Original Article

DOI: 10.17354/ijss/2016/220

Laboratory Findings and Clinical Correlation in Assessing the Severity of Perinatal Asphyxia

Dinakara Prithviraj[1], Bharath Reddy[2], Deepthi[3], Abhijit Shetty[3]

[1]Associate Professor, Department of Pediatrics, Vydehi Institute of Medical Sciences, Bengaluru, Karnataka, India, [2]Assistant Professor, Department of Pediatrics, Vydehi Institute of Medical Sciences, Bengaluru, Karnataka, India, [3]Junior Resident, Department of Pediatrics, Vydehi Institute of Medical Sciences, Bengaluru, Karnataka, India

Abstract

Introduction: Perinatal asphyxia contributes significantly to neonatal morbidity and mortality.

Objective: The study was to done to investigate the predictive values of various biochemical markers, neurosonographic, and echocardiographic findings in assessing the severity of perinatal asphyxia.

Materials and Methods: A prospective observational study conducted on babies admitted to the neonatal intensive care unit (NICU) during the period of January 2012 to January 2016 in Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India with perinatal asphyxia. About 80 babies were included in the study with perinatal asphyxia. The clinical and neurological examination was done for all the neonates included in the study. Blood samples for different systemic biomarkers were taken from all the babies within 15 min following their admission, then at 48 h and at 72 h of admission to the NICU. The patients with hypoxic-ischemic encephalopathy (HIE) were divided into three groups (Stage 1: Mild, Stage 2: Moderate, and Stage 3: Severe) according to the Sarnat and Sarnat staging system. The predictive values of these biochemical markers in determining the stage of HIE were assessed.

Results: Out of 80 babies included in the study 57.5% were male babies. The mean gestational age and birth weight were 39± 2.0 weeks and 2907 ± 420 g, respectively. The cesarean section rate was 38.75%. According to the classification of Sarnat and Sarnat, 37 (46.25%) patients had Stage 1, 23 (28.75%) had Stage 2, and 20 (25%) had Stage 3 HIE. About 10 babies died during and after the study period. There was statistically significant increase in cardiac markers (creatine kinase BB [CK-BB], troponin I, CK-BB), hepatic markers (alanine aminotransferase, prothrombin time/international normalized ratio) and increase in lactate in the cases of severe HIE stage.

Conclusion: HIE is the most severe manifestation of perinatal asphyxia which can be predicted by early laboratory evaluation of biomarkers so as that early treatment can be initiated.

Key words: Hypoxic-ischemic encephalopathy, Perinatal asphyxia, Sarnat and Sarnat staging

INTRODUCTION

Perinatal asphyxia is a condition wherein there is an impairment of transfer of the respiratory gasses resulting in hypoxemia and hypercapnia, accompanied by metabolic acidosis. The WHO defines perinatal asphyxia as "Failure to initiate or sustain breathing at birth."[1] Perinatal asphyxia is a third most common cause of neonatal death (23%) after preterm birth (28%) and sepsis (26%). The asphyxial injury may involve virtually every organ system of the body, but hypoxic-ischemic encephalopathy (HIE) is the most common sequelae.[1]

HIE characterized mainly by abnormal muscle tone and reflexes, an altered level of consciousness, and commonly by convulsions is an outcome of perinatal asphyxia.[2] HIE is a cause of death in newborns, and who survive are prone to serious neurological disorders such as cerebral palsy.[2]

Access this article online

www.ijss-sn.com

Month of Submission : 02-2016
Month of Peer Review : 03-2016
Month of Acceptance : 03-2016
Month of Publishing : 04-2016

Clinical Manifestations

Neonatal encephalopathy is defined as "A clinically defined syndrome of disturbed neurological function in the earliest

Corresponding Author: Dr. Dinakara Prithviraj, Department of Pediatrics, Vydehi Institute of Medical Sciences, Bengaluru - 560 066, Karnataka, India. Phone: +91-9742274849. E-mail: Drdinakar.nishanth@gmail.com

days of life in the term infant, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness, and often by seizures."[3]

