"A PROSPECTIVE STUDY ON CARDIAC TROPONIN I AND ECG CHANGES IN DIAGNOSIS OF MYOCARDIAL INJURY DUE TO PERINATAL ASPHYXIA IN TERM NEONATES''

By

Dr. VIDYA SHREE. B

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In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE
IN
PAEDIATRICS

Under the Guidance of

Dr. BEERE GOWDA .Y.C.

PROFESSOR,

DEPARTMENT OF PAEDIATRICS

SDUMC, KOLAR

DEPARTMENT OF PAEDIATRICS
SRI DEVARAJ URS MEDICAL COLLEGE
KOLAR – 563101

APRIL / MAY 2022

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Date:

Place: Kolar

Dr. BEERE GOWDA .Y.C
Professor
Department of Paediatrics
Sri Devaraj Urs Medical College
Tamaka, Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA.

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Dr. SUDHA REDDY V.R.
Professor and HOD
Department of Paediatrics,
Sri Devaraj Urs Medical College,
Tamaka, Kolar

Date:
Place: Kolar

Dr. P.N.SREERAMULU,
Principal,
Sri Devaraj Urs Medical College, Tamaka, Kolar

Date:
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Date:

Place: Kolar

Signature of Member Secretary

Sri Devaraj Urs Medical College

Tamaka, Kolar -563101

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Vidyashree .B

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Dr. Beeregowda. Y.C.
Professor of Paediatrics
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ABSTRACT

Background:

Perinatal asphyxia is the commonest cause of preventable cerebral injury among neonates. Birth asphyxia is a multi – system disorder with consequence that extend beyond the central nervous system . Reduced tissue perfusion, hypoxic ischemic injury, acidosis, hypercapnia, and brain injury are all symptoms of birth asphyxia, overall being potentially fatal. Asphyxiated neonates who survive can have co-morbid condition, like motor as well as cognitive deficits originating from cerebral hypoxic-ischemia. The most important cause of neonatal mortality related to hypoxic-ischemia is myocardial damage; there is significant myocardial morbidity among survivors. Myocardial injury occurs at a rate of 28–73 percent in neonates with hypoxia, and cardiac impairment is frequently ignored due to a lack of appropriate diagnostic tests. It is important to identify myocardial injury as early as possible by using specific marker like cardiac troponin I and ECG change in diagnosis of myocardial damage, hence this study was carried out.

Objectives:

1. To measure the serum cardiac troponin I levels in asphyxiated term neonates.
2. To record the ELECTROCARDIOGRAPHIC changes in asphyxiated term neonates.
3. To find the association of cardiac troponin I levels and ECG changes in diagnosis of myocardial injury in asphyxiated term neonates.

Material and Methods :

A prospective study included 50 neonates born at term with the evidence of birth asphyxia. Detailed perinatal history, Clinical systemic examination, Laboratory investigations, Neonatal ECG Electrode Placement and ECG findings were recorded. cTni and ECG was done at 6 hours and repeated at 12 to 24 hours. The outcomes measures were serum cTnI levels, ECG changes and mortality due to myocardial injury.

Data analysis :

The data entry was done in the Microsoft EXCEL spread sheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0.

Results:

- Mortality was seen in 6 out of 50 neonates (12%). ECG showed abnormality in 34 cases.
- The levels of cTnI increased from the initial hours with values of 1.98 at 6 hours and 2.47 at 12 to 24 hours showing that the values are increased in perinatal asphyxia.
- For initial 6 hours, cardiac troponin I cut-off values of >1.28 significantly predicted ECG changes with 100% accuracy. Moreover, cardiac troponin I showed increasing trend with grade of ECG abnormality (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 1.97 vs. 2.33 vs. 3.52 vs. 3.92, $p<0.0001$).
- Even at 12-24 hours, cardiac troponin I cut-off of >1.82 significantly predicted ECG abnormality with 100% accuracy.

- Moreover, cardiac troponin I showed a significant increasing trend with grade of myocardial injury (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 2.35 vs. 2.93 vs. 4.07 vs. 4.3, $p<0.0001$). Mean cardiac troponin I within 6 hours (ng/mL) was significantly higher in died patients than discharged (3.76±0.3 vs. 1.58±1.04, $p<.0001$).
- Mean cardiac troponin I at 12 to 24 hours (ng/mL) in died patients was significantly higher than discharged (4.22±0.17 vs. 2.05±1.16, $p<.0001$).

Conclusion:

Cardiac troponin levels significantly increase during neonatal asphyxia. Receiver operative characteristic curve (ROC) analysis showed that troponin I can be a useful diagnostic marker for myocardial injury at 6 hours with the cut off of more than 1.28 and at 12 to 24 hours with the cut off of more than 1.82, in patients with neonatal asphyxia. Moreover, cardiac troponin I was also associated with increasing grade of myocardial injury as shown by ECG changes. Hence our study concludes that elevated cardiac troponin I and its association with ECG changes can be a useful diagnostic marker of myocardial injury due to perinatal asphyxia. However further large multi centric trials are needed to validate it as standard diagnostic tool in the management of asphyxiated neonates

KEY WORDS: Perinatal asphyxia, Cardiac troponin I, ECG, Myocardial injury**.**

ABBREVATIONS

AUC	Area under the ROC curve
ATP	Adenosine triphosphate
BNP	Brain natriuretic peptide
CKMB	Creatine kinase myocardial band
cTnI	Cardiac Troponin I
CO	Cardiac output
CBF	Cerebral blood flow
CFT	Capillary refilling time
CVP	Central venous pressure
ECG	Electrocardiogram
ECHO	Echocardiogram
EF	Ejection fraction
HIE	Hypoxia ischemic encephalopathy
LDH	Lactate dehydrogenase
LSCS	Lower segment caesarean section
MODS	Multi-organ dysfunction syndrome
NNPD	National Neonatal Perinatal Database
NNF	National neonatology forum
NPV	Negative predictive value
PA	Perinatal Asphyxia
PPV	Positive predictive value
PPHN	Persistent pulmonary hypertension

PROM	Prolonged rupture of membranes
ROC	Receiver operating characteristic curve
RLJH&RC	R.L.Jalappa Hospital And Research centre
SD	Standard deviation
SDUMC	Sri Devaraj Urs Medical College
SDUAHER	Sri Devaraj Urs Academy of Higher Education And Research
TMI	Transient myocardial ischemia
WHO	World health organisation

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INTRODUCTION

INTRODUCTION

Perinatal asphyxia (PA) is the commonest as well as significant cause of preventable cerebral injury among neonates. In India, it is the leading cause of new-born mortality.[1]

The incidence of perinatal asphyxia in India is reported to be about 8.4% (Apgar score < 7 at 1 minute). Estimated that among 136 million annual births, about (10 million) 5%-10% respond to stimulation to initiate breathing effort, 3% to 6% require positive pressure ventilation(6 million), and only less than 1% (<1 million) require advanced resuscitation (0.1% chest compression and 0.05% require drugs).[2]

Tanna K et al[3] reported that in India moderate birth asphyxia is present in nearly 2.8% and severe PA in 5.6% of all live births. In perinatal asphyxia, nearly all organ systems of body are affected. Multiple organs are affected in majority of the cases; however, brain may sometimes be the only organ having dysfunction after asphyxia.[1]

The order of frequency of systemic organ involvement in all birth asphyxia overall has been cerebral > hepatic > pulmonary > renal > cardiac. In an autopsy series, involvement of cardiac manifestation is noted commonly than other systemic organs.[4]

Birth asphyxia also causes "decreased tissue perfusion, hypoxic ischemic injury, acidosis, hypercapnia," and causes brain injury, overall being potentially fatal. Asphyxiated neonates who survive can have co-morbid condition, like motor as well as cognitive deficits originating from cerebral hypoxic-ischemia.[5]

Cardiac injury is the leading cause of neonatal mortality in hypoxic-ischemia, with considerable myocardial morbidity among survivors. Myocardial damage occurs at a rate of 28–73 percent in neonates suffering from hypoxia.[6]

The beneficial parameters used for prediction of the outcome among asphyxiated neonates are Apgar scores, umbilical pH, and clinically seizures within 24 hours after birth. In addition, laboratory parameters, which indicate peripheral organ dysfunction, are used widely for diagnosis of asphyxia.[7]

Cardiac enzymes are widely utilized as a reliable marker of cardiac injury in new-born's, with the additional advantage of being an early indicator of cardiac injury. Their roles are complementary to clinical evaluation, Electrocardiography(ECG), and Echocardiography(ECHO), and they are specially used as screening techniques following myocardial ischemia in a variety of contexts.[8]

Biochemical markers such as Creatinine kinase(CK) as well as its iso-enzyme MB is generally used for detection of the myocardial injury. But, the limitation related to such markers was that these are affected by gestational age, gender, modes of delivery, and birth weight. Myocardial damage can also be evaluated by clinical methods, electrocardiography, echocardiography, as well as cardiac biomarkers.[9]

Among these cardiac biomarkers, Cardiac Troponin I (cTnI) is highly sensitive as well as specific biomarker in diagnosis of microscopic cardiac injury, which is released early in response to myocardial ischemia. Troponin I is reported to be important prognostic tool among neonates with perinatal asphyxia.[1]

The cTnI is considered as the gold standard biomarker. The asphyxiated new born have increased levels of serum cTnI which indicates to be excellent indicator for myocardial injury.[3]

However, some confounding factors affect cardiac troponin levels and thus limit its importance in the diagnosis of perinatal asphyxia as well as myocardial damage; these include preterm delivery or adrenalin administration.

In the new born with perinatal asphyxia with cardiac dysfunction, troponins appear after 4 to 6 hours in blood. It peaks between 12 and 24 hours and is increased for nearly 21 days.[10]

The major challenges for the Paediatrician's managing perinatal asphyxia is its unpredictability, and the fact that once it is initiated, minimum intervention can be done to minimize its harmful effects. Thus, it is easily understood why several previous researches evaluated the early predictors for PA, and protective measures for prepartum as well as postpartum periods.[11]

Hence in this study was conducted to evaluated the role of cTnI and ECG changes to diagnose the myocardial injury in relation to perinatal asphyxia.

NEED FOR STUDY

Birth asphyxia is one of the leading causes of neonatal morbidity & mortality in especially in developing countries like India and even in developed countries. Anticipation, early identification and intervention are important factors which alter the outcome of perinatal asphyxia.[1]

In R L Jalappa Hospital, Kolar, in the year 2018, total deliveries were 2000 live births, of which 25.6% required admission to NICU, out of which more of the admissions are due to perinatal asphyxia because of various causes leading to HIE, also causes multi organ dysfunctions (MODS) including myocardial ischemia. It was observed that many of the neonates required fluid management to correct the shock with a perinatal asphyxia in such new-borns the cause of death may be due to myocardial dysfunction.

In recent years, to assess myocardial dysfunction, there are numerous biochemical markers have been identified like, CKMB, Lactate dehydrogenase (LDH), Cardiac Troponin I, myoglobin, myeloperoxidase, Brain natriuretic peptide (BNP) etc.[12]

Cardiac – specific isomorphs of troponin I has been proved as an early specific markers of myocardial damage of acute coronary syndromes in adult. Asphyxiated neonates have higher cTnI concentration than controls .Troponin I is an inhibitory protein complex located on the actin filament in all striated muscles , represents a sensitive and specific marker in the analysing the magnitude of the injuries in neonates.[13]

But literature on accuracy of these markers in confirming the myocardial dysfunction is sparse. However there is paucity of reports from our country where mothers

frequently present late to hospital with obstetric complications and baby suffer from birth asphyxia with high mortality. So, It becomes important to detect myocardial dysfunction as early as possible by using specific marker like cardiac troponin I and ECG changes in diagnosis of myocardial damage .

Therefore the present study was done to explore the myocardial involvement in neonates with perinatal asphyxia by cTnI and ECG changes.

AIMS & OBJECTIVES

OBJECTIVES OF THE STUDY

1. To measure the serum cardiac troponin I levels in asphyxiated term neonates.

2. To record the ELECTROCARDIOGRAPHIC changes in asphyxiated term neonates.

3. To find the association of cardiac troponin I levels and ECG changes in diagnosis of myocardial injury in asphyxiated term neonates.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

PERINATAL ASPHYXIA

Definition:

Asphyxia is a Greek terminology which implies "loss of pulse". **World Health Organization** (WHO) - describes perinatal asphyxia as "Failure to initiate or sustain respiration after birth".[14]

National Neonatology Forum(NNF) of India has put forth definition of asphyxia as "when baby has gasping or inadequate breathing or no breathing at the end of one minute".[15]

NNF grades perinatal asphyxia as the second leading cause of Neonatal mortality. It records about 20 %.[15]Birth asphyxia is a condition that occurs during the first and second stages of labour when gas exchange and blood flow are compromised, resulting in hypoxemia, hypercarbia, and foetal acidosis.[16]

National Neonatal – Perinatal Database (NNPD) Network-

1. "**Moderate PA**: Slow/gasping breathing or an Apgar score of 4 to 6 at 1 minute.
2. **Severe PA:** No breathing or an Apgar score of 0-3 at 1 minute of age."

American Academy of Paediatrics& American College of Obstetrics and Gynaecology- Presence of all of following criteria:-

1. Profound metabolic or mixed acidemia (pH< 7.00) and base deficit ≥ 12 mmol/l in umbilical cord blood.
2. Persistence of low Apgar scores less than 3 for more than 5 minutes
3. Signs of neonatal neurologic dysfunction (e.g., seizures, encephalopathy, tone abnormalities).
4. Evidence of multiple organ involvement (such as that of kidneys, lungs, liver, heart and intestine).[17]

Consequently CNS, kidney, heart and lung suffers hypoxic injury to about 28%, 50%, 25% and 23% respectively. The magnitude of Multi- Organ Dysfunction Syndrome (MODS) ascertains early outcome of asphyxiated neonate. Long term sequelae are not linked to these organ dysfunctions with the exception of central nervous system, as it leads to hypoxic ischemic encephalopathy (HIE).[16,18,19]

Incidence:

In developed countries , the rate of perinatal asphyxia is two per 1000 births ,but the rate can be up to 10 times higher in developing countries due to insufficient access to maternal and neonatal care. Of those infants affected, 15-20% die in the neonatal period, and up to 25% of survivors are left with permanent neurologic abnormalities.[20]

A higher incidence is noted in new-born's of diabetic or toxaemic mothers, those with intrauterine growth restriction, breech presentation, and new-born's who are postdates. The incidence of PA is estimated to be much higher (10 to 15 times) in low- to middle-income countries (LMIC).[21]

Gebregziabher et al[22] (2017) conducted a cross-sectional study at Northern Europe including 267 neonates. Out of these, perinatal asphyxia was present in 48 neonates, with the prevalence being 18%.

The prevalence rate found in the study by Gebreheat et al was 22.1%.[23] In another study, Alemu et al.[24] found that out of 262 study participants, the perinatal asphyxia was present in 32.8% neonates.

Workineh et al.[25]reported in a systematic review conducted at East and Central Africa that the pooled prevalence of perinatal asphyxia was 15.9%.

Manandhan et al.[26]conducted a cross-sectional study in Nepal including 1,284 neonates, 3.66% were asphyxiated. Babu et al.[27]conducted a cross-sectional study including 364 neonates with 6.6% incidence of perinatal asphyxia .

AETIOLOGY:

Asphyxia is commonly found to occur during antepartum as well as intrapartum period. During the postpartum period, the abnormalities in cardiac, respiratory and nervous system result in asphyxia.[28,29]

The maternal factors causing perinatal asphyxia include "maternal hemodynamic compromise (amniotic fluid embolus), uterine conditions (uterine rupture), or placenta and umbilical cord (placental abruption, umbilical cord knot or compression), and infection". The occurrence of asphyxia can be before birth or immediately after birth in compromised patient that need resuscitation.[30,31]

Most of the cases of perinatal asphyxia take place during the intrapartum period, and nearly 20% of the cases take place during the antepartum period, and other cases take place during early postnatal period. Several maternal events cause perinatal asphyxia; these factors include haemorrhage, hemodynamic collapse, and amniotic fluid embolism. The placental factors (such as acute abruption), cord factors (such as tight nuchal cord, cord prolapse/avulsion), uterine factors (such as rupture), and intrapartum infection (such as maternal fever in labor) causes neonatal asphyxia. For determining the etiology, it is required to take detailed obstetrical and peripartum history.[32]

Perinatal asphyxia leads to profound systemic and neurologic complications because of reduced blood flow and oxygen to fetus or infant during the peripartum period. Perinatal asphyxia commonly causes that is caused due to the transit myocardial ischemia. When the cardiac dysfunction is severe, it lead into congestive cardiac failure, shock, and eventually new-born's death.[30]

Risk Factors For Birth Asphyxia :

- Lack of maternal oxygenation
- Reduced blood flow from mother to placenta
- Reduced blood flow from placenta to fetus.
- Impaired gas exchange across the placenta or at the fetal tissue level
- High requirement of fetal oxygen.[33,34]

Babu et al[27] reported that the maternal risk factors in asphyxiated new-borns included primiparity (54.9% in cases vs. 35% in controls) hypertension (18.1% vs. 4%),

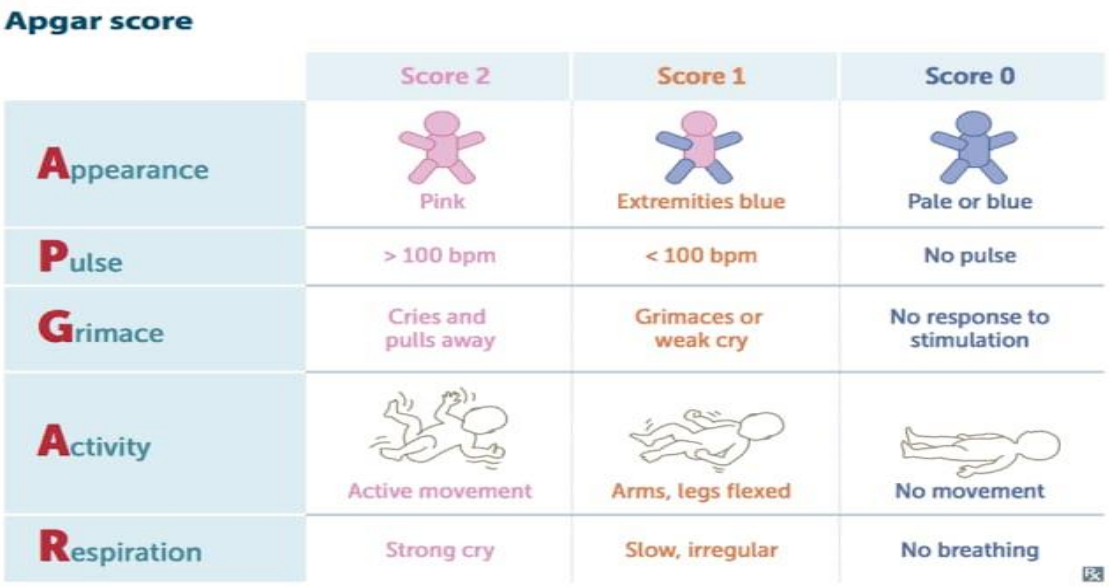
toxaemia of pregnancy (25.3% vs. 15%), antepartum haemorrhage (6.9% vs. 0%), prolonged rupture of membranes (PROM) (35.2% vs. 5%), increased duration of second stage of labour (37.4% vs. 4%) and Oxytocin use during labour (18.7% vs. 0%).

Majeed et al [35]reported that in 125 neonates with asphyxia, the risk factors were increasing/decreasing maternal age, non-attendance for antenatal care (64%), prolonged rupture of membranes (24%), non-cephalic presentation (20%), and multiple births increased risk in 4.8%. Other factors were particulate meconium (9.6%) and vaginal bleeding (34.44%) of neonates.

Table 1 - Aetiology of Hypoxic Ischemia[36,37,38]

Maternal	Placental	Umbilical cord	Foetal
Hypertension	Abnormal placenta	Prolapse	Anemia
Chorioamnionitis	Abruption	Entanglement	Twin to twin transfusion
Pulmonary or cardiac disorder	Infraction	True knot	Feto-maternal haemorrhage
Diabetes	Fibrosis	Compression	Severe iso immune haemolytic disease
Maternal vascular disorder	Hydrops	umbilical vessels abnormalities	Cardiomyopathy
In utero exposure to cocaine	Uterine rupture		Cardiac arrhythmia

Figure 1 - APGAR SCORE [21]



Apgar score is used for assessing the state of the neonate at 1 minute and then 5 minutes following birth. The neonate is surveyed for 5 key signs assigned a score of 0, 1 and 2.According to NNPD Network Perinatal asphyxia is defined based on APGAR score.

