INTRODUCTION

Asphyxia [as- ffik-se-ah] (Greek; “a stopping of the pulse”) Birth asphyxia is defined by the World Health Organization as “the failure to initiate and sustain breathing at birth immediately after delivery” (WHO).\(^1\) Perinatal asphyxia is a common problem and has an incidence varying from 0.5 - 2% of live births.\(^2\) –\(^3\) WHO estimates that 4 million neonatal deaths occur yearly due to perinatal asphyxia, representing 38% of deaths of children under 5 years of age.\(^4\)

In India, the rural and urban regions of the Uttar Pradesh and Maharashtra have mortality of 23% and 25% attributed to birth asphyxia, respectively.\(^5\) Perinatal asphyxia represents the third most common cause of neonatal death (23%) after preterm (28%) and severe infections (26%).\(^7\)

Hypoxic ischemic organ damage can occur at ante partum period (50%), at intrapartum period (40%) or after delivery as postpartum asphyxia (10%).\(^8\) Hypoxic Ischemic Encephalopathy (HIE) should be suspected in encephalopathic newborns with a history of foetal and or neonatal distress and laboratory evidence of asphyxia.

Asphyxia may be suspected and HIE reasonably included in the differential diagnosis when there is:
• Prolonged (>1 hour) antenatal acidosis in newborn blood gas analysis.
• Foetal HR <60 beats per minute.
• Apgar score ≤3 at ≥10 minutes.
• Need for positive pressure ventilation for >1 minute or first cry delayed >5 minutes
• Onset of seizures within 12 to 24 hours of birth
• Burst suppression or suppressed background pattern on EEG or amplitude-integrated Electroencephalogram (aEEG).

Severe perinatal asphyxia as defined by National Neonatal Perinatal Database as no breathing or an Apgar score of 0-3 at 1 minute of age results in myocardial ischemic injury. The incidence of clinical cardiac dysfunction in perinatal asphyxia varies from 24-60%. Cardiac dysfunction is caused by transient myocardial ischemia. Neonate with cardiac dysfunction in perinatal asphyxia presents with respiratory distress, congestive heart failure, and myocardial ischemia leading to cardiogenic shock. The electrocardiogram (ECG) may show ST depression in the mid precordium and T-wave inversion in the left precordium. Echocardiographic findings include decreased left ventricular contractility, especially of posterior wall; elevated ventricular end-diastolic pressures; tricuspid insufficiency; and pulmonary hypertension. In severely asphyxiated newborns, dysfunction more commonly affects the right ventricle. A fixed HR may indicate severe brainstem injury. Myocardial involvement leading to cardiogenic shock remains one of the most challenging in the management and a significant cause of mortality in neonates suffering from perinatal asphyxia. Echocardiographic evaluation at bed side is not always available and has long learning with inter observer variation. Moreover, right ventricular dysfunction is difficult to detect and at the most semi quantitative.

B-type natriuretic peptide (BNP) and N-terminal-pro-BNP (NT-pBNP) have a crucial role in the screening and the diagnosis of cardiac disease, respiratory distress and monitoring of the treatment response in neonates and children. Natriuretic peptides are ring-shaped amino acid sequences with specialized actions. Four natriuretic peptides have been described till now, namely A, B, C and D. Atrial natriuretic peptide (ANP) is synthesised and released by atrial myocytes. ANP lowers the blood pressure and has diuretic, natriuretic and kaliuretic properties.

Brain natriuretic peptide named after its discovery in porcine brains, is much higher in the ventricles of the heart. C-type natriuretic peptide is found in the brain and coronary vessels. It regulates vascular tone and lacks natriuretic properties. The D type known as Dendroaspis natriuretic peptide (DNP) is found in snake venom and it has no function in humans.

BNP is a 32 amino acid ring structure, and the sequence is present on chromosome 1. BNP acts on a cyclic guanosine monophosphate (cGMP)-coupled receptor via a transmembrane domain. The ring structure of the BNP must be intact to ensure receptor binding to natriuretic peptide receptors A and B (NPR-A/B). The ventricles of the heart are the main site of BNP synthesis and release in response to volume, pressure loading, and ventricular stress. Pro BNP is the inactive precursor and is cleaved into BNP, which is the active component, and N-terminal pro-BNP (NT-pBNP) is an inactive by product. The half-life of BNP is about 20 min and that of NT pBNP is 60 min. The actions of BNP are diuresis, natriuresis, arterial and venous vasodilatation, and antagonizing the renin–angiotensin system. The net effect is a reduction of intravascular volume, and ventricular preload and afterload. Recently, it has shown to be associated with the regulation of pulmonary vasculature. BNP is excreted after cleavage by membrane-bound neutral peptidase, which is found in the kidneys and vascular tree. It can also be cleared from the blood by direct binding to the natriuretic peptide receptor C, endocytosis and lysosomal degradation.

