CLINICAL AND DEMOGRAPHIC FACTORS ASSOCIATED WITH CLEFT LIP AND PALATE IN SOUTH INDIA: A HOSPITAL BASED STUDY

Jyotsna Murthy, G. Venkatesh Babu, L.V.K.S. Bhaskar*
1Department of Plastic Surgery, Sri Ramachandra University, Chennai, India
2Department of Biomedical Sciences, Sri Ramachandra University, Chennai, India
3Sickle Cell Institute Chhattisgarh, Raipur, India

Abstract- Cleft lip and palate is one of the most common visible congenital deformities. Approximately 30% of oral clefts are syndromic and are associated with some anomalies. Global surveys have shown that the frequency of cleft lip and palate varies greatly from country to country. The present study analysed demographic and associated anomalies in children attending the high volume Smile Train center in South India. Two thousand and five children were examined in outpatient department by plastic surgeon and also screened by a pediatrician for associated anomalies and syndromes. Detailed family history and personal history were collected by the nurse coordinator. The collected data was analysed using SPSS software. In the present study cleft lip with cleft palate (CLP) was more frequent (58%) than cleft lip only (CL) (17%) and isolated cleft palate (CPO) (25%) The CLP and CL were more common in males and CPO was more common in females. Parents of 30.47% cases had the consanguineous marriage and 23% showed positive family history of clefts. Only 1.35% of oral clefts are associated with various syndromes, but 14.01% oral clefts were associated with malformations in several other organs. The results of the present study provide demographic details of the cleft children in the South India.

Keywords - cleft lip and palate, syndromes, associated anomalies

1. Introduction:
Cleft lip, with or without cleft palate, is the most common congenital deformity of face and mouth and exhibit variable phenotype. The lip forms between fourth and seventh weeks and palate forms between sixth and ninth weeks of pregnancy. Generally, facial clefting results when lateral nasal process and maxillary processes forming craniocfacial complex do not fuse completely. The affected individuals may have both cleft lip and palate, or either on its own. Cleft lip and palate is more frequent in males and isolated cleft palate in females but their prevalence varies by ethnic group and geographic location. Africans have the lowest prevalence rates (1/2500) and North American Indians and Orientals have the highest prevalence rates (1/500). Approximately 70 % of the cleft lip and palate cases are of non-syndromic and occur as an isolated condition, but 30% of oral clefts are syndromic and are associated with some anomalies.1, 2

The etiology and mode of transmission of cleft lip and palate is very complex, because of the congenital anomalies that associated with it. The etiological factors include heredity, consanguinity, foetal environment, demographic factors other factors like drugs, vitamins, alcohol consumption, smoking, infections, diet etc. The patients with cleft lip and palate present complex biologic, sociologic and psychologic problems and their rehabilitation involves several disciplines. Earlier studies reported a drastic decline in the quality of life and psychosocial performance in children with clefts.3-7 In some instances reduced psychosocial, educational, and economic achievements was observed even in adulthood.8, 9

Cleft lip and palate is a polygenic and multi-factorial involving both genetic and environmental influences.10 Although, several sub-phenotypes such as dermatoglyphic features, dental anomalies and handedness have been studied extensively for nonsyndromic cleft lip and palate,11, 12 the studied on estimating the rates of oral clefts and associated anomalies is incomplete. Hence, the present study is a humble effort in the direction of accomplishing to analyse the retrospective data on the spectrum of cleft lip and palate and associated anomalies in south Indian population.

2. MATERIALS AND METHODS:
Two thousand five retrospective cleft lip and palate cases analyzed according to the following variables: general information such as gender, cleft phenotype, familial history, associated malformations. All patients with Oral Clefts are screened for history, consanguinity, affected members in family and relatives, gestational history, drug intake, smoking, alcohol consumption etc. History of OC deformity in sibling parent and grandparent are traced and registered in our cleft care directory. The children were screened by surgeon and pediatrician of the cleft team for the cleft type and associated anomalies. Principles outlined in the Declaration of Helsinki were strictly
followed during data collection. The data collected were analysed using the SPSS software (version 11.0, Chicago, IL). The statistical significance of the data, $\chi^2$ test was employed, p-values $<$0.05 were considered as statistically significant.

Figure 1: Presentation of different cleft phenotypes (CL, CLP, and CPO) in 2005 cases.

