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**Original Research Article**

# A prospective study on cardiac changes (electrocardiographic, enzymatic and echocardiographic) in birth asphyxiated neonates admitted in tertiary care centre

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## ABSTRACT

**Background:** Reduced myocardial performance and cardiac output following perinatal asphyxia may significantly complicate perinatal management and may contribute to increased end-organ damage and mortality. Hence the present study was done with the aim to assess the usefulness of echocardiography, electrocardiography (ECG), and cardiac enzymes in evaluating myocardial damage in perinatal asphyxia neonates and to assess their correlation with different stages of hypoxic-ischemic encephalopathy (HIE) and outcome.
**Methods:** The study was conducted in the NICU, Department of Pediatrics, Government Chengalpattu Medical college hospital between August 2017 and August 2018 using 70 birth asphyxiated term babies. The asphyxiated babies were resuscitated as per NRP guidelines and were stratified into HIE stages as per Levene system of classification and were managed as per clinical condition. ECG grading, echo changes were noted. Creatinine kinase-MB (CKMB) levels were measured and documented after 12 hours of life among these babies and were analysed.
**Results:** Of 70 cases, 36 (51.4%) had mild, 26 (37.1%) moderate and 8 (11.4%) severe HIE. Abnormal ECG was observed in 63 cases. Raised CKMB levels were found in 67 (95.7%) and abnormal echo findings were noted in 46 (65.7%) babies. ECG, echo changes and CKMB levels showed increasing abnormalities with increasing severity of HIE (p=0.000, 0.030 and 0.001 respectively). 8 babies in present study expired.
**Conclusions:** Cardiac abnormalities among asphyxiated neonates requires high index of suspicion. ECG abnormalities, echo changes, elevated CK-MB levels in babies with HIE can help us identify neonates at risk of complications and guide in timely intervention that can prevent mortality of these babies and help us achieve better neurological outcome in these babies.

**Keywords:** Cardiac dysfunction, CK-MB enzyme, ECG changes, Echocardiography, Perinatal asphyxia

## INTRODUCTION

Perinatal asphyxia is one among the most important causes of mortality and morbidity among newborns in developing countries. As per National Neonatal-Perinatal Database (NNPD) Report 2002-2003 perinatal asphyxia was the commonest cause for still birth accounting to 45.1% among still birth cases.[1] Among institutional deliveries, incidence is 5% and accounts for 24.3% of neonatal deaths. The way an asphyxiated newborn is managed determines the mortality and also the extent to which we can have a neurologically good and developmentally normal child. The survivors of asphyxia have been found to have an increased risk of intellectual disability, hearing and visual impairments and also behavioral disorders in childhood.[2]

The incidence of cardiac dysfunction in perinatal asphyxia can be identified by the clinical presentations. Apart from that echocardiogram, electrocardiography (ECG) and determination of cardiac enzyme levels were considered as useful diagnostic tools to detect myocardial involvement. Only few studies were done in asphyxiated neonates to assess the cardiac changes by using ECG, echocardiogram and cardiac enzymes.[3,4]

Therefore, the present study was done with the objective to assess the usefulness of echocardiography, ECG, and cardiac enzymes in evaluating myocardial damage in perinatal asphyxia neonates and to assess their correlation with different stages of HIE and outcome.

## METHODS

This prospective study was conducted at the Neonatal Intensive Care Unit (NICU), Department of Pediatrics, Chengalpattu Medical College and Hospital, Chengalpattu during the period from August 2017 to August 2018. After getting approval from institutional ethics committee and consent from the parents 70 neonates aged between 0 and 28 days of life were included in the study.

### *Inclusion criteria*

- Neonates born at term with evidence of birth asphyxia as indicated by APGAR score of less than 7/10 at five minutes, metabolic acidosis (pH<7.2) and clinical evidence of hypoxic-ischemic encephalopathy (HIE).

