PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DEFECTS IN ASYMPTOMATIC NEWBORN BABIES

BY

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Dissertation Submitted To

BLDE University, Vijayapur, Karnataka

In partial fulfilment of the requirements for the degree of

MD

IN

PEDIATRICS

Under the Guidance of

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2017

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ACKNOWLEDGEMENT

Words would not be sufficient to express my deepest gratitude and indebtedness to my honorable and esteemed teacher and guide **Dr. S.V.PATIL** $_{\textbf{MD}}$, Professor & H.O.D, Department of Pediatrics, an outstanding and revered teacher for his avid interest, unremitting encouragement and invaluable guidance throughout the course of my study. Indeed it's an honor for getting the opportunity to express my most sincere gratitude to him for his valuable suggestions given at all the steps of the study. Not only has he provided me with the analytical and conceptual tools to complete my study but he has also had a profound influence on both my personal growth and professional pursuits.

I am also extremely fortunate to have a caring, approachable and supportive department, who have advised and mentored me and made it conceivable for me to expedite this dissertation. I am thankful to Prof, **Dr.Bhavana. B**, Prof, **Dr.S.S. Kalyanshettar,** Prof, **Dr.R.H.Gobbur**, Prof, **Dr.A.S.Akki**, and Assoc. Prof, **Dr.M.M.Patil** for their congenial supervision, assiduous concern and positive feedback at all steps of this work.

My sincere thanks to all my batchmates, seniors and juniors who have helped and encouraged me during my work.Iam very grateful to all the non teaching staff of Department of Pediatrics, who has helped me during this work.

I am deeply indebted to my **parents** and all my **family members** for their help, constant encouragement and moral support that led me to successfully complete this dissertation work. Last but not the least**,** my sincere gratitude to all my study subjects whose cooperation has contributed to this study.

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LIST OF ABBREVIATIONS

ASD	**:**	Atrial septal defect
CCHD	**:**	Critical congenital heart disease
CHD	**:**	Congenital heart disease
COHb	**:**	Carboxyhaemoglobin
dTGA	**:**	Dextro - Transposition of the great arteries
ECG	**:**	Electrocardiogram
ECHO	**:**	Echocardiography
Hb	**:**	Haemoglobin
HLHS	**:**	Hypoplastic left heart syndrome
IMR	**:**	Infant motality rate
IVC	**:**	Inferior vena cava
LA	**:**	Left atrium
LED	**:**	Light emitting diode
LR+	**:**	Likelihood ratio of a positive test
LR-	**:**	Likelihood ratio of a negative test
LV	**:**	Left ventricle
MetHb	**:**	Methoxyhaemoglobin
NICU	**:**	Neonatal intensive care unit
Nm	**:**	Nanometre
NPV	**:**	Negative predictive value

P2	**:**	Pulmonary component of second heart sound
PBF	**:**	Pulmonary blood flow
PA	**:**	Pulmonary Artery
PDA	**:**	Patent Ductus Arteriosus
PPV	**:**	Positive predictive value
PS	**:**	Pulmonary stenosis
RA	**:**	Right atrium
RV	**:**	Right ventricle
RVOT	**:**	Right ventricular outflow tract
S1	**:**	First heart sound
S2	**:**	Second heart sound
Sn	**:**	Sensitivity
Sp	**:**	Specificity
SVC	**:**	superior vena cava
TAPVR	**:**	Total Anomalous pulmonary venous return
TOF	**:**	Tetralogy of Fallot
VSD	**:**	Ventricular septal defect

ABSTRACT

BACKGROUND AND OBJECTIVE

Congenital heart disease (CHD) is a leading cause of infant mortality, accounting for more deaths than any other type of malformation.[1]

The incidence of CHD varies between 4-10/1000 live births in India.[2]

About 1 in every 4 babies born with a heart defect has a critical congenital heart defect (critical CHD, also known as critical congenital heart disease).

This study was designed to screen for CCHD using pulse oximeter in the asymptomatic newborns admitted in the post natal ward and Correlate results with ECHO finding in pulse oximetry positive cases.

METHODS

In Asymptomatic new borns measurement of oxygen saturations using pulse oximeter on the Right hand and foot was carried out after 24hrs of birth . Saturations above 95% was regarded as having negative screen .Those with saturation below 90% were subjected to Echocardiography. Patients with saturations between 90 and 95 % were subjected to a second pulse oximetry screen 6-12 hrs later. Screening was done after 24 hrs of birth. Detailed clinical examination was done in all newborns after pulse oximetry. Any positive findings in CVS was noted. Those Newborns who have negative screen, were asked to report if any symptoms develop.

RESULTS

Out of total 400 neonates were screened and 7 cases of hypoxemia were identified.They were subjected to ECHO and4 had diagnosed to have critical

congenital heart disease (TGA,TAPVC,DORV) and two cases had ASD and one was normal.Negative screen did not report back with any symptoms.

The incidence of CCHD in the present study was found to be 1%.

The predictive value of a positive test of Pulse oximetry was found to be 57.1% in our study.

CONCLUSIONS

Pulse Oximetry is a cheap and simple test to screen for CCHD before they become symptomatic.

Key Words : CCHD, Pulse Oximetry, ECHO.

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INTRODUCTION

Congenital Heart Disease:

Congenital heart disease (CHD) is a leading cause of infant mortality, accounting for more deaths than any other type of malformation.[1] Congenital Heart Disease (CHD) is defined as a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially is of functional significance. This definition excludes functionless vascular anomalies like -persistent left superior vena cava, cardiomyopathies due to genetic defects, electrophysiological disturbances like long QT syndrome, WPW syndrome. The incidence of CHD varies between 4-10/1000 live births in India.[2]

About 1 in every 4 babies born with a heart defect has a critical congenital heart defect (critical CHD, also known as critical congenital heart disease). Critical congenital heart diseases consist of a subgroup of congenital heart diseases which needs surgery or catheter intervention in the neonatal period.[3]

Surgery greatly improves survival, particularly for infants with potentially life-threatening critical disorders.[2]If defects are not detected early, there is a risk of circulatory collapse, which can result in shock and acidosis with a substantial adverse effect on prognosis. [4-6]

Magnitude of Congenital Heart Disease

The average worldwide incidence of CHD is approximately 0.8% of live births.

There is wide difference in reported incidence worldwide, ranging from 4-50 per thousand live births. This largely depends upon the type of the study population

selected and mainly due to the results of variations in ascertainment methods.[7]The birth prevalence for CCHD is 2 - 3/1 000 live births globally. [8,9]

There is steep rise in prevalence of reported CHD due to prenatal sonographic examination and screening by echocardiography. Reporting by these screening tools may also detect CHD lesions of little clinical importance like small ASD, small muscular VSD etc.

The Indian scenario of CHD prevalence

According to a status report CHD accounts for 10% of the present infant mortality in India.[10]

There have been many studies some of them either hospital based or community based showing incidence of CHD varying from 0.8 to 5.2 cases per thousand births in India at different locations and incidence of various lesions has varied in these studies[10-16]

Impact of CHD/CCHD

About 2-3 in 1000 newborn infants will be symptomatic with a congenital heart disease in the 1st year of life. The diagnosis is established by 1 week of age in 40-50% of patients and by 1 month of age in 50-60% . Despite advances in both palliative and corrective surgery and increase in the number of survivors it still remains the leading cause of mortality in children with congenital malformations. [17]

CHD causes high morbidity and mortality among infants, and affects the quality of life during childhood and adulthood, depending on the progression of the disease. It also affects social interactions and the quality of life for parents of children with CHD.

Congenital heart defects are classified into two broad categories acyanotic and cyanotic.

Congestive heart failure is the primary concern in infants with acyanotic heart disease. In infants with cyanotic heart disease, hypoxia is more of a problem than congestive heart failure.

Suspicion of a congenital heart defect should be raised by the presence of feeding difficulties in association with tachypnoea, sweating over forehead and subcostal retractions, or severe growth impairment. [19]

If not diagnosed early in life, many of these defects may result in life threatening events or significant morbidity like end organ damage to major organs like kidneys, brain or eyes or congestive cardiac failure, cardiogenic shock and sudden death.

Sometimes when an infant is born, fetal (before birth) blood- pumping system can continue to work hiding the signs and symptoms of CCHD. This makes it possible for an infant with CCHD to appear healthy and be discharged home without knowing they have a heart defect[18.]

With early diagnosis of CCHD, Infants can benefit from successful surgical repair or palliation that is available with advances in paediatric cardiology. But missed or late CCHD diagnosis continues to be a clinical problem. [20,21,22]

Role and limitation of clinical examination

Although for more than 30 years of standard practice has called for clinical examination of the cardiovascular system as the routine newborn examination, studies suggest that routine cardiovascular examination misses nearly half the newborns with significant CCHD. Even though a thorough physical examination of every neonate is now universally accepted as a good practice it is apparent that an appreciable proportion of babies with congenital cardiac malformations are not detected by this routine examination.[23-25]

Heart murmurs, one of the hallmarks of noncritical heart disease diagnosed later in life may be absent or misleading because of the underlying variation in anatomy, prolonged decline of pulmonary vascular resistance or reduced ventricular function.[26]

For example, babies with an isolated interruption of the aortic arch may have no murmur while the ductus remains patent, would have normal femoral pulses. They would therefore be likely to pass a routine examination only to become rapidly and severely unwell within a few days as the duct closes.[23-25]

Diagnostic tools for CHD

a) Prenatal screening :

Studies suggest that 30 to 60 % of congenital heart defects can be detected prenatally by four-chamber screening. High- resolution four-chamber transvaginal echocardiography can provide detailed imaging of the cardiac anatomy in the fetus and can detect major abnormalities, although routine prenatal screening for CHD remains controversial. [27]

In one study, however, relying on only a four-chamber view would have resulted in overlooking 23 % of the defects. Detailed fetal echocardiography with outflow tract views can be particularly helpful in detecting anomalies of the great arteries and is indicated in pregnancies in which the risk of CHD is increased.[28]

b) Electrocardiogram :

An electrocardiogram (ECG) is indicated if CHD or an arrhythmia is suspected. However if the index of suspicion is high on the basis of other findings, a normal ECG does not exclude the presence of CHD.

c) Chest Radiographs :

Chest radiographs of an infant with congestive heart failure demonstrates cardiomegaly and increased or decreased pulmonary vascular markings. However it may not be conclusive during first few days of life.[29]

d) Echocardiography :

As all above modalities of diagnosis are inconclusive, definitive evaluation requires cardiac imaging by Echocardiography and it remains the primary diagnostic modality. Echocardiography is both sensitive as well as specific tool to diagnose CHD and CCHD but it requires costly equipment and skilled and trained personnel.

e) Cardiac catheterization

When echocardiography fails to provide confident evaluation of CHD, then diagnostic cardiac catheterization is performed at specialized centres with known risk to confirm diagnosis and for decision over further management.

f) Screening by pulse oximetry

Though Echocardiography is the gold standard for diagnosis of CCHD and can be performed by neonatologist or paediatric cardiologist with acceptable accuracy, it is not feasible as a routine screening test in most of the settings. Simple, cost effective, feasible, bedside screening test is thus required.

CCHD in the newborn may have low oxygen saturations unrecognized clinically.

Pulse oximetry is a well established, non invasive test for quantification of hypoxemia.

Use of this screening method for early detection of CCHD is based on clinically undetectable hypoxemia in potentially life-threatening cases. [30,18]. Improvement with early detection is particularly true for critical, duct dependent lesions in which closure of the ductusarteriosus can result in acute cardiovascular collapse and death.

Hence the need for a sensitive diagnostic tool at primary, secondary and tertiary care level units was long felt. The answer to this lies in screening of newborns with pulse oximetry after birth and confirmation with echocardiography[31,32]. In this scenario, we planned to study the effectiveness of pulse oximetry screening in detection of CCHD at our tertiary care hospital.

AIMS AND OBJECTIVES

(1) To screen for CCHD using pulse oximeter in the asymptomatic newborns admitted in the post natal ward.

(2) Correlate results with ECHO finding in pulse oximetry positive cases.

REVIEW OF LITERATURE

a)HISTORY OF PULSE OXIMETRY [33]

Oximetry is the measurement of oxygen saturation in arterial by transmitting light through a translucent area of a patient. This is done noninvasively and the oxygen saturation level is computed based on the measurement. This device is responsible for saving thousands of lives each year.

Before pulse oximeter, the oxygen saturation was measured by a painful arterial blood gas and it typically took a minimum of 20-30 minutes to obtain the result. This delay is not acceptable as severe brain damage can occur within 5 minutes of low oxygenation. According to reports, 2,000 to 10,000 patients died because of undetected hypoxemia per year and there is no estimation of patient morbidity.

The following briefly outlines the development of this important device.

1864: Geory Gabriel Stokes discovered that hemoglobin is the oxygen carrier in blood.

1935: Matthes developed the first oxygen saturation meter. It used a 2-wavelength light source with red and green filters, which was later changed to red and infrared filters.

1941: "Oximetry testing" is first used to measure oxygen saturation level with a pulse oximeter.

1940's: Millikan, a British scientist, used a dual light source to create the first practical aviation ear oxygen meter. During Second World War, many pilots were saved from under pressurized cabins by using oximetry testing.

1964: Hewlett Packard built the first ear oximeter by using eight wavelengths of light. The oximeter was used primary in sleep laboratories and in pulmonary functions. The unit was expensive, clumsy, and large.

1972: Takuo Aoyagi, a Japanese bioengineer at Nihon Kohden, developed a pulse oximeter based on the ratio of red to infrared light absorption in blood. He obtained a Japanese patent. Another Japanese research, Minolta, obtained an US patent based on the same concept. Oximetry became clinically feasible.

1981: Biox introduced the first commercial pulse oximeter. Initially it was focused on respiratory care and later expanded into operating rooms. Since then, other manufacturers have entered the market and the pulse oximeter technology has improved significantly.

1987: Pulse Oximetry becomes part of a standard procedure in administrating general anesthetic in US. The use of oximetry quickly spread to other hospital units, such as emergency rooms, recovery rooms, neonatal units, and intensive care units.

1995: Fingertip pulse oximeters first appeared on the market.

2000: Medicare accepted physiciansï¿½ billing for in-office oximeter readings.

2007: FDA published a notice in Federal Register (Vol. 72, No. 138 / Thursday, July 19, 2007) titled "Draft Guidance for Industry and Food and Drug Administration Staff; Pulse Oximeters Premarket Notification Submissions [510(k)s]; Availability" for comment by October, 2007. Shortly after, FDA approved pulse oximeters appeared on the market.

b)Magnitude of Congenital Heart Disease

The average worldwide incidence of CHD is approximately 0.8% of live births.

The incidence 0f CHD varies between 4-10/1000 live births in India[2].

c)FETAL CIRCULATION[34]

The knowledge of fetal and perinatal circulation i of vital importance in understanding various congenital heart diseases and their pathophysiology.

The placenta is the primary organ for nutrient and respiratory exchange between the maternal and fetal compartments however in adults all gas exchange occurs in the lungs.

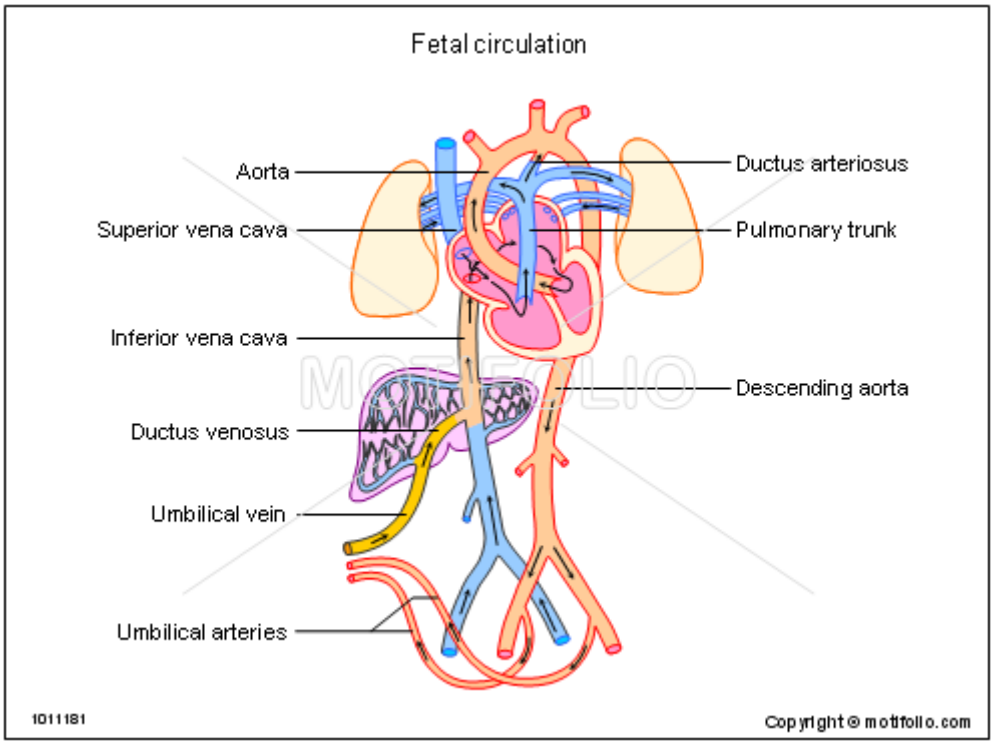
There are four shunts in fetal circulation:

- Placenta
- Ductus venosus
- Foramen ovale
- Ductus arteriosus

The placenta receives the largest amount of combined i.e., right and left ventricular output (55%) and has the lowest vascular resistance in the fetus.[34]

The superior vena cava (SVC) drains the upper part of the body (15% of combined ventricular output) and the inferior vena cava (IVC) drains the lower part of the body and the placenta (70% of combined ventricular output). [34]

Because the blood is oxygenated in the placenta, the oxygen saturation in the IVC (70%) is higher than that in the SVC (40%)



The highest P02 is found in the umbilical vein (32 mm Hg).[34] Most of the SVC blood goes to the right ventricle (RV). About one third of the IVC blood with higher oxygen saturation is directed by the crista dividens to the left atrium (LA) through the foramen ovale and the remaining two thirds enters the RV and pulmonary artery (PA).