Sarnat and Sarnat classified HIE into three clinical stages: Mild (Stage 1), moderate (Stage 2), and severe (Stage 3) encephalopathy. HIE infants have various levels of consciousness and the behavioral changes ranging from irritability to stupor or coma.[4] In most cases, systemic hypoxia-ischemia results in multiorgan dysfunction. The lungs of asphyxiated newborns can be injured by hypoxia, as a result of inhaled meconium, secondary to cardiac dysfunction, or compromised due to pulmonary hypertension. Accordingly, gas exchange is impaired and assisted ventilation may be needed.[4]

The Apgar score is used to describe the newborn's physical condition at birth. Any hypoxic insult may cause depression of the Apgar score. A prolonged depression of the Apgar score is associated with death or severe neurodevelopmental outcome.[3] Hypoxia-ischemia causes direct damage to the myocardium reacted by the increase of cardiac enzymes.[4] The other multisystem effects regard kidneys, liver, and bone marrow. Fluid retention and hyponatremia may occur due to inappropriate secretion of antidiuretic hormone.[5] Bone marrow depression causes an increase in release of nucleated red blood cells (NRBC) and thrombocytopenia. Alteration in blood glucose levels may be observed, hypoglycemia being most common.[4]

Diagnosis

Clinical evaluation and laboratory values are used to assess and manage the asphyxiated babies. The best indicator for intrapartum asphyxia is severe metabolic acidosis (pH <7.0 and base deficit ≥12 mmol/L) in umbilical cord arterial blood at delivery.[6] Cranial and doppler ultrasonography, computerized tomography, and magnetic resonance imaging are the most used brain imaging techniques.

Biochemical Markers

Neonatal asphyxia causes multiorgan failure involving mainly the kidney, liver, brain, and heart which is associated with poor prognosis.[6] The kidney is one of the most important organs commonly involved in the multiple organ dysfunction caused by perinatal asphyxia. Evaluations of blood urea and serum creatinine levels are the tests most frequently used to assess renal injury caused by perinatal asphyxia.[6] Accordingly, markers of tubular dysfunction, such as urinary β2 microglobulin, have been found to be better indicators of early renal injury.[8] Myocardial injury normally develops when this compensation mechanism fails. Electrocardiogram, echocardiography, and measurement of cardiac enzymes are used to assess myocardial dysfunction.[7]

MATERIALS AND METHODS

A prospective observational study was conducted on babies admitted to the neonatal intensive care unit (NICU) from Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, from January 2012 to January 2016 with perinatal asphyxia. During this 4-year period, we analyzed about 97 cases and as per our inclusion criteria of which 17 cases were excluded for various reasons. 80 neonates fulfilling the following criteria were finally analyzed after approval from the Ethical Committee for the study and written consent from the parents.

Inclusion Criteria

1. All newborns with perinatal asphyxia were included if at least one of the three were present:

A. Intrapartum signs of fetal distress, as indicated by non-reassuring non-stress test on continuous electronic fetal monitoring and by meconium staining of the amniotic fluid
B. Apgar score of <1 at 1 min or <7 at 5 min of life
C. The requirement of positive pressure ventilation
D. Profound metabolic or mixed acidemia (pH < 7.10) in an umbilical artery blood sample, if obtained
E. Mild, moderate, or severe HIE, as defined by Sarnat and Sarnat staging.[5]

Exclusion Criteria

1. Preterms with gestation <36 weeks or weight less than 1800 g,
2. Major congenital malformation, chromosomal abnormalities, or any metabolic disorders,
3. Birth trauma,
4. Septic shock,
5. Neonates born to mothers who have received magnesium sulfate or opioids within 4 h before delivery.

