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Original Research Article

Frequency and Pattern of Congenital Heart Diseases in Patients of Down Syndrome

Article History:

Name of Author:
Waqas Alam[1], Kiramat Ullah[2], Ulfat Raza[3], Muhammad Shahan Jan[4], Mahnoor Shah[5], Furqan Taj[6]

Affiliation: *[1,3,4,5] Training Medical Officer, Department of Pediatrics, Mardan Medical Complex, Mardan, Pakistan*
[2]Assistant Professor, Department of Pediatrics, Mardan Medical Complex, Mardan, Pakistan
[6]Training Medical Officer, Department of Pediatrics, Hayatabad Medical Complex, Peshawar, Pakistan.

Corresponding Author:
Waqas Alam
Email: *waqasalam196@gmail.com*

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Abstract: ***Objective:*** To determine the frequency and patterns of congenital heart diseases in patients with Down syndrome. ***Study design:*** Cross sectional study. ***Study duration and setting:*** June 2025 to September 2025. Department of Pediatrics, Mardan Medical Complex, Mardan ***Methodology:*** This study was conducted on 60 patients enrolled using non-probability consecutive sampling, aged two months to fifteen years with Down syndrome. Patients with a history of major congenital anomalies other than Down syndrome, prior antibiotic use, severe pulmonary hypertension, chest radiation or cardiac surgery within past six months were excluded. Echocardiography was performed for the diagnosis of congenital heart diseases. Patterns such as atrioventricular septal defect, secundum atrial septal defect, ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, pulmonary atresia and transposition of great arteries were assessed. Data were analyzed with SPSS 27. Chi-square and Fisher exact tests were used for stratification, keeping p value significant at ≤ 0.05. ***Results:*** The median age of the patients was 21 months (IQR: 7-55). Congenital heart disease was observed in 21 (35.0%) cases. In cases of congenital heart disease, Ventricular septal defect was present in 7 (33.3%) cases, patent ductus arteriosus and atrioventricular septal defect each in 5 (23.8%) cases respectively. Atrial septal defect was observed in 4 (19.0%) cases, Tetralogy of Fallot in 2 (9.5%) cases, while pulmonary atresia and transposition of great arteries were observed in 1 (4.8%) cases respectively. ***Conclusion:*** Congenital heart disease was observed in 35.0% (n = 21) patients with Down syndrome. Ventricular septal defect was the most common pattern of congenital heart disease, followed by patent ductus arteriosus and atrioventricular septal defect.

Keywords: Down syndrome, congenital heart disease, ventricular septal defect, echocardiography, patent ductus arteriosus, atrioventricular septal defect

INTRODUCTION

Down syndrome is a common chromosomal abnormalities and is linked to spectrum of congenital anomalies particularly congenital heart diseases.1 Most frequently recorded cardiac lesions involve the atrioventricular septal defects, atrial septal defects and patent ductus arteriosus.2 Embryological foundation of congenital heart disease within the Down syndrome is related to abnormal endocardial cushion development because of the gene dosage effects of chromosome 21. Such genetic imbalance interferes with the normal cardiac morphogenesis leading to complex structural abnormalities.3 Altered signalling pathways concerning the cardiac transcription factors leads to defective septation. Presence of such anomalies considerably influences clinical course of the affected individuals contributing to early-onset heart failure and increased vulnerability to respiratory infections.4

Timely diagnosis of congenital heart disease among the children with Down syndrome is critical as timely management can enhance the survival. Advances within the prenatal screening and neonatal cardiac assessment have enhance the early diagnosis. In low income countries late diagnosis is a critical challenge due to restricted access to specialised care.5,6 Delay generally leads to development of irreversible pulmonary vascular disease in uncorrected septal defects. It has been reported that early corrective surgery considerably minimize the mortality and

enhances the developmental outcomes.7

In underdeveloped countries, burden is considered to be higher due to the delayed diagnosis and restricted genetic counselling services.8 Current improvements within the paediatric cardiology have improved the understanding of genotype-phenotype association in the Down syndrome. There remains a need for the further research to better define the local disease patterns and related risk factors within the diverse populations.9,10 Such data is vital for developing the screening strategies alongside improving the early referral systems. Comorbid conditions including the hypothyroidism and respiratory infections further complicate the management of Down syndrome cases of congenital heart disease. Such associated conditions generally worsen the cardiac symptoms thereby worsening the prognosis.11

Given the significant clinical impact of congenital heart diseases in Down syndrome. There is a dire need for regional specific data in developing countries. Understanding the burden and spectrum of CHDs in such vulnerable population will help in planning the early diagnostic protocols and optimising management strategies. This study is therefore conducted to determine the frequency and pattern of congenital heart diseases among patients with Down syndrome to assist the clinicians in early identification and appropriate management which ultimately improves the outcomes in such high risk population.

