Spectrum of congenital heart diseases in children with Down Syndrome at Usmanu Danfodiyo University Teaching Hospital, Sokoto

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Abstract

Objective: Congenital heart diseases (CHD) frequently occur in children with Down syndrome. A few studies in Nigeria have highlighted the pattern of CHD in such patients, but results are variable with no data from the study area for comparison. This study aims to determine the pattern of CHD among children with Down syndrome as seen at UDUTH, Sokoto

Methods: A prospective study conducted between 1st October 2011 and 31st April 2015. Subjects included all children with phenotypic features of Down syndrome (DS) who were seen at the Pediatric cardiology clinic and had echocardiography diagnosis of congenital heart diseases.

Results: Of the 41 cases of DS seen during the study period, 32 (78.0%) children aged 2 weeks to 22 months (Mean +SD = 5.6 ± 4.0 months) were diagnosed with CHD. Male to female ratio was 2.2:1. Atrioventricular septal defect (AVSD) was the commonest CHD seen in 18 (56.3%) patients. Nine (28.1%) patients had isolated ventricular septal defect (VSD), three (9.4%) had VSD coexisting with atrial septal defect (ASD) while one (3.1%) patient each had isolated ASD and Fallot's tetralogy respectively. Only three (9.4%) patients had surgical closure abroad, with good postoperative outcome in two of the patients.

Conclusion: AVSD is the commonest CHD in our series, which is similar to previous reports. Increased access to definitive intervention is advocated since surgical outcome in such patients may be favorable.

Key words: Down syndrome, congenital heart diseases, pattern, Sokoto

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Spectre des maladies cardiaques congénitales chez les enfants atteints du syndrome de Down à l'hôpital universitaire de Usmanu Danfodiyo, Sokoto

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Résumé

Objectif: les maladies cardiaques congénitales (CHD) se produisent fréquemment chez les enfants atteints du syndrome de Down. Quelques études au Nigeria ont mis en évidence le modèle de la maladie coronarienne chez ces patients, mais les résultats sont variables sans données de la zone d'étude pour la comparaison. Cette étude vise à déterminer le motif de la maladie coronarienne chez les enfants atteints du syndrome de Down comme on le voit à UDUTH, Sokoto

Méthodes: Une étude prospective menée entre le 1er Octobre 2011 et 31stApril 2015. Les sujets inclus tous les enfants avec des caractéristiques phénotypiques du syndrome de Down (DS) qui ont été vus à la clinique de cardiologie pédiatrique et ont eu un diagnostic de l'échocardiographie de maladies cardiaques congénitales.

Résultats: Sur les 41 cas de DS vu au cours de la période d'étude, 32 (78,0%) des enfants âgés de 2 semaines à 22 mois (moyenne + SD = 5,6 ± 4,0 mois) ont été diagnostiqués avec la maladie coronarienne. Homme ratio était de 2,2: 1. Atrioventricular défaut septal (CAV) a été le CHD fréquente vu dans 18 (56,3%) patients. Neuf (28,1%) patients avaient isolé défaut septal ventriculaire (CIV), trois (9,4%) avait VSD coexistant avec défaut auriculaire septal (ASD) ASD tandis que l'un (3,1%) des patients chacun avait isolé et la tétralogie de Fallot, respectivement. Seulement trois (9,4%) patients ont eu la fermeture chirurgicale à l'étranger, avec un bon résultat postopératoire chez deux des patients.

Conclusion: CAV est la plus fréquente CHD dans notre série, qui est similaire aux précédents rapports. Un accès accru à l'intervention définitive est préconisée depuis résultat chirurgical chez ces patients peut être favorable.

