus, for Muslims, consanguineous marriages could be taken as Sunnah (deeds of the Prophet). In Hindu religion; Southern part of India has a long tradition of uncle – niece and first cousin marriage\textsuperscript{22}.

In the study, union between the first cousins (85\%) was the most preferred marriage. Similar observations have been reported by others\textsuperscript{4, 9, 16, and 28}, however another study on the Chilean population\textsuperscript{7} showed marriage between second cousins as the most preferred consanguineous marriage. However; for a particular race, tribe or say a place too, the specific pattern of consanguineous union differs. Author says, it mostly depends upon the traditional custom and beliefs\textsuperscript{22}. For example, first cousin union between a man and his Father’s Brother’s Daughter (FBD) is preferred in Arab Muslim communities. Uncle – niece and union between a man and his Mother’s Brother’s Daughter (MBD) is favored in South India\textsuperscript{21}, Han Chinese\textsuperscript{49} and The Tuareg of North Africa\textsuperscript{50}.

The present study showed that fathers and mothers were significantly more educated in the consanguineous group. Fathers (males) more educated in consanguineous group was in conformity with the studies of Judi R and Saxena P C\textsuperscript{106} and Hussain R and Bittles A H\textsuperscript{107}, the plausible explanation is that more educated males become a valuable asset for the
family, hence marrying their cousins in a way preserves the family property. Contrary to the above studies, Barbour B and Salameh P\textsuperscript{[15]} and Kerkeni E et.al.\textsuperscript{[108]} showed that males who were educated had the lowest prevalence of consanguineous marriage.

An inverse relation between consanguinity and women’s education status has been reported by Hussain R and Bittles A H\textsuperscript{[107]} and Barbour B and Salameh P\textsuperscript{[15]}, though the present study showed that more educated women were associated with consanguineous group, reason being that, Aligarh city is fortunate enough to have a world renowned Aligarh Muslim University and also a female is allowed to continue her education, while search goes on for a suitable partner, hence tends to be more educated. Blue collar occupation (self employed) was significantly higher in the study in consanguineous group; similar results were reported in Yemen\textsuperscript{[106]} and Tunisia and Croatia\textsuperscript{[108]}

In the research study, mothers with Class I Molar relationship were significantly higher in consanguineous group and different classes of molar relationship of fathers were also significantly higher in the consanguineous group. On to their respondents, the first permanent molar relationship did not show any association with either of the study groups, may be because 310 respondents of non-consanguineous group and 56 of consanguineous group in the study did not have an erupted first permanent molar, hence relationship could not be recorded. While different types of deciduous second molar relationship had a significant association with consanguinity; which in the future has got a predilection to develop into either classes of permanent first molar by mandibular growth and late and early mesial shift of molars.

Federick in 1836 reported that malocclusions whether skeletal or dental can be transferred from generations to generations; hence interplay of genes\textsuperscript{[89]}. The famous example of “Hapsburg jaw” pedigree analysis concluded that Class III malocclusions with prognathism were genetically determined. Results of various pedigree studies suggest the possibility of autosomal inheritance pattern for Class II Division 2 malocclusion and multifactorial inheritance pattern for Class II Division 1\textsuperscript{[90]}, hence supporting the present study; however, Lauc T, Rudan P, Rudan I and Campbell H\textsuperscript{[87]} showed that there is no consistent effect of inbreeding on molar relationship.
The different classes of incisal relationship of mothers and fathers, Class I and Class II Division I incisal relation of the respondent was significantly higher in the consanguineous group. The effect of inbreeding on overjet, overbite i.e. Incisal relationship has been confirmed in two studies \cite{87 and 109}, concluding that the occlusal relationship in humans are to some extent controlled by a large number of genes, which are recessive in nature.

Spacing in mothers and their respondents for the present study did not show any significant association with either of the study groups, while in fathers spacing was significantly higher in the non-consanguineous group. Crowding in mothers and fathers was significantly higher in consanguineous group while crowding in their respondents did not show any association with either of the study groups. The findings were supported by Normendo D, Almeida M A O, Quintao C C A \cite{88} where the role of heredity was emphasized and exacerbated through inbreeding.

