Original article

Congenital heart disease in a cohort of Sudanese patients with cleft defects

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Abstract:

Background and objectives:

Cleft defects are among the most visible congenital defects worldwide and congenital heart disease (CHD) being one of the most common associated anomalies. This study aimed to assess the prevalence of CHD among a cohort of Sudanese patients with cleft lip and/or palate.

Patients and Methods:

All patients who presented to Soba University Hospital with cleft lip and/or palate from March 2009 to March 2015 were included.

Results:

Out of 381 patients included; 168 patients (44%) had cleft lip and palate (CLP), 156 (41%) had cleft lip (CL) and isolated cleft palate (CP) was found in 57 patients (15%). Facial dysmorphic features were identified in 57 (15%) and cardiac defects in 42 (11%) patients. Ventricular septal defect (VSD) was diagnosed in 16 patients (38%), and ASD in 12 (30.9%). Other macroscopic anomalies were identified in 57 patients (15%) and were associated with CHD (P<0.001). Significant association was found between the type of cleft and CHD (P<0.002), as cardiac defects were maximally observed among CP cases (21%) followed by CLP cases (13%) then CL cases (5.12%). Significant association was also found between facial dysmorphic occurrence and CHD (P < 0.001).

Conclusion:

CHD is a common anomaly in cleft population. The pattern of CHD is consistent with the literature with VSD being the most frequent. The cardiac defects are most prevalent in CP group. Echocardiography is justified for screening of CHD due to the relatively higher incidence of CHD among clefts patients than in general population

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Introduction:

Cleft lip and/or cleft palate conditions are some of the relatively common congenital anomalies seen worldwide with an incidence of 7 to 10 in10,000 livebirths[(1)]. In the United States there are almost 7000 children born annually with cleft conditions [(2)]. Children with cleft lip/palate defects often have other associated anomalies [(3, 4, 5)] with more than 20% of clefts patients having these associated anomalies [(4)]. Congenital heart disease (CHD) is one of the commonest associated anomalies among

cleft population [6, 7]. Studies from USA and India reported a prevalence of 10% and 15%, respectively [6, 7]. A systematic review of twelve series found an estimate of 7.42% of CHD among non-syndromic cleft lip and/or palate patients [5].

The occurrence of CHD in a cleft patient could have several peri-operative implications and may increase risks of developing specific complications like peri-operative arrhythmias, pulmonary hypertension, infective endocarditis and respiratory tract infections [7]. Hence, before undergoing any surgical intervention, a mandatory preoperative evaluation of the patient should be done by a multidisciplinary team including paediatric cardiologists, anesthetists, and maxillofacial surgeons [7].

The current study aimed to assess the prevalence of congenital heart disease (CHD) among a cohort of Sudanese cleft population using echocardiography screening. To the best of our knowledge it is the first study in the Sudan dealing with this issue.

Patients and Methods:

This is a descriptive, hospital-based, single-center study which was carried out between March 2009 and March 2015 at Soba University Hospital (SUH), Sudan. All patients with cleft lip and/or cleft palate defects who presented to Plastic and Reconstructive Unit during the study period and underwent clinical assessment of cleft defects and echocardiographic screening for detection of CHD were included in the study. Exclusion criterion was cleft patients who haven't had echocardiographic screening. An informed consent form was obtained from all parents after explaining the nature of the study. The ethical clearance was obtained from the Ethics Committee of Soba University Hospital.

Clinical examination of cleft patients was conducted to assess the morphological type, laterality, severity of defect and to look for facial dysmorphic features and associated macroscopic non-cardiac anomalies. The cleft defects were classified as follows: cleft lip (with or without cleft alveolus) (CL), isolated cleft palate (including submucosal one) (CP), and combined cleft lip and plate (CLP). An echocardiographic assessment was performed for all included patients using a trans-thoracic two-dimensional image echocardiography with Doppler studies to detect cardiac defects.

Data were collected using a predesigned questionnaire. Demographic data, physical examination of cleft anomalies and echocardiographic findings were recorded. Data were analyzed using the SPSS software package (version 22 Windows) to determine the statistical significance of differences. The Pearson test was used and probability test (*P* value) with $P< 0.05$ was considered as significant at 95% confidence interval.

Results:

Three hundred eighty one patients with cleft lip and/or cleft palate were studied. The patients' age ranged from 15 days to 19 years, with the mean age being 4.5 ± 3 years. One hundred ninety five patients (51.2%) were less than 2 years of age and 57 patients (15%) were above the age of 10 years. There were 122 female patients (32%) and 259 male patients (68%) with a male: female ratio of 2.1:1. Family history of clefts was reported in 30 (8%) of the cases.