PATHOPHYSIOLOGY:

Asphyxia causes a number of physiological and biochemical alteration. In mild asphyxia there is a transient increase in heart rate followed by decrease in heart rate, mild increase in blood pressure and central venous pressure in order to maintain the cerebral perfusion. Redistribution of cardiac output (CO) to heart, brain, and adrenal glands ("Diving Reflex").[39]

With severe prolonged asphyxia , there is a loss of pressure autoregulation and CO2 vasoreactivity with severe prolonged asphyxia, resulting in cerebral hypoperfusion. It

further accentuated when there is cardiovascular abnormalities with hypotension and decrease in cardiac output.[39]

Increased glucose utilisation in the brain and a reduction in glycogen and phosphocreatine concentrations result in anaerobic metabolism and cellular energy failure when cerebral blood flow(CBF) is reduced. Cellular dysfunction occurs when oxidative phosphorylation and ATP generation are reduced. TMI is common among new-born's who have had perinatal hypoxia.[39]

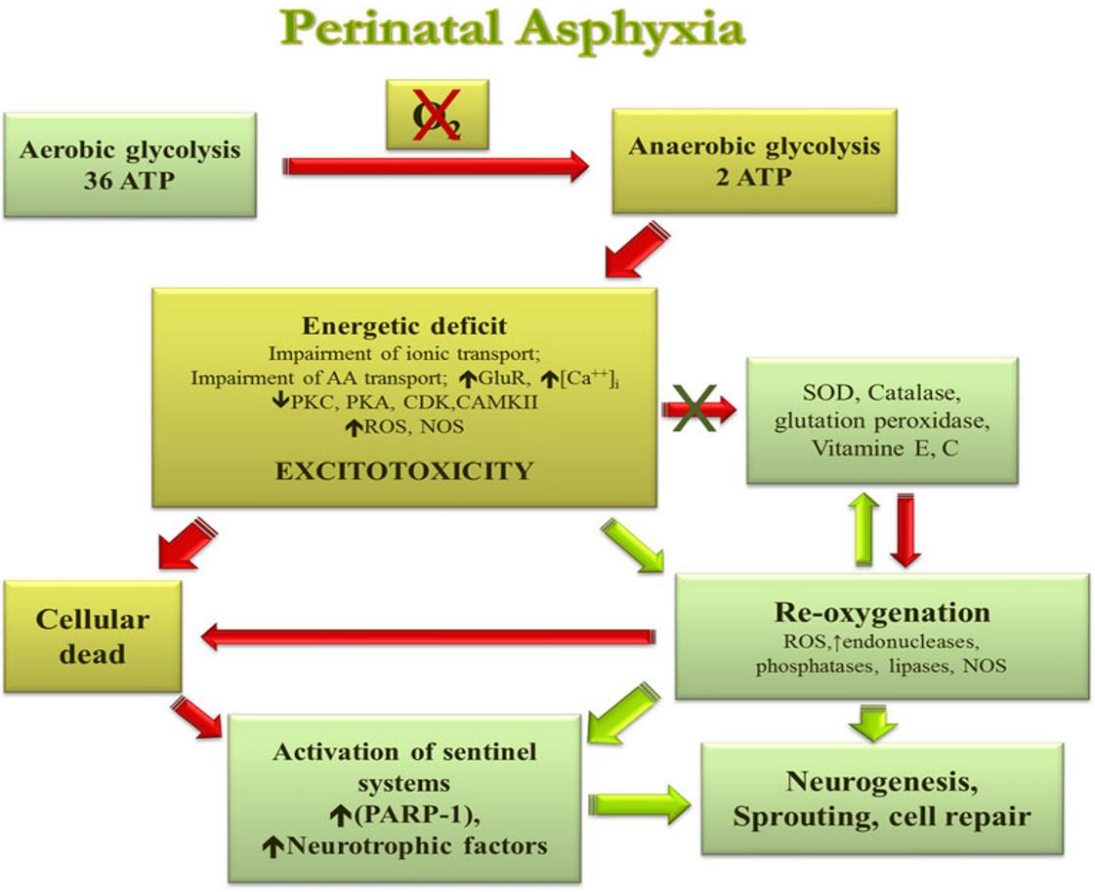


Figure 2- Pathophysiology of Perinatal Asphyxia.[40]

Table 2- Characteristics Of Energy Failures Related To HIE[21]

Primary energy failure	Secondary energy failure
Decrease in CBF, oxygen substrates and ATP	Continuing of excite toxic – oxidative cascade
Excito toxic – oxidative cascade	Activation of microglia- inflammatory response
Loss of ionic homeostasis across membranes	Activation of caspase proteins
Entry of intracellular calcium	Reduction in levels of growth factors, protein synthesis
Mitochondrial disruption	Continuing Apoptosis and necrosis
Brain acidosis	

Figure 3 - Free Radicals Production In HIE[11]

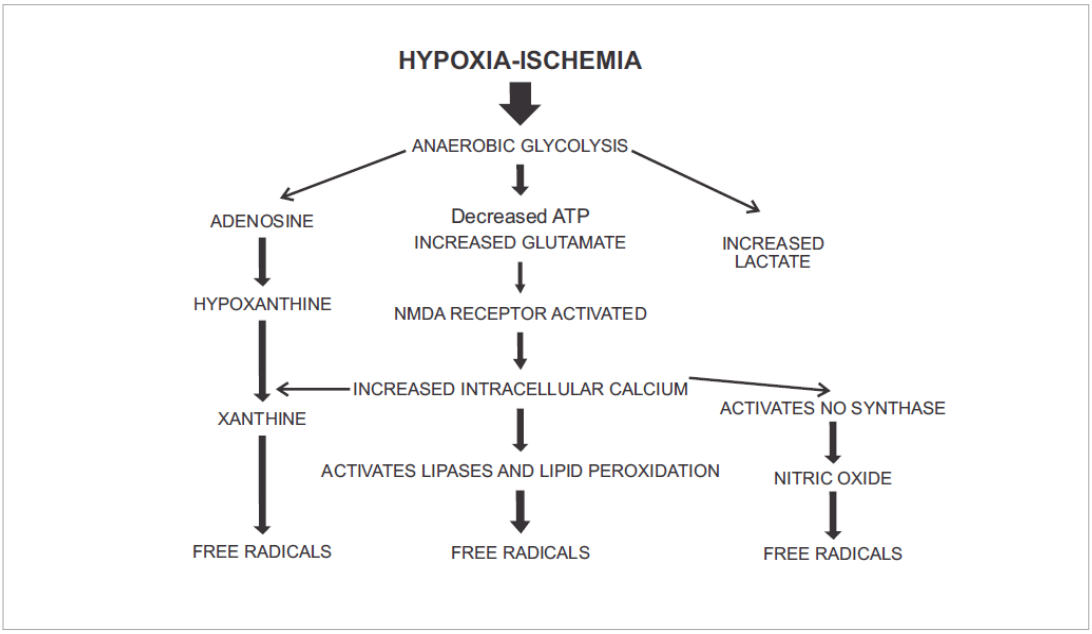


Table 3: Multi-organ Dysfunction Associated With Perinatal Asphyxia.[41]

Organ	Effect
Cardiovascular	Transient Myocardial ischemia, decreased left ventricular contractility, tricuspid insufficiency, Pulmonary hypertension and systemic hypotension
Central nervous system	Hypoxic ischemic encephalopathy, seizures, cerebral enema, intracranial haemorrhage, hypotonia and spasticity
Pulmonary	Pulmonary hypertension, pulmonary haemorrhage, meconium aspiration and pulmonary edema
Kidney	Acute tubular necrosis, cortical necrosis, renal failure, oliguria
Liver	Elevation of Hepato-cellular enzymes, altered metabolism, Hypoglycaemia and hyperbilirubinemia
Gastrointestinal	Bowel ischemia and necrotizing enterocolitis
Hematologic	Disseminated intravascular coagulation, thrombocytopenia due to decreased production by the bone marrow

Myocardial Development From Fetal To Neonatal Transition :

The adult and neonatal cardiomyocytes have considerable structural and metabolic changes. Maturation begins at birth , when the partial pressure of oxygen rises and the pulmonary and systemic circulation pressure undergoes significant modifications.[42]

The requirement for more contractile force causes hyperplasia , which is followed by cardiac cell mass hypertrophy. In a oxygen enriched environment , the metabolic transformation from glycolytic to nearly completely oxidative metabolism reflects the conversion of the substrate from lactic acid to fatty acid .[42]

Gap junctions are located differently in foetal and adult cardiomyocytes, with an adult-like arrangement near the end of the first year of life. The birth distribution shows a less well-coordinated syncytium than in adult myocardium, resulting in decreased contractile force, especially under certain situations (e.g., ischemia).[43]

Even if the antioxidant capacity increases during the last trimester of pregnancy, it is still immature at delivery. Between the first and third months of extrauterine life, the activity of superoxide dismutase (SOD) and catalase increases significantly. In addition, the increased generation of antioxidants reduces the capacity to react.[44]

Physiopathology of The Cardiovascular Response To Perinatal Asphyxia:

Cardiac output increases in adults to maintain oxygen supply to the vitals organ systems. In contrast the cardiac output of the foetus which is already high, remains constant under such conditions. The foetus compensate by increasing the blood flow to essential organs such as heart, brain and adrenals while decreasing flow to less vital

organ such as lungs, abdominal viscera , muscles and bones. Normally foetal heart and brain receive 7% of cardiac output, whereas during hypoxia these organs requires up to 26% of CO to maintain adequate tissue oxygenation.[45]

In early phase of asphyxia, cardiac output is maintained by selective regional vasoconstriction, which lowers blood flow to the less critical organs. Oxygen transport to the brain and heart suffers when asphyxia proceeds to the severe stage. The myocardial then draws on its glycogen reserve to generate energy. The glycogen store is eventually depleted, and the myocardium is exposed to decreased Po2 and pH. Hypoxia and acidosis interact to cause a reduction in myocardial function.[45]

Cardiac dysfunctions results from hypoxic ischaemic damage to sub-endocardial tissue, Papillary muscles and myocardial injuries leading to such as myocardium dysfunction, valvular dysfunction, rhythm abnormalities , congestive cardiac failure, transient myocardial ischemia, tricuspid and mitral regurgitation.[46]

Cardiovascular Effects Of Birth Asphyxia:

Among infants who have perinatal birth asphyxia, the most common complication is the cardiovascular dysfunction. The sequel afterbirth asphyxia associated with cardiovascular system that include valvular insufficiency, transient myocardial ischemia(TMI), left ventricular contractility decreased and output to pulmonary hypertension and systemic hypotension.[47]

New-borns with transient myocardial ischemia

TMI is generally present among infants who have perinatal asphyxia. It must be claimed in the case of new-borns with asphyxia with respiratory distress, a weak or absent pulse, or a baby with a significant audible murmur. The T wave is flat or inverted, and the ST depression on the ECG. The posterior wall of the left ventricle shows diminished contractility on ECHO. Left ventricular ejection fraction can be used to predict prognosis.[47]

Transient tricuspid insufficiency in new-born

In an asphyxiated neonate, tricuspid insufficiency is a common cause of heart murmur. Ischemic damage of tricuspid valve papillary muscle as well as pulmonary hypertension results in tricuspid insufficiency. Many time, tricuspid regurgitation will regress once the underlying issues are resolved.[48]

Mitral Incompetence

Mitral regurgitation is less frequent than tricuspid regurgitation. It is a vital pointer of myocardial ischemia. ECHO gives an evidence of impaired left ventricular contractility . It settles in due course in most instances.[49]

PERSISTENT PULMONARY HYPERTENSION OF NEW-BORN

After birth, there is a right-to-left shunt in the foetal circulating pattern due to high pulmonary vascular resistance. This shunt connects the ductus arteriosus to the foramen ovale. Respiratory distress and cyanosis are common symptoms of PPHN.

Chronic foetal hypoxia causes pulmonary smooth muscle hyperplasia, which leads to higher pulmonary vascular resistance. On ECHO, the pulmonary artery is dilated, and the right heart with the atrial and ventricular septate protruding into the left atrium and ventricle, respectively.[50]

DILATED CARDIOMYOPATHY

It includes cardiac dilatation, reduced cardiac contractility as well as congestive cardiac failure. Cardiac output is maintained by the ventricular dilatation and tachycardia, in spite of reduced systolic shortening fraction. Factors encompassing myocardial dysfunction: Ischemia, hypoxia, pulmonary hypertension, lactic acidosis, Hypothermia, hypocalcaemia, hypercarbia, anaemia and polycythaemia.[51]

HYPOTENSION AND CONGESTIVE CARDIAC FAILURE

Blood pressure is initially preserved due to the redistribution of blood through peripheral vasoconstriction . In case asphyxia continued , when the fetus is apenic , blood pressure drops. Transient myocardial ischemia leading to primary myocardial dysfunction causes congestive heart failure . The neonates with congestive cardiac failure presents with "tachypnoea tachycardia, hepatomegaly, diaphoresis, poor perfusion, feeding difficulties, growth failure, and cardiovascular collapse".[47]

CARDIAC DYSARRTHYMIA-Ventricular fibrillation, tachycardia, sinus node arrest, extreme bradycardia .[47]

CARDIAC TROPONIN:

Cardiac Troponin I and T are cardio regulatory proteins of the Tropomyosin complex that controls the calcium mediated interaction of actin and myosin. They are markers of myocardial injury[3]. Troponin T is not normally detectable in the serum and their levels are not influenced by sex, mode of delivery, gestation age and birth weight of the neonate.[52]

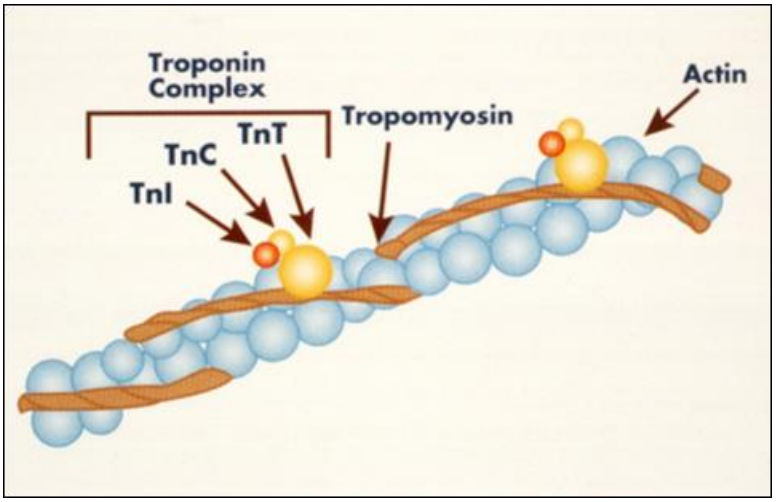


Figure 4 - TROPONIN I PROTEIN COMPLEX[53]

Troponin T in maternal blood does not crosses the placenta owing to heavy molecular weight. Cardiac Troponin T starts rising in the serum 2 -4 hours after myocardial injury, peaks at 48 hours and remains elevated for 7-10 days. Furthermore they are competent prognostic indicator of mortality in asphyxiated new-born.[54]

They are highly sensitive and specific in diagnosing myocardial injury in newborns with clinical and laboratory evidence of asphyxia. Normal values of Troponin T in the newborn are 0 to 0.097µg/L. Previously Serum Creatine Kinase Myocardial bound fraction was employed as a marker of myocardial injury in perinatal hypoxia. An elevation of CK-MB fraction >5% to 10 % might point towards myocardial injury.

Cardiac Troponin T is demonstrated to be having higher specificity as well as sensitivity when compared with CK-MB.[55]

ECG CHANGES:

Electrocardiographic changes in perinatal asphyxia were categorized into four grades as put forth by **Jedikin et al**[56]

- Grade 1: Equivocal flat or inverted T wave in one lead only.
- Grade 2: Suggestive – flat or inverted T in several leads with abnormal Q wave in any lead.
- Grade 3: Moderate – flat or inverted T in several leads or bundle branch block with abnormal Q plus and abnormal ST segments.
- Grade 4: Severe – Classical segmental infarction pattern with abnormal Q waves with markedly elevated ST segments.[56]

ECHOCADIOGRAPHIC CHANGES:

Echocardiographic changes present among new-born's with asphyxia with myocardial injury include: "valvular regurgitation tricuspid or mitral valve incompetence, Right ventricular hypokinesia and Left ventricular hypokinesia supported by low ejection fraction (EF), pulmonary hypertension and right atrial/right ventricle dilatation". Ejection fraction is associated with the change in volume of the left ventricle with

cardiac contraction. The normal mean ejection fraction is 66%, the range being 56–78%.[57]

CLINICAL EVIDENCE OF MYOCARDIAL INJURY:

There is a loss of cerebral autoregulation and it is pressure passive in neonatal asphyxia. Hypotension and reduced cardiac output are manifestations of myocardial damage, which further compromises the cerebral perfusion. Measurement of appropriate end organ perfusion is done by "Capillary filling time < 3 seconds(CFT), Systemic mean arterial Blood pressure to the bare minimum of 45 to 50mm Hg, urine output >1ml/kg/hour and Normal Central venous pressure 5-8 mm Hg in term neonates(CVP)". Reduced CVP and increased CFT stand for decreased intravascular volume as well as requirement for inotropic support.[58]

Previous empirical studies:

Trevisanuto et al[8] (2006) conducted a study including 52 neonates: 13 asphyxiated neonates and 39 without asphyxia in whom cTnI levels were measured between 24 and 48 hours after birth. It was found that median troponin I level in the subjects was greater than controls (0.36 vs. 0.04 µg/l; $p<0.05$). In asphyxiated babies, troponin levels were not significantly correlated with other markers of asphyxia, which doesn't indicate of myocardial damage in asphyxiated neonates.

Szymankiewicz M et al,[59] (2006) conducted a study including 43 neonates: 21 newborns with asphyxia and 22 without asphyxia in whom cTnI concentrations were measured between 12 and 24 hours after birth. It was observed that the cTnI levels were greater among those with asphyxia than without asphyxia (0.287 vs. 0.112

ng/mL, P<0.05).They came to Conclusion that levels of serum cTnI are markers of prediction of myocardial injury at an early stage in neonates with neonatal asphyxia.

Simović et al[60] (2014) conducted a study including 91 neonates: 55 with asphyxia and 36 without asphyxia in whom Serum troponin concentrations were measured between 24 and 48 hours after birth. Observed that the value was 0.08 μg/L. Significantly greater cTnI levels (p<0.05) in asphyxiated new-born's . An increase in cTI by 0.135 microg/L predicted the risk of death with the sensitivity and specificity of 84.6% and 85.9%, respectively.

Roopa et al[61] (2014) conducted a study including 59 neonates with or without asphyxia. There were 18 neonates with asphyxia and myocardial injury, 22 neonates with asphyxia but no myocardial injury, and 19 neonates without asphyxia among the 59 new-born's. In new-born's with asphyxia and myocardial injury, all four indicators (CKMB, cardiac troponin I, myoglobin, and brain natriuretic peptide) were higher than in neonates with asphyxia but no myocardial injury. The diagnostic value of the marker cTnI was the highest.

Pal P et al[1] (2015) conducted a study including 60 neonates: 40 with asphyxia and 20 without asphyxia in whom troponin levels were measured between 24 and 48 hours after birth. They observed that severely asphyxiated neonates had significantly higher cTn I levels compared to moderate asphyxiated neonates and controls (4.6 vs. 1.8 vs. 0.6 ng/ml, P<0.05). They concluded that there was linear relationship between cTn I levels and birth asphyxia. cTn I levels level are helpful in prediction of the mortality as well as outcomes in perinatal asphyxia.

Prithviraj et al[62] (2016) conducted a prospective study on babies admitted to the NICU. About 80 babies with PA. Out of which according to the classification of Sarnat and Sarnat 37(46.25%) patients had stage 1, 23 (28.75%) had stage 2 and 20 (25%) stage 3. There was statistically significant increase in cardiac markers (creatinine kinase CKMB, Cardiac troponin I).

Zhou et al[63] (2016) conducted a study including 164 neonates with asphyxia in whom cTnI concentrations were measured within 24 hours after birth. Observed that cTnI levels were significantly correlated with the traditional markers of asphyxia, mode of delivery, and duration of hospitalization. Increased levels of cTnI were found to be significant predictors of mortality in asphyxiated neonates. Concluded that levels of serum cTnI measured within 24 hours of birth significantly predict mortality in neonatal asphyxia.

