# Critical Congenital Heart Disease in Newborn: Early Detection, Diagnosis, and Management

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**A B S T R A C T**

Critical congenital heart disease (CHD) is a type of CHD that requires early intervention in the first year of life to survive. Morbidity and mortality increase significantly if newborns with critical CHD experience delay in the initial diagnosis and management. The infants may develop cyanosis, systemic hypoperfusion, or respiratory distress as the primary manifestations of critical CHD. Pulse oximetry screening for early detection of critical CHD must be performed in newborns after 24 hours of age or before discharge from hospital. Generally, infants with critical CHD require patency of the ductus arteriosus with an infusion of prostaglandin to maintain pulmonary or systemic blood flow. After initial management, the infants must be immediately referred to the tertiary care centre for definitive intervention.

## 1. Introduction

Congenital heart disease (CHD) is a structural abnormality in the heart or intrathoracic major blood vessel that is present at birth.[1] CHD is the most common congenital abnormality in newborns and has been recognized as one of the leading causes of death in the first year of life. The global incidence of CHD is estimated at 8 per 1000 live births.[2] The causes of CHD are multifactorial, involving genetic susceptibility and environmental factors. Maternal diabetes, rubella infection, alcohol, Down syndrome, Noonan syndrome, and phenylketonuria are some of the known etiologies of CHD. However, about 90% of CHD can occur without an underlying cause.[3]

Critical CHD is a form of CHD that requires early intervention in the first year of life to survive.[4] Critical CHD is found in 25% of infants with CHD.[5] The progress of medical science, surgical, and intervention techniques in the modern era has made it possible for almost all CHD, including critical CHD, can be intervened so that the survival rate increases. Intervention in critical CHD is typically performed in the first weeks of life to optimize hemodynamically and prevent end-organ dysfunction.[6]

Although infants with critical CHD are mostly symptomatic, some of them (4-31%) can be undetected until discharged from hospital. The risk of morbidity and mortality increases significantly if there is a delay in early recognition and management, as well as referring infants with critical CHD to the tertiary care centre for definitive surgical or catheter-based

intervention.[7] This review article aims to provide an understanding of early detection, diagnosis, and management of critical CHD in the newborn.

## 2. Physiology of fetal circulation

Knowledge of the physiology of fetal circulation and its transition to extrauterine life is essential for understanding critical CHD. Fetal circulation is very different from normal circulation after birth. Fetal pulmonary circulation is not functioning properly due to high pulmonary vascular resistance. The placenta provides oxygenated and nutritious blood to the fetus via the umbilical vein. In the liver, some blood from the umbilical vein goes to the hepatic circulation, and the remainder goes into the inferior vena cava through ductus venosus. After reaching the heart, most of the blood from the right atrium flows into the left atrium through foramen ovale. Blood in the left atrium flows into the left ventricle, then into the aorta to reach the systemic circulation. Some blood from the right atrium goes to the right ventricle and pulmonary artery. Blood in the pulmonary artery flows into the proximal part of the descending aorta through the ductus arteriosus, without passing through the lungs. Deoxygenated blood from the fetus returns to the placenta via umbilical arteries. Therefore, the presence of central shunts (ductus arteriosus, ductus venosus, and foramen ovale) is significant for fetal circulation.[8,9]

After birth, the ductus arteriosus, ductus venosus, and foramen ovale will be closed as an adaptation to extrauterine life. In a healthy term newborn, the ductus arteriosus undergoes functional closure within the first 24-72 hours of life. In newborns with critical CHD, the blood flow in the pulmonary or systemic circulation may be impaired, unless shunts are obtained from other routes, for example through the patent ductus arteriosus (PDA), atrial septal defect (ASD), or ventricular septal defect (VSD), or a combination of these. Critical CHD may not manifest before birth because the fetus gets oxygenated blood from the placenta and the presence of central shunts, which support systemic blood flow. After the ductus arteriosus closes, infants with critical CHD can rapidly develop acute heart failure, shock, and death. This can occur in the first week of life if the critical CHD is not detected and does not receive initial management. Generally, infants with critical CHD require patency of the ductus arteriosus to maintain adequate pulmonary or systemic blood flow, before the definitive intervention.[9,10,11]

