

Profile of clinical features, congenital heart disease and other comorbidities in children with Down syndrome in a tertiary care centre in Nigeria

*Wilson E Sadoh¹, Fidelis E Eki-udoko¹, Isoken A Isah¹

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Abstract

Background: Down syndrome (DS) is a common chromosomal disorder associated with congenital heart disease (CHD) which could lead to severe morbidity or mortality.

Objective: To determine the frequency and spectrum of clinical features, CHD and other comorbidities in children with DS in a tertiary care centre in Nigeria.

Method: Consecutive children with clinical features of DS were recruited. The frequency of clinical features and co-morbidities were noted. All the children had echocardiographic evaluation to identify those with CHD.

Results: A total of 64 children was recruited of which 36 (56%) were male. Fifty one (80%) had CHD of which atrio-ventricular septal defect (AVSD) was the commonest, being found in 20 (39%) children. Common clinical features present were oblique eyes in 64 (100%), depressed nasal bridge in 60 (94%) low set ears in 53 (83%) and epicanthal folds in 50 (78%).

Conclusions: Prevalence of CHD amongst DS children in this study was 80% with AVSD being the commonest. The most prevalent clinical features seen in these children were oblique eyes, epicanthal fold, depressed nasal bridge, low set ears, hypertelorism and hypotonia.

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Introduction

Down syndrome (DS) is the commonest chromosomal disorder¹. In a large Nigerian

¹University of Benin Teaching Hospital, Nigeria

*Correspondence: ehidiamen.sadoh@uniben.edu
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hospital, the incidence was reported to be 1 in 87 live births². The incidence is associated with advanced maternal age³. DS is a significant cause of mental retardation in children and is associated with other morbidities such as leukaemia, Hirschsprung disease and cardiovascular anomalies^{1,4,5}. The most severe comorbidities are the cardiovascular anomalies and when untreated, they are often the cause of death in affected children⁶.

A variety of congenital heart disease (CHD) has been described in patients with DS. Atrioventricular canal defect (AVSD) has been reported to be the commonest CHD seen in children with DS^{1,7} while others have reported a preponderance of ventricular septal defect⁸. Otaigbe et al⁹ in Port Harcourt, Nigeria evaluated 31 children with DS, all of whom had CHD which included a fairly wide spectrum of both acyanotic and cyanotic CHD. The most common CHD was patent ductus arteriosus (PDA), contrary to the report of the study done by Onalo and co-worker¹⁰ in Abuja Nigeria where AVSD was the predominant CHD found amongst 20 children with DS studied. However, the sample sizes of the earlier Nigerian studies were rather small^{7,9,10}.

There are typical dysmorphic features seen in DS patients that aid its clinical diagnosis¹. The prevalence of these features varies from setting to setting as reported by various workers^{1,11,12}. The differences may be due to the genetic variability. DS has high genotype variability and three types have been described viz. non-disjunction, unbalanced translocation and mosaicism¹.

Objectives

The present study was conducted to determine the frequency and spectrum of clinical features, CHD and other comorbidities in children with DS seen at the University of Benin Teaching Hospital, Benin City, Nigeria, a tertiary care centre.

Method

All children clinically diagnosed to have DS who presented in the children's emergency room, paediatric wards and consultant out-patient clinics were referred to the echocardiographic laboratory of the University of Benin Teaching Hospital (UBTH), Benin City, Nigeria. It is the hospital policy to refer all suspected cases of DS for

cardiologic evaluation. The study was carried out between July 2012 and December 2013. Ethical approval for the study was obtained from the research and ethics committee of the UBTH.

Using a pre-tested proforma, socio-demographic parameters of the children and parents and the clinical features of the children were obtained including age, gender, socioeconomic class (SEC), maternal and paternal ages. Each child then had a thorough clinical examination. Using a checklist, the clinical features associated with DS were noted. Other clinical signs of cardiovascular origin such as cyanosis, respiratory distress, chest wall abnormalities and cardiomegaly (displaced apex beat) were looked out for and documented. The presence of the co-morbidities of pneumonia, congestive cardiac failure (CCF) and pneumonia complicated with CCF, for which the patients were referred for cardiologic evaluation, were also noted. The diagnosis of pneumonia was based on clinical findings and typical pulmonary infiltrates seen on chest radiograph. The diagnosis of heart failure was based on the clinical diagnostic tool by Omokhodion¹³. The SEC was determined using the methods described by Olusanya et al¹⁴. The patients' weights were measured using a bassinet weighing scale for infants and an appropriate weighing scale for older children, using standard

methods. The Z scores of the weight for age were computed using the WHO growth charts for children¹⁵.