Mots clés: syndrome de Down, les maladies cardiaques congénitales, Motif, Sokoto

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INTRODUCTION

Down syndrome is the commonest chromosomal abnormality in humans, with an incidence of 1 in 1,000 to 1 in 1,100 live births worldwide . First recognized by John Langdon Down in 1866, this genetic disorder is primarily caused by chromosomal non-disjunction, resulting in trisomy 21 . It is usually diagnosed on the basis of typical phenotypic features and this is confirmed by Karyotyping. Some of the phenotypic features of this syndrome include hypertelorism, depressed nasal bridge, medial epicanthic folds, low set ears, upward slanting palpebral fissures, single transverse palmar crease, clinodactyly and hypotonia. In addition, multiple organ systems such as the cardiovascular, gastrointestinal, hematologic, endocrine and central nervous systems may be involved to a variable degree . Cardiovascular manifestations in form of congenital heart disease (CHD) occurs in up to 40-60% of the patients and is responsible for most of the morbidity and mortality in children with Down syndrome . Hence, early recognition of these lesions and timely intervention will improve the life expectancy and quality of life in affected children and reduce the emotional stress faced by their parents/caregivers.

Previous studies have described the pattern of congenital heart defects in children with Down syndrome (DS), but results are variable. While atrioventricular canal defect (AVCD) was found to be the most common lesion by some studies , others have reported ventricular septal defect (VSD) and patent ductus arteriosus (PDA) as most prevalent among their study patients. Similarly, conflicting results have been reported regarding the outcome of surgery for congenital heart diseases in children with DS, with some of the recent studies showing no evidence of increased mortality in such patients . In resource-limited countries where access to cardiac surgery is difficult and frequently delayed, the outcome may be less favorable compared to that in the general population. This is because patients with DS are more prone to early development of pulmonary hypertension, which may adversely affect surgical outcome.

There is presently no data from the study area on the pattern and outcome of congenital heart disease among children with Down syndrome. Hence, this study was conducted to determine the pattern and outcome of CHDs among children with phenotypic features of Down syndrome attending the Paediatric Cardiology clinic of Usmanu Danfodiyo University Teaching Hospital, Sokoto. Such information is needed for comparison with other studies and to guide management of patients who present to the study area.

MATERIALS AND METHODS

Study area: This study was conducted at the Paediatric Department of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, Northwestern Nigeria. The Hospital is multidisciplinary and caters for a large number of patients within the sub-region and from neighbouring countries such as Niger and Benin Republics.

Study design: This was a prospective study conducted between 1st October 2011 and 31st April 2015.

Study subjects: Subjects included all children with phenotypic features of Down syndrome (DS), who were seen at the Paediatric Cardiology clinic and had echocardiographic diagnosis of congenital heart disease. Excluded from the study were: patients older than 15years (Paediatric age limit at UDUTH), children who already had definitive surgery at first presentation and those who died before diagnosis of cardiac lesion could be confirmed by echocardiography. Patients who satisfied the eligibility criteria were recruited consecutively after getting informed written consent from the caregivers and/or assent for children aged more than seven years. The study was approved by the Hospital Ethics Committee

Procedure: At presentation, demographic information such as age, gender, mobile phone numbers were obtained. Each patient had detailed general examination including inspection for presence of dysmorphic features of Down syndrome, measurement of anthropometric indices and pulse oxygen saturation, as well as cardiovascular evaluation. Thereafter, the patients had Chest-X ray and then 12-lead Electrocardiography (ECG). The latter was performed by an ECG technician using Dr-Lee ECG machine (Model 310A, Italy), which was fitted with paediatric ECG probes. For children that were not cooperative, light sedation was achieved by oral administration of chloral hydrate at a dose of 50mg/kg. Results of the ECG tracings were read by the principal author.

