Congenital heart diseases and other major anomalies in patients with Down syndrome

Fuad I. Abbag, *MBChB, FRCP(C).*

ABSTRACT

Objectives: To determine the frequency and types of congenital heart diseases (CHDs) and other congenital anomalies among Down syndrome (DS) patients, and the short-term survival rate.

Methods: This is a retrospective review of 98 DS patients seen in Aseer Central Hospital from July 1994 to June 2005. The clinicians notes, echocardiography reports and operative notes were examined.

Results: The mean follow up period was 30 ± 40.1 months. Ninety-three patients had echocardiography; CHDs were found in 57 patients (61.3%). Ventricular septal defect (VSD) was the most common (33.3%) followed by atrioventricular septal defect (22.8%), atrial septal defect (21.1%), patent ductus arteriosus (14%) and tetralogy of Fallot (5.3%). Three patients (5.3%) developed inoperable obstructive pulmonary vascular disease (OPVD) and 3 were deemed inoperable for other reasons. The CHD was clinically suspected in 96%. The most common noncardiac anomalies were gastrointestinal, affecting 22 patients (22.4%): duodenal atresia 8 patients, imperforate anus 7 patients and Hirschsprung disease 4 patients. Sixteen patients (16.3%) died at a mean age of 19 months, 15 of them (93.8%) had anomalies.

Conclusions: The most common CHD in DS is VSD and the most common noncardiac anomaly is gastrointestinal. Down syndrome patients should be screened by echocardiography early in life to avoid OPVD. The mortality in DS is highest among those with congenital anomalies, and therefore, early intervention is crucial.

Saudi Med J 2006; Vol. 27 (2): 219-222

Down syndrome (DS) is a common disorder that occurs in approximately 1:600 newborns; however, this incidence greatly increases among children born to mothers over 35 years of age. Affected children almost always have mental retardation. They commonly have congenital heart disease (CHD) and gastrointestinal anomalies. Few decades ago the frequency of CHD was underestimated (approximately 20%), but in the last 2 decades the reported frequency has increased to approximately 50%;[1,2] this apparent increase is due to improvement in the diagnostic tools[2] and probably in the physicians attitude towards DS patients. The most common CHD in the western literature is atrioventricular septal defect (AV canal). This study was conducted to evaluate the frequency of various types of CHDs, and other major congenital malformations among DS children and short-term survival rate since this has never been studied in our region.

Methods. This study was conducted in Aseer Central Hospital (ACH) which is the main tertiary hospital for the Aseer region, in Abha city. Aseer region, which has a population of 1,200,000, is located in the southwest of Saudi Arabia part of which lies at an altitude of 3,200 meters above the Red Sea level. The ACH records from July 1994 to June 2005 were reviewed searching for children

From the Department of Child Health, College of Medicine, King Khalid University, Abha, *Kingdom of Saudi Arabia*.

Received 13th August 2005. Accepted for publication in final form 29th November 2005.

Address correspondence and reprint request to: Dr. Fuad I. Abbag, Department of Child Health, College of Medicine, King Khalid University, PO Box 641, Abha, *Kingdom of Saudi Arabia*. Tel. +966 (7) 2247800 Ext. 2203. E-mail: fuadabbag@yahoo.com

diagnosed to have DS. The case notes of these children were reviewed with particular attention to physician's notes, echocardiography reports, ECG traces, imaging reports, surgical and operative notes, and pathology reports. The types of CHD were noted and the physical examination (PE) and ECG findings recorded by the attending pediatrician and or the pediatric cardiologist were studied to see if the presence of CHD was suspected from PE or ECG, or both. The CHDs were classified as minor or major defects. Defects were considered major if they caused significant symptoms, required early surgical intervention or seemed to affect the prognosis. The size of the septal defect was categorized as small if the defect diameter was ≤ 3 mm and large if it was at least as large as the aortic orifice; size between these 2 was categorized as moderate. The age at the diagnosis of CHD and the course were noted. The presence of other congenital anomalies and short-term survival were noted. Causes of mortality and the age at death were noted.

