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The Types of Congenital Heart Disease in Down Syndrome Patients: Single-center Review of Cases in Benghazi, Libya

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Abstract:

Congenital heart disease (CHD) is a primary cause of mortality among children with Down syndrome (DS). CHD prevalence and types in DS vary worldwide, likely influenced by socio-demographics, genetics, and geography. This study evaluates CHD occurrence and types among children with DS in eastern Libya from 2010 to 2017. Of 181 children with DS examined via echocardiogram, 67 (37%) had normal cardiac anatomy, while 114 (63%) had CHD. Among the CHD cases, 88 (77%) had single cardiac anomalies, and 26 (22.8%) had multiple defects. The most common single defect was atrial septal defect (ASD), present in 39/114 (34%), followed by an atrioventricular septal defect (AVSD) in 23/114 (20%) and ventricular septal defect (VSD) in 11/114 (6.9%). Patent ductus arteriosus (PDA) was identified in 5 cases (4%), tetralogy of Fallot (TOF) in 4 cases (3.5%), mitral regurgitation (MR) in 1.7%, aortic regurgitation (AR) in 0.9%, Ebstein's anomaly in 0.9%, and double outlet right ventricle (DORV) in one case (0.9%). This study supports that CHD distribution in DS varies by ethnicity and region, with ASD being the most common. No association with maternal age was found. Paternal consanguinity in tribal societies may contribute to chromosomal abnormalities and CHD.

Keywords: Down Syndrome, Congenital Heart Disease, Ventricular Septal Defect, Patent Ductus Arterioles, Atrial Septum Defect.

INTRODUCTION

Down syndrome, or trisomy 21, is the foremost prevalent chromosomal anomaly, occurring at an evaluated rate of 16 per 10,000 live births (Weijerman et al., 2010). There is a well-established association between Down syndrome and congenital cardiac defects; nearly 50% of children with Down syndrome have congenital heart disease, which increases the risk of mortality and morbidity, particularly within their first year (Dimopoulos et al., 2023; Weijerman et al., 2010). The estimated number of children in Libya with moderate to severe congenital heart disease (CHD) who require surgical or medical intervention within their first year of life is around 500 (Aburawi, 2006). A study on CHD frequency in children with Down syndrome in western Libya indicated that atrial septal defect (ASD) is the foremost common CHD in DS (Elmagrpy et al., 2011).

Reports suggest that the frequency of congenital heart disease (CHD) in children with Down syndrome may vary geographically. In Western literature, as well as in Turkey and Morocco, atrioventricular septal defect (AVSD) is the most common CHD (Benhaourech et al., 2016; Dimopoulos et al., 2023; Nisli et al., 2008; Tandon & Edwards, 1973). Conversely, studies from other Arab countries show different prevalence patterns. For instance, in Egypt, ventricular septal defect (VSD) is the most common CHD in patients with trisomy 21. In studies from western Saudi Arabia and Ethiopia, unique patterns emerge, such as patent ductus arteriosus (PDA) being the most frequent single defect. Research from Sudan and Nigeria reveals CHD patterns similar to those in developed nations, with AVSD being the most common CHD among children with Down syndrome (Ali, 2009; Wahab et al., 2006) In developing countries, the diagnosis of Down syndrome typically relies on phenotypic features. Recently, maternal age has not been considered a primary risk factor for Down syndrome; other factors, such as maternal smoking and obesity, are now implicated (Animasahun et al., 2016; Ferguson‐Smith & Yates, 1984).

MATERIALS AND METHODS

Settings:

The study was retrospective and descriptive. We reviewed patient medical files from June 2010 to July 2017. The genetic clinic registry documented 222 cases of Down syndrome within seven years. All these patients' charts included physical examinations, echocardiography, abdominal and brain ultrasound, blood tests for thyroid function, and celiac screening. During the echocardiography screening, we utilized the VIVID 5 echocardiographic assessment.

Data Collection:

The study was performed at the Genetic Clinic of Hawari General Hospital in Benghazi, a tertiary and university hospital. We reviewed seven-year patient records from June 2010 to June 2017, including all Down syndrome (DS) cases. Data Collection Procedure: data were manually extracted from the clinic logbooks and patient records and transferred to a structured questionnaire. Collected data included the patient's current age, sex, parental contact information, age at initial diagnosis, history of consanguinity, maternal age at conception, and echo report details. The diagnosis was established based on phenotypic clinical features, which include characteristics such as mongoloid faces, single palmar crease, protruding tongue, a depressed nasal bridge, flat occiput, small and low-set ears, upward-slanted palpable fissure in eyes, epicanthic fold, hypotonia. Short neck and Chromosomal studies were also considered in some cases to confirm the diagnosis.

