Original Article

Facial Clefts

Familial Predisposition and Gender Discrimination in Patients with Facial Clefts in Local Population

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ABSTRACT

Objective: To objective of this study was to know Familial Predisposition and Gender Discrimination in Patients with Facial Clefts in Local Population.

Study Design: Retrospective observational study.

Place and Duration of Study: This study was carried on the data was retrieved from the documented files of patients presenting for plastic surgery at Shalimar Hospital and Children's Hospital and Arif Memorial Hospital from September 2009 to September 2012.

Methods and Material: The current study was conducted to cross link the occurrence of facial clefts with family history and gender. The profile of 126 patients was collected which were under treatment at various hospitals and was analyzed and evaluated.

Results: Results of the study demonstrated clear gender discrimination; with the incidence of bilateral cleft lip and palate more in males, and unilateral cleft lip and palate had a female predominance. A close association of patients with a positive family history was also seen in the study, 50% of patients with unilateral cleft lip and 50% of patients with bilateral cleft lip exhibited a positive history. 75% of patients with unilateral cleft lip and palate and 25% of the patients with bilateral cleft lip and palate had positive family history. All patients with unilateral cleft palate had a positive family history. A close association demonstrated between the gender, positive family history and facial clefts led us to postulate that a probability of a genetic predisposition cannot be overlooked.

Conclusion: The call of the day is that the future researches pertaining to facial clefts should aim their energies in isolation and localization of the Genetic and/or environmental factors responsible for the congenital malformation. The cleft per se could disappear from the Earth in a near future owing to the gene therapy and prenatal or, perhaps pre-conception screening, which will be able to eliminate the menace before it can disfigure the face of humanity.

Key Words: Facial Clefts, Cleft palate, Cleft lip

INTRODUCTION

Surveillance studies have shown that cleft lip and cleft palate is one of the commonest Cranio-facial anomalies occurring in approximately 1 in 500 live births [1]. They accounts for 65% of all head and neck anomalies[2]. These clefts are conspicuous as they result in abnormal facial appearance and defective speech [3]. Palatal clefts have also been associated previously with a progressive hearing loss [4].

Clinical and epidemiological studies on the incidence of cleft lip and palate were carried out in Pakistan in 2004 which showed that it was 1.91 per 1000 live births. Cleft lip alone was 42% and cleft palate 24% and combined cleft lip and palate was 34% [5].

The development of head and neck begins in the 4th week of intrauterine life, even before a woman is aware that she is pregnant. The initiation of face development is by the appearance of five facial primordia around the stomodeum. These include one frontonasal prominence, and paired maxillary and mandibular prominences. A major contribution is also provided by an ectodermal placode formed at the inferior part of fronto-nasal prominence, termed Nasal placode. The nasal placode proliferates to form the medial and lateral nasal prominences which contribute in the development of nose, upper lip and primary palate by formation of the inter-maxillary segment[3].

Facial clefts, that is, of lip and palate occur whenever there is a failure of union of these facial primordia with each other or with the nasal prominences. A unilateral cleft lip is produced from failure of maxillary prominence on affected side to unite with medial nasal prominence. A bilateral cleft lip results from failure of both maxillary prominences to meet and unite with merged medial nasal prominences[2]. A median cleft lip is rare and is produced due to incomplete merging of two medial nasal prominences in midline. Cleft palate results from lack of fusion of palatine shelves[6].

The incidence of facial clefts has been also associated with a magnitude of factors including alcohol abuse, smoking, malnutrition, retinoic acid and positive family history[7, 2]. A close association between occurrence of facial clefts and congenital heart disease has also been reported [8].

Clinical and epidemiologic studies of defined geographic populations can serve as a means of establishing data important for the diagnosis, treatment, and counseling of patients with cleft lip and cleft palate. Several descriptive epidemiologic studies have been

carried out in many countries worldwide; however, no such study in Pakistan has correlated the occurrence of facial clefts with gender predisposition and family history. The purpose of this study is to document the frequency with which the clefts appear in males and females and the association of facial clefts with family history.

MATERIALS AND METHODS

This is retrospective observational study. The study group consisted of all children with cleft lip alone and cleft palate alone and cleft palate with or without cleft lip. Data was retrieved from the documented files of patients presenting for plastic surgery at Shalimar Hospital and Children's Hospital and Arif Memorial Hospital. Firstly all patients with cleft lip and palate were recognized and categorized. Those who were born with cleft on their lip were called CL patients. Those who were born with cleft on their palate were called CP patients and those who have clefts on their lips extending to their palate were called as CL+CP patients[9].

RESULTS

Total number of patients with facial cleft was 126. patients with cleft lip were 31, cleft lip and palate were 43, cleft palate were 35, cleft lip and nasal deformity were 2, median cleft lip were 2 and with cleft lip, palate and nasal deformity were 3.

Following variants of facial clefts were analyzed.

Gender: Total number of patients was 126 with 64 males and 62 females.

A) Cleft lip:

Out of 31 patients with cleft lip, 25 patients have unilateral cleft lip, among which 48% were males and 52% were females.

3 patients were suffering from bilateral cleft lip, out of which 66.67% were females and 33.33% were males (Table 1).

3 patients were diagnosed to have median cleft lip. 66.67% of them were males and 33.33% were females (Table 1).

B) Cleft lip and palate:

Unilateral cleft lip and palate was found in 32 patients. 43.75% of these patients were males and 56.25% were females.

Bilateral cleft lip and palate was present in 10 cases. 70% of them were males and 30% were females (Table 1).