Regarding the morphological pattern of the cleft defects, combined cleft lip and palate (CLP) was the most frequently observed anatomical type seen in 168 patients (44%) (Figure 1). Both CLP and cleft lip (with/without) cleft alveolus (CL) cases were more commonly observed among males (59% and 61%, respectively), whereas isolated CP cases were mainly seen in females (66%). This association between cleft type and sex was found to be significant ($P<0.002$). Family history of cleft defects was reported in 30 of cases (8%), but there was no significant association between morphological pattern and family history ($P = 0.13$).

Out of 381 patients reviewed, forty two (11%) patients had cardiac anomalies detected by an

echocardiographic screening. Ventricular septal defect (VSD) was the most commonly reported anomaly (either as a single lesion or as a part of combined lesions) in 16 (38%) patients (Figure 2). Most of them (n= 39, 92.9%) were acyanotic congenital heart disease. The majority of cardiac anomalies (n=31, 73.8%) were observed among patients who were younger than five years.

An association was found between morphological type of cleft defect and occurrence of CHD. 21% of patients with isolated cleft palate, 13% of patients with CLP and 5.1% of isolated CL patients have CHD (P<0.002) **(**Table 1**).** On assessing sex distribution of CHD: twenty three (55%) of cleft patients with CHD were males whereas 19 (45%) were females. Nevertheless; no significant differences were observed (P=0.516). Facial dysmorphic features were identified in 57 (15.7%) patients, in whom 30 (52%) had CHD. Furthermore, a significant association was found between occurrence of facial dysmorphic features and existence of cardiac defects (P<0.001) (Table 2).

Other macroscopic non-cardiac anomalies were observed in 15% (n=57) of cases. In fact, six patients had multiple anomalies. Skeletal anomalies were the most commonly observed. In 38 patients the upper limbs were mostly affected (with polydactyly and syndactyly being the most frequent defects seen in 16 and 12 patient, respectively; central nervous system (CNS) anomalies (14 patients); followed by abdominal wall defects (seven patients), and other rare defects e.g. (ear and eye anomalies) were reported in three patients. Furthermore, a significant association was found between occurrence of CHD and existence of other non-cardiac associated anomalies (P<0.001) as 34 patients (60.7%) of those who had non-cardiac anomalies had an associated CHD.

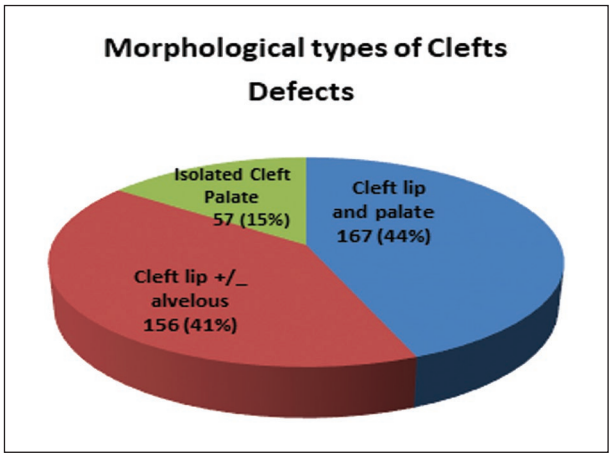
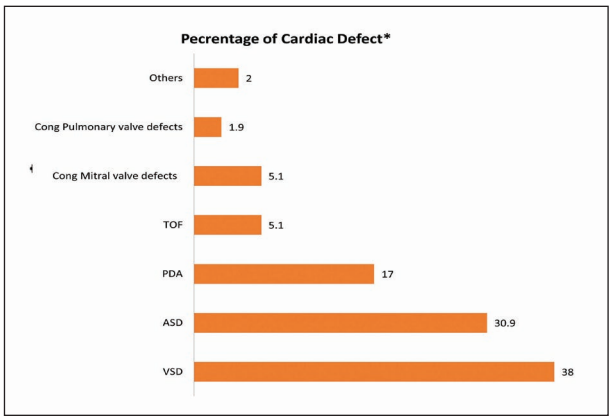


Figure 1: Distribution of morphological types of clefts defects.



VSD: ventricular septal defect, ASD: atrial septal defect, PDA: patent ductus arteriosus,

TOF: teratology of Fallot.