The result is that the brain and coronary circulation receive blood with higher oxygen saturation (P02 of 28 mm Hg) than the lower half of the body (Po_2 of 24 mm Hg) Less oxygenated blood in the PA flows through the widely open ductusarteriosus to the descending aorta and then to the placenta for oxygenation.

Dimensions of Cardiac Chambers

Because the lungs receive only 15% of combined ventricular output, the branches of the PA are small. This is important in the genesis of the pulmonary flow murmur of newborns.[34]

The right ventricle (RV) is larger and dominant than the left ventricle (LV).

The RV handles 55% of the combined ventricular output, and the LV handles 45% of the combined ventricular output. In addition, the pressure in the RV is identical to that in the LV unlike in adults. Hence electrocardiograms (ECGs) of newborns show more RV force than adult ECGs.

Changes in Circulation after Birth:

The primary change in circulation after birth is a shift of blood flow for gas exchange from the placenta to the lungs. The placental circulation disappears, and the pulmonary circulation is established.

The fetal heart is unable to increase stroke volume when the heart rate falls because it has a low compliance. Therefore, the fetal cardiac output depends on the heart rate; if heart rate drops, as in fetal distress, a drastic fall in cardiac output results.

The changes are described in brief below:

I) The removal of the placenta results in the following:

a) An increase in systemic vascular resistance (SVR) because the placenta has the lowest vascular resistance in the fetus

b) Stoppage of blood flow in the umbilical vein causes closure of the ductus venosus

II) Lung expansion results in the following:

a) A reduction of the pulmonary vascular resistance (PVR), an increase in pulmonary blood flow, and a fall in PA pressure

b) Functional closure of the foramen ovale as a result of increased pressure in the LA in excess of the pressure in the right atrium (RA).

The RA pressure falls as a result of closure of the ductus venosus

c) Closure of patent ductus arteriosus (PDA) as a result of increased arterial oxygen saturation

The PVR is as high as the SVR at or near term. The high PVR is maintained by an increased amount of smooth muscle in the walls of the pulmonary arterioles and alveolar hypoxia resulting from collapsed lungs.

With expansion of the lungs and the resulting increase in the alveolar oxygen tension, there is an initial rapid fall in the PVR. This rapid fall is secondary to the vasodilating effect of oxygen on the pulmonary vasculature.

Between 6 and 8 weeks after birth, there is a slower fall in the PVR and the PA pressure and is associated with thinning of the medial layer of the pulmonary arterioles. [34]

Closure of the Ductus Arteriosus

Functional closure of the ductus arteriosus occurs within 10 to 15 hours after birth by constriction of the medial smooth muscle in the ductus.[34]

Anatomic closure is completed by 2 to 3 weeks of age by permanent changes in the endothelium and sub intimal layers of the ductus.

Important factors in closure of the ductus are:

- Oxygen
- Prostaglandin F2 (PGE2) levels
- Maturity of the newborn
- Acetylcholine and bradykinin also constrict the ductus

Oxygen and the Ductus.

A postnatal increase in oxygen saturation of the systemic circulation (from Po_2 of 25 mm Hg in utero to 50 mm Hg after lung expansion) is the strongest stimulus for constriction of the ductal smooth muscle causing closure of the ductus.

The responsiveness of the ductal smooth muscle to oxygen is related to the gestational age of the newborn.

The ductal tissue of a premature infant responds less intensely to oxygen than that of a full-term infant due to its decreased sensitivity to oxygen-induced contraction.

It may also be due to persistently high levels of PGE2 in preterm infants.

Reopening of a Constricted Ductus.

Before true anatomic closure occurs, the functionally closed ductus may be dilated by a reduced arterial Po2 or an increased PGE_2 concentration.

The reopening of the constricted ductus may occur in asphyxia and various pulmonary diseases as hypoxia and acidosis relax ductal tissues. Ductal closure is delayed at high altitude. There is a much higher incidence of PDA at high altitudes than at sea level.

Responses of Pulmonary Artery and Ductus Arteriosus to Various Stimuli

The PA responds to oxygen and acidosis in the opposite manner from the ductus arteriosus. [34]

STIMULUS	PULMONARY ARTERY	DUCTUS ARTERIOSUS
OXYGEN	Relaxes	Constricts
HYPOXIA	Constricts	Relaxes
ACIDOSIS	Constricts	Relaxes

Premature Newborns

Two important problems that premature infants may face are

- The rate at which PVR falls
- The responsiveness of the ductus arteriosus to oxygen

The ductus arteriosus is more likely to remain open in preterm infants after birth because premature infants' ductal smooth muscle does not have a fully developed constrictor response to oxygen.

In addition, premature infants have persistently high circulating levels of PGE2 caused by their decreased degradation in the lungs and the premature ductal tissue exhibits an increased dilatory response to PGE_2.

In premature infants, the pulmonary vascular smooth muscle is not as well developed as in full-term infants. Therefore, the fall in PVR occurs more rapidly than in mature infants. This accounts for the early onset of a large leftto-right shunt and congestive heart failure.[34]

Types of critical congenital heart disease (CCHD) defined as target lesions for pulse oximetry screening. [35]

Duct dependent systemic circulation:

- Interrupted aortic arch
- Complex/critical coarctation of the aorta
- Hypoplastic left heart syndrome
- Critical aortic valve stenosis

Duct dependent pulmonary circulation:

- Pulmonary atresia-various forms
- Variants of congenital heart disease with severe pulmonary stenosis/atresia
- Critical pulmonary valve stenosis

Total anomalous pulmonary venous drainage

Transposition of the great arteries

Complex cyanotic congenital heart disease

- Transposition of the great arteries-ventricular septal defect
- Functional univentricular heart-various forms

SPECIFIC CRITICAL CONGENITAL HEART DISEASES

HYPOPLASTIC LEFT HEART SYNDROME[36]

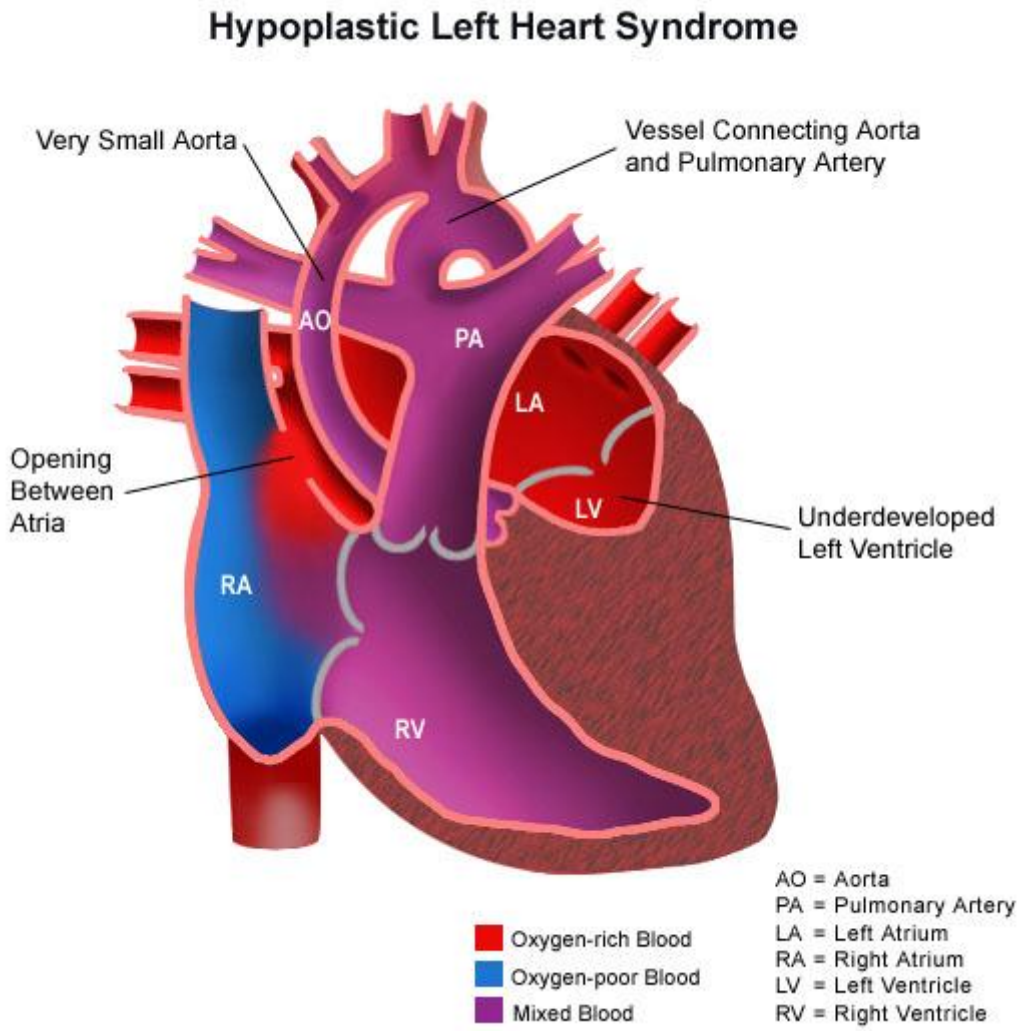
It is a related group of anomalies which include underdeveloped left side of the heart.

Atresia of the Aortic or Mitral orifice and Hypoplasia of ascending aorta

Left ventricle maybe: 1. Moderately hypoplastic

2. Very small and non functional

3. Atretic



Hence in neonate the right ventricle maintains both pulmonary and systemic circulation via ductus arteriosus.

Pulmonary venous blood passes via an ASD or dilated foramen ovale from left to right atrium and mixes with systemic circulation. Ventricular septum is usually intact.

Hence it is a total mixing lesion.[36]

The major abnormalities are:

- Inability to maintain systemic circulation
- Pulmonary overcirculation or pulmonary venous hypertension, depending on atrial level communication.

CLINICAL FEATURES

- Cyanosis
- Poor or absent peripheral pulses and perfusion
- Shock
- Respiratory distress
- Right parasternal heave
- Nondescript systolic murmur
- Non cardiac manifestations of associated syndromes : Turners' syndrome, Edward syndrome, Patau syndrome, Holt Oram syndrome.

INVESTIGATIONS

XRAY CHEST: Cardiomegaly and increased pulmonary vascularity.

ECG: Prominent P wave, Right ventricular hypertrophy

ECHOCARDIOGRAM: Diagnostic modality of investigation

- Absent or small mitral valve and aortic root
- Small left chambers
- Dilated right chambers

On a Doppler there is retrograde flow of blood in ascending aorta via ductus arteriosus and absence of anterograde flow.

TREATMENT

Surgical therapy has been associated with improved survival.

Commonly employed surgical procedures in specialized centres are Norwood and Sano procedure.[36]

First stage repair is designed to construct a reliable source of systemic blood flow and to limit pulmonary blood flow to avoid heart failure or pulmonary vascular disease.

Preoperatively it is important to maintain patency of ductus arteriosus using prostaglandin- infusion.

Third stage repair, which can be performed at 2-3 years of age aims at directing all systemic venous return to pulmonary circulation

PROGNOSIS

Untreated patients mostly succumb by 1st or 2nd week of life.[36]

Upto 30% of patients are reported to have major or minor central nervous system abnormality and upto 40 % have other dysmorphic features.[36]

Long term follow up after Norwood procedure shows reduced neuro developmental outcome. The exact reason for this is poorly understood. [36]

TRANSPOSITION OF GREAT ARTERIES[37]

Complete transposition of the great arteries (D-TGA) is one of the most common cyanotic congenital heart defect in newborns.

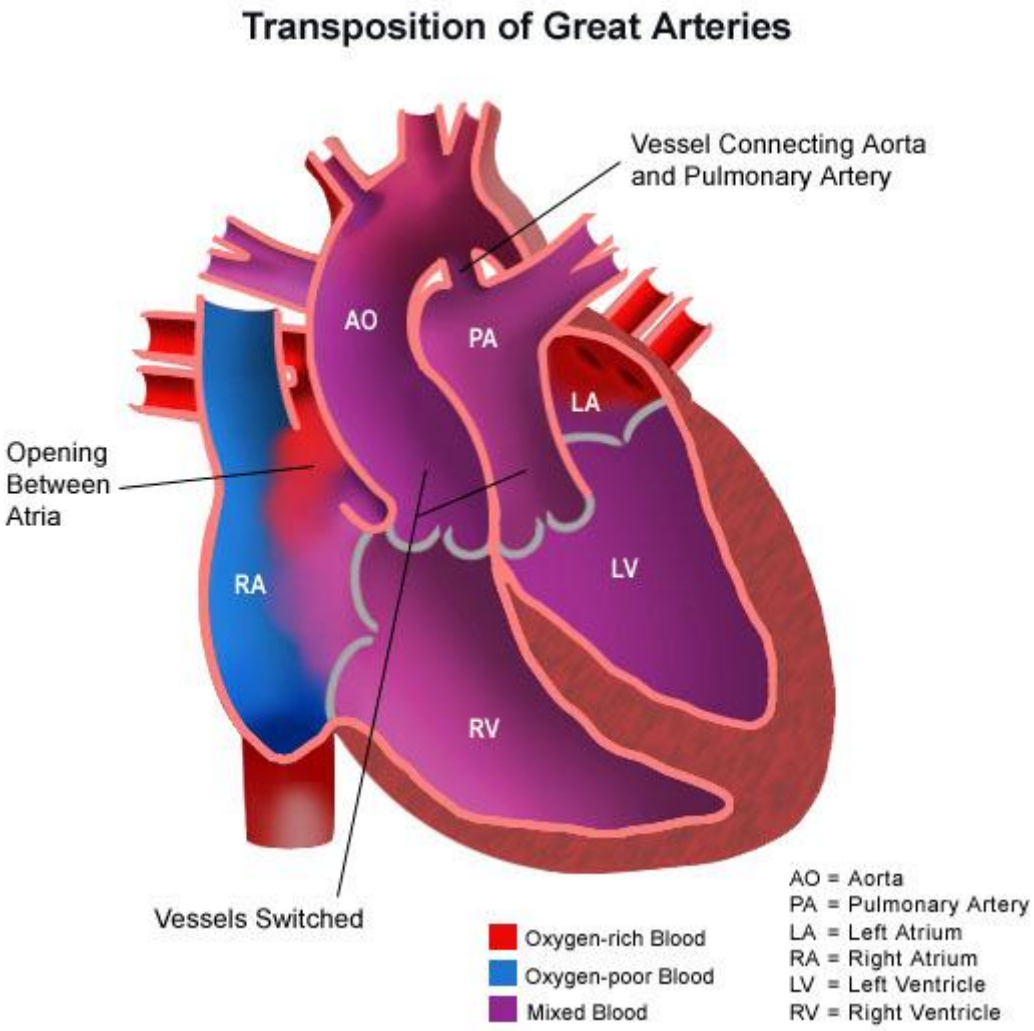
In this condition, the aorta arises from the RV and PA arises from LV.

As a result, the normal anteroposterior relationship of the great arteries is reversed.

The aorta is anterior to the PA (transposition), but the aorta remains to the right of the PA. Thus, the prefix D is used for dextroposition.[37]

In levo-transposition of the great arteries, L-TGA, or congenitally corrected TGA, the aorta is anterior to and to the left of the PA therefore, the prefix L is used.[37]

The atria and ventricles are in normal relationship. The coronary arteries arise from the aorta, like in a normal heart.



Desaturated blood returning from the body to the RA flows out of the aorta without being saturated. Well-oxygenated blood returning to the left atrium (LA) flows out of the PA and returns to the LA.

This results in a complete separation of the two circuits. The two circuits are said to be in parallel rather than in series, as in normal circulation

This defect is incompatible with life unless communication between the two circuits occurs to provide the necessary oxygen to the body.

Communication can occur at the atrial, ventricular, or ductal level or at any combination of these levels.

Most frequently only a small communication exists between the atria, usually a patent foramen ovale (PFO)[37]

CLINICAL FEATURES

- Severe cyanosis
- Respiratory distress
- Metabolic acidosis
- Hypothermia
- Low oxygen saturation
- Usually no heart murmur is noticed in D TGA
- S2 is single

INVESTIGATIONS

XRAY CHEST - Cardiomegaly with increased pulmonary vascularity

ECG - right ventricular hypertrophy (normally seen in neonates)

TGA WITH ASD

The presence of a large atrial septal defect (ASD) is most desirable in infants with TGA.

When a large ASD is present, infants have good arterial oxygen saturation, as high as 80% to 90% because of good mixing. However it is found in very few cases.

It is the actual idea behind atrial balloon septostomy (Rashkind procedure)[37] .Although these infants are not hypoxic or acidotic cardiogenic heart failure develops because of volume overload to the left side of the heart.

Because the RV is the systemic ventricle, RVH becomes evident on the ECG.

TGA WITH VSD

When associated with a large ventricular septal defect (VSD), only minimal arterial desaturation is present, and cyanosis may be missed.[37]

Therefore, metabolic acidosis does not develop, but left-sided heart failure results within the first few weeks of life.

