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CARDIAC TROPONIN-I AS A MARKER OF MYOCARDIAL DAMAGE IN NEWBORNS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY

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ABSTRACT: BACKGROUND: Perinatal asphyxia is a common problem with the incidence varying from 0.5-2% of live births. The incidence of cardiac dysfunction in perinatal asphyxia varies from 24-60%. However there is paucity of reports from our country where mothers often report to hospital quite late with obstetric complications and neonates suffer from birth asphyxia with high mortality. So it becomes important to detect myocardial dysfunction and to provide early treatment. **OBJECTIVES:** To assess the usefulness of cardiac marker in evaluating myocardial damage in hypoxic ischemic encephalopathy. **MATERIALS AND METHODS:** Prospective case control study was conducted on 50 neonates comprising the cases and 50 neonates comprising the controls meeting the inclusion and exclusion criteria born in Basaweshwar Teaching and General Hospital and Sangameshwar Teaching and General Hospital, Gulbarga. After written informed consent, venous blood sample was taken by aseptic precaution within 72 hours of birth. Blood was centrifuged and serum tested for, Cardiac troponin I-done by Electro-Chemiluminescence Immunoassay (ECLIA). **RESULTS:** The mean cTnI value of asphyxiated neonates was 47.23 ± 37.50 pg/L, compared to control group 4.33 ± 1.97 pg/L which was statistically significant. Serum cTnI concentrations significantly greater with increasing severity of HIE. Mean cTnI concentrations were: 9.56 ± 5.05 pg/L in HIE-I, 49.84 ± 15.88 pg/L in HIE-II, and 106.9 ± 31.01 pg/L in HIE -III. Mean cTnI value among cases with shock was 71.796 ± 32.16 pg/L and those without shock was 15.79 ± 11.64 pg/L. There was significant difference of mean cTnI value among cases with myocardial involvement and without myocardial involvement with P-value < 0.001 . **CONCLUSION:** In asphyxiated neonates, cardiac troponin I concentrations within 72h of birth correlate strongly with clinical grade of hypoxic ischemic encephalopathy. Early cardiac troponin I concentrations provide a useful proxy marker for the anticipated severity of myocardial damage. **KEYWORDS:** Perinatal asphyxia; Cardiac troponin-I; Myocardial damage; Hypoxic ischemic encephalopathy (HIE).

INTRODUCTION: Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. Globally, hypoxia of the newborn (birth asphyxia) or the fetus ("fresh stillbirth") is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year.¹ Perinatal hypoxia-ischaemia can cause multi-organ injury and dysfunction of brain, heart, lungs, kidneys and bone marrow.

Cardiac dysfunction results from hypoxic ischaemic damage to sub-endocardial tissue, papillary muscle and myocardium.² Cardiac-specific isomorphs of troponins T and I in adults have proved to be sensitive and specific biochemical markers of myocardial damage in acute coronary syndromes.³ Asphyxiated neonates have higher cardiac troponin I (cTnI) concentrations than controls.⁴ cTnT and cTnI have been proposed to be biochemical indices of myocardial injury in

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neonates with asphyxia, respiratory distress syndrome (RDS), and septic or cardiogenic shock. Although the half-life of cTnI is relatively short (90 min), its diagnostic time range is unusually wide (ranging from a few hours to 10–14 days after the episode of myocardial injury).⁵ Early detection of myocardial injury in neonates with hypoxic-ischaemic encephalopathy (HIE) may help to predict morbidity, mortality and early treatment. Therefore the present study was planned to explore the myocardial involvement in neonates with HIE by assessment of cardiac enzyme changes.

MATERIALS AND METHODS: This prospective case control study was conducted on asphyxiated and non-asphyxiated term neonates admitted in Basaweshwar Teaching and General Hospital (BTGH) and Sangameshwar Teaching General Hospital (STGH) Neonatal Intensive Care Unit (NICU) from November 2013 to November 2014. The study included two groups:

The case group (Study Group): It included 50 neonates fulfilling the following Criteria:

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

- Apgar score of less than 7/10 at 1 minute.
- Metabolic acidosis [pH<7.2].
- Clinical evidence of hypoxic-ischemic encephalopathy [HIE], as defined by Sarnat and Sarnat 1976.
- Evidence of multi organ dysfunction [renal, cardiovascular, respiratory and nervous systems].
- Resuscitation with >1 minute of positive pressure ventilation before stable spontaneous respiration.

EXCLUSION CRITERIA: Preterm babies, neonates with congenital malformation and neonates with sepsis.

THE CONTROL GROUP: It included 50 term apparently healthy neonates without signs of perinatal asphyxia as evidenced by clear liquor and one minute Apgar score ≥ 7 at 1 minutes.

FROM ALL NEONATES INCLUDED IN THE STUDY THE FOLLOWING DATA WAS COLLECTED:

Written informed consent was obtained from all parents. Detailed maternal history, meconium staining of amniotic fluid, birth events, Apgar score, sex of the baby and birth weight were recorded on the study proforma. Clinical and neurological examination was done for all the neonates included in the study. The asphyxiated neonates (case group) were monitored for seizures, hypotension, hypotonia and HIE in the immediate neonatal period in the NICU. Myocardial involvement assessed by clinically looking for CFT, pulse volume, tachycardia and bradycardia. Grading system used to grade the severity of HIE was SARNAT and SARNAT staging.

The cases were also observed for other systemic effects of asphyxia and cardiac involvement. 2ml of venous blood was taken by aseptic precaution within 72 hours after birth. Blood is centrifuged and serum tested for, Cardiac troponin I- done by Electro-Chemiluminescenc Immunoassay (ECLIA). Normal value of cTnI by above method is <14pg/L peaks between 14-36 hr and remain up to 7 days. Blood sample also collected for septic screening (CBC, CRP and Blood Culture). ABG was done within 1 hour of admission in these cases.

