Type of the Paper (Review)

Prevalence of Congenital Heart Disease in Pediatric Patients with Down Syndrome in Fayoum Governorate

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Abstract

Introduction: Congenital heart disease (CHD) is the leading cause of mortality and morbidity during the first two years of the Down Syndrome (DS) patient's life. Studies showed that 40-63.5% of DS patients had CHD. The defects can involve the heart walls, valves, veins, and arteries. They might develop congestive heart failure, pulmonary vascular disease, pneumonia, or failure to thrive.

Aim of the study: The current study aimed to define the prevalence and patterns of congenital heart disease (CHD) among children with Down syndrome (DS) in Fayoum Governorate.

Subjects and Methods: The study recruited 150 pediatric DS patients from the cardiology and genetic clinics of Fayoum University Hospital, outpatient clinics of Fayoum General Hospital, and Fayoum Insurance Hospital. The current cross-sectional study was conducted for one year and nine months, January 2018 to September 2019.

Results: Echocardiographic examination of cases revealed that (54.7%) had CHD. Atrial septal defect (ASD) was the most frequent lesion (67.1%), followed by ventricular septal defect (VSD) (32.9%), patent ductus arteriosus (PDA) (18.3%), and atrioventricular septal defect (AVSD) in (13.4%) of cases.

Conclusion: There was a high incidence of CHD among pediatric DS patients. Acyanotic lesions were the most common ASD and VSD. Investigations included the 2D mode with color Doppler in Echocardiographic examination is considered the gold standard for diagnosis of CHD.

Keywords: Down Syndrome; Congenital Heart Disease; Echocardiogram.

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1. Introduction

Down syndrome (DS) is an autosomal trisomy 21. DS was first described in 1866 by John Langdon Down. It is the most common chromosomal abnormality. The incidence of DS in world literature varies from 1/600 to 800 [1].

Because of a defect in the distribution of chromosomes in DS, affected individuals have three copies of chromosome 21, clinical manifestations are variable, and cannot establish the type of chromosomal abnormality, therefore the diagnosis requires a karyotype determination [2].

Down syndrome is one of the leading causes of mental disability, hypotonia, characteristic body features, heart defects, and other systemic congenital malformations. However, not all defects occur in each patient; there is a wide range of phenotypic variations. The impact on each patient is individual, with some individuals being severely affected while others are healthy and able to function as independent adults [3].

Down syndrome is one of the leading causes of intellectual disability and millions of these patients face various health issues including learning, memory, congenital heart disease (CHD), Alzheimer's disease (AD), leukemia, cancers, and Hirschprung disease (HD). The incidence of trisomy is influenced by maternal age and differs in the population (between 1 in 319 and 1 in 1000 live births) [4].

DS has high genetic complexity and phenotype variability. Trisomic fetuses are at elevated risk of miscarriages and DS people have an increased incidence of developing several medical conditions. Recent advancement in medical treatment with social support has increased the life expectancy for the DS population. In developed countries, the average life span for the DS population is 55 years [5].

The prevalence of congenital heart disease (CHD) in DS is approximately 43%. At the same time, children with DS comprise approximately 10% of all children with CHD. The most common cardiac malformations associated with DS include atrioventricular canal, patent ductus arteriosus and atrial septal defect (ASD), and ventricular septal defect (VSD) [6,7].

CHD is a major cause of morbidity and mortality in patients with DS. Current American Academy of Pediatrics (AAP) guidelines for health care in individuals with DS recommend universal neonatal echocardiography in the newborn period [8]. CHDs are the most common cause of death in children with DS during the first two years of life [8]. Such malformations include all structural and functional cardiac defects present at birth, even if discovered later in life. These malformations can be single or multiple and usually lead to significant implications for the children and their families. These children may develop congestive heart failure, pulmonary vascular disease, pneumonia, or failure to thrive.

2. Subjects and methods

2.1. Subjects

This study was conducted on 150 Pediatric patients with Down syndrome in the cardiology and genetic clinics of Fayoum University Hospital, outpatient clinics of Fayoum General Hospital, and Fayoum Insurance Hospital. This cross-sectional study was conducted during the period of one year and nine months from January 2018 to September 2019.

