ORIGINAL ARTICLE

Patterns of Orofacial Clefts in Patients with Consanguineous Parents

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ABSTRACT

Background: Orofacial clefts are very common congenital anomalies and include cleft lip, cleft lip and palate and cleft palate alone. The development of congenital anomalies is multifactorial which include environmental and genetic factors and consanguinity. As consanguineous marriages are commonly practiced, the present study is designedto evaluate the patterns of orofacial clefts in patients with consanguineous parents in local population.

Methods: Data was collected from Shalamar Hospital, Children Hospital and Arif Memorial Hospital, Lahore and observed retrospectively. Data was analyzed by using SPSS.

Results: Out of 126 patients with facial clefts 103 had positive family history of consanguinity. 25 patientswith consanguineous parents were suffering from cleft lip and 35 from cleft lip and palate. Cleft palate alone was observed in 31 patients and one of the patients was found to have cleft lip and nasal deformity in concert. 11 patients with consanguineous parents were suffering from cleft lip, palate and nasal deformity. Gender disparity among patients with consanguineous parents wasobservable as well; an overall higher frequency of isolated cleft lip (CL) was seen in males than in females with a higher incidence of unilateral cleft lip in males in contrast to a higher incidence of bilateral cleft lip in females. Incidence of cleft palate (CP) and cleft lip and palate (CL+P) showed preponderance in females than in males.Results of the current study elucidate a close association between consanguinity and the development of cleft anomalies.

Conclusion: The impact of this practice should be addressed by premarital or at least prior to conception screening with the provision of appropriate counseling to prevent this disorder well-timed.

Keywords: Consanguinity, Cleft lip, Cleft palate.

INTRODUCTION

Birth defects are the most frequent cause of childhood disability and mortality in developed and developing counteries[1]. Orofacial clefts are among the commonest malformation in man[2]. Major congenital anomalies associated with facial clefts compriseof cleft lip (CL), cleft palate (CP), cleft lip and palate (CLP) and isolated cleft palate[1].A child havingcleft lip and palate is born in the world after every two minutes, about 660 children per day and 235 thousand new cases of facial clefts are added per year. The incidence of cleft lip and palate varyin relation to race, geography and socioeconomic status[3].

As far as development is concerned, clefts of palate are produced due to insufficient union of palatine processes.Possibilities mayinclude small size of shelves, unsuccessful elevationof shelves, defective process of fusion andinability of the tongue to descend in between the shelves[4].If only one side of maxillary process fall short to unite with nasal prominence the condition isidentified as unilateral cleft lip whereas bilateral cleft is present on both sides. The incisive foramen is regarded as a reference landmark for differentiation of anterior and posterior cleft malformation. Those anterior to incisive foramen include lateral cleft lip, cleft upper jaw and cleft between primary and secondary palate. Those that lie posterior to incisive foramen include cleft (secondary) palate and cleft uvula[5].

Normal and abnormal morphogenesis of face is a complex process depending on many cell types, signaling molecules, genes, growth factors and tissues, so orofacial clefts are multifactorial in origin including hereditaryas well asbiological factors[6]. Maternal dietary habits, use of vitamin supplements, alcohol abuse, smoking andanticonvulsant medication are variousenvironmentalcauses that have been associated with clefts. Genetic factors compriseTGF B3, MSX 1, IRF 6, FGF, FOXE 1, JAG 2 and TBX22. Besides environmental and genetic factors, consanguinity has also been implicated in the development of CLP and other congenital malformation[7]. Consanguinity means descent from a common ancestor. Despite modern civilization, consanguineous marriages have been practiced by

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many societies from time immemorial due to customary values, rituals and to maintainpossessions inintegrated form within the family[8].

Scientific studies have shown that consanguinity leads to increased incidence of hydrocephalus, polydactyly, bilateral cleft lip and palate, Down syndrome, cardiovascular malformations, blood disorders, blinding and breathing problem for children at birth[8].

The current study is undertaken to assess the patterns of orofacial clefts in patients with consanguineous parents. This information may help us in designing treatment plans through cleft lip and palate clinics and offer rehabilitation, education and genetic counseling.

MATERIAL AND METHODS

A retrospective observationalstudy was made. The study group included children with cleft lip alone, cleft palate alone and cleft palate along with cleft lip. Data was taken from the documented records of patients coming for plastic surgery at Shalamar Hospital, Lahore, Children's Hospital, Lahore and Arif Memorial Hospital, Lahore. Initially all patients with cleft lip and palate were recognized and categorized. Those who were born with cleft on their lip were labeledasCL patients, those with cleft on their palate as CP patients and those who have clefts on their lips extending to their palate as CL+CP patients[9].

RESULTS

Total patients with orofacial clefts were 126 comprising 64 males and 62 females. Data was analyzed by using SPSS.

Family history of parental consanguinity: Out of 126 patients with facial clefts 103 (49 males and 54 females) had positive family history of consanguineous marriages and 23 had negative history of consanguineousmarriages.

Cleft lip: Among 25 patients with cleft lip alone, 13 male patients had cleft lip, which is unilateral in 84.61%, bilateral in 7.69% and median in 7.69%.

There were 12 female patients of cleft lip, which is unilateral in 69.23%, bilateral in 15.38% and median in 15.38%.

Cleft lip and palate: Out of 35 there were 14 male patients who had cleft lip and palate with positive family history of consanguineous marriages, 7.14% had cleft of soft palate and 92.86% had clefts of soft and hard palate together.

There were 21 female patients with cleft lip and palate and all (100%) of them had clefts of soft and hard palate together.