Results. Ninety-eight children with DS were reviewed. There were 56 males (57.1%) and 42 females (42.9%). Patients were followed up for a mean period of 30 ± 40.1 months. A 2-dimensional echocardiographic assessment, aided by Doppler and Color flow mapping, was performed in 93 of them (95%) and CHDs were found in 57 patients (61.3%). The mean age at diagnosis of CHD was 7 ± 10.3 months. The most common form of CHD was ventricular septal defect (VSD), found in 19 of the 57 patients (33.3%), followed with decreasing frequency by AV canal defect in 13 patients (22.8%), secundum atrial septal defect (ASD) in 12 patients (21.1%), patent ductus arteriosus (PDA) in 8 patients (14%), tetralogy of Fallot (TOF) in 3 patients (5.3%), and so forth (**Table 1**). The most common type of VSD was the perimembranous, found in 10 patients, followed by muscular VSD in 5 and inlet VSD in 4. The VSDs were large in 8 patients, small in 7 and moderate in 4. The AV canal defects were of the complete type in 9 patients and of the partial or incomplete type in 4. The ASDs, the third most common defect, were moderate in 7 patients, large in 3 and small in 2. The CHD was major in 44 patients (77.2%). Spontaneous closure of the septal defects occurred in 4 instances: 3 (15.8%) of the VSDs (2 small and one moderate; all were perimembranous) and one with moderate ASD. Sixteen patients had surgery or transcatheter occlusion with one death, 12 patients were referred for surgical repair and 2 were lost to follow up. In 3 patients, the cardiac lesions were considered inoperable due to unfavorable anatomy and pulmonary hypertension; their diagnoses were TOF associated with hypoplastic right ventricle (RV) and pulmonary arteries, AV canal with hypoplastic RV and tricuspid atresia. Inoperable obstructive pulmonary vascular disease (OPVD) developed in 3 patients who were significantly older than the others at the diagnosis of CHD; mean age at diagnosis was 52 ± 25 months (range, 2-6 years) and 5 ± 8.8 months (range, 1 week to 4 years) respectively (p<0.05). Their respective diagnoses were large VSD, AV canal and large ASD. The presence of CHD was suspected from the PE and ECG in 55 (96%) of the 57 patients, the 2 patients in whom CHD had not been suspected were diagnosed to have PDA and ASD respectively. All patients with AV canal had superior QRS axis on ECG. The most common noncardiac congenital anomalies (**Table 1**) were related to the gastrointestinal tract, found in 22 patients (22.4%), the most common of which was duodenal atresia (DA) affecting 8 patients. Twelve (55%) of these had associated CHD and all had surgery. Sixteen patients (16.3%) of the whole group died at a mean age of 19 ± 42 months. Fifteen (93.8%) of the deaths occurred in patients with congenital anomalies: 6 (13.3%) of those with isolated CHD, 6 (50%) of those with both CHD and gastrointestinal anomalies, 2 (20%) of those with isolated gastrointestinal anomalies and

Table 1 - Congenital heart diseases and major noncardiac anomalies in 98 patients with Down syndrome.

Types of anomalies	N (%)
Congenital heart diseases (N=57)	
Ventricular septal defect*	19 (33.3)
Atrioventricular septal defect**	13 (22.8)
Atrial septal defect	12 (21.1)
Patent ductus arteriosus	8 (14)
Tetralogy of Fallot	3 (5.3)
Pulmonary atresia	1 (1.8)
Tricuspid atresia	1 (1.8)
Noncardiac anomalies (N=25)	
Duodenal atresia†	8
Imperforate anus	7
Hirschsprung disease	4
Tracheo esophageal fistula‡	2
Omphalocele	1
Bilateral cleft lip and palate	1
Craniosynostosis	1
Micropenis	1

*4 of them had patent ductus arteriosus,
**One patient had mild coarctation, †3 of them had annular pancreas,
‡One of them had a tracheal stenosis and agenesis of right lung

the one with cleft lip and palate. Five of the 8 deaths among those with gastrointestinal anomalies occurred in patients with DA (4 of the 5 had CHD as well). The immediate cause of death in the 6 patients with isolated CHD was pneumonia in 4 and septicemia in 2, while in 8 patients with gastrointestinal anomalies it was postoperative septicemia in 6, gastric perforation in one and unknown in one.

