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Nutritional Status and Pulmonary Hypertension in Children with Down Syndrome Presenting with Congenital Heart Disease: Retrospective Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author JMC conceived and designed this study while authors BFC, OCD and ATC helped in critical revision of the article. Author BFC also did the Data analysis/interpretation. All authors have read and approved the manuscript.

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ABSTRACT

Introduction: Children with Down syndrome are predisposed to having congenital heart defect.
Objectives: This study is aimed to describe the clinical correlates, nutritional status and pulmonary hypertension in children with Down syndrome who presented with congenital heart disease.
Patients and Methods: A retrospective study of children with Down syndrome who presented with congenital heart disease from 2016 to 2020 was carried out. Nutritional status was assessed with WHO Anthro software while pulmonary hypertension was assessed with standard procedures.
Results: Out of 758 echocardiography done over the period of 5 years for children suspected of having cardiac disease, three hundred and eight one had confirmed congenital heart disease of which twenty-eight of them had Down syndrome 7.34% (28/381). Ten 10/28 (35.7%) of them had pulmonary hypertension. This is commonly noted among infants than older ages.

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Among 28 children with Down syndrome, twenty-three had complete information for weight and height which was used to assess their nutritional status, 47.8% (11/28) presented with wasting and stunted, 8.7% (2/28) of those with Down syndrome were wasted and 8.7% (2/28) with stunting. Down syndrome is commoner in children with AV canal defect 50% (14/28) followed by PDA 21.4% (6/14). Fast breathing 86.7% (13/15) as the most common symptom followed by cough 64.3% (9/14)

Conclusion: Children with Down syndrome who had congenital heart disease are at increased risk of malnutrition and pulmonary hypertension.

Keywords: Down syndrome; nutritional status; pulmonary hypertension; congenital heart disease.

1. INTRODUCTION

Down syndrome (DS) is the commonest chromosomal abnormality seen in children [1]. Down syndrome presents with a clear physical and clinical abnormalities, nevertheless, the use of cytogenetic analysis is used to delineate few cases that are due to mosaicism and translocation [2,3]. Despite, mental retardation and hypotonia commonly seen in children with Down syndrome, they are associated with other malformations [3,4]. It has been documented that about 56.9% of children who had congenital heart defects presents with Down syndrome [2]. The prevalence of Down syndrome was seen to be 4.4 per 10,000 total births and accounts for 1.5% of all congenital abnormalities [5]. Pulmonary hypertension and malnutrition are two major issues seen in children with congenital heart disease but this is accentuated among children with Down syndrome. For example, in a study, it is noted that 80% of children with Down syndrome who had congenital heart disease presents with pulmonary hypertension. They have 2.4 times chance of developing pulmonary hypertension compared with children with congenial disease who had no Down syndrome [6]. Different degrees of malnutrition is also seen in children with Down syndrome [7].

There is paucity of information on children with Down syndrome who had congenital heart disease, moreover few studies are seen in this vicinity regarding impact of nutrition and pulmonary hypertension in children with Down syndrome. This study is therefore conducted to ascertain the clinical correlates, nutritional status and pulmonary hypertension in children with Down syndrome.

2. METHODS

2.1 Study Design

This was a retrospective study conducted in four hospital Institutions namely university of Nigeria, Niger Delta University, Blessed children hospital and Triple care hospital over a 5-year period from 2016-2020.These major tertiary health care centres are referral centre for children with congenital heart disease all over the country. Children with Down syndrome who are aged 2 months to 17 years were recruited consecutively from children with confirmed congenital heart disease by means of echocardiography. Echocardiography was done by the consultant paediatric cardiologist using *GE Vivid Q* echocardiography machine and E2 Sonoscape medical Corp 2018.

Demographic variables such as age, gender, place of domicile were taken. Echocardiographic measurements of cardiac structures and functions especially right ventricular function.

2.2 Participants

These were children aged 2 months to 15 years, who attended the paediatric cardiology clinic in the hospital of study.

2.3 Inclusion Criteria for Subjects

Children with Down syndrome who had echocardiographic confirmation of congenital heart disease and who gave permission were recruited in the study

2.4 Exclusion Criteria for Subjects

Children with Down syndrome with no evidence of congenital heart disease were excluded.