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STATISTICAL METHODS: Results on continuous measurements were presented on Mean $\pm$ SD (Min-Max). Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Chi-square/Fisher Exact test, student t test and SPSS 11.5 version software used for statistical analysis. P value <0.05 taken as statistically significant.

RESULTS: This prospective study was conducted in Neonatal Division of Department of Pediatrics, BTGH and STGH M R Medical College Gulbarga for the period of 1 year from November 2013 to November 2014.

In present study 56% were males and 44% were females in study group, 58% were males and 42% were females in the control group. 74% babies were born to primigravida and 26% babies for multigravida in study group, 56% babies were born to primigravida and 44% babies for multigravida in control group. Demographic features like sex, parity, birth weight and mode of delivery were statistically not significant among the study and control group.

In study group 28% had MSAF and 72% had clear amniotic fluid. Mean Apgar score was 2.9 ± 1.25 at 1 min and 7.36 ± 1.12 at 5 min among study group. Mean Apgar score at 1 min was 8.16 ± 0.808 and at 5 min was 9.18 ± 0.433 among control group with $p < 0.001$.

Among 50 neonates of study group, 16 (32%) cases were HIE-I, 25 (50%) cases were HIE-II and 9 (18%) cases were HIE-III. Mean birth weight of HIE-I cases was 2.7 ± 0.46 kg, mean birth weight of HIE-II cases was 2.82 ± 0.32 kg and mean birth weight of HIE-III cases was 2.71 ± 0.57 kg. Demographic features like sex, parity and birth weight were statistically not significant.

Mean Apgar score at 1 minute was 4.375 ± 0.599 , at 5 minutes was 8.48 ± 0.496 among HIE-I cases, mean Apgar score at 1 minute was 2.56 ± 0.46 , at 5 minutes was 7.32 ± 0.52 among HIE-II cases and mean Apgar score at 1 minute was 1.22 ± 0.41 , at 5 minutes was 5.55 ± 0.37 in HIE-III cases which was significant.

Mean cTnI value among the study group was 47.23 ± 37.50 pg/L and mean cTnI value among the control group was 4.33 ± 1.97 pg/L which was highly significant. Among 50 neonates in the study group 5 died and 45 survived. Mean cTnI value in HIE-I cases was 9.56 ± 5.05 pg/L, in HIE-II cases was 49.84 ± 15.88 pg/L and in HIE-III cases was 106.9 ± 31.01 pg/L which was highly significant with $p < 0.001$. In present study, 56% cases had shock and 44% cases were without shock among study group. Mean cTnI value among cases with shock was 71.796 ± 32.16 pg/L and those without shock was 15.79 ± 11.64 pg/L.

	Study Group	Control Group	p-value
Sex: Male	28(56%)	29(58%)	$p > 0.05$
Female	22(44%)	21(42%)	
Parity: Primi	37(74%)	28(56%)	$p > 0.05$
Multi	13(26%)	22(44%)	
Birth weight (mean $\pm$ SD)	2.83 ± 0.371	2.764 ± 0.274	$p > 0.05$
Apgar score 1min	2.9 ± 1.25	8.16 ± 0.808	$p < 0.001$
(mean $\pm$ SD) 5min	7.36 ± 1.12	9.18 ± 0.433	
cTnI (pg/L) (mean $\pm$ SD)	47.23 ± 37.5	4.33 ± 1.97	$P < 0.001$

Table 1: Baseline characteristics and cTnI value comparison among study and control groups

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DISCUSSION: In the present study an attempt has been made to ascertain whether cardiac troponin-I as early marker of myocardial dysfunction. Only few studies have been done previously. To our knowledge this is first study in India. We have taken term babies for study with mean GA (38±2) weeks. In the present study, myocardial involvement was assessed by presence or absence of shock (Hypotension).

In our study demographic data like sex, parity, mode of delivery, birth weight is similar in both study group and control group. There was no significant difference of demographic data among study and control group with $P>0.05$. In earlier studies demographic data like sex, gestational age, parity, birth weight and mode of delivery were matched between cases and controls that was comparable to our study. In present study 28% cases of study group had MSAF while none in control group had MSAF which is highly significant.

In present study Apgar score at 1 min and 5 min were highly significant between cases and controls which were comparable with earlier studies.^{7,8} In present study mean cTnI value significantly high among cases compared to controls which was comparable with other studies with $P<0.001$.^{7,8}

In our study demographic data like birth weight, gender and parity are similar among HIE stages and was comparable with study done by Aravind TS et al.¹⁰ Mean Apgar score at 1 min and 5 min were statistically significant among stages of HIE which was comparable with earlier studies with $P<0.001$.¹⁰

Study showed mean cTnI value was significantly different among stages of HIE. HIE-I cases had lower cTnI value compared to HIE-II and HIE-III cases and HIE-II cases had lower cTnI value compared to HIE-III cases. So mean cTnI value is predictor of HIE stages. In present study 56% cases in study group had cardiac involvement(shock) and none in control group had cardiac involvement which is comparable with incidence quoted by Mandal Ravi⁶ (44%) and Jyoti Agrawal⁹ (24–60%). In present study none among HIE-I had shock, 19 out of 25 cases of HIE-II had shock and all cases of HIE-III cases had shock and ionotrope requirement which was significant with $P<0.001$. Those cases with shock had high mean cTnI value compared to cases without shock which was comparable with earlier study.⁸ So cardiac troponin I as early biochemical marker of myocardial involvement. Death cases had significantly high mean cTnI value compared to improved cases. So mean cTnI value also helps to predict the outcome of the asphyxiated neonates. Limitation of study were we have not done ECG and echocardiography to confirm the cardiac involvement.

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