Original Article

Spectrum of Congenital Heart Diseases in Down Syndrome Patients

Junaid Iqbal, Annam Sammie, Shabeer Hussain Shah, Najm ul Huda Siddiqui, Fazal Mabood and Saad Muhammad

ABSTRACT

Objective: This work sought to identify the range of cardiac pathologies found in Down's syndrome patients and establish the correlation existing between different pathologies and maternal age: a known risk factor for DS.
Study Design: A purely descriptive cross sectional design
Place and Duration of Study: This study was conducted at the Department of Pediatrics, Ayub Teaching Hospital Abbottabad from December 1, 2023 up to June 30, 2024.
Methods: Down's syndrome patient was determined by clinical presentation with reference to Hall's criteria. The patients that met the inclusion criteria were selected for the study. The diagnostic test i-e echocardiography was performed in all the patients. All the collected data was entered and analyzed on Statistical Package for the Social Science (SPSS) version 23.
Results: In this study the mean age of the patients was 31.97 ± 43.16 months, and sex distribution was having a male predilection of 0.9: 1. The mean value of maternal age of the patients was 34.28-year ± 5.18 years. In our study sample, the density of congenital heart disease variants was 54 of 70.12. Of all the congenital heart problem AVSD was the most prevalent in the study.
Conclusion: Cardiac anomalies are especially present in Down syndrome, the prevalence of CHD ranges from 60-70% in this population with 70.12% in this study. The neonates might have different types of heart defect but with the most frequent being the AVSD. In addition, the occurrence of VSD is proportional to the rise in maternal age when the rest of the defe that were considered do not show any correlation with it.

Key Words: Atrioventricular septal defects Congenital heart defects, Down syndrome.

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INTRODUCTION

Down syndrome is characterized by an additional copy of human chromosome 21, and is the most frequent genetic disease leading to intellectual disability, described in 1866 by J.L.H. Down. Its incidence is 1 in 700 births but varies with maternal age, increasing from 1:At 1600 it had been under 1: 25 of the year to 1: 350 at age 35 and 1:40 at age 43[1,2]. The greater proportion at conception is by those that end in miscarriages. T21n is caused by non-disjunction in 95% of the total cases while mosaicism and translocation contribute the remaining 5%. The extra copy of q21, q22 leads to common morphological characteristics that are common with other syndromes such as mental retardation, brachycephaly and other morphological features[3-5].

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It is associated with low IQ, Down's syndrome (DS), congenital heart defects, seizures, and other sight problems, among others, and a higher risk in children developing leukemia. It is diagnosed according to dysmorphic features at birth. A total of 50% of infants with Down's syndrome risk having CHD and the most frequent ones are atrioventricular septal defects (AVSD), ventricular septal defects (VSD), and atrial septal defects (ASD)[6, 7]. In addition to this most patients portray symptoms such as patent ductus arteriosus (PDA), left to right shunt (L to R shunt), coarctation of aorta (CoA), tetralogy of Fallot (TOF), double outlet right ventricle (DORV and mitral valve prolapse (MVP). Koh et al in Saudi Arabia observed a frequency of 40.6% among children with Down's syndrome[8,9]. This study aimed to determine the spectrum of cardiac abnormalities that manifest in Down's syndrome patients and assess the relationship of various pathologies with the maternal age: a known risk factor for DS. This will contribute to the global body of knowledge on the disease and the malformation and assist health care practitioners to develop strategies for minimizing the impact of the disease on patients and on rate of mortality and morbidity.