Cleft palate: Among 31 patients with cleft palate alone, 13 patients with positive family history of consanguineous marriages were males. 46.15% of them had cleft of both soft and hard palate and 53.85% had cleft of soft palate. None of them was suffering from cleft of hard palate alone. 18 patients with cleft palate and positive family history of consanguineous marriages were females. 55.56% of them had cleft of both soft and hard palate and 44.44% had cleft of soft palate. None of them was suffering from cleft of hard palate alone.

Cleft lip and nasal deformity: One of the male patients with positive history of consanguineous marriage was suffering from cleft lip and nasal deformity.

Cleft lip, palate and nasal deformity:33.33% of the male patients and 66.67% of the female patients had cleft lip, palate and nasal deformity along with positive family history of consanguineous marriages.

Table1. The frequency of facial clefts among patients with positive history of consanguinity.

Type of cleft	Positive history of consanguinity	
	Males	Females
Cleft lip	26.53%	22.22%
Unilateral	84.61%	69.23%
Bilateral	7.69%	15.38%
Median	7.69%	15.38%
Cleft lip and palate	28.5%	38.88%
Soft palate	7.14%	-
Soft and hard palate	92.86%	100%
Cleft palate	26.53%	33.33%
Soft	53.85%	44.44%
Soft and hard palate	46.15%	55.56%
Cleft lip and nasal deformity	100%	-
Cleft lip, palate and nasal deformity	33.33%	66.67%

DISCUSSION

Orofacial clefts put in significantly to long term disability in children in addition to remarkable emotional and economical strain for affected family and individuals[1].Recent researches have proposed the involvement of multiple genes and various ecologicalfactors in the etiology of non syndromic clefts[10]. In additionto genetic and environmental factors, consanguinity has also been involved in development of facial clefts and other anomalies present at birth[9].First degree consanguineous marriages contribute about 5 to 8% to the risk of having birth defects as compared to about 2 to 3%in case of non-consanguineous marriages[11].Consanguineous marriages invigoratethe danger of autosomal recessive disorders by means of the expression of recessive injuriousalleles,

particularlywithin the progeny of first degree cousins[12]. Consanguineous marriages is a practice that remains strongly and convincinglyingrained within our society mostly among first and second cousins.

In our study out of 126 patients with facial clefts 103(81.7%) showed positive history of consanguinity as compared to only 23(18.2%) with negative history.Aziza Aljohar in 2007 studied pattern of orofacial clefts of hospital based population in Saudi Arabia observed consanguineous marriages among 54.4% of patients' parents. He further demonstrated that 31.9% of cases with family history of CL/P showed first cousin marriages[1].

Another study conducted in Teheran included 25 CL+P cases, demonstrated31.8% of CL+P infants were the result of consanguineous marriages. However, in the group of infantswith no CL+P, just 8% showed history of consanguineous parents[9].

A significant association was also showed by Shafi et al in 2003 amongthe offspring born of consanguineous parents and the occurrence oforofacial clefts. They, however, also reportedtheco-occurrence of facial clefts with associated malformations predominantly heart defects. The co-existence of the two is possibly due to a defect in repositioning or differentiation of neural crest cells, thefocal contributor in the development of both[13].

The types of clefts are distributed differently; the frequency differs among various population groups. Our results showed that the most frequent cleft type was the combined cleft lip and palate (CL+P) representing 34% of all cleft deformities. Isolated cleft palate (CP) and isolated cleft lip (CL) constituted 30% and 24% of all cleft deformities respectively. Comparable results were found by Aquino et al in 2011, they reported CL+P was the most common cleft followed by isolated CP and CL respectively[7]. Conversely, a study conducted in France by Stoll et al in 1991stated higher rates of isolated CP as compared with CL+P[14].

Gender disparity was also obvious in the study; an overall higher frequency ofisolated cleft lip was seen in males than in females with a higher incidence of unilateral cleft lip in males compared to a higher incidence of bilateral cleft lip in females. Incidence of CP and CL+P showed preponderance in females as compared to males. Isolated clefts of soft palate were more common in males; however clefts of both soft and hard palate were more prevalent in females (Table 1). These results are in concurrence with outcome of a study conducted in Saudi Arabiafrom June 1999 to December 2005 which demonstrated higherfrequency of isolated clefts lip in boys and cleft palate in girls with a boy to girl ratio of 1.2:1 for CL and 0.9:1 for CP. However, they reported a higher prevalence of cleft lip withcleft palate in males compared to females[1].

In 1987, JWomersley and DH Stone also described a male predominance for cleft lip and female for cleft palate[15].In contrast, a more recent study carried out in Brazil from 2006 to 2009 reported a male preponderance in all types of clefts[7].

Mladina et al in 2009proposed the likelihood of occurrence of a gene accountable for the onset of facial clefts and the associated gender predisposition observed in the studies[16]. Moreover, several environmental factors have been correlated with etiology of facial cleftssuch as maternal nutritional status, vitamin supplements throughout pregnancy and use of certain medication or hormones[17].

Previous reports and results of the current studyplace our country among the countries of the world with a high incidence of consanguinity. Consanguineous marriages are an important factor in the development of cleft anomalies in addition to other genetic abnormalities and should be discouraged. The impact of this practice is documented and it should be addressed by premarital or at least prior to conception screening, which recognizes carrier status with the provision of appropriate counseling to prevent this disorder. Additional efforts shouldbe put in for the understanding and education of the community and patients regarding these deformities. Moreover, future studies focusing on specific genetic and environmental risks are desired to shed supplementary light on association between consanguinity and facial clefts.

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