Associated anomalies in cleft lip and palate: analysis of 811 consecutive patients

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Introduction: Clefts are common birth defects and may be associated with oro-facial congenital anomalies. It has not been established if specific types of anomalies are frequently related with clefts, or which organ is most commonly affected. This study aimed to assess the prevalence of associated anomalies in consecutive cleft lip and palate patients treated at two referral centres in Northern Nigeria.

Methods: Cleft lip and palate at two referral hospitals in Northern Nigeria from January 2012 to December 2015 were studied. Data were analysed using Statistical Package for Social Sciences (SPSS) version 16.

Results: A total of 811 cleft lip and palate patients were managed. Fifty-five percent (447) were male and 45% (364) were female while 71% (578) were children and 29% (233) were adults. The prevalence of associated anomalies was 11.5%. The most common associated anomaly among cleft patients was facial anomaly (64% of cleft patients). Associated anomalies were most prevalent in patients with isolated cleft palate. Hypertelorism was the commonest type of facial anomaly recorded.

Conclusion: Our study showed a low incidence of associated anomalies with a higher incidence in isolated cleft palate cases.

Key Words: Cleft lip, Cleft Palate, Associated Facial Anomaly, Congenital anomaly

Introduction

Oro-facial clefts are common birth defects in humans and may be associated with other congenital anomalies. The majority of these clefts are non-syndromic [1]. The incidence and the types of associated anomalies vary between different studies. However a frequency of 3% to 63% has been reported which is a reflection of varying data collection [2]. It has not been established if there are specific types of anomalies that are often related to cleft, or which organ is most commonly affected [3].

Establishing the presence of associated anomalies in patients with cleft is necessary for adequate screening and evaluating such patients, so that an appropriate treatment can be given [3]. It is also essential that every child should be thoroughly examined immediately after birth for associated anomalies, because children with severe malformation may not survive long [1]. There is little information on the frequency of associated anomalies in cleft in Africa. The aim of this study was to assess the prevalence of associated anomalies in a group of consecutive cleft lip and palate patients treated at two referral centres in Northern Nigeria.

Methodology

A retrospective study of all patients with cleft lip and palate managed at two referral hospitals (University of Maiduguri Teaching Hospital and Mercyland Specialist Hospital Maiduguri in Borno State in Northern Nigeria) under the SmileTrain project over a 4-year period (January 2012 to December 2015) was undertaken. The records of all patients with cleft were noted and analysed. Patients with syndromic cleft or incomplete data were excluded from the study.

Clefts were classified into 4 types: isolated unilateral cleft lip, bilateral cleft with or without palate, unilateral cleft lip and palate, isolated cleft palate. The associated congenital anomalies were classified according to the principal organ, system and/or area affected (facial, ocular, central nervous system, cardiovascular, auricular, upper and lower extremity, urogenital, and gastrointestinal). All the patients enrolled were reviewed by every cleft team member. The diagnosis of the associated anomalies was based on their expert opinions.

The evaluation of associated malformations was based on a thorough history, physical examination

and investigations which included haematological tests, biochemical tests, chest x-rays, two-dimensional echocardiogram, ultrasound scans and computed tomograghy as preliminary evaluation was deemed necessary. Patients' clinical information included age, gender, type of cleft, and presence of associated anomalies. Data were analyzed using SPSS version 16. A p-value less than 0.05 was considered significant. The study was approved by the Ethical Committees of the two hospitals.

Results

A total of 811 cleft patients were managed during the study period consisting of children 578 (71%) and adult 233 (29%). The gender distribution was 308 (38%) males and 268 (33%) females (M:F = 1.4:1).

Unilateral cleft lip with or without alveolus was the most frequent subtype (576 patients, 71%), followed by bilateral cleft lip with or without palate (123 patients, 15%). Table 1 shows the distribution of associated anomalies.

The most common associated anomaly among cleft patients was facial anomaly, in 64% of cleft patients, followed by ocular anomaly in 22%. See Figures 1 and 2.