### *Exclusion criteria*

- Preterm neonates, neonates with congenital heart disease, major congenital malformations, myopathies and neonatal sepsis.

Newborns with asphyxia are categorized into different stages based on the severity of asphyxia.[5] All neonates were managed as per NRP guidelines and APGAR scoring was done at 1 and 5 minutes of life.[6-8]

Babies were given oxygen via hood, CPAP and mechanical ventilation as needed depending on the clinical condition. IV fluids and IV antibiotics were given to babies who required respiratory support. IV Inotropes and anticonvulsants were given as per need.

Feeding was started to babies who had mild HIE and also for sick babies after stabilization. Blood samples for creatinine kinase-MB (CK-MB) were taken after 12-14 hours of life and within 24 hours by taking 1-2ml of blood and analysed by quantitative determination base on immune inhibition IFCC methodology using semi auto-analyzer. A 12 lead ECG was taken within 24 hours of life and was graded as per Jedeikin et al into four grades.[9]

ECHO was done after 24 hours of life to look for left ventricular dysfunction, mitral and tricuspid regurgitation and also for evidence of PPHN.

### *Statistical analysis*

The collected data were entered in Microsoft excel sheet and analysed using SSPE software version 21. Chi square test was done to compare the parameters among the babies who were discharged and those who expired and for the parameters with the different stages of HIE.

## RESULTS

The basic general characteristics of neonates after their delivery were presented in Table 1. A total of 7o neonates were included in the study. Most of them were male babies (57.1%). Maximum (41.4%) neonates were weighing between 2.5 to 3kg. Normal vaginal delivery constituting more than half (52.9%) of the total deliveries.

Most of the babies were born through clear liquor (72.9%). out of 70, 43 (61.4%) neonates needed BMV for duration of <1 minute and 27 for more than 1 minute. about 56 (80%) of the neonates had an APGAR of 3-5 out of 10 at one minute of life.

5 minute APGAR score was >5 in 43 neonates. About 25 neonates required Intubation in the delivery room out of 70 and one baby needed chest compression during resuscitation. 75.7% had a cord blood pH between 7.0 and 7.2 and pH of <7 was noted in 24.3% of babies.

As per Levene staging, 51.4% of newborns belonged to HIE stage 1, 37.1% belongs to HIE stage 2 and about 11.4% neonates were severely asphyxiated with HIE stage 3. Out of 70 neonates, about 54 (77.1%) of neonates had no shock and 16 (22.9%) developed shock.

Abnormal ECG was observed in 63 neonates. Most number of newborns (37.1%) had Grade 2 ECG changes. Echo was abnormal in 46 babies. Most of the newborns (57.1%) had CK-MB values between 25 and 100 IU/l. Most of the babies stayed in NICU for a period between 3 and 7 days (48.6%).

As shown in Table 2, out of 70 neonates 62 were discharged and 8 were died during hospital stay. No significant correlation was noted between gender, mode of delivery, Apgar scores at 1 minute and 5 minutes with outcome (p>0.05).

However statistically significant correlation was seen between outcome and colour of liquor (p=0.017), duration of BMV (p=0.04), HIE staging (p=0.00), presence of shock (p=0.00), ECG findings (p=0.00), echo findings (p=0.03), CK-MB levels (p=0.001) and hospital stay in days (p=0.001).