METHODOLOGY

This study was conducted in the Department of Pediatrics, Mardan Medical Complex, Mardan, after taking ethical approval from the institute (No. 630/BKMC). A sample of 60 patients was selected for this study using WHO sample size calculator, using the following assumptions, frequency of patent ductus arteriosus 8.5%,12 margin of error 7% and confidence interval 95%. Patients were selected using non-probability consecutive sampling.

Patients aged 2 months to 15 years, presenting with Down syndrome were included in this study. Down syndrome was defined as a child presenting with flat facial profile and hypotonia (muscles are on the loose, floppy side) and trisomy confirmed by karyotyping. Patients with a history of major congenital anomalies other than Down syndrome, antibiotic treatment for any reason, severe pulmonary hypertension, radiation therapy to the chest area and cardiac surgery within the past 6 months.

Informed consent was taken from parents/guardians of patients after explaining the purpose/benefits of the study. Basic demographics such as age, maternal age and residence were recorded at inclusion in the study. The presence of CHD was confirmed using echocardiography by a trained pediatric cardiologist. The echocardiography examination was carried out using M-mode, color two-dimensional (2D) pulse, and continuous-wave Doppler echocardiogram. Two-dimensional echocardiographic pictures were recorded in the standard parasternal long-axis, short-axis, apical four-chamber, subcostal, and suprasternal views. In patients with congenital heart diseases, they following patterns were assessed; Atrioventricular septal defect (AVSD), it was defined as any one of the following: Cardiothoracic ratio >0.60, widened superior mediastinum, and diameter of the right descending pulmonary artery >16 mm on chest X-ray. Visualization of a single atrioventricular valve orifice rather than separate mitral and tricuspid valves with multiple leaflets, and ventricular end-diastolic volume >40–70 mL/m² on echocardiography. Secundum atrial septal defect (ASD), it was defined as a variably sized area of septal "dropout," or absence of tissue, in the mid/central interatrial septum about the fossa ovalis delimited by inferior and superior rims of septum, and interatrial flow when assessed with color flow Doppler on echocardiography. Ventricular septal defect (VSD), it was defined as in a parasternal long-axis view, a muscular septal defect, either trabecular or outlet, or a membranous/perimembranous septal defect can be visualized on echocardiography. Patent ductus arteriosus (PDA), it was defined as a high-velocity jet directed from the far field toward the main pulmonary artery, continuous flow throughout systole and diastole, and larger lesions on echocardiography. Tetralogy of Fallot (TOF), it was defined as anterior malalignment of the conal septum resulting in a large subaortic ventricular septal defect, overriding aorta, right ventricular outflow tract obstruction or pulmonary stenosis, and right ventricular hypertrophy on echocardiography. Pulmonary atresia, it was defined as complete absence of pulmonary valve tissue with no detectable forward flow from the right ventricle to the pulmonary artery on color and pulsed wave Doppler echocardiography, with pulmonary blood supply typically dependent on a patent ductus arteriosus or major aortopulmonary collateral arteries. Transposition of great arteries (TGA), it was defined as the aorta arising from the morphologic right ventricle and the pulmonary artery arising from the morphologic left ventricle on two-dimensional echocardiography, typically with parallel orientation of the great arteries rather than the normal spiral arrangement.

Data was analyzed using SPSS 27. For numerical variables such as age, and maternal age, median with interquartile ranges were used, after assessing for normality using Shapiro Wilk test. Categorical variables were presented using frequency and percentages, which were congenital heart disease, pattern of congenital heart disease, gender, and residence. Fisher exact test and Chi Square test was used for stratification. p value was considered significant if ≤ 0.05. Confidence Intervals were also calculated for the overall frequency of congenital heart diseases.

RESULTS

Sixty children with Down syndrome were enrolled in the study. The median age of the children was 21 months with an interquartile range 7 to 55 months. The median maternal age was 34 years with an interquartile range 28 to 38.75 years. According to gender distribution there were 34 (56.7%) male patients and 26 (43.3%) female patients.

Congenital heart disease was identified in 21 (35.0%; 95% CI: 0.231-0.484) children (Table I). Regarding the pattern of CHD individual acyanotic lesions, ventricular septal defect was observed in 7 patients (33.3%). Patent ductus arteriosus was present in 5 cases (23.8%), while atrioventricular septal defect was similarly found in 5 cases (23.8%). Atrial septal defect secundum was observed in 4 children (19.0%). Among the cyanotic lesions, tetralogy of Fallot was observed in 2 patients (9.5%), while pulmonary atresia and transposition of the great arteries were each observed in one patient (4.8%) respectively (Table II).

Table III presents the distribution of mixed lesions. Age and gender distribution did not show significant association with congenital heart disease, although CHD was more frequent in female patients (Table IV).