## 3. Congenital heart disease classification

CHD can be generally classified into three main categories based on clinical point of view, including critical CHD, clinically significant CHD, and clinically non-significant CHD.[12]

### Critical CHD

Patients with critical CHD generally have hypoplastic or small right or left ventricle and severe obstructive lesions in the valves or great arteries in the right or left heart system. Therefore, patients with critical CHD cannot tolerate the transition from fetal circulation to extrauterine circulation and will depend on the central shunts, especially the patency of the ductus arteriosus to obtain adequate circulation. Neonates with critical CHD can be asymptomatic at birth if the ductus arteriosus still open. When the duct closes, these neonates may experience severe metabolic acidosis, brain injury, necrotizing enterocolitis, heart failure, cardiovascular collapse, and death.[3,13] Critical CHD can be classified into three types of lesions: right heart obstructive lesions left heart obstructive lesions and mixing lesions **(Table 1).**

**Table 1**. Classification of Critical CHD[9,12]

| Right heart obstructive lesions (duct-dependent pulmonary circulation) |
| --- |
| Pulmonary atresia with intact ventricular septum |
| Critical pulmonary stenosis |
| Tetralogy of Fallot with pulmonary atresia |
| Tricuspid atresia |
| Severe Ebstein's anomaly |
| **Left heart obstructive lesions (duct-dependent systemic circulation)** |
| Hypoplastic left heart syndrome |
| Critical aortic stenosis |
| Coarctation of the aorta |
| *Interrupted aortic arch* |
| **Mixing lesions** |
| Transposition of the great arteries |
| Total anomalous pulmonary venous return |
| Truncus arteriosus |

**Clinically significant CHD**

Clinically significant CHD includes structural cardiac malformations that cause substantial impairment of cardiac function but usually do not require early intervention. The examples of this group include large VSD, complete atrioventricular septal defect (AVSD), large ASD, and tetralogy of Fallot (TOF) with good pulmonary artery anatomy.[12]

**Non-significant CHD**

Non-significant CHD includes structural cardiac malformations without significant impairment of cardiac function. The examples of this group include small VSD, small ASD, and mild pulmonary stenosis..[12]

**4. Clinical manifestation of CHD**

The clinical manifestations of critical CHD can be vary depending on the type of CHD. In general, there are three main clinical manifestations of critical CHD: cyanosis, systemic hypoperfusion, and respiratory distress.[14]

**a. Cyanosis**

Cyanosis is a bluish discolouration of the skin and mucous membranes due to increased levels of deoxygenated haemoglobin in the blood. Cyanosis becomes evident when the blood oxygen saturation level is <80% or the deoxygenated haemoglobin concentration is below five g/dL. Central cyanosis is associated with arterial desaturation and involves the lips, tongue, and mucous membranes. In contrast, peripheral cyanosis (acrocyanosis) is not related to arterial desaturation and usually seen only in the upper or lower extremities.[15]

Central cyanosis is always pathological, and it can be due to cardiac or pulmonary causes. Critical CHD with obstructive right heart lesions often manifests primarily as central cyanosis. Peripheral cyanosis can occur in infants with normal cardiac anatomy as a result of several non-cardiac conditions such as exposure to cold temperatures and sepsis. It is not always easy to distinguish central cyanosis due to cardiac or pulmonary causes. Pulmonary causes of cyanosis usually improve with oxygen supplementation or agitation, while cardiac cyanosis does not improve with oxygen supplementation and may worsen on crying or activity.[16]

Differential cyanosis (i.e., lower limb cyanosis without accompanying upper limb cyanosis) can be found in persistent pulmonary hypertension of the newborn and some left heart obstructive lesions, such as interrupted aortic arch and coarctation of the aorta (CoA). Patient with these conditions, the preductal part of the body receives oxygen-rich blood from the left atrium and left ventricle. In contrast, the postductal part of the body receives oxygen-poor blood from the right atrium, right ventricle, pulmonary artery, and