2.2. Inclusion criteria

DS pediatric patients from birth to 16 years old with documentation of a positive karyotype.

2.3. Methods

After an explanation of the nature of the study, oral consent was taken from one of the parents for the procedure. All cases were fully examined by echocardiography to detect any congenital heart diseases. The examiner was a pediatric cardiologist. An examination was done after feeding to calm the baby. A mild oral sedative (Chloral Hydrate) was used for crying pediatric patients, with a dose of 0.5-1mg per kg.

2.4. Statistical analysis

SPSS v. 22 was used for statistical analysis of data. The level of significancy was assessed at *P-value < 0.05*.

3. Results and Discussion

Cases' ages ranged from 0.5 -126 months (median age of 16 months). Regarding sex, half of the studied patients (50%) were females. More than half of the studied cases had positive findings in echocardiographic examination (54.7%). Atrial septal defect (ASD) was the most frequent finding (67.1%), followed by Ventricular septal defect (VSD) (32.9%), Pulmonary hypertension (23.2%), Patent ductus arteriosus (PDA) (18.3%), Atrioventricular septal defect (AVSD) (13.4%), Tricuspid regurge (13.4%), Mitral regurge (3.7%), Mitral valve prolapse (MVP) (3.7%), Tetralogy of Fallot (TOF) (1.2%), Pericardial effusion (1.2%), Pulmonary stenosis (1.2%), Cardiac mass (1.2%), and Coronary fistula (1.2%) (Table 1).

Table 1: Echocardiographic findings of the study population.

Parameters		**Frequency (n=150)**
Echo results	Negative	68 (45.3%)
	Positive	82 (54.7%)
CHDs cases (n=82)	ASD	55 (67.1%)
	VSD	27 (32.9%)
	AVSD	11 (13.4%)
	PDA	15 (18.3%)
	TOF	1 (1.2%)
	Pulmonary hypertension	19 (23.2%)
	Mitral regurge	3 (3.7%)
	MVP	3 (3.7%)
	Tricuspid regurge	11 (13.4%)
	Pericardial effusion	1 (1.2%)
	Pulmonary stenosis	1 (1.2%)
	Cardiac mass	1 (1.2%)

Coronary fistula	1 (1.2%)

The current study showed that an echocardiographic examination of cases revealed that (54.7%) had CHD. ASD was the most frequent lesion identified (67.1%), followed by VSD (32.9%), PDA (18.3%), and AVSD (13.4%). There was no statistically significant gender difference in the frequency of CHD (*P=0.3*). The median age of studied cases was significantly lower in positive echocardiographic findings, as compared to those with normal echocardiography (12 vs. 31.5, *P<0.0001*). On the other hand, there was no statistically significant correlation between sex and the findings of echocardiography. In the contrast, there was a statistically significant correlation between anthropometric measurements (weight, height, head circumference (*P=0.0001*) and the presence of abnormal echocardiography (Table 2).

Table 2: Relation between Echocardiographic findings, Socio-demographic, and anthropometric measurements.

Variable		Positive	Negative	*P-value*
Age (months)		12 (0.5-60)	31.5 (0.5-126)	<0.0001[*a]
Body measurements	**Weight (kg)**	8 (2.2-19)	13.5 (3.8-40)	<0.0001[*a]
	Height (cm)	69.5 (43-102)	86 (51-145)	<0.0001[*a]
	HC (cm)	42.5 (30-48)	45 (36-49)	<0.001[*a]
Sex	**Male**	38 (46.3%)	37 (54.4%)	0.325[b]

Female	44 (53.7%)	31 (45.6%)

[a] Mann Whitney U test, [b] Chi-square test, *Significant.