**Table 1: General and clinical characteristics of study population.**

| Variables | | Number of neonates (N=70) | Percentage |
|---|---|---|---|
| Sex | Male | 40 | 57.1 |
| | Female | 30 | 42. 9 |
| Birth weight | <2kg | 1 | 1.4 |
| | 2-2.5kg | 7 | 10 |
| | 2.5-3 kg | 29 | 41.4 |
| | 3-3.5 kg | 28 | 40 |
| | >3.5 kg | 5 | 7.1 |
| Mode of delivery | LN | 37 | 52.9 |
| | LSCS | 24 | 34.3 |
| | Vacuum | 7 | 10 |
| | Forceps | 2 | 2.85 |
| Liquor | Clear | 51 | 72.9 |
| | Meconium stained | 19 | 27.1 |
| BMV duration | 30 secs to 1 min | 43 | 61.4 |
| | >1 min | 27 | 38.6 |
| 1 min APGAR | <3 | 12 | 17.1 |
| | 3-5 | 56 | 80 |
| | >5 | 2 | 2.9 |
| 5 min APGAR | <3 | 0 | 0 |
| | 3-5 | 27 | 38.6 |
| | >5 | 43 | 61.4 |
| Intubation in delivery room | Yes | 25 | 35.7 |
| | No | 45 | 64.3 |
| Cord blood pH | <7 | 17 | 24.3 |
| | 7-7.2 | 53 | 75.7 |
| HIE staging | Stage 1 | 36 | 51.4 |
| | Stage 2 | 26 | 37.1 |
| | Stage 3 | 8 | 11.4 |
| Presence of shock | Yes | 16 | 22.9 |
| | No | 54 | 77.1 |
| ECG grading | Grade 1 | 17 | 24.3 |
| | Grade 2 | 26 | 37.1 |
| | Grade 3 | 18 | 25.7 |
| | Grade 4 | 2 | 2.9 |
| | Normal | 7 | 10 |
| ECHO changes | Normal | 24 | 34.3 |
| | Abnormal | 46 | 65.7 |
| CKMB level (IU/l) | <25 | 3 | 4.3 |
| | 25-100 | 40 | 57.1 |
| | 100-250 | 19 | 27.1 |
| | >250 | 8 | 11.4 |
| Hospital stay (in days) | <3 | 5 | 7.1 |
| | 3-7 | 34 | 48.6 |
| | >7 | 31 | 44.3 |

The severity of HIE staging in relation to various parameters were given in Table 3.

It showed that no statistically significant difference was observed for gender mode of delivery and Apgar score at 1 minute with different stages of HIE grading.

**Table 2: Correlation of various parameters with outcome.**

| Categories | Discharge (N=62) | Death (N=8) | P value | Significance |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 35 (87.5) | 5 (12.5) | 0.550 | NS |
| Female | 27 (90) | 3 (10) | | |
| **Mode of delivery** | | | | |
| NVD | 35 (94.6) | 2 (5.4) | 0.550 | NS |
| LSCS | 20 (83.3) | 4 (16.7) | | |
| AVD | 7 (77.8) | 2 (22.2) | | |
| **Colour of liquor** | | | | |
| Clear | 48 (94.1) | 3 (5.9) | 0.017 | S |
| Meconium stained | 14 (73.7) | 5 (26.3) | | |
| **Duration of BMV** | | | | |
| 30 secs to 1 min | 39 (90.7) | 4 (9.3) | 0.0480 | S |
| >1 min | 23 (85.2) | 4 (14.8) | | |
| **1 minute Apgar** | | | | |
| <3 | 10 (83.3) | 2 (16.7) | 0.737 | NS |
| 3-5 | 50 (89.3) | 6 (10.7) | | |
| >5 | 2 (100) | 0 | | |
| **5 minute Apgar** | | | | |
| <3 | 0 | 0 | 0.480 | NS |
| 3-5 | 39 (90.7) | 4 (9.3) | | |
| >5 | 23 (85.2) | 4 (14.8) | | |
| **HIE staging** | | | | |
| Stage 1 | 36 (100) | 0 | 0.000 | S |
| Stage 2 | 24 (92.3) | 2 (7.7) | | |
| Stage 3 | 2 (25) | 6 (75) | | |
| **Presence of shock** | | | | |
| Yes | 9 (56.2) | 7 (43.8) | 0.000 | S |
| No | 53 (98.1) | 1 (1.9) | | |
| **ECG grading** | | | | |
| Normal | 6 (85.7) | 1 (14.3) | 0.000 | S |
| Grade 1 | 17 (100) | 0 | | |
| Grade 2 | 25 (96.2) | 1 (3.8) | | |
| Grade 3 | 14 (77.8) | 4 (22.2) | | |
| Grade 4 | 0 | 2 (100) | | |
| **ECHO findings** | | | | |
| Normal | 24 (100) | 0 | 0.030 | S |
| Abnormal | 38 (82.6) | 8 (17.4) | | |
| **CKMB levels** | | | | |
| <25 | 3 (100) | 0 | 0.001 | S |
| 25-100 | 39 (97.5) | 1 (2.5) | | |
| 100-250 | 16 (84.2) | 3 (15.8) | | |
| >250 | 4 (50) | 4 (50) | | |
| **Hospital stay (in days)** | | | | |
| <3 | 3 (60) | 2 (40) | 0.001 | S |
| 3-7 | 33 (97.1) | 1 (2.9) | | |
| >7 | 26 (83.9) | 5 (16.1) | | |