Discussion. Down syndrome is a common disorder associated with many congenital anomalies that cause significant morbidity and mortality. The most common anomaly in this study is CHD affecting 61.3% of those properly screened by echocardiography; this is slightly higher than the frequency reported in the western studies, 44-50%.[1,2] The most common type of CHD in this study is VSD 33.3%; this is different from the finding in the Caucasian patients where AV canal was reported as the most common type of CHD accounting for 45%,[1] but relatively similar to the finding in Chinese patients with DS where VSD was the most common lesion accounting for 43.6%.[3] Cyanotic CHDs are less common in DS patients. The most common cyanotic CHDs in this study is TOF occurring in 5.3%; this frequency is similar to that in the Caucasians, 4%.[1] A previous study has shown that the most common type of acyanotic CHD and cyanotic CHD in our pediatric population in general are VSD (32.5%) and TOF (4.5%);[4] these are quite similar to the findings in our patients with DS. There are few noticeable differences between the general population and DS patients as the latter are characterized by increased frequency of AV canal, rarity of obstructive left-sided lesions, decreased frequency of cyanotic CHD (with the exception of TOF) and absence of transposition of the great arteries; these observations were previously documented.[3,5] The frequency of AV canal in DS patients in this study is 22.8% while it was only 3.6% in the general population.[4] The rarity among DS patients of obstructive left-sided lesions such as hypoplastic left heart syndrome, aortic valve stenosis, coarctation of the aorta and interrupted aortic arch has been documented in the Far East[3] as well as in western population.[1,5] A comparison between AV canal in DS and AV canal in the general population demonstrated that the anatomy in DS patients is simpler, namely significant left-sided anomalies are rare.[6] The frequency of cyanotic CHDs in DS patients in this study is 8.8% while it is 16.4% in our general population.[4] The CHDs in DS patients are mainly acyanotic defects with left to right shunt with frequency of 91.2%; this is higher than that in the general population (62.3%).[4] The left to right shunt causes pulmonary congestion giving rise to respiratory distress, and increases DS patients susceptibility to pneumonias (infectious or aspiration pneumonia) which together with heart failure probably constitute the most common causes of death in DS infants with CHD; pneumonia accounts for majority of the death causes among those with isolated CHD in this study. The second most frightening complication of defects with left to right shunt is obstructive pulmonary vascular disease. This complication occurs in the general population with such defects, but in DS patients it is more common and it occurs earlier than usual. This complication occurred in 5.3% of the patients in this study. It can be avoided in majority of patients by early diagnosis and intervention to close the defect before one year of age. Since CHD occurs in more than half of DS patients and since significant cardiac lesion may not be detected by PE, it seems very sound to recommend screening of all DS patients by echocardiography and preferably during the neonatal period. The sensitivity of PE in detecting CHD in neonates with DS was 80% in one study.[7] The sensitivity of PE and ECG in detecting CHD in the present study is 96%, which is higher than expected, this is probably due to significant proportion of the patients in this study being relatively older children in whom it is easier to detect the signs of cardiac diseases. The CHD in DS patients can be repaired at slightly higher death rate than in the general population 2.7%.[8] The postoperative period is commonly complicated by pulmonary infection[8] to which DS patients are particularly susceptible. The other serious postoperative complication is severe pulmonary hypertension, which usually occurs in 2% of non-syndromic patients but increased to approximately 10% in DS patients and to 14% after correction of AV canal defect.[9] Spontaneous closure of the common types of VSDs (namely the perimembranous and muscular) may occur in DS patients, 15.8% in this study; however, as this does not usually occur when the VSD is large, all patients with large VSDs should be referred during infancy to the surgeon regardless of the type and the presence or absence of cardiac symptoms. Inlet VSDs in particular do not usually close spontaneously and therefore should be closed surgically as early as possible. The AV canal defect should be repaired at around 6 months of age.