On the other hand in a Croatian study \cite{87} the authors reported that inbreeding had little/no effect on crowding/spacing and higher the genetic contribution as an etiological factor, the prognosis after treatment worsens. History of trauma for the present study did not show any association with either of the study groups for mothers, fathers or their respondents, hence emphasizing the role/impact of inbreeding.

The present study brought out that fusion, talons cusp, non-syndromic supernumerary teeth, congenitally missing/impacted teeth, ectopic eruption, hypoplastic/hypocalcemic defect, molar incisor hypomineralization, cleft lip – palate and microdontia were significantly higher in mothers of consanguineous group. In fathers – fusion, gemination, congenitally missing/impacted teeth, ectopic eruption, hypoplastic/hypocalcemic defect, molar incisor hypomineralization were significantly higher in consanguineous group as compared to non-consanguineous.

Their respondents had the presence of – fusion, gemination, talons cusp, non-syndromic supernumerary teeth, congenitally missing/impacted teeth, ectopic eruption, hypoplastic/hypocalcemic defect, molar incisor hypomineralization, cleft lip – palate,
microdontia and dens evaginatus which were significantly higher in consanguineous group. The absence of radiographic evaluation for the dental developmental anomalies and the age group inclusion criteria for the respondents as 6 – 9 years, may have acted as limitations for the present study in bringing out the actual presence and hence the association of dental anomalies in the study population with either of the groups.

For cleft births, Elahi MM et. al. [71] and Lakshmayya N D, Srinivasa R M, Goel S [92] supported consanguinity as one of the etiologic agent for oral clefts whereas studies conducted in Kuwait [72] and Nigeria [73] found no association between consanguinity as an etiological agent and oral clefts.

If any disturbance occurs with the various stages in the life cycle of the tooth, the following developmental defects are seen - **initiation** (tooth agenesis/congenitally missing teeth, ectopic eruption, non syndromic supernumerary teeth), **proliferation** (non–syndromic supernumerary teeth), **histodifferentiation** (non syndromic supernumerary teeth, Talons cusp, dens Evaginatus), **morphodifferentiation** (fusion, gemination, microdontia, non syndromic supernumerary teeth) and **apposition** (hypoplasia). A strong genetic component with each stage of the life cycle of tooth is predicted, however the interplay of genetic factors remain unknown and is an area of further research [91].

Tooth agenesis or congenitally missing teeth was significantly higher in the present study in the consanguineous group. Similar results were revealed by other workers [80, 86, 93 and 94]. Garib D G, Alenkar B M, Ferreria F V, Ozawa T O [80] concluded that genetics probably presents itself as the prime etiological factor for tooth agenesis. There are ethnical differences too in the prevalence of tooth agenesis. Asians tend to show an inclined prevalence [110]. However Chen YH, Cheng NC, Wang YB, Yang CY [81] and Kapdan A et.al. [82] found no association of tooth agenesis with consanguinity.

Non–syndromic supernumerary teeth have shown a true co–relation with consanguineous marriages in studies conducted in Saudi Arabia [37] and Lebanon [83]. Similar results were revealed in the present study with respect to non–syndromic
supernumerary teeth. The study indicated that fusion, gemination, talons cusp and microdontia were significantly higher in consanguineous group, which were in conformity with the studies by Garib D G, Alenkar B M, Ferreria F V, Ozawa T O \cite{80} and Suprabha BS, Sumanth KN, Baaz K, George T \cite{93}.

However, 2,611 pre-school children, aged 2 and 6 year old were evaluated in a study conducted in Taiwan for the prevalence of congenital dental anomalies like hypodontia, hyperdontia, fusion, gemination etc, but no association with consanguinity could be ascertained.\cite{81}. A similar study was carried out in Turkey in 2012, where 1,149 children, aged 2 – 5 years were evaluated for dental anomalies namely fusion, gemination, microdontia, hyperdontia; but again no relation could be established with consanguinity\cite{82}.

Ectopic eruption was significantly higher in consanguineous group in the present conducted study. Bjerklin K, Kurol J, Valentin J \cite{111} also confirmed the genetic aetiology of ectopic eruption. However, Garib D G, Alenkar B M, Ferreria F V, Ozawa T O \cite{80} stated that ectopic eruption was related to space deficiency in either of the arches. In the present study, hypoplastic /hypocalcemic defect and molar incisor hypomineralization (MIH) were significantly higher in consanguineous group, which were similar to the results reported by others \cite{36, 77 and 80}.