S-Statistically significant; NS-Not significant.

Other findings like colour of liquor (p=0.001), duration of BMV (p=0.003), Apgar score at 5 min (p=0.003), presence of shock (p=0.00), ECG grading (p=0.005), echo findings (p=0.002) and CK-MB levels (p=0.00) showed significant difference among different stages of HIE.

**Table 3: Comparison of various parameters with severity of HIE.**

| Parameters | Categories | HIE stage 1 n (%) | HIE stage 2 n (%) | HIE stage 3 n (%) | P value | Significance |
|---|---|---|---|---|---|---|
| Gender | Male | 20 (50) | 14 (35) | 6 (15) | 0.550 | NS |
| | Female | 16 (53.3) | 12 (40) | 2 (6.7) | | |
| Mode of delivery | NVD | 18 (48.6) | 16 (43.2) | 3 (8.1) | 0.145 | NS |
| | LSCS | 16 (66.7) | 5 (20.8) | 3 (12.5) | | |
| | AVD | 2 (22.2) | 5 (55.6) | 2 (22.2) | | |
| Colour of liquor | Clear | 32 (62.7) | 17 (33.3) | 2 (3.9) | 0.001 | S |
| | Meconium stained | 4 (21.1) | 9 (47.4) | 6 (31.6) | | |
| Duration of BMV | 30 secs to 1 min | 29 (67.4) | 10 (23.3) | 4 (9.3) | 0.003 | S |
| | >1 min | 7 (25.9) | 16 (59.3) | 4 (14.8) | | |
| 1 minute Apgar | <3 | 6 (50) | 4 (33.3) | 2 (16.7) | 0.953 | NS |
| | 3-5 | 29 (51.8) | 21 (37.5) | 6 (10.7) | | |
| | >5 | 1 (50) | 1 (50) | 0 | | |
| 5 minute Apgar | <3 | 0 | 0 | 0 | 0.003 | S |
| | 3-5 | 7 (25.9) | 15 (55.6) | 5 (18.5) | | |
| | >5 | 29 (67.4) | 11 (25.6) | 3 (7) | | |
| Presence of shock | Yes | 1 (6.2) | 7 (43.8) | 8 (50) | 0.000 | S |
| | No | 35 (64.8) | 19 (35.2) | 0 | | |
| ECG grading | Normal | 3 (42.9) | 4 (57.1) | 0 | 0.005 | S |
| | Grade 1 | 11 (64.7) | 6 (35.3) | 0 | | |
| | Grade 2 | 14 (53.8) | 10 (38.5) | 2 (7.7) | | |
| | Grade 3 | 8 (44.4) | 6(33.3) | 4 (22.2) | | |
| | Grade 4 | 0 | 0 | 2 (100) | | |
| ECHO | Normal | 19 (79.2) | 5(20.8) | 0 (0) | 0.002 | S |
| | Abnormal | 17 (37.0) | 21(45.7) | 8 (17.4) | | |
| CKMB levels | <25 | 3 (100) | 0 | 0 | 0.000 | S |
| | 25-100 | 27 (67.5) | 13(32.5) | 0 | | |
| | 100-250 | 3 (15.8) | 11(57.9) | 5 (26.3) | | |
| | >250 | 3 (37.5) | 2 (25) | 3 (37.5) | | |

S-Statistically significant; NS-Not significant.