2.5 Study Tool

Echocardiography was performed with the aid of Hewlett-Packard (HP) model SONO 2000 Ultrasound Imaging System. The probe has a transducer with multi-frequency in the range 5.5-12MHz for children

2.6 Assessment of Nutritional Status

Height was measure in centimetres and weight in Kilograms using stadiometer. WHO Anthro software was used to calculate *Z* scores for weight for age (WAZ), weight for height (WHZ), and height for age (HAZ)

2.7 Estimation of Pulmonary Hypertension

Systolic gradient across tricuspid regurgitation velocity was used to calculate pulmonary pressures by adding values of right atrial pressure. Values above 25 mm Hg was taken as pulmonary hypertension. The use of early diastolic pulmonary regurgitation velocity of >2.2m/s, reversal of right ventricle/left ventricle ratio of more than a unit and a domed shape contour in-mid systole with notch formation at late systole was applied in the assessment of pulmonary hypertension [8,9]. Bernoulli equation was then used to calculate pulmonary pressure (PASP=4 V^2+right atrial pressure) [10,11].

2.8 Data Analysis

Analysis was done with IBM SPSS statistics for windows, version 20 (IBM Corp, Chicago). Proportions and percentages were used to analysed categorical variables and presented in form of tables. Discrete variables including age, weight and height were presented as means and standard deviations. The z-scores of weight for height, weight-for-age, weight for height, height/length-for-age and body mass index (BMI) were calculated with WHO anthro and anthro plus software. WHO classification was used to assess the nutritional status of children with Down syndrome. P value was set at $p < 0.05$.

3. RESULTS

3.1 Demographic Characteristics

381 children were diagnosed of congenital heart disease over the period of study. 312 of them were assessed for features of Down syndrome and 28 out of the 312 had features of Down syndrome, leaving the prevalence of Down syndrome among children with congenital heart disease as 9.0%. Table 1 shows the demographic characteristics of children with Down syndrome, 60.7% of them being males and majority were infants. The patients' mean age, weight and height/length were respectively, 21.3 ± 38.2 months, 9.7 ± 11.5 kg and 78.1 ± 30.2 cm.

Table 1. Demographic characteristics of patients with Down syndrome

Sex	**N**	**%**
Male	17	60.7
Female	11	39.3
Total	28	100.0
Age group		
<12months	18	64.3
>12 Months	10	35.7
Total	28	100

3.2 Clinical Correlates

Various frequency of clinical symptoms suggests fast breathing 86.7% (13/15) as the most common symptom followed by cough 64.3% (9/14) and this is as in Table 2.

Among the 28 children with Down syndrome, 50% (14/28) had AV canal defect while 21.4% (6/28) had patent ductus arteriosus (PDA). Other cardiac lesions observed in these children are as in Table 3.

Table 2. Frequency of different symptoms among patients with Down syndrome

Symptoms	**N**	**N**	**%**
Cough	14	9	64.3
Fast breathing	15	13	86.7
Cyanosis	17	8	40.1
Excessive sweating	12	3	25
Easy fatigability	13	7	53.8
Chest pain	14	0	0.0

N (number of patients accessed for the symptom);
n (number of patients with the symptom),
% (100 X N/n)

Table 3. Frequency of different congenital heart disease among patients with down syndrome

Congenital heart dx	N	%
AV canal defect	14	50.0
PDA	6	21.4
VSD	4	14.3
ASD	3	10.7
TOF	1	3.6
Total	28	100

PDA; patent ductus arteriosus. VSD; ventricular septal defect, ASD; atrial septal defect, TOF; tetrology of Fallot

3.3 Down Syndrome and Pulmonary Hypertension

Out of twenty-eight children with Down syndrome, 10/28 (35.7%) of them had pulmonary hypertension. Pulmonary hypertension was commoner in infants, 70.0% (7/10) than older children. It was also commoner in males, 60% (6/10) than female, 40%.

3.4 Down Syndrome and Nutritional Status

Among 28 children with Down syndrome, twenty-three had complete information for weight and height which was used to assess their nutritional status, which is as presented in Table 4.