There is a lack of data on normative values of BNP and NT-pBNP in neonates. The reference ranges quoted in the literature vary depending on timing of the test, the kits used and the population studied. Natriuretic peptides do not to cross the placenta and therefore any variation in neonates must be explained intrinsically. This study was intended to know if any correlation in severity of perinatal asphyxia with concentrations of NT-pBNP and to establish if it is useful to identify in myocardial dysfunction.

METHODS

This study was conducted in the neonatal intensive care unit, Department of Pediatrics, Vani Vilas Hospital, Bangalore Medical College and Research Institute from Nov 2017 to May 2019. The study was cross sectional. Written Informed consent was taken from the parents of study subjects after fulfilling the inclusion criteria as soon as the neonate was admitted to NICU.

- Profound metabolic or mixed acidemia (pH< 7.00) in umbilical cord blood.
- Persistence of low Apgar scores less than 3 for more than 5 minutes
- Signs of neonatal neurologic dysfunction (e.g., seizures, encephalopathy and tone abnormalities).
- Evidence of multiple organ involvement (such as that of kidneys, lungs, liver, heart and intestine).

The neonates that were excluded from the study were preterm infants, antenatally diagnosed cardiac disease and with major congenital malformation.

Based on previous study P.S. Rajakumar et al, myocardial dysfunction in newborns with perinatal asphyxia was 76.6%.

International Journal of Contemporary Pediatrics | May 2020 | Vol 7 | Issue 5 | Page 998
The details were entered in a predesigned proforma. This included history regarding antenatal risk factors for perinatal asphyxia such as age of the mother, history of pregnancy induced hypertension, anemia, bleeding, infection and systemic disease. Intrapartum factors like mode of delivery, history of prolonged rupture of membrane, difficult labor, meconium staining of amniotic fluid, malpresentation and cord prolapse were also entered. Examination findings including vitals and detailed anthropometry were recorded and a complete neurological examination and other systemic examination were done as per established standards. The neonates were treated as per the NICU treatment protocol for birth asphyxia of the hospital. During the NICU stay, heart rate, respiratory rate, blood pressure and oxygen saturation are monitored continuously. Clinical assessments included assessments of the neurologic status twice daily, the grade of HIE (Stage I, Stage II or Stage III), the type of respiratory support needed, the presence of seizures, involvement of multorgan dysfunction. Hospital recommended guidelines for investigations were done as and when needed. 2ml of venous blood drawn in plain tube between 3-6 hours of life from asphyxiated infants is analyzed for NT-pBNP. The Hotgen kit was used for quantitative measurement of human NT-ProBNP in serum or plasma employing combination of up converting phospher technology and immunochromatography. The Microsoft Excel and SPSS (SPSS Inc. Chicago v 18.5) software packages were used for data entry and analysis respectively. The results were averaged (mean±standard deviation) for each parameter for continuous data was analyzed using student t test and for proportions using chi-square test.

**RESULTS**

Among 120 neonates 88(73.3%) were male and 32(26.7%) were female. In the study group, 30(25%) babies were of low birth weight (<2500 grams) and 90(75%) babies were having normal weight at birth (>2500 grams). 77.5 percent of babies (93) were born between 37-39 weeks and 22.5 percent were born after 40 weeks (postdated). The mean and standard deviation of birth weight was 2786.9±475.684 grams and range of 1800 to 3820 grams. 41.7 percent of babies (50) delivered had meconium staining of the liquor and 58.3 percent had clear liquor. 80 percent of the babies (96) were born vaginally, 4.2 percent of deliveries were assisted with either forceps or vacuum. Rest 15.8 percent were taken for emergency lower segment caesarean section. 40 babies were resuscitated with tactile stimulation, 53 babies were resuscitated with positive pressure ventilation using bag and mask. 26 newborns were intubated and 1 newborn required chest compressions and endotracheal adrenaline. APGAR scores at 1 minute of life following resuscitation, 5.8 percent had score of less than 3, 70.8 percent had scores between 3 and 5 and 23.3 percent had score above 5. No babies had Apgar score of less than 3 at 5 minutes of life. 32.5 percent had scores between 3 and 5; rest 67.5 babies had scores above 5. Among 120 newborns in the study with perinatal asphyxia 44 (36.7%) babies had stage 1, 48 (40.0%) babies had stage 2, and rest 28 (23.3%) babies had stage 3. Stages were done according to modified Sarnat stages of hypoxic ischemic encephalopathy. 55.8 percent had respiratory distress and 19.2 percent had shock at the time of admission in neonatal intensive care unit following perinatal asphyxia. Table1.

