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Original Research Article

A study on cardiac troponin t in early diagnosis of myocardial injury due to perinatal asphyxia and its comparison with other modalities

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ABSTRACT

Background: Perinatal Asphyxia is a multi-system disorder and its effects are not limited to central Nervous System. MODS determine the early outcome of asphyxiated neonate. Cardiac impairment occurs in about 25% of neonates with asphyxia. Often cardiac impairment is overlooked due to the lack of sensitive diagnostic test.
Methods: A hospital based prospective analytical study performed over 50 Asphyxiated neonates admitted in our NICU from September 2016 to January 2017 myocardial dysfunction was evaluated using clinical, electrocardiography, echocardiography and cardiac troponin-T card test.
Results: In the present study, among the 50 neonates 32 had clinical evidence of myocardial injury. Troponin T card test has the highest sensitivity of about 84.37%, positive predictive value of 93.1% and negative predictive value of 76% in diagnosing myocardial injury in contrast to ECG and ECHO. In terms of Specificity ECHO has the highest specificity of about 94.4% when compared to ECG and Trop T. Among all the diagnostic modalities used in this study, Troponin T best predicts the severity and outcome of Perinatal asphyxia.
Conclusions: Troponin T card test is a valuable tool for early detection of myocardial injury due to perinatal asphyxia. In resource limited setting where the accessibility to 12 lead ECG, ECHO, and aid of cardiologist are not available, Trop T card test will serve as an effective handy screening tool in diagnosing myocardial injury

Keywords: Cardiac troponin T, ECG, ECHO, Myocardial injury, Perinatal asphyxia

INTRODUCTION

Perinatal asphyxia is a common problem with the incidence varying from 0.5-2% of live births. It accounts for 9.7/1000 live births and contributes to 30% of neonatal mortality in Nepal. The incidence of perinatal asphyxia (PA) varies between 1% and 5%.[1] PA has a high impact on neonatal mortality and morbidity and may lead to ischemic myocardial damage, as well as poor neurological and gastrointestinal outcomes.[1-4] Ischemia and myocardial necrosis occurs in 25-51% of newborn infants with severe PA. It is an important cause of admission to neonatal intensive care units (NICU) with multi organ dysfunction.[2] When an asphyxic event occurs, it leads to a series of physiological mechanisms in order to preserve the function of vital organs (brain and heart), whereas other organs such as the kidneys, gastrointestinal tract, and skin are affected to a varying degree based on the duration of the episode. However, in spite of compensatory mechanisms, it may progress to hypoxic-ischemic encephalopathy (HIE) involving the brain and heart.[3] The incidence of cardiac dysfunction in perinatal asphyxia varies from 24-60%. Apart from the clinical presentation, electrocardiography (ECG), echocardiogram and determination of cardiac enzymes are useful tools to detect myocardial involvement. In contrast to adults, recognition of myocardial ischemia is far more difficult in neonates. Only a few studies have assessed the myocardial dysfunction with the assay of cardiac enzymes and ECG abnormalities.[4]

METHODS

A hospital based prospective analytical study performed over 50 asphyxiated neonates admitted in our NICU from September 2016 to January 2017. Myocardial dysfunction was evaluated using clinical, electrocardiography, echocardiography and Cardiac troponin-T card test. A 12-lead ECG was recorded and 4 ml of venous blood was collected for cardiac enzymes estimation in each asphyxiated neonate within 72 hours of life.

Infants with ECG changes of grade 1 or 2 were diagnosed to have mild, whereas those with changes of grades 3 or 4 were considered to have severe injuries. Cases with congenital heart diseases, major central nervous system malformations, and neonatal sepsis were excluded.

All the neonates were managed in NICU as per hospital protocol. They were given oxygen by hood (5-6 L/min), nasal continuous positive airway pressure, mechanical ventilation (based on saturation of oxygen (SpO_2) and arterial blood gas findings), intravenous fluids, vitamin K, inotropes (Dopamine and/or Dobutamine each by 1–20 µg/kg/min) and anticonvulsants (Phenobarbitone 20 mg/kg as loading dose, followed by 3-5 mg/kg/day, and phenytoin sodium was also added with the same dose in non-responder to phenobarbitone), wherever required. First line antibiotics (cefotaxime and gentamycin) were given to those cases where risk factors for sepsis were present and required mechanical ventilation. Feeding was started once patient showed improvement, initially started as nasogastric feeding and then followed by spoon or breast feeding.