Babies included in the study as per criteria were studied for demographic details, such as gestational age, birth weight, and risk factors for perinatal asphyxia, were also recorded. Gestational age was assessed from last menstrual period and New Ballard score. Arterial blood gas (ABG) analysis was done from the umbilical arterial blood. Thorough clinical and neurological examination was done for all the neonates included in the study. Blood samples are taken from all the patients in these three groups within 15 min following their admission, then at 48 h and at 72 h of admission to the NICU. Blood samples are analyzed for

ABG, HCO_3, base deficit levels, whole blood cell (WBC) count parameters (hemoglobin [Hb], total leukocyte count [TLC], platelet count), renal parameters (blood urea nitrogen [BUN], creatinine, and urinary micro globulins), liver parameters (aspartate aminotransferase, alanine aminotransferase, fibrinogen levels, prothrombin time/international normalized ratio [PT/INR]), cardiac enzymes (creatine kinase BB [CK-MB], CK-BB, troponin levels) lactate dehydrogenase (LDH), C-reactive protein (CRP), lactate, uric acid (UA) and electrolyte levels. The patients with HIE were divided into three groups (Stage 1: Mild, Stage 2: Moderate, and Stage 3: Severe) according to the Sarnat and Sarnat staging system within 48-72 h following their admission to the NICU. The predictive values of these biochemical markers in determining the stage of HIE were assessed. All the babies looked for any cerebral edema, any intracranial bleeds, cardiac activity (ventricular contraction, persistent pulmonary hypertension of the newborn [PPHN], left ventricular output), and corticomedullary differentiation of the kidney on ultrasound.[9]

Blood lactate levels analyzed by a gas analyzer Gem Premier 3000; reference values 0.3-3 mmol/L; serum level of troponin I determined along with other biomarkers (CK-MB and CRP) by enzyme-linked immunosorbent method on enzyme-linked fluorescent assay (cTnI reference range is from 0.01 to 2.8 μg/L.[10] The following variables were analyzed along with the 1st and 5th min Apgar score.

CK-MB fraction level was determined by a biochemical analyzer Beckman Coulter. Serum concentration of CRP was determined by the biochemical analyzer Beckman Coulter. The reference value in the clinical lab of Vydehi Hospital was irrespective of age is <0.35 ng/mL.[11]

Statistical Analysis

Descriptive statistics (mean and standard deviation) are calculated. To display the mean values of biochemical markers descriptive statistics – median and quartiles. To compare the mean values of variables two populations were used: Mann–Whitney test and ANOVA. The correlation of two numerical characteristics was examined using Spearman's and Pearson's correlation coefficient. The suitability of numeric variables was tested using receiver operating characteristic curves.

RESULTS

Out of 80 babies included in the study, 57.5% were male. The mean gestational age and birth weight were 39±2.0 weeks and 2907 ± 420 g, respectively. The cesarean section rate was 38.75%. According to the classification of Sarnat and Sarnat, 37 (46.25%) patients had Stage 1, 23 (28.75%) had Stage 2, and 20 (25%) had Stage 3 HIE (Table 1).

There was a total of 25% of preterm, 44% were term neonates, and 31% were postterm admitted in the study

