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The detailed profile of congenital heart diseases in 254 children with Down syndrome in Saudi Arabia

Naif Alkhushi[1,2,3*]

Abstract

Background Down syndrome is the most common chromosomal abnormality in humans. It is associated with several congenital anomalies, including a spectrum of congenital heart diseases. Understanding the true prevalence and distribution of congenital heart diseases is essential for health resource planning, outcomes, and family counseling.

This study aimed to assess the prevalence and distribution of congenital heart disease in children with Down syndrome. It is a retrospective cohort review that included all patients treated at King Abdulaziz University Hospital. Frequencies were estimated using the SPSS software and comparisons were made using Student's *t* test.

Results The ages of the 254 subjects ranged from less than 1 year to 53 years. Of these, 44.5% were female and 40.6% were Saudi nationals. Congenital heart disease was present in 66.5% with a significant difference between Saudi nationals 44.6%) and non-Saudi nationals 71.5% ($P=0.01$). The atrioventricular septal defect was the most common pathology, representing 33.1% of all congenital heart diseases followed by perimembranous ventricular septal defect 18.9%, and right ventricular pathology 10.2%.

Conclusion The prevalence of congenital heart diseases in Saudi children with Down Syndrome is similar to that reported worldwide. Septal defects and right-sided pathologies are the dominant forms of congenital heart diseases, with atrioventricular septal defect and perimembranous ventricular septal defect representing the most common pathologies.

Keywords Congenital heart diseases, Down syndrome, Atrioventricular septal defect

Background

Down syndrome (DS) is the most common chromosomal abnormality in children [1]. The estimated prevalence in the USA was 6.7/10,000 individuals in 2013, with an incidence of 1 in 779 live births [2]. Its prevalence has doubled over the past 60 years owing to the improved survival of infants and children with DS. It is influenced by maternal age, early detection, and early termination of pregnancy, with advances in antenatal diagnosis [2]. Down syndrome is caused by a genetic alteration that leads to an extra copy of one or more of the 310 genes present on Hsa21 via translocation, non-disjunction, or mosaicism of chromosome 21 [3]. The clinical profile

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of this syndrome includes specific facial dysmorphisms, hypotonia, and intellectual disabilities. Individuals with DS are at an additional risk of various pathological consequences in the cardiovascular, respiratory, gastrointestinal, endocrine, and musculoskeletal systems, in addition to hearing and vision disturbances [4, 5].

Congenital heart diseases (CHD) are present in 40–54% of children with DS worldwide [6–9]. They are a major cause of morbidity and mortality in this population, with significant improvements in outcomes over the past few decades. In Saudi Arabia, the reported prevalence is higher reaching up to 81% [10–13]. The reported high prevalence is likely exaggerated by the inclusion of minor pathologies such as patent foramen ovale (PFO), small patent ductus arteriosus (PDA), small muscular ventricular septal defects (VSD), and non-congenital pathologies like mild tricuspid valve regurgitation. Most echocardiographic assessments of these newborns were performed before discharge from the nursery, which is likely to have exaggerated the diagnosis of PDA. In contrast, the Saudi population is known to have a high prevalence of consanguineous marriages, with an inherently increased risk of genetic disorders. Understanding the prevalence of CHD and its distribution in children with DS is important for health resource planning, understanding outcomes, and family counseling. This study examined the overall prevalence and specific distribution of CHDs. In addition, we examined the prevalence and distribution after excluding patients with minor, hemodynamically insignificant pathologies.

Methods

Ethical approval was obtained from King Abdulaziz Hospital Research Ethics Committee (Ref: 324–20). The Hospital Information System was searched for all codes linked to the diagnosis of Down syndrome or trisomy 21. Medical record data, age, sex, and nationality were collected. The echocardiographic reports were reviewed. Patients with a PFO only were considered normal. In newborns, follow-up echocardiography was used to establish a diagnosis. This procedure is typically done at 2–6 weeks of age. This was done to avoid an exaggerated diagnosis of a small PDA. Atrial septal defect (ASD), VSD, and PDA were further categorized as small, moderate, or large. When there was more than one pathology, the most hemodynamically significant was used to ascertain the distribution within the CHD cohort. Hemodynamic significance was defined as a pathology that will need medical treatment or intervention whether by cardiac catheterization or surgery to correct it shortly after the diagnosis. The prevalence of each pathology was estimated independently of other associated pathologies with adherence to the standard nomenclature and classification of congenital heart diseases.