RESULTS

Among the 50 newborns in the study, 29 infants (58%) were males. Among all the newborns (asphyxiated) in the study, the majority were resuscitated using bag and mask (40%) and bag and tube (44%) mode. Classification Among the newborns in the study, the majority (56%) of them obtained moderate birth asphyxia (APGAR) score, while 44% of the infants had severe asphyxia.

There is a significant association between HIE staging and presence of ECG changes in the study population. There is a significant association between HIE staging and presence of myocardial injury clinically in the study population. All the diagnostic modalities used for diagnosing myocardial damage in the asphyxiated infants were significantly associated with the outcome as evidenced by the chi-square test. This indicates that these can be used as predictors of mortality due to myocardial involvement in infants with perinatal asphyxia. *p value significant if <0.05. Infants who had positive troponin-T test had 43 times more risk of having myocardial injury clinically when compared to infants with the negative troponin-T test.

Sensitivity = 27/32 = 84.37, specificity = 16/18 = 88.88. Positive predictive value = 27/29 = 93.10 (probability of clinical disease when the troponin-t test is positive). Negative predictive value = 16/21 = 76.19. Infants who had echocardiographic changes pertaining to perinatal asphyxia have 9.5 times more risk of having myocardial injury clinically when compared to infants with normal echocardiographic changes. In terms of sensitivity and specificity, troponin T has a better sensitivity (84.4%) and specificity (88.9%) when compared to ECG and echocardiogram. The probability of progression to clinical signs or shock due to myocardial injury in an infant with the positive troponin-t test (PPV) is very high (93.1%). Furthermore, the probability of not progressing to clinical signs or shock following a negative troponin-T test (NPV) was 76.2%. There is a significant association between ECHO changes and Troponin T test. P value: <0.001.

About 50% of the infants were in HIE stage 2 and 38% were on the stage 3 of HIE staging, according to Sarnat and Sarnat classification.

Table 1: Distribution of new-borns according to hypoxic-ischemic encephalopathy (HIE) staging.

HIE staging	Frequency	Percentage
1	6	12
2	25	50
3	19	38
Total	50	100

The majority (50%) of the infants had no ECG changes. However, 34% had flat or inverted T waves in 1 or 2 leads and 16% had these changes in 3 or more leads.

Table 2: Distribution of newborns according to ECG changes.

ECG	N	%
No changes	25	50%
Flat or inverted t waves in 1or 2 leads (I)	17	34%
Flat or inverted t waves in >=3 leads (II)	8	16%
II+ST wave changes (III)	0	0%
Abnormal Q waves (IV)	0	0%
Total	50	100%

Table 3: Distribution of infants according to Echocardiographic findings.

ECHO	N	%
Mitral regurgitation	0	0
Normal	26	52
Pulmonary hypertension	1	2
Pulmonary HT and Tricuspid regurgitation	2	4
Tricuspid regurgitation	21	42
Total	50	100

About 52% of the infants had normal ECHO findings and tricuspid regurgitation (42%) was the commonest echo finding pertaining to asphyxia. Majority (54%) had elevation in troponin T levels as evidenced by a positive card test.

Table 4: Distribution of newborns according to Troponin T card test.

Troponin T card test	Frequency	Percentage
Negative	21	42.0
Positive	29	58.0
Total	50	100.0

Infants who had signs of circulatory shock and needed inotropic support were diagnosed to have myocardial injury clinically. About 32 infants were diagnosed with myocardial injury.

Table 5: Distribution of infants according to clinical diagnosis of myocardial injury.

Myocardial injury	Frequency	Percentage
Present	32	64.0
Absent	18	36.0
Total	50	100.0

Table 6: Distribution of sample according to HIE (Hypoxic-ischemic encephalopathy staging) and ECG changes.

HIE staging	ECG			Total
	Flat or inverted t waves in >=3 leads	Flat or inverted t waves in 1or 2 leads	No changes	
1	0	2	4	6
2	3	5	17	25
3	5	10	4	19
Total	8	17	25	50

Pearson Chi-Square value: 10.993.P value (significant at 0.05 level): 0.027 Interpretation: There is a significant association between HIE staging and presence of ECG changes in the study population.

Pearson Chi-Square value: 18.060. P value (significant at 0.05 levels): <0.001 Interpretation: There is a significant association between HIE staging and positive Troponin T card test in the sample population.