Table 1: Demographic data of the patients

Demographic data	Staging according to Sarnat and Sarnat staging (staging done at 48 h of life)			*P* value
	Stage 1 *n*=37 (%)	Stage 2 *n*=37 (%)	Stage 3 *n*=37 (%)	
Preterm babies *n*=20 (25%)	13 (35)	3 (14)	4 (20)	0.176
Term babies *n*=35 (44%)	20 (54)	10 (43)	5 (25)	0.135
Post term babies *n*=25 (31%)	4 (11)	10 (43)	11 (55)	0.001
SGA/IUGR *n*=30 (37.5%)	6 (16)	10 (43)	14 (55)	0.154
Gestational age (in weeks)	38.4 (37.1-39.5)	39.1 (38.2-40.5)	39.5 (38.6-41.6)	0.284
Male *n*=46 (57.5%)	16 (43)	16 (70)	14 (70)	0.112
Female *n*=34 (42.5%)	21 (57)	7 (30)	6 (30)	
Apgar score (mean)	7	6	5	0.101
Mode of delivery				
Vaginal *n*=37 (46.25%)	19 (52)	9 (40)	9 (45)	1.212
LSCS *n*=31 (38.75%)	17 (46)	10 (43)	4 (20)	
Assisted *n*=12 (15%)	1 (2)	4 (17)	7 (35)	
Materno fetal factors				
No antenatal checkups *n*=10 (12.5%)	6 (16)	2 (8)	2 (10)	0.001
PROM/PPROM *n*=12 (15%)	8 (22)	3 (14)	1 (5)	0.001
Fetal distress *n*=13 (16%)	3 (8)	5 (21)	5 (25)	1.121
Meconium stained liquor *n*=15 (18%)	3 (8)	5 (21)	7 (35)	0.001
Prolonged labor *n*=8 (10%)	4 (11)	2 (8)	2 (10)	1.116
Antepartum hemorrhage *n*=8 (10%)	3 (9)	3 (14)	2 (10)	1.241
Eclampsia *n*=4 (5%)	0	3 (14)	1 (5)	1.023
Without any risk factors *n*=10 (12.5%)	10 (27)	0	0	0.001

PROM: Premature rupture of membranes, PPROM: Preterm premature rupture of membranes, LSCS: Lower segment caesarean section, SGA: Small for gestational age, IUGR: Intrauterine growth restriction

group with perinatal asphyxia. There were statistically significant higher number of babies of postterm in Stage 3 then those with Stage 1 and 2 HIE ($P = 0.001$); there was no difference between Stage 1 and 2 HIE between preterm, term, and postterm babies (Table 1). Around 18% of the babies with meconium stained liquor had asphyxia of which 35% had Stage 3 HIE.

No statistically significant difference was detected among the three groups with regard to Hb and WBC levels. However, platelet count was the lowest in the patients with Stage 3 HIE, more so for the blood levels taken at the time of admission. Among the biochemical renal parameters, there was no difference in BUN values whereas creatinine levels were high in Stage 3 HIE compared to that of Stage 1 and 2 (Table 2).

The levels of serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase are significantly higher in Stage 3 HIE done at 48 h and 72 h compared to that Stage 1 and 2 and at admission levels of Stage 3. Fibrinogen levels are lowest in Stage 3 HIE compared to that Stage 1 and 2 HIE. There were significant higher PT/INR levels in Stage 3 babies compared to that of Stage 1 and 2. There was no difference in glucose levels in all the stages of HIE (Table 2).

There is a statistically significant elevation in cardiac enzyme levels (CK-MB and CK-BB) and LDH in children in Stage 3 HIE compared to babies from Stage 1 and 2. There was statistically significant low pH, HCO_3 and increase in the base deficit and lactate levels in Stage 3 HIE babies compared to that of Stage 1 and 2 (Table 3).

There is a statistically significant increased levels of CRP in Stage 2 and 3 compared to Stage 1 HIE. There is a significant decrease in sodium levels in babies of Stage 3 HIE compared to that Stage 1 and 2.

In the study out of 80 babies, 10 babies died, seven died at the end of 48 h, and three after 72 h. There were statistically significant high levels of CK-BB, troponin I, CRP, lactate and a very low levels pH at admission in non-survivors (Table 3).

A higher number of Stage 3 HIE babies had diffuse cerebral edema with intracranial bleeds and higher resistive index. Stage 3 babies had poor ventricular contraction with decreased ventricular output and increased PPHN. Higher number of Stage 3 babies had poorly differentiated corticomedullary differentiation in ultrasound of kidneys compared to that of Stage 1 and 2 (Table 4).

