Clinical Presentation and Outcome of Management of Congenital Heart Diseases Associated with Down Syndrome in a Tertiary Care Hospital

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Abstract:

Introduction: Treatment of children with Down syndrome having congenital heart defects has not been reported well in Bangladesh. This study has been carried out to inform practitioners about findings from cases in Combined Military Hospital, Dhaka.

Methods: Three years retrospective observational study (clinical data, hospital course and follow-up) was carried out on 114 patients (49 males and 65 females, age range 1 month to 12 years) who underwent diagnostic and therapeutic work up in the pediatric cardiology department CMH Dhaka between January 2018 and December 2020.

Results: Among 114 patients ,64 were (57%) were infants and 50 were older children (43%) , twenty-five had congestive cardiac failure and eighteen had hypothyroidism. The study showed that 33.3% were atrioventricular septal defect (AVSD), 28.1% were patent ductus arteriosus (PDA),8.75% were tetralogy of Fallot (TOF) ,5.25% were coartation of aorta (COA) ,3.5% were patent ductus arteriosus with coarctation of aorta 3.5%, double outlet right ventricle with pulmonary stenosis were 3.5%, ventricular septal defect were 7% whereas atrial septal defect along with ventricular septal defect were 5.3% ,atrial septal defect were 3.5%, transposition of great arteries with multiple ventricular septal defect were 1.8%.Forty (35%) patients using per cutaneous intervention,had 100% procedural success and no mortality .45 patients underwent surgery,few of them were not operated due to severe pulmonary hypertension.

Conclusion: Congenital heart disease was more frequent in DS children,having worse prognosis.Children with DS required special attention due to increased risk of pulmonary hypertension. Delayed treatment was an important risk factor for poor prognosis.So early diagnosis is needed in order to provide optimal intervention and surgery ,before occurrence of irreversible PAH.

Keywords: Down syndrome, Congenital heart disease, Pulmonary hypertension.

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Introduction

Down syndrome (DS) is the most common chromosome abnormality among live born infants[1]. The phenotype of DS is characterized by more than 80 clinical features, including cognitive impairments, muscle hypotonia, short stature, facial dysmorphisms, congenital heart disease and several other anomalies. Indeed,

Congenital heart diseases(CHD) are considered to be the most important clinical phenomenon of DS as they contribute to significant morbidity and mortality. The most common heart defect seen in infants with DS is an atrioventricular septal defect. Other heart defects seen in infants with DS include ventricular septal defect,atrial septal defect and patent ductus arteriosus[2]. It is known that factors such as pulmonary hypertension can be associated with a significant mortality risk in the patients [3]. Regarding management of CHD with DS patient has been historically more controversial. In the early years of congenital heart surgery, patients with DS were not offered surgery and intervention [4]. There is a lack of clarity regarding the indications for and outcomes after

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interventional and surgical management in DS patient in infancy and early childhood. Although aggressive medical management, intervention and surgical treatment for CHD in patient with DS is routine practice in the current era, that is not always the case. Intervention is now a widely accepted alternative to surgery in many patients with single noncomplex congenital heart disease. Advances in paediatric cardiovascular surgery and cardiac interventional catheterization since the new millennium have shown improved outcomes in selected groups of patients with CHD [5,6]. Over recent decades, there has been a substantial raise in the life expectancy of children with DS with an improvement in average life expectancy from 12 years in the 1940s to 60 years today. This raise in life expectancy has mainly been due to the successful early surgical treatment of CHD in children with DS[7,8]. But patients are needed to be assessed properly whether they need surgical procedure at all or just intervention is sufficient for their treatment. But this has not yet been investigated in Bangladesh. The retrospective study included the evaluation of medical records, chest radiography,12-lead electrocardiogram (EEG), echo-cardiograms and treatment outcomes of all patients with CHD.

Methods:

Selection of data for this study

The study has been conducted on 114 children with DS associated with CHD,admitted in a tertiary care hospital,CMH Dhaka betweenJanuary 2018 and December 2020.Most children were referred from other regions of the country.The study aimed to evaluate the proper diagnosis in order to understand specific management. The retrospective observational study include the medical records, chest radiography,12-lead electrocardiogram (ECG),echocardiogram,intraoperative findings,interventional and surgical outcomes of all patients of DS with CHD. Pulmonary hypertension was defined as a pressure gradient estimated by Doppler (continuous Doppler) on tricuspid valve regurgitation(+ 10 mm Hg) over 30 mmHg or a systolic pulmonary artery pressure of more than half systemic systolic pressure.