CLINICAL FEATURES - systolic murmur due to VSD, S2 is single

X-RAY CHEST - Cardiomegaly with increased pulmonary vascularity ECG- biventricular hypertrophy, right hypertrophy as right ventricle serves systemic circulation and left hypertrophy due to volume overload [37]

TGA WITH PULMONARY STENOSIS

With an associated pulmonary stenosis (PS), although the VSD helps good mixing, the volume of fully saturated blood returning from the lungs is inadequate.

Because PBF is not increased, the left cardiac chambers are not under increased volume work; therefore, cardiac enlargement and heart failure: do not develop.[37]

CLINICAL FEATURES

- Severe hypoxia
- Severe acidosis
- Ejection systolic murmur due to pulmonary stenosis
- Single S2

XRAY CHEST - normal heart size with decreased or no pulmonary vascularity

ECG - biventricular hypertrophy

TREATMENT

- Prostaglandin infusion
- Supportive management by correcting acidosis, hypoglycaemia, hypothermia
- Rashkind balloon atrial septostomy - can also be done for individuals with large VSD with poor mixing
- Arterial switch Jatene procedure - treatment of choice in D TGA with intact ventricular septum

TETRALOGY OF FALLOT[38]

Includes the following four abnormalities:

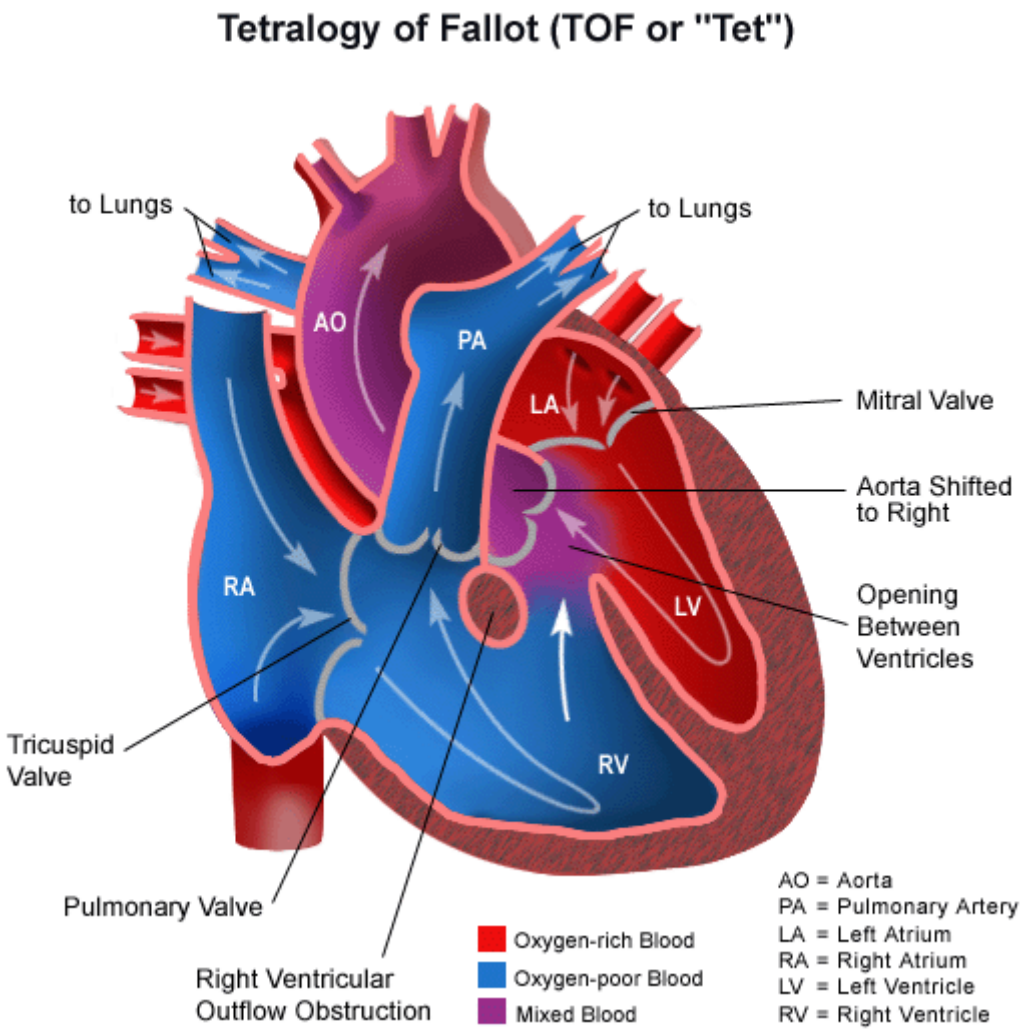
a. Ventricular septal defect (VSD)
b. Pulmonary stenosis (PS)
c. Right ventricular hypertrophy (RVH)
d. Overriding of the aorta

Physiologically TOF-requires only two abnormalities[38]:

- Large VSD- enough to equalize systolic pressures in both ventricles
- Stenosis of the right ventricular outflow tract (RVOT) in the form of
  - Infundibular stenosis
  - Valvular stenosis
  - or both

The direction and the magnitude of the shunt through the VSD is determined by the severity of the RVOT obstruction. With mild stenosis, the shunt is left to right, and the clinical picture resembles that of a VSD. This is called “acyanotic” or “pink TOF” - as cyanosis is minimum.[38]

With a more severe stenosis, the shunt is right to left, resulting in “cyanotic” TOF.



The pulmonary valve might be atretic with right to left shunting of the entire systemic venous return through the VSD.

Here the PBF is provided through a patent ductus arteriosus (PDA) or multiple collateral arteries arising from the aorta.

In TOF regardless of the direction of the ventricular shunt, the systolic pressure in the RV equals that of the LV and the aorta.

The size of VSD must be nearly as large as annulus of aortic valve to equalize pressures in both ventricles.[38]

CLINICAL FEATURES

- ❖ Cyanosis, which becomes more pronounced when baby is crying
- ❖ Difficult Feeding
- ❖ Failure to gain weight
- ❖ Poor development
- ❖ Squatting during episodes of cyanosis
- ❖ Varying degrees of cyanosis and clubbing are present.
- ❖ Apical impulse is shifted outwards. (RV tap)
- ❖ A systolic thrill felt at the upper and mid left sternal border.
- ❖ An ejection click maybe audible
- ❖ S2 is usually single (soft P2).
- ❖ A loud ejection systolic murmur is often heard in the upper left sternal border. This murmur originates from PS

In Acyanotic TOF there is : Ejection systolic murmur due to PS pansystolic murmur due to VSD

XRAY: Mild cardiomegaly with increased pulmonary vascularity

ECG : Right or both ventricle hypertrophy

In cyanotic TOF there is :	Severe cyanosis
	Ejection systolic murmur due to PS - harsh or soft depending on whether PS is moderate or large Single S2 i.e. P2
XRAY	No cardiomegaly with decreased pulmonary vascularity
EGG	Right ventricular hypertrophy
In TOF with pulmonary atresia:	Severe cyanosis
	No murmur
XRAY	Small cardiac shadow with decreased pulmonary blood flow
ECG	Right ventricular hypertrophy

COMPLICATIONS

- ❖ Cerebral thrombosis
- ❖ Bacterial endocarditis

TREATMENT

- ❖ Depends on severity of right ventricular outflow tract obstruction.
- ❖ Supportive therapy inform of prevention of hypothermia, hypoglycaemia dehydration
- ❖ Prostaglandin infusion if severe RVOT obstruction is present

- Corrective open heart surgery with severe RVOT obstruction, can be done at any age using resection of RVOT obstructing muscle and patch closure of VSD

- Modified Blalock Taussig aortopulmonary shunt

PROGNOSIS

Post operative survival rates improve however patients are pooled with problems like

- Decreased exercise tolerance
- Conduction disturbances
- Pulmonary regurgitation with right ventricular dilatation
- Bacterial endocarditis

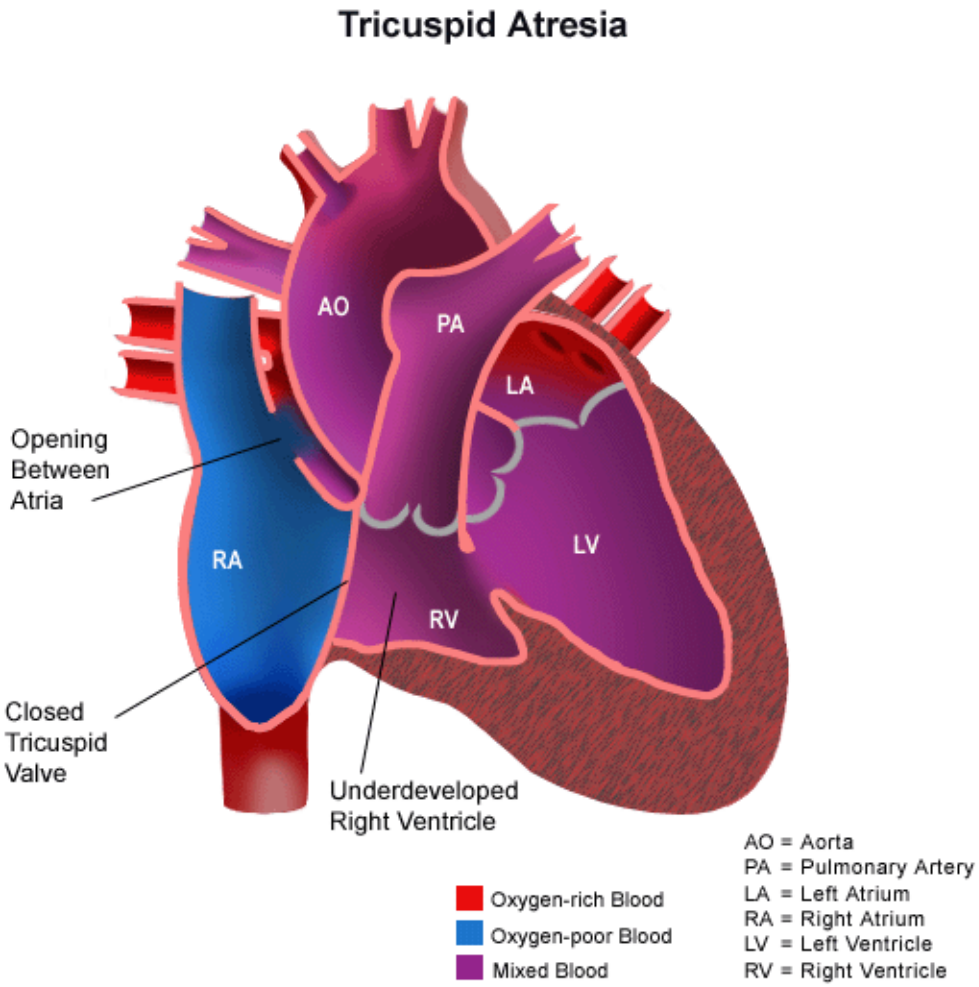
TRICUSPID ATRESIA[39]

Tricuspid atresia results from an abnormal development of the endocardial cushion tissue, that is, an incomplete shift of the common AV canal to the right. [39]

In tricuspid atresia, the tricuspid valve and a portion of the RV do not exist. Functionally no outlet from right atrium to right ventricle is present.

Because no direct communication exists between the RA and RV, systemic venous return to the RA must be shunted first to the LA through an ASD or PFO. Hence RA pressure is elevated in excess of the LA pressure, and enlargement of the RA occurs.

There is usually a VSD or PDA for the pulmonary arteries to receive some blood for survival.



The physiology of circulation and clinical features depend on presence of other associated defects like transposed great vessels.

In patients with normally related great arteries the pulmonary blood flow is generally reduced as it comes through a small VSD, hypoplastic RV, or small pulmonary arteries.

In infants with transposed great arteries the pulmonary blood flow is usually increased.[39]

Here the magnitude of pulmonary blood flow determines not only the level of arterial oxygen saturation but also the degree of enlargement of the cardiac chambers.[39]

CLINICAL FEATURES

- ❖ Variable presentations are noted.
- ❖ Profound cyanosis if great vessels are normally related.
- ❖ Holosystolic murmur parasternally
- ❖ Single S2

XRAY	Right atrial enlargement
	Concave pulmonary artery segment
	Decreased pulmonary vascularity
ECG	Left ventricular hypertrophy
	Left axis deviation

TREATMENT

Intravenous prostaglandin infusion

Blalock Taussig procedure

Pulmonary banding if unobstructed pulmonary flow and heart failure

Modified Fontan operation

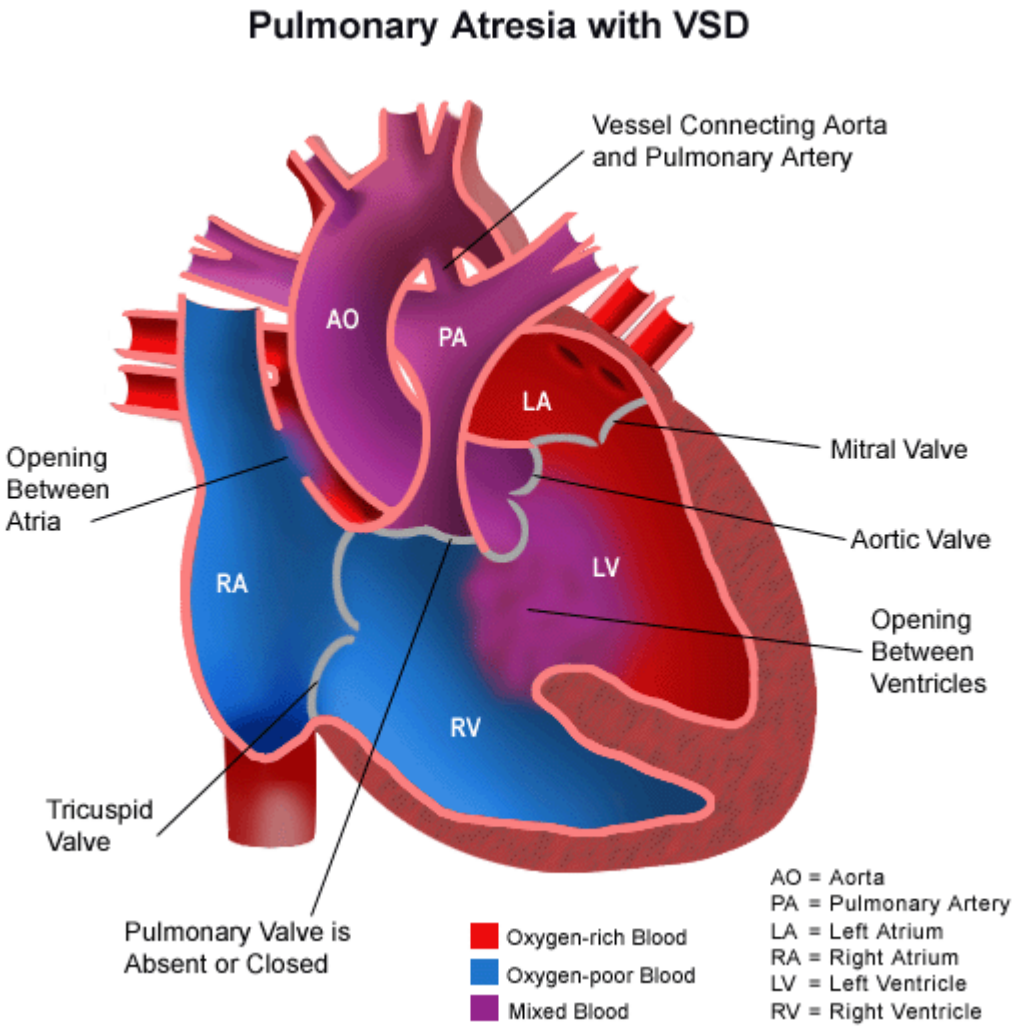
PULMONARY ATRESIA[39]

In pulmonary atresia direct communication between the RV cavity and the PA does not exist.

The PDA (or collateral arteries) is the major source of blood flow to the lungs. The systemic venous return to the RA must go to the LA through an ASD or a PFO. Hence the RA enlarges and hypertrophies to maintain a right-to-left atrial shunt.

The RV is usually hypoplastic with a thick ventricular wall.

Systemic and pulmonary venous returns mix in the LA and go to the LV to supply the body and lungs.



Because the PDA is the major source of PBF and it may close after birth, the PBF is usually decreased.[39]

When multiple collateral arteries are the only source of PBF, they are usually not adequate and PBF is reduced.

Therefore, the infant is severely cyanotic and the overall heart size is normal or only slightly increased.

Closure of the ductus results in a rapid deterioration of the infant's condition unless there are enough collateral arteries supplying PBF.

CLINICAL FEATURES

- Severe cyanosis
- Single S2
- Murmur of PDA

X RAY Pulmonary oligaemia

Normal heart size

ECG Left ventricular hypertrophy

TREATMENT

- Prostaglandin infusion
- If right ventricle is well developed - Surgical pulmonary valvulotomy or radioablation catheter and balloon valvuloplasty
- If right ventricle hypoplastic - Glenn and Fontan procedures

TOTAL ANOMALOUS PULMONARY VENOUS RETURN[39]

Here the pulmonary veins drain abnormally to the RA, either directly or indirectly through its venous tributaries.

An ASD is usually present to send blood from the RA to the LA.

TAPVR may be divided into the following three types:

1) Supracardiac: The common pulmonary vein drains to the superior vena cava through the vertical vein and the left innominate vein.

2) Cardiac: The pulmonary veins empty into the RA directly or indirectly through the coronary sinus.

3) Infracardiac (or subdiaphragmatic): The common pulmonary vein traverses the diaphragm and drains into the portal or hepatic vein or the inferior vena cava.

Physiologically there are only 2 types

1. Obstructive

2. Non obstructive

The infracardiac type is usually obstructive, and the majority of the cardiac and supracardiac types are non obstructive.