DISCUSSION

Perinatal asphyxia causes multiorgan dysfunction mainly the nervous system leading to encephalopathy, which may take 72 h for neurological manifestations to appear. As it requires nearly 3 days for the systemic manifestations and categorization into different stages, early laboratory analysis will be helpful so that initiation of the treatment is started, as treatment is effective only when it is administered in the first 6 h of life.

In a study done by Vishnu *et al.*, there was an increase in NRBC and TLC in Stage 2 and 3 of HIE, whereas a decrease in platelet count in Stage 3. In our study, there was no difference in Hb and TLC count among different stages of HIE. Whereas, decreased platelet count and increase in NRBCs were seen in babies with Stage 3 HIE.[9]

As per literature, there is an increase in tubular proteins (notably in beta-2 microglobulins and myoglobulins) along with an increase in BUN and creatinine in the early stages of renal failure secondary to perinatal asphyxia. The study done by Banerjee *et al.* revealed that an elevated levels of urinary β2 microglobulin with HIE babies, irrespective of clinical staging; conversely, serum creatinine and blood urea were shown to be increased only in newborns with severe HIE (Sarnat Stage 3). Furthermore, a recent study highlighted that the increase of urinary β2 microglobulin is directly related both to asphyxia grading (Apgar score) and to Sarnat and Sarnat staging of HIE.[7] In our study, BUN was normal, whereas creatinine and urinary beta-2 microglobulins in urine were elevated in HIE Stage 3 babies.[10]

Increase in liver enzymes is observed due to effect of hypoxia on liver and other multi organs. The effect increases as the level of hypoxia increases. In our study, we observed a significant worsening in the results of liver and kidney function tests as the stage of HIE progressed.[11]

In study done by Fernandez *et al.* measured the serum CK-BB (brain isoenzyme) activities of 33 full-term newborns in the 4th and 10th h of life and discovered that babies who died of severe HIE or developed neurologic sequelae had significantly higher serum CK-BB activities than babies who did not have neurological abnormalities. Based on this observation, they claimed that a high serum CK-BB activity is a sensitive marker of brain injury. In our study, the babies with HIE Stage 3 had higher CK-BB levels compared to that of the children in Stage 1 and 2.[12]

Holzmann *et al.* showed that fetal scalp blood sampling is an early marker of intrapartum hypoxia, and they claimed

Table 2: Laboratory data of the cases as per stages of HIE

Laboratory data	Stage 1			Stage 2			Stage 3			*P* value (within groups)	*P* value (Bet groups)
	At admitted	48 h	72 h	At admitted	48 h	72 h	At admitted	48 h	72 h		
Hb	17.2±2.8	16.8±2.6	16.6±2.2	16.8±2.6	16.7±2.1	18.2±3.2	17.9±2.9	17.2±2.2	18.2±3.2	0.524	P1-2: 0.621 P2-3: 0.546 P3-1: 0.462
WBC count	22608±4408	19201±3324	18213±2126	26212±6218	22163±4312	23121±5120	26149±6129	25129±6145	24121±8120	0.342	P1-2: 0.254 P2-3: 0.126 P3-1: 0.193
Platelet count	286012±44123	261212±36145	254162±32132	192183±52412	184782±48149	141213±46121	112141±36129	108941±49213	141213±46121	0.001	P1-2: 0.326 P2-3: 0.001 P3-1: 0.001
BUN	18±3	17±4	18±2	18±3	17±4	17±5	22±4	21±3	17±5	0.632	P1-2: 0.764 P2-3: 0.675 P3-1: 0.365
Cr	0.5±2	0.4±1	0.4±1	0.5±2	0.6±1	0.6±1	0.9±3	0.8±2	0.8±1	0.001	P1-2: 0.231 P2-3: 0.001 P3-1: 0.001
UA	6.8±0.4	6.7±0.3	6.7±0.2	6.8±0.4	6.7±0.3	8.4±0.2	9.2±0.3	10.4±0.3	9.6±0.2	0.001	P1-2: 0.321 P2-3: 0.001 P3-1: 0.001
Urinary macroglobulin	1.81±0.21	1.73±0.15	1.69±0.19	2.9±0.21	3.1± 0.12	2.8±0.20	4.2±0.19	4.4±0.24	4.8±0.23	0.001	P1-2: 0.621 P2-3: 0.001 P3-1: 0.001
SGOT	62	64	62	62	64	76	84	102	121	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
SGPT	44	42	41	44	42	72	89	96	72	0.001	P1-2: 0.367 P2-3: 0.001 P3-1: 0.001
Fibrinogen	196	184	181	196	184	154	142	138	144	0.001	P1-2: 0.531 P2-3: 0.001 P3-1: 0.001
PT	1.2	1.15	1.12	1.32	1.28	2.2	2.4	2.6	2.2	0.001	P1-2: 0.219 P2-3: 0.001 P3-1: 0.001
Glucose	56±10	64±6	66±8	52±8	61±4	62±5	61±4	64±5	66±3	0.543	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
CPK-MB	340±126	412±184	422±182	618±218	1212±136	1180±148	2812±464	2612±512	2182±412	0.001	P1-2: 0.453 P2-3: 0.001 P3-1:0.001