Echocardiography: Transthoracic

Echocardiography (TTE) was performed using Sonoscape SSI 5000 echo-machine, mounted with a 2.5MHz linear array transducer. Cardiac imaging was through apical, parasternal long axis (PLAX), parasternal short axis (PSAX), subcostal and suprasternal notch views. The location and size of anatomic defects were determined using 2-dimensional-echocardiography (2D); whereas flow direction and pressure gradients were assessed with colour Doppler and continuous wave Doppler respectively. M-mode was used for measurement of ventricular function. Echocardiographic evaluation was performed by the principal investigator, who had previously underwent one year post fellowship training in Pediatric Cardiology at India and has had more than 5 years working experience in Pediatric Cardiology Unit of UDUTH, Sokoto.

Treatment and follow up: All parents/guardians of children with confirmed CHD were counseled accordingly. The need for surgery, where necessary, was discussed with the parents or guardians. When indicated, medical treatment with anti-heart failure medications (Frusemide, spironolactone and captopril), antibiotics for concomitant respiratory infections and nutritional rehabilitation were commenced. Patients were followed up after hospital discharge at the paediatric cardiology clinic. Those with other identified co-morbidities such as neurologic abnormalities were also referred to appropriate specialty clinics for evaluation and follow up.

Data analysis: The demographic, clinical and echocardiography data of all the patients with confirmed congenital heart diseases were entered and analyzed using SPSS statistical software version 20 (*Armonk, NY: IBM Corp*). Quantitative data were expressed as means and standard deviation while categorical variables were expressed as proportions. The proportions of male and female subjects across various age groups were compared using Chi-square test while Fishers exact test was used to compare children with AVSD and those with other lesions. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of patients

A total of 41 children with phenotypic features of Down syndrome were seen at the paediatric cardiology clinic during the study period. Thirty-two (78.0%) of these had echocardiographic diagnosis of Congenital heart disease (CHD). There were 22 males and 10 females (M: F ratio= 2.2:1). The mean +SD age was 5.6 ± 4.0 months (range 2weeks to 22 months), while mean maternal age was 31.4 + 6.8 years (range 18-42 years). Table 1 shows the age and gender distribution of children with DS and congenital heart disease. Majority of them (62.5%) were under the age of six month.

The patients presented with various symptoms including difficulty in breathing, cough, failure to thrive and bluish discoloration of the lips and tongue. However, 3(9.4%) patients were asymptomatic (table 2).

Pattern of CHD

Acyanotic congenital heart diseases (ACHDs) accounted for 96.9% of all congenital heart diseases while cyanotic CHD constituted only 3.1% of the cases. The spectrum of the various lesions among the study cohort is shown in table 3. Atrioventricular septal defect (AVSD) was the commonest congenital cardiac defect, with a prevalence of 56.3%. Ventricular septal defect (VSD) was the next most common CHD, occurring in isolation (28.1%) or in association with atrial septal defect (9.4%). Tetralogy of Fallot (TOF) was the only cyanotic CHD observed among the study subjects and occurred in one patient (3.1%) only. Of the 18 children with AVSD, 7 (38.9%) were females compared to only 3 (21.4%) females out of the 14 children diagnosed with other congenital heart lesions. However, the difference was not statistically significant (Fisher's Exact Test, p= 0.45). Figure 1 shows a 2-dimensional echocardiographic image of one of the study patients with complete AVSD.

Treatment and outcome:

Three of the 32 (9.4%) patients had surgical intervention at India (AVSD repair in 2 and VSD closure in one patient); while one patient (3.1%) had spontaneous closure of VSD. Nine patients (28.1%) were lost to follow up while the remaining 19 (59.4%) patients are still on follow up at both the Pediatric Cardiology and Pediatric Neurology clinics. The two patients that had surgery for atrioventriuclar septal defect (AVSD) were aged 14 and 22 months respectively while the third patient who had VSD repair was 9 months old. Though surgery was

successfully performed in all the patients, they all had prolonged post operative hospital stay. Unfortunately, the 22-month-old girl that had AVSD repair developed severe postoperative pulmonary artery hypertension (PAH) and subsequently died at India.