All forms of TAPVR involve mixing of oxygenated and deoxygenated blood before or at the level of right atrium Hence it is a total mixing lesion.

The mixed right atrial blood passes into right ventricle and pulmonary artery or into left atrium and left ventricle via an ASD or PFO thus being only source of systemic blood flow.

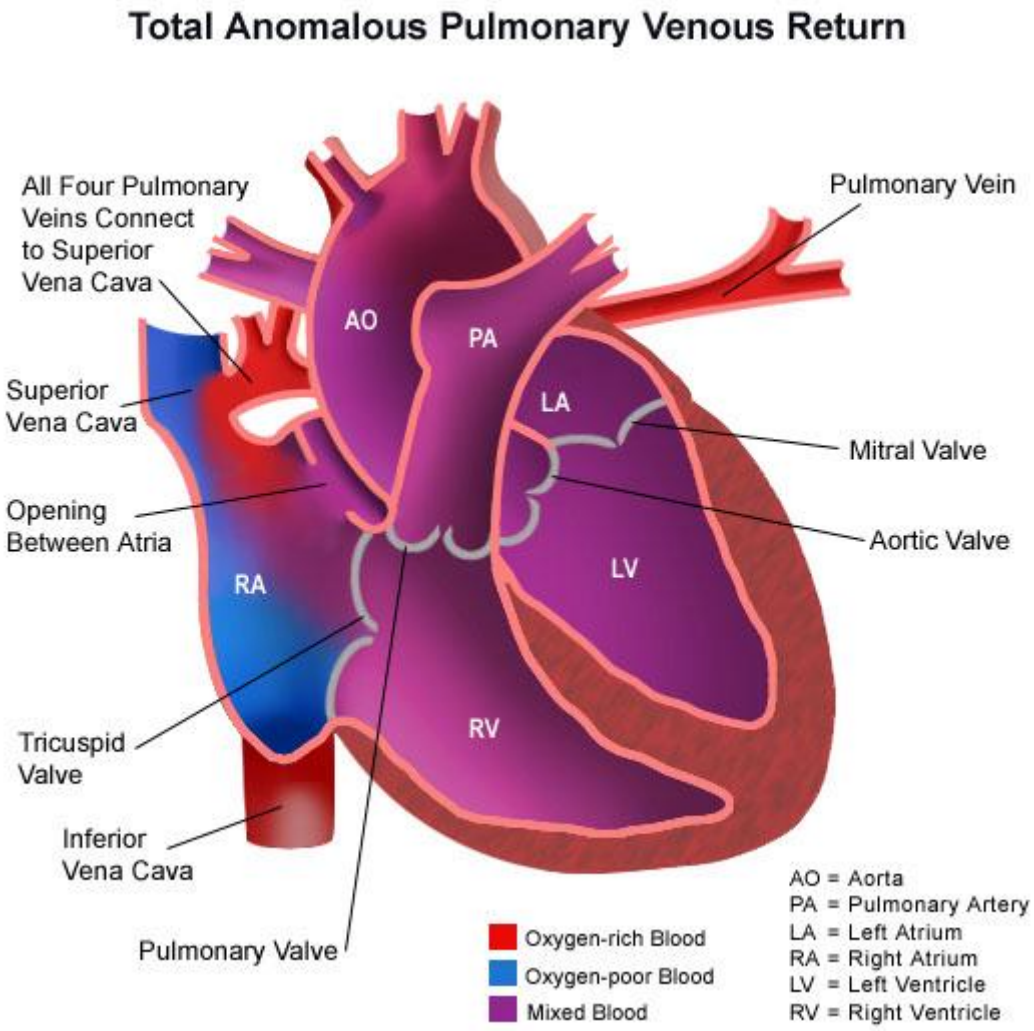


Fig. 20 TOTAL ANOMALOUS PULMONARY VENOUS RETURN

The clinical manifestations depend on the presence or absence of obstruction of venous channels. If pulmonary venous return is obstructed, severe pulmonary hypertension develops.

Obstructed TAPVR is a pediatric surgical emergency. Prostaglandin therapy is ineffective.

CLINICAL FEATURES

Obstructed TAPVR (Infracardiac):

- Severe cyanosis
- Respiratory distress
- Murmurs may or may not be present

Non obstructed TAPVR (Supra cardiac or cardiac):

- Cyanosis
- Moderate desaturation
- Systolic murmurs along left parasternal area
- Gallop rhythm

XRAY	Enlargement of RA, RV, prominent PA segment, increased pulmonary artery markings
ECG	Right ventricular hypertrophy
	Right bundle branch block

TREATMENT

- Surgically anastomosing pulmonary venous confluence into left atrium and interrupting any connection to systemic circuit
- If veno occlusive disease is present heart - lung transplant may be only option

PROGNOSIS

Long term prognosis is guarded.

Pulmonary vascular hypertension might develop post operatively

d)Pulse oximetry[40,41]

Pulse oximetry is useful monitoring tool as it is simple, non-invasive and accurate under most circumstances. It measures the percentage of haemoglobin in the arterial blood that is saturated with oxygen (SaO_2) along with pulse rate. Oxygen saturation is defined as the oxygen content expressed on percentage of oxygen capacity. If all haemoglobin molecules are bonded with the oxygen molecule (O_2), the total body haemoglobin is said to be fully saturated (between 97-100% reading). When haemoglobin dissosciates the oxygen molecule to tissue cells at capillary levels, the saturation progressively decreases and normal venous saturation is about 75%.

Cyanosis is very difficult to detect clinically because of variation in lighting conditions and variability among individual observers. Cyanosis and bradycardia are late signs of hypoxemia and pulse oximetry monitoring represents a very significant advancement in patient safety because even today physicians fail to detect severe arterial desaturation clinically. It is worth remembering that SP O_2 will not decrease until the PaO_2 is below 11.3 kPa (85 mm of Hg) because of shape of the oxygen disassociation curve.

Furthermore, when the low threshold alarm sounds as saturation falls below the default setting of 90 % in pulse oximetry, the corresponding Pa02 is 7.7 kPa (i.e. 57.8 mm of Hg) on the standard oxygen disassociation curve and as per definition denotes hypoxemia.

- **Hypoxemia -** is defined as an SaO_2 of 90 % or less = PaO_2 of 7.7 kPa or 58 mm of Hg

- **Severe Hypoxemia -** is defined SaO_2 of 85 % or less (= Pa O_2 6.7 kPa or 50 mm of Hg)

Principle of pulse oximetry

Oxygen breathed in through the lungs attaches to red blood cell protein haemoglobin. The newly oxygenated blood then circulates to the tissues. Arterial haemoglobin saturated with oxygen is bright red and venous haemoglobin with less oxygen is darker with different light absorption wave lengths. Thus pulse oximetry is based upon two physical principles.

a) Light absorbance of oxygenated haemoglobin is different from that of reduced haemoglobin as the oximeter's two wavelengths of light which include red and infrared light.

b) The absorbance of both wavelengths has a pulsatile component, which is due to fluctuation in volume of arterial blood between the source and the detector. Given these two facts, clever engineering techniques have produced an invaluable monitor for oxygenation, evolved over last 70 years.

Modern pulse oximetry was borne with the realization that pulsatile changes in light transmission through living tissue are due to alteration of the arterial blood volume in the tissues. Measurement of pulsatile components would eliminate the variable absorption of light by bone, tissue, skin pigment etc. from analysis. The most important fact of pulse oximetry therefore, is that only pulsatile absorbance between the light source and photo detector is that of arterial blood.

Two wavelengths of light used are 660 nanometer (red) and 940 nm (near infrared). At the 660 nm, reduced haemoglobin absorbs about ten times as much light as oxyhaemoglobin. At the infrared wavelength (940nm), the absorption coefficient of oxyhaemoglobin is greater than that of reduced haemoglobin.

The pulse oximeter directly senses the absorption of red and infrared light and the ratio of pulsatile to non-pulsatile light of the red and infrared wavelengths are translated through complex signal processing to a function of the arterial oxygen saturation through this spectral analysis.

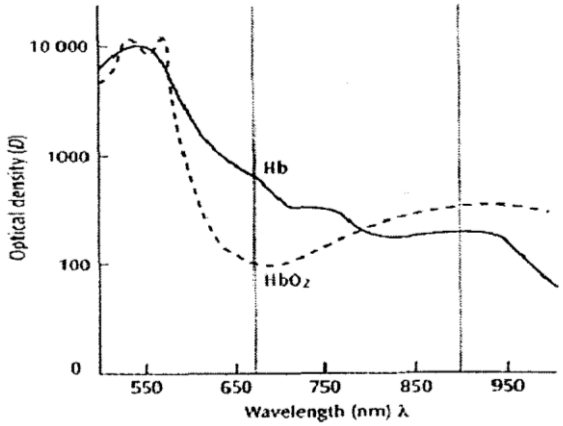


Fig: 1 Absorption spectrum of reduced (Hb) haemoglobin (Solid line) and oxygenated (HbO_2) haemoglobin (dashed line). D is the optical density (an index of the opaqueness of the medium) and A is the wavelength in nanometers. 810 nm is one of the isobestic points at which the absorbance of the two forms of haemoglobin is the same. The two vertical lines denote wavelengths in the red and infrared parts of the spectrum used by the light-emitting diodes of pulse oximeters.

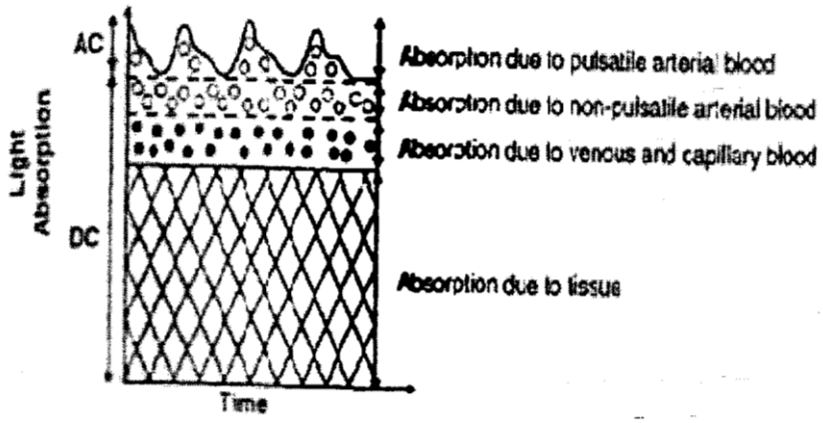


Fig: 2 shows that the pulsatile (AC) and non pulsatile (DC) components of light absorption can be separated

The pulse oximetry combines two technologies of:

1) Spectrophotometry
2) Optical Plethysmography.

Spectrophotometry:

Measures haemoglobin oxygen saturation and the clinical applications are largely concerned with detecting and quantifying hypoxemia and

Optical Plethysmography:

Measures pulsatile changes in arterial blood volume at the sensor site. The pulse oximeters plethysmographic capability has been proposed as a monitor of circulatory adequacy. But it should be understood that pulsatile perfusion required to generate a pulse signal on a given pulse oximeter, is not either necessary or sufficient to guarantee adequacy of circulation for a given application. Plethysmographic wave form help clinicians distinguish an artificial signal from the true signal.

Physics behind pulse oximeter:

Detection of oxygen saturation of haemoglobin by spectro photometry is based on Beer-Lambert law, which relates the concentration of a solute to the intensity of light transmitted through a solution.

Thus, in a container of known dimension a concentration of known solute in clear solution can be calculated from the measurement of the intensity of transmitted and incident light of known wavelength.

If there is one solute, the absorption A is a product of path length (D), the concentration (C) and extinction coefficient (E) i.e. A = DCE.

Each solute has a specific extinction co-efficient for absorption of light at specific wavelength. The absorbance of different wavelengths is dependent on the different solute concentrations (reduced and oxygenated haemoglobin), and is detected by transmitting light of specific wavelengths across the solution and measuring the intensity on the sensor side.

Design of pulse oximeter

1) Modern pulse oximeters consists of a peripheral probe together with a microprocessor unit displaying a waveform, oxygen saturation and pulse rate.

2) Each pulse oximeter probe contain two LEDs which emit two wavelengths of light, through a cutaneous vascular bed. The probe is commonly placed on the digits or earlobe. A photo detector on other side measure the intensity of transmitted light at each wavelength from which oxygen saturation is derived

3) The microprocessor can select out the absorbance of the pulsatile fraction of blood i.e. that due to arterial blood (AC), from the non-pulsatile venous or

capillary blood and other tissue pigments (DC), thus eliminating the effect of tissue absorbance to measure the oxygen saturation of arterial blood.

From the proportion of light absorbed by each component of two frequencies it then calculates the ratio ('R') of pulse added absorbance. In the red region, oxyhaemoglobin absorbs less light than haemoglobin, while the reverse occurs in the infrared region.

The oxygenated haemoglobin allows red light to transmit through while the deoxygenated haemoglobin allows infrared to transmit through. The ratio of absorbencies at these two wavelengths is calibrated empirically against direct measurements of arterial blood oxygen saturation (SaO_2) in neonates and the resulting calibration algorithm is stored in a digital microprocessor within the pulse oximeter.

During subsequent use, the calibration curve is used to generate the pulse oximeter's estimate of arterial saturation (SpO_2).

In pediatric cardiology measurement of hypoxemia is used in:

- Detection of CCHD - the presence of clinically unsuspected hypoxemia is perhaps the most famous disclosure that pulse oximeter has made.
- To gauge pulmonary blood flow in medical and surgical management of infants with cyanotic CHD and decreased pulmonary blood flow.
- In post operative pediatric cardiac intensive care, a small decrease in oxygen saturation maybe first sign of pulmonary hypertensive crisis. Continuous monitoring permits adjustment of ventilator parameters.

Limitations of Pulse Oximetry

Pulse oximeter are sometimes unreliable in the newborn as minor changes in skin temperature as well as minor adjustments in contacts can cause motion artefacts and poor signal manifesting as:

1) "Low signal to noise ratio" and results in poor function with poor perfusion conditions. Most important limitation of pulse oximetry is that they are inaccurate in patients who need them the most. Eg. hypotension, hypothermia, low cardiac output, hypovolemia, peripheral vascular disease or during infusion of vasoactive drugs etc. often preclude detection of SpO_2 from fingers or at least delays detection of hypoxemia. In such situation ear probes may clearly detect SpO_2 or pulse oximeters with signal extraction technology may perform better during low perfusion states.

2) "Too much noise" due to motion, ambient light venous pressure waves, hyperaemia ,improper position etc. In these conditions incorrect SpO_2 with an erroneous heart rate may be displayed or may default to zero.

3) Difficulty in detecting high oxygen partial pressures - at high saturation levels small changes in saturation are associated with relatively large changes in PaO_2. Thus the pulse oximeter has a limited ability to distinguish high but safe levels of arterial oxygen from excess oxygenation which may be harmful, as in premature newborns.

4) Erratic performance with irregular rhythms e.g. rapid atrial fibrillation

5) Abnormal pulses - Venous pulsation like in tricuspid regurgitation cause low SpO_2 readings because a mixture of arterial and local venous oxygen saturation

levels is shown. Application of mild pressure on the sensors has been found to be effective in reducing venous artefacts as it appears to reduce or eliminate the venous volume is optically probed tissue

6) Optical shunting - when a sensor is applied poorly or lifted from the skin, some emitters light may reach the detector while not passing through perfused issues. This is optical shunting. Optical shunting results in artificial reduction in plethysmographic pulse amplitude since some of the detected light is never exposed to pulsating arterial blood content. Whether the shunting underestimates or overestimates the true SpO_2 depends upon whether the red or infrared signals are more strongly shunted.

7) Response time - Signal averaging time for pulse oximetry represents the amount of time used by device to calculate the displayed SpO_2 value

8) The shorter the signal averaging time, the more sensitive the device will be to changes in SpO_2 value. However, the device will also be more prone to false alarms due to artefacts or errors.

   Conversely, as the signal averaging time is increased, the number of alarm due to error or artefacts is decreased. But, the amount of time needed to detect true hypoxemia is increased (upto 1 mm.) because SpO_2 values are averaged over a long time.

9) Abnormal hemoglobin - COHb (Carboxy Hb) and Met Hb (Methoxy Hb) also absorb light as pulse oximeters two wavelengths and this leads to error in estimating the percentage of reduced and oxyhaemoglobin (functional haemoglobin saturation).

When presence of either of these dyshemoglobinemia is suspected, pulse oximetry should be supplemented by in vitro multi wavelengths co-oximetry (fractional haemoglobin saturation).

10) Failure to detect hypoventilation - Hypoventilation and hypercarbia may occur without a decrease in haemoglobin oxygen saturation, especially if patient is receiving high supplemental oxygen. So pulse oximetry cannot be relied upon to assess the adequacy of ventilation or to detect disconnection or oesophageal intubation.

11) Ambient light - if ambient light is very strong or is flickering at frequencies similar to that of LED, it may interfere with rate and saturation measurement. Opaque covering of the probe is helpful in minimizing the effects of ambient light.

12) Inaccurate readings at low saturation values - Within the oximetry memory is a series of oxygen saturation values obtained from experiments in human volunteers until saturation values of 80% were obtained. Since the microprocessor has no memory of values less than 80%, accuracy cannot be ascertained at low SpO_2 readings below 75- 80%.