All the children with a clinical diagnosis of DS underwent transthoracic echocardiographic evaluation using 2D, M mode and Doppler interrogation using an Aloka Prosound SSD-4000SV (Aloka, Meerbusch, Germany) machine. The analysis of the reports was done according to the recommendations of the American Society of echocardiography¹⁶. The presence and types of CHD on echocardiography were documented.

Statistical analysis

The data was entered into SPSS version 16 (Chicago IL) spread sheet and analysis done with the same tool. Simple proportions were expressed in percentages. Differences in proportions were tested with X² test. Level of significance was set at *p* <0.05 level.

Results

Of the 64 children with DS, 36 (56.2%) were male. The median age was 6 months with a range of 2 days to 15 years. The socio-demographic characteristics and parental age groups of the study population are shown in table I.

Table 1: Socio-demographic characteristics and parental age groups of the study population

Characteristic	Males	Females	Total (%)	P value
<i>Age group</i>				
<6 months	16	09	25 (39.1)	0.60
≥ 6 month - <12months	08	08	16 (25.0)	
≥ 12 months	12	11	23 (35.9)	
<i>Nutritional status</i>				
Underweight	20	20	40 (62.5)	0.81
Normal weight	12	09	21 (32.8)	
Overweight	01	02	03 (04.7)	
<i>Socioeconomic class</i>				
High	12	11	23 (35.9)	0.44
Middle	16	12	28 (43.8)	
Middle	09	04	13 (20.3)	
<i>Maternal age</i>				
<35 years	17	10	48 (42.2)	0.45
≥ 35 years	19	18	16 (57.8)	
<i>Paternal age</i>				
<50 years	30	24	54 (84.4)	1.00
≥ 50 years	06	04	10 (15.6)	

The frequency distribution of DS dysmorphic features in the study population is shown in table 2. Brushfield spots were not seen in a single case in this study. Of the 64 children with clinical features of DS, 51 (79.7%) children had CHD. Of the 51 cases 49 (96.1%) were acyanotic CHD while two (3.9%) were cyanotic CHD. Forty one (80.4%) had isolated cardiac defects while 10 (19.6%) had

multiple cardiac defects. Three patients had surgery, two with complete atrio-ventricular septal defect (AVSD) and one with ventricular septal defect (VSD).

The distribution of the types of cardiac anomalies by gender is shown in table 3.

Table 2: The frequency of Down syndrome clinical features seen in the study population

Clinical feature	Males	Females	Total (%)
Oblique eyes	36	28	64 (100)
Depressed nasal bridge	36	24	60 (93.8)
Low set ears	29	24	53 (82.8)
Epicanthal folds	22	28	50 (78.1)
Hypertelorism	28	19	47 (73.4)
Hypotonia	23	23	46 (71.9)
Microglossia	14	18	32 (50.0)
Short hands	12	14	26 (40.6)
Brachycephaly	12	14	26 (40.6)
Short neck	12	14	26 (40.6)
Umbilical hernia	11	12	23 (35.9)
Oval palate	10	10	20 (31.3)
Single Simian crease	06	09	15 (23.4)
Hyperextension of limbs	07	07	14 (21.9)
Strabismus	01	04	05 (07.8)
Ulnar loops	01	04	05 (07.8)
Clinodactyly	01	0	01 (01.6)

Table 3: Distribution of the types of CHD according to gender

Cardiac anomaly	Males	Females	Total (%)
Isolated AVSD	11	09	20 (39.2)
Isolated ASD	08	03	11 (21.6)
Isolated VSD	06	03	09 (17.6)
VSD + ASD	01	02	03 (05.8)
ASD + PDA	01	02	03 (05.8)
AVSD + PDA	0	01	01 (02.0)
VSD + PDA	0	01	01 (02.0)
VSD + ASD + PDA	01	0	01 (02.0)
Single ventricle	0	01	01 (02.0)
PTA	01	0	01 (02.0)
Total	29	22	51 (100.0)

AVSD = Atrio-ventricular septal defect, ASD = Atrial septal defect, VSD = Ventricular septal defect, PDA = Patent ductus arteriosus, PTA = Persistent truncus arteriosus,

The frequency distribution of some clinical findings and co-morbidities in the 64 children with clinical features of DS is shown in table 4.

Of the 14 children with co-morbidities, 06 (42.9%) had bronchopneumonia, 05 (35.7%) had

bronchopneumonia and congestive cardiac failure (CCF) and 03 (21.4%) had isolated CCF. All 09 (14.1%) cases with cyanosis had cardiac anomalies. The anomalies included 06 (66.7%) children with AVSD and one each (11.1%) with persistent truncus arteriosus (PTA), VSD and single ventricle.