Gouda et al[64] (2017) conducted a prospective observational study including 100 neonates: 50 asphyxiated newborns and 50 without asphyxia in whom Serum cTnI concentrations were measured within 12 hours after birth. It was observed that asphyxiated neonates had significantly higher cTnI concentrations than controls. There was an increase in serum levels of cTnI with increasing severity of HIE. . However, no such correlation was found with chronologic or fetal age. There was no effect of cTnI levels on sex, mode of delivery, and blood oxygenation in neonates.

A prospective case-control study was conducted by Kumar PS et al,[49] (2018) in tertiary care centre to determine the cardiac involvement by measuring serum creatine

kinase- myocardial band (CKMB) and ECG changes in perinatal asphyxiated term neonates. CKMB levels were significantly elevated in Hypoxic ischemic encephalopathy (HIE) stage 3 when compared with HIE stage 1. There was a statistically significant difference in the mean CKMB levels between the normal and grade 4 ECG groups. They concluded that evaluation of CKMB Levels and ECG as a marker of severity of perinatal asphyxia shows promising results. Troponin I additional to enzymes and ECG will improve the sensitivity and specificity of cardiac evaluation as tool for assessing the severity of perinatal asphyxia.

Jiang et al[65] (2019) conducted a study including 18 with asphyxia + myocardial injury, 22 neonates with asphyxia and no myocardial injury, and 19 controls, in whom Serum cTnI concentrations were measured between 12 hours and 7 days after birth. They observed cTnI levels were significantly highest in newborns with asphyxia and myocardial injury. hs-cTnI at cut-off value of 0.087 µg/L, for asphyxia-induced myocardial injury, the sensitivity was 55.6%, specificity 95.5%, and diagnostic accuracy was 77.5%. Author concluded that levels of serum cTnI significantly predict mortality in neonatal asphyxia.

Issa A et al,[10] (2021) conducted a study including 170 neonates: 85 with asphyxia and 85 without asphyxia in whom Serum cTnI concentrations were measured within 72 hours after birth. It was noticed that median troponin I level in the subjects was greater than controls (1.26 vs. 0.79 ng/ml, $P< 0.05$). The troponin I levels in HIE I was 1.26, in HIE II was 1.11, and in HIE III was 3.58 ng/ml. They Concluded that levels of serum hs-cTnI are markers of prediction of myocardial injury within 72 hours in neonates with neonatal asphyxia.

MATERIAL & METHODS

MATERIAL AND METHODS

1. **Study Site:** This study was conducted in the Department of Paediatrics, R.L. Jalappa Hospital and Research Centre, Kolar, Karnataka.

2. **Source of data :**50 neonates born at term gestation with evidence of birth asphyxia and admitted to NICU of RLJH during the period of study .

3. **Study Design:** A Prospective study

4. **Study Duration :**The duration of study was from January 2020 to December 2020.

5. **Methods of collection of data :**

Inclusion Criteria :

Neonates born at term with the evidence of birth asphyxia as indicated by:

1. Intrapartum signs of fetal distress, as indicated by late decelerations on fetal monitoring or by thick meconium staining of the amniotic fluids.
2. Apgar score of $\leq$ 3 at 1 minute and $\leq$5 at 5 minute.
3. Metabolic acidosis (pH <7.0) in an umbilical artery blood sample.
4. Evidence of multi organ dysfunction (renal, cardiovascular, respiratory, nervous system).[62]

Exclusion criteria:

1**.** Congenital heart diseases**.**

2. Congenital malformations.

3. Neonatal sepsis

4. Respiratory distress syndrome

5. Pre eclampsia

6.IUGR

6. **Sample Size:**

This study included all the 50 term neonates with perinatal asphyxia recruited from NICU of RLJH hospital during the period of study .

The study of Singh V et al[48] observed that electrocardiography (ECG) changes were seen in 13% of infants who had birth asphyxia. Taking this value as reference, the minimum required sample size with 10% margin of error and 5% level of significance is 44 patients. To reduce margin of error, total sample size taken is 50.

Formula used is:-

$$N \geq (p(1-p))/(ME/z\alpha)2$$

Where Zα is value of Z at two sided alpha error of 5%, ME is margin of error and p is proportion of infants with electrocardiography (ECG) changes.

Calculations:-

n>=((.13*(1-.13))/(.1/1.96)2=43.45=44 (approx.)

7. Sampling Technique:

Consecutive sampling was done after applying the relevant inclusion and exclusion criteria.

8. **Ethical considerations**

Ethical clearance was obtained from the Institutional Ethical Committee, prior to the start of the study. Written informed consent was taken from all study participants. Risk and benefits involved in the study and the voluntary nature of participation were explained before obtaining consent .Confidentiality and privacy was ensured at all stages.

9. Methodology

This study was conducted in RLJH&RC affiliated to Sri Devaraj Urs Medical College (SDUMC), a constituent college of Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER).

This study was started after obtaining ethical clearance from the Institutional Ethical Committee. Data of neonates who satisfied the eligibility criteria was included in the study. The parents were explained about the study and a written informed consent was obtained from them (Annexure).

Data collection tools: The detailed information regarding gestational age and gravida was collected, based on predesigned data sheet and findings of relevant clinical examination (Annexure).

Neonates with evidence of birth asphyxia were examined clinically, and laboratory tests as per proforma were done and documented. All asphyxiated neonates were subjected to following-

1. Detailed perinatal history with special emphasis on-
    - Gestational age was assessed by New Ballard scoring system.

- Detailed maternal history included maternal age, comorbidities like DM and HTN.

2. Labour events: prolonged or obstructed labour, abnormal presentation, meconium stained liquor, premature rupture of membrane, maternal infection, mode of delivery.[61]

3. Laboratory Assessment –

Parameter – Cardiac troponin I (cTnI)

Normal value – 0.63(±0.58) ng/ml with range of 0.001-4.3ng/ml . less than 1.8 is considered the upper limit of normal range.[66]

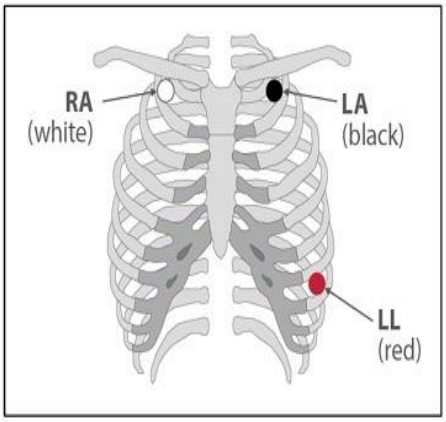
Sample-3 ml of serum venous blood

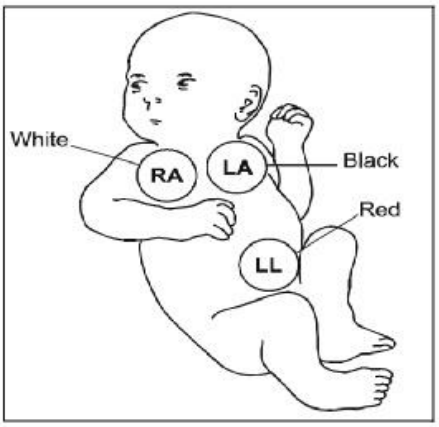
Timing of Sample -3 ml of serum was taken by aseptic precaution within 6 hours and repeated at 12-24 hours of life.

4. **Neonatal ECG Electrode Placement:** ECG lead placement on a neonate was usually directed towards obtaining the best possible respiration data through the ECG thoracic impedance technique.

Thoracic impedance was usually measured between the right arm and left arm electrode patches. These patches were placed on the chest directly across from each other to optimize the measurements of the neonates chest movements and measure within 6 hours and repeated at 12 to 24 hours.

Figure 5-Neonatal 3 – Wire Lead Placement





- The RA (White) electrode was placed under patient left clavicle, mid-calvicular line within the rib cage frame.
- The LA (Black) electrode was placed at right sternal border, fourth intercostal space within the rib cage frame.
- The LL (Red) electrode was placed at on the patients' lower left abdomen within the rib cage frame.[67]

ECG –"Electrocardiographic changes and grading had been described by Rowe and colleagues. [56]

- Grade 1: Equivocal flat or inverted T wave in one lead only.
- Grade 2: Suggestive – flat or inverted T in several leads with abnormal Q wave in any lead.
- Grade 3: Moderate – flat or inverted T in several leads or bundle branch block with abnormal Q plus and abnormal ST segments.
- Grade 4: Severe – Classical segmental infarction pattern with abnormal Q waves with markedly elevated ST segments."

- Sterilization of ECG leads was done by using 70% isopropyl alcohol by soaking it for 10 minutes.
- Parameters such as mode of delivery, liquor status, fetal distress, gender, birth weight, mode of resuscitation, APGAR score and outcomes were recorded.

10 Outcome measures:

- Comparison of cardiac troponin I(ng/mL), ECG findings between within 6 hours and at 12-24 hours
- ROC characteristics of Cardiac troponin I within 6 hours(ng/mL) for predicting abnormal ECG within 6 hours
- Cardiac troponin I at 12-24 hours for predicting abnormal ECG at 12-24 hours
- Association of cardiac troponin I within 6 hours with ECG within 6 hours
- Association of cardiac troponin I at 12-24 hours with ECG at 12-24 hours
- ROC of Cardiac troponin I within 6 hours and at 12-24 hours(ng/mL) for predicting mortality
- Association of cardiac troponin I and ECG findings with mortality.

Statistical analysis

The presentation of the Categorical variables was done in the form of number and percentage (%). The quantitative data with normal distribution were presented as the means ± SD and the data with non-normal distribution as median with 25th and 75th percentiles (interquartile range). The data normality was checked by using Kolmogorov-Smirnov test. The cases in which the data was not normal, we used non parametric tests. The following statistical tests were applied for the results:

The association of the variables which were quantitative in nature were analysed using Independent t test (for two groups) and ANOVA test (for more than two groups) and Paired t test was used for comparison across follow up.

The comparison of the variables which were qualitative in nature were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

Receiver operating characteristics curve was used to find out cut off point of Cardiac troponin I for predicting abnormal ECG and mortality.

For statistical significance, p value of less than 0.05 was considered statistically significant after assuming all the rules of statistical tests.

Statistical software: The data entry was done in the Microsoft EXCEL spread sheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0.

RESULTS

RESULTS

A Prospective study was conducted in Department of Paediatrics, Sri Devaraj Urs Medical College, Tamaka, Kolar. 50 neonates born at term with the evidence of birth asphyxia were included in the study. Detailed perinatal history, Clinical examination, Laboratory investigations, Neonatal ECG Electrode Placement and ECG findings were recorded and results are as follows.

Table 4:-Distribution of Study Subjects according to Gestational age (weeks).

Gestational age(weeks)	Frequency	Percentage
37 to 39 weeks+5 days	39	78.00%
>=40 weeks	11	22.00%
Mean ± SD	38.74 ± 1.2	
Range	37-41.71	

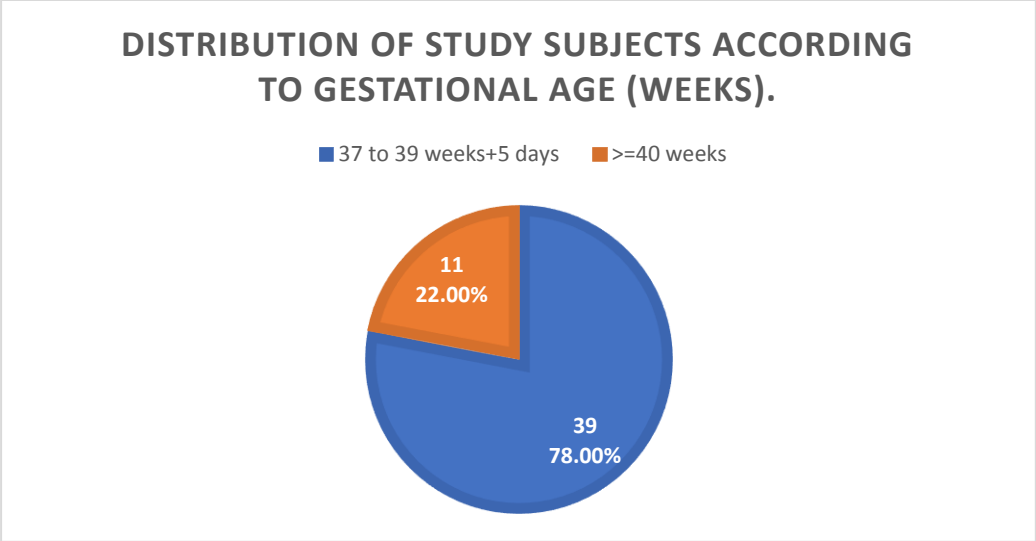


Figure 5:- Distribution of Study Subjects according to Gestational age

In present study, in majority 39 (78%) of neonates, gestational age (weeks) was 37 to 39 weeks+5 days. Gestational age(weeks) was >=40 weeks in only 11(22%) out of 50 neonates . Mean value of gestational age(weeks) of study subjects was 38.74 ± 1.2 .

It is shown in Table 4, Figure 5.

Table 5:-Distribution of Study Subjects according to Gravida Status.

Gravida	Frequency	Percentage
Primi	34	68.00%
Multi	16	32.00%
Total	50	100.00%

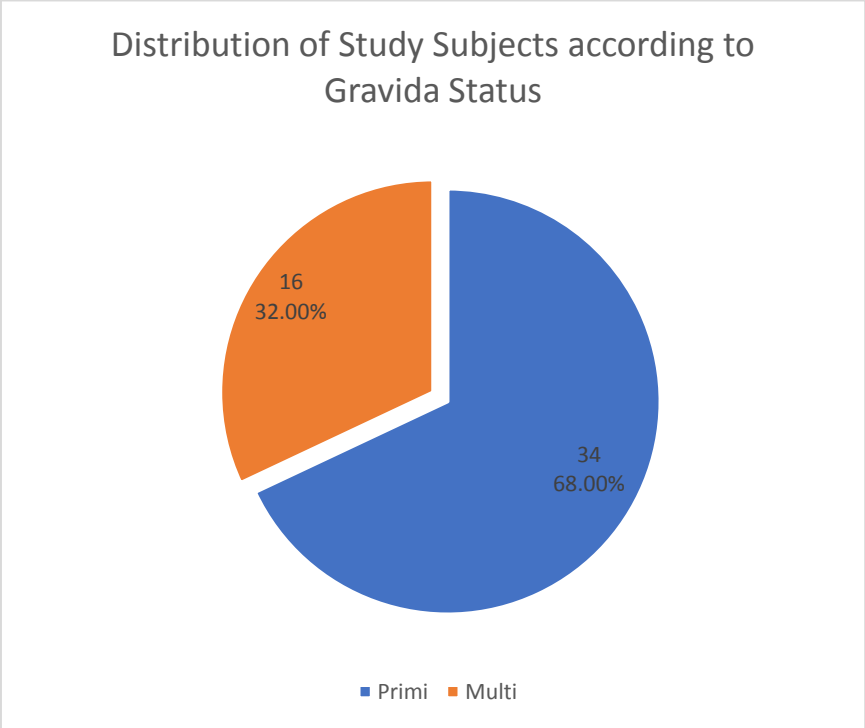


Figure 6:- Distribution of Study Subjects according to Gravida Status

In present study, majority 34 (68%) of neonates were Primi gravida and only 16 (32%) out of 50 neonates were multi gravida.

It is shown in Table 5, Figure 6.

Table 6:-Distribution of Liquor Status Among Study Subjects.

Liquor status	Frequency	Percentage
Clear	19	38.00%
Meconium	31	62.00%
Total	50	100.00%

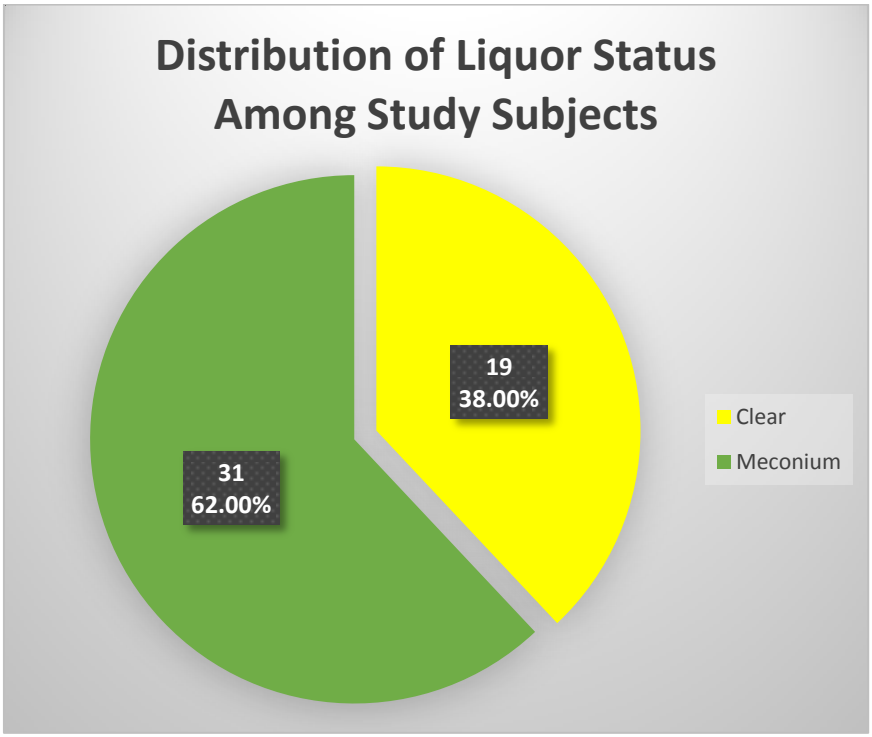


Figure 7:-Distribution of liquor status Among Study Subjects.

In present study, in majority 31 (62%) of neonates, liquor status was meconium. Liquor status was clear in only 19 (38%) out of 50 neonates.

It is shown in Table 6, Figure 7.

Table 7:-Distribution of fetal distress Among Study Subjects.

Fetal distress	Frequency	Percentage
No	17	34.00%
Category 1	13	26.00%
Category 2	11	22.00%
Category 3	9	18.00%
Total	50	100.00%

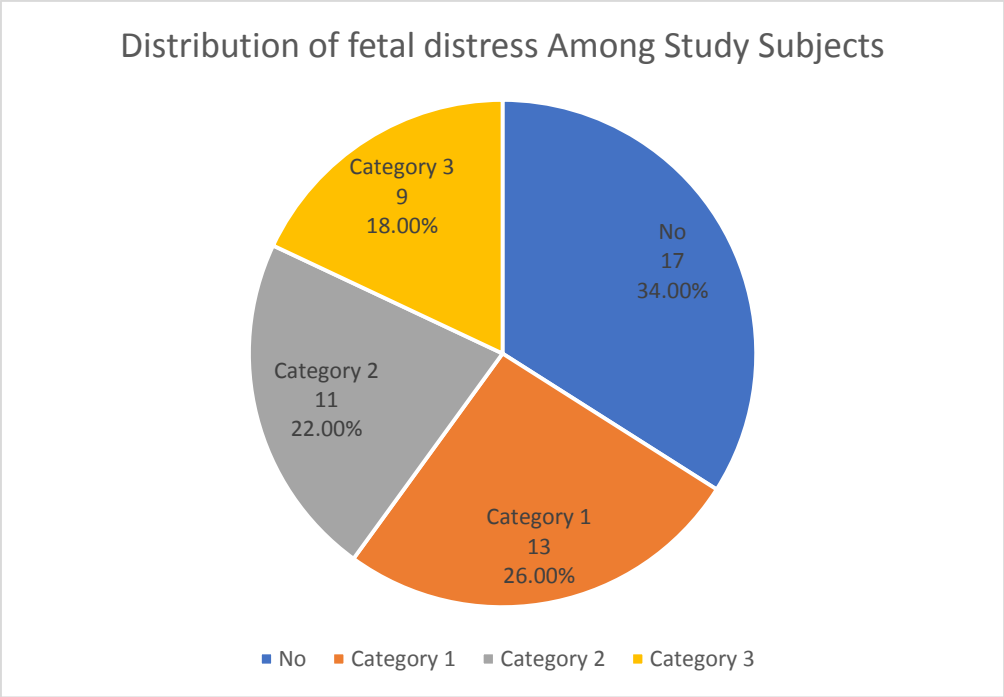


Figure 8:-Distribution of fetal distress Among Study Subjects.