Table: 7 Distribution of sample population according to HIE (Hypoxic-ischemic encephalopathy staging) staging with mortality.

HIE staging	Outcome		Total
	Recovered	Death	
1	6	0	6
2	22	3	25
3	11	8	19
Total	39	11	50

Pearson Chi-Square value: 7.625.P value (significant at 0.05 levels): 0.022. Interpretation: There is a significant association between HIE staging and mortality in the study population.

DISCUSSION

In this study, parameters like ECG changes involving T wave, ST segment and Q wave, echocardiographic features like valvular regurgitation, ejection fraction, shunts, pulmonary hypertension, and troponin-T elevation as evidenced by positive card test, were evaluated for their relationship with severity of asphyxia and outcome of the cases.[5] The role of cardiac enzymes in the detection of ischemic damage to the heart is well established in adults. But recently, their role in the detection of ischemia in newborns due to perinatal birth asphyxia has been under debate. Initially, CK-MB and troponin-I were studied for their diagnostic role in asphyxiated newborns.[6]

Karnik et al showed that troponin-I had better sensitivity than CK-MB and the study also concluded that there is no predictive value for CK-MB. Agrawal et al also compared troponin-I and CK-MB and got similar results, claiming the superiority of troponin-I over CK-MB in the diagnosis of myocardial damage in newborns with birth asphyxia. Of later, cardiac troponin-T has been under investigation for the same purpose.

Costa et al and Marta et al proved the elevation of cardiac troponin-T was significant in asphyxiated newborns.[7] Gunes et al reinforced that troponin-T elevated to a greater extent in severe asphyxia than mild asphyxia and cardiac troponin-T had much better sensitivity than CK-MB.

Many comparative studies were done to investigate cardiac troponin-T against CK-MB for diagnostic significance in asphyxiated newborns. Rajakumar et al and Boo et al reproduced the better results for troponin-T in comparison with CK-MB. Clark et al also showed that cardiac troponin-T levels in the serum correlated with the severity of asphyxia and pediatric mortality score. Based on these researches of late, a single use card test was designed to detect the elevation of troponin-T in serum.[8]

While most of the above-mentioned studies investigated serial measurements of troponin-T, this study investigated a simple card test done in anti-coagulated venous blood, which has the advantage of bedside testing and much quicker results. The test was done on day 1 between 12-24 hours as cardiac troponin-T tends to rise in this time-limit. The troponin T card test is designed to yield a positive result for cardiac troponin concentrations ≥0.08 ng/ml. The efficacy of this test in terms of sensitivity and specificity was evaluated in comparison to clinical diagnosis of myocardial injury.

According to Sarnat and Sarnat classification, 6 infants were in HIE stage I, while 25 and 19 neonates were in stage II and III, respectively.[9] A 12 lead ECG was taken in all the 50 infants to determine the ischemic changes due to asphyxia. As the severity of asphyxia increased according to the HIE staging, the prevalence of ECG changes also increased in the sample population. In terms of sensitivity and specificity, ECG was much inferior to echocardiogram and troponin-T card test with a positive predictive value of 80% and negative predictive value of only 52%.[10] This low negative predictive value reflects that a normal ECG does not rule out a potential underlying myocardial ischemia. Although it has good positive predictive value and sensitivity of 62%, ECG cannot be used as a solitary diagnostic modality for early detection of myocardial injury. Echocardiographic changes also were significantly associated with the outcome, as infants with these changes were at more risk of having a worse outcome.

When compared to ECG, an echocardiogram was far better in terms of specificity and predictive values in diagnosing the myocardial injury which manifests clinically but in terms of sensitivity (62.5%), it was at par with ECG. In fact, the specificity of an echocardiogram (94.4%) was higher than troponin-T card test (88.9%).[11] This reflects the importance of screening all the asphyxiated infants for structural myocardial damage facilitating early diagnosis and management, in turn improving the outcome of these infants. Regarding the troponin-T levels in infants with echocardiographic changes, these infants had 44 times more risk of testing positive in the card test. So, it can be said that almost everyone who has significant structural ischemic changes in echocardiogram is expected to test positive for elevation in troponin-T. No regional wall motion abnormalities and shunts were observed in the study population.

