The distribution of clefts of the primary and secondary palates by sex, type, and location

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Abstract: The frequency and patterns of distribution of cleft lip, cleft lip and alveolus, cleft lip and palate, and isolated cleft palate, together with the possible association between sex, type of cleft, and affected side were studied from records of 278 individuals with clefts. These records were obtained from four cleft centers in the New York City area and constituted a racially mixed urban sample. The type of the cleft varied between sexes. Males had significantly higher rates of cleft lip and palate ($p<0.0001$), and females had higher rates of isolated cleft palate ($p<0.0001$). No sex differences were found for cleft lip or cleft lip and alveolus. Unilateral clefts of both the primary and secondary palates were found to occur over three times more frequently than bilateral clefts, and left side predominance was demonstrated.

Key words: Cleft lip, Cleft palate frequency, Primary palate, Secondary palate, Sidedness

Orofacial clefting, including cleft lip with or without cleft palate, is the most common craniofacial anomaly. Consequently, it is important to analyze distribution of this anomaly and to describe its characteristics. This is particularly relevant when an opportunity exists to pool a relatively large sample of affected individuals in a single location, such as a large urban area. Comprehensive care for this condition tends to attract the families of these individuals to the cleft care centers. The metropolitan New York City area has several such centers, and thus it could be considered an appropriate place to study epidemiology and demography of orofacial clefts.

The incidence of cleft lip and/or palate has been studied in numerous epidemiological investigations in various regions of the world.[1-5] The reports suggest that wide ethnic and racial variations exist.[6] High incidence rates have been reported for Asian populations, intermediate rates for Caucasian populations, and low rates in Black African populations.[7] The overall incidence rates for cleft lip, cleft lip and palate, and isolated cleft palate ranged from 0.79 to 3.74 per 1000 individuals for Asians, 0.91 to 2.69 for Caucasians, and 0.18 to 1.67 for Blacks.[7] In the United States, clefts appear to be most common among Native Americans, they are of intermediate prevalence among Caucasians and Asian-Americans, and are least common among African Americans.[8-12] The reported incidence of cleft lip and palate was greater than for cleft lip alone or for isolated cleft palate. In most reports, males outnumbered females in both cleft lip and cleft lip and palate, while isolated cleft palate was predominant in females. A worldwide study reported an increase in the frequency of congenital malformations, and orofacial clefting represented 15% of all such anomalies.[13-26] This increase was explained by the decrease in postnatal mortality, partially due to improved surgical techniques and

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better neonatal care. These factors seem to have contributed to an increased number of children surviving with a cleft anomaly.[28-30]

Epidemiologic data on clefts in many studies is of limited value when all orofacial cleft types are combined without distinction between isolated cleft lip, cleft lip and palate, and isolated cleft palate. Embryologically and etiologically, clefts of the primary palate differ from clefts of the secondary palate. Isolated cleft lip, cleft lip and alveolar process, and cleft lip with cleft palate are considered variations of the same developmental anomaly. Cleft palate associated with cleft lip and alveolar process appears to be a secondary event, occurring subsequent to the formation of a cleft in the primary palate. Closure of the secondary palate may be prevented by the tongue being postured high in the primary cleft area and then failing to descend in time for the palatal shelves to approximate and fuse.[31] This could possibly explain why clefts of the secondary palate occur more frequently with bilateral than with unilateral cleft lip.

Clefts of the primary and secondary palate have been reported to develop from failure of the respective maxillary processes to approximate, the epithelium to fuse, and the mesenchyme to penetrate through the epithelial membranes.[32] Ultimately, it may also rupture after the palate has already fused.[33]

Clefts of the lip, as well as those of the secondary palate, may show varying degrees of completeness on one or both sides. As fusion of the processes of the primary palate begins in the region of the floor of the nose and proceeds downward and forward, a teratogenic insult at any time could result in clefting of the lip and alveolar process from that point onward.[34] Therefore, the cleft may be of a different degree or severity, from a mild notch of the vermilion border to incomplete or complete cleft of the lip and alveolar process, unilaterally or bilaterally.