In present study, 17 (34%) of neonates did not have fetal distress followed by category 1 (26%) and category 2 (22%). Fetal distress was of category 3 in only 9 out of 50 neonates (18%).

It is shown in Table 7, Figure 8.

Table 8:-Distribution of Mode of Delivery Among Study Subjects.

Mode of Delivery	Frequency	Percentage
Normal vaginal delivery	23	46.00%
LSCS	21	42.00%
Vacuum assisted vaginal delivery	6	12.00%
Total	50	100.00%

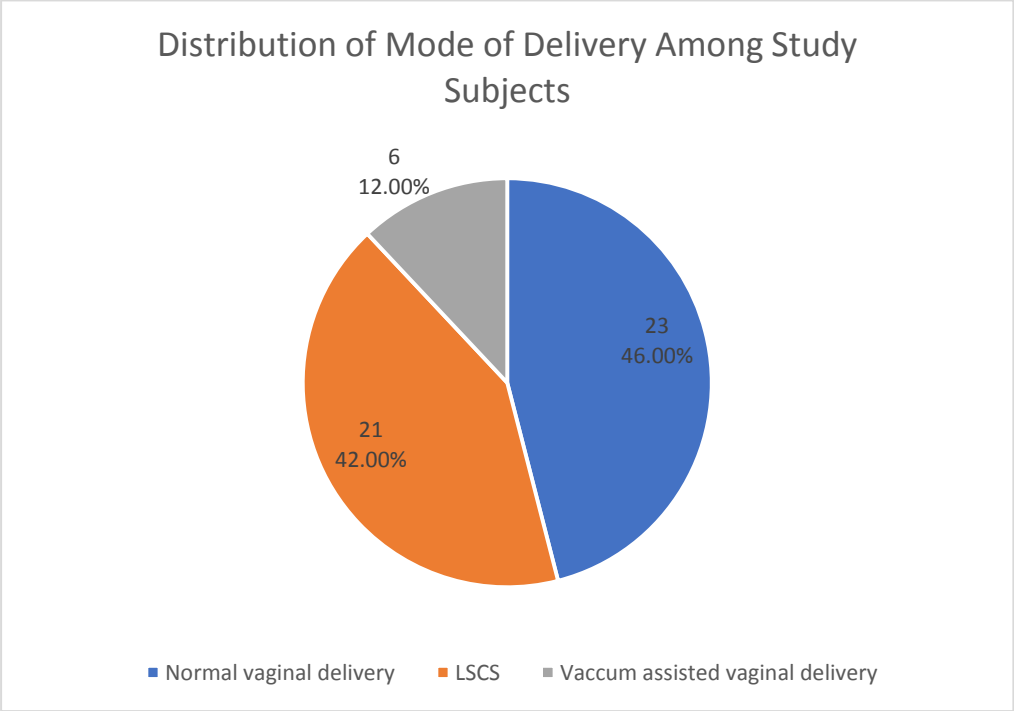


Figure 9:-Distribution of Mode of Delivery Among Study Subjects.

In present study, in majority 23 (46%) of neonates, Mode of Delivery was normal vaginal delivery followed by LSCS 21 (42%). Mode of Delivery was vacuum assisted vaginal delivery in only 6 (12%) out of 50 neonates

It is shown in Table 8, Figure 9.

Table 9:-Distribution of Gender According to Study Subjects.

Gender of baby	Frequency	Percentage
Female	24	48.00%
Male	26	52.00%
Total	50	100.00%

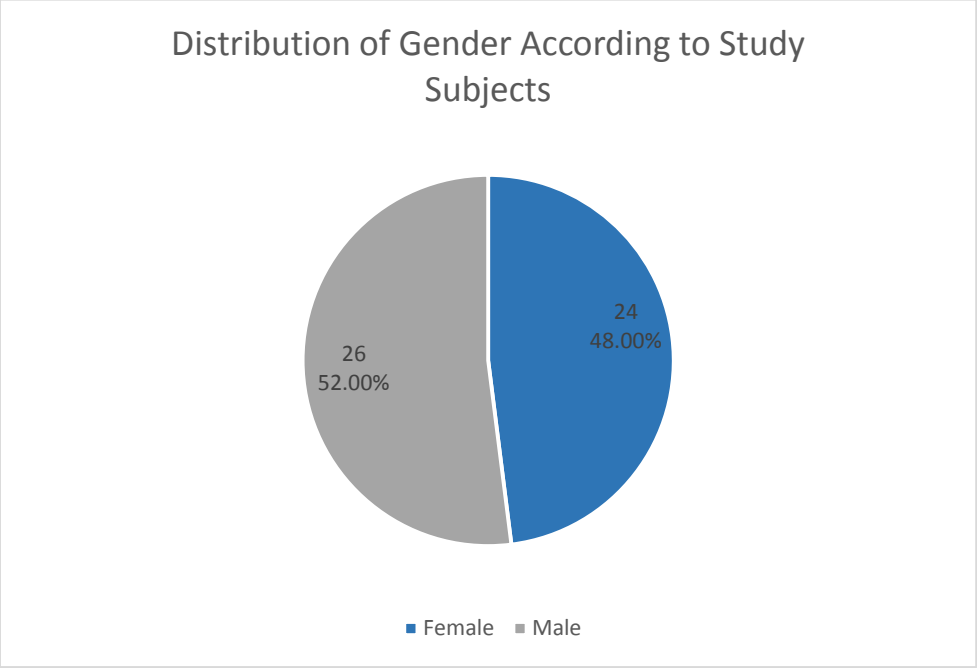


Figure 10:-Distribution of Gender According to Study Subjects.

In present study, in majority 26 (52%) of neonates were male and female in only 24(48%) out of 50 neonates .

It is shown in Table 9, Figure 10.

Table 10:-Distribution of Birth Weight (kg) Among Study Subjects.

Birth Weight(kg)	Frequency	Percentage
2.5 to 3 kg	18	36.00%
>3 kg	32	64.00%
Mean ± SD	3.15 ± 0.33	
Range	2.58-4.1	

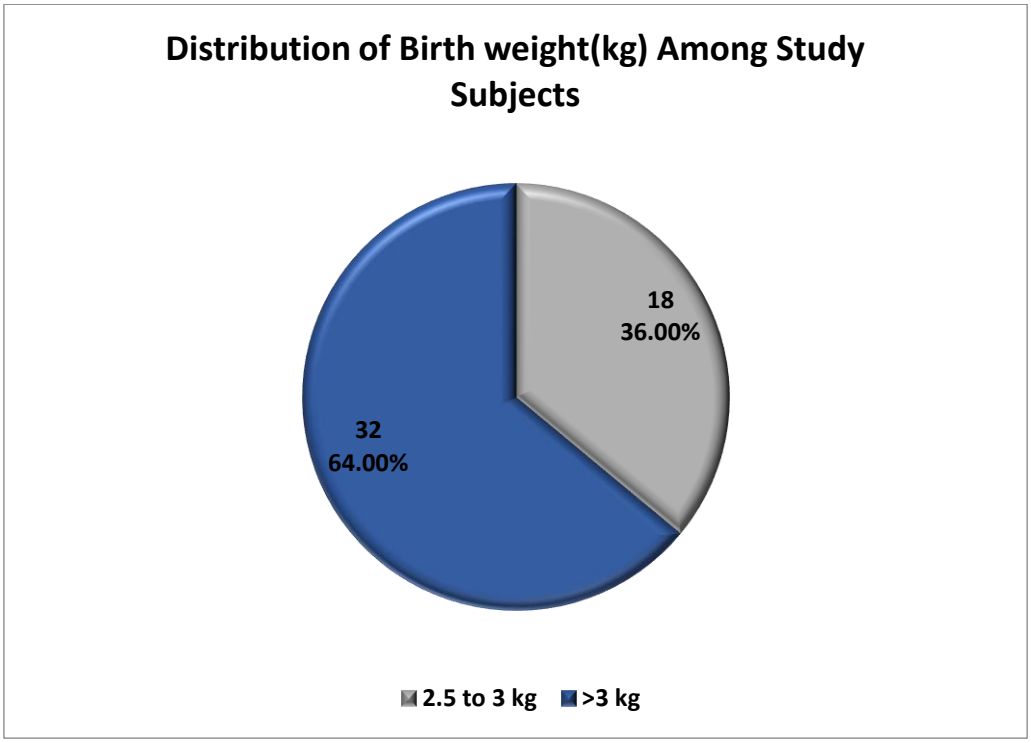


Figure 11:-Distribution of Birth Weight (kg) Among Study Subjects.

In present study, in majority 32 (64%) of neonates, Birth weight(kg) was >3 kg. Birth Weight(kg) was 2.5 to 3 kg in only 18 (36%) out of 50 neonates. Mean value of birth Weight(kg) of study subjects was 3.15 ± 0.33 .

It is shown in Table 10, Figure 11.

Table 11:-Distribution of Mode of Resuscitation Among Study Subjects.

Mode of resuscitation	Frequency	Percentage
Bag and mask	27	54.00%
Bag and tube	23	46.00%
Total	50	100.00%

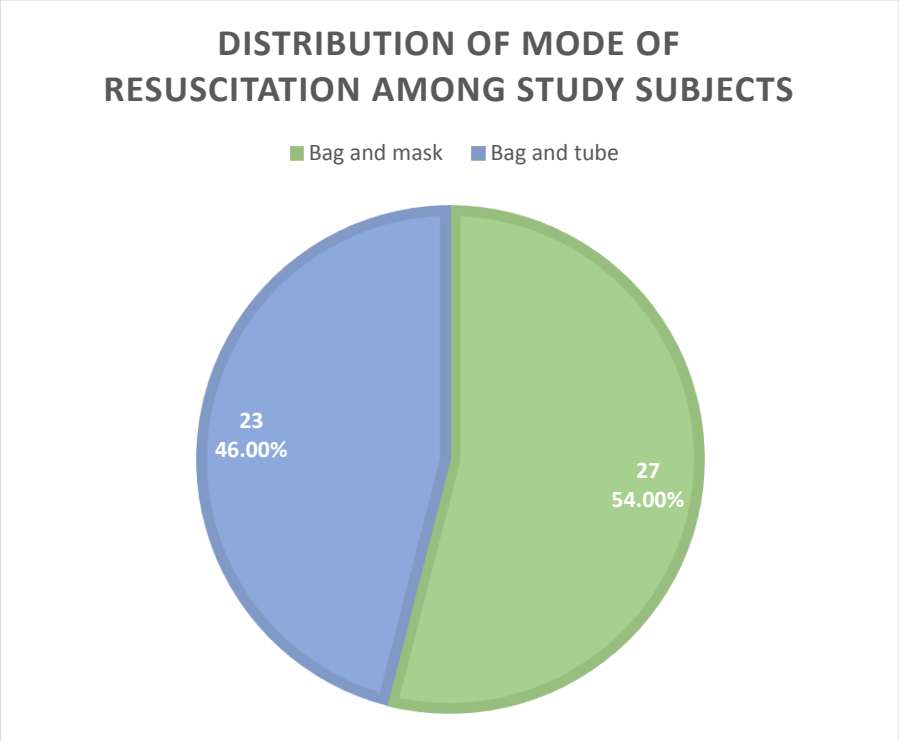


Figure 12:-Distribution of Mode of Resuscitation Among Study Subjects.

In present study, in majority 27 (54%) of neonates, Mode of Resuscitation was Bag and Mask. Mode of resuscitation was bag and tube in only 23(46%) out of 50 neonates.

It is shown in Table 11, Figure 12.

Table 12:-Descriptive statistics of APGAR Score of Study Subjects.

APGAR score	Mean ± SD	Range
at 1 minute	2.2 ± 0.81	1-3
at 5 minutes	4.24 ± 0.82	3-5

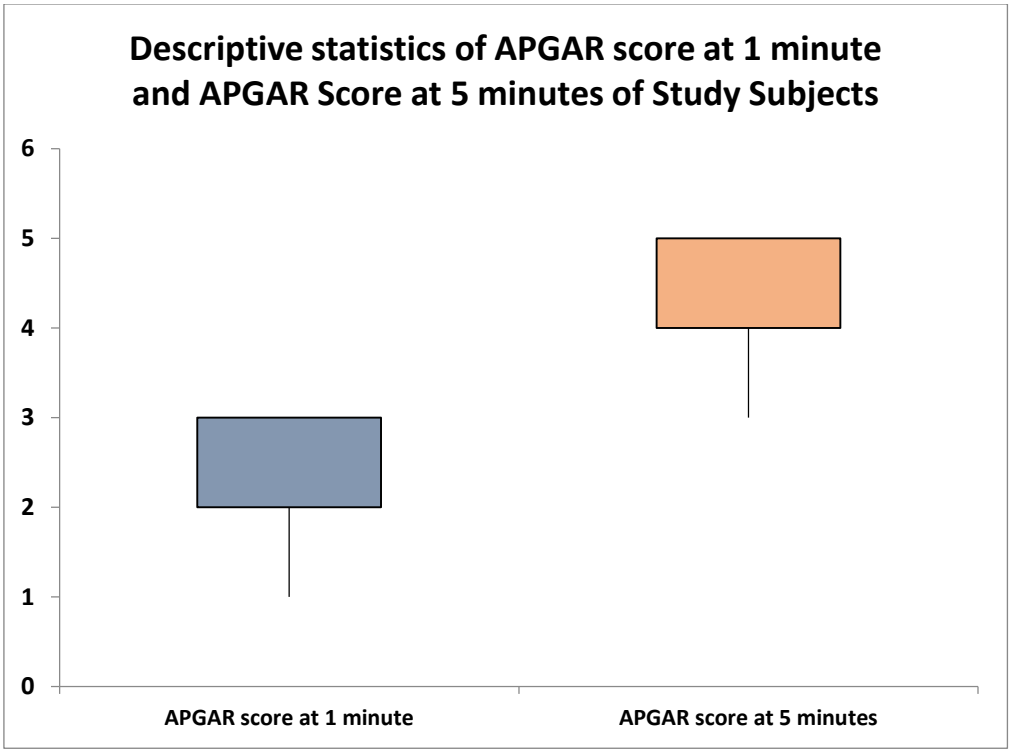


Figure 13:-Descriptive statistics of APGAR Score at 1 minute and APGAR score at 5 minutes of Study Subjects.

Mean value at 1 minute and at 5 minutes of study subjects was 2.2 ± 0.81 and 4.24 ± 0.82 respectively.

It is shown in Table 12, Figure 13.

Table 13:-Distribution of Outcome of Study Subjects.

Outcome	Frequency	Percentage
Death	6	12.00%
Discharge	44	88.00%
Total	50	100.00%

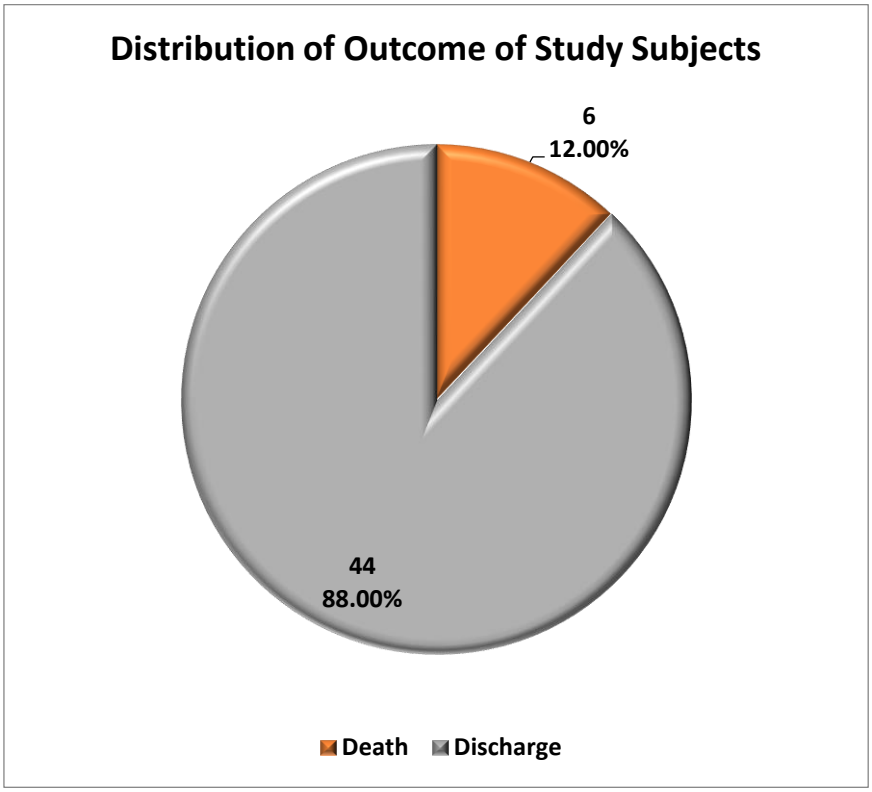


Figure 14:-Distribution of Outcome of Study Subjects.

In present study, majority 44 (88%) of neonates were discharged and only 6 (12%) out of 50 neonates died.

It is shown in Table 13, Figure 14.

Table 14:-Comparison of Cardiac troponin I(ng/mL) between within 6 hours and at 12 to 24 hours.

Cardiac troponin I(ng/mL)	Within 6 hours(n=50)	At 12 to 24 hours(n=50)	Total	P value
Normal	16 (32%)	13 (26%)	29 (29%)	0.509‡
Elevated	34 (68%)	37 (74%)	71 (71%)	
Mean ± SD	1.85 ± 1.21	2.31 ± 1.3	2.08 ± 1.27	<.0001*
Range	0.15-4	0.22-4.4	0.15-4.4	

* **Paired t test,** ‡ **Chi square test**

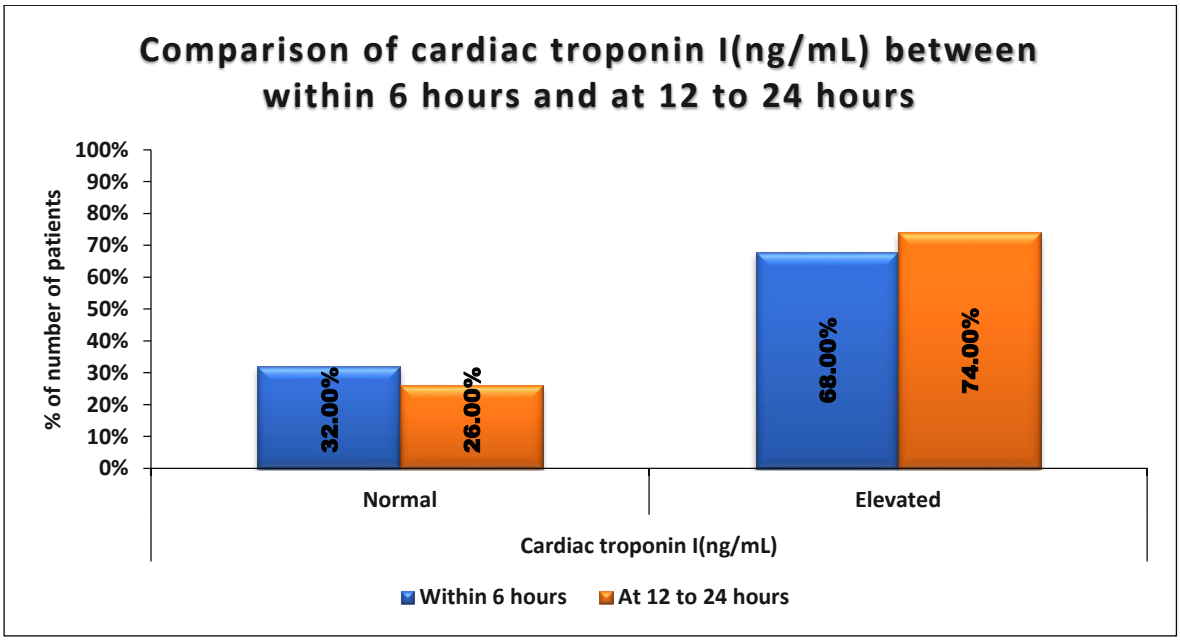


Figure 15:-Comparison of Cardiac troponin I(ng/mL) between within 6 hours and at 12 to 24 hours.

Distribution of cardiac troponin I(ng/mL) was comparable between within 6 hours and at 12 to 24 hours. (Normal:- 32% vs 26% respectively, Elevated:- 68% vs 74% respectively) (p value=0.509). On quantitative assessment, mean ± SD of cardiac troponin I(ng/mL) at 12 to 24 hours was 2.31 ± 1.3 which was significantly higher as compared to within 6 hours (1.85 ± 1.21).(p value <.0001)

It is shown in Table 14, Figure 15.