DISCUSSION

Congenital heart diseases are recognized as one of the most common systemic co-morbidities in children with Down syndrome . The present study has found a high prevalence of CHDs (79.3%) among children with Down syndrome. This finding is comparable to that of Asani *et al* in Kano, Northwestern Nigeria, which reported a prevalence of 77.1% among the 35 subjects evaluated. Ekure *et al* in Lagos has similarly reported a prevalence of 87% among a cohort of 54 subjects with Down syndrome whereas Otaigbe *et al* in Port Harcourt, reported the highest prevalence of 100% among 38 subjects studied. The very high prevalence obtained in the latter study is not clear, but high rates of exposure to environmental toxins due to petroleum exploration activities in the region has been suggested as one of the possible explanations .

It is of note that the aforementioned studies (5,7,10) were hospital based and might therefore over-estimate the prevalence of CHDs in children with Down syndrome. This is because symptomatic children with suggestive symptoms of CHDs are more likely to be referred to the hospital than those who are otherwise normal or asymptomatic. Consequently, hospital sample may not represent the actual community burden and pattern of CHDs in patients with DS. Population-based prevalence of CHDs in children with this chromosomal anomaly has been shown to be generally lower (ranging between 40-60%) than hospital-derived estimate . A community study in Brazil, for example, reported a prevalence of 46.8% among children diagnosed with DS. Hence, as suggested by Freeman *et al*, true estimation of the prevalence and types of heart defects in Down syndrome should be done using a population-based sample. This is however difficult in developing countries, where health and birth records are not optimal.

The pattern of CHD in the study cohort showed preponderance of acyanotic lesions, as only one patient had cyanotic CHD in form of tetralogy of Fallot. Like many other studies, atrioventricular septal defect (AVSD) was the commonest type of CHD in the present study. This is in contrast to some studies that found other lesions to be the most common . Ekure in Nigeria , and both Abbag and Al-Jarallah in Saudi Arabia have reported ventricular septal defect (VSD) as the most common heart defect in children with Down syndrome; whereas some studies in Brazil and in Turkey have both demonstrated atrial septal defect (ASD) as the commonest lesion among their study cohorts. Curiously, patent ductus arteriosus (PDA) was the most frequent in a study by Otaigbe *et al* in Port Harcourt, South-South Nigeria. The results from these studies highlight the wide variability in the pattern and prevalence of cardiac lesions among children with DS. Whether this variability could be related to geographic, genetic or other epidemiologic factors need to be further explored.

More than 60% of the patients were diagnosed below the age of six months, which is consistent with reports from other studies . This may imply that such patients do come to light relatively early due to obvious dysmorphic features or early onset of clinical symptoms as a result of their congenital heart defects or other associated comorbidities. It has been advocated that all newborn infants with features of Down syndrome should have early cardiac evaluation to exclude congenital heart defects . This is because of the risk for early onset pulmonary vascular disease in such patients, which may contraindicate surgery and adversely affect their prognosis .

Due to the small number of patients, it is difficult to reliably compare the gender variations in the relative prevalence of specific cardiac lesions among the study subjects. The higher number of males with CHD as well as AVSD in this study may be due to the preponderance of male subjects with DS compared to females. Asani *et al* in their study of children with DS, have shown a higher prevalence of CHD in males with DS than female subjects whereas; Otaigbe *et al* in Port-Harcourt reported equal incidence in both genders. But these studies were also limited by small sample size.

Access to definitive intervention was very low among the study patients, as only three of them were able to afford the cost of surgery at India. The challenges of cardiac surgery in Nigeria and indeed many parts of Africa have previously been highlighted . These include endemic poverty, high cost of surgery, poorly equipped health facilities and lack of personnel with capacity to offer routine cardiac intervention

locally . In the past, the benefit of cardiac surgery in children with Down syndrome was doubted and some caregivers may be unwilling to spend their resources on a condition in which the other associated neurologic and physical features may not be amenable to treatment . It has now been shown that such intervention is associated with actuarial survival benefit and improved quality of life . In the present study, all the three patients that had surgery had prolonged postoperative hospital stay, but death occurred in one of the patients who was aged 22 months at the time of surgery. The other two patients have remained stable on follow up. Hence, unless where contraindicated, Down children with CHD should have timely correction of their cardiac lesions to enhance prognosis. Concerted effort to urgently make cardiothoracic surgical services locally available and accessible is necessary.