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Table I: Frequency of congenital heart disease (CHD)

Congenital Heart Disease	n	%	95% CI	
Yes	21	35.0%	0.231	0.484
No	39	65.0%		

Table II: Pattern of congenital heart disease

		n	%
Ventricular Septal Defect (Acyanotic)	Yes	7	33.3%
	No	14	66.7%
Patent Ductus Arteriosus (Acyanotic)	Yes	5	23.8%
	No	16	76.2%
Atrioventricular Septal Defect (Acyanotic)	Yes	5	23.8%
	No	16	76.2%
Atrial Septal Defect Secundum (Acyanotic)	Yes	4	19.0%
	No	17	81.0%
Tetralogy of Fallot (Cyanotic)	Yes	2	9.5%
	No	19	90.5%
Pulmonary Atresia (Cyanotic)	Yes	1	4.8%
	No	20	95.2%
Transposition of Great Arteries (Cyanotic)	Yes	1	4.8%
	No	20	95.2%

Table III: Distribution of mixed lesions

	n	%
VSD + AVSD	1	25.0%
PDA + AVSD	1	25.0%
VSD + PDA	1	25.0%
VSD + ASD	1	25.0%

Table IV: Stratification of congenital heart disease with age and gender of patients

		CHD				p value
		Yes		No		
		n	%	n	%	
Age distribution (Months)	2 to 12	10	35.7%	18	64.3%	1.000[b]
	13 to 60	8	33.3%	16	66.7%	
	61 to 180	3	37.5%	5	62.5%	
Gender	Male	9	26.5%	25	73.5%	0.113[a]
	Female	12	46.2%	14	53.8%	

[a]Chi square test; [b]Fisher exact test

DISCUSSION

The present study found that 35.0% (n = 21) children with Down syndrome had congenital heart disease. This figure aligns with Korejo et al. they reported 33.9% frequency of CHD in children with down syndrome.13 This frequency is lower than the 50% prevalence of CHD reported by Khokhar et al respectively.14 It is also lower than the 66.1% pooled prevalence reported by Sharaf et al.15

The pattern of lesions in the present study showed that acyanotic defects were most common presentation. This aligns with Burki et al. who reported that 85% of congenital heart defects in their Down syndrome patients were acyanotic.16 Endocardial cushion defects and incomplete septation account for majority of anomalies in Down syndrome.17

Ventricular septal defect was the most common lesion present in 33.3% of cases with congenital heart disease. VSD occurs when the interventricular septum does not close normally during embryonic development. Small VSDs often close by its own, the closure rates reach up to approximately 75% by 120 months of age.18

Patent ductus arteriosus and atrioventricular septal defect were each observed in 23.8% of CHD cases. Atrial septal defect was present in 19.0% CHD cases. Regarding cyanotic lesions, tetralogy of Fallot was observed in 9.5% cases, while pulmonary atresia and transposition of the great arteries were observed in 4.8% cases. Korejo et al. reported atrial septal defect in 21.4% cases, and tetralogy of Fallot in 10.7% cases.14 Areeba et al. reported Patent ductus arteriosus in 31.9% cases, and atrioventricular septal defect in 12.8% cases.19 Iqbal et al. in their study found that ventricular septal defect was the second most common lesion in their CHD cases, present in 19.7% of patients.20

Hairder et al. in their study explained that the increased gene dosage from the extra chromosome 21 triggers extra transcription pathways and additional production of protein. This results in faulty septo-morphogenesis of the heart. They reported that reduced TWIST1 expression impairs standard epithelial-mesenchymal transition (EMT) and valve development, driving the overexpression of RYR2 and NCX to establish a cardiomyocyte-specific profile in Trisomy 21 cells.

The present study found a trend towards female gender in congenital heart disease. CHD was present in 46.2% females compared to 26.5% in males, though this did not reach statistical significance. Haider et al. reported that females have 1.72 times higher odds of developing cardiac defect compared to males. Geleta et al. similarly reported that female gender had higher odds of developing multiple cardiac anomalies.

The study have several limitations. The small sample size of the study limited the power of subgroup analyses. The single centre design limits generalisability to other centers. The study did not perform long term follow up. The study also failed to assess thyroid function, another common comorbidity in Down syndrome that can influence cardiovascular function.

CONCLUSION

In conclusion, the current study found that the frequency of congenital heart diseases in patients with Down syndrome was 35% (n = 21). Acyanotic lesions accounted for the majority of the lesions, with ventricular septal defect being the most common, followed by patent ductus arteriosus and atrioventricular septal defect. Congenital heart diseases were more common in female gender. Routine echocardiographic screening should be performed for children with Down syndrome at diagnosis. Early detection and timely referral to paediatric cardiology services are recommended.

Declarations

Conflict of interest was not declared by the authors
Consent was taken from all patients
No funding was received
Ethical approval taken (No. 630/BKMC)

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