Table 1
Distribution of clefts by sex and type

Sex	Cleft lip	Cleft lip and alveolus	Cleft lip and palate	Cleft palate	Total	%
Male	3 (1%)	20 (7%)	128 (46%)	7 (3%)	158	57
Female	3 (1%)	24 (9%)	70 (25%)	23 (8%)	120	43
Total	6 (2%)	44 (16%)	198 (71%)	30 (11%)	278	100

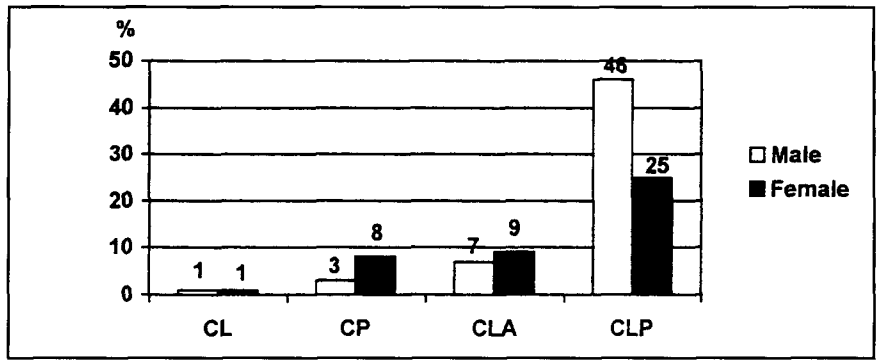

Figure 1
Distribution of clefts by sex and type.

Similarly, fusion of the secondary palate begins from the incisive foramen area and proceeds posteriorly. Thus, fusion interference will result in a mild cleft of the uvula or soft palate up to a complete cleft of the hard and soft palate. A high correlation has been reported between the degree of clefts in the primary palate and clefts of the secondary palate.[35] In addition, a submucosal cleft palate appears to be a milder expression of the clefting process where bony and muscular deficiencies occur in the midline, but without a complete or "open" cleft.

The present investigation was undertaken to study the distribution of various types of orofacial clefts in a large urban population. Additionally, differences between sexes, location of cleft, and side were evaluated.

Material and methods

The records of 278 individuals affected with unilateral or bilateral cleft lip and/or palate were obtained from four cleft palate centers in the New York City metropolitan area (Montefiore Medical Center, Center for Craniofacial Disorders [n=56]; New York University College of Dentistry, Department of Orthodontics [n=42]; New York University Medical Center, Institute for Reconstructive Plastic Surgery [n=75]; Suffolk Cleft Palate Rehabilitation Center [n=105]). The sample comprised 158 males and 120 females, 5 to 18 years of age (mean age 10.4 years), of mixed socioeconomic background and varied racial and ethnic origin. Because New York City is one of the primary ports of entry for immigrants, a variety of ethnic groups have settled in the vicinity. It was impractical to divide the sample by race or ethnic origin. The sample included only individuals whose clefts were not "syndromic clefts," that is where clefting was part of a

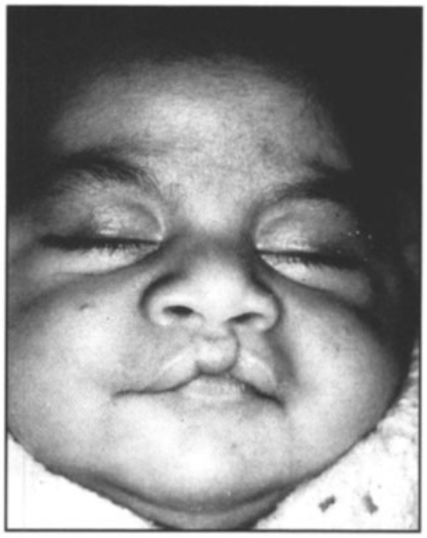

Figure 2
Bilateral isolated cleft lip. Left: Complete; Right: Incomplete

more complex craniofacial syndrome. The reported data pertain to patients with clefts who were enrolled for treatment or observation in the centers. Studied individuals were classified according to the findings of their clinical examinations, listed centers and not on the number of infants born with clefts in the New York City region. Classification of the clefts described in these patients' records were further verified by examination of the radiographs. The findings were analyzed using the standard descriptive statistical parameters. Significance was tested using the chi-square test.

