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Review Article

Comprehensive Approach to Congenital Heart Defects

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ABSTRACT
Congenital heart defects (CHD) are cardiovascular malformations that generally occur due to aberrant development of a normal structure in the fetus, or failure of such a structure to progress beyond an early stage of embryonic or fetal development. Malformations are due to complex multi-factorial genetic and environmental causes. Congenital heart defects, in a definition proposed by Mitchell *et al*, is a gross structural abnormality of the heart or intrathoracic great vessels that are actually or potentially of functional significance. A comprehensive approach to every aspect of CHD, covering from embryology, fetal malformations, pathology, clinical approach, investigations, interventions to the surgery is very essential to reduce the morbidity and mortality in children with CHD.
Key words: Congenital malformation, Great vessels, Fetus, ASD,VSD,TOF.

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INTRODUCTION

Congenital heart defects (CHD) are the commonest of all congenital lesions and the most common type of heart defects among children.[1] These defects generally result from the aberrant development of a normal structure in fetus or failure of progress beyond the early stage of embryonic or early fetal development. Cardiac mal-development early in the embryo leads to significant morbidity and mortality. The CHD as defined by Mitchell et al is a gross structural abnormality of the heart or intra thoracic great vessels that are actually significance.[2] The estimated prevalence of CHD is 8 to 10 per 1000 live births, with a higher rate of stillbirth, spontaneous abortion, and prematurity.[3] The relative frequency of the most common lesions varies with different reports but nine common lesions form 80% of congenital heart defects.[4] Recent advances in diagnosis and surgical treatment over the past 40 years have led to dramatic increases in survival for children with serious heart defects.

Etiopathogenesis

The etiological factor of most Congenital heart defects is unknown. In the present scenario, the complex genetics, and inheritance of CHD remains incompletely understood. In the past, the circumstances were even more worst because many children with CHD did not survive to reproductive age and fetal echocardiography was not available. In most of the cases, it is multi-factorial in origin and is a result of both genetic predisposition and environmental factors. Known genetic causes of heart disease includes inherited chromosomal abnormalities such as trisomy 21, 13, and 18, as well as a range of newly recognized genetic point mutations, point deletions and other genetic abnormalities as seen in syndromes such as CATCH 22, familial ASD with heart block, Alagille syndrome, Noonan syndrome, and many more. Known ante-natal environmental factors include maternal infections (*Rubella*), drugs (alcohol, hydantoin, lithium and thalidomide) and maternal illness (diabetes mellitus, phenylketonuria, and systemic lupus erythematosus).[5] High levels of stress were more likely to have high levels of a hormone called corticotrophin-releasing hormone (CRH) in their blood. Researchers have found a link between high levels of CRH and preterm labor or congenital heart defect in the baby. The researchers speculate that increased levels of stress-related hormones may affect both maternal blood pressure and fetal growth and development.[6] The fraction of cardiac malformations that support intrauterine circulation compromise the spectrum of congenital heart defect (CHD). The anatomic features of most CHD in humans have been carefully analyzed. Genetic alterations and null mutations have targeted the cardia and vascular system and established abnormalities in cardiovascular ontogeny as a primary cause of embryonic demise.[7] In recent years it has become evident, based on ultrasound and fetal echocardiographic studies that the incidence is considerably higher than that usually thought earlier. Prenatal ultrasound examination has documented not only congenital heart lesions but also cardiac arrhythmias and myocardial dysfunction as important causes of fetal morbidity and mortality. The cardiac anomalies and arrhythmias are the most common causes of non-immune hydropsfetalis. Thus, of all deaths related to a congenital heart defects, 50 percent occurred in six months, and 80 percent by 1 year of age. It is thus appropriate that attention should be focused on heart disease in the neonate.[8] The table IA lists the various genes implicated in CHD. The CHD caused by various disorders are listed in Table IB. The classification of CHDs depending on the pathogenesis is given in Table 2.

Family History

A careful family history spanning at least three generations should be obtained during the evaluation of any child with CHD. The possibility of consanguinity should be investigated, as it is a clue for autosomal recessive inheritance and a recognized factor for increased risk of recurrence. The risk of recurrence increases if close relatives are also affected.[15] Relatives of patients with syndromic CHD should be carefully evaluated for minor manifestations of the disorder. It is especially important in those with mandolin syndromes that are known to have a high degree of variability of expression (e.g. Noonan syndrome, Kartagener syndrome, hypertelorism-hypospadias syndrome, and Waardenburg syndrome).[16]

Table 1 A: Genes Implicated in the Etiology of Congenital Heart Defects[9]