(Contd)...

Table 2: ***(Continued)***

Laboratory data	Stage 1			Stage 2			Stage 3			*P* value (within groups)	*P* value (Bet groups)
	At admitted	48 h	72 h	At admitted	48 h	72 h	At admitted	48 h	72 h		
CK-BB	14.4±2.1	15.1±1.9	15.4±2.1	18.8±2.6	18.7±2.1	18.2±1.9	26.2±2.3	31±1.9	29.7±2.6	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
Troponin I	0.19±0.05	0.21±0.06	0.24±0.04	0.34±0.11	0.38±0.13	0.44±0.15	0.77±0.21	0.84±0.25	0.96±0.15	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
LDH	762±92	482±86	562±96	1121±121	1098±102	1114±106	772±282	2142±302	2784±482	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
pH	7.32±0.07	7.36±0.04	7.39±0.03	7.2±0.12	7.3±0.04	7.32±0.03	7.14±0.12	7.21±0.09	7.28±0.04	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
HCO_3	18.2±3.2	19.1±2.8	19.6±2.1	18±3	17±4	18±2	13.6±4.1	14.1±3.2	15.2±2.8	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
BE	−8.1±4.1	−7.9±3.8	−7.2±2.4	0.6±2	0.7±1	0.7±1	−16.2±2.1	−12.8±1.8	−9.1±2.1	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
Lactate	3.6	4.2	3.9	6.8±0.4	6.7±0.3	6.7±0.2	6.8	11.2	10.4	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
CRP	0.32±0.11	0.36±0.16	0.31±0.10	0.45±0.21	0.42±0.18	0.40±0.16	2.49±1.22	2.32±0.96	1.32±1.11	0.001	P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
Na	136±4.02	135±4.3	136±4.12	196	184	181	130±4.8	127±5.1			P1-2: 0.453 P2-3: 0.001 P3-1: 0.001
Ca	8.2±0.2	8.3±0.1	8.3±0.1	7.8±0.3	7.9±0.2	7.9±0.1	7.6±0.2	7.8±0.1			P1-2: 0.301 P2-3: 0.311 P3-1: 0.231

Hb: Hemoglobin, WBC: Whole blood cell, BUN: BLood urea nitrogen, Cr: Creatinine, UA: Uric acid, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, PT: Prothrombin time, CPK-MB: Creatine phosphokinase-MB, CK-BB: Creatine kinase-BB, LDH: Lactate dehydrogenase, CRP: C-reactive protein

that lactate levels might be an earlier marker than the pH value when a hypoxic process is present. In our study, the mortality is high in babies with high lactate levels and babies of Stage 3 HIE.[13,14]