Patient assessment, treatment and data recording:

Inclusion criteria of symptomatic patients of congenital heart diseases with DS,were based on the following symptoms included the presence of baseline respiratory distress e.g. tachypnea, retraction, hypoxia, apnea, increased work of breathing and feeding difficulty. All patients were evaluated by interventional pediatric cardiologist for possible percutaneous cardiac intervention, including patients' weight and transthoracic echocardiography to assess anatomy of the defect. The pulmonary hypertension was assessed only by decrease in echocardiographic measurement.

Intervention was performed in CMH Dhaka, include PDA, ASD, VSD device closure and COA stenting. Rest of the patient with complex heart disease referred for surgical corrections include ASD, VSD,Coarctation of the aorta, TOF, complete AV canal defect and surgery for single ventricle physiology.

All interventionswere performed with the patient under deep sedation with continuous trans thoracic echocardiogram guidance. In the percutaneous cases, a hemodynamic assessment of the degree of left-to-right shunt was performed. Heparin was administered in all patients. A full assessment of the defect and surroundings rim was performed, Angiography was performed to assess the size and location of the defect. Antibiotic prophylaxis was given during the procedure and then for next 3 days and indicated patients were placed on an aspirin regiment after the procedure. All patients had a chest radiograph, electrocardiogram and echocardiogram at 24 hours and on the first, sixth and twelfth months after the procedure and yearly thereafter.

Analysis: All collected data were sorted according to a designed checklist from the CMH databases. After extraction of data from the CMH database, and sorting with consideration of above inclusion criteria, a total of 114 DS with CHD patients were selected. The assessment of the data showed that the treatment was done in the following way in Figure 1 which shows how to review DS with heart issues. After that the patent treatment were decided based on the results and recommended for either intervention or surgery.

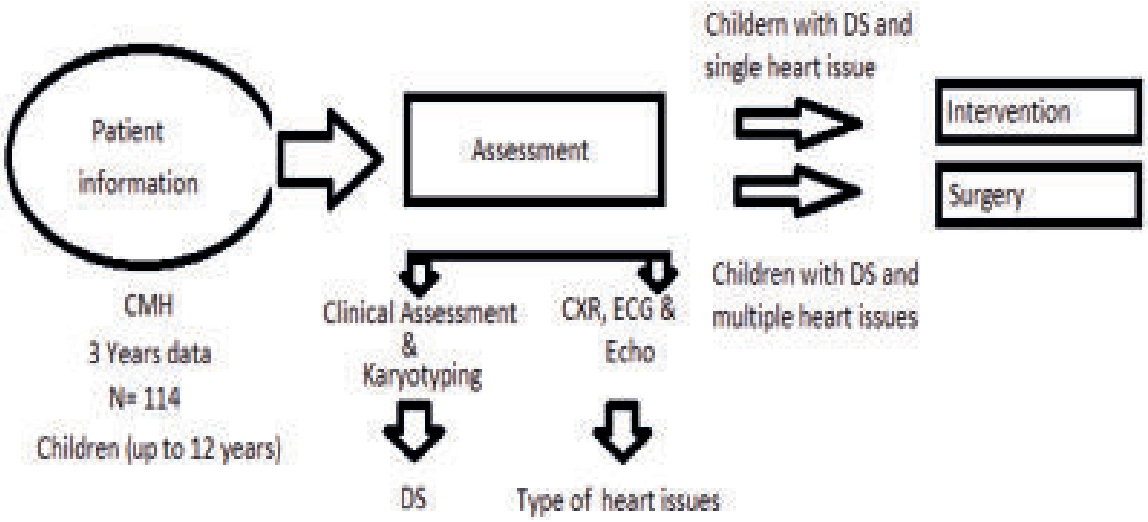

Fig.-1: *Patient treatment process*

After finding this process in Figure 1, data analysis was done in software tools to analyses the outcome and present that for visual purpose.

Data processing and analysis tools: Data were compiled into an Excel spreadsheet (Microsoft Corporation, Redmond, USA) which was used to tabulate demographic and etiological information. Simple proportions were used for categorized data. All data were analyzed through standard statistical methods by using SPSS software, Version 16.0 (statistical package for social science SPSS Inc. Chicago, USA)

Ethical approval:A permission was obtained from the concerned department and ethical review committee for compiling and publication of data records.

