Pattern of Cardiac Affection among Down Syndrome Pediatric Patients Attending Assiut University Children's Hospital

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Abstract:
Aim: The study aims to evaluate the pattern of cardiac affection in pediatric DS patients.

Methods: From February 2022 to June 2023, a tertiary University Hospital conducted a descriptive prospective case series study involving 102 children. The socio-demographic characteristics, marital history, and examination were all included in the questionnaire.

Results: In total, 102 children with DS were recruited for this study. A total (45.1%) patients had clinical cardiac affection, and (54.90%) without cardiac affection. The majority of participants were < 1 year old (63.7%), males (58.8%), and the majority of patients came from rural areas (87.3%). The majority of mothers were multiparous (27.45%). The current study found that the mother's age was not a risk factor for Down syndrome, as the study revealed a median maternal age of 35.5(18-50), because translocations usually occur at a young age. Both groups had insignificant differences regarding demographics, obstetric and comorbidities, except residence, where the majority of both groups came from rural areas with a higher frequency of rural residency among those without cardiac affection (94.65 vs. 78.3%; p= 0.01). The current study found that the most frequent cardiac lesions were ASD with VSD (AVSD), which were present in (52.17%) children, isolated ASD (15.2%), isolated VSD (6.5%), and VSD& PFO (6.5%).

Conclusions: Both cardiac and non-cardiac DS children had insignificant differences with regard to demographic and anthropometric measurements. Primary health care has become essential to help these children have longer, more productive lives, with more attention to growth.

Keywords: Pattern of Cardiac affection; Down Syndrome; Assiut University Hospital.

Introduction:

A genetic disease called Down syndrome (DS), commonly referred to as trisomy 21, is brought on by the presence of all or a portion of a third copy of chromosome 21 [1]. Nearly all people with Down Syndrome have congenital cardiac anomalies, the most frequent of which are atrioventricular septal defect (42%), ventricular septal defect (22%), and atrial septal defect (16%) [2]. CHDs severely impair the quality of life of individuals with DS [3].

A fetal echocardiography examination is advised during pregnancy. A postnatal cardiology check ought to be carried out. Another echocardiogram must be performed within the first month following delivery [3].

Children with Down syndrome (DS) have lower birth weights and grow more slowly than children without DS. Advances in and increased access to medical care have

improved the health and well-being of individuals with DS [4] [5].

Statural growth, as an indicator of development, often represents a child's health status. The growth retardation of children with DS commences prenatally. Morris et al. [6] [7].

Patients and Methods

A case series study was conducted in Assiut University Children's Hospital and Assiut University Cardiology Hospital. This study was conducted from February 2022 to June 2023.

(The Inclusion criteria) All children with Down Syndrome aged under four years attended Assiut University Children's Hospital and Assiut University Cardiology Hospital.

Ethical Considerations:

The study adhered to Assiut University's Ethical Committee regulations and was approved by the committee with approval number (IRB No:17101640).

Data Collection:

The data were collected by a semistructured questionnaire that was divided into three sections: The first section included the demographic data of the child, such as name, age, sex, residence, birth order, and telephone number. The second section included questions about marital history, educational level, mother's work, age at the patient's birth, antenatal care and folic acid supplementation, consanguinity, and passive smoking during the first trimester.

The third section: included: General examination was done including vital signs (pulse, blood pressure, respiratory rate, temperature), skin color (pallor, cyanosis) and any skin abnormalities (scars, pigmentation)and the charactertistic features(flattened face especially the bridge of the nose, almond-shaped eyes that slant up, short neck, small ears, tongue that tend to stick out of the mouth, small hands and feet, a single line across the palm (palmar crease)small pinky fingers that sometimes curve toward the thumb). Anthropometric measurements: weight, length, head circumference, weight for height, BMI, and mid-arm circumference. Local examination included chest, heart, abdominal, and neurological examination [5].

Statistical Analysis:

SPSS (Statistical Package for the Social Sciences, version 20, IBM, and Armonk, New York) was used to gather and analyze the data. The Shapiro test was employed to ascertain if the data adhered to a normal distribution.