C) Cleft palate:

There were 35 cases of cleft palate. 16 patients of cleft palate were males and 19 of them were females. 50% of the male patients had cleft of both soft and hard palate and 50% had cleft of soft palate alone. Cleft of hard palate alone was found in none of them.

47.37% of female patients had cleft of soft palate and 52.63% had cleft of both soft and hard palate. Cleft of hard palate alone was not found in any female patients (Table 1).

D) Cleft lip and nasal deformity:

There were 2 patients with cleft lip and nasal deformity. 50% of them were males and 50% were females (Table 1).

E) Cleft lip, palate and nasal deformity:

There were 3 patients with cleft lip, palate and nasal deformity. 33.33% of which were males and 66.67% were females (Table 1).

Table No.1: Sexual distribution of facial clefts

	Diagnosis	Males	Females
1.	Cleft lip		
2.	Unilateral	48%	52%
3.	Bilateral	66.67%	33.33%
4.	Median	66.67%	33.33%
5.	Cleft lip and palate		
6.	Unilateral	43.75%	56.25%
7.	Bilateral	70%	30%
8.	Cleft palate		
9.	Soft palate	50%	47.37%
10.	Soft and hard palate	50%	52.63%
11.	Cleft lip and nasal deformity	50%	50%
12.	Cleft lip, plate and nasal deformity	33.33%	66.67%

Table No.2: The frequency of positive family history of facial clefts.

	Diagnosis	Positive family history of facial clefts
1.	Cleft lip	
	Unilateral	50%
	Bilateral	50%
2.	Cleft lip and palate	
	Unilateral	75%
	Bilateral	25%
3.	Cleft palate	
	Unilateral	100%

Positive family history of facial clefts:

Out of 126 patients 9 had positive family history of facial clefts and 117 had negative family history.

5 Patients with positive family history of facial clefts were males and 4 were females.

A) Cleft lip:

2 patients with positive family history were suffering from cleft lip. 50% of them were unilateral and50% had bilateral cleft lip.

B) Cleft lip and palate

Positive family history was present in 4 patients with cleft lip and palate. 75% of them had unilateral cleft lip and palate and 25% was suffering from bilateral cleft lip and palate (table 2).

C) Cleft palate:

3 out of 9 patients with positive family history of facial clefts had cleft palate and all of them had unilateral cleft palate (table 2)

DISCUSSION

Genetic, environmental and drug abuse have previously been associated with the occurrence of facial clefts.

A study conducted in Poland in 2007 by Kot et al concluded that 17% of patients with cleft lip and/or palate had a positive family history which is in accordance with our study in which familial predisposition was seen in 7% of patients. The study also reported that the type of cleft in a child depends not only on the type of cleft in parent but there is greater risk of clefts in sons of mothers with cleft lip (CL) or cleft lip and palate (CL+P) or fathers with cleft lip (CL) and in daughters of mothers or fathers with cleft palate (CP) [10].

A close association between children born of a consanguineous marriage and the incidence facial clefts was also reported by Shafi et al in 2003, this study, however, also reported that facial clefts observed in patients born of a consanguineous marriage had associated malformations particularly heart disease. The co-occurrence of facial clefts with heart defects can be owed to a fact that neural crest cells make a major contributor in the development of both, any malformation in migration or differentiation of neural crest cells can lead to the two defects to co-exist[8].

Gender discrimination was also evident in the study, a higher incidence of unilateral cleft lip (CL) and cleft lip and palate (CL+CP) was exhibited in females as compared to a high frequency of bilateral cleft lip in males. Clefts of soft palate alone were more frequent in males; however clefts of both soft and hard palate were more frequent in females (Table 1). These results are in accordance with results of study done in country of Stockholm between 1991 and 1995 which reports high incidence of bilateral clefts lip (CL), cleft palate (CP) and cleft lip and palate (CL+P) in males than in females[11]. Kim S. et al reported in 2002 that the male: female ratio was 2.1:1 in cleft lip (CL) group, 2.5:1 in cleft palate (CP) group and 0.95:1 in cleft palate (CP) group1[2]. J Womersley and DH Stone reported in 1987 that males predominated for cleft lip, females for cleft palate.

Peterka M. et al. in 1996 documented that among children of mother with cleft lip, 68% were boys and 32% were girls with cleft lip or cleft lip and palate. If the mother had cleft lip and palate, the same cleft was found in 64% of boys and 15% of girls. If the mother had cleft palate, the same type was present in 37% of boys and 51% of girls. Similar results were found for affected fathers and their children with only exception among children of fathers with cleft lip and palate, the percentage of boys and girls with cleft lip was 43% and 40%, respectively[9].

The gender predisposition observed in the studies can be postulated to be caused by a gene, as previously suggested by Mladina et al in 2009. According to them the probability and possibility of presence of a gene responsible for the onset of facial clefts is great[1].specific envoirnmental factors are known to contribute to facial clefts, these include infectious agents, x-ray radiations, drugs, hormones and nutritional deficiencies. Hox family of homeobox genes expressed in rhombomeres is important in head and neck development[14]. Retinoic acid regulates Hox complex which in turn regulates head and neck development[6].

CONCLUSION

The call of the day is that the future researches pertaining to facial clefts should aim their energies in isolation and localization of the Genetic and/or environmental factors responsible for the congenital malformation. The cleft per se could disappear from the Earth in a near future owing to the gene therapy and prenatal or, perhaps pre-conception screening, which will be able to eliminate the menace before it can disfigure the face of humanity.

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