Statistical Analysis:

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23

RESULTS

Within the seven-year study period, the genetic clinic saw 312 patients. Of those, 222 had Down syndrome (71.2%), and of those, only (181/222) had an echocardiography examination. The patients' geographical distribution was as follows: 73% from Benghazi, 14% from other cities in the eastern part of Libya, 8% from the south of Libya, and 4% from the west of Libya, illustrated in Figure 1.

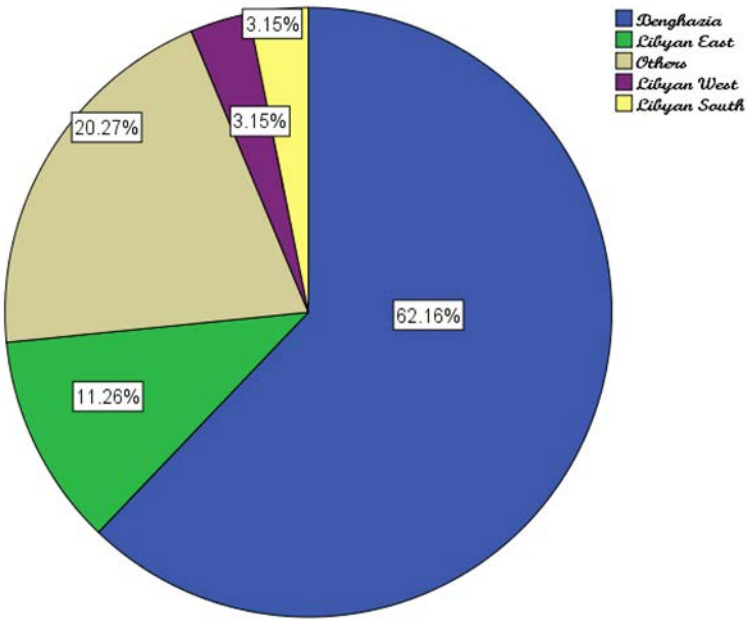

Figure (1). The geographical distribution of the patient

The presenting age at the clinic was 57% neonates, 22% less than one year, and 10% between one and five years. Seven % were between 5 and 10 years old. Lastly, 3% were over 10 years old, as shown in Figure (2).

There were 118 males and 104 females; the male-to-female ratio was 1.1:1.

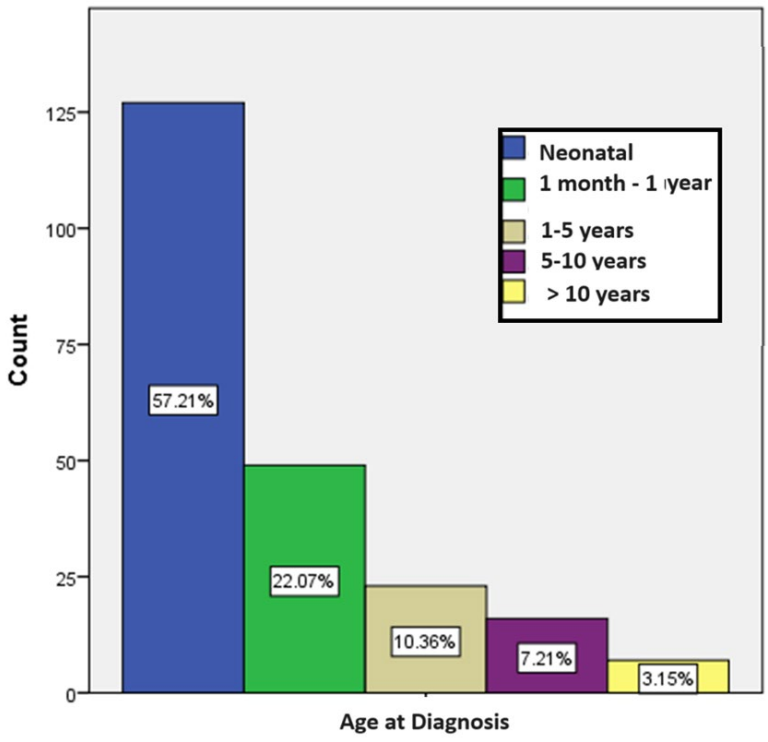

Figure (2). The age of diagnosis of congenital heart disease.

The chromosomal study was done in 42/222 36 patients (86%) were Trisomy 21: (47XX or 47XY), four patients were translocation (two have 14, 21 translocations, one has 13, 21 translocations, and one has translocation of 18, 21), and two patients were mosaic type.