Results:

One hundred fourteen patients with a diagnosis of CHD and DS were evaluated. Subjects were children from birth to 12 years old. The weight ranged from 4 kg to 35 kg. Among 114 patients ,64 were (57%) were infants and 50 were older children (43%) .Fig 2 show the number of procedure per year .Fifteen patients were not operated due to severe pulmonary hypertension.Overall, 50 patients (43.8%) had isolated ASD, VSD,PDA and COA versus 64 patients (56.1%) with complex congenital cardiac diseases.

Clinical symptom -signs and echo findings of CHD were reasons for referral of patients to cardiologist are shown in Table-1.Among them 43.33%children had wasting, 30% had moderate and 13.33% had severe wasting.

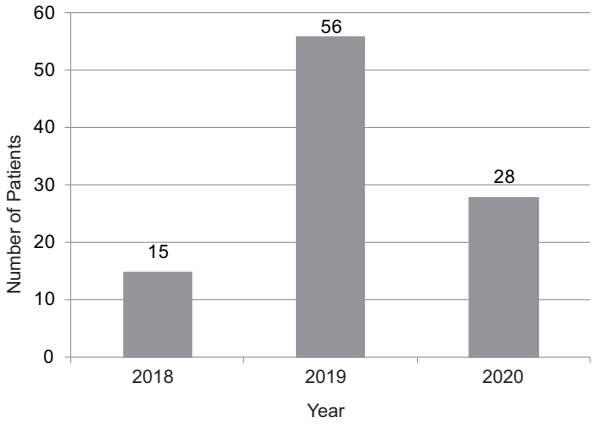

Fig.-2: *Number of patients by year(n=99)*

Table-I

Reasons for referral among study population(n=114)

Reasons for referral of cases with DS	n=114
Diagnosed at neonatal period as DS and screening for CHD	56 (49.1%)
Failure to thrive	22 (19.3%)
Cyanosis since birth	09 (7.9%)
Feeding difficulties	11 (9.7%)
Tachypnea	16 (14.0%)
Among FTT child - moderate wasting (-2 to3)	35(30.7%) out of 114
Severe wasting (<-3)	15(13.2%) out of 114

WHZ-a weight for length/height Zscore

FTT-who have failed to gain weight or height according to standard medical growth charts .

Pattern of CHD among studied population is shown in Table -2

Evidence of moderate to severe pulmonary arterial hypertension (PAH) was reported in 45 (39.47%) of cases. Three (2.6%) patients had non-cardiac abnormalities associated, such as hypospadias, and cleft palate. Eighteen (15.7%) patients had congenital hypothyroidism.

In the majority of cases, symptoms of dyspnea on exertion and/or otherwise unexplained LV enlargement constituted the indications for closure.

Among 50 we enrolled 40 cases (PDA-30,VSD-2,ASD-3 and COA-5) for angiography followed by cardiac intervention . According to the PDA classification adopted by Krichenko et al.,18 (64.2)% had Type A,12 (42.8)% had Type B . The mean PDA diameter on angiography was 4.1 ± 2.1 mm, and the mean length was 8.3 ± 3.1 mm. Most of the PDAs were restrictive and most of the ASD is secondumwith adequate rims. Few percent of VSD were perimembranous and restrictive. The median shunt fraction (Qp/Qs) was 1.8:1 with a range from 1.3 to 2.4:1.The primary indication for intervening COA was resting hypertension,and upper to lower extremity systolic gradient of >20 mm Hg associated with claudication or headaches.Out of 6 aortic

Coarctation patients,2 had native aortic coarctation and 4 had aortic recoarctation those underwent balloon angioplasty in neonatal life.

Table 4 summarizes the characteristics of the PDAs, ASDs, VSDs and COA. After angiography interventional cardiologist to certify the technical feasibility for percutaneous intervention of 40 cases and rest of them referred for cardiac surgery.