Students' test was used to express the data as mean ± standard deviation (SD) when comparing quantitative data with a normal distribution. The Mann-Whitney U test compared quantitative data with aberrant distributions expressed as medians (minimum-maximums). Number (n) and percentage (%)represent nominal data. Chi2 testing was applied to these kinds of data. The confidence level was maintained at 95%, and a P value was deemed significant if it was less than 0.05.

Results:

The study included 102 children with Down syndrome. The mean age of enrolled patients was 1.03 years, ranging between 0.10 and 3.8 years. The majority of patients (63.7%) were < 1 year old. More than half, 58.8% were males, and 87.3% came from rural areas. Only five patients had a family history of Down syndrome. (Table 1)

The majority were normal, except for mid-arm circumference, and 50.72% were classified as under n.

Table 1: Socio-demographic and parents' data of Down Syndrome children

	Cardiac affection		Total (102)	%	*P value
	No (= 56)	Yes (n= 46)			
Age group					0.47
< 1 year	35 (53.84)	30 (46.15)	65	(63.72%)	
> 1 year	21(56.75)	16 (43.24)	37	(36.27%)	
Sex					0.26
Male	35 (58.33)	25(41.66)	60	(58.82%)	
Female	21(50)	21(50)	42	(41.17%)	
Residence					0.01
Rural	53(59.55)	36(40.44)	89	(87.25%)	
Urban	3(23.07)	10 (76.92)	13	(12.74%)	
Birth order of the child					0.11
1st	8(72.72)	3 (27.27)	11	(10.78%)	
2nd	4(50)	4(50)	8	(7.84%)	
3rd	7(36.84)	12(63.15)	19	(18.62%)	
4th	7(63.63)	4(36.36)	11	(10.78%)	
5th	10(40)	15 (60)	25	(24.50%)	
6th or more	20(71.42)	8(28.57)	28	(27.45%)	
Education level of mother					0.90
Illiterate	25 (56.81)	19(43.18)	44	(43.13%)	
Primary	26 (54.16)	22(45.83)	48	(47.05%)	
Secondary	2(40)	3(60)	5	(4.90%)	
University	3(60)	2(40)	5	(4.90%)	
Mother's occupation					0.25
Yes	4 (40)	6 (60)	10	(9.80%)	
No	52 (56.52)	40(43.47)	92	(90.19%)	
Mother's age at time of birth (years)	32.66 ± 8.09	34.07 ± 6.87			0.35
Mother's obesity	8(57.14)	6(42.85)	14	(13.72%)	0.54
Passive smoking	26 (56.52)	20(43.47)	46	(45.09%)	0.46
Consanguinity	16(53.33)	14(46.66)	30	(29.41%)	0.50
Family history of Down syndrome	3(60)	2(40)	5	(4.90%)	0.59

The majority were normal, except mid-arm circumference, 50.72% were classified as undernutrition, and 47.82% were normal. (Table 2, Figure 1-4)

Table 2: Anthropometric measurements of Down Syndrome children:

Variable	Category	n = 102	Percentage
Weight (kg)	Mean ± SD	6.25 ± 3.2	
	Median (Range)	5 (2 – 20)	
	Low weight for age	49	(48.03%)
	Normal weight for age	51	(50.0%)
	Overweight for age	2	(1.96%)
Length/Height (cm)	Mean ± SD	63.76 ± 12.1	
	Median (IQR)	60 (40 – 110)	
	Low length for age	33	(32.35%)
	Normal length for age	67	(65.68%)
	High length for age	2	(1.96%)