**Table 1:** Mean, standard deviation, minimum and maximum values of birth weight (grams), gestational age (week), pH, sodium bicarbonate meq/L, and BNP ng/mL.

| Birth weight (grams) | HIE | N   | Mean  | SD    | Min. | Max. | F value* | p value |
|----------------------|-----|------|-------|-------|------|------|---------|---------|
| Stage 1              | N   | 44   | 2743.9| 501.29| 1800 | 3820 | 0.290   | 0.749   |
| Stage 2              | N   | 48   | 2817.3| 460.013| 1800 | 3650 |         |         |
| Stage 3              | N   | 28   | 2802.5| 473.072| 1900 | 3700 |         |         |
| Gestational Age (Wk) |     |      |       |       |      |      |         |         |
| Stage 1              | N   | 44   | 38.3  | 1.102 | 37.0 | 41.0 | 2.543   | 0.083   |
| Stage 2              | N   | 48   | 38.7  | 1.371 | 37.0 | 42.0 |         |         |
| Stage 3              | N   | 28   | 38.9  | 1.079 | 37.0 | 41.0 |         |         |
| pH                   |     |      |       |       |      |      |         |         |
| Stage 1              | N   | 44   | 7.37  | 0.074 | 7.21 | 7.68 | 62.073  | <0.001  |
| Stage 2              | N   | 48   | 7.24  | 0.147 | 7.01 | 7.66 |         |         |
| Stage 3              | N   | 28   | 7.01  | 0.185 | 6.54 | 7.30 |         |         |
| Sodium Bicarbonate (meq/L) |     |      |       |       |      |      |         |         |
| Stage 1              | N   | 44   | 19.89 | 3.218 | 14.90| 28.60| 62.595  | <0.001  |
| Stage 2              | N   | 48   | 15.72 | 4.665 | 10.10| 28.70|         |         |
| Stage 3              | N   | 28   | 9.36  | 3.358 | 3.70 | 16.30|         |         |
| BNP (ng/mL)          |     |      |       |       |      |      |         |         |
| Stage 1              | N   | 44   | 1.502 | 3.581 | 7.170| 5    | 19.803  |         |
| Stage 2              | N   | 48   | 4.916 | 8.001 | 674  | 5    | 35.000  |         |
| Stage 3              | N   | 28   | 8.912 | 13.927| 152  | 6    | 35.000  |         |
DISCUSSION

Perinatal asphyxia remains a severe condition leading to significant neonatal mortality and morbidity, although important advances made in past decade. The exact pathogenesis of myocardial dysfunction in birth asphyxia is still not clear; the role of hypoxia induced pulmonary vasoconstriction is the main precipitating cause of disturbed circulatory dynamics. There are logistic difficulties such as expertise and equipment in assessment of myocardial dysfunction. There are reports of NT-βBNP levels in perinatal asphyxia as a marker of cardiac dysfunction. The reduced cardiovascular reserve is associated with hypoxic brain damage and it has a high impact on neonatal mortality and adverse neurological outcomes.

In the present study, a total of 120 neonates with evidence of birth asphyxia were selected and studied. The babies were stratified based on the severity of asphyxia into three stages using modified Sarnat staging. The results and interpretations of the findings were based on the severity of HIE stages.