PDA. Due to an accurate detection of differential cyanosis in newborns, the oxygen saturation test should be performed in the preductal (right hand) and postductal (foot) part of the body. [13,15]

### b. Systemic Hypoperfusion

Neonates with sudden onset of systemic hypoperfusion or shock after the first 48-78 hours of life need to be suspected of critical CHD, especially left heart obstructive lesions such as critical aortic stenosis, CoA, interrupted aortic arch, and hypoplastic left heart syndrome (HLHS). The symptoms typically occur when the ductus arteriosus closes. These neonates may present with sudden onset of pallor, grey appearance, breathing difficulty, anuria, and metabolic acidosis. [16,17]

The closure of ductus arteriosus in the first week of life causes cardiogenic shock in newborns with duct-dependent circulation. In this situation, the way to save the infant is to reopen the duct immediately (with prostaglandin infusion) and provide supportive therapy that includes fluid treatment, respiratory care (usually requires mechanical ventilation with sedation, paralysis, and controlled ventilation), and inotropic support. Other causes of cardiogenic shock in newborns include dilated cardiomyopathy, myocarditis, and myocardial dysfunction due to tachyarrhythmias such as atrial flutter or paroxysmal supraventricular tachycardia. Other conditions that should be suspected as a differential diagnosis of neonatal shock include neonatal sepsis, meningitis, hypoglycemia, and inborn errors of metabolism. In addition to careful history taking and physical examination, chest x-ray and electrocardiography (ECG) help differentiate CHD from other causes. Cardiomegaly can suggest the suspicion of CHD as the underlying cause of shock. [13]

### c. Respiratory Distress

Persistent dyspnea or tachypnea in a newborn may indicate a heart or lung problem. CHD with large shunt lesions manifests as dyspnea, tachypnea, feeding difficulty, irritability, and respiratory distress.

Severe respiratory pain and pulmonary oedema may occur in cases of critical CHD with excessive pulmonary blood flow or lesions associated with pulmonary venous obstruction, resulting in tachypnea, chest wall retraction, and increased breathing effort. Thetypicaln lesions causing these symptoms to include left heart obstructive lesions (present with systemic hypoperfusion or collapse), transposition of the great arteries (TGA) (present with severe cyanosis), obstructed TAPVR (presents with severe cyanosis), and truncus arteriosus (presents with mild cyanosis). Simple left-to-right shunt lesions such as ASD, VSD, and AVSD rarely cause severe respiratory distress or pulmonary oedema because of the relatively high pulmonary vascular resistance in the neonatal period. [12,13]

## 5. Early Detection

### Fetal Echocardiography

Early detection of critical CHD at the prenatal period by fetal echocardiography can reduce morbidity and mortality. However, early prenatal detection is still tricky because fetal echocardiography facilities are not widely available. Fetal echocardiography is indicated in high-risk pregnancies such as a family history of CHD or genetic disorders, the use of nonsteroidal anti-inflammatory drugs in the third trimester, exposure to cardiac teratogens (e.g., lithium, anticonvulsants), and TORCH infection during pregnancy. [18]

### Pulse Oximetry Screening

Pulse oximetry screening is a simple, non-invasive, and cost-effective test that has been universally implemented for early detection of critical CHD in newborns. Pulse oximetry screening is performed 24-48 hours after birth to measure the proportion of haemoglobin in blood that is saturated with oxygen. The presence of hypoxemia or a difference between preductal and postductal saturation often precedes other signs or symptoms in newborns with critical CHD. [7]

There are seven types of critical CHD that are the primary target of pulse oximetry screening according

to the Secretary of Health and Human Service's Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC), including TGA, HLHS, pulmonary atresia with an intact ventricular septum, TOF, TAPVR, tricuspid atresia, and truncus arteriosus. Some other types of critical CHD that are classified as secondary targets, including CoA, interrupted aortic arch, double outlet right ventricle, Ebstein's anomaly, severe aortic stenosis, severe pulmonary stenosis, and single ventricular complex.[4]

