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Review Article

Congenital Heart Disease: Causes and Risk Factors

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Abstract:

Congenital Heart Defect (CHD) is a multifactorial disorder based on both genetic and environmental factors involved in development. The basic problem lies in the structure of heart leading to CHD that occurs in walls, valves, arteries and veins of heart. During cell cycle, the gene that controls this process may mutate, causing disturbance in any portion of heart leading to disturbed blood flow, blood flow in wrong direction or complete blockage. Defect may range from simple with no manifestations to complex with severe symptoms. Simple defects need no treatment while some babies with complex birth defects during birth require special care, vaccination, medication or otherwise treated with surgery. The incidence of CHD has declined from 80 to 20% due to progress in heart surgery techniques, medical treatment and interventional cardiology. Various genetic and non-genetic increase the susceptibility for CHD. The diagnosis and treatment of CHD has greatly improved in recent years. Almost all the children with CHD survive to adulthood and spend healthy and active lives after being treated.

Key words: Congenital heart defect, birth defects, genetic, non-genetic, mutation, surgery.

Introduction:

Congenital heart disease (CHD) is the congenital organ deformity in the neonates and irregularity occurs before birth. CHD is also known as cyanotic heart disease or congenital cardiovascular malformation. The occurrence of CHD is nearly constant and ranges from 8–10/1000 [1]. About 90% of children with this defect can survive until their adulthood. CHD is considered as a multifactorial disorder involving both genetic and environmental factors contributing to the development of disease [6]. Less than 20% of CHD is due to chromosomal variation or appears as monogenic syndrome due to single gene alterations [2]. The etiology of this disease is still unknown. In certain cases, at the time of pregnancy, use of certain medications, alcohol, tobacco or presence of any infection due to rubella virus or poor nutrition or obesity in the mother contribute to such defects [3,4]. Heart diseases can be treated either by surgery or catheter interference during the first year of life otherwise can be cured without treatment. The critical phase of CHD is experienced by 25% of population suffering. In most cases, diuretics are administered to eliminate fluid retention and regulate irregular heartbeat [5]. According to a report, 40,000 children in Pakistan are born with CHD [7]. During cell cycle, the gene TNNT2 that controls the heart development may cause the disturbance of any portion of heart in its suppressed state. A decline from 80% to 20% has been observed due to advances in heart surgery, medical treatment and interventional cardiology. All other CHDs need regular control even after the successful primary interventional or operative treatment. For such patients optimum care must sustain from their childhood to late adulthood.

Causes of Congenital Heart Disease:

CHD is a multifactorial disorder characterized by range of symptoms including death during the first year of life [8].

Cyanotic CHD is the appearance of bluish skin of baby caused by the deficiency of oxygen. Cyanotic CHD includes diseases such as

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Tetralogy of Fallot, tricuspid atresia, pulmonary atresia and truncus arteriosus.

Non-Cyanotic CHD displays a group of symptoms, which may be present all at once or alone. It is caused due to genetic mutations, chromosomal mutations or environmental factors like drugs (alcohol or retinoic acid for acne). Some of the disorder run in the families like Down syndrome, Trisomy 13 and Turner syndrome [9].

Genetic Disorder: In most cases, CHD is caused due to genetic changes including deletion or mutation in a segment of DNA [10]. Approximately 5-8% of CHD is due to chromosomal abnormalities like trisomy 13, 18 and 21 while trisomy 21 being the most common genetic cause [11,12]. Deletion of long arm of chromosome 22 or small chromosomal irregularities also lead to congenital heart defects.

Environmental Factors such as infections like rubella virus (German measles) and maternal obesity are also responsible for CHD [13,14].

Physiological Mechanisms of Congenital Heart Disease:

Gene mutation disturb the cell cycle that controls the process of heart development and any defect or disturbance in any portion of heart during formation eventually cause CHD [15,16]. CHD occurs when there is disturbance in heart development. In most cases, during fifth week of pregnancy the heart development is disturbed. At this time, the heart is in developing phase into tube like structure. Due to disturbance in blood flow, the blood movement slows down and goes in wrong direction, which causes the blockage.

During 19th day of pregnancy, formation of endocardial tube occur which develops into a pair of vascular element. The cell undergoes programed cell death by the fusion of tube and on day 21, heart cell forms their shape around it. During day 22 heart starts to beat while it is arranged in bilateral symmetry with paired vessels on each side. From day 22 to 23, the heart tube folds and twists with the ventricle moving left to center and the atria moving near the head, while blood flow starts on day 24 [17]. On day 28, expansion of heart tissue area begins inward which last till 2 weeks forming septum primmum (membranous) and endocardial cushion (muscular) which ultimately fuse and convert into four chambers of heart. If there is a failure in fusion then faulty leakage of blood occurs that allows the blood to move in wrong direction. The blood fuses from left ventricle (oxygenated blood) to right ventricle (deoxygenated blood).

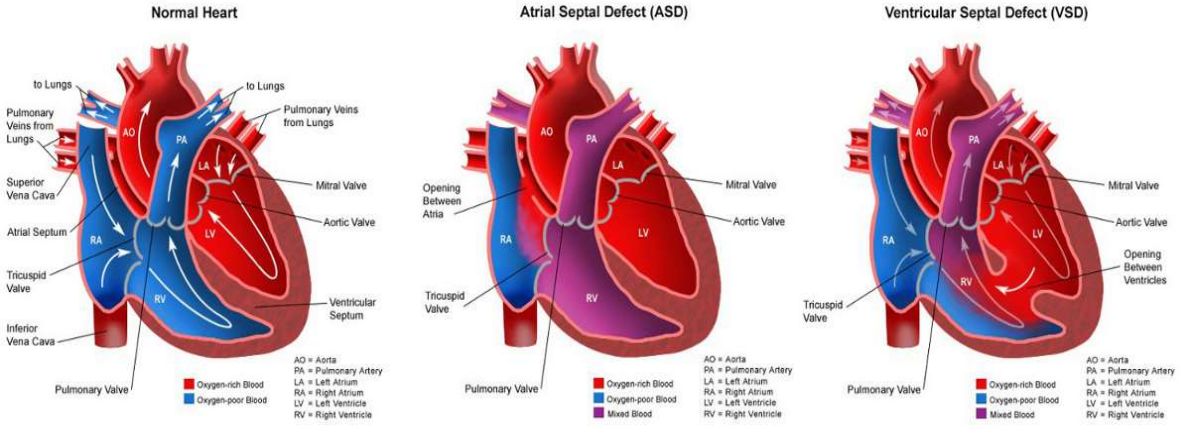

Figure 1: Physiological mechanism of Congenital Heart Defect

Prognosis & Diagnosis:

Heart defects are most likely treated with surgery and less likely by medication. Treatment with surgery makes 90% chance for survival into adulthood and healthy life but without any treatment death will occur when patient reaches at the age of 20 [18,19]. People with severe leakage of pulmonary valve are suggested to get their valve replaced. Powerful techniques enables successful diagnosis such as chest X-ray

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shows the presence of heart with Tetralogy of Fallot. Echocardiology is a safe but an expensive technique as compared to other techniques involving harmful radiations.

Clinical Manifestations:

Clinical signs depend on the type of defect. Some of the defects without any threat to the quality of include narrowing of the aorta, VSD and ASD problems [20]. It is not mandatory with every defect to appear with some manifestations however, low breathing rate and bluish skin are some common complications [21]. Irregular sound expressed due to abnormal blood flow through heart is audible through stethoscope. Symptoms of CHD include low breathing rate, bluish skin, excessive breathing, sweating and loss o weight in infants. In addition to these symptoms, other complications include difficulties with development and growth, endocarditis and high blood pressure in pulmonary arteries.

Complexity of Heart Defect:

Heart Defects of Low Complexity are uncorrected heart defects, isolated small atrial septal defects (ASD II), Preventive ventricular septal defects (VSD), congenital aortic stenosis

Heart Defects of Moderate Complexity include Ebstein's anomaly, Tetralogy of Fallot, Septal faults with related abnormalities, Unbalanced pulmonary venous joining, Persistent ductus arteriosus, Sinus venosus defects, Aortic isthmus stenosis.