Results

The sample of 278 individuals was first separated by sex and then divided into four groups according to the type of the orofacial cleft (Table 1 and Figure 1).

The distribution of cleft lip (CL)and cleft lip and alveolus (CLA) was approximately equal between males and females. Cleft lip and palate (CLP) was found nearly twice as often in males as in females (128 to 70, respectively), while isolated cleft palate (CP) occurred over three times more frequently in females than in males (23 to 7, respectively, Table 1).

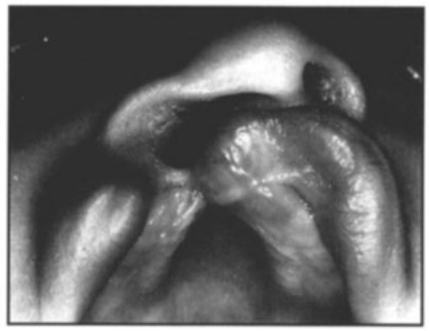

Figure 3A

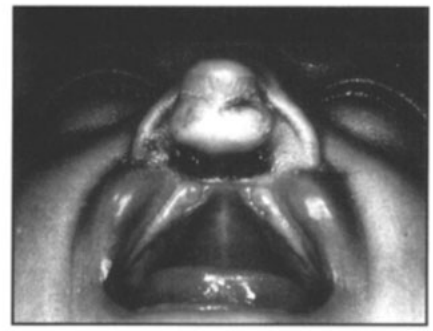

Figure 3B
Cleft of the lip and alveolar ridge. A: Unilateral complete; B: Bilateral complete

Figure 4A

Figure 4B
Cleft of the lip and palate. A: Unilateral complete; B: Bilateral complete

Isolated cleft lip—characterized by the cleft extending through the upper lip partially or completely up to the base of the nostril, but not through the alveolar ridge (Figure 2). This group was the smallest, with only six individuals equally distributed between males and females. Clefts were located on the left side in two males and in two females, and on the right side in one male and one female. There were no bilateral clefts in this group.

Cleft lip and alveolar ridge—characterized by clefting in the upper lip and maxillary alveolar process, ending posteriorly at the incisive foramen (Figure 3). This form of cleft can be complete or incomplete. A complete cleft of the primary palate extends through all the involved structures, whereas incomplete cleft of the primary palate may not extend through the upper lip to the nostril, or through the alveolar ridge to the incisal foramen. In this study we intended to include both complete and incomplete clefts of the primary palate, however each of the clefts in this group involved both the lip and alveolar process to a greater or lesser extent. The group included 44 individuals, 20 (45%) males and 24 (55%) females. The clefts were found on the left side in 11 (25%) males and 11 (25%) females, and on the right side in 8 (18%) males and 8 (18%) females. Bilateral clefts of the lip and alveolar ridge occurred

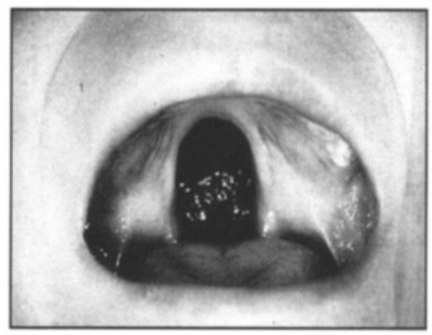

Figure 5
Isolated cleft palate

in 1 (2%) male and 5 (12%) females. Consequently, some clinically insignificant differences are reported in frequencies of this type of clefting between males and females.