HC (cm) (102)	Mean ± SD	39.82 ± 4.1	
	Median (Range)	40 (31 – 53)	
	Delayed (small for age)	35	(34.31%)
	Normal head circumference	66	(64.70%)
	Large head growth for age	1	(0.98%)
Weight for length (n=82) (<2years)	Stunted(low height for age)	38	(46.34%)
	Normal	42	(51.21%)
	Increase weight for length	2	(2.43%)
BMI (n=20)	Underweight	3	(15%)
	Normal weight	17	(85%)
MAC/cm (n=69)	Mean ± SD	11.99 ±2.61	
	Median (Range)	11 (8 – 21)	
	Undernutrition (<-3 z score)	35	(50.72%)
	Normal	33	(47.82%)
	Overweight (>3 z score)	1	(1.44%)
Cardiac Examination	Clinically Free	56	(54.90%)
	Murmur	46	(45.09%)

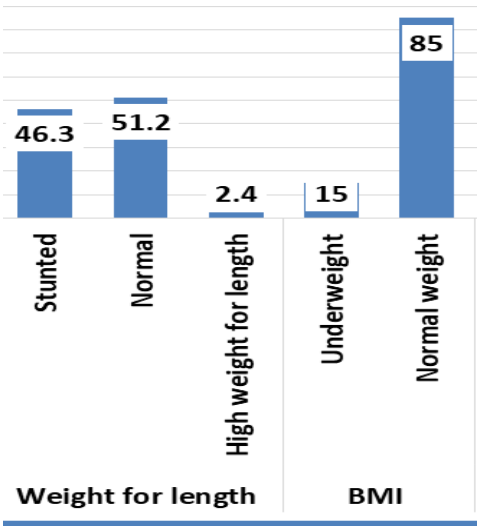

Figure 1 Weight &Length\Height

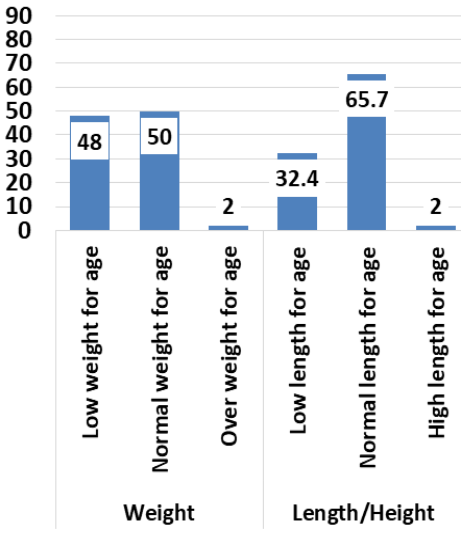

Figure 2: Weight for length&BMI

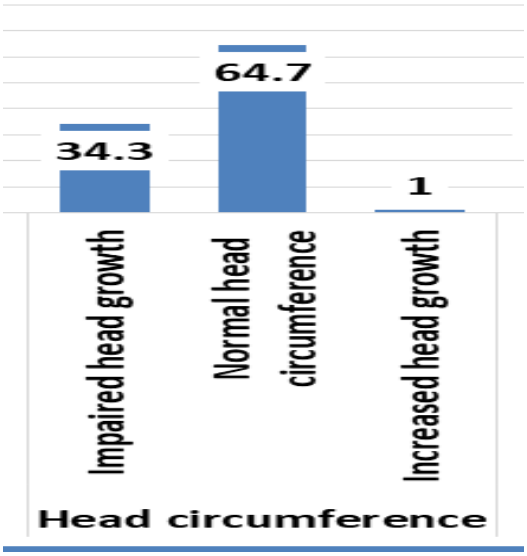

Figure 3: Head circumference

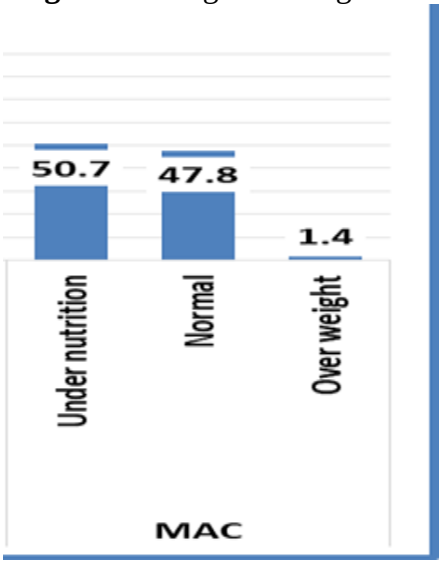

Figure 4: Mid arm circumference

Based on clinical evaluation, 45.1% of patients had cardiac affection (cardiac group) and 54.9% had a clinically free cardiac examination (non-cardiac group). (Figure 5)