Table 15:-Comparison of distribution of Cardiac troponin I(ng/mL) between within 6 hours and at 12 to 24 hours.

Distribution of Cardiac troponin I(ng/mL)	Within 6 hours(n=50)	At 12 to 24 hours (n=50)	Total	P value
0 to <1.8	16 (32%)	13 (26%)	29 (29%)	
1.8 to 2.8	25 (50%)	18 (36%)	43 (43%)	
>2.8 to 3.8	6 (12%)	10 (20%)	16 (16%)	0.142‡
>3.8	3 (6%)	9 (18%)	12 (12%)	
Total	50 (100%)	50 (100%)	100 (100%)	

‡ **Chi square test**

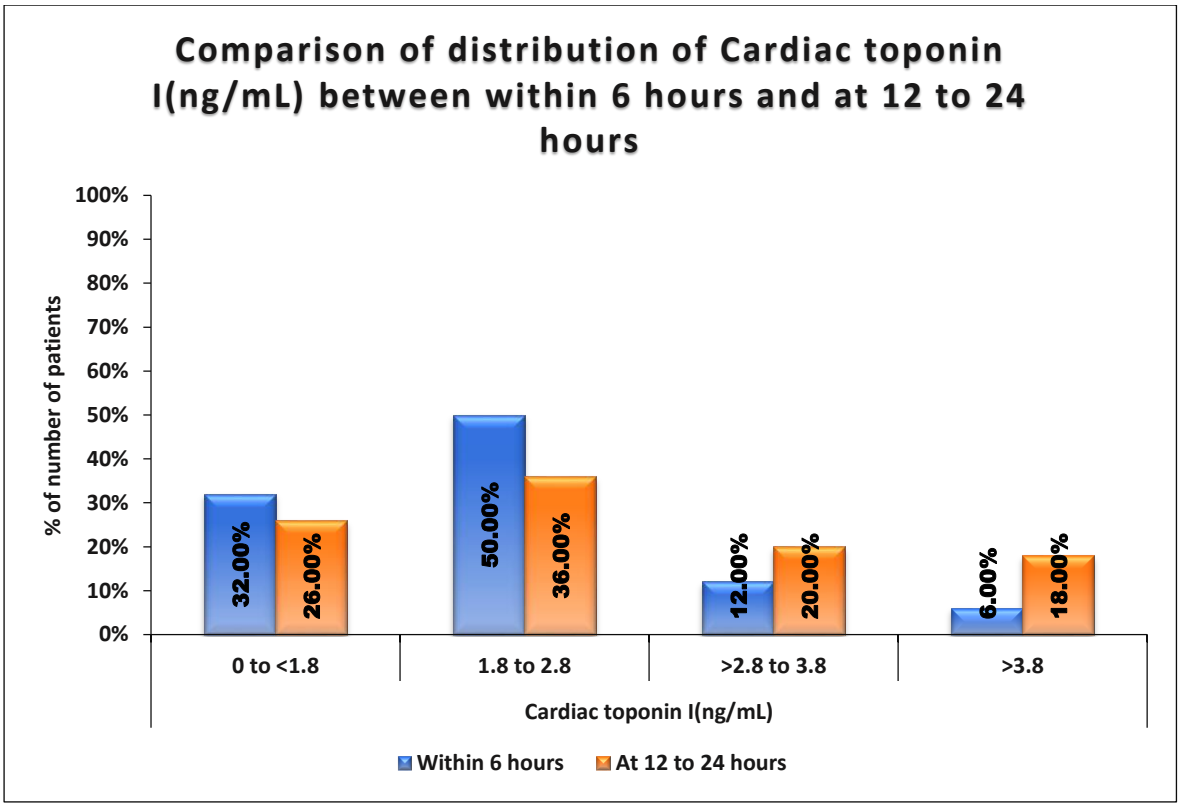


Figure 16:-Comparison of distribution of Cardiac troponin I(ng/mL) between within 6 hours and at 12 to 24 hours.

Distribution of cardiac troponin I(ng/mL) was comparable between within 6 hours and at 12 to 24 hours. (0 to <1.8:- 32% vs 26% respectively, 1.8 to 2.8:- 50% vs 36% respectively, >2.8 to 3.8:- 12% vs 20% respectively, >3.8:- 6% vs 18% respectively) (p value=0.142).

It is shown in Table 15, Figure 16.

Table 16:-Comparison of ECG findings between within 6 hours and at 12 to 24 hours.

ECG findings	Within 6 hours(n=50)	At 12 to 24 hours(n=50)	Total	P value
Normal	16 (32%)	14 (28%)	30 (30%)	0.997†
Grade 1	14 (28%)	16 (32%)	30 (30%)	
Grade 2	11 (22%)	11 (22%)	22 (22%)	
Grade 3	5 (10%)	5 (10%)	10 (10%)	
Grade 4	4 (8%)	4 (8%)	8 (8%)	
Total	50 (100%)	50 (100%)	100 (100%)	

† **Fisher's exact test**

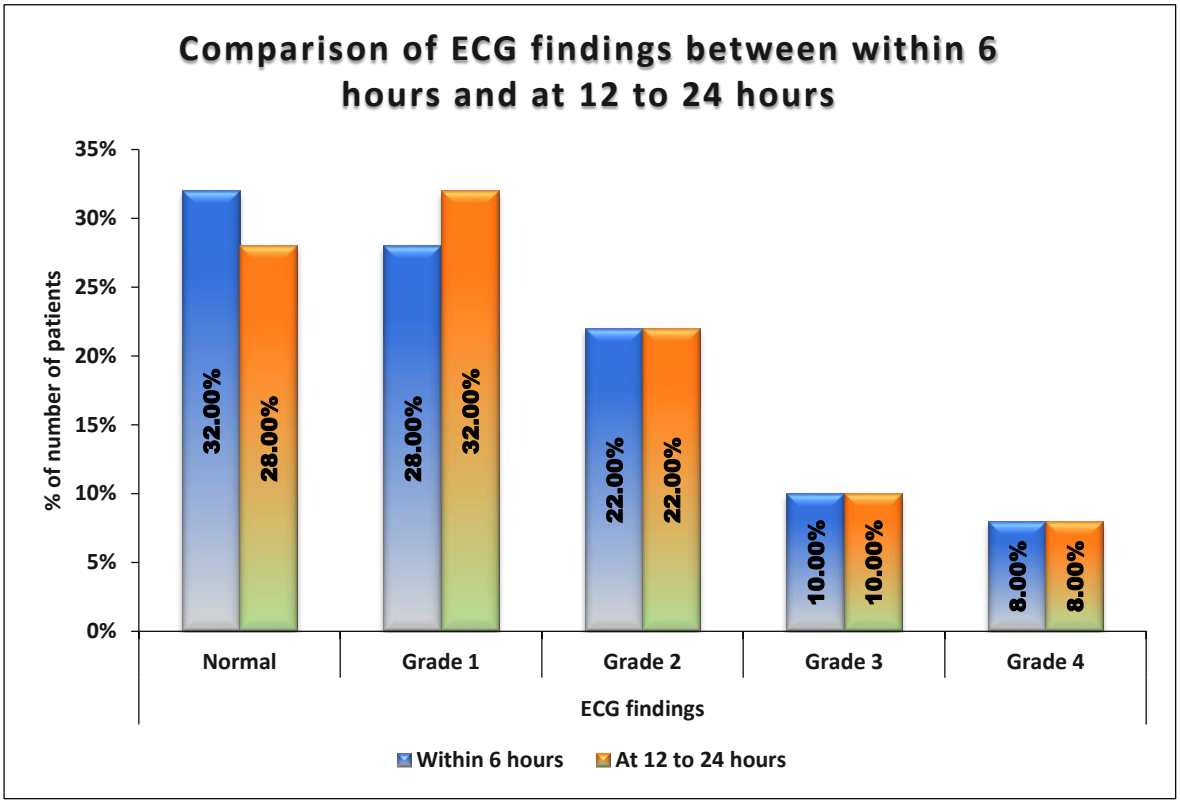


Figure 17:-Comparison of ECG findings between within 6 hours and at 12 to 24 hours.

Distribution of ECG findings was comparable between within 6 hours and at 12 to 24 hours. (Normal:- 32% vs 28% respectively, Grade 1:- 28% vs 32% respectively, Grade 2:- 22% vs 22% respectively, Grade 3:- 10% vs 10% respectively, Grade 4:- 8% vs 8% respectively) (p value=0.997).

It is shown in Table 16, Figure 17.

Table 17:-Receiver operating characteristics of Cardiac troponin I within 6 hours(ng/mL) for predicting abnormal ECG within 6 hours.

Abnormal ECG within 6 hours	Cardiac troponin I within 6 hours(ng/mL)
Area under the ROC curve (AUC)	1
Standard Error	0
95% Confidence interval	0.929 to 1.000
P value	<0.0001
Cut off	>1.28
Sensitivity(95% CI)	100%(89.7 - 100.0%)
Specificity(95% CI)	100%(79.4 - 100.0%)
PPV(95% CI)	100%(89.7 - 100.0%)
NPV(95% CI)	100%(79.4 - 100.0%)
Diagnostic accuracy	100.00%

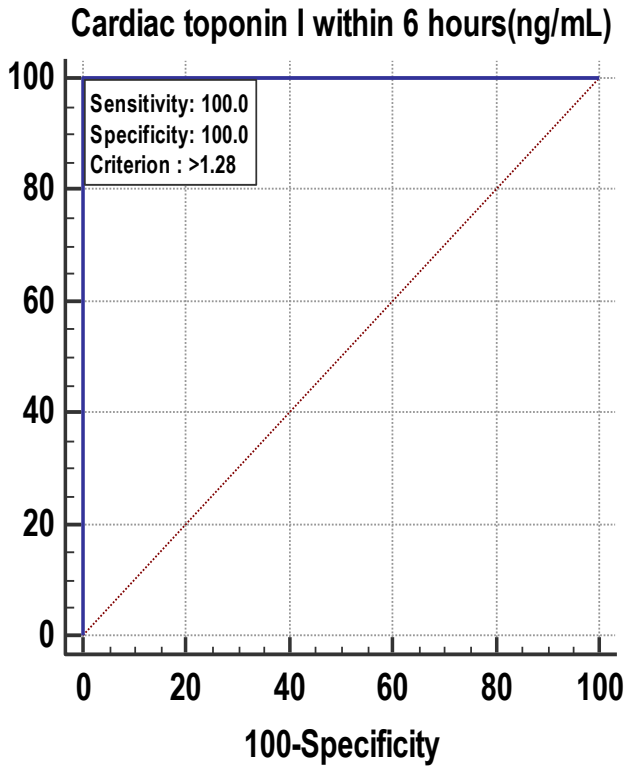


Figure 18:-Receiver operating characteristics of Cardiac troponin I within 6 hours(ng/mL) for predicting abnormal ECG within 6 hours.

Interpretation of the area under the ROC curve showed that the performance of cardiac troponin I within 6 hours(ng/mL) (AUC 1; 95% CI: 0.929 to 1.000) was outstanding. Cardiac troponin I within 6 hours(ng/mL) was the significant predictor of abnormal ECG at cut off point of >1.28 with 100% chances of correctly predicting abnormal ECG. The above table shows that the neonates who had abnormal ECG, 100% of neonates had cardiac troponin I within 6 hours(ng/mL) >1.28. If cardiac troponin I within 6 hours(ng/mL) >1.28, then there was 100% probability of abnormal ECG and if Cardiac troponin I within 6 hours(ng/mL)<=1.28, then 100% chances of no abnormal ECG. Among neonates who did not have abnormal ECG, 100% of neonates had Cardiac troponin I within 6 hours(ng/mL)<=1.28.

It is shown in Table 17, Figure 18.

Table 18:-Receiver operating characteristics of Cardiac troponin I at 12 to 24 hours(ng/mL) for predicting abnormal ECG at 12 to 24 hours .

Abnormal ECG at 12 to 24 hours	**Cardiac troponin I at 12 to 24 hours(ng/mL)**
Area under the ROC curve (AUC)	0.996
Standard Error	0.00484
95% Confidence interval	0.921 to 1.000
P value	<0.0001
Cut off	>1.82
Sensitivity(95% CI)	94.44%(81.3 - 99.3%)
Specificity(95% CI)	100%(76.8 - 100.0%)
PPV(95% CI)	100%(89.7 - 100.0%)
NPV(95% CI)	87.5%(61.7 - 98.4%)
Diagnostic accuracy	96.00%

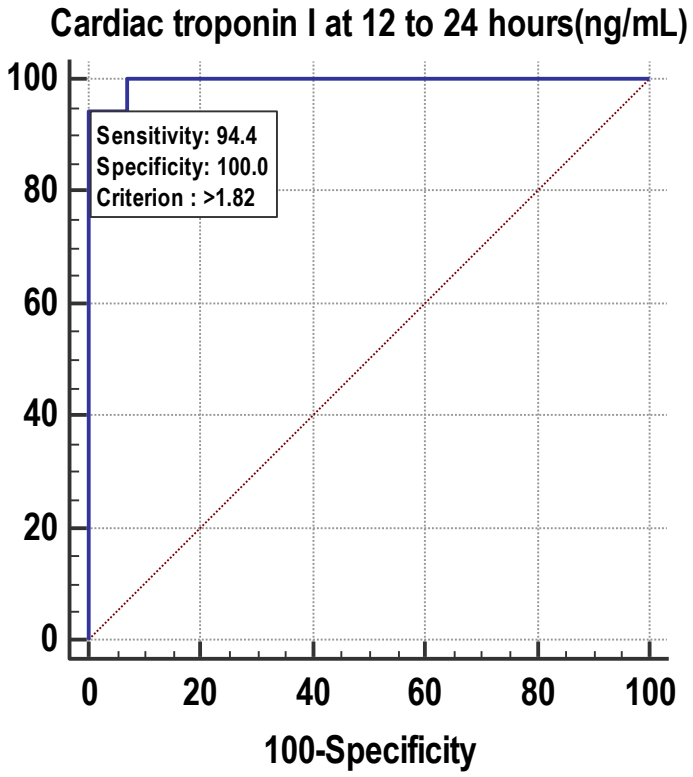


Figure 19:-Receiver operating characteristics of Cardiac troponin I at 12 to 24 hours(ng/mL) for predicting abnormal ECG at 12 to 24 hours .

Interpretation of the area under the ROC curve showed that the performance of cardiac troponin I at 12 to 24 hours(ng/mL) (AUC 0.996; 95% CI: 0.921 to 1.000) was outstanding. Cardiac troponin I at 12 to 24 hours(ng/mL) was the significant predictor of abnormal ECG at cut off point of >1.82 with 99.6% chances of correctly predicting abnormal ECG. The above table shows that the neonates who had abnormal ECG, 94.44% of patients had cardiac troponin I at 12 to 24 hours(ng/mL) >1.82. If cardiac troponin I at 12 to 24 hours(ng/mL) >1.82, then there was 100% probability of abnormal ECG and if Cardiac troponin I at 12 to 24 hours(ng/mL)<=1.82, then 87.5% chances of no abnormal ECG. Among neonates did not have abnormal ECG, 100% of neonates had Cardiac troponin I at 12 to 24 hours(ng/mL)>1.82.

It is shown in Table 18, Figure 19.

Table 19:-Association of cardiac troponin I within 6 hours (ng/mL) with ECG within 6 hours.

Cardiac troponin I(ng/mL) within 6 hours	Normal(n=16)	Grade 1(n=14)	Grade 2(n=11)	Grade 3(n=5)	Grade 4(n=4)	Total	P value
0 to <1.8	16 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	16 (32%)	<.0001†
1.8 to 2.8	0 (0%)	14 (100%)	11 (100%)	0 (0%)	0 (0%)	25 (50%)	
>2.8 to 3.8	0 (0%)	0 (0%)	0 (0%)	5 (100%)	1 (25%)	6 (12%)	
>3.8	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (75%)	3 (6%)	
Mean ± SD	0.37 ± 0.3	1.97 ± 0.21	2.33 ± 0.27	3.52 ± 0.26	3.92 ± 0.1	1.85 ± 1.21	<.0001§
Range	0.15-1.28	1.8-2.6	2-2.8	3.2-3.8	3.79-4	0.15-4	

† **Fisher's exact test,** § **ANOVA**

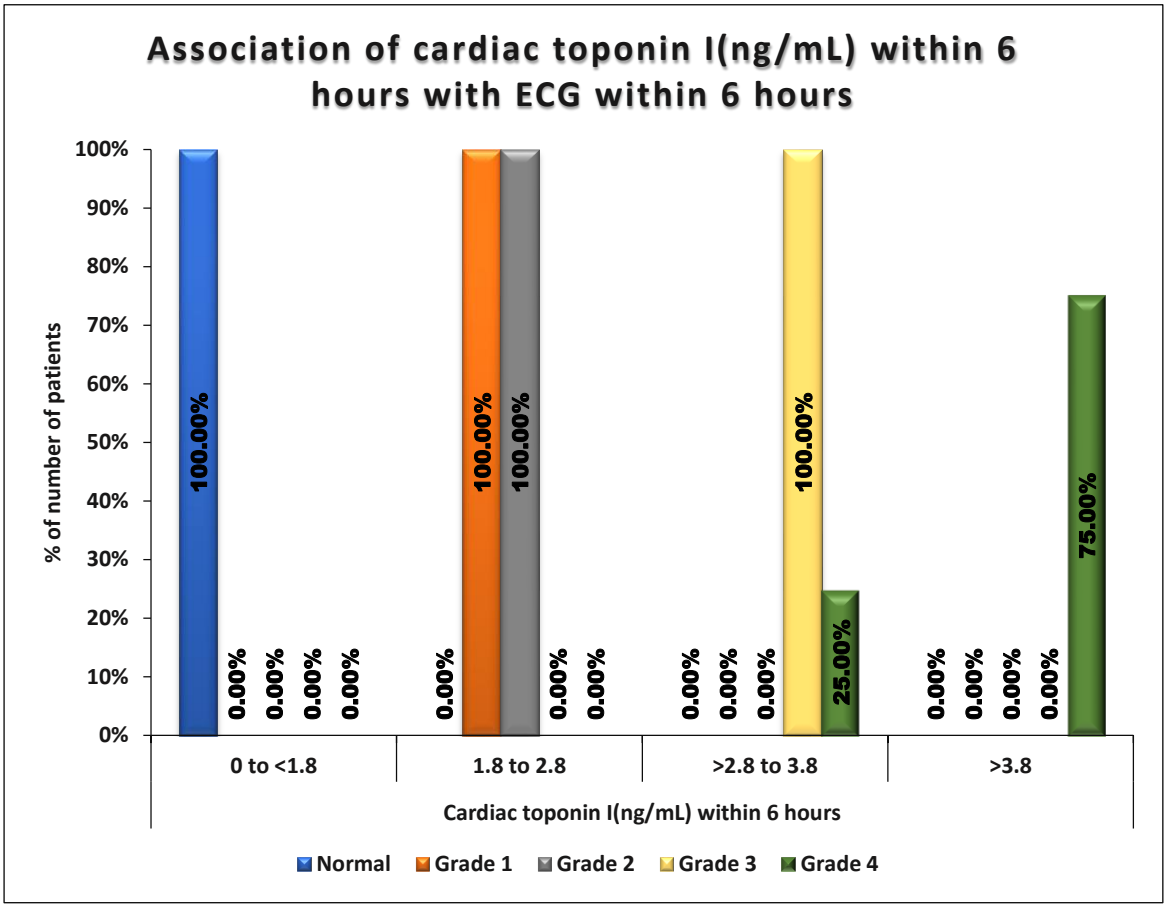


Figure 20:-Association of Cardiac troponin I within 6 hours (ng/mL) with ECG within 6 hours.

Proportion of neonates with cardiac troponin I 0 to <1.8 was significantly higher in normal (100%). Proportion of neonates with cardiac troponin I 1.8 to 2.8 was significantly higher in grade 1 (100%), grade 2 (100%). Proportion of neonates with cardiac troponin I >2.8 to 3.8 was significantly higher in grade 3 (100%). Proportion of neonates with cardiac troponin I >3.8 was significantly higher in grade 4 (75%). (p value <0.0001)

Mean ± SD of cardiac troponin I(ng/mL) within 6 hours in grade 4 (3.92 ± 0.1) was highest followed by grade 3 (3.52 ± 0.26), grade 2(2.33 ± 0.27), grade 1(1.97 ± 0.21) and in normal (0.37 ± 0.3) was lowest. (p value <.0001) .