Anomalies of the gastrointestinal tracts are the second most common congenital malformation associated with DS in this study occurring in 22.4%; the most common gastrointestinal anomaly is DA (with or without annular pancreas) followed by imperforate anus and Hirschsprung disease; the 3 account for 86% of the cases. The DA and annular pancreas are strongly associated with DS; a 300 times risk

increase in DS compared with the general population was seen.[10] The DS patients have increased mortality and this usually occurs in the presence of associated congenital anomalies. The mortality is highest among those with DA especially when associated with CHD as these patients are prone to infections. Surgical repair of DA and the other gastrointestinal anomalies in DS patients should be attempted and pessimistic views should not be endorsed to the parents. The mortality in those with DA was high in this study and in another small study (56%),[11] but one should not be discouraged by this as larger studies reported a death rate of 18%,[12] and 14%.[13] In order to decrease the postoperative death, appropriate nursing care and very strict implementation of infection control measures to decrease infections have to be striven for.

Pediatricians have to be aware of the common problems and congenital anomalies associated with DS and their prognosis in order to be able to initiate a timely referral to the concerned specialties and to educate the parents regarding the early and late complications of DS.

References

1. Freeman SB, Taft LF, Dooley KJ, Allran K, Sherman SL, Hassold TJ, et al. Population-based study of congenital heart defects in Down syndrome. ***Am J Med Genet*** 1998; 80: 213-217.
2. Khoury MJ, Erickson JD. Improved ascertainment of cardiovascular malformations in infants with Down's syndrome, Atlanta, 1968 through 1989. Implications for the interpretation of increasing rates of cardiovascular malformations in surveillance systems. ***Am J Epidemiol*** 1992; 136: 1457-1464.
3. Lo NS, Leung PM, Lau KC, Yeung CY. Congenital cardiovascular malformations in Chinese children with Down's syndrome. ***Chin Med J Eng*** 1989; 102: 382-386.
4. Abbag F. Pattern of congenital heart disease in the southwestern region of Saudi Arabia. ***Ann Saudi Med*** 1998; 18: 393-395.
5. Marino B. Congenital heart disease in patients with Down's syndrome: anatomic and genetic aspects. ***Biomed Pharmacother*** 1993; 47: 197-200.
6. Marino B, Vairo U, Corno A, Nava S, Guccione P, Calabro R, et al. Atrioventricular canal in Down syndrome. Prevalence of associated cardiac malformations compared with patients without Down syndrome. ***Am J Dis Child*** 1990; 144: 1120-1122.
7. McElhinney DB, Straka M, Goldmuntz E, Zackai EH. Correlation between abnormal cardiac physical examination and echocardiographic findings in neonates with Down syndrome. ***Am J Med Genet*** 2002; 113: 238-241.
8. Malec E, Mroczek T, Pajak J, Januszewska K, Zdebska E. Results of surgical treatment of congenital heart defects in children with Down's syndrome. ***Pediatr Cardiol*** 1999; 20: 351-354.
9. Lindberg L, Olsson AK, Jogi P, Jonmarker C. How common is severe pulmonary hypertension after pediatric cardiac surgery. ***J Thoracic Cardiovas Surg*** 2002; 123: 1155-1163.
10. Kallen B, Mastroiacovo P, Robert E. Major congenital malformations in Down syndrome. ***Am J Med Genet*** 1996; 65: 160-166.
11. Buchin PJ, Levy JS, Schullinger JN. Down's syndrome and the gastrointestinal tract. ***J Clin Gastroenterol*** 1986; 8: 111-114.
12. Singh MV, Richards C, Bowen JC. Does Down syndrome affect the outcome of congenital duodenal obstruction? ***Pediatr Surg Int*** 2004; 20: 586-589.
13. Dalla Vecchia LK, Grosfeld JL, West KW, Rescorla FJ, Scherer LR, Engum SA. Intestinal atresia and stenosis: a 25-year experience with 277 cases. ***Arch Surg*** 1998; 133: 490-496.