In all the 40 patients, the device and stent was successfully deployed with appropriate position confirmed both by angiography and TTE. No device or stent embolization occurred. Furthermore, there was no left pulmonary artery or aorta stenosis developed after PDA device closure and no left ventricular outflow tract obstruction developed after ASD or VSD device

Table-II

Pattern of CHD among studied population (n=114)

Diagnosis	n=114
Atrioventricularseptal defect	38(33.3)
Ventricular septal defect	08(7)
Tetralogy of Fallot	10(8.75)
Coarctation of the aorta	06(5.25)
Atrial septal defect	04(3.5)
Atrial septal defect + ventricular septal defect	06(5.3)
Patent ductusarteriosus	32(28.1)
PDA +Coarctation of the aorta	04(3.5)
TGA + multiple VSD	02(1.8)
DORV+ Pulmonary stenosis	04(3.5)

Table-III

Indications for PDA, ASD and VSD device closure and COA stenting (n=50)

Indication	n = 114
Significant left to right shunt (LV enlargement)	12(10.5%)
LA enlagement with LA:Ao ratio of > 1.5	06(5.2%)
Pulmonary hypertension with PASP (<50% of systemic)	14(12.2%)
Pulmonary hypertension with L-R shunt (>PASP 50% of systemic)	08(7.0%)

closure.patient was uneventful during procedure and no significant complications develop during or after procedure. The most prevalent procedures were PDA device closure, ASD device closure followed by COA stenting and VSD device closure as shown in Table 5. And the most prevalent procedures were complete AVSD repair 25 (21.9%) out of 38 AVSD cases, followed by total VSD and ASD closure 6 (5.2%) .And palliative surgery done 9% of total cases that shown in Table 6.

Table-IV

PDA, ASD and VSD characteristics (angiography)

Data type	PDA, ASD , VSD and COA
Type A (Number and %)	18 (64.2%)
Type B (Number and %)	12 (42.8%)
PDA diameter, mean ±SD (mm)	4.1±2.1
PDA length, mean ±SD (mm)	8.3±3.1
COA length(native coar and recoarc),mean=SD(mm)	10± 4.4
ASD length, mean ±SD (mm)	10.5± 2
VSD length ,mean + _SD (mm)	2.2 +1.1
Hemodynamic data: Median of Qp: Qs (Ratio and Range)	1.8 (1.3-2.4:1)
Hemodynamic data: Median of PVR (wood unit and range)	1.7 (1.3-4.9)
Hemodynamic data: Median of PASP (mmHg) with range in bracket	45 (30- 65)
Hemodynamic data Median of Mean PA pressure (mmHg) with range in bracket	35 (26-56)

Table-V

Cardiac intervention performed in patients with Down syndrome

Cardiac intervention	Patients with intervention	N=40
PDA device closure	30	75%
ASD device closure	03	7.5%
VSD device closure	02	6.6%
COA stenting	05	16.6%
Total intervention	40	100% of N and 35% of total cases

Table-VI

Surgical procedures performed in patients with Down syndrome

Surgical procedures	Patients with surgery	N= 69
Complete AVSD repair	25	(21.9%)
VSD repair	02	(1.75%)
ASD +VSD repair	03	(2.6%)
Surgery for PDA with COA	04	(3.5%)
COA repair	01	(0.87%)
Rastelli repair	04	(3.5%)
Modified Blalock-Taussig shunt	02	(1.75%)
Tetralogy of Fallot repair	06	(5.2%)
Glenn procedure	08	(7%)
Total surgery	55	79.7%of N and 48.2% of total cases

Discussion:

Since january 2018, 114 patients with CHD and DS were treated. About 50% of individuals with DS are affected by CHD [9,10].We aimed to establish proper diagnosis and management required in children with DS and CHD by evaluation of 114 children in a Bangladeshi setting. Clinical symptoms occur in infancy as a result of high pulmonary blood flow associated with PAH[11,12].Failure to thrive ,congestive heart failure and frequent pulmonary infections were invariably observed children in this study[11].

Overall 114 CHDs were diagnosed in our study population,50 patients (43.8%) had a isolated ASD,VSD.PDA and COA versus 64 patients (56.1 %) with complex cardiac diseases . .

The present study showed that the main CHD in DS patients was AVSD present in 38(33.3%) of diagnosis. An Irish study published in 2018 also evidenced AVSD as more frequent, present in 30% of cases [13]. A Swedish study (Bergström et al. [14]) published in 2016 reported similar prevalence, with 42% AVSD. A study in Germany also evidenced the AVSD as more frequent followed by VSD, 51.2% and 25.1% respectively [15]. However, a Bangladeshi study published in 2017 by Fatema NN on the Cardiovasc. J .published that in DS patients PDA as more frequent followed by VSD and transcatheter closure is effective and safe[16].

PDA was the main lesion with 32 (28.07%) cases. Usually, PDA accounts for 5%–10% of all CHDs. But, it can be associated with various other CHD[17]. The presence of a hemodynamically significant PDA with left-to-right shunt may result in left ventricular (LV) volume overload with signs and symptoms of heart failure. In patients with evidence of LV volume overload, closure is needed to prevent complications such as LV dysfunction, arrhythmias, and pulmonary arterial hypertension (PAH). PAH before surgery was identified in more than 60% cases,suggesting that special attention is needed in postoperative care.