### TABLE 1: CLEFT PHENOTYPE BY SEX AND THE SEX RATIO

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Total (%)</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>Male: Female ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCLP</td>
<td>865 (43.1)</td>
<td>511 (25.5)</td>
<td>354 (17.7)</td>
<td>1.44:1</td>
</tr>
<tr>
<td>BCLP</td>
<td>308 (15.4)</td>
<td>185 (9.2)</td>
<td>123 (6.1)</td>
<td>1.50:1</td>
</tr>
<tr>
<td>UCL</td>
<td>337 (16.8)</td>
<td>194 (9.7)</td>
<td>143 (7.1)</td>
<td>1.36:1</td>
</tr>
<tr>
<td>CPO</td>
<td>495 (24.7)</td>
<td>223 (11.1)</td>
<td>272 (13.6)</td>
<td>0.82:1</td>
</tr>
</tbody>
</table>

$\chi^2$ p value $<$0.001 (d.f=3)

### TABLE 2: DISTRIBUTION OF FAMILY HISTORY OF CLEFTING AMONG DIFFERENT CLEFTS

<table>
<thead>
<tr>
<th>Cleft Group</th>
<th>Family history negative</th>
<th>Family history positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLP</td>
<td>1090 (54.36)</td>
<td>83 (4.14)</td>
</tr>
<tr>
<td>CPO</td>
<td>470 (23.44)</td>
<td>25 (1.25)</td>
</tr>
<tr>
<td>CL</td>
<td>300 (14.96)</td>
<td>37 (1.85)</td>
</tr>
</tbody>
</table>

$\chi^2$ p value =0.006 (d.f=2)

### 3. RESULTS

In the present study it is evident that the cleft lip with cleft palate (CLP) was more frequent (58%) than cleft lip only (CL) (17%) and isolated cleft palate (CPO) (25%) (Figure 1). The distribution of cleft phenotype by sex among the 2005 cases is presented in Table 1. CLP and CL were more common in males than in females (sex ratios were 1.44 and 1.36 respectively), whereas CPO was more common in females than in males (sex ratio is 0.82). The distribution of different cleft phenotypes between male and female is significant ($p=0.001$) (Table 1). A positive family history of clefts was observed in 145 cases (7.23%). Family history influence is more in subjects with both lip and palate (4.14%) than that of CL (1.85%) and CPO (1.25%) (Table 2). The parents of 611 (30.47%) cases had the consanguineous marriage, and the percentage of consanguineous marriage in parents of CLP cases (17.46%) was higher than that of CL and CPO cases (4.74% and 8.28% respectively), but it is not statistically significant ($p=0.174$) (Table 3). 14.01% oral clefts (281 cases: 159 CLP, 107 CPO and 15 CL) were associated with malformations in heart, upper limb, lower limb, genital, skin, eyes, ears, mental/growth retardation, skull, and mandible (Table 4). Various syndromes that associated with cleft lip and palate patients are documented in table 5. A total 27 patients (1.35%); 10 CLP, 16 CPO, and 1 CL showed associated syndromes. Of the total syndromes identified the Pierre Robin Sequence (PRS) is common (10cases) followed by Medial Facial Dysplasia (5 cases) and velo-cardio-facial syndrome (3 cases). Other rare syndromes associated are Hemifacial Microsomia (2 cases), Van der Wood syndrome (2 cases), Apert syndrome (1 case), Robin SC syndrome (1 case) and Treacher Collin syndrome (1 case).

### TABLE 3: DISTRIBUTION OF CONSANGUINITY AMONG DIFFERENT CLEFT PHENOTYPES

<table>
<thead>
<tr>
<th>Cleft Group</th>
<th>No consanguinity</th>
<th>Consanguinity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLP</td>
<td>823 (41.05)</td>
<td>350 (17.46)</td>
</tr>
<tr>
<td>CPO</td>
<td>329 (16.41)</td>
<td>166 (8.28)</td>
</tr>
<tr>
<td>CL</td>
<td>242 (12.07)</td>
<td>95 (4.74)</td>
</tr>
</tbody>
</table>

$\chi^2$ p value =0.174 (d.f=2)

### TABLE 4: DISTRIBUTION OF ASSOCIATED ANOMALIES AMONG CLEFT PHENOTYPES

<table>
<thead>
<tr>
<th>Organ</th>
<th>CLP</th>
<th>CPO</th>
<th>CL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>46(28.9)</td>
<td>14(13.1)</td>
<td>4 (26.7)</td>
<td>64(22.8)</td>
</tr>
<tr>
<td>Upper limb</td>
<td>18(11.3)</td>
<td>11(10.3)</td>
<td>2 (13.3)</td>
<td>31(11.0)</td>
</tr>
<tr>
<td>lower limb</td>
<td>16(10.1)</td>
<td>5 (4.7)</td>
<td>1 (6.7)</td>
<td>22 (7.8)</td>
</tr>
<tr>
<td>Genital</td>
<td>5 (3.1)</td>
<td>5 (4.67)</td>
<td>1 (6.67)</td>
<td>11 (3.9)</td>
</tr>
<tr>
<td>Skin</td>
<td>1 (0.63)</td>
<td>1 (0.93)</td>
<td>0 (0.00)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>Eye</td>
<td>29(18.2)</td>
<td>13(12.2)</td>
<td>5 (33.3)</td>
<td>47 (16.7)</td>
</tr>
<tr>
<td>Ear</td>
<td>22(13.8)</td>
<td>10 (9.4)</td>
<td>0 (0.0)</td>
<td>32 (11.4)</td>
</tr>
<tr>
<td>MR/GR</td>
<td>9 (5.7)</td>
<td>11 (10.3)</td>
<td>1 (6.7)</td>
<td>21 (7.5)</td>
</tr>
<tr>
<td>CFA</td>
<td>8 (5.0)</td>
<td>11 (10.3)</td>
<td>1 (6.7)</td>
<td>20 (7.1)</td>
</tr>
<tr>
<td>Mandibular</td>
<td>5 (3.1)</td>
<td>26(24.3)</td>
<td>0 (0.0)</td>
<td>31 (11.0)</td>
</tr>
</tbody>
</table>