Trends in Pulse Oximetry

Pulse oximetry can detect mild hypoxemia, which is characteristic for many forms of CCHD, and may not be recognised by clinical examination.[26]

It identifies cases of critical congenital heart defects that go undetected with antenatal ultrasonography.[42]

One-year survival for infants with critical congenital heart defects has been improving over time, yet mortality remains high. Survival has been greatest for those diagnosed after 1 day of age and may increase more with screening using pulse oximetry.[43]

Pulse oximetry is a safe, feasible method that adds value to existing screening in developed countries.[42] In light of clinical evidences, CCHD was added to the US Recommended Uniform Screening Panel for newborns in 2011.[44]

Studies have shown that even in UK the screening is found to be cost-effective for detection of cardiac defects. [45]

Scenario in developing countries

Non-cardiac disorders commonly identified by low oxygen saturation in the newborn period include congenital pneumonia and septicaemia, pulmonary hypertension of the neonate, meconium aspiration syndrome, and pneumothorax.

These disorders can be as life-threatening as CCHD and so their early recognition and treatment after pulse oximetry screening is an additional benefit of the procedure.

In the high infant mortality rate (IMR) areas, most of the neonatal deaths are attributed to preventable causes like pneumonia and birth asphyxia.

However, once the IMR values start declining due to improvement in these factors the proportion of childhood deaths due to congenital malformations like CCHD becomes more important. [8]

A prospective study on clinical utility of pulse oximetry for newborn CCHD screening was published from Kerala.[46] The feasibility of performing neonatal heart

surgeries with in-hospital mortality almost comparable to developed nations has also been already reported from Kerala. [47]

Hence, the focus has to shift towards early detection of critical CHD, more efficient transport of neonates with a CCHD to a tertiary centre before clinical deterioration and reducing the pre-operative morbidity.

Early detection of hypoxemia by pulse oximetry screening will also allow judicious allocation of scarce resources towards the management of infectious and respiratory disorders that substantially contribute to neonatal mortality and morbidity.[45]

Studies Related To Pulse Oximetry

Thangaratinam S et al conducted a metaanalysis in the year ,2012 and screened 552 studies and identified 13 eligible studies with data for 229421 newborn babies. The overall sensitivity of pulse oximetry for detection of critical congenital heart defects was 76·5% (95% CI 67·7–83·5). The specificity was 99·9% (99·7–99·9), with a false-positive rate of 0·14% (0·06–0·33). The false-positive rate for detection of critical congenital heart defects was particularly low when newborn pulse oximetry was done after 24 h from birth than when it was done before 24 h (0·05% [0·02–0·12] vs 0·50 [0·29–0·86]; p=0·0017).[48]

In another study done by Mahle et al, its been documented that screening should be performed with motion-tolerant pulse oximeters. It is appropriate to use either disposable or reusable pulse oximetry probes. Screening should not be undertaken until 24 hours of life or as late as possible if early discharge is planned to reduce the number of false- positive results[44]

In a study done by Mahle et al, it has been documented that pulse oximetry has gained wide acceptance as a noninvasive method to determine oxygen saturation (SpO2). The method does not require calibration and is able to provide instantaneous data that correlate well with blood gas measurements.[49]

Mebergalf et al conducted a study in all live born infants in Norway in 2005 and 2006 and arterial oxygen saturation (SpO2) was measured in apparently healthy newborns, with SpO2 < 95% was considered significant. Out of 57959 live births in the hospitals performing pulse oximetry screening, 50008 (86%) were screened. A total of 136 CCHDs (1.2 per 1000) were diagnosed, 38 (28%) of these prenatally. Of the CCHDs detected after birth, 44/50 (88%) were detected before discharge in the population offered pulse oximetry screening (25 by pulse oximetry), compared to 37/48 (77%) in the non-screened population ($p = 0.15$). Median times for diagnosing CCHDs in-hospital before discharge were 6 and 16 h after birth respectively ($p < 0.0001$). In the screened population 6/50 (12%) CCHDs were missed and recognized after discharge because of symptoms. Two of the six missed cases failed the pulse oximetry screening, but were overlooked (echocardiography not performed before discharge). If these cases had been recognized, 4/50 (8%) would have been missed compared to 11/48 (23%) in the non-screened population ($p = 0.05$). Of the cases missed, 14/17 (82%) had left-sided obstructive lesions.[50]

Turska A etal conducted a study in the year between 2007 - 2008 and from a population of 52,993 newborns were screened ,a group of 51,698 asymptomatic infants was isolated. CCHD was diagnosed solely by pulse oximetry in 15 newborns, which constituted 18.3% of all CCHD; 14 (0.026%) false positives were obtained and there were four false negative results. The sensitivity of the test was 78.9% and specificity 99.9%. The positive predictive value was 51.7% and negative 99.9%.[51]

Ewer AK have documented that even though Pulse oximetry screening is not a perfect test; with a sensitivity of around 75% for CCHD,14 it is clear that about a quarter of babies with these defects will not be detected. A combination with other routine screening procedures the vast majority of CHD cases will be identified.12 The commonest conditions missed by pulse oximetry are those causing obstruction to the aorta (eg, coarctation and interrupted aortic arch), which unfortunately are also frequently missed by antenatal ultrasound and routine examination.[52]

d)Echocardiography For Evaluation of Congenital Heart Disease[53,54]

Echocardiography refers to evaluation of cardiac structures and function with images and recordings produced by ultrasound. It is cost effective investigation which helps in arriving at accurate anatomical diagnosis upon which further management depends. In vast majority of cases surgery or trans catheter intervention is planned solely based on echocardiography.

There are four basic modes: B mode, Doppler and Colour flow imaging, M mode.

- B(Brightness) mode is also called 2 D ECHO, where the images are displayed real time in various shades of grey depending on their echo- reflectance.

- Doppler mode helps to evaluate the velocity of blood across valves and in the blood vessels.

- Colour flow imaging uses the Doppler's principles where the directions of blood is easily identified by colour coding (Blue Away Red Towards - 'BART'). If the blood flows towards the transducer, it is coded red and if it moves away, it is coded blue. Colour flow imaging also demonstrates whether the flow is laminar or turbulent.

- M mode is rarely performed mode in pediatric echocardiography. It refers to recording of the movement of intracardiac structures at a particular plane in single dimension like opening and closure of valves, movements of walls and septi. It displays a one dimensional slice of cardiac structures varying over time.

Three dimensional echocardiographic reconstruction is valuable for understanding cardiac morphology.

Each mode is not mutually exclusive but complimentary to each other. Higher the frequency of the ultrasound, higher is the resolution power and lower is the tissue penetration capacity. A transducer frequency of 8-12 MHz is ideal.

Sedation protocol

In neonates pharmacological sedation is seldom required. Feeding itself is good enough to keep the neonate quiet in majority of cases.

Standard Transducer Positions and Echocardiography Examination views in neonates

Echocardiography for congenital heart disease (CHD) requires the use of views that are not often used while performing echocardiography in adults. The systemic and disciplined use of these views to perform an echo for a patient with CHD provides a great deal of information and it is possible to provide a complete diagnosis in many neonates.

There are five views that are specifically useful for evaluation of CHD in neonates. Echocardiography examination is done in following order.

Started with

1) Subxiphoid (Sx) View then

2) Apical Four Chamber View (A4CV) is obtained followed by

3) Parasternal Long Axis View (PLAV) and Parasternal Short Axis View (PSAV).

4) High Parasternal Or Ductal View is evaluated and lastly

5) Suprasternal View is obtained.

In Parasternal Long View (PSLV), the pointer of transducer should be facing right shoulder. In all other views, the pointer should be facing to the left. The transducer has to be swept in horizontal and vertical planes in each location to assess the relation between various structures. In the screen, the image is displayed as a sector. The tip of sector is the site of transducer and conventionally it is at 12 o' clock position. However, in A4CV, the ventricles are displayed above and atria are displayed below with the conventional display. Anatomical correct image is obtained if the image is rotated so that the tip of sector is at 6 o'clock position, and assessment of chambers and vessels becomes easier.

It is recommended that echocardiography images should be displayed on the screen in the anatomically correct manner. For anatomically correct display the apex of the imaging sector is at the bottom of the screen in the subxiphoid and the apical views. This is different from what is commonly practiced by adult cardiologists. In each view, one has to optimize the gain and keep the colour sector smallest to region of interest.

Echocardiography for CHD requires systematic evaluation of number of structures. Familiarities with the structures that are visualized using these views provide useful framework for performing a complete study. There are several benefits of performing echocardiography in a disciplined fashion using a specific sequence starting with subxiphoid views to avoid chances of error and allows thorough identification of situs, chambers of heart, cardiac position and imaging of great vessels and pulmonary veins. [54]

Limitations of Echocardiography

There are situation where echocardiography has major limitations.

- In general, ultrasound tends to get scattered by air. It cannot, therefore be used to see vascular structures inside lungs.

- The reliability of echocardiogram is critically dependent on the presence of good window. A solid tissue in close proximity with the heart allows good transmission and provides an excellent view. The liver and thymus are examples of organs that provide acoustic windows and enable acquisition of good windows.

- The examination is subjective and operator dependent and needs special expertise in pediatric echocardiography with large learning curve and extensive training.

- Morphology of congenital lesions needs to be understood by a proper training programme of sufficient duration at center with exposure to many cases after obtaining basic skills in paediatric cardiology.

Sources of Error:

Echocardiography is a powerful tool and has the potential of identifying most forms of CHD with great precision. Core principles are:

1) Echo should be performed after clinical evaluation to ensure that clinical question is answered

2) Correct transducer and equipment is used.

3) Result of echo should be interpreted in context of clinical situation and should not be viewed in isolation

4) Echo diagnosis should be internally consistent for e.g. a small VSD cannot co-exist with severe pulmonary hypertension unless there is alternative explanation e.g. large PDA

5) The echo diagnosis should be comprehensive as per checklist because CHD often do not conform to predictable stereotypes and surprises are common place

6) Recognize limitations of echocardiography

Problem of missed or late CCHD diagnosis

CCHD is defined as CHD lesions that are ductal dependent or may require surgical or catheter intervention in the first month of life. [32].

Despite prenatal evaluation a significant proportion of newborns are not diagnosed after birth or before discharge. A study demonstrates that, between 1989

and 2004 in California USA, an average of 10 infants per year died from missed CCHD diagnosis.[32]

Mellander and Sunnegardh reported that the proportion of CHD cases detected only after discharge of newborn increased from 13% in 1993-1995 and 21% in 1996-1998 to 26% in 1999-2001.

This problem may be aggravated by recent trends of earlier discharge and other changes in postnatal care.[55]

The first manifestation of CCHD may be acute with circulatory collapse and the need for cardio-pulmonary resuscitation or death i.e. delayed diagnosis is associated with significant morbidity and mortality. [31]

The incidence of severe physiologic compromise resulting from previously unrecognised CCHD has been estimated to be 1 per 15,000 to 1 per 26,000 live births.

There is broad consensus now that screening for CCHD is warranted .[35] .However, there is controversy regarding the use of prenatal ultrasound, as close clinical observation during the transitional period and thorough physical examination alone may be sufficient for timely diagnosis of CCHD.

This may be true in certain specific settings of well equipped and resourceful tertiary centres but the prerequisites mentioned are probably not encountered in the majority of hospitals or maternity units.

For example in a study by April L Dawson et al birth hospital nursery level and CCHD type were found to be associated with late CCHD detection.[56]

MATERIALS AND METHODS

STUDY SETTING

The study was conducted in the post natal ward in the tertiary care hospital .

STUDY DESIGN

This was a hospital based prospective observational study. All neonates fulfilling selection criteria, born and admitted in postnatal ward during study period were included in the study.

STUDY METHOD

In Asymptomatic new borns measurement of saturations using pulse oximeter on the Right hand and foot was carried out after 24hrs of birth.[73] Saturations above 95% was regarded as having negative screen .Those with saturation below 90%were subjected to Echocardiography. Patients with saturations between 90 and 95 % were subjected to a second pulse oximetry screen 6-12 hrs later. Screening was done after 24 hrs of birth.

Detailed clinical examination was done in all newborns after pulse oximetry. Any positive findings in CVS was noted.

STUDY DURATION

This study was conducted over a period of one and half years beginning from October 2014 to April 2016.

SAMPLE SIZE

All asymptomatic consecutive neonates born during the study duration (including late preterm neonates) were included in the study.

The incidence of CCHD has been found to be ranging from 4-10/10000 in India. [2]

With the incidence of CCHD 0.9/100 population at 95% confidence interval and plus or minus one margin of error, the calculated sample size is 342.

$N = z\ alpha*p*(1-p)/d^2$

Therefore, a minimum of 342 cases were included in the study.

Where, N = sample size

p = incidence rate

d=margin of error plus or minus one

zalpha=z value at 95%

INCLUSION CRITERIA:

- All the asymptomatic newborn neonates (term and late preterm) delivered in the tertiary care hospital.
- Parents who gave informed consent.

EXCLUSION CRITERIA:

Newborn with respiratory symptoms and signs.

Newborn with symptomatic cardiac diseases

All neonates with prenatal sonographic diagnosis of duct dependent circulation

DATA COLLECTION

Neonates included in the study were asymptomatic neonates (term and late preterm) delivered in the tertiary care hospital. The study was commenced after obtaining clearance from the institutional ethical committee. Parents of all neonates were given written informed consent forms for this study and neonates of those who were unwilling were excluded from the study. All those neonates who had a diagnosis of duct dependent circulation on antenatal sonogram were also excluded.

Oxygen saturation was measured with "Nelcor Probe", which was held manually in both upper and lower limbs after 24 hours after birth. It was ensured that the baby's limbs were warm and a consistent wave form was noticed before final readings were taken. Pulse oximetry of Gold way Philips company ut 600a, was used. Two readings at 10 min interval were taken, mean of both was used .

Parental concern was taken into consideration before and after Pulseoximetry screening/ECHO. Anxiousness regarding the individual procedures were taken care of and its relevance was also explained in detail to the parents. Following the procedures, their queries were answered in terms of their understanding. Those babies with an ECHO suggestive of CCHD were given more parental attention with regard to nature and prognosis of condition and they were also given awareness regarding the need of higher centre referral.

Parents of Neonates with negative screen were explained to report in case of any symptoms related to heart disease or any other symptoms like bluish discolouration, inability to feed, swelling of body.

Interpretation of test

1) A pulse oximetry reading >95% was considered as test negative result.
2) A saturation value of < 90 % in right arm and right limbs or a difference of upper and lower limb value >3% was considered as test positive result and neonates were subjected to echocardiogram.
3) For a saturation value between 90-95%, oxygenation and warming of limbs were ensured and neonate was re-evaluated after six hours. If it is less than 90%, neonates were subjected to Echocardiogram (ESaote Mylab25Gold with Neonatal probe PA023E).

Cases with hypoxemia (<90%) were subjected to a detailed second clinical examination using examination of peripheral pulses, cyanosis, careful palpation, percussion and auscultation, chest radiograph, pulse oximetry and echocardiography.

STATISTICAL ANALYSIS

Statistical analysis of data was done by using descriptive and inferential statistics using Predictive Value of a Positive test.

Software used in analysis were:

- SPSS 17.0 version

RESULTS

Table 1: Distribution of neonates according to sex, gestational age and birth weight.

Characteristics	Frequency (n)	Percentage
Sex		
Male	225	56.2
Female	175	43.8
Gestation Age		
Late Preterm	14	3.5
Term	386	96.5
Birth Weight (gm)		
0-1500	1	0.2
1501-2000	11	2.8
2001-2500	112	28
2501-3000	180	45
3001-3500	68	17
>3500	28	7
Total	400	100
Mean birth weight : 2.77 ± 0.45 Kg		

A total of 400 newborns were included in the study. 56.2% of neonates were males and 43.8% of neonates were females.

Term gestation newborns were more in the study compared to late preterm gestation.

Among the birth weight distribution of the newborns in the study, those newborns in the weight range of 2501-3000 grams were maximum [n=180 (45%)]. The least number of newborns was for the weight range 0-1500 grams [n=1 (0.2%)].

Mean birth weight for the newborns of this study was 2.77 ± 0.45kg.