Heart Defects of High Complexity include Cyanotic heart defects, Patients after Fontan repair, Reverse of the great arteries (TGA), Conflicting joining between atria, ventricles, and great arteries, Patients with implanted conduits [22].

Genetic causes of Congenital Heart Disease:

Sometime the baby inherits the genetic health condition from one or both parents that lead to CHD, and, owing to this reason, certain types of congenital heart defect run through the families.

Down syndrome: Down's syndrome is widely known genetic condition that causes CHD. Children born with this disorder may lead to genetic abnormality that can cause range of disabilities. Around 50% of children with this syndrome have congenital heart defect.

Turner syndrome: Turner syndrome only affect the females and about 50% of children with this disorder experience congenital heart defect and a problem of artery valve narrowing.

Noonan syndrome: About 80% of children with Noonan syndrome lead to congenital heart defect. In 50% of such cause, pulmonary stenosis is the consequence.

Phenylketonuria (PKU): Phenylalanine is actually a chemical with role in nerovous and circulation system. In PKU, body is unable to break this chemical. Due to disturbance in chemical breakdown, it causes learning difficulties in children. Dietary supplements and low proteins are usually recommended for treating PKU. During pregnancy, if a mother suffers from this disorder then chances for the babies to get CHD increase to six folds.

Mutations: Due to mutation, heart development may affect and lead to congenital malformation like arterial septal defect. Mutations play a critical role in causing CHD. About 30% of congenital heart defect patients are diagnosed with syndromic phenotypes with extra cardiac manifestation. Others express deletion or mutation in one gene like Noonan, Alagille and Holt-Oram syndrome [23]. Remaining 70% exhibit non-syndromic new gene with Mendelian inheritance as mostly seen in families with several effects [24-26].

Non-genetic causes of Congenital Heart Disease:

Maternal Diabetes: Around 3-6% of women, having diabetes birth a baby lead to heart defect and there are greater chances for transposition of arteries. High risks are reported in diabetes type I and type II as compared to gestational diabetes as release of high level of insulin

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hormone in blood causes disturbances in development of fetus.

Alcohol: During pregnancy, drinking too much alcohol cause a poisonous effect on the tissues of fetus and leads to fetal alcohol syndrome eventually causing congenital heart defect. Pregnant women should not drink alcohol.

Rubella (German measles): If a woman gets this infection during 8 to 10 weeks of pregnancy, it influences bad effect on unborn baby. German measles usually spread from person to person. Vaccination is compulsory for all gestational phase women. German measles disorder may lead to congenital heart disease along with many other birth defects.

Flu: During the first three months of pregnancy women getting flu, have twice chances to birth a baby with CHD. Therefore, vaccination is compulsory for all pregnant women.

Smoking: Smoking is also associated with congenital heart defect so avoid smoking during this period otherwise there are 60% chances for this disease in babies.

Organic Solvents: Use of organic solvents such as nail polishes, glue, paints etc. during pregnancy increase three fold risk for babies to born with CHD.

Medication: During the first trimester of pregnancy, if mother takes the painkiller like ibuprofen and certain acne medication like isotretinoin and topical retinoids then chances are twice for babies with heart defect.

Conclusions:

Around 40,000 children suffer with congenital heart defect in Pakistan on annual basis. By every passing year, this defect has decayed from 80 to 20% owing to the advancement in heart surgery and medical treatment. Many genetic and non-genetic factors contribute to the prognosis and development of congenital heart disease. Diagnosis and treatment of CHD have greatly improved over the years. Patients need special care, medication, vaccination from childhood to high adulthood. Acute complications are treated with medication and special care. Whereas, further surgery or catheter interventions help patients with post complication such as heart failure, pulmonary hypertension and endocarditis. There is a great challenge for management to handle the patient during pregnancy or non-cardiac surgery, therefore, constructive counseling of the patient is always mandatory.

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