

A STUDY ON PLASMA BIOCHEMICAL PHENOMENA IN HYPOXIC-ISCHAEMIC ENCEPHALOPATHY CASES IN TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Perinatal asphyxia can lead to hypoxic ischaemic encephalopathy (HIE). The mortality due to hypoxic ischaemic encephalopathy is as high as 28.8% and morbidity is 30% of surviving newborn due to hypoxic ischaemic encephalopathy.

Aims and Objectives- To study the plasma biochemical phenomena in neonates with hypoxic ischaemic encephalopathy in relation with severity of HIE.

MATERIALS AND METHODS

It is a hospital-based prospective study done in tertiary care hospital in SCB Medical College Hospital and SVP PG Institute, Cuttack from November 2015 to October 2017.

RESULTS

The babies with perinatal asphyxia develop hyponatraemia, hypocalcaemia, hyperkalaemia, high serum urea and creatinine, high serum ALT, AST, ALP, decrease in serum albumin and increase in Prothrombin time in proportion to the severity of asphyxia.

CONCLUSION

A significant number of babies with birth asphyxia and deranged biochemical parameters either died or discharged with severe neurological sequelae. It can be concluded that deranged biochemical parameters are early indicators of poor outcome. Studies should be held on the effects of early correction of these metabolic derangements with their outcomes, so that it may invent a new horizon of treatment for birth asphyxia babies.

KEYWORDS

Hypoxic-Ischaemic Encephalopathy, Apgar Score, Biochemical Phenomena.

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BACKGROUND

Perinatal asphyxia is one of the most common primary causes of mortality (28.8%) and morbidity among neonates in India and is the commonest cause of stillbirths (45.1%).^[1] Birth asphyxia is the most common and important cause of preventable cerebral injury occurring in the neonatal period.^[2] Full recovery may not occur and many children are left with lifelong neurological impairment and in some cases incapacitating disability.^[3] This creates a great burden for the family as well as for the society. According to World Health Organisation estimates in the developing countries 3% of all infants (3.6 millions) suffer from moderate-to-severe birth asphyxia, of which 23% (840, 000) die and approximately the same number develop serious sequelae.^[4] Prevention is more important than treatment. Sodium, potassium and calcium are the major electrolytes in human body and any deviation from their normal levels in blood might cause convulsions,

shock and other types of metabolic abnormalities. Calcium is an important second messenger in our body and also helps carrying out muscle function and acts as cofactor for several enzymatic activities. Body should maintain optimum level of these electrolytes in blood.^[5] Perinatal asphyxia causes diminished oxidative phosphorylation and ATP production. This energy failure impairs ion pump function causing accumulation of intracellular sodium, chloride, water and calcium; extracellular potassium leading to electrolyte imbalance which affects the outcome of asphyxiated babies.^[6]

The kidney is the most common organ to be affected in perinatal asphyxia.^[6] The proximal tubule of the kidney is especially affected by decreased perfusion, leading to acute tubular necrosis with oliguria. Hence, blood urea nitrogen and serum creatinine may be elevated.

Liver cell injury commonly occurs after perinatal asphyxia and is similar to shock liver syndrome. It is represented as an early, abrupt and transient (within 24 - 72 hours after) insult increase in aminotransferases [Aspartate transferase (AST) and alanine transferase (ALT)], alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) plasma activity. Later on the peak aminotransferase level returns to near normal within 10 days.^[7] The prognosis of hypoxic hepatitis itself is safe, and it rarely progresses into complete hepatic failure. With improved survival of sick asphyxiated neonates because of improvements in medical care, the clinical entity of liver involvement is being increasingly recognised, and so this work was planned to recognise the

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prevalence of liver involvement in birth asphyxia and to study the severity and type of hepatic dysfunction in relation to Apgar score and HIE grading of asphyxiated newborns.

Good supportive care is essential in the first 72 hours after asphyxia to prevent ongoing brain injury in the penumbra region. Strict monitoring and prompt correction is needed for common problems including temperature maintenance, blood sugar, blood pressure, serum electrolytes, renal parameters and oxygenation.

Studies to find out changes in serum sodium, potassium and calcium, liver enzyme levels in different degrees of asphyxia are still lacking.^[5] Considering the above consequences of birth asphyxia, this study has been designed to observe the serum biochemical values in asphyxiated newborns and to correlate with different degree of asphyxia.

Aims and Objectives

To find out the levels of serum electrolytes (Na⁺, K⁺, Ca²⁺) serum urea, serum creatinine, serum albumin, serum SGOT, serum SGPT, serum ALP, Prothrombin time in asphyxiated babies.