The total number of associated anomalies was 93 (11.5%) with single anomaly recorded in each patient. There was a high occurrence of associated anomalies in isolated cleft palate patients where 6 patients (40%) out of the 15 cases, presented with associated anomalies, followed by patients with combined cleft lip and palate (16 out of 97 cases, 16.5%); the least number was recorded in bilateral cleft lip with or without palate patients with 11 (8.9%) out of 112 patients. There was a significant relationship between cleft deformity and associated anomalies (P=0.001). See Figure 3.

Among cleft patients with facial anomalies, 29 patients (49%) had hypertelorism followed by nasal deformity in 14 (24%). There was however no significant relationship between facial anomalies and cleft type (P = 0.384) - see Table 2. Table 3 revealed the most common ocular anomaly to be strabismus followed by exophthalmos. There was no significant relationship between cleft type and ocular anomalies (P= 0.072).

Discussion

A cleft lip or palate can be a single anomaly or a part of multiple congenital anomalies [1]. In general, most congenital anomalies can be divided into three types:

a. Disruptions: A rare anomaly related to breakdown of the original normal foetal developmental process, e.g. craniofacial cleft resulting from amniotic bands.

b. Deformations: These occur secondary to mechanical forces leading to anomalies of a lesser degree when compared to disruption, e.g. club foot, cleft palate, Pierre Robin sequence etc.

c. Malformations: A morphologic defect in an organ

Table 1. Distribution of associated anomalies among cleft patients

Site of Anomaly	CLA	BCLP	UCLP	ICP	Total (%)
Facial	38	6	12	3	59 (64)
Ocular	14	3	3	-	20 (22)
CNS	3	1	-	-	4 (4)
Lower extremities	3	1	-	-	4 (4)
Cardiovascular	-	-	-	2	2 (2)
Auricular	-	-	-	1	1 (1)
GIT	1	-	-	-	1 (1)
Upper extremities	1	-	-	-	1 (1)
Urogenital	-	-	1	-	1 (1)
Total	60	11	16	6	93 (100)

Key:

UCLA = Cleft Lip with/without Alveolar cleft

BCLP = Bilateral Cleft Lip with Cleft Palate

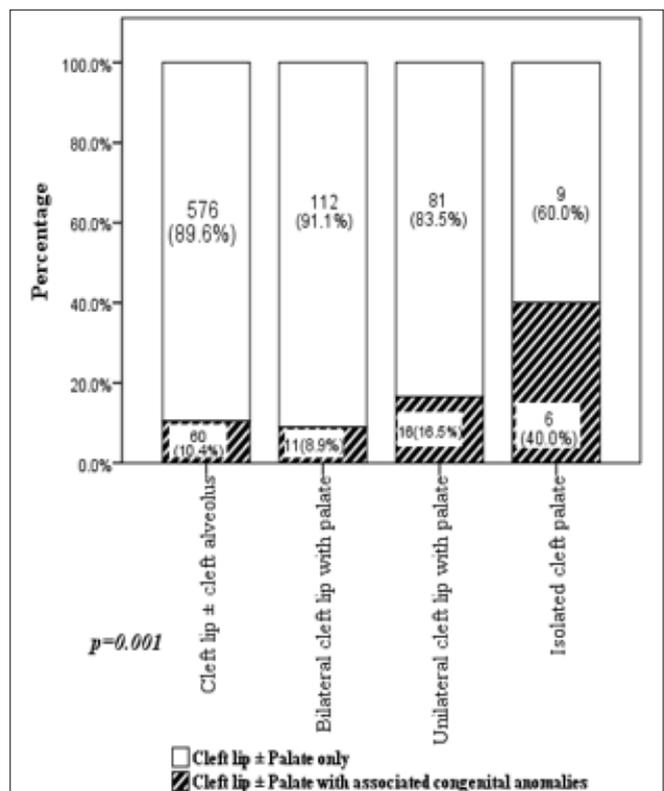UCLP = Unilateral Cleft Lip with Cleft Palate

ICP = Isolated Cleft Palate

Figure 1. Bar chart showing association between cleft type and associated anomalies