The gender, birth weight and gestational age distribution of the babies and colour of the liquor was not found to have a significant correlation with the severity of HIE staging in the present study. This was similar to the results shown by Agarwal et al, and Jain et al. Among the total 20 deaths, 9 babies had a meconium stained liquor at birth and all babies were graded with severe HIE stage 3. This difference was not significant statistically and the findings were in accordance with the reports of Lakshmanan et al. The findings of this study suggest that both the 1 minute and 5-minute APGAR scores were having a significant correlation stage of perinatal asphyxia. This was in contrary to the studies by Shadique et al, where statistical significance was not seen, however studies by Lakshmanan et al, showed statistical significance of APGAR scores with stages of perinatal asphyxia.

| Study | Sample size | Age range | Kit | BNP levels |
|-------|-------------|-----------|-----|------------|
| Koch and Singer 28 | 12 | Day 0 to day 1 Plasma | Biosite | Mean: 231.6 pg/ml SD: 197.5 |
| Koch and Singer 28 | 14 | Day 4 to day 6 Plasma | Biosite | Mean: 48.4 pg/ml SD: 49.1 |
| Kunii et al 29 | 11 | Day 0 Cord blood | Shiono RIA BNP | Mean: 10.4 pg/ml SD: 11.9 |
| Kunii et al 29 | 11 | Day 1 Plasma | Shiono RIA BNP | Mean: 118.8 pg/ml SD: 83.2 |
| Kunii et al 29 | 11 | Day 7 Plasma | Shiono RIA BNP | Mean: 15.3 pg/ml SD: 7.8 |
| Bar-Oz et al 30 | 122 | Day 1 Cord blood | Elecsys 1010/2010 | Mean: 578.8 ng/I SD: 351.3 |
| Bar-Oz et al 30 | 33 | Day 1 Plasma | Elecsys 1010/2010 | Mean: 3043.4 ng/I SD: 1783.2 |
| Mir et al 31 | 153 | Day 1 Venous/cord | Biomedica | Mean: 641 fmol/mL Range: 254-1272 |
| Mir et al 31 | 153 | Day 3 Venous/cord | Biomedica | Mean: 246 fmol/mL Range: 110-430 |

| Study -BNP level pg/ml | Stage 1 HIE | Stage 2 HIE | Stage 3 HIE | p value |
|------------------------|-------------|-------------|-------------|---------|
| Dharmendra Jain et al 33 | n = 10 | 482.40±114.83 | 957.00±336.94 | 1823.27±477.91 | <0.001 |
| Present study | n = 44 | 1,502.86±3,581.17 | 4,916.31±8,001.674 | 8,912.41±13,927.152 | 0.003 |

| Study | Death | BNP levels | p value |
|-------|-------|------------|---------|
| Dharmendra Jain et al 33 | Discharge | 1888.6±598.6 pg/ml | p value < 0.01 |
| Simovic AM, et al 34 | Asphyxiated newborns (n = 55) | 993.05±1259.51 pg/ml | p value 0.003 |
| | Healthy newborns (n = 36) | 278.98±190.47 pg/ml | |
| Present study | Death (n = 20) | 10,319.52±14,742.4 pg/ml | p value 0.002 |
| | Discharge (n = 100) | 3,452.66±6,984.858 pg/ml | |

Table 2: Reference ranges for B-type natriuretic peptide (BNP) in neonates.

Table 3: Comparison of mean, standard deviation of B-type natriuretic peptide (BNP) in neonates with Stages of hypoxic ischemic encephalopathy.

Table 4: Comparison of mean, standard deviation of B-type natriuretic peptide (BNP) in neonates of hypoxic ischemic encephalopathy with mortality.
This difference could probably be attributed to the difference of the number of newborns enrolled in the studies with severe asphyxia.

Koch and Singer determined the concentration of NT-Pro BNP in 12 normal newborns on day one with a mean of 231.6 pg/ml and standard deviation 197.5 pg/ml.\textsuperscript{28} Subsequently on day 4 to day 6 found a lower mean of 48.4 pg/ml and standard deviation of 49.1 pg/ml. Table 2.

Levels of BNP and NT-p BNP surge at birth, plateaus on day 3-4. This is followed by a steady fall to reach a constant level in infancy.\textsuperscript{31} The surge is multifactorial, including the loss of the placental low-pressure system. Exposure to the initially supra-systemic pulmonary pressures subjects the ventricle to greater volume and pressure loading. Furthermore, the placenta has a role in clearance of natriuretic peptides and loss of this clearance system contributes to the high levels.\textsuperscript{32} Therefore high levels of BNP at birth have a crucial regulatory role in the hemodynamic changes associated with transition to extra uterine life. Kidney maturation, a rise in systemic vascular resistance and a fall in pulmonary pressures explain the subsequent fall in the peptide levels.