It is shown in Table 19, Figure 20.

Table 20:-Association of Cardiac troponin I(ng/mL) at 12 to 24 hours with ECG at 12 to 24 hours.

Cardiac troponin I(ng/mL) at 12 to 24 hours	Normal(n=14)	Grade 1(n=16)	Grade 2(n=11)	Grade 3 (n=5)	Grade 4 (n=4)	Total	P value
0 to <1.8	13 (92.86%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (26%)	<.0001†
1.8 to 2.8	1 (7.14%)	13 (81.25%)	4 (36.36%)	0 (0%)	0 (0%)	18 (36%)	
>2.8 to 3.8	0 (0%)	3 (18.75%)	7 (63.64%)	0 (0%)	0 (0%)	10 (20%)	
>3.8	0 (0%)	0 (0%)	0 (0%)	5 (100%)	4 (100%)	9 (18%)	
Mean ± SD	0.59 ± 0.39	2.35 ± 0.45	2.93 ± 0.34	4.07 ± 0.1	4.3 ± 0.14	2.31 ± 1.3	<.0001§
Range	0.22-1.82	1.8-3.08	2.3-3.5	3.93-4.2	4.1-4.4	0.22-4.4	

† **Fisher's exact test,** § **ANOVA**

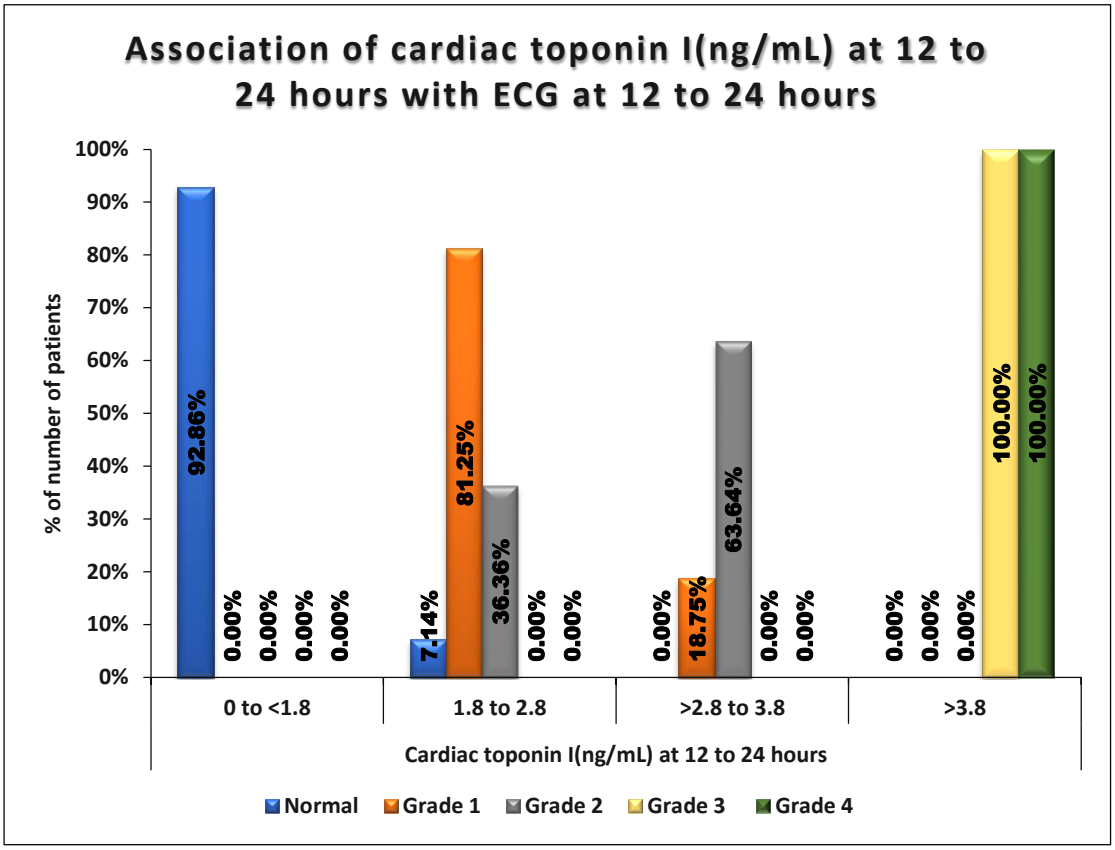


Figure 21:-Association of Cardiac troponin I(ng/mL) at 12 to 24 hours with ECG at 12 to 24 hours.

Proportion of neonates with cardiac troponin I 0 to <1.8 was significantly higher in normal (92.86%). Proportion of neonates with cardiac troponin I 1.8 to 2.8 was significantly higher in grade 1 (81.25%). Proportion of neonates with cardiac troponin I >2.8 to 3.8 was significantly higher in grade 2 (63.64%). Proportion of neonates with cardiac troponin I >3.8 was significantly higher in grade 3 (100%), grade 4 (100%). (p value <0.0001)

Mean ± SD of cardiac troponin I(ng/mL) at 12 to 24 hours in grade 4 (4.3 ± 0.14) was highest followed by grade 3 (4.07 ± 0.1), grade 2(2.93 ± 0.34), grade 1(2.35 ± 0.45) and in normal (0.59 ± 0.39) was lowest. (p value <.0001)

It is shown in Table 20, Figure 21.

Table 21:-Receiver operating characteristics of Cardiac troponin I within 6 hours and at 12 to 24 hours(ng/mL) for predicting mortality.

Mortality	Cardiac troponin I within 6 hours(ng/mL)	Cardiac troponin I at 12 to 24 hours(ng/mL)
Area under the ROC curve (AUC)	0.981	0.981
Standard Error	0.0165	0.016
95% Confidence interval	0.895 to 1.000	0.895 to 1.000
P value	<0.0001	<0.0001
Cut off	>2.8	>3.93
Sensitivity(95% CI)	100%(54.1 - 100.0%)	100%(54.1 - 100.0%)
Specificity(95% CI)	93.18%(81.3 - 98.6%)	95.45%(84.5 - 99.4%)
PPV(95% CI)	66.7%(29.9 - 92.5%)	75%(34.9 - 96.8%)
NPV(95% CI)	100%(91.4 - 100.0%)	100%(91.6 - 100.0%)
Diagnostic accuracy	94.00%	96.00%

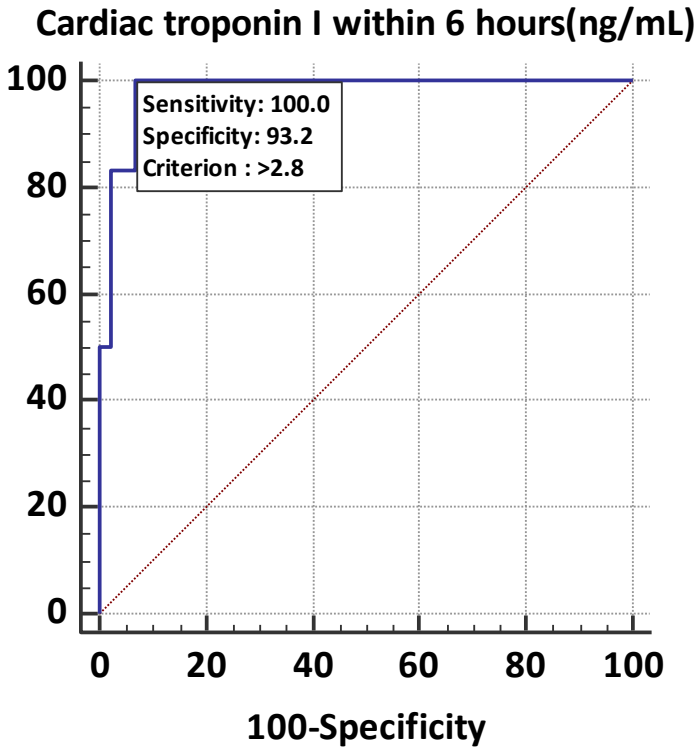


Figure 22:-Receiver operating characteristics of Cardiac troponin I at 12 to 24 hours (ng/mL) for predicting mortality.

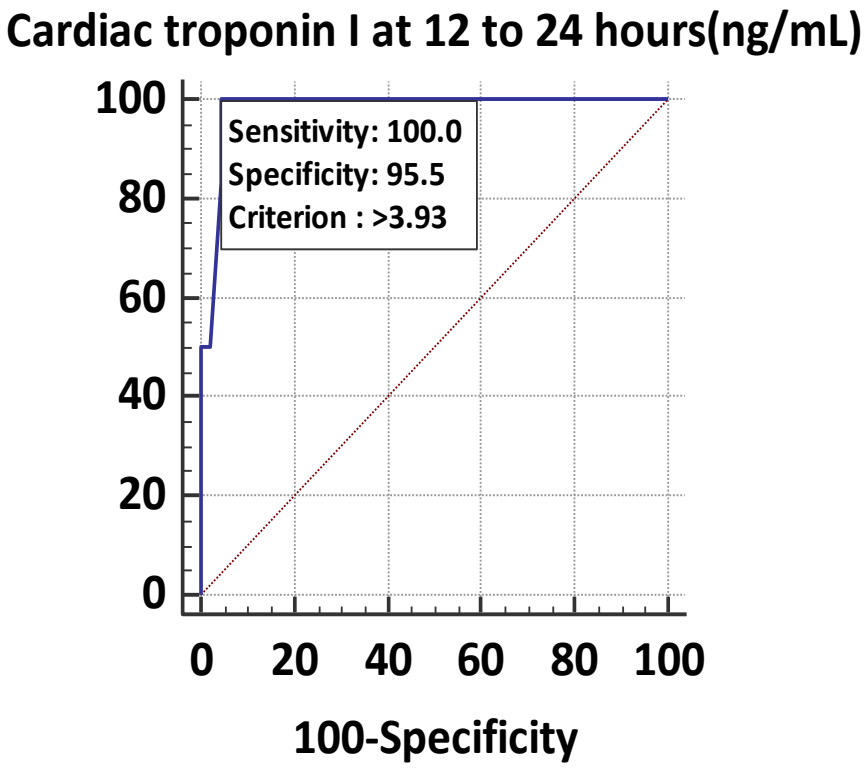


Figure 23:-Receiver operating characteristics of Cardiac troponin I at 12 to 24 hours(ng/mL) for predicting mortality.

Interpretation of the area under the ROC curve showed that the performance of cardiac troponin I within 6 hours(ng/mL) (AUC 0.981; 95% CI: 0.895 to 1.000) and cardiac troponin I at 12 to 24 hours(ng/mL) (AUC 0.981; 95% CI: 0.895 to 1.000) was outstanding.

Cardiac troponin I within 6 hours(ng/mL) and at 12 to 24 hours(ng/mL) had sensitivity of 100%. On the other hand, cardiac troponin I at 12 to 24 hours(ng/mL) had specificity of 95.45% followed by cardiac troponin I within 6 hours(ng/mL) (93.18%). Highest positive predictive value was found in cardiac troponin I at 12 to 24 hours(ng/mL) (75%).

It is shown in Table 21, Figure 22 and 23.

Table 22:-Association of Cardiac troponin I(ng/mL) with Mortality.

Cardiac troponin I(ng/mL)	Death(n=6)	Discharge(n=44)	Total	P value
Cardiac troponin I within 6 hours(ng/mL)				
Mean ± SD	3.76 ± 0.3	1.58 ± 1.04	1.85 ± 1.21	<.0001¶
Range	3.2-4	0.15-3.8	0.15-4	
Cardiac troponin I at 12 to 24 hours(ng/mL)				
Mean ± SD	4.22 ± 0.17	2.05 ± 1.16	2.31 ± 1.3	<.0001¶
Range	4-4.4	0.22-4.2	0.22-4.4	

¶ **Independent t test**

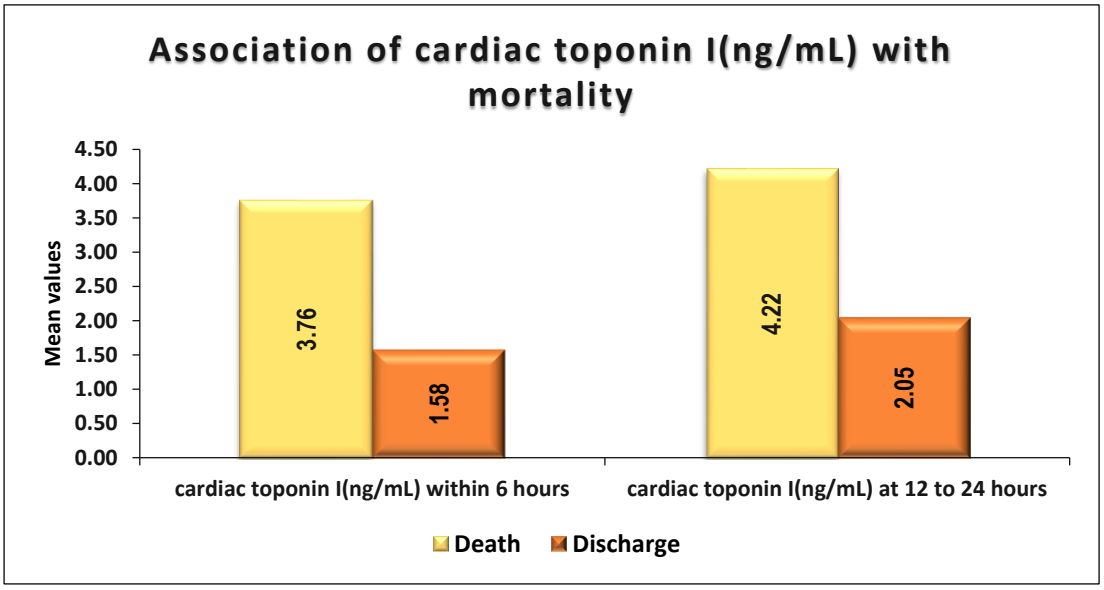


Figure 24:-Association of Cardiac troponin I(ng/mL) with mortality.

Mean ± SD of cardiac troponin I(ng/mL) within 6 hours in death was 3.76 ± 0.3 which was significantly higher as compared to discharge (1.58 ± 1.04).(p value <.0001)

Mean ± SD of cardiac troponin I(ng/mL) at 12 to 24 hours in death was 4.22 ± 0.17 which was significantly higher as compared to discharge (2.05 ± 1.16).(p value <.0001)

It is shown in Table 22, Figure 24.

Table 23:-Association of ECG findings with mortality.

ECG findings	Death(n=6)	Discharge(n=44)	Total	P value
ECG within 6 hours				
Normal	0 (0%)	16 (100%)	16 (100%)	<.0001†
Grade 1	0 (0%)	14 (100%)	14 (100%)	
Grade 2	0 (0%)	11 (100%)	11 (100%)	
Grade 3	2 (40%)	3 (60%)	5 (100%)	
Grade 4	4 (100%)	0 (0%)	4 (100%)	
ECG at 12 to 24 hours				
Normal	0 (0%)	14 (100%)	14 (100%)	<.0001†
Grade 1	0 (0%)	16 (100%)	16 (100%)	
Grade 2	0 (0%)	11 (100%)	11 (100%)	
Grade 3	2 (40%)	3 (60%)	5 (100%)	
Grade 4	4 (100%)	0 (0%)	4 (100%)	

† **Fisher's exact test**

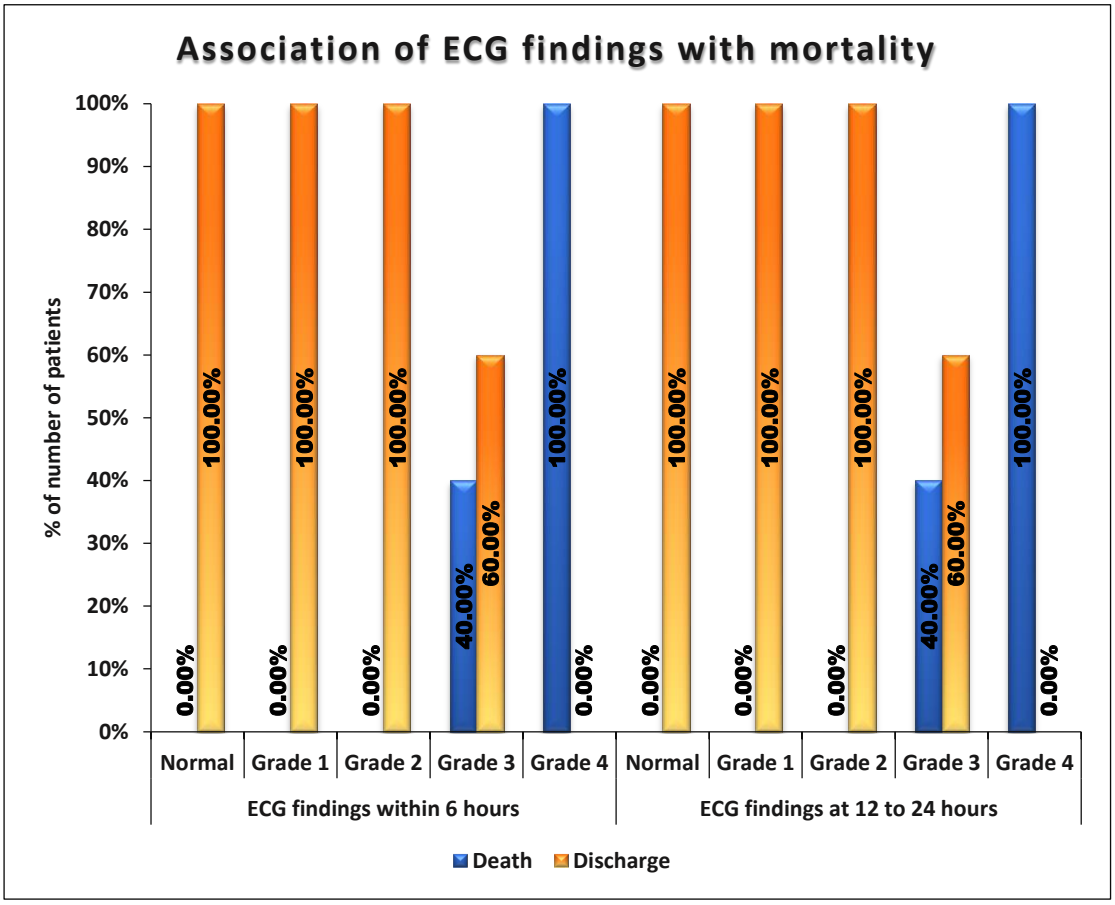


Figure 25:-Association of ECG findings with mortality.

Proportion of died neonates was significantly higher in **ECG within 6 hours**:-grade 4(100%) as compared to normal(0%), grade 1(0%), grade 2(0%), grade 3(40%).

(p value <.0001)

Proportion of died neonates was significantly higher in **ECG at 12 to 24 hours**:-grade 4(%) as compared to normal(0%), grade 1(0%), grade 2(0%), grade 3(40%).

(p value <.0001)

It is shown in Table 23, Figure 25.

Table 24:-Comparison of ECG abnormality between within 6 hours and at 12 to 24 hours.