Pulse oximetry screening is recommended for newborns ≥24 hours of age. Early screening may be done, but it has lower sensitivity and specificity because some types of critical CHD may not show hypoxemia and generally newborns still have low oxygen saturation level within the first 24 hours of life. There are no guidelines on how late a newborn can be screened, but screening should be done prior to discharge from the hospital. Screening should be performed in the right hand (preductal) and foot (postductal).[19] The algorithm for screening of critical CHD with pulse oximetry can be seen in **Figure 1.**
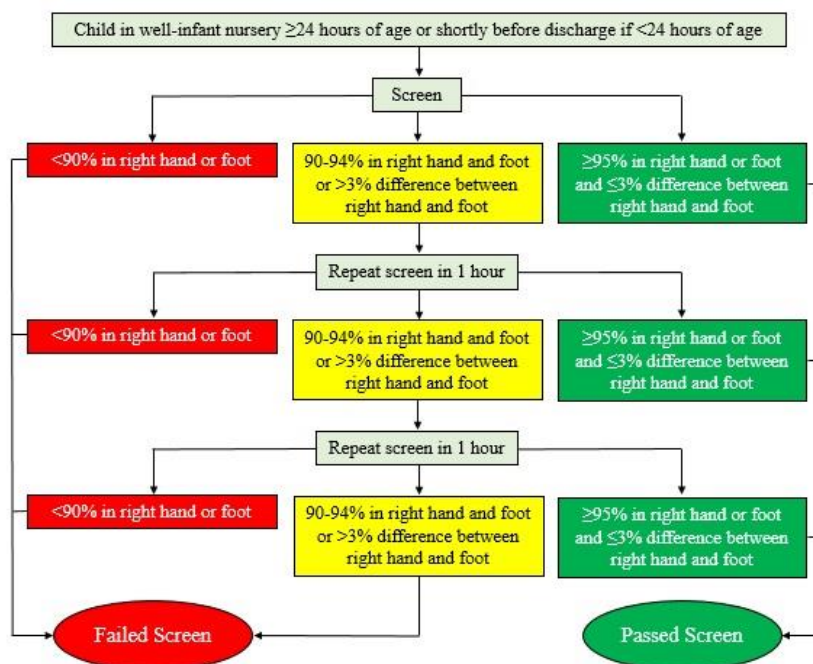


Figure 1. Algorithm for Pulse Oximetry Screening in the Newborns[20]

Typically newborns have an oxygen saturation of ≥95% after 24 hours of age. Pulse oximetry screening result is positive when an oxygen saturation of <90% is obtained in the right hand or foot. If the oxygen saturation is between 90-94% in the right hand and foot or there is a difference of >3% between the right hand and foot, the examination should be repeated in 1 hour, with a maximum of 2 repetitions. Infants who have positive screening result need echocardiography and should be referred to tertiary care centre with pediatric cardiology facilities for further evaluation and management after other possible causes of hypoxemia has been excluded. Infusion of prostaglandin can be given immediately if oxygen saturation is <90% with suspicion of critical CHD. Infants who have negative screening result can continue routine newborn care without further workup, but it should be kept in mind that negative screening result does not entirely exclude critical CHD.[21]

## 6. Diagnosis

Diagnosis is made based on history taking, physical examination, and supporting assessments

which include chest radiography, ECG, and echocardiography. Echocardiography is needed to make a definitive diagnosis of CHD. Hyperoxia test can help to differentiate between the cardiac and non-cardiac cause of cyanosis.[22]

### History of disease assessment

On history taking, it is essential to explore the presence or absence of risk factors for CHD, such as the family history of CHD, history of drugs consumed and the illness suffered by the mother during pregnancy. The risk of CHD increases if there is a history of CHD in the mother, father, or siblings. The history of antenatal examinations, such as ultrasound or fetal echocardiography, should be inquired. Perinatal events causing respiratory distress and cyanosis immediately at birth may lead to suspicion of non-cardiac cause. An uneventful delivery with sudden onset of shock or cyanosis after 24-48 hours of labour should lead to fear of duct-dependent circulation.[17,23]