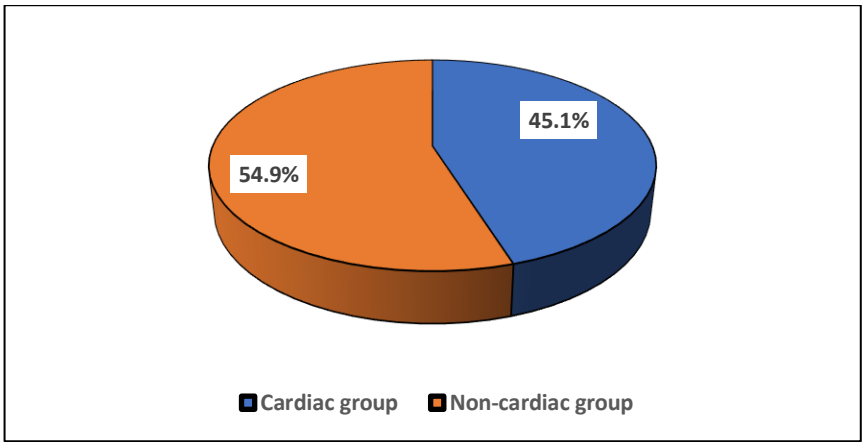

Figure 5: Distribution of patients based on cardiac affection

Regarding socio-demographic data, the two groups had no significant differences (p> 0.05). However, when it came to place of residence, the majority of both groups were from rural areas, and those without cardiac affection were more likely to live in rural areas (94.65 vs. 78.3%; p= 0.01). (Table3)

Table 3: Socio-demographic and parents' data of Down Syndrome children

	Cardiac affection		Total (102)	%	*P value
	No (= 56)	Yes (n= 46)			
Age group					**0.47**
< 1 year	35 (53.84)	30 (46.15)	65	(63.72%)	
> 1 year	21(56.75)	16 (43.24)	37	(36.27%)	
Sex					**0.26**
Male	35 (58.33)	25(41.66)	60	(58.82%)	
Female	21(50)	21(50)	42	(41.17%)	
Residence					**0.01**
Rural	53(59.55)	36(40.44)	89	(87.25%)	
Urban	3(23.07)	10 (76.92)	13	(12.74%)	

Table 3: Socio-demographic and parents' data of Down Syndrome children ***(Cont.)***

	Cardiac affection		Total (102)	%	*P value
	No (= 56)	Yes (n= 46)			
Birth order of the child					**0.11**
1st	8(72.72)	3 (27.27)	11	(10.78%)	
2nd	4(50)	4(50)	8	(7.84%)	
3rd	7(36.84)	12(63.15)	19	(18.62%)	
4th	7(63.63)	4(36.36)	11	(10.78%)	
5th	10(40)	15 (60)	25	(24.50%)	
6th or more	20(71.42)	8(28.57)	28	(27.45%)	
Education level of mother					**0.90**
Illiterate	25 (56.81)	19(43.18)	44	(43.13%)	
Primary	26 (54.16)	22(45.83)	48	(47.05%)	
Secondary	2(40)	3(60)	5	(4.90%)	
University	3(60)	2(40)	5	(4.90%)	
Mother's occupation					**0.25**
Yes	4 (40)	6 (60)	10	(9.80%)	
No	52 (56.52)	40(43.47)	92	(90.19%)	

Mother's age at time of birth (years)	32.66 ± 8.09	34.07 ± 6.87			**0.35**
Mother's obesity	8(57.14)	6(42.85)	14	(13.72%)	0.54
Passive smoking	26 (56.52)	20(43.47)	46	(45.09%)	0.46
Consanguinity	16(53.33)	14(46.66)	30	(29.41%)	0.50
Family history of Down syndrome	3(60)	2(40)	5	(4.90%)	0.59

Nominal data were compared using the Chi2 test, and continuous data were compared using the Student t test.

