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Original Article

Congenital heart disease in children with Down syndrome in Afghanistan

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Abstract

Background Congenital heart disease (CHD) is frequently cited as the main cause of death in the pediatric Down syndrome (DS) population. The prevalence and spectrum of CHD patterns in DS varies widely worldwide; this variation could be due to sociodemographic, genetic, and/or geographic factors.

Objective To verify the prevalence, pattern, and frequency distribution of CHD in children with Down syndrome.

Methods A three-year retrospective study was conducted in children aged 0-14 years with Down syndrome who underwent echocardiography for possible CHD from January 2014 to December 2016, based on the Pediatric Unit CHD Registry of the Cardiac Research Institute, Kabul Medical University. Clinical, echocardiographic, and outcome data were collected and sorted according to confirmation of the syndrome and echocardiography result.

Results During the three-year study period, 420 DS patients were identified, 286 (68%) of whom had CHDs. The prevalence of isolated and multiple CHD in the 420 children with DS were 38% (160 patients) and 30% (126 patients), respectively. Ventricular septal defect (23%) and atrial septal defect (16.4%) were the most common isolated defects. The combination of VSD and ASD (19.9%) were the most frequent multiple CHDs. The most common associations of CHD were VSD + ASD (19.9%) and VSD + PDA (9%).

Conclusion A high prevalence of CHDs was noted in children with Down syndrome. VSD and ASD are the most commonly diagnosed isolated CHDs in our study. ASD + VSD is the most common multiple CHD pairing. To our knowledge, this is the first extensive study in Afghanistan to demonstrate the pattern and prevalence of CHD associated with Down syndrome. **[Paediatr Indones. 2018;58:312-6; doi: http://dx.doi.org/10.14238/pi58.6.2018.312-6]**.

Keywords: *congenital heart disease; Down syndrome; echocardiography*

Down syndrome (DS) is the most common chromosomal anomaly among children, with a prevalence of 1/700 live births.[1] Congenital heart disease (CHD) undoubtedly affects the progress and survival of children with DS.[2] The worldwide CHD prevalence was estimated to be 6 to 13 per 1,000 live births.[3,4] This prevalence could be higher in Asian countries due to higher rates of consanguineous marriage, diabetes, and obesity.[5-7]

Congenital heart disease (CHD) is the leading cause of mortality and morbidity in the first two years of life in the DS population;1,4 40% to 63.5% of DS patients have CHD.4 The profiles and types of these CHDs may vary in different geographical areas around the world.[7,8] A 2013 study in Norway also suggested seasonal variation of the occurrence of DS and birth defects, providing indirect evidence of the causal role of environmental factors, since genetic factors do not exhibit seasonality.[9]

It is important to be familiar with the prevalence and anatomical characteristics of CHD in DS, as

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well as the associated complications and causes of morbidity and mortality, in order to apply preventative measures and to improve patient quality of life. In addition, because the type of CHD and the timing of repair affect the prognosis, timely treatment of cardiac abnormalities is crucial for optimal survival.[10] The CHDs are the most frequent congenital anomalies in DS cases.[8] The most common CHDs in patients with DS are atrioventricular septal defect (AVSD), patent ductus arteriosus (PDA), atrial septal defect (ASD), ventricular septal defect (VSD), and tetralogy of Fallot (TOF) with AVSD, according to a Norwegian study.[9] The prevalence of CHD in children with DS in Afghanistan has not been well investigated; it could be higher than in Western countries due to higher rates of consanguineous marriage and less access to prenatal care by pregnant women. Despite the high prevalence of CHD in children with DS, little progress has been made in identifying associated factors and causes. There has been a dearth of studies on CHD in children with DS in Afghanistan. Therefore, we aimed to verify the prevalence, pattern, and frequency distribution of congenital heart disease (CHD) in children with Down syndrome at the Cardiac Research Institute of Kabul Medical University.

Methods

A three-year retrospective study was conducted in children aged 0-14 years with Down syndrome, who underwent echocardiography for possible congenital heart disease from January 2014 to December 2016, based on the Pediatric Unit CHD Registry at the Cardiac Research Institute of Kabul Medical University.

The diagnosis of DS was made by local clinicians, based on clinical features and genetic confirmation. Children diagnosed with DS in the region are routinely referred to the Cardiac Research Institute of Kabul Medical University for cardiac assessment. The inclusion criteria comprised all children with DS diagnosis based on typical clinical features and confirmed by cytogenetic studies. The exclusion criteria comprised children with dysmorphic features and not confirmed to be DS by cytogenetic studies. All participants underwent 2-dimensional echocardiographic examination and Doppler studies.