ECG abnormality	Within 6 hours(n=50)	At 12 to 24 hours(n=50)	P value
Normal	16 (32.00%)	14 (28.00%)	0.663‡
Abnormal	34 (68.00%)	36 (72.00%)	
Total	50 (100.00%)	50 (100.00%)	

‡ **Chi square test**

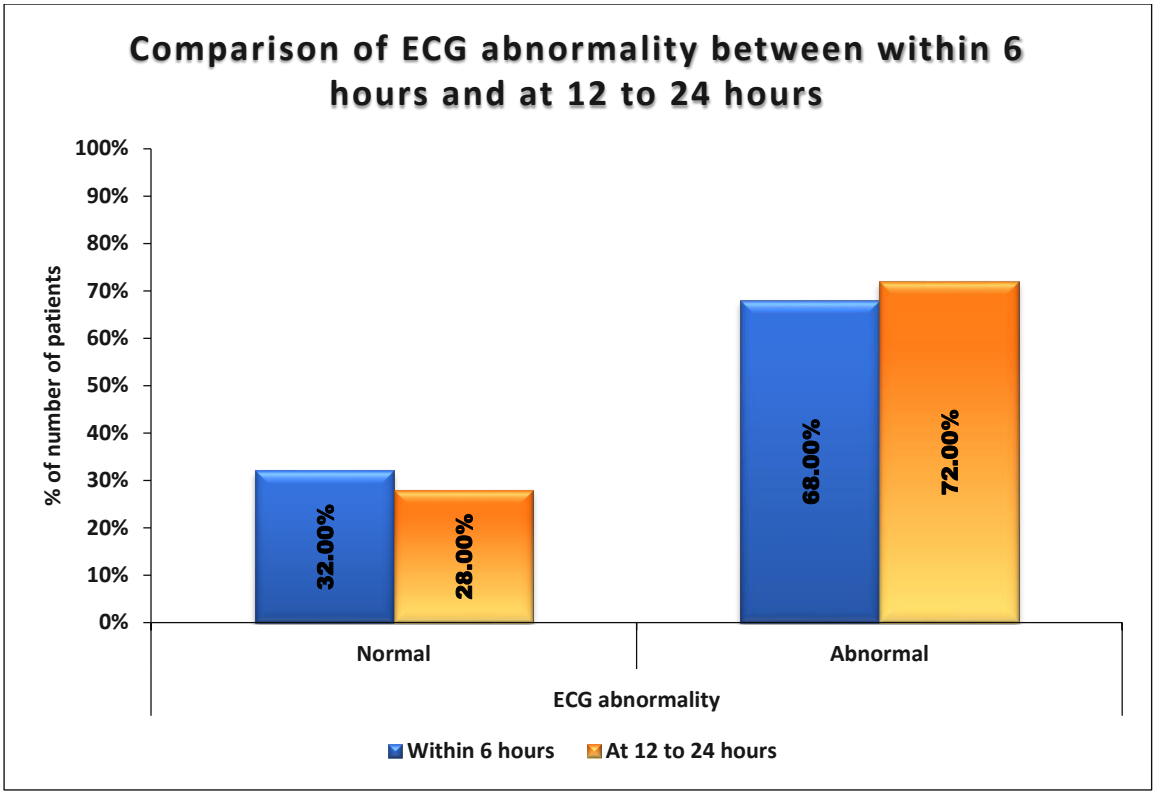


Figure 26:-Comparison of ECG abnormality between within 6 hours and at 12 to 24 hours.

Distribution of ECG abnormality was comparable between within 6 hours and at 12 to 24 hours. (Normal:- 32% vs 28% respectively, Abnormal:- 68% vs 72% respectively)

(p value=0.663).

It is shown in Table 24, Figure 26.

DISCUSSION

DISCUSSION

In this prospective observational study, the most important finding was that cTnI showed significant association with myocardial injury and mortality in children with perinatal asphyxia.

We observed that the levels of cardiac troponin increased from the initial hours with values of 1.98 at 6 hours and 2.47 at 12 to 24 hours thereby showing that the values are increased in perinatal asphyxia.

The findings were in line with other studies. In the study by Matter et al[68] cardiac troponin I was measured at 12-24 hours where it was found that serum troponin concentrations were significantly higher in asphyxiated neonates compared to those without asphyxia (0.17 vs. 0.03 µg/l, P<0.001).

In the study by Jiang et al,[65] the cardiac troponin was measured at 12 hours and 7 days, the values were 0.1325 and 0.018 µg/l, respectively. In the study by Simović AM et al,[60] levels of cardiac troponin I were measured at 24-48 hours after birth. It was found that the value was 0.08 µg/L.

In the study by Szymankiewicz M et al,[59] the cardiac troponin I levels were measured between 12 and 24 hours, the mean cTnT levels were higher in asphyxiated infants than controls (0.287 vs. 0.112 ng/mL, P<0.001).

In the study by Issa A et al[10] cardiac troponin I was measured 24-78 hours after birth. The mean value was significantly higher in cases than controls (1.26 vs.0.79, P<0.001).

Trevisanuto et al [8] measured cardiac troponin I level at 12 hours and found that asphyxiated neonates had significantly higher median cTnI levels than controls (0.36 vs. 0.04 g/l; p<0.01). The cTnI levels were more than detection limit for the assay in all asphyxiated neonates. Out of these, 10 neonates had cTnI levels more than the decisional level for myocardial damage (0.15 g/l).

In a case control study by Pal P et al [1] cTn I levels in severely asphyxiated neonates were significantly higher than moderately asphyxiated neonates and control group neonates (4.6 vs. 1.8 vs. 0.6 ng/ml, P <0.05).

Though the study results of our study and other studies show that started troponin levels can be a standard marker among new-born's with asphyxia its practical use is limited by confounders suggest preterm delivery administration of adrenaline gestational age and birth weight.[3,68]

Perinatal asphyxia causes multi organ dysfunction with myocardial involvement being a common condition leading to adverse outcomes. Cardiac dysfunction can be so severe that it leads to congestive heart failure and shock, which can result in the death of a new-born. The ECG and cardiac enzymes can be utilised to show that myocardial function is impaired.[1]

In present study, ECG showed abnormality in 34 cases. ECG changes have been suggestive of myocardial ischemia in new-born's which include generalized T-wave inversion or flattening, ST segment elevation or depression, abnormal Q wave and bundle branch block.

While evaluation we found that for initial 6 hours, cardiac troponin I cut-off values of >1.28 significantly predicted ECG changes with 100% accuracy. Moreover, cardiac troponin I showed increasing trend with grade of ECG abnormality (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 1.97 vs. 2.33 vs. 3.52 vs. 3.92, $p<0.0001$). The present study findings corroborated with many previous research such as by Sadoh et al [69]and Yildirim et al,[70] where the cardiac troponin levels were found to be a useful indicator of myocardial injury.

Similar findings were reported by Kiruthika N,[71] observed that mean troponin I levels was significantly higher among neonates with abnormal ECG in comparison to those with normal ECG (3.1 vs. 0.65 ng/ml, $p<0.05$). This concludes that mean troponin I levels in cases with cardiac dysfunction (as evidenced by ECG abnormality) was found significantly higher in cases with severe asphyxia.

Even Tanna K et al [3] found a direct correlation to be present between ECG changes and cardiac troponin levels which showed increasing abnormalities with increasing with severity of HIE.

Issa et al [10] found that the median value of HIE III was about three times that of HIE I and >3 times that of HIE II.

Besides 6 hours, even at 12-24 hours, cardiac troponin I cut-off of >1.82 significantly predicted ECG abnormality with 100% accuracy. Moreover, cardiac troponin I showed a significant increasing trend with grade of myocardial injury (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 2.35 vs. 2.93 vs. 4.07 vs. 4.3, p<0.0001).

Among other studies, Jiang et al[65] measured cardiac troponin levels at 12-24 hours and found that hs-cTnI levels at 12 hours at an optimal cut-off value of >0.087 µg/L differentiated between the myocardial injury and non-myocardial injury groups with the sensitivity, specificity, PPV, NPV, and accuracy of 55.6%, 95.5%, 90.9%, 72.4%, and 77.5%, respectively. Hs-cTnI levels at 12 hours accurately predicted myocardial injury in 10 out of the 18 cases among neonates with myocardial injury.

Sundarajan et al[72] reported that there was significant association between ECG changes and Troponin T (P < 0.001). Troponin I test showed the highest sensitivity of about 84.37%, PPV of 93.1% and NPV of 76% in diagnosing myocardial injury in contrast to ECG .In terms of specificity, troponin T showed better specificity (88.9%) in comparison with ECG. They also found significant association of HIE grading with cTn I levels (P<0.05).

In the study by Agrawal et al[51] also, there was significant association of ECG findings and increased cardiac troponin I were with the different grades of HIE (p<0.05).

In the study by Prithviraj et al,[62] the mean cardiac troponin levels at 48 and 72 hours in stage 1 were 0.21±0.06 and 0.24±0.04, respectively, in stage 2 were 0.38±0.13 and 0.44±0.15, respectively, and in stage 3 were 0.84±0.25 and 0.96±0.15, respectively

(p=0.001); thereby showing the role of increasing values of CTi with grade of myocardial injury.

Acute myocardial infarction is diagnosed, by the commonly preferred markers for detecting the myocardial injury include cardiac troponins T & I because their sensitivity and specificity is high. Cardiac troponin, which is a protein, is released from myocytes during irreversible myocardial damage. It is reported to demonstrate high specificity to the cardiac tissues; it is reliable for establish correct diagnosis of myocardial infarction, when there is history of ischemic pain or changes in ECG reflect ischemia.[1]

Cardiac troponin level depend on the size of infarct, which indicate the prognosis after an infarction.[3] Moreover, the time of myocardial injury holds important since the values goes on increasing from 6 hours to 12 hours to 24 hours.

Myocardial injury has been specifically discussed because it leads to adverse outcomes such as neonatal death. In our study, 6 (12%) children died. Among other studies, Sundarajan et al[72] reported that out of 50 asphyxiated infants, 11 died. In the study by Rajakumar et al[16], out of 30 asphyxiated new-born's, 9 died. Kanik et al[73] reported that 9 out of 34 infants died.

In relation to neonatal mortality, we found that cTn I was significantly associated with mortality at 6 hours (death vs. discharge: 3.76 ± 0.3 vs. 1.58 ± 1.04, P<0.0001) and at 12-24 hours (death vs. discharge: 4.22 ± 0.17 vs. 2.05 ± 1.16, P<0.0001). Similarly, ECG was also significantly associated with mortality. Overall, cardiac

troponin I at a cut-off of >2.8 (6 hours) and >3.93 (12-24 hours) predicted mortality in 94% and 96% cases, respectively.

In corroboration, Matter et al[68] found that serum cardiac troponin I was significantly higher among non survivors. The cardiac troponin I at cut-off value of 0.15 lg/l, had specificity and sensitivity of 100% and 70%, respectively in mortality prediction among neonates with asphyxia.

For predicting mortality Simović AM et al,[60]established a cardiac troponin I cut off of more than 0.135 µg/L with the sensitivity and specificity of 84.6% and 85.9%, respectively. They recommended cardiac troponin I as the most sensitive as well as reliable early predictor of mortality among full-term neonates having perinatal asphyxia.

Zhou et al[63] also reported that troponin I levels measured at 24 hours significantly predicted mortality in neonates with asphyxia.

Sundarajan et al[72] reported that cardiac troponin (P=0.001) as well as ECG changes (P=0.017) were significantly associated with the outcome, as infants with these changes were at more risk of having a worse outcome. This indicates that these tests are the predictors of mortality because of myocardial involvement among infants with perinatal asphyxia.

Kiruthika N[71]reported that troponin I levels was significantly higher in death babies in comparison to in discharged babies (3.71ng/ml vs. 1.69 ng/ml, $p<0.05$) as seen in our study making Troponin I levels a predictor for mortality in asphyxiated babies.

Issa et al,[10] came up with similar findings as the median troponin I levels in non-survivors were significantly higher than the survivors (4.00 vs. 1.21, $P= 0.015$). Similar findings were reported by Liu L et al.[74]since mortality was associated to the degree of myocardial ischemia and deaths.

Overall it can be said that CTnI can be used as a marker for detection of myocardial dysfunction in asphyxiated new-borns .

CONCLUSION

CONCLUSION

- Cardiac troponin levels significantly increase during the neonatal asphyxia.

- Receiver operating characteristic curve (ROC) analysis showed that troponin I can be a useful diagnostic marker for myocardial injury at 6 hours with the cut off of more than 1.28 and at 12 to 24 hours with the cut off of more than 1.82, in patients with neonatal asphyxia.

- Moreover, cardiac troponin I was also associated with increasing grade of myocardial injury as shown by ECG changes, making it a valuable tool for detection of early myocardial injury due to perinatal birth asphyxia.

- Hence this study concludes that elevated cardiac troponin I and its association with ECG changes can be a useful diagnostic marker of myocardial injury due to perinatal asphyxia.

- However further large multi centric trials are needed to validate it as a standard Diagnostic tool in the management of asphyxiated neonates.

LIMITATIONS OF THE STUDY

- In our study, cardiac troponin was not compared with other cardiac biomarkers, such as CK-MB, Brain natriuretic peptide (BNP) ,serum myoglobin .

- Another limitation was that cardiac troponin was not compared with other diagnostic modalities, like Doppler echocardiography.

STRENGTHS OF THE STUDY

1. There is scarcity of studies in India that evaluated the role of serum cardiac troponin I levels in a term asphyxiated neonates. Thus our study can act as a stepping zone for further larger studies to find out usefulness of troponin I in Indian new-born's with birth asphyxia.

2. Many of our results corroborated with other studies done at different times and in different places both in India as well as outside India. This study, thus, adds to the already existing literature about the electrocardiography changes in aasphyxiated term neonates.

3. A fairly reasonable number of cases were studied. So, it gives a fair idea of the correlate cardiac troponin I levels with ECG changes in myocardial injury in a term neonates with perinatal asphyxia encountered in a hospital setting.

4. The study was able to determine an association of CTi with the grade of myocardial injury.

SUMMARY

SUMMARY

The prospective study was conducted at R .L .Jalappa Hospital ,Tamaka, Kolar from January 2020 to December 2020 .

50 neonates born at term with the evidence of birth asphyxia were included in the study.

After obtaining written informed consent from the parents of the neonates ,Detailed perinatal history, Clinical systemic examination, Laboratory investigations, Neonatal ECG Electrode Placement and ECG findings were recorded. CTi was done at 6 hours and repeated at 12 to 24 hours. the outcomes measures were mortality due to myocardial injury.

Results

Mothers clinical and Demographic characteristics .

- Mean gestational age of mother was 38.74 weeks.
- 68% of mothers were primi gravida.
- In majority (62%) of patients, liquor status was meconium. 34% of patients did not have fetal distress followed by category 1 (26%) and category 2 (22%).
- In majority (46%), mode of Delivery was normal vaginal delivery followed by LSCS (42%). Majority (52%) of babies was males. Mean birth weight was 3.15 kg.

Neonatal characteristics

- Mean APGAR score at 1 minute and 5 minutes was 2.2 and 4.24, respectively.
- In 54.00% of neonates, bag and mask resuscitation was required.
- Mortality was seen in 6 out of 50 neonates (12%).

CTi and ECG evaluation

- In present study, ECG showed abnormality in 34 cases.

- We observed that the levels of troponin increased from the initial hours with values of 1.98 at 6 hours and 2.47 at 12 to 24 hours thereby showing that the values are increased in perinatal asphyxia.

- While evaluation we found that for initial 6 hours, cardiac troponin I cut-off values of >1.28 significantly predicted ECG changes with 100% accuracy. Moreover, cardiac troponin I showed increasing trend with grade of ECG abnormality (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 1.97 vs. 2.33 vs. 3.52 vs. 3.92, $p<0.0001$).

- Besides 6 hours, even at 12-24 hours, cardiac troponin I cut-off of >1.82 significantly predicted ECG abnormality with 100% accuracy. Moreover, cardiac troponin I showed a significant increasing trend with grade of myocardial injury (grade 1 vs. grade 2 vs. grade 3 vs. grade 4: 2.35 vs. 2.93 vs. 4.07 vs. 4.3, $p<0.0001$).

- Mortality was seen in 6 out of 50 neonates (12%).

- Mean cardiac troponin I within 6 hours(ng/mL) in died patients was 3.76 ± 0.3 which was significantly higher as compared to discharged(1.58 ± 1.04).(p value <.0001)

- Mean cardiac troponin I at 12 to 24 hours(ng/mL) in died patients was 4.22 ± 0.17 which was significantly higher as compared to discharged (2.05 ± 1.16).(p value <.0001).

- Hence we concluded that cardiac troponin I and its association with ECG changes can be a useful diagnostic marker of myocardial injury due to perinatal asphyxia.

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ANNEXURE

ANNEXURE-I

PROFORMA

A PROSPECTIVE STUDY ON CARDIAC TROPONIN I AND ECG CHANGES IN DIAGNOSIS OF MYOCARDIAL INJURY DUE TO PERINATAL ASPHYXIA IN TERM NEONATES

SL No: Date:

Name Of Mother:

Age Of Mother:

Name Of Father:

Address:

Gestational Age :

Date Of Birth:

Time Of Birth:

Place Of Birth:

Date Of Discharge /Death:

Ante Natal Data :

1. Gravida :
2. Risk factors :

Natal Data :

1. Foetal Distress(CTG Changes):
2. Liquor status :
3. Mode of Delivery: Vaginal

Vacuum assisted vaginal delivery

LSCS

4. Mode of Resuscitation :

   APGAR SCORE: 1 minute :

   5 minute :

   10 minute:

   Need for PPV >1minute :

   Spontaneous respiration established : Yes / No

   Required intubation :

5. Birth weight

CORD BLOOD ABG:

Ph- PCo2- Po2- HCo3-

LABORATORY PARAMETERS

PARAMETER	Within 6 hours of life	Repeated at 12 to 24 hours of life
CARDIAC TROPONIN I		
ECG		

ANNEXURE-II

INFORMED CONSENT FORM

Date:

I, Mr/Mrs _____ have been explained in my own vernacular language that my child _____ will be included in the study**, A PROSPECTIVE STUDY ON CARDIAC TROPONIN I AND ECG CHANGES IN DIAGNOSIS OF MYOCARDIAL INJURY DUE TO PERINATAL ASPHYXIA IN TERM NEONATES.**

Ihereby give my valid written informed consent without any force or prejudice for recording the observations of clinical and haematological parameters . The nature and risks involved have been explained to me, to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I provide consent voluntarily to allow my child as a participant in this research. I hereby **give consent to provide history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc**. For academic and scientific purpose the operation / procedure, etc may be video graphed or photographed. All the data may be published or used for any academic purpose. I will not hold the doctors / institute etc responsible for any untoward consequences during the procedure / study. A copy of this informed consent form and patient information sheet has been provided to the participant.

_____

(Signature & Name of Pt. Attendant)

_____

(Signature/Thumb impression & Name of Patient/Guardian)

(Relation with patient)

Witness :

(Signature & Name of Research person/doctor)

ANNEXURE-III

A PROSPECTIVE STUDY ON CARDIAC TROPONIN I AND ECG CHANGES IN DIAGNOSIS OF MYOCARDIAL INJURY DUE TO PERINATAL ASPHYXIA IN TERM NEONATES.

PATIENT INFORMATION SHEET

Principal investigators : Dr. VIDYA SHREE . B / Dr. BEERE GOWDA Y.C.

I, Dr. VIDYA SHREE.B , Post graduate student in Department of Paediatrics at Sri Devaraj Urs Medical College, will be conducting a study titled **"A PROSPECTIVE STUDY ON CARDIAC TROPONIN I AND ECG CHANGES IN DIAGNOSIS OF MYOCARDIAL INJURY DUE TO PERINATAL ASPHYXIA IN TERM NEONATES."** for my dissertation under the guidance of Dr. BEERE GOWDA.Y.C, Professor of Department of Paediatrics. The participants of this study i.e. include 50 term neonates admitted to NICU in view of with perinatal asphyxia.

You will not be paid any financial compensation for the participating in this research project.

All the data will be kept confidential and will be used only for research purpose by this institution. You are free to provide consent for the participation of your child in the study. You can also withdraw your child from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.

Name and Signature of the Principal Investigator

Date:

Place : Kolar.

ಮಾಹಿತಿನೀಡಿದಒಪ್ಪಿಗೆನಮೂನೆ

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ/ಶ್ರೀಮತಿ _____

ನನ್ನಮಗುವನ್ನುಅಧ್ಯಯನದಲ್ಲಿಸೇರಿಸಲಾಗುವುದುಎಂದುವಿವರಿಸಲಾಗಿದೆ,

ಕಾರ್ಡಿಯಾಕ್ಕ್ರೀಪೋನಿನ್ಮತ್ತುಇಸಿಜಿಬದಲಾವಣೆಗಳಕುರಿತುಪ್ರತಿನಿತ್ಯಹೃದಯಸ್ನಾಯುವಿನಗಾಯದರೋಗನಿರ್ಣಯದಲ್ಲಿನಿರೀಕ್ಷಿತಅಧ್ಯಯನ.

ಕ್ಲಿನಿಕಲ್ಮತ್ತುಹೆಮಟೊಲಾಜಿಕಲ್ನಿಯತಾಂಕಗಳಅವಲೋಕನಗಳನ್ನುದಾಖಲಿಸಲುನಾನುಯಾವುದೇಬಲಅಥ

ವಾಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆನನ್ನಮಾನ್ಯವಾದಲಿಖಿತತಿಳುವಳಿಕೆಯನ್ನುನೀಡುತ್ತೇನೆ.

ಒಳಗೊಂಡಿರುವಸ್ವಭಾವಮತ್ತುಅಪಾಯಗಳನ್ನುನನಗೆವಿವರಿಸಲಾಗಿದೆ, ನನ್ನತೃಪ್ತಿ.