In our study, the levels of serum lactate and LDH levels are high in Stage 3 of HIE and, as the stage of HIE progressed, the results of the two tests used in measuring serum lactate and LDH levels showed a statistically significant increase.[15] Basu *et al.* showed that the newborns with asphyxia had significantly higher plasma UA levels than healthy newborns and that there was a positive correlation between UA levels, HIE stage, and APGAR score. In our study, the levels in Stage 3 HIE babies had significantly higher UA levels.[16,17]

Table 3: Biomarkers in children between asphyxiated survivors and non-survivors

Biomarkers	Asphyxiated survivors (*n*=70)	Asphyxiated non survivors (*n*=10)	*P* value
pH	7.14±0.08	7.08±0.11	<0.001
CK-BB	18.1±3.1	29.32±2.8	<0.001
Lactate	6.2±1.4	9.1±3.1	<0.001
Troponin I	0.46±0.12	0.84±0.09	<0.001
CRP	1.2±0.32	2.6±1.1	<0.001

CRP: C-reactive protein, CK-BB: Creatine kinase BB

Based on the results of our study, we can claim that the troponin I, pH, CK-BB, lactate and CRP which were done at admission had higher prognostic factors in predicting the mortality before the clinical determination of the HIE stage in newborns with perinatal asphyxia according to the Sarnat and Sarnat scoring system. Further, determining the cutoff values for these biochemical markers would help clinicians to differentiate Stage 1 HIE from the advanced stages so that therapeutic hypothermia treatment can be initiated.

CONCLUSION

- HIE is predominant cause of mortality and morbidity neonates with perinatal asphyxia.
- Sarnat and Sarnat staging can be used for clinical staging of newborns with perinatal asphyxia and as a predictor of prognosis.
- Renal, cardiac, and hepatic biomarkers can be used as early predictors for morbidity and mortality for the asphyxiated neonates.
- Neurosonographic and echocardiographic findings in 48-72 h of life also can be used as prognostic factors of severity of asphyxia.
- Early prediction of the severity of asphyxia is used for treatment and intervention for better survival and outcome.

Table 4: Radiological and echocardiographic findings of the cases according to the stages of HIE

USG/ECHO parameters	Stage 1			Stage 2			Stage 3			*P* value (within groups)	*P* value (bet groups)
	At admitted	48 h	72 h	At admitted	48 h	72 h	At admitted	48 h	72 h		
Brain edema	No edema	No edema	No edema	No edema	10 minimal edema	14 minimal edema	5 diffuse edema	12 diffuse edema	10 diffuse edema	0.001	P1-2: 0.212 P2-3: 0.001 P3-1: 0.001
IVH	No	No	No	No	2 (grade 2)	4 (grade 3)	1	3	4	0.001	P1-2: 0.121 P2-3: 0.001 P3-1: 0.001
Intracranial bleed	No	No	No	No	1 baby	1 baby	1 baby	2 babies	4 babies	0.001	P1-2: 0.326 P2-3: 0.001 P3-1: 0.001
Doppler of ACA-RI	0.8	0.8	0.8	0.8	0.6	0.9	0.8	0.6	0.55	0.632	P1-2: 0.764 P2-3: 0.675 P3-1: 0.365
ECHO ventricular contraction	Good	Good	Good	Not good	Good	Good	Not good	Not good	Not good	0.001	P1-2: 0.231 P2-3: 0.001 P3-1: 0.001
PPHN	40	28	20	50	32	28	52	34	36	0.112	P1-2: 0.321 P2-3: 0.102 P3-1: 0.119
Left ventricular output	260	260	280	170	200	260	110	140	170	0.001	P1-2: 0.621 P2-3: 0.001 P3-1: 0.001
Abdominal ultrasound Cort-medullary differentition	Normal study			Minimally lost (hyper echogenicity increased but able to differentiate minimally)			Completely lost (complete hyper echogenicity)			0.001	P1-2: 0.621 P2-3: 0.001 P3-1: 0.001