CONCLUSION

This study has shown a high prevalence of CHD in children with Down syndrome, with AVSD being the most common type of heart lesion. Majority of the affected patients have limited access to definitive treatment, emphasizing the need to establish functional cardiac centers in the country. There is need for multicenter population-based studies in the country to ascertain the actual community prevalence and types of CHDs in children with Down syndrome.

Study limitations: Being a hospital-based study with small sample size, the result may not be truly representative of the population in the study area. Karyotyping was performed in only two patients, as facilities for such investigation were presently not available locally. The number of patients that had surgery is too small to allow for meaningful statistical analysis of surgical outcome.

Conflict of interest: None

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Table 1: Age and gender distribution of children with Down syndrome and CHD

Age (Months)	Male n (%)	Female n (%)	Total n (%)
0-6	14 (70.0)	6 (30.0)	20 (62.5)
6.1-12	6 (66.7)	3 (33.3)	9 (28.1)
>12	2 (66.7)	1 (33.3)	3 (9.4)
Total	**22 (68.8)**	**10 (31.2)**	**32 (100.0)**

$x^{2=}$ 0.39 df=2, p= 0.98

Table 2: Presenting symptoms in children with Down syndrome and CHD

*Presenting symptoms	n (%)
Cardiac murmur	31 (96.9)
Cough	26 (81.3)
Poor weight gain	19 (59.4)
Delayed motor milestones	14 (43.8)
Asymptomatic	3 (9.4)
Cyanosis	2 (6.3)

* Some patients have more than one symptom

Table 3: Spectrum of congenital heart diseases seen in children with Down syndrome

Type of CHD	Male n (%)	Female n (%)	Total n (%)
Atrioventricular Septal Defect (AVSD)	11 (61.1)	7(38.9)	18(56.3)
Isolated Ventricular Septal Defect	7 (77.8)	2(22.2)	9(28.1)
VSD + ASD	2(66.7)	1(33.3)	3(9.4)
Isolated Ostium Primum ASD	1(100.0)	0(0.0)	1(3.1)
Tetralogy of Fallot	1(100.0)	0(0.0)	1(3.1)
Total	**22(68.8)**	**10(31.2)**	**32(100.0)**

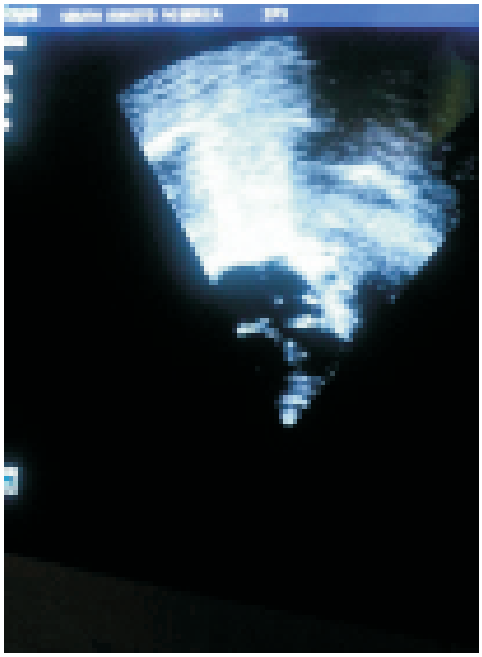

Figure 1: A 2 dimensional echo of a 10-month old girl with Down syndrome showing complete atrioventricular septal defect (see arrow showing the central defect).