

Management of Congenital Heart Diseases Associated with Down Syndrome

Down syndrome (DS) is the most common chromosome-related disorder. In the United States (U.S.) roughly 6,000 babies are born with DS every year (about 1 in every 700 babies) and more than 400,000 people are living with the condition in the U.S.¹. and it is present 28.3/10,000 in all pregnancies in Japan². It affects around one in 400-1,500 babies born in different populations depending on several factors³.

DS was first described by an English physician John Langdon Down in 1866, but its association with chromosome 21 was established almost 100 years later by Dr. Jerome Lejeune in Paris⁴. Incidence of DS is increasing throughout the globe and in December 2011, the United Nations General Assembly declared 21 March as World Down Syndrome Day⁵. The General Assembly decided, with effect from 2012, to observe World Down Syndrome Day on 21 March each year.

DS is caused by the presence of three copies of part or all of chromosome 21.

There are three different types of down syndrome.

- Trisomy 21 (nondisjunction): it is the most common type, where every cell in the body has three copies of chromosome 21 instead of two, which accounts for 95% of cases.
- Mosaicism : here a mixture of normal and cell containing 47 chromosomes are present, accounts for only about 2% of all cases of down syndrome (facts about down syndrome, 2021). mosaic down syndrome may have fewer characteristics of down syndrome
- Translocation : here each cell has part of an extra chromosome 21, or an entirely extra one, accounts for about 3% of cases of down syndrome.

The etiology of DS is unknown. Maternal age is the only factor that has been linked to an increased chance of having a baby with Down syndrome resulting from nondisjunction or mosaicism. However, due to higher birth rates in younger women, 51% of children with

Down syndrome are born to women under 35 years of age.⁶

DS children have physical, cognitive and behavioral symptoms.

Physical signs of down syndrome include: short stature and short neck, poor muscle tone, flattened facies with depressed nasal bridge, small ears, almond-shaped eyes, small hands and feet, single deep horizontal crease across the palm of the hand.

Common learning and behavioral symptoms of down syndrome include: delay in speech and language development, attention deficit, sleep apnea, delayed cognition, delayed toilet training.

Not all people with down syndrome have all these symptoms. symptoms and their severity are different from person to person.

Diagnosis⁷

- Prenatal ultrasound: examines the baby's physical features and may visualize certain organ abnormalities that are associated with down syndrome and measure the folds of tissue and extra fluid at the back of the neck.
- Either a triple or quad-screen test measures alpha-feto protein (AFP) and the hormone estriol and correlated with down syndrome and these tests do not provide a definitive diagnosis of down syndrome.
- Amniocentesis is the most definitive diagnostic test for down syndrome during pregnancy. it can be done after the 15th week of pregnancy with very low risk of complications.
- Chorionic villus sampling (CVS): this can be done during the first trimester, using cells taken from the placenta.
- Percutaneous umbilical blood sampling (PUBS): this is also done in the second trimester using blood removed from the umbilical cord.
- In DS due to chromosomal abnormality almost all systems are affected. These patients may have

intellectual and developmental disabilities, congenital heart defects, gastrointestinal, (GI) abnormalities, *Hematologic Disorders, Neurologic Disorders, Endocrinological Disorders, Musculoskeletal Disorders, Refractive Errors and Visual Abnormalities, Otorhinolaryngological (ENT) Disorder, Lung defects, Weak immune system, Overweight or obesity, Breathing issues, including sleep apnea, asthma, and pulmonary hypertension.*

Among those Congenital Cardiac Defects (CHD) are by far the most common and leading cause associated with morbidity and mortality in the patients with Down syndrome especially in the first 2 years of life. The incidence of CHD in babies born with Down syndrome is up to 50%. The most common cardiac defect associated with Down syndrome is an atrioventricular septal defect (AVSD), and this ABOUT 40% of the congenital cardiac defects in Down syndrome. The second most common cardiac defect in Down syndrome is a ventricular septal defect (VSD), which is seen in about 32% of the patients with Down syndrome. AVSD, AND VSD account for more than 50% of congenital cardiac defects in patients with Down syndrome. The other cardiac defects, atrial septal defect (10%), tetralogy of Fallot (6%), and isolated PDA (4%), about 30% of the patients have more than one cardiac defect. Because of such a high prevalence of CHD in patients with Down syndrome, it has been recommended that all patients get an echocardiogram within the first few weeks of life⁴.