Figure 1a: Sex Distribution of the children

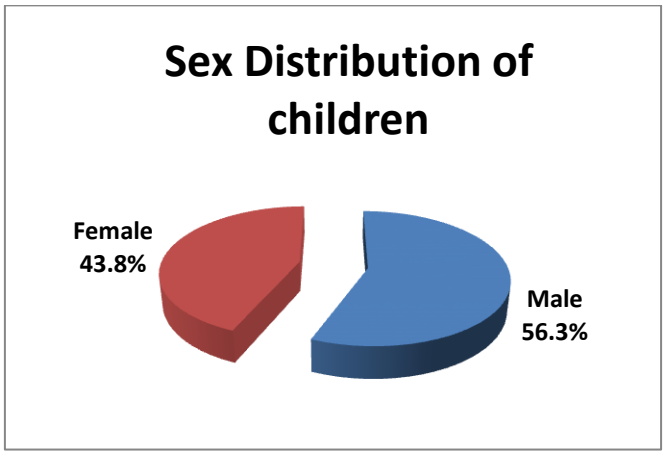


Figure 1b: Distribution of neonates according to Gestation Age

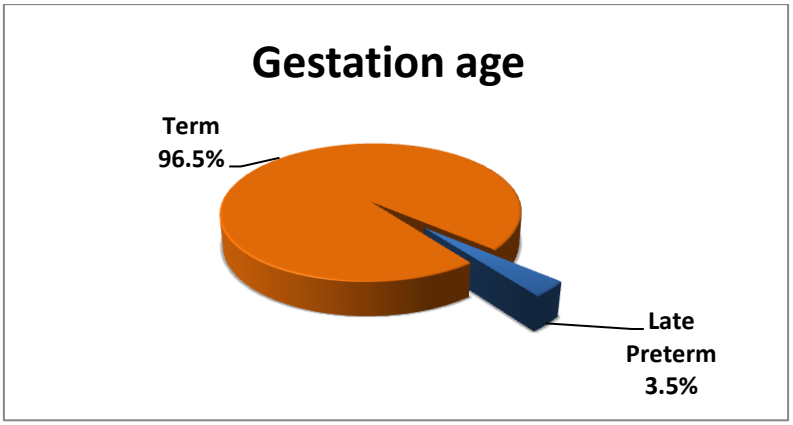


Figure 1c: Distribution of neonates according to Birth Weight (gm)

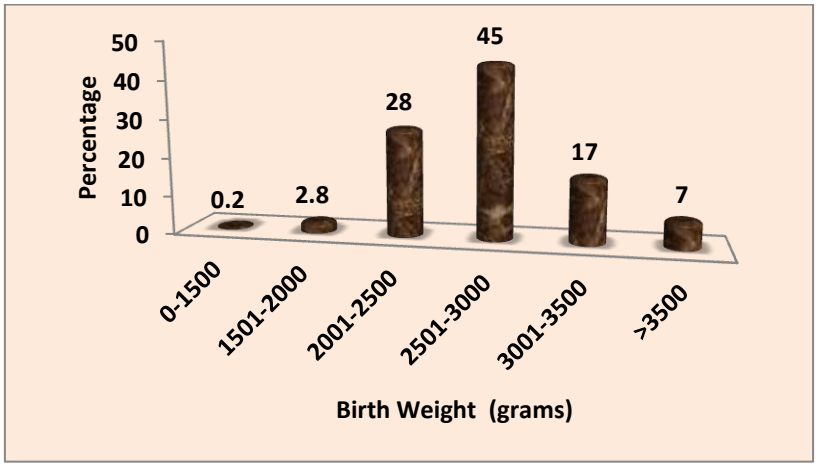


Table 2-Mean and SD of anthropometric parameters, heart rate, respiratory rate of study population

Characteristics	Minimum	Maximum	Mean	SD
Birth weight (gm)	900	4260	2770	450
Length (cm)	44	52	48.63	1.57
Head circumference (cm)	33	36	34.35	0.67
HR (beats per minute)	130	144	137.51	2.44
RR (cycles per minute)	32	46	38.58	1.87

Mean birth weight of neonates was 2770 ± 450grams with a maximum weight of 4260 grams and minmum of 900 grams.

Mean length was 48.63 ± 1.57 cm with a maximum length of 52cm and minimum of 44cm.

Mean head circumference was 34.35 ± 0.67cm with a maximum of 36cm and minimum of 33cm.

Mean heart rate of newborn was 138 ± 2 beats per minute.

Mean respiratory rate of newborn was 39 ± 2 cycles per minute.

Table 3: Distribution of neonates according tothe Pulse Oximetry Saturation

Pulse Oximetry Saturation	Frequency	Percent
<90%	7	1.8
90%-95%	3	0.8
>95%	390	97.5
Total	400	100

Figure 2a: Distribution of neonates according tothe Pulse Oximetry Saturation

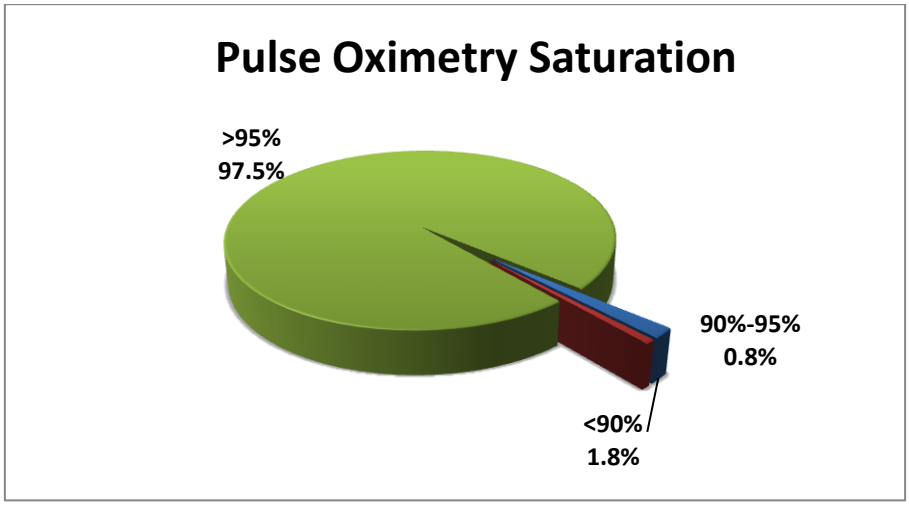
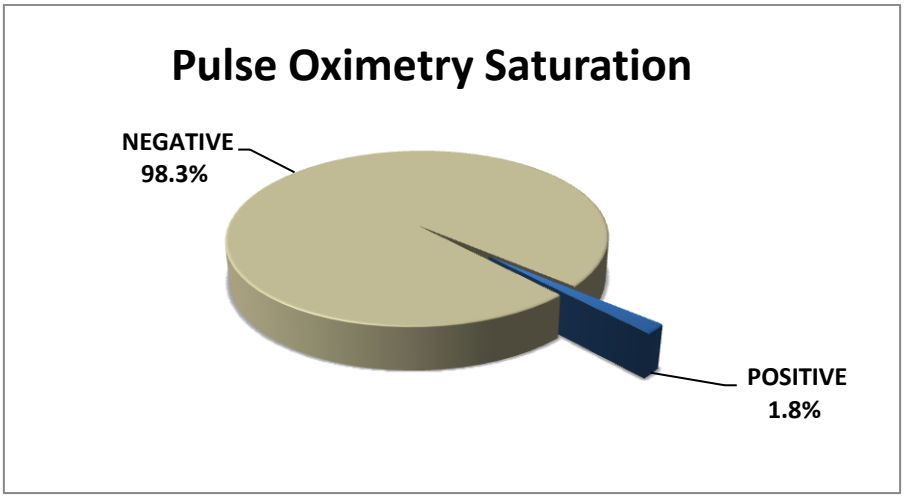


Figure 2b: Distribution of neonates according tothe Pulse Oximetry Saturation



In this study, those neonates who were subjected to pulse oximetry saturation test were found to have a saturation of >95% in 97.5% , 90-95% saturation in 0.8% and <90% saturation in 1.8%.

Table 4: Comparison of pulseoximetry findings with the anthropometric parameters, heart rate and respiratory rate of study population.

Characteristics	Pulse Oximetry Positive (Oxygen saturation <90%) [N=7]		Pulse Oximetry Negative (Oxygen saturation >90%) [N=393]		p value
	Mean	SE	Mean	SE	
Birth weight (gm)	2428	0.17	2772	0.02	0.044*
Length	48.93	0.60	48.62	0.08	0.613
Head circumference	34.43	0.23	34.35	0.03	0.759
HR	137.43	0.72	137.51	0.12	0.929
RR	38.57	0.57	38.58	0.09	0.996

Note *significant at 5% level of significance

Mean birth weight of neonates with pulseoximetry saturation of <90%, was significantly lesser (2428 ± 0.17 grams) than the mean birth weight of neonates with pulseoximetry saturation of >90% (2772 ± 0.02 grams).

There was no significant difference noted in the mean length, head circumference, heart rate and respiratory rates among pulse oximetry positive and pulseoximetry negative neonates.

Figure 3: Comparison of Mean Birth weight (gm)of neonates with the Pulse Oximetry saturation

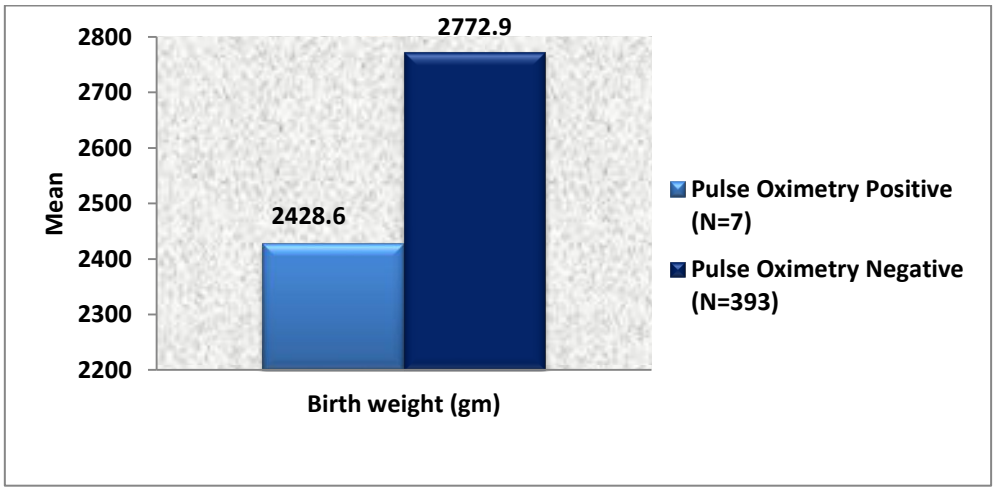
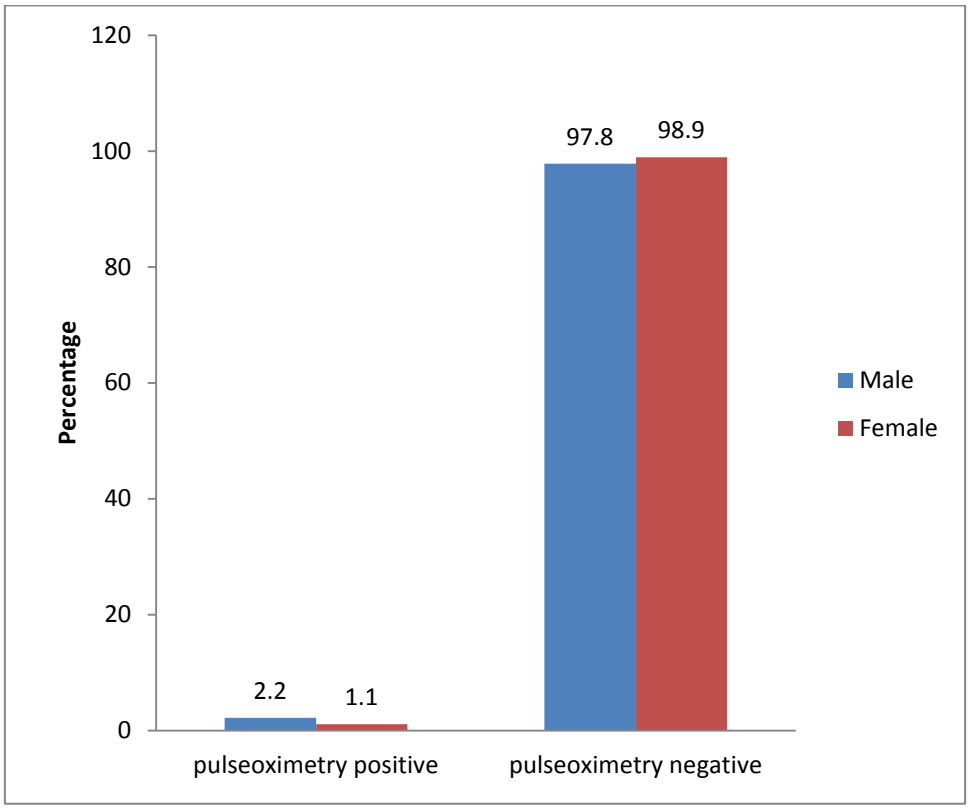


Table 5: Distribution of Pulse Oximetry Saturation according to sex of neonates

Sex of Neonates	Pulse Oximetry Positive (N=7)		Pulse Oximetry Negative (N=393)		Total	Chi square p value
	N	%	N	%		
Male	5	2.2%	220	97.8%	225 (100%)	<0.001*
Female	2	1.1%	173	98.9%	175 (100%)	

Note *significant at 5% level of significance

Figure 4: Distribution of Pulse Oximetry Saturation according to sex of neonates



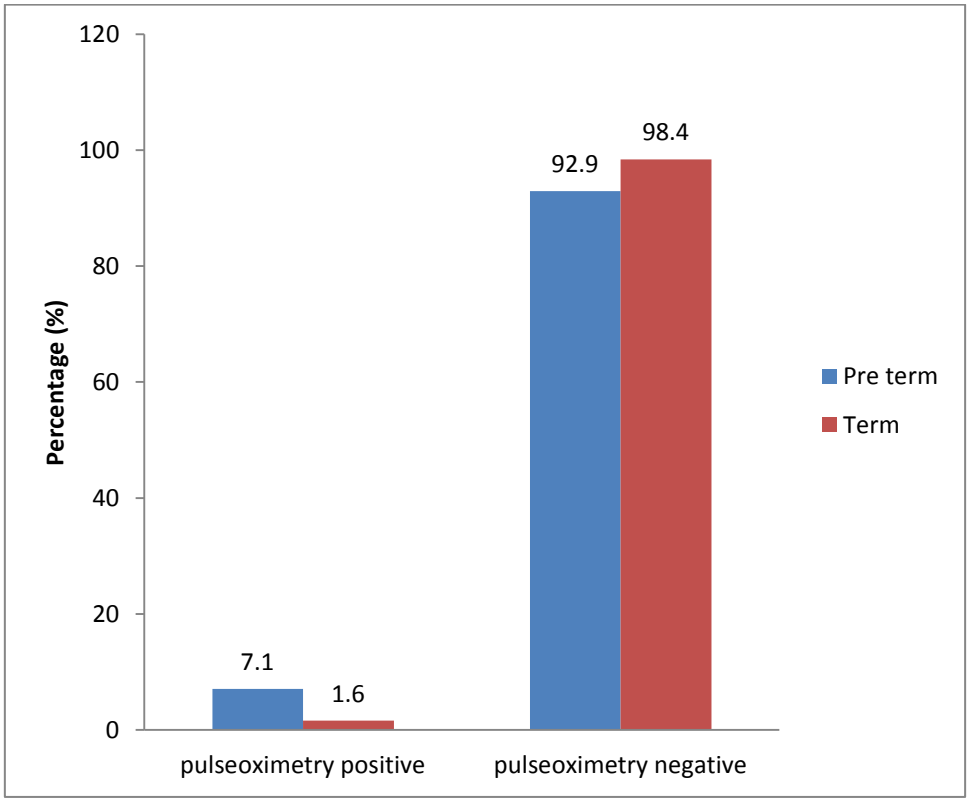
Higher percentage of male babies (2.2%) had positive pulse oximetry (O2 saturation <90%) when compared to female babies (1.1%). This association was found to be statistically significant.

Table 6: Distribution of Pulse Oximetry Saturation according to gestational age of neonates

Gestational age	Pulse Oximetry Positive (N=7)		Pulse Oximetry Negative (N=393)		Total	Chi square p value
	N	%	N	%		
Late Pre term	1	7.1%	13	92.9%	14 (100%)	<0.001*
Term	6	1.6%	380	98.4%	386 (100%)	

Note *significant at 5% level of significance

Figure 5: Distribution of Pulse Oximetry Saturation according to gestational age of neonates



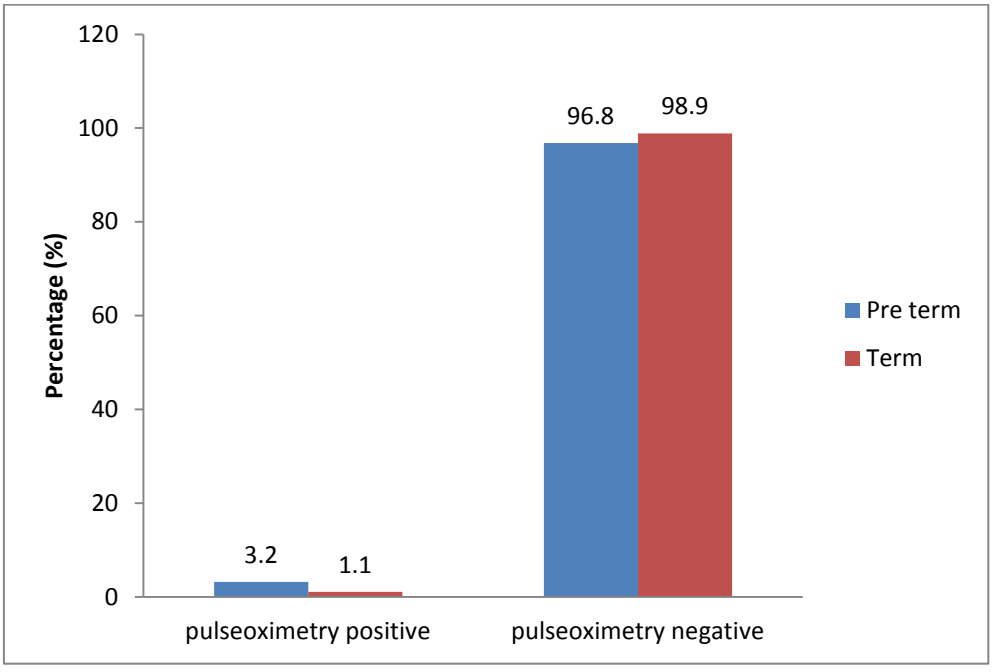
Higher percentage of Late pre term babies (7.1%) had positive pulse oximetry (O2 saturation <90%) when compared to term babies (1.6%). This association was found to be statistically significant.