Molar Incisor Hypomineralization is a clinical condition of systemic origin, affecting one or more permanent first molars along with incisors. Molar incisor hypomineralization and enamel hypoplasia occur due to disruptive function of ameloblast cells. These cells are most sensitive in terms of their metabolic function being affected by systemic conditions \cite{112}.

For Molar incisor hypomineralization and enamel hypoplasia – effect of poor general health, nutritional deficiency, local infection, birth trauma, pre term births, nephrotic syndrome, excessive use of antibiotics, exanthematous disease (measles, chicken pox) etc as etiological factors cannot be ruled out\cite{112}. However, in the present study there were no
children with medical histories that could influence hypoplasia. Only medical conditions reported were heat exhaustion, night blindness, viral hepatitis A and scabies. Dental caries is an infectious and multifactorial disease caused by interaction between microorganisms, substrate, tooth and time. The evidence in support of an inherited susceptibility to dental caries is quite limited [75].

From a preventive aspect, the relative influence of genetics and environment should be known as that would help in modifying and recommending the preventive measures. Genes are involved in tooth eruption, tooth morphology, saliva, oral flora, arch shape, dental spacing, and immune response – hence capable of influencing the individual susceptibility to dental caries [113].

In the clinical examination of the present study, DMFT score for non–consanguineous group was 2.02 ± 1.42 and 1.82 ± 0.90 for consanguineous group. The deft score for non–consanguineous group was 3.02 ± 2.13 and for consanguineous group 4.06 ± 2.32 – which was statistically significant (p<0.001). Major contribution was offered by the decayed component, probable explanation being that dental care is still considered to be neglected in developing countries. Furthermore; poor accessibility, availability of dental health services and cost also play their role.

Smadi L et.al [114] reported a deft and DMFT score of 3.2 and 0.2 respectively, while Poornima P et.al [115] found a score of 2.77 and 0.26 respectively in their studies. The DMFT score was lower as compared to deft score in the present study, as majority of respondents in non–consanguineous group were 8 year old while in consanguineous group; majority was represented by 7 year old respondents- where only a few permanent teeth had erupted.

The study of risk factors as confounding factors for dental caries had varied results in the study. The frequency of cleaning teeth daily (p = 0.012) and consumption of milk with sugar every day (p < 0.001) was significantly higher in non–consanguineous group. Use of tooth brush (p <0.001) and tooth paste (p < 0.001) as a cleaning aid, knowledge about
fluoride in tooth paste (p<0.001), consumption of cream biscuits /cakes once a week (p=0.008), soft drinks every day (p<0.001), sweets/candy several times a week (p < 0.001) and tea with sugar (p<0.001) were significantly associated risk factors in consanguineous group. Amongst demographic factors – educated parents, self employment (proxy for socio economic status) and first and second birth order were significantly higher in consanguineous group.

Consumption of cream biscuits/cakes once a week, soft drinks every day, sweets/candy several times a week (2 – 3 times) and tea with sugar are documented risk factors associated with dental caries \cite{116,117}. These refined and additional sugar provide more carbohydrate source to promote acid production, hence favouring a high DMFT/deft score.

Using tooth brush and paste as a cleaning aid and having knowledge about fluoride in the same group with above quoted favourable eating habits for the causation of dental caries – can be attributed to the social desirability to provide correct answers, similar views were expressed by Zhu et.al. \cite{118}. Another probable possible explanation could be the role of genes in saliva, tooth morphology, immune response, oral flora; rendering the respondents more susceptible to dental caries in the present study, again an interesting area of further research.

In the present study parents of consanguineous group were lesser illiterate and more self employed as compared to the non – consanguineous group. Middle school education was the most prevalent educational status for both fathers and mothers in the consanguineous group, though just not enough in today’s industrialized world to make them understand and put them in a better position to arrange for the dental needs of their children. Hence, after studying the confounding factors in the present study and the statistically significant association of deft with consanguineous group, one can conclude that dental caries which has multifactorial aetiology, both environmental and genetic factors had an influence in the causation of dental caries in the present study.