IVH: Intraventricular hemorrhage, ACA RI: Anterior cerebral artery resistance index, ECHO: Echocardiography, PPHN: Persistent pulmonary hypertension of the newborn

REFERENCES

1. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976;33:696-705.
2. van de Riet JE, Vandenbussche FP, Le Cessie S, Keirse MJ. Newborn assessment and long-term adverse outcome: A systematic review. Am J Obstet Gynecol 1999;180:1024-9.
3. Committee on Obstetric Practice, American College of Obstetricians and Gynecologists. ACOG Committee Opinion. Number 326, December 2005. Inappropriate use of the terms fetal distress and birth asphyxia. Obstet Gynecol 2005;106:1469-70.
4. Ferriero DM. Neonatal brain injury. N Engl J Med 2004;351:1985-95.
5. Rennie JM, Hagmann CF, Robertson NJ. Outcome after intrapartum hypoxic ischaemia at term. Semin Fetal Neonatal Med 2007;12:398-407.
6. Massaro AN, Chang T, Kadom N, Tsuchida T, Scafidi J, Glass P, *et al.* Biomarkers of brain injury in neonatal encephalopathy treated with hypothermia. J Pediatr 2012;161:434-40.
7. Wiberg N, Källén K, Herbst A, Olofsson P. Relation between umbilical cord blood pH, base deficit, lactate, 5-minute Apgar score and development of hypoxic ischemic encephalopathy. Acta Obstet Gynecol Scand 2010;89:1263-9.
8. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976;33:696-705.
9. Milutinovic S, Karadzic R, Pavlovic M, Tomasevic M, Stankovic A. Biochemical cardiac markers application in cardiology. Apoll Med Aesculap 2006;4:16-22.
10. Volpe JJ. Neurology of the Newborn. 4th ed. Philadelphia: WB Saunders Company; 2001. p. 217-76.
11. Vannucci RC. Hypoxic-ischemic encephalopathy: Clinical aspects. In: Fanaroff AA, Martin RJ, editors. Neonatal-Perinatal Medicine. IVth ed. Philadelphia, PA: Mosby-Yearbook, Inc.; 1997. p. 877-91.
12. Hansen AR, Soul JS. Perinatal asphyxia and hypoxic - Ischaemic encephalopathy. In: Cloherty JP, Eichenwald EC, Hansen AR, Stark AR, editors. Manual of Neonatal Care. 7th ed. Philadelphia: Lippincott Williams and Wilkins, a Walters Kluwer Business; 2012. p. 711-28.
13. Ferriero DM. Neonatal brain injury. N Engl J Med 2004;351:1985-95.
14. Beken S, Aydin B, Dilli D, Erol S, Zenciroglu A, Okumus N. Can biochemical markers predict the severity of hypoxic-ischemic encephalopathy? Turk J Pediatr 2014;56:62-8.
15. Antonelli M, Azoulay E, Bonten M, Chastre J, Citerio G, Conti G, *et al.* Year in review in intensive care medicine 2010: I. Acute renal failure, outcome, risk assessment and ICU performance, sepsis, neuro intensive care and experimentals. Intensive Care Med 2011;37:19-34.
16. Basu P, Som S, Choudhuri N, Das H. Contribution of the blood glucose level in perinatal asphyxia. Eur J Pediatr 2009;168:833-8.
17. Banupriya C, Ratnakar, Doureradjou P, Mondal N, Vishnu B, Koner BC. Can urinary excretion rate of malondialdehyde, uric acid and protein predict the severity and impending death in perinatal asphyxia? Clin Biochem 2008;41:968-73.

How to cite this article: Prithviraj D, Reddy B, Deepthi, Abhijit. Laboratory Findings and Clinical Correlation in Assessing the Severity of Perinatal Asphyxia. Int J Sci Stud 2016;4(1):220-227.

Source of Support: Nil, **Conflict of Interest:** None declared.