Table 7: Distribution of Pulse Oximetry Saturation according to birth weight of neonates

Birth weight	Pulse Oximetry Positive (N=7)		Pulse Oximetry Negative (N=393)		Total	Chi square p value
	N	%	N	%		
LBW & very low birth weight	4	3.2%	120	96.8%	124 (100%)	<0.001*
>2500 gm	3	1.1%	273	98.9%	276 (100%)	

Note *significant at 5% level of significance

Figure 6: Distribution of Pulse Oximetry Saturation according to birth weight of neonates

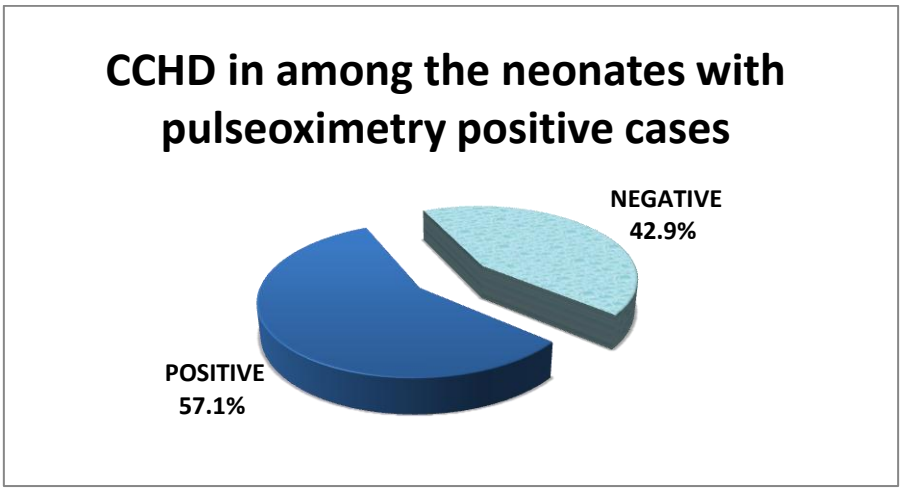


Higher percentage of Low birth weight and very low birth weight babies (3.2%) had positive pulse oximetry (O2 saturation <90%) when compared to babies with birth weight >2500grams (1.1%). This association was found to be statistically significant.

Table 8: Distribution of the CCHD among Pulse Oximetry positive cases (N=7)

CCHD	Frequency	Percent
POSITIVE	4	57%
NEGATIVE	3	43%
Total	7	100%

Figure 7: Distribution of CCHD among pulse oximetry positive cases



All 7 neonates with oxygen saturation of <90% in pulse oximetry were subjected to ECHO. It was found that 4 out of 7 neonates were diagnosed to be suffering from CCHD.

Table8 : CCHD incidence among the study population (N=400)

CCHD	Frequency	Percent
POSITIVE	4	1%
NEGATIVE	96	99%
Total	7	100%

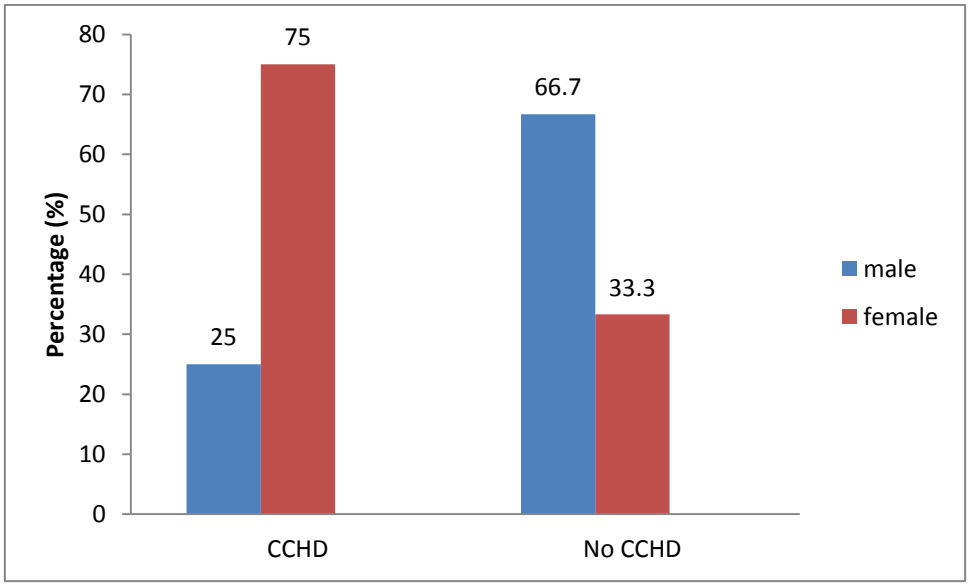
The incidence of CCHD in the present study was found to be 1%

Table 9: Distribution of CCHD according to sex of neonates

Sex of Neonates	CCHD POSITIVE (N=4)	CCHD NEGATIVE (N=3)	Chi square p value
Male	1 (25%)	2 (66.7%)	0.271
Female	3 (75%)	1 (33.3%)	
Total	4 (100%)	3 (100%)	
Male : Female	**1:3**		

Note *significant at 5% level of significance

Figure 8: Distribution of CCHD according to sex of neonates



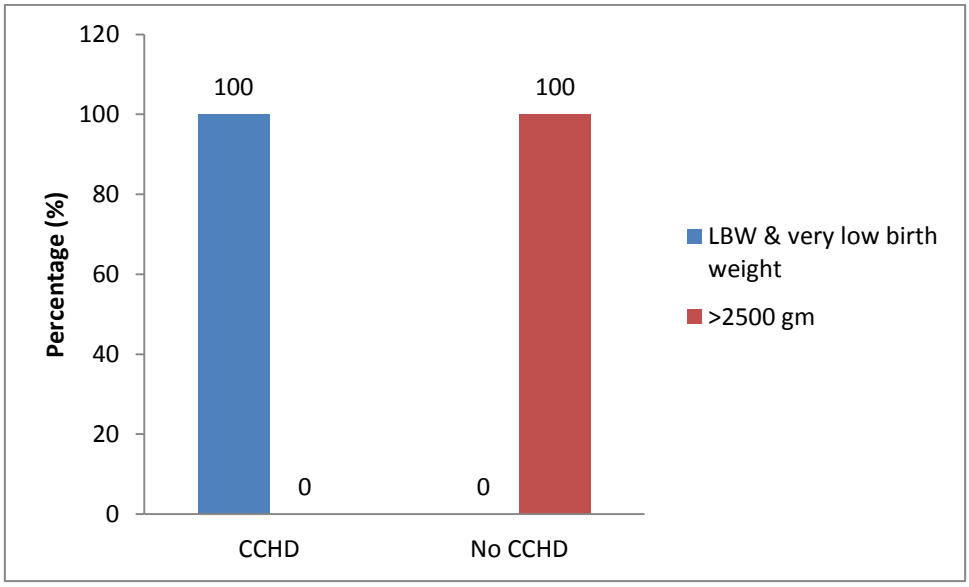
25% of neonates suffering from CCHD were males and 75% of neonates suffering from CCHD were females.

Table 10: Distribution of CCHD according to birth weight of neonates

Birth weight	CCHD POSITIVE (N=4)	CCHD NEGATIVE (N=3)	Chi square p value
LBW	4 (100%)	0 (0)	<0.001*
>2500 gm	0 (0 %)	3 (100%)	<0.001*
Total	4 (100%)	3 (100%)	

Note *significant at 5% level of significance

Figure 9: Distribution of CCHD according to birth weight of neonates



All 4 (100%) of neonates suffering from CCHD were Low birth weight babies. None of the babies who were born with birth weight of >2500gms were found to be suffering from CCHD. This association was statistically significant.

TABLE 11 : Predictive Value of positive test

	Pulse Oximetry Positive	**Pulse Oximetry Negative**	**Total**
CCHD POSITIVE	4	0	4
CCHD NEGATIVE	3	393	396
Total	7	393	400

True positive = 4

False positive = 0

True negative = 393

False negative = 3

True positive rate (Sensitivity)= TP/(TP+FN)

=57.14 %

False positive rate = FP/(FP+TN)

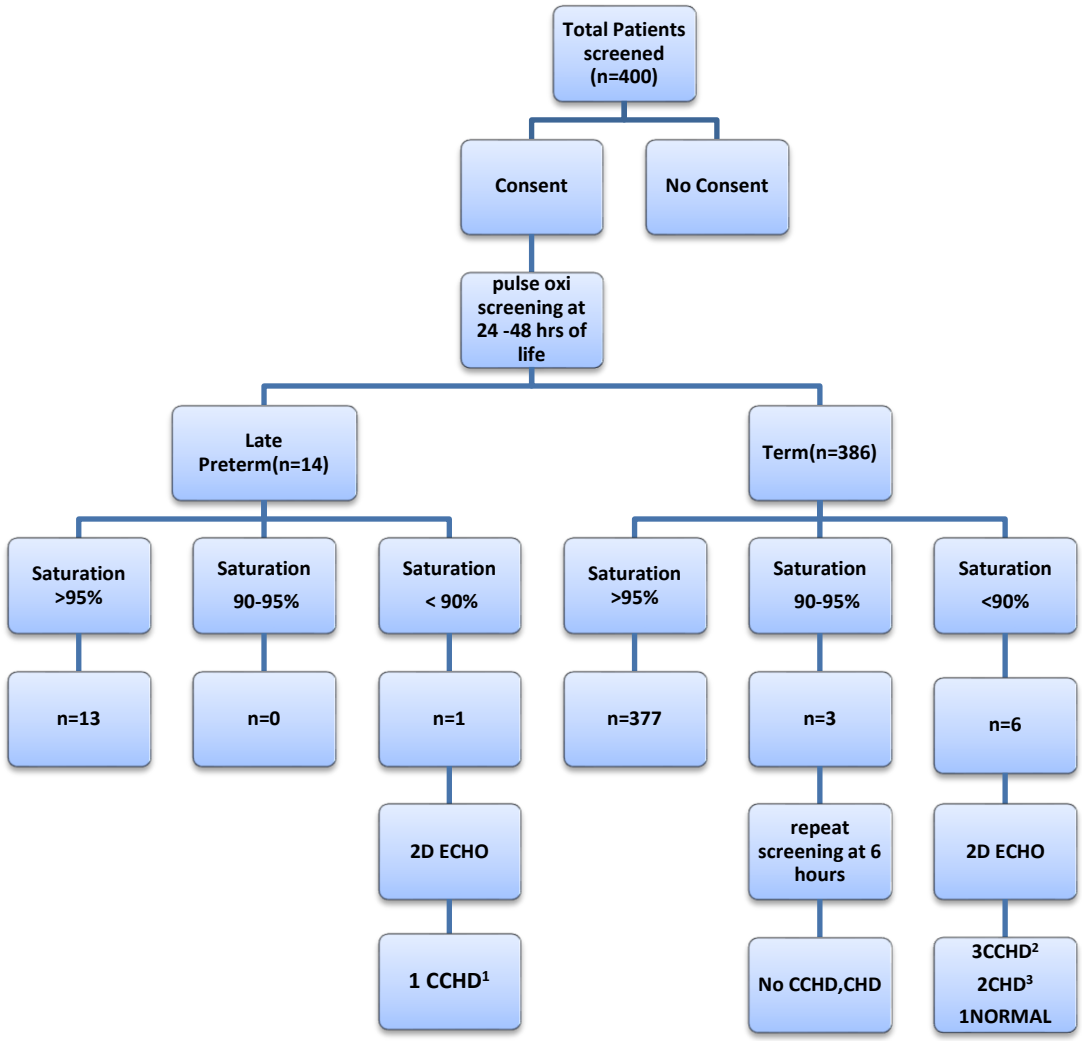
=0.0%

The predictive value of a positive test of Pulse oximetry was found to be 57.1% in our study.

Table 12 :TYPES OF CRITICAL CONGENITAL HEART DISEASES OBSERVED

CRITICAL CONGENITAL HEART DISEASE	NUMBER OF CASES
TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION	01
TRANSPOSITION OF GREAT ARTERIES	01
DOUBLE OUTLET RIGHT VENTRICLE	02

FLOW CHART OF STUDY DESIGN



1-TGA

2-TAPVC, 2DORV.

3-2ASD.

Figure 10 :Demonstration of pulse oximetry on a neonate.

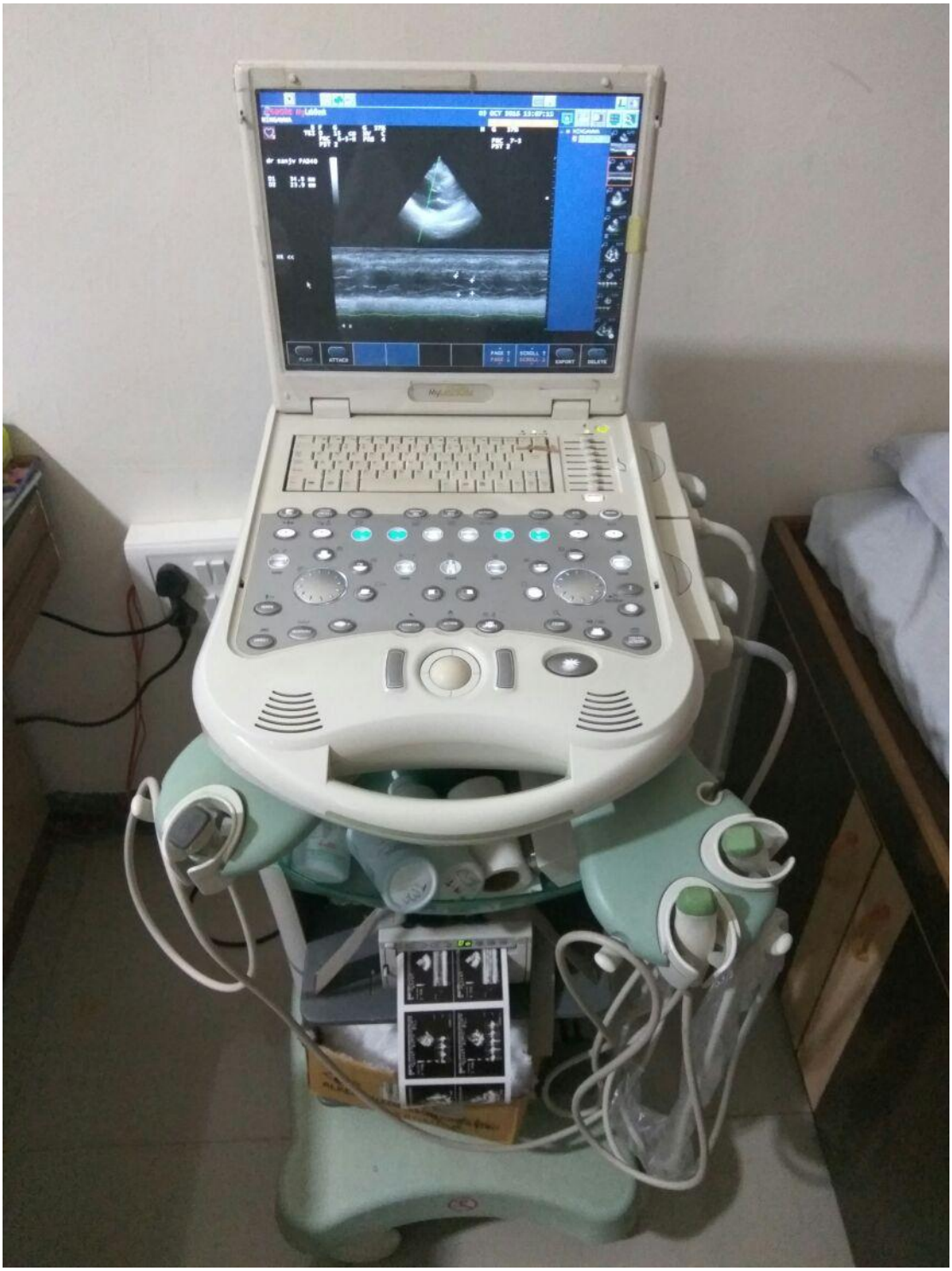


Figure 11: 2D ECHO Machine

DISCUSSION

In a developing country like India, where infant mortality rate is high, the dream of achieving millennium development goal is far from real. If focus on emerging causes of morbidity and mortality are not addressed at the appropriate time, this cannot be solved.

The number of diagnosed cases of congenital heart diseases has been increasing over time due to the use of echocardiogram,not only after birth but antenatally also.

However, the number of missed cases of CCHD or the impact of a delayed diagnosis of a CCHD is not known worldwide.

The limited availability of echocardiogram machines and cost of echocardiography are major confounding factors in considering its use for purpose of screening.

In a study by Matthew et al, those neonates who had more severe disease are more likely to be diagnosed earlier and with associated poorer survival.[43]

This observation re-emphasizes the magnitude of threat posed by a silent, birth defect in a neonate who may be sent home only to be received back in the emergency room with cardiovascular collapse.

Pulse oximetry screening for detection of hypoxemia in neonates with critical congenital heart disease is being discussed globally.

The first reports suggesting the use of pulse oximetry as a screening test for CCHD were published in 1995.[58] After that many studies using pulse oximetry showed the usefulness of this test.[59,60]

These were followed by single unit studies before several large cohort studies were undertaken.

Firstly, a cohort study of 39,821 newborns in a single region in Sweden recorded a sensitivity of 82.9% and a specificity of 98%.[59] No infant who underwent oximetry died of duct dependent systemic or pulmonary circulation compared to 5 such deaths in regions without pulse oximetry.

This was followed by a German study of 3,364 term neonates who underwent pulse oximetry between 6 and 36 hours. Of the 18 neonates with abnormal results, 50% had critical congenital heart defects .Sensitivity was determined to be 82% and specificity 99.9%.[60]

In a prospective multicentered trial in SAXONY, Germany, Pulse oximetry screening was performed in healthy term and post-term newborns at the age of 24-72 hours. In 42,240 newborns from 34 institutions during a 2 year period were included in a study 72 children were excluded due to prenatal diagnosis/or clinical signs of CCHD before pulse oximetry screening.795 newborns did not receive pulse oximetry screening, mainly due to early discharge after birth. In 41,445 newborns pulse oximetry screening was performed and showed true positive in 14,false positive in 40, true negative in 41,384 and false negative in 4 children. Sensitivity, specificity, positive and negative predictive value were 77.78%,99.9%,25.93% and 99.99% respectively.[35]

A large multi-centre study was undertaken involving 20,555 newborn babies.[42] This study reported an incidence of major congenital heart disease of 2.6:1 000 live births with 24 babies with a CCHD detected.