METHODS

Subsequent to the clearance by the institutional review board, a descriptive cross-sectional study was

conducted at the Department of Pediatrics. This study was conducted from December 1, 2023 to June 30, 2024. The sample size was calculated using the WHO software for health research studies at 95% confidence level and a prevalence of congenital heart disease of 40.6% as found in Down's syndrome and an absolute accuracy of 11 % .9 consecutive non probability simple random sampling was employed aimed at children of both sexes, age 0-15years with features of typical Down's syndrome. Down's syndrome was identified based on the presence of characteristic clinical features as defined by Hall's criteria, which include: Using the terms: mongoloid facies, brachycephaly, named micrognathia, macroglossia, low set ears, Sloping palpebral fissures with epicantic folds, short and broad hands, short neck with transverse single crease in palm, delayed developmental milestones and hypotonia. The exclusion criteria included extremely low birth weight infants, and circumstances in which there was a documented positive history of TORCH infections in the mother or teratogenic drug exposure during pregnancy. Patients who satisfied these inclusion criteria above where then enrolled in the study and their parents provided written consent. These patients therefore went through some tests that included echocardiograms with doppler analysis. The patient's name, age, gender, address/ hospital number/ ward, and whether they have congenital heart disease, and if yes, the type was also documented on a proforma.

Data Analysis Procedure: The data was analyzed with SPSS version 23. Quantitative variables such as age and maternal age were presented as mean ± standard deviation. Categorical variables like gender and cardiac defect type were described using frequencies and percentages. All results were displayed in tables and diagrams. Data was stratified by age, gender, and maternal age with respect to the outcome variable, presence of cardiac defect. A post-stratification chi-square test was performed at a 5% level of significance.

RESULTS

In this present total 77 patients were enrolled. The mean age of the patients was 35.75±18.75 months. In our study 37(48.1%) patients were male while 40(51.9%) patients were females. Male to female ratio of the patients was 0.9:1. According to this study the mean value of maternal age of the patients was 34.28±5.18 years (table 1). The frequency of congenital heart disease (CHD) variants in our study sample was 54 (70.12%). Among the various types of congenital heart problem AVSD was the most common. The study results showed the frequency of AVSD was noted in 33 (42.9) patients. The results narrated in figure 1 show frequencies (percentages) of all other congenital heart conditions as well. Since the increasing maternal age is a known risk factor of DS; the association of each of the CHD type with maternal age was studied and are summarized in table 2. Among the studied CHD types only VSD should positive association with increasing maternal age with a p-value of 0.04.

Table No. 1: Descriptive statistics of the study group (n=77)

Variable	Mean±SD	Frequency (percentage)
Age months	35.75±18.75	
Maternal Age (yrs.)	34.28±5.18	
Gender (male:female)		37(48.1%):40(51.9%)

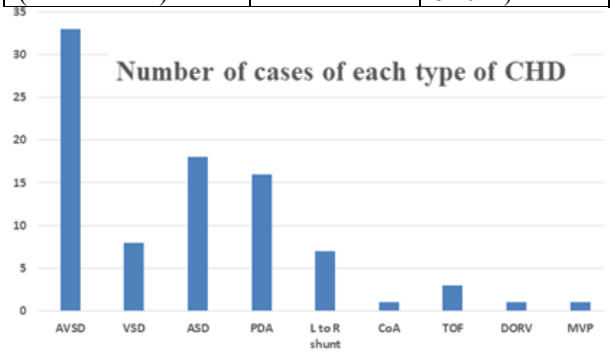

Figure No. 1: Frequency of the whole spectrum CHD in the study population.

(atrioventricular septal defects (AVSD), ventricular septal defects (VSD), and atrial septal defects (ASD), patent ductus arteriosus (PDA), left to right shunt (L to R shunt), coarctation of aorta (CoA), tetralogy of Fallot (TOF), double outlet right ventricle (DORV) and mitral valve prolapse (MVP))

Table No. 2: Association of various CHDs with maternal age

Variable	Maternal age (Mean±SD)	t-value	p-value
AVSD (present:absent)	34.09±4.96: 34.43:5.39	-0.28	0.77
VSD (present:absent)	37.75±4.26: 33.88±5.15	2.03	0.045
ASD (present:absent)	33.88±5.48: 34.4±5.12	-0.36	0.71
PDA (present:absent)	32.81±3.08: 34.67±5.56	-1.28	0.2
Left to Right shunt (present:absent)	32.28±6.49: 34.48±5.04	-1.07	0.28
Coarctation of aorta (present:absent)	41.0±0: 34.19±5.15	1.31	0.19
AVSD with TOF (present:absent)	36.66±1.52: 34.18±5.25	0.81	0.42
DORV (present:absent)	35.0±0: 34.27±5.21	0.13	0.89
MVP (present:absent)	27.0±0: 34.38±5.14	-1.42	0.15