Table 4: Frequency distribution of clinical features and co-morbidities

Features/ Co-morbidities	Frequency	% of total
Murmur	34	53.1
Respiratory distress	28	43.8
Co-morbidities	14	21.9
Displaced apex beat	13	20.3
Bulging chest	10	15.6
Cyanosis	09	14.1

A total of seven (10.9%) deaths were recorded. Two of the deaths occurred at home after discharge from the hospital and five occurred in the hospital during the study period. The deaths were related to severe respiratory problems and the underlying

congenital heart defects. Sixteen (25%) of the 64 children with DS were lost to follow up while 38 (59.4%) are being followed up in the clinic.

Discussion

The prevalence of cardiac anomalies of 79.7% in this study is similar to the 77.1% recorded by Asani *et al*⁷ in Kano, Nigeria but lower than the 100% recorded by Otaigbe *et al*⁹ in Port Harcourt, Nigeria. The higher value recorded in the Port Harcourt study has been attributed to the fact that referral for echocardiography was based on the suspicion of possible cardiac defect while in the present study, all the children seen with DS were referred for echocardiographic evaluation irrespective of whether cardiac anomaly was suspected or not. The prevalence in our study is however higher than the 40 to 60% reported incidence studies globally¹⁷⁻¹⁹.

The majority of the children with DS in this study were underweight. This may be due to the fact that the prevalence of CHD was high in this study and the majority of the CHD were shunt lesions that could lead to recurrent pneumonia and heart failure. These co-morbidities would contribute to the underweight seen in these children. The finding of high prevalence of underweight children with DS is in tandem with the Brazilian study that showed that 78.2% of study subjects were underweight¹¹.

The commonest CHD in this study was AVSD which is consistent with the Kano⁷ and Abuja¹⁰ studies in Nigeria and other previous works outside the country^{6,20}. This is however at variance with the Port Harcourt⁹ study which recorded patent ductus arteriosus (PDA) as the commonest and a study in Riyadh, Saudi Arabia⁸ which recorded VSD as the commonest. It is not clear why there is a varied pattern in the distribution of CHD in different localities; it is possible that the genetic heterogeneity of the condition may be contributive.

The spectrum of CHD included complex congenital heart disease such as single ventricle and PTA. The presence of complex congenital heart defect was similarly reported in the Port Harcourt⁹ study where they found double outlet right ventricle. This finding of complex congenital heart diseases has been reported in other previous studies outside the country^{8,21}. Most (80.4%) of the CHD recorded in this study were isolated lesions which is consistent with the Kano study and other studies outside the country^{7,8,22}. In the Port Harcourt study⁹, however, the majority (71%) of the patients with DS had multiple cardiac defects. It is not clear what is responsible for this finding. It is possible that it could be environmental; the higher prevalence of CHD in the oil rich Niger-Delta region of Nigeria has been alluded to in an earlier study²³.

Two thirds of the patients with DS in this study were born to mothers younger than 35 years. This is consistent with previous studies that have shown

a higher prevalence of DS born to younger mothers^{4,9}. The occurrence of a growing number of children with DS born to younger mothers presents a strong reason for advocating DS screening for pregnant mothers as is done in some other countries^{24,25}. Two factors may militate against a successful screening programme in the country. It is expensive and may be beyond the reach of majority of Nigerians; however the cumulative cost of caring for a DS child certainly outweighs the cost of screening²⁶. The other factor is managing the outcome of a positive screening result. Nigerian couples may be unlikely to accept termination of pregnancies because of their religious beliefs.

This study demonstrated that the clinical features present in patients with DS in the study locality in at least 70% of cases are oblique eyes, depressed nasal bridge, low set ears, epicanthal folds, hypertelorism and hypotonia. There is variation in the frequency of clinical features from locality to locality. For instance, single simian crease was present in 23.4% of the patients in this study; this is lower than the 39% recorded in the Port Harcourt study⁹ and the 83.9% in the Brazilian study¹¹. There were no Brushfield spots identified in this study, which is similar to a Korean study²⁷, but at variance with a Jordanian study²⁸ where 9% of children with DS had Brushfield spots. The difference in findings may be due to the known low frequency of Brushfield spots in DS individuals with dark coloured irides²⁹.

Although in older infants and children, the features of DS are easily identifiable and thus a clinical diagnosis is made with a high level of certainty, in some others especially newborns, clinical diagnosis is less clear. The limitation of this study is the absence of cytogenetic studies to confirm DS in the suspected children. This was because the facility was not available.

Conclusions

- Prevalence of CHD amongst clinically diagnosed DS children in this study was 80% with AVSD being the commonest.
- The most prevalent clinical features seen in children with DS in this study were oblique eyes, epicanthal folds, depressed nasal bridge, low set ears, hypertelorism and hypotonia.

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