Dharmendra Jain et al, published a similar study determining the levels of B type natriuretic peptide concentrations in HIE stages.\textsuperscript{33} This study was in accordance to the increasing concentrations of B type natriuretic peptide with increasing severity of hypoxic ischemic encephalopathy. The myocardial dysfunction was most severe in stage 3 perinatal asphyxia with highest BNP values with statistical significance p value. Table 3.

The mean B type natriuretic peptide concentrations were significantly elevated in non survivor group. This was attributable to higher level of cardiac dysfunction in the newborns with perinatal asphyxia. NT-Pro BNP can serve as a marker of cardiac dysfunction and higher levels was associated with poor outcome. Table 4.

CONCLUSION

N-Terminal Pro BNP levels within the first 48hrs after birth was significantly higher in newborns with perinatal asphyxia, with the levels rising proportionally to the clinical stages of HIE. Early N-Terminal Pro BNP concentrations may provide a useful marker for the anticipated severity of myocardial dysfunction.

ACKNOWLEDGEMENTS

Authors would like to thank Sri Jaganath P S, for helping in compiling and analyzing the data.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. World Health Organization. Basic Newborn Resuscitation: A Practical Guide, Geneva, Switzerland: World Health Organization; 1997. Available at: www.who.int/reproductive health/publications/newborn_resus_citation/index.html.
2. Rowe RD, Hoffman T. Transient myocardial ischemia of the newborn infant: a form of severe cardiorespiratory distress in full-term infants. J Pediatr. 1972;81:243-50.
3. Flores-Nava G, Echevarría-Ybargüengoitia IL, Navarro-Barrón IL, García-Alonso A. Transient myocardial ischemia in newborn babies with perinatal asphyxia (hypoxic cardiomyopathy). Biol Med Hosp Infant Mex. 1990;47:809-14.
4. Aslam HM, Saleem S, Afzal R, Iqbal U, Saleem SM, Shaikh MW et al. Risk factors of birth asphyxia. Italian J Pediatr. 2014 Dec 1;40(1):94.
5. Baqui AH, Darmstadt GL, Williams EK. Rates, timing and causes of neonatal deaths in rural India: implications for neonatal health programs. Bull World Health Organ. 2006;84:706-13.
6. Bang AT, Bang RA, Baitule S, Deshmukh M, Reddy MH. Burden of morbidity and the unmet need for health care in rural neonates: a prospective observational study in Gadchiroli, India. Indian Pediatr. 2001;38:952-65.
7. Antonucci R, Porcella A, Pilloni MD. Perinatal asphyxia in the term newborn. JPNIM. 2014;3(2):e030269.
8. Dilenge ME, Majnemer A, Shevell MI. Long-term developmental outcome of asphyxiated term neonates. J Child Neurol. 2001;16:781-92.
9. Manual of Neonatal Care, 7th edition, John P. Cloherty, Eric C. Eichenwald, Anne R. Hansen, Ann R. Stark, New Delhi, Wolters Kluwer; 2015:711.
10. National Neonatal and Perinatal Database Report 2002-2003.1-58. Available at: https://www.newbornwhocc.org/pdf/nmpd_report_2002-03.PDF.
11. Rajakumar PS, Bhat BV, Sridhar MG, Balachander J, Konar BC, Narayanan P, et al. Cardiac Enzyme Levels in Myocardial Dysfunction in Newborns with Perinatal Asphyxia. Indian J Pediatr. 2008;75(12):1223-5.
12. Vesely DL, Cliffs E. Atrial natriuretic hormones. New Jersey: Prentice Hall, 1992.
13. Sudoh T, Kangawa K, Minamino N, Matsuo H. A new natriuretic peptide in porcine heart. Nature. 1988;332(6159):78-81.
14. Saito Y, Nakao K, Itoh H, Yamada T, Mukoyama M, Arai H, et al. Brain natriuretic peptide is a novel cardiac hormone. Bioch Biophys Res Communica. 1989;158(2):360-8.
15. Vesely DL, Douglass MA, Dietz JR, Gower Jr WR, McCormick MT, Rodriguez-Paz G, et al. Three peptides from the atrial natriuretic factor prohormone amino terminus lower blood pressure...
and produce diuresis, natriuresis, and/or kaliuresis in humans. Circulation. 1994;90(3):1129-40.