Table 4. Nutritional status of children with Down syndrome presenting with congenital cardiac defect

Nutritional status	Frequency	%
Wasted	2	8.7
Stunted	2	8.7
Wasted and stunted	11	47.8
Well nourished	7	30.4
Overweight	0	0.0
Obese	1	4.3
Total	28	100.0

Nutritional status was based on the Z-score of weight and height/length

4. DISCUSSION

This study showed that the prevalence of Down's syndrome in children with congenital heart disease is 9.0% and is commoner among children with AV canal defect [12]. Abdul et al. noted a prevalence rate of 38% and commonly seen in children with ventricular septal defect (23%). Somasundaram et al. [13] also noted VSD as the commonest heart defect in children with Down syndrome. While Murato [14] documented ASD as a commonly seen defect in Down syndrome. The prevalence obtained in this study is different from that of other authors probably because of sample size and geographical location. Nevertheless, the high prevalence of Down syndrome in children with AV canal is in tandem with that obtained in several studies [15,16].

The prevalence of pulmonary hypertension among children with Down syndrome seen in this study was 35.7%. Children with Down syndrome normally present with adeno-tonsillar hypertrophy, upper airway obstruction such as tracheal stenosis, oropharyngeal and subglottic compromise coupled with the presence of left to right shunt lesions and hypotonia of the musculatures. These features could explain the high prevalence of pulmonary hypertension among them. There was also a high prevalence of pulmonary hypertension in infants than older children with Down syndrome as seen in this study. Younger children with Down syndrome have been noted to have about 1.2–5.2 times risk of having pulmonary hypertension than their older counterparts [17,18]. This propensity to developing pulmonary hypertension at early age could be due to endothelial damage and poor lung functional capacity [19,20].

Pulmonary hypertension is commoner in male children with Down syndrome compared to their female counterpart as documented in this study. There has been a "sex paradox" in pulmonary arterial pressure, in that, elevated pulmonary arterial pressure is commoner in females because of increased turnover of BMPR2 mutants, yet males present with increased severity and pathological sequel of pulmonary hypertension [21,22].

Again the possibility that females are naturally endowed with double X chromosomes- a chromosome that elaborates bradykinin and endothelial relaxation factor than Y chromosome could also explain this gender difference. It is important to take cognizance of the fact that endothelium-derived relaxing factor (EDRF) - an endogenous vasodilator is elaborated more in X chromosome [23]. Endothelium-derived relaxing factor causes relaxation of the vascular smooth muscle by activating guanylate cyclase. This subsequently increases cyclic guanylate monophosphate which causes vasodilatation [24].

The commonest type of malnutrition noted in children with Down syndrome, in this study, is wasting and stunting seen in 47.8% of them. AbdAllah et al. [25] in their study noted short stature as the commonest variant of malnutrition and attributed this to deficiency of micronutrient. We could not decipher the cause of stunting in our study since micronutrient deficiency was not explored. However pulmonary hypertension, hypoxia and poor intake could all explain this high prevalence of malnutrition seen in this study.

The commonest symptoms seen among children with Down syndrome are fast breathing and cyanosis. Cyanosis is as a result of admixture of saturated and de-saturated blood at the level of the large in-let VSD [26]. Vasomotor instabilities, which is very common in children with Down could also explain this [26]. Fast breathing is usually as a result of patients with clinically significant atrioventricular valve regurgitation may also have symptoms of CHF, such as tachypnea, excessive sweating, and failure to appropriately gain weight [26].

Its association with congenital heart disease is well known. Studies have shown that 40%-60% of children with Down syndrome present congenital heart disease. However, among children with congenital heart diseases, 4%-10% are associated with Down syndrome [27].

5. CONCLUSION

Children with Down syndrome who had congenital heart disease are at increased risk of malnutrition and pulmonary hypertension.

6. RECOMMENDATIONS

A high index of suspicion is necessary to avert the numerous complications and morbidity that may arise from pulmonary hypertension and malnutrition among children with Down syndrome presenting with congenital heart disease.

7. STRENGTH OF THE STUDY

This is the first time this work is done in our locale. Again no work describes both nutritional status and malnutrition in children with Down in a stratum.

8. LIMITATIONS

This work is limited by the fact that nutritional status and pulmonary hypertension in children with congenital heart disease with Down syndrome was not compared with their counterparts who had congenital heart disease but had Down syndrome.

CONSENT AND ETHICAL APPROVAL

This complies with national guidelines. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standard. Ethical approval was obtained from the Ethics and Research committee of the University of Nigeria Teaching hospital Enugu (IRB number of 00002323) and date of issue was 14/04/2020.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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