## DISCUSSION

In present study, a total of 70 neonates with evidence of birth asphyxia were selected and studied. The babies were stratified based on the severity of asphyxia into three stages using Levene staging of asphyxiated neonates.[5] The results and interpretations of the findings were based on the severity of HIE staging and also on the outcome of the neonates based on whether they were discharged or expired.

Gender distribution of the babies and mode of delivery was not found to have a significant correlation with either outcome or with the severity of HIE staging in present study. This was similar to the results shown by Agarwal et al and Jain et al.[10,11] In present study, about 51 babies delivered were found to have clear liquor and about 19 babies had meconium stained liquor. Among the total 8 deaths, 5 babies who died had a meconium stained liquor at birth and 6 babies were graded with sever HIE. This difference was significant statistically and the findings were contrary with the reports of Lakshmanan et al.[12]

Our findings suggest that both the 1 minute and 5 minute APGAR were not having a significant correlation with the outcome. Also 1 minute APGAR was found to have no correlation with HIE severity but 5 minute APGAR had a significant correlation (p-0.003) with HIE severity which is in accordance with the results of Agarwal et al and Jain et al.[10,11]

On contrary to the previous studies, majority of the patients in present study belongs to HIE stage 1 (51.4%) showing a significant correlation between the severity of

HIE and the outcome of the neonates. present study showed that about 16 babies (22.9%) developed shock and its incidence was found to be statistically significant correlation between increasing severity of HIE and also the outcome of the neonate. However, Mandal et al found shock in 44% of neonates which was higher than present findings.[13]

ECG, echocardiography are important tools to pick up the severity and extent of cardiac involvement among birth asphyxiated neonates. In present study, among the 63 abnormal ECGs, Grade 1 changes were seen in 26.9%, Grade 2 in 41.2%, Grade 3 28.5% and Grade 4 changes were noted in 3.1% of the babies which shows that most babies in present study had Grade 2 ECG changes which is in corroboration with study done by Rajakumar et al.[14]

The echo changes expected to occur in asphyxia are depressed ventricular function, mitral regurgitation, tricuspid regurgitation. About 65.7% of neonates in present study had abnormal echo findings. None of the babies with normal ECHO expired. All the babies that expired with abnormal echo belonged to HIE stage 3. Echo changes in present study were found to have a statistically significant correlation with outcome (p=0.030) and HIE staging (0.002) of the neonates. Similar results were noted by Lakshmanan et al and also by Aleksandra et al.[12,15]

CKMB is one of the important clues in identifying the cardiac involvement which can play a pivotal role in early identification of babies who are at risk of developing cardiac complications. In present study it was found that the mean CKMB levels were 133.9 IU/l which was comparable to the study done by Saira et al who had a mean CKMB level of 122.46 IU/l.[16] On contrary to this, Mandal et al reported CK-MB values as high as a 823.5 IU/l.[13] In present study, no baby was expired with normal CKMB levels. The enzyme levels showed significant rise with increasing severity of HIE; indicating more myocardial ischaemia in severe HIE than mild and moderate cases. The mortality rate was increased with increase in CKMB levels.

Limitation: The estimation of enzyme levels of troponin T, which is very specific for myocardial ischemia, was not done due to logistic issues in present study.

## CONCLUSION

In conclusion, present results confirm that colour of liquor, BMV duration, presence of shock, ECG changes, echo abnormalities, CKMB levels, were found to have a significant correlation with increasing severity of HIE and adverse outcome. Hence, early detection of these issues can help in providing better treatment and improves the survival rate of the neonates.

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