The sensitivity reported was 75% (95% Cl 53.29 - 90.23) for critical cases, 49.06% (95% Cl 35.06 - 63.16) for a major CHD with a specificity 99.16% (95%Cl 99.02 - 99.28) and false positive rate of 0.8%.[42]

When reviewed within a systematic review and meta-analysis, [45] some key observations were described:

- Pulse oximetry detected 30 additional cases of a CCHD per 100 000 live births.
- The false positive rate, if tested at >24 hours was 0.05 (0.02 -0.12), which equates to a specificity of 99.95% and sensitivity of 77.5 (61.8 - 88.0). The cost effectiveness of this study was analyzed in terms of Quality Adjusted Life Years.

ANTENATAL ULTRASONOGRAPHY

In this study of 400 neonates, babies with a prenatal diagnosis of duct dependent circulation on antenatal sonogram were excluded as we wanted to test result using pulse oximetry only.

The prenatal detection of congenital heart disease (CHD) in low risk pregnancies (for cardiac defects) ranges from 5 to 40%.[62,63]

A study from Germany has reported 60% of CCHD diagnosed on antenatal ultrasonography.[35]

Antenatal screening for birth defects, has now become routine in many parts of the world with history taking, blood tests, antenatal ultrasound. Even advanced methods such as amniocentesis and chromosomal analysis has become part of the prenatal assessment.[57]

However, screening fetal echocardiography is not a universal test and in fact, is limited to the developed countries and tertiary centres in low and middle income countries.

Clinical examination of neonates in the postnatal ward has been the routine practice of ruling out possibility of a heart defect. However, a complete evaluation encompasses careful inspection, palpation including peripheral pulses and auscultation.

However, according to Reide et al [35] such neonates who receive treatment for an antenatally detected duct dependent lesion from birth cannot be withheld. Hence, pulse oximetry in these newborns reflects the underlying haemodynamic status rather than acting as a screening tool.

Another study, by Cuneo et al showed that the accuracy of antenatal diagnosis improved with the integration of a pediatric cardiologist into the perinatal team.[64]

In the present study this aspect was not considered.

GENDER

The study population consisted of 56.2% male and 43.8% female neonates. (Table 1).Among babies who had CCHD (4 in number)25%were males and 75% were females were diagnosed which was consistent with a study by Shiwei Liu et al and Chaddha et al.[70,71]

No gender was considered to be a risk factor for one year survival with CCHD.[43]

GESTATION

Majority of the neonates (96.5%) were born full term (Table 1). There were only 13 late preterm babies.

Critical congenital heart diseases were noticed in 7.1% of late preterm and 1.6% of term neonates. This was similar to Laas et al[65] and Godfrey et al[66] who found significant association between prematurity and congenital heart disease.

This means if all preterms are included in study, more chances of detection of CCHD is possible .we included only late preterm in our study (Table 6).

BIRTH WEIGHT

The maximum number of neonates (45%) observed in the study fell in the weight group between 2.5-3 Kg. (Table 1)

It was observed that the majority of neonates who had critical congenital heart disease were having low birth weight.(3.2% vs 1.1% $p < 0.05$).The weights of the babies with diagnosed CCHD were respectively 2.3,1.9,2.3,2.06kg.

Archer et al,[67] also found serious congenital heart disease was more common in neonates with very low birth weight. Mortality was also higher amongst those in very low birth weight group.

In a other study done by Krammer HH et al, birth weights of 843 children with congenital heart disease were compared to the respective data of a normal west German population. On average, CHD group had significantly lower birth weights,

but the weight deficit was far less obvious then in previous studies. The decrease in birth weight was distinct only in children with TOF and ASD. Hence this study showed that patients with CHD were more often small for gestational age (15%) or had a low birth weight(8.6%).[72]

Other parameters like head circumference, heart rate, respiratory rate were comparable in both group in our study as all were apparently normal babies.

Protocol Issues

Secretary's Advisory Committee on Heritable Disorders in Newborns and children (SACHDNC) Protocol in 2010, According to which an infant would have a positive screen if at more than or equal to 24 hours of life following criteria were met

a) Pulse oximetry reading was less than 90% in either the right hand or either foot.
b) Both readings from the right hand and either foot were <95% on three measurements each separated by one hour.
c) A persistent >3% difference in right hand and either foot measurement on 3 measurement each separated by one hour.

Thus an infant who had > or = 95% in either extremity with < or = 3% difference in the pre – and post ductal oxygen saturation would have a negative screen and no further work up is needed.

KOCHILAS et al demonstrated that the SACHDNC protocol was the most efficient protocol with the fewest false –positive pulse oximetry screens.[73]

In this study of 400 neonates, we found seven cases positive for hypoxaemia on pulse oximetry. Those with profound hypoxemia (SPO2 <90%) were subjected to echocardiogram and 4 out of 7 neonates were found to be positive for CCHD.

In this study group of neonates, there was no difference in pulse oximetry readings in the upper and lower extremity.

Three neonates with pulse oximetry values between 90-95% were noticed. Their pulse oximetry was repeated after 6 hours and it subsequently improved(after 6 hours). However, they were not found to have any CCHD on Echocardiography.

Out of total seven echocardiograms done, three did not show any cardiac defect. The number of false positive cases were two cases of ASD and one case was normal. We performed pulse oximetry after 24 hours of life. Many studies reported that when screening is done between 24-48 hours of life, the number of false positives is far less.[35,43,68]

Detected CCHD

In a study done by ZENG et al 33% of infants with CCHD were diagnosed. This included TOF, HLHS, Pulmonary atresia, TGA, Tricuspid atresia and Truncus arteriosus. These conditions may be life threatening and may need immediate intervention.[74]

We found four CCHD in our study, This included two DORV, one TGA, one TAPVC.

All patients found to be having a CCHD were referred to a higher centre for further management.

It is a routine practice in our hospital to follow all discharged neonates at 15 days of life and subsequently at 6 weeks for vaccination except high risk neonates who are followed every 15 days in high risk clinic every Thursday. No other cases labelled as CCHD returned to our hospital.

Predictive value screening

Predictive value of a positive test indicates, the probability that a patient with a positive test result had the disease which is tested for. The predictive value of a positive test for CCHD was found to be 57.14%in our study which is better when compared to other study.

A study by Reide et al reported a positive predictive value of 25.93%[35] for CCHD. Another study by Zhao et al found the analysis of both clinical evaluation and pulse oximetry as: Sn=932% (879-962); Sp=971% (971- 972); PPV=38% (32-45); NPV= 9999% (9998-100); LR+ = 326% (325- 326); LR- = 007% (006-009) and found that pulse oximetry adds to the current methods of diagnosing CCHD. [69]

The results of this study bring out the inherent limitations of clinical screening for CCHD in newborns immediately after birth, especially in the context of limited resource environments. It is not feasible to do echocardiogram for every neonate especially in areas with high birth rate like India.

However, reports with good follow up data, higher coverage of echocardiography and better diagnostic value of antenatal ultrasonography have suggested sensitivity, specificity, positive and negative predictive value to be 77.78%, 99.90%, 25.93% and 99.99%, respectively.[35]

In our study, within the setup of a tertiary based hospital, the incidence of critical congenital heart disease was found to be 1 per 1000 live births.

Thus, in resource limited environment, pulse oximetry screening for CCHD makes valuable contribution towards early diagnosis of CCHD. The added advantage is diagnosis of other morbidities and its utilization in further monitoring of those with hypoxemia.

In UK, a study looking at cost-effectiveness of screening determined that pulse oximetry required further testing within their setting in order to accurately determine costs based on primary data.[61]

A study done in India [46] introduced pulse oximetry screening as a tool to be used in a less resourceful setting. Its use is employed at the different cadres of healthcare practitioners: the on-site paediatrician performed clinical evaluation while pulse oximetry was performed by a study nurse.

Bedside echocardiography was performed by a research officer while only those babies with abnormal echocardiograms were reviewed by a paediatric cardiologist.

In this context, the sensitivity of pulse oximetry without clinical examination was low (<20%). This study explained the limitations of technical and human factors as well as limited skill to perform echocardiography.

Overall Pulse Oximetry appears to be a simple, cheap and useful method.

Parents Reaction

In our study, 400 neonates were analyzed and only neonates whose parents gave consent were included. We noticed that though most parents were anxious regarding pulse oximetry screening, they found it to be safe and acceptable for their babies. Indeed, the idea of screening for CCHD by pulse oximetry was accepted with enthusiasm.

Strength and Limitations of the study

Strength

1) Sampling of the study was done in such a manner that all consecutive neonates whose parents gave consent were included to avoid any selection bias.

2) As there is paucity of data regarding magnitude of CCHD in India, this study can serve as a baseline data to compare and follow for further studies.

Limitations

1. As the study was conducted in a tertiary care hospital, the findings cannot be generalized to the population as a whole. This is the inherent limitation of a hospital based study compared to community based study.
2. Due to resource constraints it was not feasible to do 2D echocardiogram of each neonate.
3. Cases and controls could not be followed for their final outcome.

SUMMARY

Our study was conducted in the Pediatric Department of a Medical college in India over a period of one and a half years.

It was an prospective observational study and each consecutively born neonate (400 in number) in our hospital over one and half years were included. All cases were evaluated on the clinical basis and 2D ECHO was done for a final diagnosis.

All consecutively born neonates, whose parents gave consent were included in the study and those without an antenatal diagnosis were subjected to pulse oximetry screening after twenty four hours of birth. Screening was done on right upper and lower limbs. Three Subgroups were made based on oxygen saturation and those with severe hypoxaemia(Sao2<90%) were subjected to echocardiogram. In those for whom hypoxaemia was less severe (Sao2 90-95%), pulse oximetry was repeated after six hours. These neonates were also subjected to echocardiogram for a confirmatory diagnosis, if saturation was below 90%.Those with Sao2 >95% were considered normal.

The results are summarized below:

1) Out of total 400 neonates screened, 7 cases of hypoxemia were identified and monitored. Out of this, 4 had CCHD (TGA, TAPVC, two were DORV),two cases were ASD and one was normal

2) Predictive accuracy of Pulse Oximetry screening test is good with a “Predictive value of a positive test “in our study is 57.14%.

CONCLUSIONS

- Congenital heart diseases are a major cause of morbidity and mortality in children. Out of these, a subpopulation of critical congenital heart diseases requires early diagnosis. They may need medical and surgical management in the neonatal period itself.

- Critical congenital heart diseases are invariably associated with hypoxaemia and this principle is utilised while using a pulse oximeter for the screening.

- Many a times CCHD do not exhibit clinical signs or symptoms but deteriorate rapidly with fatal outcome.

- Pulse oximetry is an effective adjunct to antenatal ultrasonography and appropriate clinical examination in the diagnosis of critical congenital heart diseases even in resource limited environment.

- It facilitates early referral and treatment of neonates diagnosed with critical congenital heart disease to a centre equipped for their care.

- Resource generation in the form of pulse oximeters and hospital staff trained to do pulse oximetry is feasible in a developing country like India.

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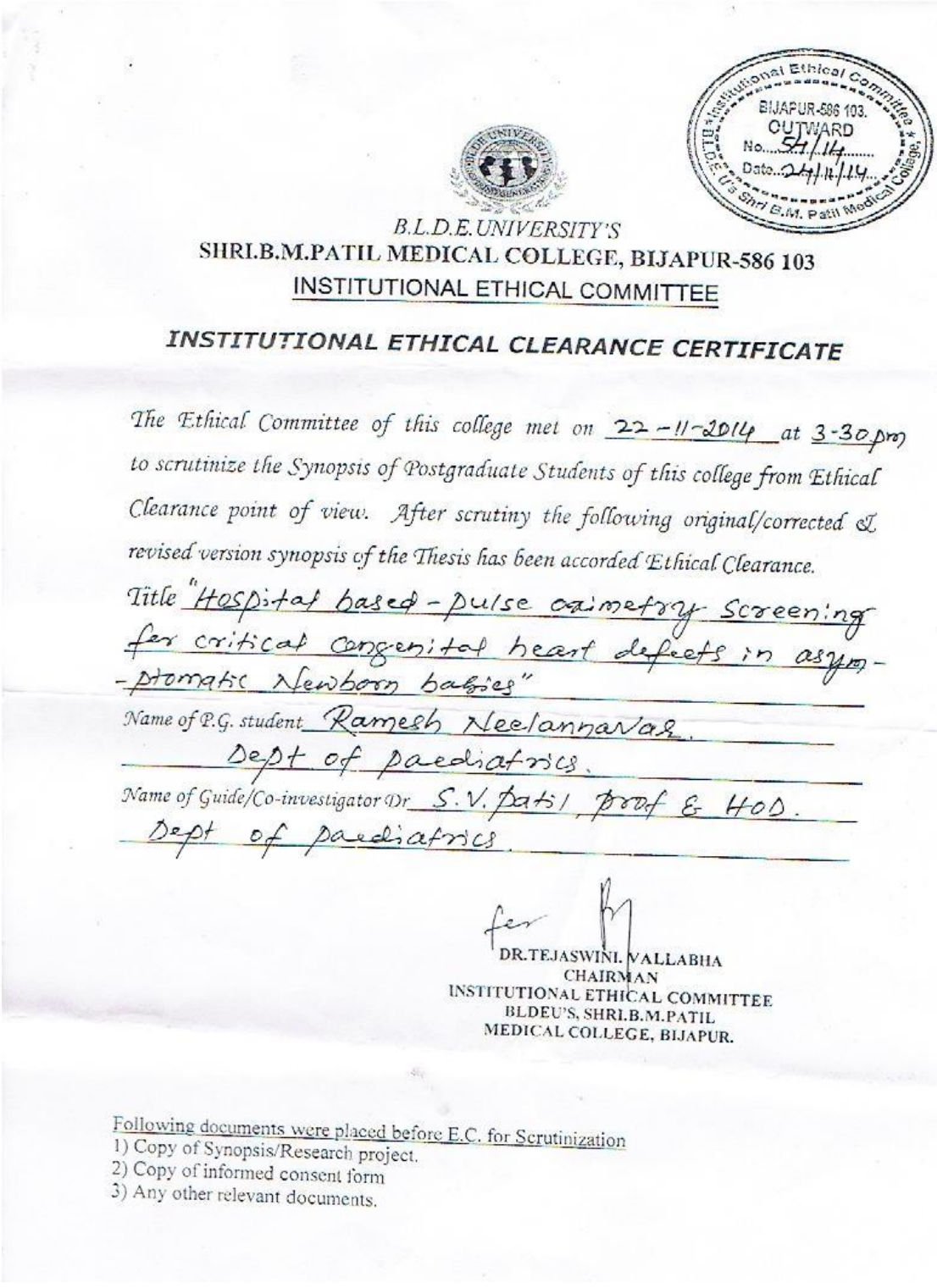
ANNEXURES

ETHICAL CLEARANCE CERTIFICATE



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SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "Hospital based - pulse oximetry screening for critical congenital heart defects in asymptomatic Newborn babies"

Name of P.G. student Ramesh Neelannavar.
Dept of paediatrics.

Name of Guide/Co-investigator Dr S.V. Patil, Prof & HOD.
Dept of paediatrics.

for
DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

CONSENT FORM

PARENTS / GUARDIAN CONSENT STATEMENT:

We confirm that Dr. Ramesh Neelannavar is doing a study on pulse oximetry screening for critical congenital heart defects in asymptomatic newborn babies Dr.Ramesh Neelannavar has explained to us the purpose of research and the study procedure. We are willing to allow our baby to undergo screening and the possible discomforts as well as benefits. We have been explained all the above in detail in our own language and we understand the same. Therefore we agree to give consent to participate as a subject in this research project.

_____ _____

(Parents / Guardian) Date

_____ _____

(Witness to signature) Date

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time; Dr.Ramesh Neelannavar at the department of pediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Ramesh Neelannavar may terminate my participation in the study after he has explained the reasons for doing so.

PROFORMA

Name

Age

Sex –Male /Female

Address

IP No.

DOB

Mother Age

Socioeconomic Class – Lower / Middle/Higher

Racial and Ethnic differences

(Any genetic predisposition)

Antenatal history

 Antenatal check-ups done/not done

Natal and Neonatal History

Delivery type – Normal / Caesarean / Others

Gestation Age : Preterm/term/post term

Anthropometry at birth

 Birth weight

 Length

 Head circumference

Physical examination

Vitals R R

PR

Temp

General examination

Pallor / Jaundice/Cyanosis, Edema /Clubbing

Other relevent findings -

Cardiovascular examinassions

Precordium

Auscultation

- Heart sounds I, II Murmur

- Other sounds

Other systems

RS

P/A

CNS

Pulse oximetry reading after >24 hrs<48hrs

ECG - Finding

ECHO - Result

KEY TO MASTERCHART

A	:	In patient number
B	:	Name of the baby
C	:	Days in life
D	:	Sex of neonate
E	:	Date of Birth
F	:	Age of the mother
G	:	Socio economic status
H	:	Ante natal visits.
I	:	Mode of Delivery
J	:	Gestation
K	:	Birth weight
L	:	Length of the neonate
M	:	Head Circumference
N	:	Temperature
O	:	Heart rate
P	:	Respiratory Rate
Q	:	General Physical examination
R	:	Systemic examination

S : Pulse Oximetry saturation

T : Echocardiography

U : CCHD Positive

V : CCHD Negative