The majority of children with cardiac defects had an atrial septal defect and a ventricular septal defect, 21(52.17%) (Table 4)

Table 4: Pattern of cardiac affection in Down Syndrome children

Type of cardiac affection	n=46	Percentage
(ASD&VSD(complete AV canal)	24	(52.17%)
ASD	7	(15.21%)
VSD	3	(6.52%)
ASD&PDA	1	(2.17%)
ASD& partial AV canal	1	(2.17%)
ASD&VSD&PDA	1	(2.17%)
PFO&PDA	1	(2.17%)
Dextrocardia&PFO	1	(2.17%)
CompleteAVcanal&VSD	1	(2.17%)
VSD&PFO	3	(6.52%)
PFO&VSD&Fallot	1	(2.17%)
VSD&PDA	1	(2.17%)

ASD: Atrial septal defect, **VSD**: Ventricular septal defect, **Complete AV Canal**: Complete atrioventricular canal, **PDA**: Patent ductus arteriosus, **PFO**: Patent foramen ovale.

Discussion

Down syndrome (DS) is one of the most frequently occurring chromosomal abnormalities and is an autosomal trisomy 21. DS occurs once in every 600 to 800 live births and is frequently associated with congenital heart disease (CHD). Children with DS represent approximately 10% of all children with CHD [9] [10].

In our study, the majority of patients were < 1 year old (63.7%), males (58.8%), and came from rural areas (87.3%). The majority of mothers were multiparous (27.45%), which agrees with previous studies from Egypt, Iran, and India [11].

Regarding mothers' educational level, 44 (44.1%) mothers were illiterate, while 48 (47.1%) and 10 (9.8%) mothers had primary and secondary/university educational level, respectively. Only five patients had a family history of Down syndrome.

Shalaby et al. 2011 [12] reported that consanguineous marriage, parental residence location (rural/urban), parental educational status, father's behaviors, and mother's reproductive success are probable risk factors for Down syndrome.

The current study found that the advanced age of the mother is not a risk factor for the occurrence of Down syndrome, as the study reveals a median maternal age of 35.5(18-50), and had Down syndrome, child partially agrees with this study [13] [14] [15] [16].

DS is associated with intellectual disability, congenital malformations (especially of the heart), dysmorphological features, and dysfunction of several other organs. Short stature is a characteristic feature of DS. Growth retardation of DS individuals starts prenatally [17] [18] [19].

The current study recruited a total of 102 children with Down syndrome. The main findings in the current study were; 1) a total of 46 (45.1%) patients had clinically cardiac affection and 56 (54.90%) without

cardiac affection, 2) both groups had insignificant differences as regard demographic, obstetric and comorbidities with exception of residence where majority of both groups came from rural areas with higher frequency of rural residency among those without cardiac affection (94.65 vs. 78.3%; p= 0.01).

The effect of maternal age on the association of CHD and DS is unclear; some studies reported a greater risk for CHDs in young mothers, whereas others observed no maternal age effect [20] [21]. The current study did not find any association between maternal age and the CHDs in our DS children.

A total of 16 (29.4%) children had positive consanguinity. Still, the current study observed no effect of consanguineous mating on the occurrence of CHDs in DS, which disagrees with the previous Egyptian studies. The low frequency of consanguineous mating in urban compared to rural areas [22] [23] [24].

In the current study, only 5 (4.90%) children had a positive family history of DS, with no significant difference between the two subgroups. The risk of congenital cardiac anomalies in children with DS was not associated with the parents' consanguinity; instead, having a maternal age above 32 years was associated with a lower occurrence of congenital cardiac anomalies in children with DS [25] [26] [27].

The most frequent lesions were ASD/ VSD (AVSD) (52.17%) and ASD alone (15.21%). A previous study conducted among 722 individuals with DS reported that 93.6% were standard trisomy, 4.7% carried a Robertsonian translocation, and 1.7% were mosaics. The age ranged from 2 days to 18 years. The male-to-female ratio was 1.2 [28].