### Physical examination

The physical examination should include vital signs, skin colour, heart murmur, upper and lower limb pulses, a sign of liver enlargement, and capillary refill time (CRT). Vital signs include preductal and postductal blood pressure, respiratory rate, body temperature, pulse oximetry measurement, and body weight. Afebrile infants with severe respiratory distress may raise suspicion of CHD. A femoral pulse that is absent or weaker than the brachial pulse may indicate CoA. Low perfusion with prolonged CRT may indicate a circulatory collapse in obstructive left heart lesions.[15]

CHD may occur in the presence or absence of a heart murmur. A heart murmur in infants can be physiological or pathological. Six cardinal signs suggest pathological murmur: pan systolic murmur, a grade of 3/6 or greater, punctum maximum at the upper left sternal border, harsh quality of the murmur, early midsystolic click, and abnormal second heart sound. The absence of murmur cannot rule out critical CHD, because murmur may not be found in some critical CHD such as TGA with an intact ventricular septum, obstructed TAPVR, HLHS, critical aortic stenosis, and acute pulmonary stenosis.[14,15]

### Hyperoxia Test

Hyperoxia test can be performed in critically ill infants with cyanosis to differentiate between the cardiac or pulmonary cause of cyanosis. This test is performed by measuring arterial blood gas while breathing room air, then re-measuring the arterial blood gas after the patient has lived 100% oxygen for 10 minutes. If the cause of cyanosis is a pulmonary problem, then the administration of 100% oxygen will increase the partial pressure of oxygen ($pO_2$) to above 150 mmHg. If the $pO_2$ remains below 100 mmHg, the cyanosis is probably caused by a shunting lesion that bypasses the lung, such as cyanotic CHD. The hyperoxia test should be performed carefully because 100% oxygen is a pulmonary vasodilator and it can exacerbate respiratory distress in infants with duct-dependent lesions by decreasing pulmonary vascular resistance and increasing pulmonary blood flow, resulting in pulmonary overcirculation.[15,24]

### Chest x-ray

A chest x-ray is needed to exclude pulmonary disease and also to evaluate the size or shape of the heart and pulmonary vascularization in cases of suspected CHD. Cardiomegaly may indicate CHD. Some CHD has characteristic features on chest x-ray, such as egg-on-a-string in TGA, boot-shaped in TOF, snowman appearance on TAPVR, hilar-waterfall in truncus arteriosus, rib notching in CoA, and box-shaped heart in Ebstein's anomaly. Pulmonary vascularity can be increased (plethora) in mixed lesions such as TGA, truncus arterious, and TAPVR. In contrast, pulmonary vascularity can be decreased (oligemia) in obstructive lesions such as tricuspid atresia, pulmonary atresia, and Ebstein's anomaly.[25,26]

### Electrocardiography

ECG can aid the diagnosis of CHD, especially when the echocardiography is not available. A variety of ECG changes can be used to identify structural abnormalities, such as axis abnormalities and cardiac hypertrophy. With increasing age, the axis changes from the right axis deviation to normal axis within the first six months of life. Superior axis deviation can be found in AVSD or ostium primum ASD. Right axis deviation with right ventricular hypertrophy can be found in TOF and its variants. Left axis deviation with left ventricular hypertrophy can be found in tricuspid atresia.[12,15]

### Echocardiography

Echocardiography is an essential tool to establish a definitive diagnosis of critical CHD and guide management strategies. Echocardiography can assess the structural abnormalities of the heart, volume/diameter of heart chambers, wall thickness, ventricular systolic and diastolic function, and valve pressure gradient. In cases of suspected critical CHD, echocardiography should be performed as soon as possible.[27]