### TABLE 5: PRESENTATION OF SYNDROMES AMONG DIFFERENT CLEFT PHENOTYPES

<table>
<thead>
<tr>
<th>Cleft Group</th>
<th>No syndrome</th>
<th>Syndromic</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLP</td>
<td>1163 (58.0)</td>
<td>10 (0.50)</td>
</tr>
<tr>
<td>CPO</td>
<td>479 (23.89)</td>
<td>16 (0.80)</td>
</tr>
<tr>
<td>CL</td>
<td>336 (16.76)</td>
<td>1 (0.05)</td>
</tr>
</tbody>
</table>

### 4. DISCUSSION

In the present study it is evident that the CLP was more frequent than CL and CPO. The CLP and CL were more common in males and CPO was more common in females. Parents of 30.47% cases had the consanguineous marriage and 23% showed positive family history of clefts. 14.01% oral clefts were associated with malformations in heart, upper limb, lower limb, genital, skin, eyes, ears, mental/growth retardation,
skull and mandible. 1.35% of oral clefts are associated various syndromes.

Results of the present study are consistent with a Danish study in which sex distribution of oral clefts was more males than the females, and also combined cleft lip and palate is more followed by isolated cleft lip and isolated cleft palate. Prevalence or incidence of orofacial clefts differ among different populations. It is well known that the prevalence of oral clefts is low among blacks compared to whites. Although, Nigerians showed a lower birth rate of cleft anomalies (0.4:1000 live births), the frequency of cleft lip only was predominant (49%) than the cleft palate only (19%), and of cleft lip and palate (32%) (15). A retrospective study in Northeast Mexico showed an incidence of clefts as 1.1:1000 births with male predominance. In Northern Ireland the incidence of oral clefts are 1.28 per 1000 live births (1.781), and the clefts more in males than females (17). The incidence of clefts in Stockholm County in Sweden was 2.0/1000 live births and no difference in incidence values of children with isolated cleft lip, children with cleft lip and palate, and children with isolated cleft palate. Using raw counts from non-overlapping published studies of Asian populations it was calculated that the prevalence rates for syndromic plus nonsyndromic cleft lip with or without cleft palate in Chinese, 1.30; Japanese, 1.34; Other Asian, 1.47 per 1000 live births (19). The birth prevalence of cleft lip and palate is estimated to be 1.94 per 1000 live births in the Philippines (20). Indian being most populous areas of the world showed the birth prevalence of clefts is somehwere between 27,000 and 33,000 clefts per year (21). A recent meta-analysis revealed the cleft frequency rate per 10000 for cleft lip with or without palate is 9.3 and for cleft palate only is 1.7 (21). The birth rate of clefts was found to be 1.09 for every 1000 live births in Indian population. Most of the studies are institutional based and does not represent correct figures. Furthermore, many studies underestimated the true frequency oral clefts because they have not considered the stillbirths, elective terminations, spontaneous abortions, post-natal loss of children during analysis. Population based studies are more appropriate to estimate prevalence but very few has been reported in literature.

A prospective neurosonographic study was undertaken in 190 Taiwanese patients with NSCLP revealed 3.2% malformations of the central nervous system (23). A Swedish population based study reported that 1% of the cleft lip and palate cases presented associated malformations but these were more frequent in cleft lip and palate (28%) than in isolated cleft palate (22%) or isolated cleft lip (8%) individuals (24). In contrast to this a study from North-eastern France showed more frequency of associated malformations in infants with cleft palate (46.7%) than cleft lip and palate (36.8%) or isolated cleft lip (13.6%) (25). In American population 32.2% of all cleft patients had associated congenital malformations and these were more common in CP (38.7%), than CLP (26.4%) (26).

Approximately 30% of orofacial clefts are syndromic. In Latvia 16% of CL/CP patients showed recognized genetic syndromes or associated anomalies (27). In the present study only 1.35% of oral clefts are associated various syndromes. This is consistent with a previous report from our group showed that only 36 patients are syndromic in a total of 2600 indicating many of these orofacial clefts are nonsyndromic (28). An Australia registry and clinic based analyses of birth defects and syndromes associated with cleft Lip/palate also revealed less frequency of syndromes (29). The main limitation of the present study is that it used data from only one hospital. However, this study demonstrates that the identification of syndromes and anomalies associated with oral cleft are essential to assess the risk faced by the child and also help to provide necessary treatment and improve survival of these children.

ACKNOWLEDGEMENTS:

Dr. Jyotsna Murthy acknowledges funding from Smile train. Dr.L.V.K.S. Bhaskar acknowledges funding from the Indian Council of Medical Research (ICMR), Government of India (Project Ref. No. 56/15/2007-BMS).

REFERENCES: