RESEARCH
www.commprac.com
ISSN 1462 2815

THE FREQUENCY OF NON-SYNDROMIC OROFACIAL CLEFTS AND THEIR CONNECTION TO CONGENITAL HEART CONDITIONS

Dr. Yelkur Pallavi [1], Dr. Radha Kumar [2]*, Dr. Thangella manasa [3], Dr. Vaanmathi Azhagar Nambi Santhi [4] and Dr. Varshini Chandrasekhar [5]

[1,5] Postgraduate MD Paediatrics, Department of Paediatrics, Saveetha Medical College, SIMATS, Chennai, India.
[2] Professor, Department of Paediatrics, Saveetha Medical College, SIMATS, Chennai, India. *Corresponding Author
[3] Senior Resident, MD Paediatrics, Department of Paediatrics, Meenakshi Medical College and Research Institute, Chennai, India.
[4] Assistant Professor, Department of Paediatrics, Saveetha Medical College, SIMATS, Chennai, India.

DOI: 10.5281/zenodo.12065455

Abstract

Introduction: Orofacial clefts (OC) are common congenital anomalies that significantly impact health, finances, and social well-being. This study examines the prevalence of non-syndromic orofacial clefts (NSOFCs), their association with congenital heart diseases (CHDs), and the demographic and clinical characteristics of affected individuals. **Methods**: A prospective study was conducted from January 2023 to January 2024, evaluating echocardiographic records of 60 patients with cleft lip (CL) and cleft palate (CP) scheduled for surgical repair. Comprehensive cardiovascular assessments, including detailed medical histories and physical examinations, were performed. All patients underwent transthoracic echocardiographic evaluations to identify CHDs. **Results**: CHDs were found in 20% of children with non-syndromic orofacial clefts. The most common CHD was Patent Ductus Arteriosus (PDA) (54%), followed by Patent Foramen Ovale (PFO) (45.4%). CHDs were more prevalent in males (53.33%) than females (46.67%). The median age at diagnosis was 12 months. Isolated cleft lip was the most frequent OC type (50%), followed by isolated cleft palate (43.3%) and cleft lip with cleft palate (6.6%). **Discussion**: The prevalence of CHDs in children with non-syndromic orofacial clefts was higher than in the general population, with PDA being the most common defect. All detected CHDs were acyanotic, consistent with some studies but differing from others. Early diagnosis through routine echocardiographic screening is crucial for effective management and prevention of complications. **Conclusion**: This study highlights the significant prevalence of CHDs among children with non-syndromic orofacial clefts and emphasizes the need for routine cardiovascular assessments. Children with non-syndromic orofacial clefts should also be screened for cardiovascular disease.

Keywords: Acyanotic Heart Defects, Cleft Lip, Cleft Palate, Congenital Heart Diseases, Echocardiographic Screening,Non-Syndromic Orofacial Clefts, Pediatric Congenital Anomalies.

INTRODUCTION

Orofacial cleft (OC) refers to a group of congenital defects that affect the facial and oral structures. It is primarily classified into isolated cleft palate (CP) and cleft lip with or without cleft palate (CL/P). While Orofacial cleft (OC) is typically not deemed a disorder that poses a risk to life, it is the prevailing congenital abnormality. Orofacial cleft(OC) has profound negative effects on the patient's health, finances, and mental well-being, as well as on their family and society as a whole (1,2). Orofacial cleft (OC) is a prevalent craniofacial abnormality, with an incidence of around 1 in 700 individuals (3). Nevertheless, due to disparities in birth rate and the effectiveness of birth defect monitoring systems internationally, there is significant heterogeneity in the global occurrence of Orofacial clefts. A study conducted by the International Perinatal Database of Typical Oral Clefts (IPDTOC) Working Group revealed significant global disparities in the occurrence of CL/P and CP, with prevalence rates varying by a factor

of six and three, respectively (4). Furthermore, the occurrence of oral clefts (OC) varies depending on whether they are associated with a specific syndrome or not. Non-syndromic clefts are responsible for the bulk of Orofacial cleft instances, accounting for 70% of cases with cleft lip and palate (CL/P) and 50% of cases with cleft palate (CP). (5) Females have a twofold higher chance of developing CP, while males have a twofold higher risk of developing CL/P (2). Curiously, in the United States, there were observed differences in the occurrence of non-syndromic OC across different ethnic groups. Asian or Indian-American individuals had the highest prevalence of non-syndromic CL/P, with approximately 1 in 500 individuals being diagnosed. African individuals had the lowest prevalence, with approximately 1 in 2500 individuals being affected. Caucasian individuals fell in between, with a prevalence of 1 in 1000 individuals (2,6).

Children with CLs and CP have a greater reported prevalence of congenital cardiac abnormalities compared to the general population. The prevalence of cardiovascular abnormalities in individuals with cleft lip and cleft palate is predicted to be 16 times higher compared to the general population [7]. A study conducted by Aimede et al. [8] found that 9.5% of patients with orofacial clefts in Abeokuta, Nigeria had a prevalence of the condition. Similarly, Otaigbe et al. [9] reported a prevalence rate of 15% for congenital heart disorders (CHD) in individuals with cleft lip/palate (CL/CP) in Port Harcourt, Nigeria. Geis et al. [10] found that the total frequency in England was 6.7%. Liang et al. [11] reported that the prevalence of congenital heart disease (CHD) in individuals with orofacial clefts is 5.4%. The most prevalent forms of congenital heart defects (CHD) are isolated atrial septal defect (ASD) and ventricular septal defect (VSD).[9] Sun et al. discovered that 13.6% of the subjects had coronary heart disease (CHD), with atrial septal defect (ASD) being the most prevalent form of CHD, accounting for 39.7% of cases. As far as the authors are aware, there has been no description of the frequency and characteristics of congenital heart disease (CHD) among children with cleft lips (CLs) and cleft palates (CP) in this specific geopolitical area. The aim of this study is to investigate the prevalence rates of non-syndromic orofacial clefts (NSOFCs) within specific populations, determine the frequency of congenital heart diseases (CHDs) among individuals with NSOFCs, and explore the demographic and clinical characteristics of individuals with both NSOFCs and associated CHDs. Additionally, this study seeks to assess potential risk factors contributing to the co-occurrence of orofacial clefts and congenital heart diseases, and to investigate the impact of early detection and intervention on the management of CHDs in individuals with NSOFCs. By addressing these objectives, the study aims to enhance understanding and improve the clinical outcomes for individuals affected by these conditions.

METHODS

This prospective study was designed to evaluate the echocardiographic records of all patients diagnosed with cleft lip (CL) and cleft palate (CP) over a one -year period, spanning from January 2023 to January 2024. The aim was to identify the presence and types of congenital heart defects (CHDs) in a total sample size of 60 patients. All patients scheduled for surgical repair of CL and CP were systematically referred to the cardiopulmonary clinic for comprehensive cardiovascular assessment. Upon referral, each patient underwent a thorough clinical evaluation, which included a detailed medical history and physical examination to screen for signs and symptoms indicative

of CHDs. Regardless of whether patients exhibited symptoms suggestive of heart disease, they were all routinely referred for echocardiographic evaluation to ensure thorough screening. The transthoracic echocardiographic studies were meticulously performed by the authors, utilizing advanced imaging techniques. The echocardiographic protocol included M-mode and two-dimensional imaging, complemented by Doppler interrogation to assess blood flow patterns and detect structural abnormalities. These evaluations were conducted using both a cardiac ultrasound system and a SonoScape ultrasound system, ensuring high-quality imaging and accurate diagnosis.

The echocardiographic assessments were performed through standard echocardiographic windows, including parasternal long-axis, parasternal short-axis, apical four-chamber, and subcostal views. These views allowed for a comprehensive evaluation of cardiac anatomy and function, facilitating the identification of various congenital heart defects, such as atrial septal defects (ASDs) and ventricular septal defects (VSDs). Data from the echocardiographic studies were meticulously recorded and analyzed. The results were expressed using frequency tables and percentages to provide a clear depiction of the prevalence and types of CHDs within the study population. The analysis aimed to elucidate the relationship between non-syndromic orofacial clefts and the incidence of congenital heart defects, contributing valuable insights to the existing body of research. Children with either cleft lip , palate and both cleft lip and palate without any dysmorphic features were included in the study. Children with dysmorphic features were excluded from study.

RESULTS

Table 1: Distribution Characteristics of the Study Population

S.NO	TYPE OF OROFACIAL CLEFT	FREQUENCY	PERCENTAGE
1	ISOLATED CLEFT LIP	30	50%
2	ISOLATED CLEFT PALATE	26	43.3%
3	CLEFT LIP WITH CLEFT PALATE	4	6.6%
4	TOTAL	60	100%

Table 2: Distribution Characteristics of the Study Population

S.NO	GENDER	FREQUENCY	PERCENTAGE
1	MALE	32	53.33%
2	FEMALE	28	46.67%
3	AGE AT DIAGNOSIS (MONTHS) MEDIAN	12 (3-36)	

Out of 60 children included in the study echocardiogram detected presence of congenital heart disease in 11 children (18.3 %) in (table 3).

Table 3: Distribution of Types of Congenital Heart Defects

S.NO	TYPE OF CONGENITAL HEART DISEASE	FREQUENCY	PERCENTAGE
1	PATENT DUCTUS ARTERIOSUS	6	54%
2	ATRIAL SEPTAL DEFECT	5	45.4%
3	TOTAL	11	100%

Table 4: Distribution of Frequency Of CHD in Male Patient

S.NO	TYPE OF CONGENITAL HEART DISEASE	FREQUENCY	PERCENTAGE
1	PATENT DUCTUS ARTERIOSUS	2	28.5%
2	ATRIAL SEPTAL DEFECT	5	71.4%
3	TOTAL	7	100%

Table 5: Distribution of Frequency of CHD ın Female Patient

S.NO	TYPE OF CHD	FREQUENCY	PERCENTAGE
1	PATENT DUCTUS ARTERIOSUS	4	80%
2	ATRIAL SEPTAL DEFECT	1	20%
3	TOTAL	5	100%

The study meticulously analysed the distribution of various types of congenital heart defects (CHDs) among a sample size of 60 patients, offering a detailed overview of the characteristics of the study population and the specific distribution of CHDs among male and female patients.

In this study examining the distribution of orofacial clefts, Isolated Cleft Lip was the most common type, occurring in 50% (30 cases) of the sample. This was followed by Isolated Cleft Palate, which was present in 43.3% (26 cases) of the patients. Cleft Lip with Cleft Palate was noted in 6.6% (4 cases) of the sample. These statistics highlight the diverse presentation of orofacial clefts within the population and the need for targeted healthcare strategies to address each type effectively.

The demographic characteristics of the study population revealed a higher prevalence of CHDs among males, who represented 53.33% (32 cases) of the sample, compared to females, who accounted for 46.67% (28 cases). The median age at diagnosis was 12 months, with a range spanning from 3 to 36 months, indicating that the majority of CHDs were identified relatively early in life. This early diagnosis is crucial for timely intervention and management of these conditions.

In a study examining the frequency of various types of congenital heart diseases (CHD), Out of 60 children included in the study echocardiogram detect presence of congenital heart disease in 11 children (18.3 %), it was found that Patent Ductus Arteriosus (PDA) was the most prevalent, accounting for 54% of the cases, with 6 instances reported. Atrial septal defect was observed in 5 individuals, making up 45.5% of the cases. Overall, the study encompassed 11 cases, providing a comprehensive overview of the distribution of these congenital heart conditions.

When analyzing the distribution of CHDs among male patients specifically, ASD was the most frequent defect, accounting for 71.4% (5 cases) of the 7 male patients. PDA followed with 28.5% (2 cases). This gender-specific distribution underscores the need for awareness and tailored medical approaches for male patients with CHDs.

Similarly, in female patients, PDA was also the most prevalent CHD, representing 80% (4 cases) of the 5 female patients. ASD was observed in 20% (1 cases). The distribution pattern in females, not similar to that in males, highlights slight variations that could be significant for clinical management and research focused on gender differences in CHD prevalence and outcomes.

DISCUSSION

The incidence rate of congenital heart disorders in children with orofacial clefts is 18.3%, indicating a higher prevalence compared to the general population. Nevertheless, it is crucial to acknowledge that the limited sample size in this study could have impacted the prevalence rate. However, the sample size in this study is slightly more than the one reported by Otaigbe et al., who discovered a prevalence rate of 15% among a group of 20 children with oral clefts.

The prevalence rate observed in this study surpasses the rates reported by Aimede et al. [8], Barbosa et al. [12], and Geis et al. [10] in their respective locales of Abeokuta, South-western Nigeria, Brazil, and England. Aimede et al. documented a prevalence of 9.5%, Barbosa et al. observed a prevalence of 9.5%, and Geis et al. recorded a prevalence of 6.7%. The prevalent rate in our study is markedly lower than the rates of 45.5% reported by Rawashdeh and Jawdat Abu-Hawas from Jordan and 45.1% reported by Sun et al. from Eastern China.

The study conducted by Sun et al. [13] found high prevalence rates of orofacial clefts, which were consistent with our findings. The study had a substantial sample size of 60 cases, indicating the robustness of the results. These data further validate the notion that orofacial clefts are influenced by a mix of genetic and environmental factors, highlighting the complex nature of this condition. [14] All occurrences of CHD were of the acyanotic type.

In the present study all the 11 children have congenital acyanotic heart disease and no child had cyanotic congenital heart disease.This outcome is consistent with the findings published by Otaigbe et al. [7] and Shafi et al. [15], who also did not observe any instances of cyanotic congenital heart disease (CHD). Nevertheless, it is in opposition to the conclusions of several other research [13,16,17] which have observed the existence of both cyanotic and acyanotic congenital heart defects (CHD) in individuals with orofacial clefts.

The investigation revealed that ASD, also known as atrial septal defect, was the most common congenital heart defect (CHD) identified, representing 50% of the cases. Furthermore, it was demonstrated that it constituted a constituent of many shunt abnormalities in 25% of the patients, aligning with the results of prior investigations [13, 15, 18]. Our analysis offers a contrasting perspective to the findings of Milerad et al. [7] and Chan et al. [17], who identified ventricular septal defect (VSD) as the most prevalent congenital heart defect (CHD).

While the identified lesions were not serious enough to delay the surgery, their identification can aid in preventing complications such as infective endocarditis, which is more prevalent in cases involving small ventricular septal defects (VSD), primum atrial septal defects (ASDs), and multiple abnormalities.[19].

The study's results affirm the importance of doing electrocardiograms on children with orofacial clefts because they have a higher likelihood of developing coronary heart disease (CHD). Performing these electrocardiograms is not essential prior to corrective surgery. Instead, their purpose is to identify congenital heart disease (CHD) at an early stage and promptly manage any potentially life-threatening complications.

Overall, this study provides a comprehensive and nuanced understanding of the distribution and characteristics of CHDs and orofacial clefts within a sizeable patient population. The data emphasize the importance of early diagnosis and the need for gender-specific healthcare strategies to effectively manage and treat these congenital conditions. The insights gained from this study are vital for improving patient outcomes and guiding future research and healthcare policies aimed at addressing congenital heart defects and orofacial clefts.

CONCLUSION

This study underscores the significant prevalence of congenital heart defects (CHDs) among children with non-syndromic orofacial clefts (NSOFCs), with Patent Ductus Arteriosus (PDA) being the most common. The findings highlight the importance of routine echocardiographic screening for early detection and management of CHDs in children with cleft lip and/or palate (CL/CP). Males exhibited a higher incidence of CHDs compared to females, suggesting a need for gender-specific medical approaches. The study's 20% prevalence rate of CHDs in children with NSOFCs is higher than many reported rates but lower than some from other regions, reflecting genetic and environmental influences. All CHDs identified were acyanotic, aligning with some studies but contrasting others, which found both cyanotic and acyanotic defects. The sample size of 60 cases supports the reliability of these findings, emphasizing the necessity for localized research. Overall, early cardiovascular assessment and intervention are crucial for preventing complications and improving outcomes for children with NSOFCs, guiding future research and healthcare strategies.

LIMITATIONS

This study has several limitations that should be considered. Firstly, the small sample size of only 60 patients limits the generalizability of the findings, and a larger cohort would provide more robust and statistically significant results. Geographical and demographic limitations also affect the study, as it was conducted in a specific area, which may not reflect the prevalence and characteristics of non-syndromic orofacial clefts (NSOFCs) and congenital heart defects (CHDs) in other regions. Differences in genetic, environmental, and socio-economic factors can influence the results.Furthermore, the study did not address long-term outcomes or follow-up of the patients, which is essential for understanding the progression and management of CHDs in individuals with NSOFCs. The exclusion of syndromic orofacial clefts limits the study's applicability to the broader population of children with clefts, as syndromic cases might have different CHD prevalence and characteristics. While echocardiography is a key diagnostic tool, it may not detect all CHDs, particularly minor or subclinical defects. Incorporating additional diagnostic methods could provide a more comprehensive assessment.

References

1) Sinno H, Tahiri Y, Thibaudeau S, Izadpanah A, Christodoulou G, Lin SJ, Gilardino M. Cleft lip and palate: an objective measure outcome study. Plast Reconstr Surg. 2012 Aug;130(2):408-414. doi: 10.1097/PRS.0b013e3182589d4b. PMID: 22842412.

2) Mossey PA, Little J, Munger RG, Dixon MJ, Shaw WC. Cleft lip and palate. Lancet. 2009 Nov 21;374(9703):1773-85. doi: 10.1016/S0140-6736(09)60695-4. Epub 2009 Sep 9. PMID: 19747722.

3) Rahimov F, Jugessur A, Murray JC. Genetics of nonsyndromic orofacial clefts. Cleft Palate Craniofac J. 2012 Jan;49(1):73-91. doi: 10.1597/10-178. Epub 2011 May 5. PMID: 21545302; PMCID: PMC3437188.

4) IPDTOC Working Group. Prevalence at birth of cleft lip with or without cleft palate: data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). Cleft Palate Craniofac J. 2011 Jan;48(1):66-81. doi: 10.1597/09-217. Epub 2010 Apr 6. PMID: 20507242.

5) Jugessur A, Farlie PG, Kilpatrick N. The genetics of isolated orofacial clefts: from genotypes to subphenotypes. Oral Dis. 2009 Oct;15(7):437-53. doi: 10.1111/j.1601-0825.2009.01577.x. Epub 2009 Jul 2. PMID: 19583827.

6) Dixon MJ, Marazita ML, Beaty TH, Murray JC. Cleft lip and palate: understanding genetic and environmental influences. Nat Rev Genet. 2011 Mar;12(3):167-78. doi: 10.1038/nrg2933. PMID: 21331089; PMCID: PMC3086810.

7) Milerad J, Larson O, Hagberg C, Ideberg M. Associated malformations in infants with cleft lip and palate: a prospective, population-based study. Pediatrics. 1997 Aug;100(2 Pt 1):180-6. doi: 10.1542/peds.100.2.180. PMID: 9240796.

8) Aimiede OS, Olalere GO, Olaosun Adedayo O, Sotannde Adeshola I (2013) Orofacial Clefts: Our Experience in Two Suburban Health Facilities. Dentistry 3: 155. doi:10.4172/2161-1122.1000155

9) Otaigbe BE, Akadiri OA, Eigbobo JO. Clinical and echocardiographic findings in an African pediatric population of cleft lip/palate patients: A preliminary report. Niger J Cardiol. 2013 Jan-Jun;10(1):6-8. doi: 10.4103/0189-7969.118574.

10) Geis N, Seto B, Bartoshesky L, Lewis MB, Pashayan HM. The prevalence of congenital heart disease among the population of a metropolitan cleft lip and palate clinic. Cleft Palate J. 1981 Jan;18(1):19-23. PMID: 6936098.

11) Liang CD, Huang SC, Lai JP. A survey of congenital heart disease in patients with oral clefts. Acta Paediatr Taiwan. 1999 Nov-Dec;40(6):414-7. PMID: 10927955.

12) Barbosa MM, Rocha CM, Katina T, Caldas M, Codorniz A, Medeiros C. Prevalence of congenital heart diseases in oral cleft patients. Pediatr Cardiol. 2003 Jul-Aug;24(4):369-74. doi: 10.1007/s00246-002-0335-9. Epub 2003 Jan 15. PMID: 12522651.

13) Sun T, Tian H, Wang C, Yin P, Zhu Y, Chen X, Tang Z. A survey of congenital heart disease and other organic malformations associated with different types of orofacial clefts in Eastern China. PLoS One. 2013;8(1):e54726. doi: 10.1371/journal.pone.0054726. Epub 2013 Jan 21. PMID: 23349958; PMCID: PMC3549991.

14) Grosen D, Chevrier C, Skytthe A, Bille C, Mølsted K, Sivertsen A, Murray JC, Christensen K. A cohort study of recurrence patterns among more than 54,000 relatives of oral cleft cases in Denmark: support for the multifactorial threshold model of inheritance. J Med Genet. 2010 Mar;47(3):162-8. doi: 10.1136/jmg.2009.069385. Epub 2009 Sep 14. PMID: 19752161; PMCID: PMC2909851.

15) Shafi T, Khan MR, Atiq M. Congenital heart disease and associated malformations in children with cleft lip and palate in Pakistan. Br J Plast Surg. 2003 Mar;56(2):106-9. doi: 10.1016/s0007-1226(03)00044-4. PMID: 12791351.

16) Wyse RK, Mars M, al-Mahdawi S, Russell-Eggitt IM, Blake KD. Congenital heart anomalies in patients with clefts of the lip and/or palate. Cleft Palate J. 1990 Jul;27(3):258-64; discussion 264-5. doi: 10.1597/1545-1569(1990)027<0258:chaipw>2.3.co;2. PMID: 2372974.

17) Chan KW, Lee KH, Pang KK, Mou JW, Tam YH. Clinical characteristics of children with orofacial cleft in a tertiary centre in Hong Kong. Hong Kong J Paediatr 2013;18:147-51.

18) Altunhan H, Annagür A, Konak M, Ertuğrul S, Ors R, Koç H. The incidence of congenital anomalies associated with cleft palate/cleft lip and palate in neonates in the Konya region, Turkey. Br J Oral Maxillofac Surg. 2012 Sep;50(6):541-4. doi: 10.1016/j.bjoms.2011.08.001. Epub 2011 Aug 30. PMID: 21880407.

19) Knirsch W, Nadal D. Infective endocarditis in congenital heart disease. Eur J Pediatr. 2011 Sep;170(9):1111-27. doi: 10.1007/s00431-011-1520-8. Epub 2011 Jul 20. PMID: 21773669.