### 7. Management

The initial management of the infant with suspected critical CHD should include hemodynamic stabilization, maintaining airway patency, providing respiratory support with oxygen administration and mechanical ventilation if necessary, intravenous access, initiation of prostaglandin E1 (PGE1/alprostadil) infusion as soon as possible to reopen the ductus arteriosus, and referring the infant to a tertiary care centre with pediatric cardiology services. In infants presenting with shock, intravenous fluids should be given immediately to increase preload. Inotropic support is required to increase systemic perfusion. Metabolic acidosis is corrected by giving bicarbonate. Empiric antibiotics should be considered in every critically ill infant. Echocardiography should be performed as soon as possible to confirm the diagnosis, but should not delay therapy. After the infant is stabilized, definitive intervention either through surgery or transcatheter should be done immediately to correct the underlying heart defect.[15,28,29]

Prostaglandin infusion is indicated as a brief therapy in neonates with critical CHD with duct-dependent circulation to maintain patency of the ductus arteriosus until definitive intervention can be done. The closed ductus arteriosus can be reopened within 30 minutes after initiation of PGE1. The opened ductus arteriosus will increase pulmonary or systemic circulation and improve the cyanosis and shock.[30] Potential side effects of prostaglandin include apnea, fever, seizure, hypotension, diarrhoea, and cortical hyperostosis, which are associated with high dose. However, these side effects are temporary and can be relieved by lowering the amount. Suppose there is no response to prostaglandin infusion. In that case, it is necessary to think about the possibility of a non-cardiac diagnosis or specific obstructive lesions such as obstructed TAPVR and TGA with intact ventricular septum, which requires emergency intervention.[17,31]

The dose of prostaglandin infusion is based on the patient's clinical presentation. It can be divided into four categories:

a. In an infant with TGA or duct-dependent circulation (left or right heart obstruction) who is diagnosed antenatally, the dose starts with 5-10 nanograms/kg/minute.

b. In a cyanotic infant who is non-acidotic and well with suspected duct-dependent circulation, the dose starts with 5-10 nanograms/kg/minute. If the response is low (no improvement in oxygen saturation and acidosis), the dose can be gradually increased every 20 minutes to a maximum of 100 nanograms/kg/minute.

c. An infant with a non-palpable femoral pulse who is non-acidotic and well, the dose starts with 10-15 nanograms/kg/minute. This infant may need a longer time to respond clinically. The dose can be gradually increased every 20 minutes to a maximum of 100 nanograms/kg/minute.

d. In an infant with acidosis and suspected duct-dependent circulation, the dose starts with 50 nanograms/kg/minute. This infant usually requires mechanical ventilation for severe hypoxemia, acidosis, or cardiorespiratory failure. The amount can be gradually increased to a maximum of 100-200 nanograms/kg/minute.[32]

During PGE1 administration, close monitoring of vital signs, oxygen saturation, and systemic perfusion is needed. The aim is to achieve palpable pulses, resolution of acidosis, and improvement of oxygen saturation (75-85%). After stabilization, the dose of PGE1 can be tapered off to the least effective dose that keeps the ductus arteriosus open. The infant then should be immediately consulted and referred to a tertiary care centre for further evaluation and management.[31,32]

## 8. Prognosis

Newborns with critical CHD are at increased risk of developmental disorders, disabilities, arrhythmias, heart failure, stroke, and sudden cardiac arrest.[9] The survival rate of newborns with critical CHD has been increased, but mortality is still high. Early diagnosis and management can improve the survival rate. The first-year mortality rate in infants diagnosed with critical CHD early (antenatal or predischarge from the hospital) is lower (16%) than those diagnosed after hospital discharge (27%).[33]

## 9. Conclusion

CHD is a structural abnormality in the heart or intrathoracic major blood vessel that is present at birth. Critical CHD refers to lesions that require early intervention in the first year of life to survive, either through surgery or transcatheter. Infants with critical CHD may develop cyanosis, respiratory distress, or shock within the first week of life when the ductus arteriosus closes. Pulse oximetry screening should be performed in newborns after 24 hours of age or before discharge from hospital for early detection of critical CHD. Infants with suspected critical CHD with duct-dependent circulation should immediately be given prostaglandin infusion to keep the ductus arteriosus open and maintain pulmonary or systemic circulation. Echocardiography is required as soon as possible to establish the diagnosis. After initial stabilization and management, the infant should be referred immediately to the tertiary care centre for definitive intervention.

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