Statistical analysis was performed using SPSS software. The student's t-test was used to compare the prevalence between Saudi and non-Saudi individuals.

Results

A total of 254 subjects were included, with ages ranging from less than 1 to 53 years. The mean age was 8.2 years. 53.1% were younger than 7 years and 11% were older than 18 years. Females represented 44.5%, and Saudi nationals represented 40.6%.

The prevalence of CHD in the entire cohort was 66.5%, with a significant difference between Saudi nationals 44.6%) and non-Saudi nationals 71.5% ($P=0.01$).

The prevalence of hemodynamically significant CHD after the exclusion of small ASDs, VSDs, and PDA was 52.4%. Combined pathologies of two or more CHDs were present in 18.9% of children with Down syndrome. These were predominantly ASD, VSD, and PDA.

The distribution of CHD is shown in Table 1 and Figs. 1 and 2.

The prevalence of each pathology in children with Down syndrome is shown in Table 2.

Discussion

This study demonstrated a high prevalence of CHD in children with DS in Saudi Arabia, despite strict definition criteria. Although our hospital is a tertiary care center, which could have affected the results, the great majority of children with DS are born in our hospital or referred for genetic assessment in a designated DS clinic. The study included many adults who either presented to the emergency department with various complaints or were followed up in adult medical or surgical clinics. All these heterogeneities would make this cohort more representative of the general population. This prevalence is comparable to the studies done in Madina (58.6%), Aseer (61.3%), and Riyadh (49%) regions [13–15]. This was significantly lower than that reported in a previous study from the same center by Al-Aama et al. at 86.6% [10]. It was likely due to the exclusion of PFO from the present study. The prevalence of CHD in Saudi nationals is significantly lower than that in non-Saudi nationals and is comparable to the internationally reported prevalence [7, 9, 16, 17]. This discrepancy could be explained by referral bias, as our hospital is the main referral center for complex cardiac surgery in non-Saudi expatriates.

Although the overall prevalence of CHD in DS is an important finding, a more relevant finding for understanding the impact of these pathologies is knowing their detailed distribution and the prevalence of individual pathologies. In this study, the atrioventricular

Table 1 The distribution of CHD in children with Down syndrome

Dominant congenital heart pathology	All pathologies Number 169 (%)	Hemodynamically significant pathologies Number 133 (%)
Secundum atrial septal defect	2 (1.2)	2 (1.5)
Partial atrioventricular septal defect	9 (5.3)	9 (6.8)
Complete atrioventricular septal defect	47 (27.8)	47 (35.3)
Perimembraneous VSD	48(28.4)	38 (28.6)
Inlet VSD	1 (0.6)	1 (0.8)
Muscular VSD	11 (6.5)	0
Tetralogy of Fallot	5 (3)	5 (3.8)
Tetralogy of Fallot/AVSD	5 (3)	5 (3.8)
Double outlet right ventricle	5 (3)	5 (3.8)
Patent ductus arteriosus	32 (18.9)	17 (12.8)
Coarctation of the aorta	2 (1.2)	2 (1.5)
Pulmonary stenosis	1 (0.6)	1 (0.8)
Pulmonary atresia with intact ventricular septum	1 (0.6)	1 (0.8)

