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ORIGINAL ARTICLE

FREQUENCY OF CLEFT LIP AND PALATE IN CHILDREN OF CONSANGUINEOUS PARENTS AT TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: *To determine the frequency of cleft lip and palate in relation to inter-family or out of the family marriages.*

A birth defect can present as a single defect, syndromic fatal or nonfatal. Cleft lip and / or palate is one of the most common genetic defects that effect every 2 individuals out of 1000 live births. Inter-cousin marriages are the primary cause of these genetic defects. A case-control study was conducted in a tertiary care hospital to determine the frequency of occurrence of cleft lip and palate patients in children of consanguineous marriages.

Methodology: *Data of 60 subjects were collected (30 cases and 30 controls) using a pre structured Performa which included age, gender, location of cleft, cleft lip, cleft alveolus, cleft palate cleft lip and palate, cleft side, familial relation of parents, presence, and absence of cleft. SPSS version 24.0 was used for statistical analysis. Odds ratio (OR) were done for statistical analysis and $P < 0.05$ was considered statistically significant.*

Results: *Our results showed that cleft lip and / or palate was higher in males than female subjects, male accounted for 72.2% and female 27.8%. Consanguineous marriages accounted for 60% of cases and non-consanguineous marriages resulted in 30% of the cases that presented with cleft lip / and palate.*

Conclusion: *The odds (OR=2.000) of developing cleft lip and / or palate in children of consanguineous parents is two times greater than children of non-consanguineous parents.*

Key words: *Infant, Newborn, Cleft Lip, Cleft Palate, Consanguinity, Genes, Recessive, Teratogens, Incidence, Prevalence, Hepatolenticular Degeneration, Thalassemia, Polycystic Kidney Diseases, Patient Care Team*

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INTRODUCTION

Clefts are slits or openings in upper lip that either involves palate or presents without palate involvement (CL/P). Clefts develop during fatal life and are present at birth. The main categories are isolated cleft palate and cleft lip with or without cleft palate (CL/P). CLP can occur in isolation or as part of a broad range of cardiac, chromosomal, genetic or teratogenic syndromes.[1,2] Consanguineous marriage is a marriage between two blood related or close relatives, where the spouses are either first or second cousins. Interfamilial marriages are common and appreciated in the patriarchal society of Pakistan.[3] In interfamilial marriage due to the genetic commonalities of relatives, their children are more likely to develop autosomal recessive diseases.[4] Genetic effects of consanguinity can be traced to the fact that the inbred individual may carry two copies of a gene that was present in a single copy in the common ancestor of his/her consanguineous parents. A recessive gene may thus come to light for the first time in an inbred descendant after having remained hidden for generations. Hence, consanguinity impacts the occurrence of a few acquired mutations including different aggregates like polydactyly, spinocerebellar degeneration, brain tube defects, anencephaly, and diseases for example polycystic kidney disease, thalassemia , Wilson disease, Parkinson.[5-7]

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One of the most common congenital anomaly is cleft lip and/or palate (CL/P) as its global prevalence is around 2 of every 1000 live births.[8] Cleft lip and/or palate can occur in subtypes of syndromic and non-syndromic CL/P.[2] Syndromic cleft lip/palate (SCL/P) accounts for around 30% of cases and presents with additional defects. NON syndromic have no other malformation than CL/P.[2] Non syndromic Cleft lip with or without palate(CL/P) occurs among the most common gap malformation of the orofacial region.[9] Effects on speech, hearing, appearance, and psychology can lead to long lasting adverse outcomes for health and social integration. After definitive repair, children remain at increased risk for middle ear disease, velopharyngeal dysfunction, and malocclusion and require ongoing follow-up with a multidisciplinary team.[10]

Cleft lip with or without palate is the most widely recognized in born craniofacial oddity, its prevalence fluctuates between various ethnicities. In relation to the occurrence of orofacial clefts, international studies have revealed a significant association between consanguineous marriages and the risk of the occurrence of clefts but there has been very little research done in our community to examine the relationship between consanguinity and CL/P.[11,12] Hence, our rational is to study the frequency of CL/P in our community.

The aim of this study was to find out the frequency of inter cousin marriages on the incidence of cleft lip with or without palate.

MATERIALS AND METHODS

Sample size and ethical considerations

A case control study was conducted on 60 subjects, in which 30 were cleft lip/palate patients and 30 were normal controls, in Orthodontic Department of Peshawar dental college and hospital within duration of 6 months. Ethical approval of the study was taken from the Institutional Review Board (IRB) and informed consent was taken from all the participants.

Inclusion and exclusion criteria

The inclusion criteria were based on Cleft patients with or without a documented syndrome and familial relationship of parents. Parents who were not willing to participate were excluded from the study.

Data collection

All the demographic data of the patients, i.e. gender, origin, family history regarding cleft palate, and consanguineous marriage, were collected using a preformed annexure, Within duration of six months.

Statistical analysis

Statistical analyses were performed using IBM, SPSS software (V.24). Chi-Square test were performed to determine the significance of our results. Results that have a p-value of <0.05 were considered to be statistically significant.