Previous Egyptian studies have reported lower values from DS with CHDs ranging from 36.9% to 40% [22] [23]. However, the frequency of CHDs in DS is lower in the current study compared to previous studies from Lebanon (54.2%), Saudi Arabia (58.6%), Iraq (53%), Norway (58%), and Mexico (58%) [25] [29] [30].

The current study found that the most frequent cardiac lesions were ASD with VSD, which were present in 24 (52.17%) children, isolated ASD (15.2%), isolated VSD (6.5%), and VSD& PFO (6.5%). Geographical differences in the pattern of CHDs in DS have been reported; AVSD is more common in Western countries [29] [20] [31].

In Egypt, ASD, VSD, and AVSD were reported to be the most prevalent CHD in 3 different studies [22] [23] [32].

Other studies from Saudi Arabia, Algeria, and Morocco reported AVSD was the most prevalent CHD in their DS patients, and research from Iraq, where VSD was the most common CHD among Iraqi DS patients [9] [33] [34] [30].

Another study by stoll et al 2015, had Cardiac anomalies in 44%, AVSD (30%) was the most common cardiac anomaly, followed by ASD(25%), VSD(22%), PDA(5%), coarctation of aorta (5%), and tetralogy of Fallot (3%) [35] [32] [36].

The most common congenital heart defects were Atrioventricular septal defects (AVSD; with or without other CHD) and ventricular septal defects (VSD; with or without other CHD) have been reported and represent approximately 45% and 35% of CHD associated with DS, respectively [37] [38] [39].

As trisomy 21 is insufficient to cause CHD, factors contributing to the association of CHD and DS are currently being investigated. One proposed contributing factor recently addressed is gender [40] [21]. In agreement with studies from Libya, we observed a higher frequency of CHD in the female gender (p=0.03, OR: 1.393, IC: 1.032 to 1.880), implying that this gender is more susceptible to CHD in DS patients. In the present study, AVSD and ASD were more prevalent in females. These results are in accordance with previous studies [20] [40] [21]. We did not observe a sex difference in the prevalence of VSD, which is in agreement with a meta-analysis that included 12 publications [40] [21] [41] [40].

On the other hand, PDA was the most common cardiac malformation observed in Guatemalan children with DS, followed by VSD, ASD, and then AVSD. The most common cardiac malformations in Mexican children with DS were ASD, VSD, and PDA, while the AVSDs were less common than the other malformations [42] [43] [44] [45].

Conclusions:

Consanguineous marriage, parental residence (rural/urban), parental educational status, father's behaviors, and mother's reproductive success are probable risk factors for Down syndrome. Advanced maternal age is associated with DS. Both cardiac and non-cardiac DS children had insignificant differences with regard to demographics, except for residence.

Recommendations:

- Maintenance of optimal health is a major factor in the lifelong functioning of children with Down Syndrome.
- Research for developing growth charts for children with Down Syndrome in Egypt is needed as a local reference.
- Echo screening must be done for all children with DS.

List of abbreviations: **ASD**: Atrial septal defect, **AVSDs:** Atrioventricular septal defects, **Complete AVCanal**: Complete atrioventricular canal, **CHDs:** Congenital heart defects, **DS:** Down Syndrome, **VSD**: Ventricular septal defect.

Ethical approval and consent to participate:

The study adhered to Assiut University's Ethical Committee regulations and was approved by the committee with approval number (**IRB No.**:17101640). **Trial registration:** ASMPCOSP, NCT05056285. Registered 24 August 2022, https://classic.clinicaltrials.gov/ct2/show/NCT05056285.

Consent for publications:

Not applicable.

Availability of data and materials:

The data sets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Authors contributions:

Authors (Amira G. Osman, Farghaly HS, Shaimaa M. Khalaf, Dalia G Mahran) contributed equally to the study. All authors have read and agreed to the submitted version of the manuscript.

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