MATERIALS AND METHODS

After obtaining Ethical Committee clearance from the Institution, the present study was carried out in the Department of Paediatrics, SCB Medical College and Hospital, Cuttack and S.V.P.P.G.I.P, Cuttack from November 2015 to October 2017.

This was a prospective observational study. The study cohort consisted of the hospitalised term neonates of birth weight \geq 2.5 kg to the indoors/ S.N.C.U of S.C.B M.C.H and S.V.P.P.G.I.P, Cuttack with diagnosis of birth asphyxia as per the following defined criteria.^[7,8,9]

Inclusion Criteria

Apgar score < 7 at 5 minutes of birth, 2. Delayed onset of respiration for \geq 5 minutes, 3. Need for positive pressure ventilation at birth, 4. Metabolic acidosis (Cord Arterial Blood or Blood Gas Analysis within First Hour after Birth) indicated base deficit \geq 16 mmol/L. 5. Evidence of encephalopathy including altered state of consciousness and/ or seizures (Subtle/ tonic/ tonic-clonic types).

Exclusion Criteria

Preterm babies (< 37 Weeks of Gestational Age), 2. Babies with severe congenital malformations, 3. Suspected inborn errors of metabolism, 4. Congenital infections, 5. Babies receiving diuretics prior to evaluation, 6. IUGR babies, 7. Septic shock, 8. Low birth weight babies, 9. Babies to mothers suffering from renal diseases and on nephrotoxic drug.

Neonates presenting with perinatal asphyxia were studied according to pre-structured proforma where detail history regarding type and place of delivery, type of resuscitation required, any complication before/ during delivery, onset and duration of seizure and findings of clinical examination with special reference to central nervous system were noted and analysed according to the Sarnat and Sarnat staging system.^[8]

In the present study, 150 cases were taken randomly as per the defined inclusion criteria.

Investigations

Blood samples were collected at the time of maximum Sarnat and Sarnat stage,^[8] and sent for investigations. Following investigations were done in Department of Pathology and Biochemistry.

- a. Complete blood count, b. CRP (Q), c. Serum electrolytes
- d. Serum urea, creatinine, e. ALT, f. AST, g. ALP, h. LDH, i.TSB, j. Serum Albumin and k. PT

Serum Na, K, Ca were estimated using electro-analyzer on the basis of ion-selective electrodes. Serum urea was estimated by using GLDH/ Kinetic method. Serum creatinine was estimated using Modified Kinetic Jaffe's method.

Serum ALT, AST, ALP and LHD were estimated by modified IFCC method.

Management and Follow-Up

Babies were followed up until discharge or death. Day-to-day check-up was done with particular stress on respiratory, cardiovascular, renal and neurological system examination. Asphyxiated babies were managed as per the standard protocol and with improvement of clinical status of newborns, orogastric/ nasogastric and subsequently oral feeding was selectively started after clinical evaluation.

Newborns were examined at the time of discharge to see for any focal neurological deficit, abnormal movements, feeding difficulty or persistent convulsions requiring continuation of anticonvulsant.

Statistical Analysis

Statistical analysis was done by statistical software SPSS for windows version 21. P values were calculated using chi-square test and ANOVA (Analysis Of Variance) with post-hoc test. P < 0.05 was considered as significant and p < 0.01 as highly significant.

The value obtained were plotted in predesigned proforma, analysed in the table.

RESULTS

Degree of Asphyxia	Number of Cases				Total	(%)
	Male No. (%)	Female No. (%)	M:F Ratio	Total		
HIE- 1 (Mild)	13 (56.5)	10 (43.5)	1.3:1	23	15.33	
HIE- 2 (Moderate)	73 (84.9)	13 (15.1)	5.6:1	86	57.33	
HIE- 3 (Severe)	30 (73.2)	11(26.8)	2.7:1	41	27.34	
Total	116 (77.3)	34 (22.7)	3.4:1	150	100	

Table 1. Distribution of Birth Asphyxia with Severity

Out of 150 cases of birth asphyxia, moderate asphyxia 86 cases (57.33%) constitute the majority of cases and Male: Female ratio was 3.4: 1.

Maturity	HIE-1 No. (%)	HIE-2 No. (%)	HIE-3 No. (%)	Total No. (%)	P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
Term	20 (87)	47 (54.7)	19 (46.3)	86 (57.3)	0.009	0.003	0.38
Post-term	3 (13)	39 (45.3)	22 (53.7)	64 (42.7)			

Table 2. Degree of Birth Asphyxia with Maturity

*p value: Chi-square test applied with post-term as risk factor.