The results showed a statistically significant correlation between chest examination and the abnormal echocardiography. That was a proportion of cases with abnormal chest examination (respiratory distress, Rattling sounds, transmitted nasal sounds, and chest wheezes) was higher among patients with abnormal echocardiography than those with normal echocardiography (53.7 % vs. 16.2%) with *P=0.0001*. There was a statistically significant correlation between abdominal examination (abnormal findings: Umbilical hernia, hepatomegaly, ascites, and splenomegaly) and the abnormal echocardiography with *P=0.041*. There was a statistically significant correlation between neurological examination (abnormal finding: hypotonia) and abnormal echocardiography (*P=0.018*). There was a statistically significant correlation between cardiac examination (abnormal findings: Ejection systolic murmur, soft murmur, pan systolic murmur, palpitation, accentuated S2, and cyanosis) and the presence of abnormal echocardiography with *P=0.0001* (Figure 1).

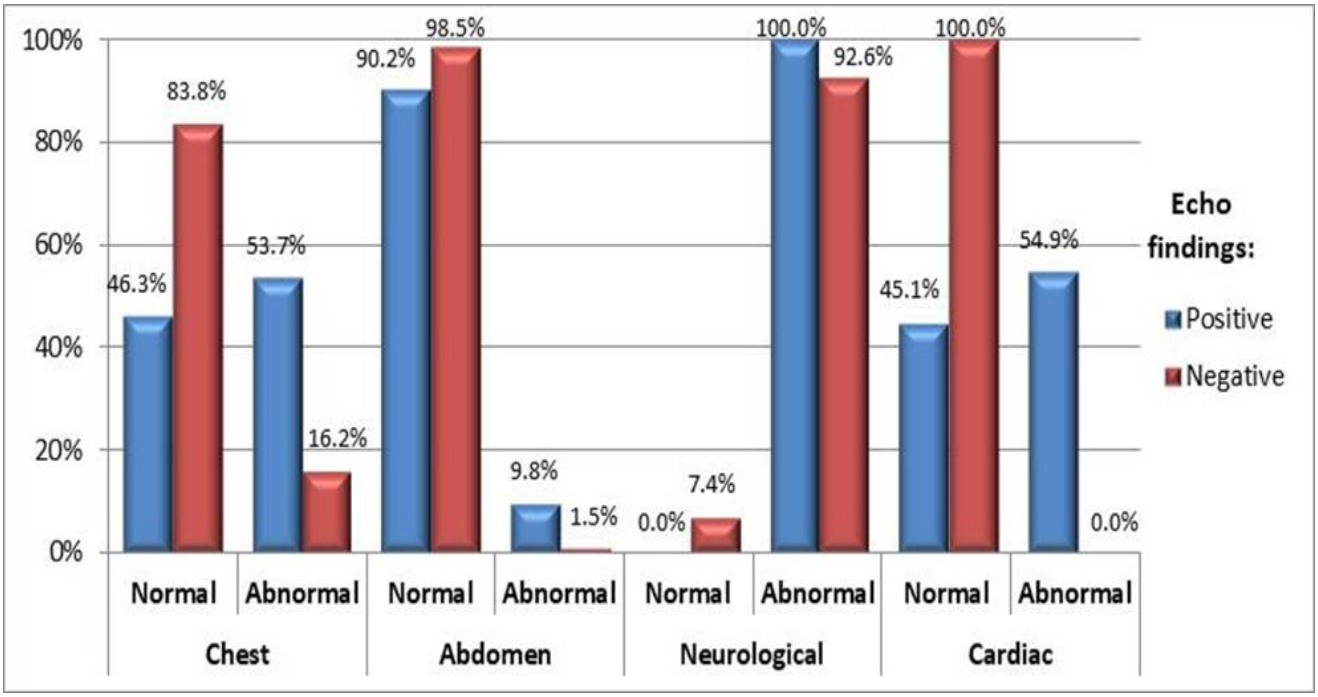

Figure 1: Clinical chest, abdomen, neurological and cardiac examination in relation to Echocardiographic findings.