Table 2. Cleft Type and Types of Facial Deformities

Type of Anomalies	CLA	BCLP	UCLP	ICP	Total (%)
Hypertelorism	21	2	5	1	29 (49)
Dysmorphic face	4	-	1	-	5 (8)
Nasal Deformities	6	3	4	1	14 (24)
Microcephally	-	-	1	-	1 (2)
Telecanthus	-	1	-	-	1 (2)
Macrocephally	4	-	-	1	5 (8)
Frontal bossing	2	-	1	-	3 (5)
Midfacial hypoplasia	1	-	-	-	1 (2)
Total	38	6	12	3	59 (100)

P-value = 0.384

Key: (See under table 1)

Table 3. Cleft Type and Types of Ocular Deformities

Ocular Deformities	CLA	BCLP	UCLP	ICP	Total (%)
Strabismus	5	-	2	-	7 (35)
Microphthalmia	1	-	-	-	1 (5)
Blindness	1	-	-	-	1 (5)
Cataract	4	-	-	-	4 (20)
Exophthalmous	3	2	1	-	6 (30)
Anophthalmia	-	1	-	-	1 (5)
Total	14	3	3	-	20 (100)

P=value= 0.072

Key: (See under table 1)

from an intrinsically abnormal developmental process, e.g. polydactyly, congenital heart anomalies, cleft lip [4].

However, with the present advancement in embryology and genetics, and its correlations, the associated anomalies need to be differentiated from syndromes, in patients with multiple congenital anomalies [4].

The reported prevalence of associated anomalies varies widely across the literature; generally a prevalence rate between 3% and 63% has been reported which is a reflection of varying data collection [2]. Our hospital-based study revealed a low rate of 11.5%, which is at variance with most hospital-based studies which are often higher than population studies. The reason for this is not known. Authors who have reviewed data from birth registries generally report lower incidences than authors who account for patients referred to their institutions [3]. Knocks and Braithwaite [5] in Northumberland reported in 1962 an incidence of 7.5%, whereas Greene

et al [6] in 1964 found that 15% of infants in the United States had other defects. A Sweden population-based study showed that 1% of patients with oral cleft had associated malformations that either required follow-up or treatment [3]. Rollnick and Pruzansky [7] observed other malformations in 44% of the reviewed children with clefts who were referred to the Centre for Genetics, Medical Centre, University of Illinois. An even higher incidence was reported by Shprintzen et al [8] who found that associated malformations were present in 63.4% of the children examined at SUNY Upstate Medical University, New York, USA. Population-based studies are believed to be more appropriate [1].

The wide variation in reports on prevalence of cleft deformity and associated anomalies is dependent on the diagnostic procedure used [9]. Another possible explanation for the variation has been a lack of agreement on what should be regarded as a congenital defect. Some other challenges other investigators have encountered are variation in the time of presentation of these cases after birth, level of knowledge of the investigators themselves and available technology, as well as variability in the clinical expressions of these associated anomalies [10]. In the two centres where our study was carried out, a team approach was adopted. Our team however lacks a genetist or a dysmorphologist.

There are also different reports in the literature as to which congenital malformations are most common in patients with cleft. Our study has shown a higher prevalence of associated anomalies in the head region with the most involvement being the face (64%) followed by the ocular region (22%). This is similar to the study of Shprintzen [8] who found most of the associated anomalies in the head and neck area. Whereas Stark [11] and Lilius [12] observed a dominance of malformations of the extremities. In a study in Sweden in 616 infants Josef et al. found cardiac anomalies as the most common associated anomaly [3]. It has however not been conclusively established whether clefts are related to specific types of congenital defects [8]. It is also not known whether the aetiology of the cleft deformity are same with that of the associated anomalies. However further genetic studies are important to be able to differentiate the aetiologies and pathogenesis of associated anomalies from cleft syndromes [2].

In our study we found that although the incidence of cleft was highest in isolated unilateral cleft lip, associated anomalies (28%) was highest in patients with isolated cleft palate. This is similar to that reported earlier by Stoll [9] and Natsume [13]. Josef et al. however reported a higher incidence of associated anomalies among patients with combined cleft lip and palate [3].