Gene	Chromosomal Location	Function	Cardiac Defects
TBX1	22q11.2	Transcription factor	TOF, PTA, IAA
TBX5	12q24.1	Transcription factor	Conduction system defects, ASD, VSD, TOF,PTA, single ventricle.
Nkx	2.5 5q34	Transcription factor	Conduction system defects, ASD, VSD, TOF, PTA, Epstein anomaly, HLHS, AS, CoA, heterotaxy.
GATA	4 8p23.1-p22	Transcription factor	ASD
ZFPM2/FOG2	8q23	Transcription factor	TOF
JAG1	20p12	Cell signaling molecule	TOF, PS, PPS
PTPN11	12q24.1	Cell signaling molecule	PS, hypertrophic cardiomyopathy
LEFTYA	1q42	Cell signaling molecule	Heterotaxy
ACVR	3p22-p21.3	Cell signaling molecule	Heterotaxy
CF	C1 2	Cell signaling molecule	Heterotaxy,TGA
ZIC3	Xq26.2	Transcription factor	Heterotaxy
CRELD1	3p25-pter	Cell adhesion molecule	Heterotaxy, AVSD
Elastin	7q11.23	Structural protein	SVAS, PAS, TOF

Table 1 B: Genetic approach and Environmentally Induced Disorder with CHD_{10}

Disorder	Pts With Chd (%)	Predominant Heart Defect(s)
Rubella syndrome	50	PDA peripheral PS
Diabetic embryopathy	3-5	TGV VSD CoA
maternal Phenylketonuria	30	TOF VSD ASD
Thalidomide embryopathy	15	TOF TGV DORV
Isotretinionembryapathy	25	TOF, TGV, IIA-B
Fetal alcohol syndrome	35	VSD,ASD,TOF
Fetal Hydantoin syndrome	10	PS,AS,PDA
Fetal trimethadione syndrome	50	VSD, TOF

Clinical Presentation

Clinical manifestations of congenital heart defect vary according to the type and severity of the defect.[10] In neonatal period the presenting feature of CHD is cyanosis, heart failure, failure to thrive, an abnormal clinical sign detected on routine examination.[11] In infancy and childhood, the usual presenting features are cyanosis, digital clubbing, murmur, syncope, squatting episodes, heart failure, arrhythmia, failure to thrive.[12] Cyanosis is an important clinical sign in the newborn. It is the primary symptom of the most common forms of the cyanotic congenital cardiac disease that present symptomatically in the newborn. If cyanosis due to congenital cardiac disease is not recognized the newborn may experience rapid and severe cardiovascular decompensation. If the newborn has an arterial oxygen saturation above 85%, cyanosis may be quite difficult to detect by visual inspection. Oxygen saturation should be measured by pulse oximetry. The Pulse oximetry should be performed on the right hand, which, in a normal aortic arch receives blood from the ascending aorta, and on either foot, which receives blood from the descending aorta. Different conditions are associated with different relationships in oxygen saturation between the upper and lower body and defining the relationship be very helpful in identifying the specific defect causing cyanosis.[13] A pulse oximetry screen is performed on an infant within the first 24 h of life, and can easily and quickly determine whether an infant has CCHD. This procedure was developed in the early 1970's, and is dependent on the different absorption spectrum that exists between oxygenated and deoxygenated hemoglobin.[14]

Associated Extracardiac Anomalies

In most patients, CHD occurs as an isolated malformation, but approximately one-third have associated anomalies and 10 to 15 percent have specific dysmorphic syndromes. The reported incidence of associated extracardiac anomalies ranges from 7.7 to 45.0 per cent.[5,6,17] A prospective study of 1016 children with congenital heart defects identified 135 (13.3 per cent) who had recognized syndromes, embryopathies, or associations (Table 3).

Management

Prevention of Congenital heart defects

Primary prevention

Modification/abolishment of risk factors, e.g. a) Vaccines b) health promotion (via exercise) vitamins especially Folic acid to be started before conceiving.

Secondary Prevention

Recognition of subclinical disease and early treatment of initial clinical manifestations to prevent progression of disease.

Teritary Prevention

Limiting disability to the least possible and aiding the recovery from complications e.g. rehabilitation efforts.[19]

Initial Treatment

Initiation of medical therapy in a newborn with a critical congenital heart defect is necessary to prevent and/or reverse clinical deterioration and complications. The general approach should follow the usual

Table 2: Classification of CHD by Pathogenetic Mechanisms[12*]

1. Abnormalities of Mesenchymal Tissue Migration (conotruncal defects)
Subarterial ventricular septal defects
Aortopulmonary window(AP window)
Double-outlet right ventricle(DORV)
Tetralogy of Fallot (TOF)
D- Transposition of the great vessels (DTGA)
Truncusarteriosuscommunis
Interrupted aortic arch, type B
Pulmonary atresia with ventricular septal defect (VSD)
2. Altered Cardiac Hemodynamics
Coarctation of aorto with intact ventricular septum
Hypoplastic left heart syndrome (HLHS)
Aortic valvular stenosis (AS)
Interrupted aortic arch, type A
Atrial septal defect, secundum type (2^{0}ASD)
Pulmonary atresia without ventricular septal defect
Perimembranous ventricular septal defect (pmVSD)
3. Abnormalities in Programmed Cell Death
Muscular ventricular septal defect
Ebstein's anomaly
4. Abnormalities of Extracellular Matrix
Endocardial cushion defects (AV canal defects)
5. Targeted Growth Defects
Total anomalous pulmonary venous return (TAPVC)
Partial anomalous pulmonary venous return Single atrium

guidelines for management of a critically ill or potentially critically ill newborn.[20]

a. Oxygen

Supplemental oxygen is often administered to cyanotic newborn with known or suspected heart disease.[20]

b. Mechanical ventilation

Mechanical ventilation of the newborn whose primary symptom is cyanosis is often unnecessary. In contrast, mechanical ventilation and sedation are often very beneficial to the newborn with decreased systemic perfusion.

c. Fluid

Careful attention to fluid status and urine output is essential when managing newborns with a critical congenital heart defect**.** In general, on the first day or two of life, a newborn with CHD, manifest the same fluid, glucose, and electrolyte requirements as infants without a congenital heart defect. Depending on the particular defect, however, fluid and electrolyte management may change dramatically in the neonatal period. Symptoms and signs of heart failure develop due to increasing pulmonary blood flow, reduced systemic output, and compensatory sodium and water retention. Free water restriction and diuretic therapy are indicated to reduce total body sodium and water.[19]

Table 3: Extracardiac malformations most frequently reported among patients with congenital heart diseases[15-18]

Extracardiac malformations
Central nervous system
Hydrocephalus
Corpus callosum agenesis
Defects of the neural tube closure
Craniofacial
Cleft lip/palate
Eyes
Microphthalmia/anophthalmia
Respiratory
Diaphragmatic hernia
Pulmonary hypoplasia/ agenesis
Tracheoesophageal fistula
Pulmonary segmentation anomalies
Digestive
Esophageal atresia/stenosis
Duodenal atresia/stenosis
Omphalocele
Anal atresia/stenosis
Musculoskeletal
Upper limbs deficiency
Polydactyly/syndactyly
Costovertebral anomalies
Dislocation of the hip
Clubfoot
Genitourinary
Renal duplication
Urethral/renal pelvis duplication
Hydronephrosis
Renal agenesis/hypoplasia
Cystic kidney disease
Ectopic kidney
Vesicoureteral reflux
Hypospadias
Spleen anomalies
Asplenia/polysplenia

Principles of Medical Management[5,6,20]

The essential care of the newborn with a critical heart defect is no different from that of a newborn with other medical conditions in that application of a few general principles will promote effective care and minimize the chance of iatrogenic misadventures. It is imperative that a concerted team approach involving neonatology, cardiology, nursing, surgery, and anesthesiology is utilized. Effective and ongoing communi-

cation is essential for optimizing care and providing a uniform approach to the management of these complex cases.

Timing of Surgery

In general, PGE1 should be administered to a cyanotic newborn with duct dependent condition along with another supportive measure. Surgery should be scheduled on a semi-elective basis after careful evaluation is complete. One exception is noteworthy: surgery is the only effective therapy for neonates with obstructed total anomalous pulmonary venous return and should be performed as soon as the diagnosis is established**.** Patients with d-transposition of the great arteries who have restrictive patent foramen ovale often need emergent balloon atrial septostomy because of profound hypoxemia. After successful septostomy these newborn are usually quite stable and corrective surgery should be delayed until any end-organic damage resolves. A newborn who present with congestive heart failure and shock because of left heart obstructive lesions (e.g., interrupted aortic arch) also can be stabilised by the administration of PGE1 and other supportive care. Surgery is done for more complex defects or when catheterization cannot correct the defect. But, in some defects might need a combination of surgery and catheterization. The kind of surgery will depend on what defect the child has. Some congenital heart defects can be completely repaired with one surgery. Defects that are more complex often require staged surgeries over time.[21]

Types of surgical procedures (Congenital Defect Repair)

a. Palliative surgery

Palliative surgery refers to procedures where complete repair of the heart defect is not possible and blood flow is controlled either with a shunt or an artificial tube implanted in the heart or with only one ventricle of the heart.