VSD ventricular septal defect, *AVSD* atrioventricular septal defect

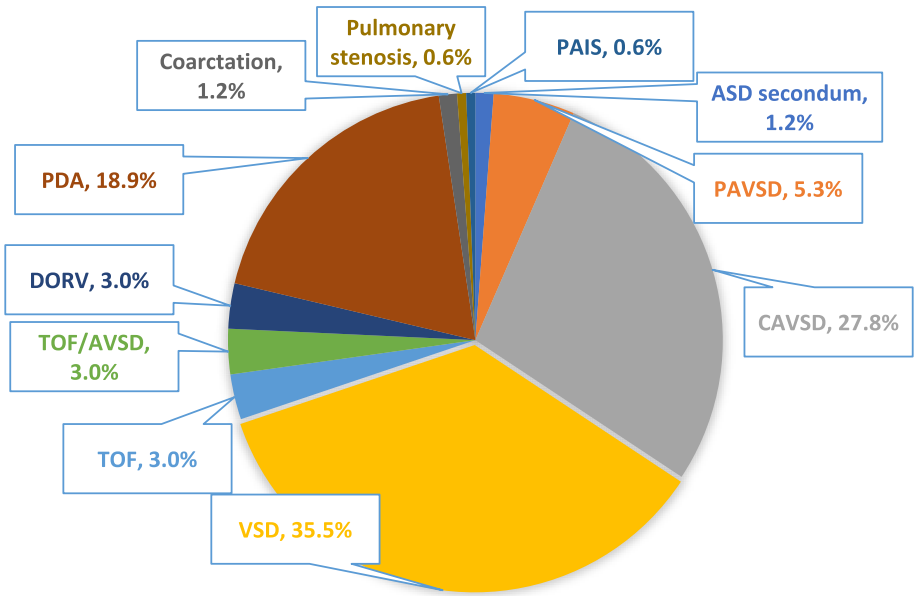

Fig. 1 The distribution of congenital heart diseases. ASD; atrial septal defect, AVSD; atrioventricular septal defect, CAVSD; complete atrioventricular septal defect, DORV; double outlet right ventricle, PAIS; pulmonary atresia with intact ventricular septum, PAVSD; partial atrioventricular septal defect, PDA; patent ductus arteriosus, TOF; tetralogy of Fallot, VSD; ventricular septal defect

septal defect was the most common pathology, representing 33.1% of all CHD followed by perimembranous VSD at 18.9% and right ventricular pathology at 10.2%, including TOF with and without atrioventricular septal defects, double outlet right ventricle, pulmonary stenosis, and pulmonary atresia. Unbalanced AVSD alone was seen in one patient only in this cohort. The prevalence of AVSD was 22% and that of hemodynamically significant VSD was 16.2%. The percentage of children with DS who have hemodynamically significant pathology that will likely require one or more surgical or catheterization interventions in the first few years of life is 52.4%.

Studies investigating the changes in CHD prevalence in children with DS have found dynamic changes in their prevalence over time [18]. This is due to improved maternal screening and neonatal care, as well as improved acceptance of DS individuals in society.