We recommend that doctors in Sub-Saharan Africa (and worldwide) dealing with cleft patients (often dental, facio-maxillary and plastic surgeons) request

Figure 2. A child with unilateral cleft lip and associated frontal bossing. Credit: Dr Adesina.

Figure 3. A child with unilateral cleft and associated bilateral congenital cataract. Credit: Dr Adesina (Consent given)

multidisciplinary evaluation of their patients for possible associated abnormalities therefore improving decision making in their management. Dealing with a severe congenital cardiac anomaly should take precedence over a simple repair of a cleft lip. This simple measure can prevent unnecessary morbidities and mortalities.

Conclusion

The prevalence of associated anomalies among oro-facial cleft patients is low. Patients with isolated cleft palate appear to be at higher risk for associated anomalies.

We recommend a team approach when evaluating the patients with cleft. Future prospective studies on associated anomalies are also recommended.

Limitations: The present study was retrospective and as such was limited to the clinical records available to the researchers. There might have been a higher number of congenital anomalies seen in the period under review but we have presented what was available in patient's records.

Acknowledgement: Photographs of the children are published with permission of the parents.

References

1. Shahin AF, Nikzad S, and Alireza L. Prevalence of Associated Anomalies in Cleft Lip and/or Palate Patients, *Iran J Otorhinolaryngol.* 2016 Mar; 28(85): 135–139.

2. Sekhon, PS, Ethunandan M, Markus, A.F. Krishnan G, Bhasker Rao C., Congenital Anomalies Associated With Cleft Lip and Palate—An Analysis of 1623 Consecutive Patients Cleft Palate–Craniofacial Journal, 2011; 48 (4).

3. Josef M, Ola L, Catharina H, Margareta I. Associated Malformations in Infants with Cleft Lip and Palate: A Population-based Study. *Pediatrics* 1997; 100; 180.

4. Venkatesh R. Syndromes and anomalies associated with cleft. *Indian J Plast Surg.* 2009 Oct; 42(Suppl): S51–S55.

5. Knocks G, Braithwaite FL. Cleft lips and palates in Northumberland and Durham. *Arch Dis Child* 1962; 38:66–70.

6. Greene JC, Vermilion JR, Hay S, Gibbens SF, Kerschbaum S. Epidemiologic study of cleft lip and cleft palate in four states. *J Am Dent Assoc* 1964; 68:387 – 404.

7. Rollnick BR, Pruzansky S. Genetic services at a center for craniofacial anomalies. *Cleft Palate J* 1981; 18:304–313.

8. Shprintzen RJ, Siegel-Sadewitz VL, Amato J, Goldberg RB. Anomalies associated with cleft lip, cleft palate, or both. 1985; *Am J Med Genet* 20:585 – 595.

9. Stoll C, Alembik Y, Dott B, Roth MP. Epidemiological and genetic study in 207 cases of oral clefts in Alsace, north-eastern France. *J Med Genet.* 1991; 28(5):325–329.

10. Wyszynski DF, Sarkozi A, Czeizel AE. Oral clefts with associated anomalies issues. Cleft methodological Palate, *Craniofac J.* 2006; 43:1–6.

11. Stark RB. Cleft Palate: A Multidiscipline Approach. New York, NY: Harper & Row, Publishers; 1968:303.

12. Lilius DP. Clefts with associated anomalies and syndromes in Finland. *Scand J Reconstr Hand Surg* 1992; 26:185–196.

13. Natsume N, Niimi T, Furukawa H, Kawai T Ogi N, Suzuki Y, et al. Survey of congenital anomalies associated with cleft lip and/or palate in 701,181 Japanese people. *Oral Surg Oral Med Oral Radiol Endod.* 2001; 91 (2):157–61.

Further reading

Roberts RM; Mathias JL; Wheaton P. Cognitive Functioning in Children and Adults with Nonsyndromal Cleft Lip and/or Palate: A Meta-analysis. *Journal of Pediatric Psychology* 2012; 37(7):786-797.