The mothers' ages were recorded in 195 patient files. 50/195 (25.5%) of mothers were more than 35, and 145/195 (74%) were less than 35 when they had their baby with Down syndrome. A family history of consanguinity was positive in 83% of patients with DS, and 16% had no history of consanguinity.

Echocardiography examination results, illustrated in Figure (3), were conducted on 181 out of 222 patients, revealing that 114 out of these 181 patients (63%) had congenital heart disease (CHD), and 67 out of 181 (37%) exhibited normal cardiac anatomy. Of those diagnosed with CHD, 88 individuals (77%) had a single cardiac defect, while the remaining 26 cases (23%) had multiple lesions.
The most frequently occurring single lesion was atrial septal defect (ASD), which was observed in 39 patients (34%), followed by atrioventricular septal defects (AVSD) in 23 patients (20%) and ventricular septal defect (VSD) in 11 patients (9.6%).

Less commonly, patent ductus arteriosus (PDA) was identified in six cases (5%), while tetralogy of Fallot (TOF) was present in four cases (3.5%). Mitral regurgitation (MR) was found in two cases (1.8%), aortic regurgitation (AR) in one patient (0.9%), and Ebstein's anomaly in 0.9% of cases. In addition, DORV TGA one patient with 0.9% ASD was frequently found in association firstly with PDA in 13 cases (11%), followed by association with VSD in 7 cases (6%). One patient presented with both ASD and pulmonary stenosis (0.9%). VSD was found in 11/114 patients (9.6%) as single lesion VSD was found to be coexistent with ASD in 7 cases (6%) and with PDA in 5 cases (4.4%). Upon reviewing the medical files, we found that only 9 patients had surgical intervention 4%, 3 patients had transcatheter intervention 1.4%, and one patient died.

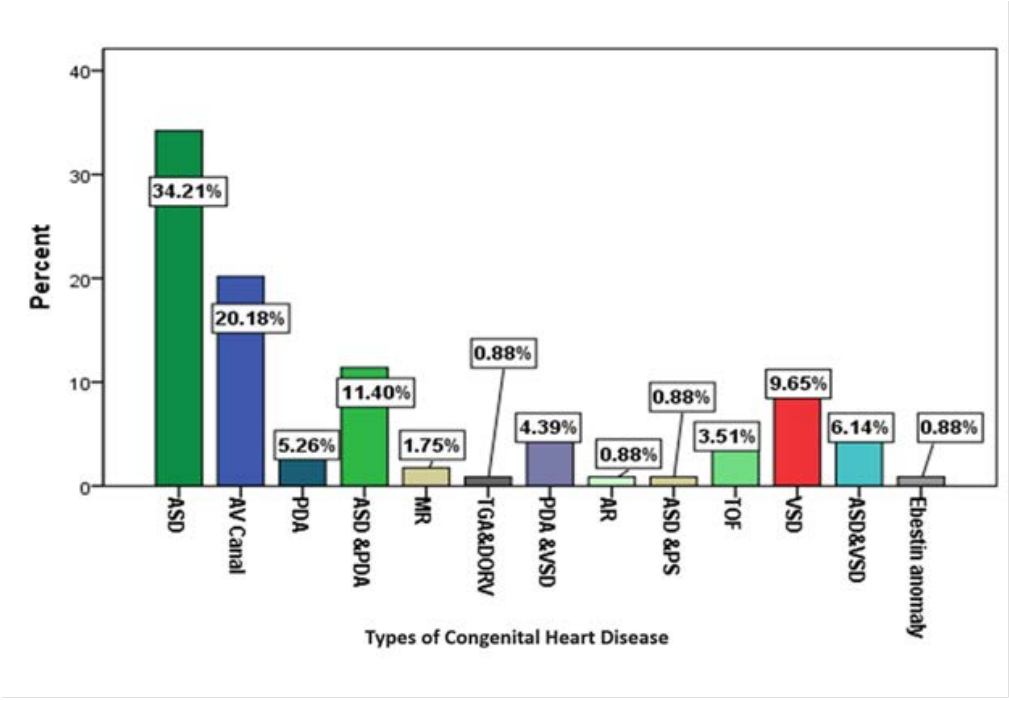

Figure (3). The frequency distribution of the various types of congenital heart disease.

DISCUSSION

The predominance of congenital heart disease (CHD) in children with trisomy 21 at our genetic clinic is remarkably high, at 62%. This figure is considerably higher than the 45% reported in Tripoli, in the western part of Libya (Elmagrpy et al., 2011). Furthermore, the prevalence observed in our study exceeds the 36.9%, 50%, and 51.7% reported in Egypt, Brazil, and Qatar, respectively (Bermudez et al., 2015; El-Gilany et al., 2017; Wahab et al., 2006). However, it is lower than the prevalence rates reported in western Saudi Arabia (86.6%) and Nigeria (95.8%) (Al-Aama et al., 2012; Susan & Chiemerie, 2022).