An echocardiographic examination of cases in this study revealed that (54.7%) had CHD.ASD was the most frequent lesion identified in 55/82 (67.1%), followed by VSD (32.9%), (18.3%) had PDA, and AVSD was detected in (13.4%). That disagreed with a study in Mansoura, in which CHD was found in 19.0%, and the most frequent was VSD (7.9%) followed by ASD (5.6%), and PDA (2.8%), AVSD (2.7%), in descending order of frequency [11]. In another study conducted on 514 DS patients in Alexandria, it was found that CHD was detected in 38.5% of patients with a prevalence of AVSD of 18.0% followed by VSD at 11% (Table 3) [12].

The current results showed that ASD was the most common anomaly reported in 67.1% of 82 studied cases, while AVSD was 13.4%. The results were different from that obtained by Morsy et al., 2016, in their study in Saudi Arabia, as AVSD was the most common anomaly reported in 40.7% of 177 children [10].

The results of the present study showed that left to right shunt VSD pattern represents the second most common CHD in children with DS (32.9%). That observation is contrary to other international studies in which VSD represents the most common pattern of CHD in children with DS in Iraq (29%) [13], Kerala, India (28.1%) [14], Kashmir, India (24%) [15], Japan (33.3%) [16], Atlanta, USA (43%) [17], and Malaysia (20%) [18].

In the international literature, the most common CHDs in DS from reports from western European countries and the USA are the following: endocardial cushion defect (43%), which results in AVSD/AV canal defect; VSD (32%); Secundum atrial septal defect (10%); tetralogy of Fallot (6%); and isolated PDA (4%). However, in Asia, isolated VSDs have been reported to be the most common defect, observed in about 40% of patients, whereas in most reports from Latin America, the secundum type of ASD is suggested to be the most common lesion [19]. Most international studies confirmed that AVSD is the most common CHD in DS patients (ranging from 18-63%) [10]. That disagreed with our study in which AVSD represents only (13.4%).

Table 3: Comparison of the frequency and patterns of CHD among DS patients between the present study and other national and international studies.

Study location	Total DS	DS with CHD	VSD	ASD	PDA	Complete AVSD
Present study	150	54.7%	32.9%	67.1%	18.3%	13.4%
Mansoura, Egypt	712	19%	7.9%	5.6%	2.8%	2.7%
Alexandria, Egypt	514	38.5%	11%	-	3%	18%
Northwest, Saudi Arabia	302	58.6%	10.7%	11.86%	8.47%	40.7%

Muscat, Oman	90	60%	25.9%	33.3%	9.3%	27.7%
Tripoli, Libya	1193	45%	14%	23%	-	19%
Khartoum, Sudan	80	100%	23%	-	-	48%
Kurdistan, Iraq	445	53%	29%	5%	14%	20%
Guatemala	349	54%	27.5%	12.5%	28.5%	9.5%
Istanbul, Turkey	1042	40%	16.5%	16.7%	-	34.2%
Kerala, India	404	63.4%	28.1%	12.5%	16.8%	27.3%
Kashmir, India	50	50%	24%	8%	4%	14%
Malaysia	71	49.3%	20%	17.1%	11.4%	20%
Japan	196	50.5%	33.3%	9%	12%	7%
Amsterdam, Netherlands	482	43%	33.3%	17.3%	5.8%	54%
Newcastle, UK	821	41.6%	31%	15%	4%	36.5%
Goteborg, Sweden	219	52.5%	9%	12.5%	32%	51%
Copenhagen, Denmark	278	28.7%	19%	4%	6%	49%
Philadelphia, USA	114	65.7%	14%	-	6%	30%
Atlanta, USA	1469	44.0%	43%	42%	-	39%

Conclusion

There was a high incidence of CHD among pediatric patients with DS. Acyanotic lesions were the most common ASD and VSD. Investigations especially 2D mode with color Doppler in Echocardiographic examination forms the gold standard for diagnosis of CHD.

Acknowledgment

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Ethical Consideration:

The study was approved by ethical committee of Fayoum faculty of medicine. An informed written consent was obtained from all parents of the cases participating in our study. The parents were informed by the researcher about the objectives of the study, the examination and investigations.

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Conflicts of Interest: All authors declare no conflict of interest.

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