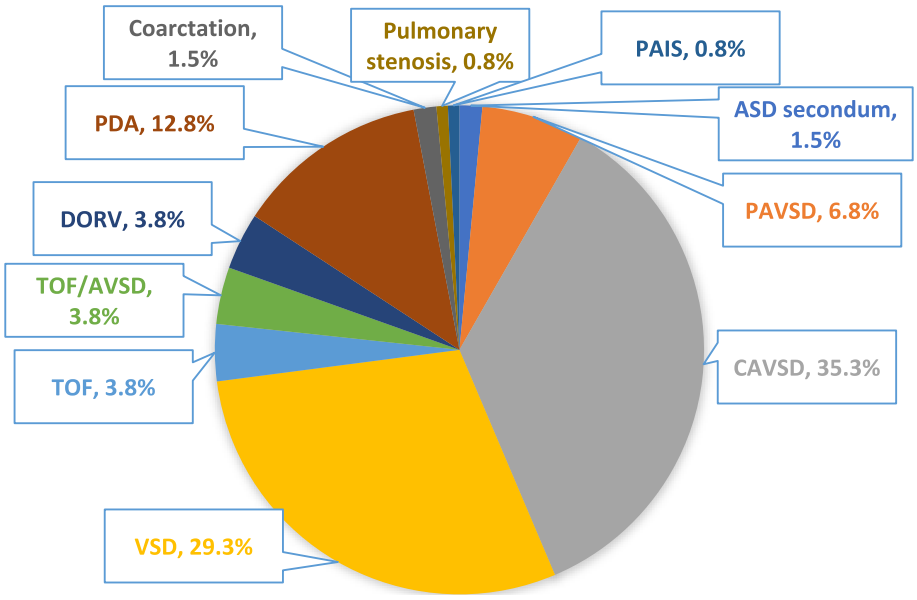

Fig. 2 The distribution of hemodynamically significant congenital heart diseases. ASD; atrial septal defect, AVSD; atrioventricular septal defect, CAVSD; complete atrioventricular septal defect, DORV; double outlet right ventricle, PAIS; pulmonary atresia with intact ventricular septum, PAVSD; partial atrioventricular septal defect, PDA; patent ductus arteriosus, TOF; tetralogy of Fallot, VSD; ventricular septal defect

Table 2 The prevalence of the individual CHD pathologies in children with Down syndrome

Congenital heart pathology	All pathologies Number (%)	Hemodynamically significant pathologies Number (%)
Secundum atrial septal defect	18 (7.1)	9 (3.5)
Partial atrioventricular septal defect	9 (3.5)	9 (3.5)
Complete atrioventricular septal defect	47 (18.5)	47 (18.5)
Perimembraneous VSD	48 (18.9)	38 (15)
Inlet VSD	1 (0.4)	1 (0.4)
Muscular VSD	14 (5.5)	2 (0.8)
Tetralogy of Fallot	5 (2)	5 (2)
Tetralogy of Fallot/AVSD	5 (2)	5 (2)
Double outlet right ventricle	5 (2)	5 (2)
Patent ductus arteriosus	56 (22)	22 (8.7)
Coarctation of the aorta	2 (0.8)	2 (0.8)
Pulmonary stenosis	1 (0.4)	1 (0.4)
Pulmonary atresia with intact ventricular septum	1 (0.4)	1 (0.4)

VSD ventricular septal defect, *AVSD* Atrioventricular septal defect

Studies on the genetics of CHD in DS in animal models and humans have suggested complex gene interactions and epigenetic factors are responsible for these variations [19–21].

The life expectancy of individuals with DS in the USA has significantly improved over the past few decades, from 26 in 1950 to 58 in 2010 [22]. Survival is negatively affected by the presence of CHD, low birth weight, and other significantly associated disorders [23]. The operative mortality of biventricular repair is similar to or lower than children without DS; however, it is significantly higher for univentricular heart repair, reaching 12 to 35% [24–29]. The length of hospital stay and quality of life of patients with DS are influenced by their associated anomalies and the nature of their acquired disorders. Children and adults with DS who survive surgery

for CHD require comprehensive health surveillance and support to achieve the best potential quality of life [30].

Conclusions

The prevalence of CHD in Saudi children with DS was similar to that reported worldwide. This was higher in the entire cohort, likely due to a referral bias. Septal defects and right-sided pathologies are the dominant forms of CHD, with atrioventricular septal defect and perimembranous VSD representing the most common pathologies. The proportion of patients with hemodynamically significant pathologies was significantly high. These pathologies require resources available only in tertiary care centers and would likely impact the survival and quality of life of individuals with DS. Health surveillance, family counseling, and resource allocation are needed to match the needs of patients with DS.

Limitations

The study is retrospective cohort and the prevalence of CHD in the non-Saudi population is likely exaggerated by referral bias.

Abbreviations

DS	Down syndrome
CHD	Congenital heart diseases
PFO	Patent foramen ovale
ASD	Atrial septal defect
PDA	Patent ductus arteriosus
VSD	Ventricular septal defect
AVSD	Atrioventricular septal defect
PAVSD	Partial atrioventricular septal defect
CAVSD	Complete atrioventricular septal defect
PAVSD	Pulmonary atresia with ventricular septal defect
PAIS	Pulmonary atresia with intact ventricular septum
TOF	Tetralogy of Fallot
DORV	Double outlet right ventricle

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Dr. Naif Alkhushi is the only author.

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Availability of data and materials

Available with the author.

Declarations

Ethics approval and consent to participate

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The consent for participation was waived as this is a retrospective chart review.

Consent for publication

Waived.

Competing interests

The author declares no competing interests.

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