ನಡೆಸುತ್ತಿರುವಅಧ್ಯಯನದಬಗ್ಗೆನನಗೆವಿವರವಾಗಿವಿವರಿಸಲಾಗಿದೆ.

ನಾನುರೋಗಿಯಮಾಹಿತಿಹಾಳೆಯನ್ನುಓದಿದ್ದೇನೆಮತ್ತುಯಾವುದೇಪ್ರಶ್ನೆಯನ್ನುಕೇಳಲುನನಗೆಅವಕಾಶವಿದೆ

ನಾನುಕೇಳಿದಯಾವುದೇಪ್ರಶ್ನೆಗೆನನ್ನತೃಪ್ತಿಗೆಉತ್ತರಿಸಲಾಗಿದೆ.

ನನ್ನಮಗುವನ್ನುಈಸಂಶೋಧನೆಯಲ್ಲಿಪಾಲ್ಗೊಳ್ಳುವಂತೆಅನುಮತಿಸಲುನಾನುಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದಒಪ್ಪಿ

ಗೆಯನ್ನುನೀಡುತ್ತೇನೆ. ಇತಿಹಾಸವನ್ನುಒದಗಿಸಲು, ದೈಹಿಕಪರೀಕ್ಷೆಗೆಒಳಗಾಗಲು,

ಕಾರ್ಯವಿಧಾನಕ್ಕೆಒಳಗಾಗಲು,

ತನಿಖೆಗೆಒಳಗಾಗಲುಮತ್ತುಅದರಫಲಿತಾಂಶಗಳುಮತ್ತುದಾಖಲೆಗಳನ್ನುವೈದ್ಯರು /

ಸಂಸ್ಥೆಇತ್ಯಾದಿಗಳಿಗೆಒದಗಿಸಲುನಾನುಈಮೂಲಕಒಪ್ಪಿಗೆನೀಡುತ್ತೇನೆ.

ಶೈಕ್ಷಣಿಕಮತ್ತುವೈಜ್ಞಾನಿಕಉದ್ದೇಶಕ್ಕಾಗಿಕಾರ್ಯಾಚರಣೆ / ಕಾರ್ಯವಿಧಾನ,

ಇತ್ಯಾದಿಗಳನ್ನುವೀಡಿಯೊಗ್ರಾಫ್ಅಥವಾಛಾಯಾಚಿತ್ರಮಾಡಬಹುದು.

ಎಲ್ಲಾಡೇಟಾವನ್ನುಪ್ರಕಟಿಸಬಹುದುಅಥವಾಯಾವುದೇಶೈಕ್ಷಣಿಕಉದ್ದೇಶಕ್ಕಾಗಿಬಳಸಬಹುದು.

ಕಾರ್ಯವಿಧಾನ / ಅಧ್ಯಯನದಸಮಯದಲ್ಲಿಯಾವುದೇಅಹಿತಕರಪರಿಣಾಮಗಳಿಗೆನಾನುವೈದ್ಯರು /

ಸಂಸ್ಥೆಇತ್ಯಾದಿಗಳನ್ನುಜವಾಬ್ದಾರರನ್ನಾಗಿಮಾಡುವುದಿಲ್ಲ.

ಈತಿಳುವಳಿಕೆಯುಳ್ಳಒಪ್ಪಿಗೆನಮೂನೆಯಪ್ರತಿಯನ್ನುಮತ್ತುರೋಗಿಯಮಾಹಿತಿಹಾಳೆಯನ್ನುಭಾಗವಹಿಸುವ

ವರಿಗೆಒದಗಿಸಲಾಗಿದೆ.

(ಪಂ. ಅಟೆಂಡೆಂಟ್‌ನಸಹಿಮತ್ತುಹೆಸರು)

_____

(ಸಹಿ/ಹೆಬ್ಬೆರಳಿನಗುರುತುಮತ್ತುರೋಗಿಯ/ರಕ್ಷಕರಹೆಸರು)

(ರೋಗಿಯೊಂದಿಗಿನಸಂಬಂಧ)

ಸಾಕ್ಷಿ :

_____

(ಸಂಶೋಧನಾವ್ಯಕ್ತಿ/ವೈದ್ಯರಸಹಿಮತ್ತುಹೆಸರು)

ನವಜಾತಶಿಶುಗಳಲ್ಲಿಪೆರಿನಾಟಲ್‌ಉಸಿರುಕಟ್ಟುವಿಕೆಯಿಂದಾಗಿಹೃದಯಸ್ನಾಯುವಿನಗಾಯದರೋಗನಿರ್ಣಯದಲ್ಲಿಕಾರ್ಡಿಯಾಕ್ ಟ್ರೋಪೋನಿನ್ I ಮತ್ತುಇಸಿಜಿಬದಲಾವಣೆಗಳಕುರಿತುನಿರೀಕ್ಷಿತಅಧ್ಯಯನ.

ರೋಗಿಯಮಾಹಿತಿಹಾಳೆ

ಪ್ರಧಾನತನಿಖಾಧಿಕಾರಿಗಳು: ಡಾ. ವಿದ್ಯಾಶ್ರೀ. ಬಿ/ಡಾ. ಬೀರೇಗೌಡವೈ.ಸಿ.

ನಾನು, ಡಾ. ವಿದ್ಯಾಶ್ರೀ.ಬಿ,
ಶ್ರೀದೇವರಾಜ್ಅರ್ಸ್ಮೆಡಿಕಲ್ಕಾಲೇಜಿನಪೀಡಿಯಾಟ್ರಿಕ್ಸ್ವಿಭಾಗದಸ್ನಾತಕೋತ್ತರವಿದ್ಯಾರ್ಥಿನಿ,
"ಕಾರ್ಡಿಯಾಕ್ಫ್ರೀಪೋನಿನ್ I
ಮತ್ತುಇಸಿಜಿಬದಲಾವಣೆಗಳಕುರಿತುಪ್ರಾಸ್ಪೆಕ್ಟಿವ್ಸ್ಟಡಿಎಂಬಶೀರ್ಷಿಕೆಯಅಧ್ಯಯನವನ್ನುನಡೆಸುತ್ತಿದ್ದೇನೆ.
ಟಮ್ನಿಯೋನೇಟ್ಸ್." ಮಕ್ಕಳವಿಭಾಗದಪ್ರಾಧ್ಯಾಪಕರಾದಡಾ.
ಬೀರೇಗೌಡ.ವೈ.ಸಿಅವರಮಾರ್ಗದರ್ಶನದಲ್ಲಿನನ್ನಪ್ರಬಂಧಕ್ಕಾಗಿ.
ಈಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸುವವರುಅಂದರೆಪೆರಿನಾಟಲ್ಉಸಿರುಗಟ್ಟುವಿಕೆಯದೃಷ್ಟಿಯಿಂದ NICU
ಗೆದಾಖಲಾದ 50 ಅವಧಿಯನವಜಾತಶಿಶುಗಳುಸೇರಿದ್ದಾರೆ.

ಈಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿಭಾಗವಹಿಸಿದ್ದಕ್ಕಾಗಿನಿಮಗೆಯಾವುದೇಹಣಕಾಸಿನಪರಿಹಾರವನ್ನುಪಾವತಿ
ಸಲಾಗುವುದಿಲ್ಲ.

ಎಲ್ಲಾಡೇಟಾವನ್ನುಗೌಪ್ಯವಾಗಿಇರಿಸಲಾಗುತ್ತದೆಮತ್ತುಈಸಂಸ್ಥೆಯಿಂದಸಂಶೋಧನಾಉದ್ದೇಶಕ್ಕಾಗಿಮಾತ್ರ
ಬಳಸಲಾಗುತ್ತದೆ.
ಅಧ್ಯಯನದಲ್ಲಿನಿಮ್ಮಮಗುವಿನಭಾಗವಹಿಸುವಿಕೆಗೆಒಪ್ಪಿಗೆನೀಡಲುನೀವುಸ್ವತಂತ್ರರಾಗಿದ್ದೀರಿ.
ಯಾವುದೇಕಾರಣಗಳನ್ನುನೀಡದೆನೀವುಯಾವುದೇಸಮಯದಲ್ಲಿನಿಮ್ಮಮಗುವನ್ನುಅಧ್ಯಯನದಿಂದಹಿಂಪಡೆ
ಯಬಹುದು.
ಭಾಗವಹಿಸಲುನಿಮ್ಮನಿರಾಕರಣೆಯುಈಸಂಸ್ಥೆಯಲ್ಲಿಯಾವುದೇಪ್ರಸ್ತುತಅಥವಾಭವಿಷ್ಯದಕಾಳಜಿಗೆನಿಮ್ಮನ್ನು
ಪೂರ್ವಾಗ್ರಹಮಾಡುವುದಿಲ್ಲ.

ಪ್ರಧಾನತನಿಖಾಧಿಕಾರಿಯಹೆಸರುಮತ್ತುಸಹಿ

ದಿನಾಂಕ:

ಸ್ಥಳ: ಕೋಲಾರ.

KEY TO MASTER CHART

A- UHID NO.

B- NAME OF THE BABY.

C- SEX.

D- BIRTH WEIGHT.

E- GESTATIONAL AGE.

F- GRAVIDA.

G- LIQUOR STATUS AT THE TIME OF DELIVERY.

H- FETAL DISTRESS AT THE TIME OF DELIVERY.

I- MODE OF DELIVERY.

J- MODE OF RESUSCITATION.

K- APGAR SCORE AT 1 MINUTE.

L- APGAR SCORE AT 5 MINUTE.

M- CARDIAC TROPONIN I LEVELS WITHIN 6 HOURS OF LIFE.

N- CARDIAC TROPONIN I AT 12 TO 24 HOURS OF LIFE.

O- ECG RECORDINGS WITHIN 6 HOURS OF LIFE.

P- ECG RECORDINGS AT 12 TO 24 HOURS OF LIFE .

Q- OUTCOME.

MASTER CHART

SL.NO	UHID No	Gestational age	Gravida	Liquor status	Fetal distress	Mode of Delivery	Sex	Birth Weight	Mode of Resuscitation	Apgar at 1min	Apgar at 5 min	Cardiac toponin i within 6 hours	Cardiac toponin I at 12 to 24 hours	ECG within 6 hours	ECG at 12 to 24 hours	Outcome
1	830257	41weeeks + 2 days	Primi	Meconium	CAT 2	LSCS	Female	2.62kg	Bag and mask	2	4	2.8ng/ml	3.5ng/ml	Grade 2	Grade 2	Discharge
2	837251	40weeks	Primi	Clear	CAT 1	Normal	Female	3kg	Bag and mask	3	5	1.89ng/ml	2.6ng/ml	Grade 1	Grade 1	Discharge
3	842535	40weeks + 2 days	Primi	Meconium	CAT 3	Normal	Male	3.2kg	Bag and tube	1	3	3.7ng/ml	4.1ng/ml	Grade 3	Grade 3	Death
4	842858	39weeks	Primi	Meconium	CAT 3	Normal	Male	3.5kg	Bag and tube	1	3	4ng/ml	4.4ng/ml	Grade 4	Grade 4	Death
5	843640	38weeks + 4 days	Primi	Meconium	CAT 2	Vacuum assisted vaginal delivery	Female	3.16kg	Bag and tube	2	4	2ng/ml	2.3ng/ml	Grade2	Grade 2	Discharge
6	847597	40weeks	Primi	Meconium	CAT 1	Normal	Female	2.8Kg	Bag and mask	3	5	1.8ng/ml	2.2ng/ml	Grade1	Grade1	Discharge
7	848616	37weeks +2 days	Multi	Clear	No	LSCS	Male	3.52kg	Bag and mask	3	5	0.8ng/ml	1.81ng/ml	Normal	Grade 1	Discharge
8	857608	39weeks +1 days	Primi	Clear	No	LSCS	Male	3.08kg	Bag and mask	3	5	0.29ng/ml	0.8ng/ml	Normal	Normal	Discharge
9	867322	38weeks	Multi	Meconium	CAT 2	Vacuum assisted vaginal delivery	Female	4kg	Bag and mask	2	4	2.34ng/ml	3.1ng/ml	Grade 2	Grade 2	Discharge
10	881322	38weeks+5 days	Primi	Meconium	CAT 3	Normal	Female	3.2kg	Bag and tube	1	3	3.6ng/ml	4.1ng/ml	Grade3	Grade 3	Discharge
11	872813	41weeks	Primi	Meconium	CAT 1	LSCS	Female	3.58kg	Bag and tube	2	5	1.99ng/ml	2.4ng/ml	Grade 1	Grade 1	Discharge
12	867250	37weeks +2 days	Primi	Clear	No	Normal	Male	2.9kg	Bag and mask	3	5	0.68ng/ml	1.82ng/ml	Normal	Normal	Discharge
13	8683366	38 weeks +2 days	Primi	Clear	No	Normal	Female	3.2kg	Bag and mask	3	5	1.85ng/ml	1.9ng/ml	Grade 1	Grade 1	Discharge
14	868649	37weeks +5 days	Primi	Clear	No	Vacuum assisted vaginal delivery	Female	3.4kg	Bag and mask	3	5	0.28ng/ml	0.6ng/ml	Normal	Normal	Discharge
15	868716	38 weeks + 1 days	Multi	Clear	No	Normal	Male	3kg	Bag and mask	3	5	0.21ng/ml	0.74ng/ml	Normal	Normal	Discharge
16	868856	39 weeks	Primi	Meconium	CAT 3	Normal	Male	3.2kg	Bag and tube	1	3	3.2ng/ml	4ng/ml	Grade 3	Garde 3	Death

17	845434	38 weeks	Multi	Meconium	CAT 3	LSCS	Female	2.89kg	Bag and tube	1	3	3.3ng/ml	3.93ng/ml	Grade 3	Grade 3	Discharge
18	860729	37weeks+4 days	Primi	Meconium	CAT 1	Normal	Male	4.1 kg	Bag and mask	2	5	1.84ng/ml	2.4ng/ml	Grade 1	Grade1	Discharge
19	862126	38weeks+ 4 days	Primi	Clear	No	Normal	Female	2.76kg	Bag and mask	3	5	0.18ng/ml	0.54ng/ml	Normal	Normal	Discharge
20	849090	39 weeeks	Primi	Meconium	CAT 2	LSCS	Female	3.45kg	Bag and tube	2	4	2.4ng/ml	3.08ng/ml	Grade 2	Grade2	Discharge
21	853064	37 weeks + 3 days	Multi	Clear	No	Normal	Female	3.24kg	Bag and mask	3	5	0.3ng/ml	0.4ng/ml	Normal	Normal	Discharge
22	901886	38 weeks +4 days	Primi	Clear	CAT 1	Normal	Male	2.8kg	Bag and mask	3	4	1.8ng/ml	2.2ng/ml	Grade 1	Grade 1	Discharge
23	896892	39 weeks + 2 days	Multi	Meconium	CAT 2	LSCS	Male	3.18kg	Bag and tube	2	4	2.4ng/ml	3.1ng/ml	Grade 2	Grade 2	Discharge
24	892181	38 weeks + 3 days	Primi	Meconium	CAT 3	Normal	Male	3.6kg	Bag and tube	1	3	4ng/ml	4.3ng/ml	Garde 4	Grade 4	Death
25	886930	37 weeks+2 days	Multi	Meconium	CAT 3	Vacuum assisted vaginal delivery	Male	3.3kg	Bag and tube	1	3	3.8ng/ml	4.2ng/ml	Grade 3	Grade 3	Discharge
26	886854	40 weeks	Primi	Meconium	CAT 1	Normal	Male	2.8kg	Bag and mask	2	5	2ng/ml	2.8ng/ml	Grade 1	Grade 1	Discharge
27	886641	41 weeks +5 days	Primi	Meconium	CAT 1	LSCS	Male	3.1kg	Bag and tube	2	4	1.81ng/ml	1.9ng/ml	Grade 1	Grade1	Discharge
28	883108	38 weeks + 3 days	Multi	Clear	No	LSCS	Female	3.32kg	Bag and mask	3	5	0.2ng/ml	0.63ng/ml	Normal	Normal	Discharge
29	883020	37 weeks + 2 days	Primi	Meconium	CAT 2	LSCS	Male	2.68kg	Bag and tube	2	4	2.5ng/ml	3ng/ml	Grade 2	Grade2	Discharge
30	882360	39 weeks	Primi	Meconium	CAT 2	LSCS	Female	2.9kg	Bag and tube	2	4	2.0ng/ml	2.7ng/ml	Grade 2	Grade 2	Discharge
31	880033	38 weeks	Multi	Meconium	CAT 1	LSCS	Female	3.4kg	Bag and mask	3	5	1.9ng/ml	2ng/ml	Grade 1	Grade 1	Discharge
32	877412	40 weeks	Primi	Meconium	CAT 2	LSCS	Male	2.69kg	Bag and tube	2	4	2.0ng/ml	2.67ng/ml	Grade 2	Grade2	Discharge
33	877381	39 weeks + 2 days	Multi	Meconium	CAT 1	LSCS	Female	3.2kg	Bag and mask	3	5	1.87ng/ml	2ng/ml	Grade 1	Grade1	Discharge
34	876094	38 weeks + 1 days	Primi	Clear	No	Normal	Female	2.87kg	Bag and mask	3	5	0.2ng/ml	0.22ng/ml	normal	normal	Discharge
35	873464	37 weeks + 5 days	Multi	Clear	No	Normal	Male	3.44kg	Bag and mask	3	5	0.28ng/ml	0.5ng/ml	Normal	Normal	Discharge

36	867250	38weeks	Primi	Clear	No	Vacuum assisted vaginal delivery	Male	2.9kg	Bag and mask	3	5	0.15ng/ml	0.67ng/ml	Normal	Normal	Discharge
37	858073	41weeks	Primi	Meconium	CAT 3	LSCS	Female	3.27kg	Bag and tube	1	3	3.9ng/ml	4.1ng/ml	Garde 4	Garde 4	Death
38	832907	38weeks +5 days	Multi	Meconium	CAT 1	LSCS	Male	3.42kg	Bag and tube	2	4	2ng/ml	3.08ng/ml	Grade 1	Grade 1	Discharge
39	833373	39weeks	Primi	Meconium	CAT 1	LSCS	Female	2.86kg	Bag and tube	2	4	1.98ng/ml	2.54ng/ml	Grade 1	Grade1	Discharge
40	837215	37weeks +3 days	Primi	Clear	No	Normal	Male	3.58kg	Bag and mask	3	5	0.29ng/ml	0.32ng/ml	Normal	Normal	Discharge
41	839625	37weeks	Primi	Clear	No	Vacuum assisted vaginal delivery	Male	2.62kg	Bag and mask	3	5	0.18ng/ml	0.3ng/ml	Normal	Normal	Discharge
42	839994	41weeks	Primi	Meconium	CAT 2	LSCS	Male	3.3kg	Bag and tube	1	3	2.45ng/ml	2.82ng/ml	Grade 2	Grade 2	Discharge
43	841189	37 weeks +4days	Multi	Clear	No	Normal	Male	3.1kg	Bag and mask	3	5	0.26ng/ml	0.35ng/ml	Normal	Normal	Discharge
44	843852	38weeks +2 days	Multi	Meconium	CAT 2	LSCS	Female	3.26kg	Bag and tube	1	3	2.1ng/ml	2.67ng/ml	Grade 2	Grade 2	Discharge
45	849925	40weeks	Primi	Meconium	CAT 1	Normal	Male	3.1kg	Bag and tube	2	4	2.6ng/ml	3.04ng/ml	Grade1	Grade1	Discharge
46	846893	38weeks	Multi	Meconium	CAT 1	Normal	Male	2.76kg	Bag and mask	2	4	2.2ng/ml	3ng/ml	Grade 1	Grade1	Discharge
47	883778	39weeks	Primi	Meconium	CAT 2	LSCS	Male	3.22kg	Bag and tube	1	3	2.6ng/ml	3.3ng/ml	Grade2	Grade2	Discharge
48	894367	37 weeks	Primi	Clear	No	Normal	Female	2.58kg	Bag and mask	3	5	0.32ng/ml	0.39ng/ml	Normal	Normal	Discharge
49	853400	39 weeks +2 days	Primi	Clear	No	Normal	Female	3.26kg	Bag and mask	3	5	1.28ng/ml	1.8ng/ml	Normal	Normal	Discharge
50	853701	38weeks + 3 days	Multi	Meconium	CAT 3	LSCS	Female	3.16kg	Bag and tube	1	3	3.79ng/ml	4.4ng/ml	Garde 4	Garde 4	Death