Unilateral clefts occurred six times more often than bilateral (38 to 6, respectively). The results suggest the left side predominance as the left side was affected approximately 50% more than the right, both in males and females. Unilateral clefting on the left side is also more prevalent than bilateral (22 to 6, respectively). Sex distribution for unilateral clefting of the lip and alveolus was equal for both sides, whereas bilateral clefting was found more often in females than in males (5:1 ratio).

Cleft lip and palate—involves the lip and alveolar process and extends posteriorly along the palatal midline to the uvula, thus including both the primary and secondary palates (Figure 4). Incomplete clefts of the lip and palate were also included in this group. An incomplete cleft of the lip and palate is one in which the cleft of the lip may not extend all the way through to the nostril, or the cleft of the palate may not extend all the way through to involve the uvula. This group of clefts was the largest. It included 198 (71%) of the total sample subjects, of which 128 (65%) were male and 70 (35%) were female. Cleft lip with palatal involvement was found on the left side in 52 (26%) males and 34 (17%) females. Clefts affected the right side in 39 (20%) males and 21 (11%) females, and they occurred bilaterally in 37 (19%) males and 15 (7%) females.

The results show that cleft lip and palate occur more often in males than in females (128 to 70, a ratio of nearly 2:1). The left side was affected approximately 50% more often than either the right side or both sides together, and more so in males than females. The left side predominance for this anomaly could be repeatedly demonstrated.

Table 2
Distribution of clefts by type and location

Cleft	Left side		Right side		Bilateral	
	No.	%	No.	%	No.	%
Lip	4		2		-	
Lip and alveolus	22		16		6	
Lip and palate	86		60		52	
Total	112	45	78	32	58	23

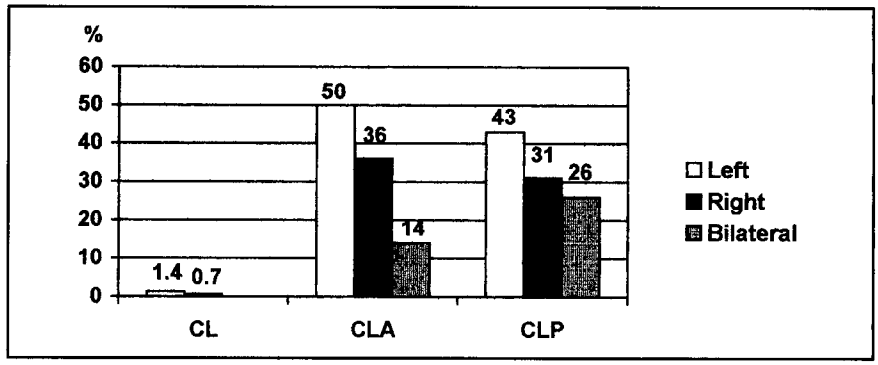

Figure 6
Distribution of clefts by type and side

Isolated cleft palate—characterized by a cleft of the secondary palate only which extends anteriorly as far as the incisive foramen (the junction of the premaxilla and the maxilla proper) and does not involve the alveolar process (Figure 5). Both complete and incomplete clefting was observed. An incomplete cleft of the secondary palate may involve either part or all of the soft palate tissues, or may extend anteriorly up to the incisive foramen, involving part or all of the hard palate,. In our study, we grouped both complete and incomplete clefts of the secondary palate. There were 30 individuals (11%) in this group, 23 (77%) females and 7 (23%) males. Isolated cleft palate occurred 3.3 times more often in females than in males (3:1 ratio).