Definition as given by Bittles \cite{2} “Inbreeding coefficient (F) represents a measure of the proportion of loci at which the offspring of a consanguineous union is expected to inherit
gene copies from both the parents” [2]. The inbreeding coefficient for the present study was 0.0538, while [21] a study conducted in Aligarh in 1998, found (F) to be 0.0477; the highest reported from any part of India. In western countries, the inbreeding coefficient is low, for example in Canada (F= 0.00004 – 0.0007), USA (F = 0 – 0.0008), Southern Europe (F = 0.001- 0.002).

There are documented reasons that encourage consanguineous marriages [2, 3, 17]: religion, culture, socioeconomic status, migration, population density, degree of ruralisation, demographic factors, illiteracy, better relationship with in – laws, strengthening of family ties, better adjustment after marriage and social stability. All these factors conclusively mean that such marriages have little gene exchange with other populations. [25]

To summarize and support the findings of the present study, multiple logistic regressions (likelihood ratio tests and parameter estimates) were performed in which consanguinity was the dependent variable and the independent variables were demographic factors (religion, paternal education, maternal education, parental occupation, birth order); dental parameters (molar relationship – first permanent and second deciduous molar, incisal relationship, spacing, crowding); history of trauma; dental developmental defects (fusion, gemination, talons cusp, non – syndromic supernumerary teeth, congenitally missing/impacted teeth, ectopic eruption, Hypoplastic/hypocalcemic defects, molar incisor hypomineralization, cleft lip – palate, microdontia, dens evaginatus).

With respect to demographic data – in Religion; Islam and Christianity had a significant association with the consanguineous group, while in Parental occupation; private employment had a weak though a significant association with the non – consanguineous group. In dental parameters – no spacing in father, mesial step of second deciduous molar relation and Class I incisal relation of the respondent had a significant association with the consanguineous group. Class I and II permanent molar relation of the father and no spacing in the respondent showed a weak but a significant association with the non – consanguineous group.

Pertaining to dental developmental defects; non - syndromic supernumerary teeth, hypoplastic/hypocalcemic defect, molar incisor hypomineralization in fathers, molar
incisor hypomineralization, fusion and cleft lip and palate in mothers, non – syndromic supernumerary teeth, congenitally missing/impacted teeth, hypoplastic/hypocalcemic defect, molar incisor hypomineralization, fusion, cleft lip – palate, microdontia and ectopic eruption in respondent had a significant association with consanguinity.

In another multiple logistic regression; dental caries was the dependent variable and consanguinity and associated risk factors (demographic, feeding practices, oral hygiene practices) were the independent variables. In the present study by multivariate logistic regression, no significant association was deduced between consanguinity and dental caries. In relation to demographic factors; Unemployment. With regard to oral hygiene practices; frequency of teeth cleaning – (never, once a week, several times a week, once a day), mode of cleaning – (wooden toothpicks), use of tooth paste and knowledge about fluoride in paste. In relation to feeding practices; frequency of sweets consumption – (every day, milk with sugar–never, several times a month, once a week, every day), tea with sugar – (several times a month, several times a week) and nocturnal bottle feeding with milk had a significant association with dental caries.

For the present research study, there is a possibility of information bias, especially regarding disease reporting, as at times the parents might have misunderstood the question. The study being a household survey, so radiographic examination was not possible. The absence of radiographic evaluation for the dental developmental anomalies and the age group inclusion criteria for the respondents as 6 – 9 years, may have acted as limitations for the present study in bringing out the actual presence and hence the association of dental anomalies in the study population with either of the groups.

Individual, family and community have to be educated through IEC programmes and awareness created amongst them, regarding the consequences of consanguineous marriages and that not only medical conditions but non - syndromic dental conditions too have an association with consanguinity. Pre - marital and pre - conceptual counselling is a logical way to allow the couples to make decisions and is more likely to be received with greater acceptance rather than discouraging consanguineous marriages.
Health care workers should have clear laid down evidence based guidelines in counselling couples related to the risks of having dental conditions in their offsprings. Collaboration between dental professionals and geneticists is needed to explore the underlying genetic factors by complete family history and to create a pedigree chart highlighting the affected and unaffected member. In this way, the early recognition of dental defects and dental conditions would permit long range planning and would definitely improve the prognosis through timely orthodontic/dental intervention.