Overall, echocardiographic changes have good specificity but the lack of sensitivity reinforces the need for another sensitive bedside test like troponin-T card test. The simple bedside cardiac troponin-T card test done in the venous blood which was investigated in this study was positive in 29 of the 50 infants indicating the level of troponin-T in these infants are higher than 0.08 ng/ml. About 17% and 40% of the infants in HIE stage 1 and 2 respectively, tested positive for troponin-T card test. But, about 95% of the infants in stage 3 of HIE staging tested positive in troponin-T card test.[12] These figures depict that likelihood of the test being positive increases with increase in the severity of asphyxia. About 38% of the infants who tested positive had the worse outcome of death while all infants with a negative test survived. So, it is obvious that infants with positive troponin-T card test are at more risk of dying than infants with a negative troponin-T card test.[13] Among all the parameters studied, troponin-T elevation as evidenced by a positive card test is the best predictor of mortality. This fact coincides with the findings in other studies like Boo et al and Clark et al.[14,15]

CONCLUSION

Present study findings regarding sensitivity of troponin-T correlates well with findings of Matter et al (Troponin-T levels correlated with Tei index and ejection fraction. Doppler tissue imaging (DTI) has high sensitivity than echo) and Boo et al (Infants with congestive cardiac failure within 48 hours of life, infants with EF <60%, non-survivors had high cardiac troponin-T levels but not CK-MB). The correlation between troponin-T and mortality observed in the study coincides with one observed by Clark et al (Positive correlation between cTnT and pediatric infant mortality score).

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REFERENCES

1. Caliskan E, Doger E, Cakiroglu Y, Duman C, TurkerG, Yucesoy I. Cord blood cardiac troponin I and creatine kinase MB levels in poor neonatal outcomes. J Turkish-German Gynecol Assoc. 2006;7:98-102.
2. Araujo K, Da Silva J, Sanudo A, Kopelman B. Plasma concentrations of cardiac troponin I in newborn infants. Clin Chem. 2004;50:1717-18.
3. Groenendaal F, Vries LS. Selection of babies for intervention after birth asphyxia. Semin Neonatol. 2000;5:17-32.
4. Baum H, Hinze A, Bartels P, Neumeier D. Reference values for cardiac troponins T and I in healthy neonates. Clin Biochem. 2004;37:1079-82.
5. Turker G, Babaoglu K, Gokalp AS, Sarper N, Zengin E, Arisoy AE. Cord blood cardiac troponin I as an early predictor of short-term outcome in perinatal hypoxia. Biol Neonate. 2004;86:131-7.
6. Trevisanuto D, Zaninotto M, Altinier S, Plebani M, Zanardo V. High serum cardiac troponin T concentrations in preterm infants with respiratory distress syndrome. Acta Paediatr. 2000;89:1134-6.
7. Vento M, Sastre J, Miguel AA, Jose V. American Thoracic Society: understanding cardiac troponin T

in the newborn period. Am J Respir Crit Care Med. 2006;173:817.
8. Trevisanuto D, Picco G, Golin R, Doglioni N, Altinier S, Zaninotto M, et al. Cardiac troponin I in asphyxiated neonates. Biol Neonate. 2006;89:190-5.
9. Clark SJ, Newland P, Yoxall CW, Subhedar NV. Concentrations of cardiac troponin T in neonates with and without respiratory distress. Arch Dis Child. 2004;89:348-52.
10. Vento M, Sastre J, Asensi MA, Viña J. Room-air resuscitation causes less damage to heart and kidney than 100% oxygen. Am J Respir Crit Care Med. 2005;172:1393-8.
11. McAuliffe F, Mears K, Fleming S, Grimes H, Morrison JJ. Fetal cardiac troponin I in relation to intrapartum events and umbilical artery pH. Am J Perinatol. 2004;21:147-52.
12. Gaze DC, Collinson PO. Cardiac troponin I should be interpreted with caution in pediatric neonatal patients. Biol Neonate. 2004;87:19.
13. Clark SJ, Newland P, Yoxall CW, Subhedar NV. Cardiac troponin T in cord blood. Arch Dis Child. 2001;84:34-7.
14. Oyvind H, Kenneth D. Cardiac troponins I and T in patients with suspected acute coronary syndrome: a comparative study in a routine setting. Clin Chem. 1998;44:1430-6.
15. Gonzalez de Dios J. Definition of perinatal asphyxia in the medical literature: the need for a consensus. Rev Neurol. 2002;35:628-34.

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