Discussion

In many studies, cleft lip and palate are recorded as a single entity, without any distinction between the various types or degrees of clefts. As the development of the primary palate (lip and premaxilla), which takes place during the fourth to seventh week of gestation, is different embryologically and etiologically from that of the secondary palate (hard and soft palate), which develop during the seventh to twelfth week, the incidence of their clefting should be recorded separately.[36] Cleft palate associated with cleft lip appears to be a secondary result of a disturbance in the development of the lip. The impediment of the tongue may prevent selfclosure of the primary cleft, eventually resulting in failure of the palatal shelves to make contact as they move into the horizontal position.[31] This could also be the reason that cleft palate occurs more frequently with bilateral cleft lip than with unilateral. Thus, it appears that isolated cleft palate and cleft lip with cleft palate represent variations in the severity of the same defective development. For these reasons, our sample was di-

vided into four groups according to the type of the anomaly. Additionally, distribution by sex and location (sidedness) was studied. Differences in the incidence of cleft lip, cleft lip and palate, and isolated cleft palate among different racial groups, between the two sexes, and their combination with other craniofacial malformations have been reported previously.[7,37,38] A wide variation in frequency, ranging from 0.43 to 2.45 per 1000, has been reported for mixed races.[13,39] These were estimates based on averaging various sources of information. Our sample was obtained from four cleft centers in metropolitan New York and included patients of varied racial and ethnic backgrounds, including Caucasians of mixed European ancestry, African and Asiatic Americans, and others. There was no clear dominance of one racial group, thus the racial and ethnic types were grouped together in our study.

In the cleft population studied (278 individuals), the overall male to female ratio was nearly 1:1, but it varied with the type of cleft. A highly statistically significant difference ($p<0.0001$) between males and females affected with cleft lip and palate (cleft of the primary and secondary palate) was found in our study. Almost no sex differences were noted in individuals affected with isolated cleft lip or cleft lip and alveolus (cleft of the primary palate only, Table 1). On the other hand, the incidence of isolated cleft palate (cleft of the secondary palate only) was found to be highly statistically significant in females ($p<0.0001$, Table 1). These, together with our findings that cleft lip and palate occurs more frequently in males, while isolated cleft palate occurs most often in females, is in agreement with several previously reported studies.[13,40-43] Our racially mixed sample replicated studies of single races, despite the fact that the incidence of clefts differs by race. The reasons for the sex dimorphism of clefts are still obscure and are a subject of further investigation.

The distribution of clefts by type and side of the face is demonstrated in Table 2 and Figure 6. Unilateral cleft of the primary and secondary palate appeared over three times more frequently than bilateral clefts. Of the total 278 individuals in our sample, 190 (68.5%) presented a unilateral cleft of the lip and alveolar process (primary palate), either alone or in combination with a cleft of the secondary palate. Left side clefts (clefts of the lip, lip and alveolus, or lip and palate) were found in 112 individuals (59%), while right side clefts were found in 78 (41%). This difference was statistically significant ($p<0.05$). Most studies are in agreement with our findings, indicating as yet unexplained, the left side predominance for this anomaly.[1,13,14,20,40,41]

One attempt to explain this phenomenon suggests that in the early stages of development, the embryo receives a somewhat greater supply of blood, due to the higher blood pressure from the right internal carotid artery, which is in a more direct line of blood flow than the left side.[44]

Bilateral clefts of the lip and palate were found in 58 individuals (21%), and isolated cleft palate was detected in only 30 individuals (11%). The reason for left side predominance of cleft anomalies, similar to several other congenital dental anomalies, is unknown. It would be valuable to know whether any growth asymmetries in the embryonic face could account for this phenomenon. Answers to this question await further investigation.

Conclusions

Various types of orofacial clefts were studied for their location and severity. The most prevalent form was the cleft lip and palate, comprising 71% of our sample. Males were affected twice as often as females for this anomaly. Other types of clefts affected females slightly more often, but not to a significant degree. Unitaleral clefts occurred significantly more often than bilateral clefts (approximately 4:1) and the left side was affected substantially more often than the right (approximately 3:2). The recurring theme of left side dominance in various craniofacial anomalies, including various types of orofacial clefts, remains an intriguing but unexplained phenomenon.

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