Clinical, echocardiographic, and outcomes data were collected and sorted according to confirmation of the syndrome and echocardiography results. Data analysis was done with *Statistical Package for Social Sciences (SPSS)* software, using simple descriptive statistics such as ratios, proportions, and percentages. Comparison of means was by student's t-test while proportions were compared using the Chi-square test. Statistical significance was defined as $P \leq 0.05$. This study was approved by the Ethics Committee of Pediatric Cardiology Department, Kabul Medical University, Afghanistan.

Results

During the three-year study period, 420 DS patients were identified, of whom 286 (68%) had CHD. The prevalence of isolated and multiple CHDs in 420 children with DS were 38% (160 patients) and 30% (126 patients), respectively. Ventricular septal defect (23%) and atrial septal defect (16.4%) were the most frequently diagnosed isolated defects. VSD + ASD (19.9%) was the most frequent multiple CHD. The most common associations of CHD were VSD + ASD (19.9%) and VSD + PDA (9%) (**Table 1**).

There were no significant differences in CHD frequency between boys and girls (**Table 2**).

There were no significant differences in age and birth weight of children with and without CHD (**Table 3**).

Discussion

This is the first study to address the spectrum of cardiac defects in DS at the Cardiac Research Institute of Kabul Medical University. This study was conducted in the only pediatric cardiac unit in Kabul City, and included patients referred from different hospitals in the whole city, thus providing data on the frequency and pattern of CHD in DS in almost the whole Kabul City. In our study, the overall prevalence of CHD in children with DS was 68%. This rate was slightly higher than other national published studies (Narchi *et al.*[8] 35.2%, Al-Jarallah[10] 49%), and some large population-based studies, such as the California Birth Defects Monitoring Program registry, Torfs CP

Table 1. Prevalence and types of CHDs in children with Down syndrome

Congenital heart diseases	Type of CHD	Number	% of CHD	% of children with DS
No heart disease		134		31.9
Heart disease		286	100	68
Isolated CHD	Total	160	55.9	38
	VSD	68	23	16.1
	ASD	47	16.4	11.1
	AVSD	25	8.7	5.9
	PDA	12	4.1	2.8
	COA	3	1.04	0.71
	PS	5	1.7	1.1
Multiple CHD	Total	126	44.1	30
	VSD+ PDA	26	9.09	6.19
	VSD + ASD	57	19.9	13.5
	VSD + PFO	13	4.5	3.09
	TOF	14	4.8	3.33
	ASD + PDA	16	5.5	3.80

ASD=atrial septal defect, AVSD=atrioventricular septal defect, CHD=congenital heart diseases, COA=coarctation of aorta, PDA=patent ductus arteriosus, PFO=patent foramen ovale, PS=pulmonary stenosis, TOF=tetralogy of Fallot, VSD=ventricular septal defect

Table 2. Gender distribution of CHD status in children with DS

		Male (n=213)	Female (n=207)	Total (N=420)	P value
DS, n(%)	CHD	139 (65.3)	147 (71.0)	286 (68)	0.43
	No CHD	74 (34.7)	60 (29.0)	134 (32)	0.35

Table 3. Age at the time of referral and birth weight of 420 children with DS, by CHD status

	CHD (n=268)	No CHD (n=134)	P value
Mean age (SD), months	15.98 (17.23)	14.8 (16.7)	0.65
Mean birth weight (SD), kg	2.57 (0.46) [N=183*]	2.74 (0.35) [N=84*]	0.13

*Birth weight of some children was not accurately recorded.

(43.9%),[6] Venugopalan P (60%),[18] Salih AF (53%),[22] Vida VL (54%),[23] Ashraf M (50%),[25] Azman BZ (49.3%),[26] Masaki M (50.5%),[27] Amark K (52.5%),[15] and McElhinney DB (65.7%).[17] This variation in the prevalence of CHD in DS can be explained by differing screening programs and diagnostic facilities, as well as the genetic, socioeconomic, and environmental variability of different study populations. Gene-environment interactions and gene-gene interactions may affect certain molecular pathways during embryogenesis. It has been suggested that genetic factors, specific embryological mechanisms, and cell characteristics may determine the pattern of heart anomalies.[23]

The differences of rate of CHD in DS could be due to different genetic, economic, and other aspects of living situations. Afghanistan is a post-war country, with most people living in poverty and having less access to medical facilities during pregnancy, which may affect the prevalence of cardiac malformation. Moreover, the rate of consanguineous marriage is very high in Afghanistan, which may increase the chance of developing cardiac malformations in children. The true prevalence of congenital heart defects in Afghanistan has not been well investigated, and may be higher than in other countries. Further study is needed with a larger sample size to investigate the true prevalence of congenital heart disease among children.

This study shows a high prevalence of CHDs in children with Down syndrome. The VSD and ASD are the most common isolated CHDs in our

subjects, while ASD + VSD is the most common multiple CHD. To our knowledge, this is the first extensive study done in Afghanistan, to demonstrate the pattern and prevalence of CHD associated with Down syndrome.

Conflict of Interest

None declared.

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