RESULTS

The 60 subjects included in the study was separated into two groups, controls and cases. Among 60 patients, 30 was CLP subjects in which 18 were Consanguineous and 12 were non- Consanguineous. Among 30 non-CLP group, 17 were Consanguineous and 13 were non- Consanguineous. Results showed that the parents of 30% of the CLP patients were first relatives while 20% were not non familial. While in non-cleft group patients 28. % of parents were married out of family. The total number of consanguineous was 35 and non-consanguineous were 25 (Table 1).

Table 2 shows the distribution of study subject according to the cleft type. The most common type was unilateral with total number of 18 among 30 CLP cases, in which 11 was consanguineous and 7 were non- consanguineous. Among 30 CLP subjects, 12 were bilateral in which 6 were consanguineous and 6 were non- consanguineous.

Furthermore, the unilateral CLP were divided into left and right on gender basis. Left unilateral CLP was found in 10 subjects which is higher in male subjects as compared to females. Right unilateral CLP were found in only 2 female subjects while it was 6 in males. The distribution of left unilateral CLP was 10 and 8 on the right side.

DISCUSSION

Children with birth defects are nerve tracking for their parents and the community. Cleft lip, with or without involvement of palate, is among the most popular defects that are present by birth around the globe. The prevalence of cleft lip obtained based on the meta-analysis of the reviewed studies in a study conducted by Nader Salari was 0.3% in every 1000 live births, and cleft lip and palate was 0.45%.[13] The etiology of birth defects is multifactorial including genetic factors, maternal age, and intake of drugs, exposure to teratogenic agents or radiation, maternal illness/infection, smoking, inter-family and alcohol consumption. According to the published literature Inter-family cousin marriages is considered one of the common causes of CLP frequency. No such data bases are available in Pakistan that update the CLP cases. We only studied the cases that were reported to the tertiary care hospital of Peshawar medical dental college.

Consanguineous marriages are more common in south Asia and Middle east, especially with the first

TABLE 1: SHOWS THE DISTRIBUTION OF CLP AND NON-CLP AMONG CONSANGUINEOUS AND NON- CONSANGUINEOUS

	Consanguineous N (%)	Non-Consanguineous N (%)	Total N (%)
CLP	18 (30%)	12 (20%)	30 (50%)
Non-CLP	17 (28.3%)	13 (21.7%)	30 (50%)
Total	35 (58.3%)	25 (41.7%)	60 (100%)

TABLE 2: SHOWS DISTRIBUTION OF UNILATERAL AND BILATERAL CLP AMONG CONSANGUINEOUS AND NON- CONSANGUINEOUS SUBJECTS

	Consanguineous	Non-Consanguineous	Total
Unilateral	11* (36.7%)	7 (23.3%)	18 (60%)
Bilateral	6 (20%)	6 (20%)	12 (40%)
Total	17 (60%)	13 (40%)	30 (100%)

TABLE 3: DISTRIBUTION OF UNILATERAL CLP AMONG BOTH GENDERS ON LEFT AND RIGHT

	Male	Female	Total
Right*	6 (33.3%)	2 (11.1%)	8 (44.4%)
Left	7 (38.9%)	3 (16.7%)	10 (65.6%)
Total	13(72.2%)	5 (27.8%)	18 (100%)

*Statistically significant p-value (P=0.003)

cousin. A study conducted in Saudi Arabia state that 56% of the marriages in Riyadh is consanguineous marriages. We studied the CLP cases on the bases of Consanguinity. In our study, we found out that 58.3% of the couples were consanguineous parents while 41.7% were non- consanguineous and also, the recurrence of CL/P is more common among interfamily relationships contrasted with relationships outside families, that is 30% in inert-family marriages and 20% in non familial. The same data were reported by Ravichandran et al with 38.1% of the cases with consanguineous marriages. However, their study was based on a large sample size of 1,171 cases. The results of non-consanguineous were in contrast to our study with 61.9%.[14]

We studied the relationship of unilateral and bilateral CLP with the Consanguinity of the cases. Among 17 Consanguineous cases, 36.7% cases were unilateral and 272.3% were bilateral cases. A study report the unilateral cases in Consanguineous marriages with 38.7% which is slightly higher than our study.[15] Our study reported 20% of bilateral consanguineous cases. Another study report the 45.7% cases of bilateral consanguinity.[16] Unilateral cleft lips were separately studied on both right and left side. Left cleft lip cases were higher (65.6%) in both genders as compared to right (44.4%). It was also found that male subjects with left cleft lip were high (38.9%) as compared to females (16.7%). In contrast, left unilateral cleft were reported 38.9% in male subjects in a study while right was 33.3%.[15]

CONCLUSION

The odds of developing cleft lip and/or palate in children of consanguineous parents is two times greater than that of non-consanguineous parents, based upon the finding of current study, it is considered that consanguineous marriages in the population studied can be thought of is a risk factor for the occurrence of non-syndromic oral cleft lip with or without palate.

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