The high prevalence of congenital heart disease (CHD) in our study can be attributed to several factors. The most significant is early diagnosis, with over 57% of our sample diagnosed during the neonatal period, which included cases of small atrial septal defect (ASD) and patent ductus arteriosus (PDA). Additionally, 83% of DS patients in our study had a history of consanguinity, while 16% had no consanguinity (El-Gilany et al., 2017; Elmagrpy et al., 2011; Sharifi et al., 2018). Another factor is that the paperwork of our genetic clinic was mandated by the government to obtain financial aid for these populations. This resulted in a high early referral rate and early cardiac screening.

Early diagnosis in our study relied on the characteristic physical features of children with trisomy 21, which presents a study limitation. Although genetic testing was unavailable in our hospital, 42 out of 222 patients (19%) obtained chromosomal studies through private facilities. Of these, 36 patients (86%) had trisomy 47XX or 47XY, 4 had a translocation, and 2 exhibited a mosaic pattern, consistent with a study in Qatar showing 98% of participants have regular trisomy (Wahab et al., 2006).

Among the cardiac anomalies observed in children with trisomy 21 in our study, isolated cardiac defects were found in 76.8% of cases, compared with 65%, 70.4%, 29%, 23%, and 80.4% reported in Tripoli, Morocco, Egypt, Saudi Arabia, and Guatemala, respectively (Al-Aama et al., 2012; Benhaourech et al., 2016; El-Gilany et al., 2017; Elmagrpy et al., 2011; Vida et al., 2005). Atrial septal defect (ASD) is the most common congenital heart disease (CHD) in our study, similar to findings in western Libya, Korea, and Brazil (Bermudez et al., 2015; Elmagrpy et al., 2011; Kim et al., 2014). ASD, whether isolated or combined with other defects, accounted for 51.8% of cases. Atrioventricular septal defect (AVSD) was the second most common CHD in our study at 20%, while in European countries, the USA, Turkey, Morocco, and Sudan, AVSD is the most prevalent CHD (Ali, 2009; Benhaourech et al., 2016; Dimopoulos et al., 2023; Nisli et al., 2008; Weijerman et al., 2010). In contrast, other countries, such as Egypt and Afghanistan, report ventricular septal defect (VSD) as the most common CHD (El-Gilany et al., 2017; Sharifi et al., 2018). The isolated VSD rate in our study, however, was only 9.6%.

In other regions, such as western Saudi Arabia, Ethiopia, and Guatemala, patent ductus arteriosus (PDA) is the most common congenital heart disease (CHD) (Al-Aama et al., 2012; Muntha & Moges, 2019; Vida et al., 2005). In our study, isolated PDA accounted for only 5% of cases, while a combination of ventricular septal defect (VSD) and PDA occurred in 4.1% of cases. The most common isolated cyanotic CHD was Tetralogy of Fallot (TOF), representing 3.5% of cases, which is comparable to rates reported in Sudan (5%), Nigeria (8.3%), and Ethiopia (2.6%) (Ali, 2009; Muntha & Moges, 2019; Susan & Chiemerie, 2022).

Our study reveals a higher prevalence of trisomy 21 among children born to younger mothers. Maternal age was documented in 195 patient files, with 145 mothers (74%) under 35 years old at the time of their child’s birth with Down syndrome, while 50 mothers (25.5%) were over 35. This con-

trasts with European studies suggesting that advanced maternal age increases the risk of chromosomal aberrations, especially autosomal trisomies (Ferguson‐Smith & Yates, 1984). However, reports from Egypt (El-Gilany et al., 2017), Nigeria (Animasahun et al., 2016), and a recent systematic review and meta-analysis have identified a significant correlation between CHD and other risk factors, such as maternal obesity, active and passive smoking, diabetes, and exposure to organic solvents during pregnancy (Wu et al., 2023).

CONCLUSION

Our study confirms that the distribution of CHDs in children with trisomy 21 may vary based on ethnicity and geographical regions. We found a significantly elevated occurrence of CHDs in children with trisomy 21 in comparison to national and international levels; ASD was the most common lesion. There was no clear association between maternal age and DS; another factor that may be contributing is that paternal consanguinity may play a significant role in the development of chromosomal aberration and CHD in tribal societies. We need further research to explore other maternal factors that may influence the incidence of DS and CHD in young mothers.

ETHICS

This study is non-interventional and poses no risk to patients and families.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

Author contributions: All named authors contributed to data collection and analysis, drafting, and revising the manuscript, which they approved as the final version.

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