(atrioventricular septal defects (AVSD), ventricular septal defects (VSD), and atrial septal defects (ASD), patent ductus arteriosus (PDA), left to right shunt (L to R shunt), coarctation of aorta (CoA), tetralogy of Fallot (TOF), double outlet right ventricle (DORV) and mitral valve prolapse (MVP))

DISCUSSION

The high incidence of congenital heart disease (CHD) in Down syndrome (DS) is well known, and numerous authors have reported figures on the frequency of congenital heart defects among DS cases. These figures vary from 35% to 65%. Atrioventricular septal defects (AVSD) and ventricular septal defects (VSD) are often associated with chromosomal aberrations such as trisomy 21, whereas hypertrophic cardiomyopathy is primarily linked to specific gene mutations. In Down syndrome, VSD and AVSD are typical malformations[9]. In this study, the percentage of AVSD in children with Down syndrome was 42.9% (33 out of 77 patients). Several local and international studies are discussed below to highlight their findings. Ali et al. reported AVSD in 48% of Sudanese children with Down syndrome[10], while Freeman et al. noted a similar prevalence of 45% in American children[11]. In Faisalabad, Pakistan, Ahmad et al. evaluated DS-associated CHD in children, reporting VSD (60.4%), AVSD (29.1%), atrial septal defect (ASD, 4.1%), patent ductus arteriosus (PDA, 4.1%), and tetralogy of Fallot (TOF, 2%) as the most prevalent defects. Among these children, 73.2% (n=93) presented during their first year of life, with a mean age of 7±4 months[12]. Another study conducted by Khan and Muhammad in Pakistan reported AVSD in 19.4% of Down syndrome children[13].The prevalence of CHDs in DS varies significantly among studies. A recent multicentric study from Saudi Arabia documented AVSD in 40.6% of children with DS[9]. In an Indian study, AVSD was the most common defect in DS patients (37.1% of 35 cases), whereas VSD was more prevalent in non-syndromic patients (68.4% of 38 cases)[14]. In Brazil, second-type ASD was most frequent (51.8%), followed by AVSD (46.6%), VSD (27.7%), TOF (6.3%), and other anomalies (12.5%)[15].In Sudan, AVSD was most common (48%), followed by ASD (23%) and TOF (6%) at presentation. Additionally, 10% of patients had Eisenmenger syndrome[9]. Hyder et al. reported isolated lesions, with VSD being the most common (60.3%), followed by PDA (13.7%) and complete AVSD (8.6%)[16].Benhaourech et al. evaluated CHD in DS, reporting 186 congenital heart defect lesions. The most common defects were AVSD (29%), VSD (21.5%), and ASD (19.9%). Associations like AVSD + ASD (10%) and VSD + ASD (7.8%) were also noted. Interestingly, when stratified against maternal age, VSD was more frequent in children born to older mothers, although the difference was statistically insignificant (p=0.04)[17,18].

Study Limitations: The single-center nature of the study limits the generalizability of its findings. However, the comprehensive analysis of various cardiac defects provides valuable insights into the spectrum of CHDs in this population. To enhance knowledge of the disease burden in Down syndrome, multicentric studies are recommended.

CONCLUSION

Congenital heart disease is very common among Down syndrome cases, affecting as any as 70.12% of the individuals. The heart defect presents in various forms with AVSD being the most common presentation. Furthermore, VSD is associated with increasing maternal age where the rest of the defects don't demonstrate any such association.

Abbreviations

- AVSD: Atrioventricular Septal Defect
- VSD: Ventricular Septal Defect
- ASD: Atrial Septal Defect
- PDA: Patent Ductus Arteriosus
- TOF: Tetralogy of Fallot
- DS: Down Syndrome
- CHD: Congenital Heart Disease

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Final Approval of version:	All the above authors
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