CHD can have a range of symptoms, because the condition refers to several different types of heart defect but General signs of congenital heart disease can include:

- Cyanosis, tachypnea, acycardia, edema, ascites, facial puffiness, shortness of breath during feeding, extreme tiredness and fatigue, fainting during exercise
- In severe cases, these clinical features may develop shortly after birth. However, symptoms sometimes don't develop until the teenage years or early adulthood.
- Decreased growth and development, repeated respiratory tract infections (RTIs), infective Endocarditis, pulmonary hypertension, heart failure

Treatment of DS

- DS is a lifelong condition and cannot be cured. To improve skills, speech, physical, occupational, and/or educational therapy is to be given. With these treatments, many child with DS live happy, productive lives
- A care team with family member of DS child is needed. Which may include:
 - Primary care providers to monitor growth, development, medical concerns and provide vaccinations.
 - Specialists depending on the needs of the person (cardiologist, endocrinologist, geneticist, hearing and eye specialists).
 - Speech therapists to help them communicate.
 - Physical therapists to help strengthen their muscles and improve motor skills.
 - Occupational therapists to help refine their motor skills and make daily tasks easier.
 - Behavioral therapists to help manage emotional challenges that can come with Down syndrome.
- There are several important treatments for the complications of DS. There can be serious complications as well as not-so-serious ones. As approximately 50% of newborns with DS have congenital heart disease^[8]. Majority of these heart defects require surgical or transcatheter intervention, most commonly in infancy.

Perioperative planning

- Structural defect may manifest in every organ system of DS patients, and comorbidities in patients with DS and CHD should be assessed before taking decision of surgery. Assessment of problems within the respiratory, gastrointestinal, endocrine, immunologic, hematologic, and neurologic systems is to be done.

Most common cardiac surgeries done in patients with Down syndrome⁹

- Complete atrioventricular septal defect repair
- Ventricular septal defect closure
- Mitral valve repair/replacement
- Partial atrioventricular septal defect repair

- Patent ductus arteriosus ligation
- Tetralogy of Fallot repair
- Atrial septal defect closure
- Coarctation/arch repair
- Tricuspid valve repair/replacement
- Tetralogy of Fallot- atrioventricular septal defect repair
- Single ventricle palliation
- Cardiac transplantation : Sometimes surgical repair or palliation is not a good option for patients with DS, and heart transplant may be considered.

Transcatheter intervention, done in infancy

Transcatheter device closure is the preferred approach for most secundum atrial septal defects. Ventricular septal defects are more often treated surgically, but transcatheter closure is an option in selected cases.[10] Multiple defects in DS are usually treated with surgery, but there is case report of infant with Down's syndrome with ASD, VSD and PDA who was treated with simultaneous transcatheter device closure as all the defects were suitable for interventional procedure¹¹.

DS Prognosis:

In 1983, the average lifespan of a person with the condition was just 25 years. With advances in the treatment and screening life span increased, to 49 years in the year 1997 [8]. Now a days the average lifespan of a person with Down syndrome in the United States is approximately 55 years⁷. Mortality : Study from Japan states main causes of death were pneumonia/respiratory infections (20.5%), congenital malformations of the circulatory system (11.2%), other diseases of the circulatory system (9.2%), and aspiration pneumonia (8.4%) and in United States, Sweden, and Denmark congenital heart defects, respiratory infections, dementia, pneumonia, and childhood leukemia are main causes of death in patients with DS.¹²

Down syndrome remains the most common chromosomal abnormality in live-born infants in the world today. The association between Down syndrome and congenital heart disease (CHD) is well known, and it is widely recognized that CHD contributes significantly to the morbidity of children with Down syndrome¹³.

Conclusion

As the incidence of CHD in DS patients is higher. Routine echocardiogram to screen cardiac status of all newborns with DS should be done by 6 weeks of age. Early diagnosis and timely treatment is mandatory to avoid pulmonary hypertension which may cause corrective surgery impossible.

A good corrective surgery of CHD in DS children can prolong their life. In Bangladesh, nowadays corrective surgery are possible in CMH which is a good hope for DS children with CHD.

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