16. Singh G, Kuc RE, Maguire JJ, Fidock M, Davenport AP. Novel snake venom ligand dendroaspis natriuretic peptide is selective for natriuretic peptide receptor-A in human heart; down regulation of natriuretic peptide receptor-A in heart failure. Circ Res 2006;99:183-90.
17. Hunt PJ, Yandle TG, Nicholls MG, Richards AM, Espiner EA. The amino-terminal portion of probrain natriuretic peptide (proBNP) circulates in human plasma. Biochem Biophys Res Commun 1995;214:1175-83.
18. Withnall R. Science review: natriuretic peptides in critical illness. Crit Care. 2004;8:342-9.
19. Reynolds EW, Ellington JG, Vranicar M, Bada HS. Brain-type natriuretic peptide in the diagnosis and management of persistent pulmonary hypertension of the newborn. Pediatrics. 2004;114:1297-304.
20. O’Mara PW, Poole SD, Brown N, Ding T, Paria B, Reese J. Regulation of the fetal and newborn ductus arteriosus (da) by natriuretic peptides. E-PAS. 2006;59:2875-314.
21. Maack T. Receptors of atrial natriuretic factor. Annu Rev Physiol. 1992;54:11-27.
22. Committee on Fetus and Newborn, American Academy of Pediatrics and Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. Use and Abuse of the Apgar Score. Pediatr. 1996;98:141-2.
23. Cantinotti M, Storti S, Parri MS, Murzi M, Clerico A. Reference values for plasma B-type natriuretic peptide in the first days of life. Clin Chem. 2009;55(7):1438-40.
24. Agrawal J, Shah GS, Poudel P, Baral N, Agrawal A, Mishra OP. Electrocardiographic and enzymatic correlations with outcome in neonates with hypoxic-ischemic encephalopathy. Ital J Pediatr. 2012;38:33.
25. Jain D, Pandey AK, Das BK, Prasad R. Cardiac Function in Perinatal Asphyxia. Sch J Appl Med Sci. 2016;4(7):2718-28.
26. Lakshmanan R, Verma YS. Cardiac changes in asphyxiated neonates-need for early detection to improve long-term outcome. Int J Contemp Pediatr. 2017;4(5):1844-50.
27. Shadique AM, Sailavasan M. A prospective study on cardiac changes (electrocardiographic, enzymatic and echocardiographic) in birth asphyxiated neonates admitted in tertiary care centre. Int J Contemp Pediatr. 2019;6:269-74.
28. Koch A, Singer H. Normal values of B type natriuretic peptide in infants, children, and adolescents. Heart 2003;89:875-8.
29. Kunii Y, Kamada M, Ohitsu K, Araki T, Katoaka K, Kageyama M, et al. Plasma brain natriuretic peptide and the evaluation of volume overload in infants and children with congenital heart disease. Acta Med Okayama. 2003;57:191-7.
30. Bar-Oz B, Lev-Sagie A, Arad I, Salmeter L, Nir A. N-terminal pro-B-type natriuretic peptide concentrations in mothers just before delivery, in cord blood, and in newborns. ClinChem 2005;51:926-7.
31. Mir TS, Marohn S, Läer S, Eiselt M, Grollmus O, Weil J. Plasma concentrations of N-terminal pro-brain natriuretic peptide in control children from the neonatal to adolescent period and in children with congestive heart failure. Pediatrics. 2002;110:e76.
32. Mir TS, Laux R, Hellwege HH, Liedke B, Heinze C, von Buelow H, et al. Plasma concentrations of aminoterminal pro atrial natriuretic peptide and aminoterminal pro brain natriuretic peptide in healthy neonates: marked and rapid increase after birth. Pediatrics. 2003;112:896-9.
33. Jain DD, Pandey DA, Das DB, Prasad DR. Cardiac function in perinatal asphyxia. J Appl Med Sci. 2016;4:2718-28.
34. Simović AM, Košutić JL, Prijić SM, Knežević JB, Vujić AJ, Stojanović ND. The role of biochemical markers as early indicators of cardiac damage and prognostic parameters of perinatal asphyxia. Vojnosanitetski pregled. 2014;71(2):149-55.

Cite this article as: Kariyappa M, Shivarudrappa S. N-terminal pro brain natriuretic peptide as a marker of myocardial dysfunction in newborns with perinatal asphyxia. Int J Contemp Pediatr 2020;7:997-1002.