Figure 2. Percentage of cardiac defects among cleft patients

**P<0.002*

Table 1. Association between morphological types of cleft defects and occurrence of cardiac defects (n=381)

Morphological type of cleft defect*	Congenital heart defects		Total
	Present n (%)	Absent n (%)	
Cleft lip +/_ cleft alveolus	8 (5.1%)	148(94.9%)	156
Isolated cleft palate	12(21%)	45 (79%)	57
Cleft lip and palate	22 (13%)	146 (87%)	168
Total	42	339	381

**P<0.002*

Table 2. Association between facial dysmorphic features and occurrence of cardiac defects among cleft patients (n=381)

Facial dysmorphic features *	Cardiac defects		Total
	Present n (%)	Absent n (%)	
Present	30(52.7%)	27(47.3%)	57
Absent	12 (3.7%)	312(96.3%)	324
Total	42	339	381

*P<0.001

Discussion:

This study assessed the prevalence of CHD in a cohort of Sudanese clefts patients using echocardiography as a tool to detect the presence of CHD. This is quite important for both clinicians and developmental biologists, as it can improve screening, evaluation and the appropriate management of these associated conditions in cleft patients [8]. Furthermore, presence of CHD in clefts patients could have implications on peri-operative course and timing of surgery [6]. As this may increase the risk of developing certain intra-operative and postoperative complications; hence, a prompt diagnosis and intimate management is needed to predict and reduce these risks [7].

The number of patients included in this study is 381, which is comparable to a similar study from the USA [6], but far smaller than other series from India [8] and China [11]. The pattern of distribution of morphological types of clefts is consistent with many previous reports, where, combined cleft lip and palate (CLP) being the most frequent defect pattern followed by cleft lip (CL) [7, 12, 13]. However; it contradicts the findings of Sekhon et al and Sun et al who reported a predominance of isolated cleft lip (CL) over CLP [8, 11]. This could be explained by the fact that surgery for isolated cleft lip is accessible in paediatric, maxillofacial and general plastic surgery units. Moreover, this pattern of variation of clefts types' distribution between different reports may

reflect a biological phenomenon which is racially or ethnically determined [14].

The prevalence of CHD in this study is 11%, which is in the range of studies from USA (10%) [6], India (15%) [7] and Turkey (15.6%) [10]. However, it is lower than that reported in a different Indian series (21%) [12]. The pattern of cardiac anomalies observed in this series is fairly comparable to other studies which report VSD as the most prevalent defect [7, 15, 16]. However, studies by Çalış and Priyadharshini concluded that ASD in the most frequent anomaly [10, 12]. These variations could be due to the difference of the methods used for screening of cardiac anomalies, i.e., by echocardiography or clinical evaluation and disparity in identifying minor lesions [7, 10]. Similar to what has been reported in the literature, the acyanotic CHD were extremely more common than cyanotic ones [7, 10-12, 15] and significant association was observed between the presence of facial dimorphism and congenital heart malformations (P<0.001), a finding which is in line with a previous report from Saudi Arabia [17].

In the Sudan, CHD represents a fairly common congenital anomaly; however, the true prevalence has not been estimated on the basis of epidemiological studies as the reported studies were hospital-based or from small population surveys [18]. If the international prevalence of CHD is applied on Sudanese population, which is 0.8% (8-12 per 1000 live births) [19], the risk of CHD in cleft population would be about 13 times (11**%**/ 0.8%) that of the general population. This significantly higher risk for CHD mandates a proper clinical and echocardiographic evaluation as suggested by many authors [7, 12]. Similar findings were revealed by other researchers that cleft patients, particularly those with palate clefts, have significantly higher risk (15.1%) of having CHD than the general population [5].

Although clinical examination is an important diagnostic tool [6], nearly 8 - 65% of cases of CHD are missed relying on clinical examination alone compared to echocardiography [12]; hence, it is suggested as the gold standard diagnostic tool for CHD [11]. Integrating echocardiographic findings to clinical examination can increase its yield by more than 50% and subsequently improve its accuracy [12].

On assessing the relationship between morphological types of cleft defects and CHD, the results showed that cardiac defects were maximally observed among isolated CP patients (12 out of 57) (21%) followed by CLP cases (22 out of 168) (13%) which is similar to other reports [6, 7, 11] and suggests a potential link between palatal and cardiac development [17]; which can be explained on embryological basis, as neural crest cells are involved in both craniofacial and cardiac development[21].

Conclusion:

CHD is a common associated anomaly in Sudanese cleft population. The pattern of CHD in cleft population is consistent with the literature where VSD is the most frequent defect. The cardiac defects are most prevalent among CP group. Routine echocardiographic evaluation is justified to screen for CHD among cleft patients.

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