b. Cardiac catheterization

Cardiac catheterization is a procedure in which a thin flexible tube called a catheter is passed into the cardia and its surrounding blood vessels. Cardiac catheterizations can be performed in 2 ways: 1. Diagnostic catheterization, 2. Interventional catheterization. The catheters are used for blood sampling, pressure measurements, dye injection (angiogram), and to repair specific areas of the heart and the surrounding blood vessels. The introduction of therapeutic interventions has made Pediatric Cardiology more attractive. The Pediatric Cardiologist does not have to depend on surgical colleagues for relieving obstructions like pulmonic stenosis, aortic stenosis, and coarctation of the aorta. They can dilate distally located peripheral pulmonic stenosis, which is not only difficult but at times impossible for a surgeon to reach. Atrial septal defect, patent ductus arteriosus, and some ventricular septal defects can be closed with various types of devices and operative surgeries,[22] Coil embolization of collaterals, pulmonary and coronary arteriovenous fistulae is being done routinely at many centers. Various catheter-based therapeutic interventions have revolutionized the management of Congenital Heart defects. The device closure of various defects gives complete cure to nearly 65% of simple Congenital Defect Repairs without a scar on the chest.[23] Hydropsfetalis with pinpoint aortic stenosis can be literally saved from death. Interventions have threatened the supremacy of surgery and at times they are adjunct to surgery.

c. Arterial switch procedure

An arterial switch procedure can be an option for neonates who have defects known as transposition of the great arteries (TGA). With this defect, the positions of the vessels that take blood away from the heart to the lungs and the body are switched. An arterial switch procedure, usually performed within the first few weeks of life, is done to correct the blood flow. This open heart procedure involves "switching" the pulmonary artery and the aorta back to their normal positions and attaching the coronary arteries to the new aorta in the correct positions.[24]

d. Blalock-Taussig (BT) shunt

Blalock-Taussig shunts, or "BT Shunts," are used for defects that affect the flow of blood from the right ventricle, through the pulmonary artery, and to the lungs. These include pulmonary atresia, pulmonary stenosis, tricuspid atresia, and tricuspid stenosis. Also called the blue baby operation, it is a palliative procedure since it doesn't correct the defect but helps to resolve symptoms until the child is older and/or the defect itself can be repaired.[24]

e. Norwood procedure

The Norwood Procedure is used for neonates with only one pumping chamber in their heart and other single ventricle defects. The Norwood can be done as part of a series of surgeries. It involves reconstructing the aorta using the pulmonary artery to allow the ventricle to easily pump blood out to the body. It also involves placing a BT Shunt to maintain blood flow to the lungs and inserting a Bi-Directional Glenn Shunt. The final step is the fenestrated Fontan.[25]

Pediatric Heart Transplantation

- Heart transplantation has been used for the treatment of end-stage pediatric heart disease for nearly 4 decades, with the first infant heart transplantation performed in the late 1960s. The development of cyclosporine-based immune suppression regimens 20 years ago stimulated an increased application of heart transplantation in pediatric patients with intractable heart Failure.[26] The Registry of the International Society for Heart and Lung Transplantation (ISHLT)[27] recorded the occurrence of 41 pediatric heart transplantations. In 1995, the registry recorded 370 pediatric heart transplantations. At that time, consensus indications,[28] for heart transplantation for pediatric heart disease included the following.
- Need for ongoing intravenous inotropic or mechanical circulatory support.
- Complex congenital heart disease not amenable to conventional surgical repair or palliation or for which the surgical procedure carried a higher risk of mortality than transplantation.
- Progressive deterioration of ventricular function or functional status despite optimal medical care with digitalis, diuretics, and angiotensin-converting enzyme (ACE) inhibitors.
- Malignant arrhythmia or survival of cardiac arrest unresponsive to medical treatment, catheter ablation, or an automatic implantable defibrillator.
- Progressive pulmonary hypertension that could preclude cardiac transplantation at a later date.
- Growth failure secondary to severe congestive heart failure unresponsive to conventional medical treatment.
- Unacceptably poor quality of life.[29]

CONCLUSION

Congenital Heart Defect is the biggest single cause of child mortality and early childhood hospitalization. The world has become small and all the advances in cardiology spread to the other parts of the world in no time. The pediatric cardiology discipline today takes care of pediatric cardiac patients from newborn (intrauterine) to grown-up congenital. The evolution of this subspecialty of cardiology is the result of years of perseverance, patience and passionate dedication of several genius minds as pioneers. But the cardiac catheterization laboratory has clearly transformed from a diagnostic facility to a place for providing definitive treatment to nearly 65% of simple CHDs without a scar on the chest. As enhanced

medical interventions have significantly improved the survival rates for infants and children, there has been an increased focus on the quality of life of these individuals and their families. Recent developments in the field of Pediatric cardiac surgery and Pediatric Cardiology especially non-surgical transcatheter interventions have changed the pre-operative or pre-procedure diagnostic workup of the cardiac malformations. However, it should be clear that the physicians and surgeons looking after Pediatric Cardiac patients are complementing each other in the care and welfare of the sick babies and children and not competing with each other.

CONFLICT OF INTEREST

None

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