An additional reason for PDA closure is infective endocarditis to prevent infection [18-20].Another Bangladeshi study in 2020 by Islam M Z,Islam F on the Cardiovasc.j.showed that VSD asmore frequent and outcome after surgical closure is good .[21].

Surgical closure of PDAs was first performed by Gross and Hubbard in 1939 and has long been considered the gold standard treatment[22].The most common complications of surgical PDA intervention include pneumothorax, bleeding, and recurrent laryngeal nerve injury.These complications would make the operation more hazardous[23].Surgical closure remains the treatment of choice in the rare patients with a PDA too large for device closure or with unsuitable anatomy, such as aneurysmal PDA.Transcatheter closure of PDA was started by Porstmann et al. in 1967 and became more widespread in 1976 after Rashkind and Cuaso developed a closure device[23,24]. The most common devices we use in our practice are the Amplatzer® Ductal Occluder (ADO, St. Jude Medical Inc., St. Paul, Minnesota, USA), the Occlutech® Duct Occluder (ODO, Occlutech, Helsingborg, Sweden), and the Nit-Occlud® PDA (PFM Medical, Cologne, Germany). In this study, we also report our 3-year experience with transcatheter closure of PDA in 30 DS patients using various devicesfocusing on safety and efficacy of device closure .

In this series 3.5% and 8% DS patient presented with ASD and VSD. Percutaneous device closure was successful in almost all ASD patients by using ASO device (Amplatzer Septal Occluders) and perimembranous VSD patients .In 1 ASD patient in whom TTE showed deficient inferioposteriorrims;device closure was unsuccessful despite multiple attempts owing to prolapse of the device into right atrium.More recently ,a study by Vogel and Colleagues[25]reported the results of successful percutaneous closure of ASD by using ASO device .The presence of residual shunt was assessed by color Doppler TTE. Furthermore, improvement in signs/symptoms for which the intervention was performed was determined by history and serial TTE during follow-up visits. Follow-up occurred at 1, 30, 90, 180, and 360 days with yearly follow-up thereafter with the longest follow-up being 5 years for the first few patients. The mean follow-up was 72 months .5 stents were implanted out of 6 aortic coarctation .Mean peak systolic gradient fell from 20mm Hg after stent implantation.

CHD with left-right shunt or increased pulmonary blood flow will certainly evolve with some degree of PAH.The five-year survival of children with Down syndrome in Norway 1994-2009 differed by associated congenital heart defects and co-morbidities. The untreated AVSD,PDA and VSD are the main causes[25,26]. The

present study demonstrated that 30 (66.6%) procedures were performed in patients already with some evidence of PAH, according to observations collected from surgical descriptions. 15(33.3%) cases were refused due to severe PAH. When untreated, these patients can progress to Eisenmenger syndrome (ES), the final stage of PAH, when the left to right shunt is reversed, with high morbidity and mortality. In order to avoid this evolution, it has been recommended to operate these patients before 6 months of age, or even between 3 and 4 months in some centers[27].

Immediate result were assessed using echocardiography in the cardiac catheterization laboratory after intervention and post operative ward after surgery. ICU hospitalization in the postoperative period with a median time of 1 day after cardiac intervention and 7 days after surgery. Patients who receive intervention in this center are shift to the ward next week, sometimes discharged directly from the ICU to home. Patients had follow-up in the paediatric cardiology department at intervals of 1 months ,3 months ,6 months and 12 months up to 5 years.patients were checked clinically and by radiography with transthoracic echocardiography .

Conclusion :

CHD has remained a common co-occurring condition in DS for decades.Careful planning for cardiac intervention or surgery is required ,evaluating for all cardiac diseases ,with careful consideration of the risk for PVD . In order to effectively, implement the patient management and define the correct treatment, whether is an transcatheter intervention beside surgery is also feasible. Increased awareness is needed in order to provide early diagnosis of CHD and enable optimal treatment ,before occurrence of irreversible PAH.

Authors' Contribution

All authors conceived of the research idea. Data were collected, processed and managed by Prof.

Fatema. Dr. Ferdous conducted the research and prepared the first draft. Prof. Fatemasupervise the research and contributed to writing discussion. All authors read and approved the final manuscript.

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