The incidence of severity of birth asphyxia increases with post maturity, as p value was < 0.01.

Mode of Delivery	No. of Birth Asphyxia No. (%)	Degree of Birth Asphyxia No. (%)			P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
		HIE-1	HIE-2	HIE-3			
Normal delivery with vertex presentation	72 (48.0)	11 (47.8)	46 (53.5)	15 (36.6)	0.629	0.379	0.074
Normal delivery with abnormal presentation(Breech)	31 (20.7)	3 (13.1)	23 (26.7)	5 (12.2)	0.273	0.921	0.064
LSCS	13 (8.7)	8 (34.8)	3 (3.5)	2 (4.9)	0.0001	0.005	0.706
Forceps/ Ventouse delivery	34 (22.6)	1 (4.3)	14 (16.3)	19 (46.3)	0.256	0.001	0.0007

Table 3. Mode of Delivery with Degree of Birth Asphyxia

*p value: Chi-square test applied

Severe degree of birth asphyxia was mostly seen in forceps/ ventouse delivery (46.3%) and it was statistically significant as 'p' value was < 0.01. LSCS was mostly associated with mild degree of asphyxia and it was statistically significant (p < 0.01).

Risk Factors	HIE-1 No. (%)	HIE-2 No. (%)	HIE-3 No. (%)	Total No. (%)	P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
Prolonged labour	12 (52.2)	47 (54.7)	36 (87.8)	95 (63.3)	0.832	0.001	0.0002
Preeclampsia	1 (4.3)	2 (2.3)	3 (7.3)	6 (4)	0.598	0.637	0.387
GDM	1 (4.3)	3 (3.5)	2 (4.9)	6 (4)	0.845	0.637	0.706
Multiple pregnancy	1 (4.3)	2 (2.3)	2 (4.9)	5 (3.3)	0.598	0.923	0.820
MSAF	1 (4.3)	36 (41.9)	26 (63.4)	63 (42)	0.001	0.0001	0.023
Cord around neck	1 (4.3)	10 (11.6)	9 (22)	20 (13.3)	0.522	0.133	0.127
Oligohydramnios	2 (8.7)	7 (8.1)	8 (19.5)	17 (11.3)	0.931	0.432	0.063
Malpresentation	3 (13)	23 (26.7)	5 (12.2)	31 (20.7)	0.273	0.921	0.064
APH	1 (4.3)	6 (7)	7 (17.1)	14 (9.3)	0.647	0.278	0.079
No Risk Factors	8 (34.8)	11 (12.8)	0	19 (12.7)	0.013	0.0003	0.039

Table 4. Risk Factors with Degree of Birth Asphyxia

*p value: Chi-square test applied.

Prolonged labour (87.8%) and meconium stained liquor (63.4%) were more commonly seen in severe degree of birth asphyxia and they were statistically significant, as their 'p' values were < 0.01. Severity of birth asphyxia increases when associated with different risk factors and it was statistically significant (p < 0.05).

Place of Delivery	HIE-1 No. (%)	HIE-2 No. (%)	HIE-3 No. (%)	Total No. (%)	P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
Hospital	21 (91.3)	66 (76.7)	21 (51.2)	108 (72)	0.210	0.003	0.0038
Outside hospital	2 (8.7)	20 (23.3)	20 (48.8)	42 (28)			
Total	23	86	41	150			

Table 5. Place of Delivery with Degree of Asphyxia

*p value: Chi-square test applied with delivery outside the hospital as a risk factor.

Incidence of severity of birth asphyxia increased with delivery outside the hospital as compared to the hospital delivery and it was statistically significant as 'p' value was < 0.01.

Biochemical Parameters	HIE-1 (X ± SD)	HIE-2 (X ± SD)	HIE-3 (X ± SD)	P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
Serum Na+ (mmol/L)	137.5±3.8	132.7±6.8	124.4±4.4	< 0.01	< 0.01	< 0.01
Serum K+ (mmol/L)	5.00±0.79	5.55±0.77	6.17±0.89	< 0.05	< 0.01	< 0.01
Serum Ca2+ (mmol/L)	1.05±0.16	0.87±0.16	0.83±0.08	< 0.01	< 0.01	>0.05 (NS)
Serum Urea (mg/dL)	26.86±8.7	48.96±26.5	88.82±34.5	< 0.01	< 0.01	< 0.01
Serum Creatinine (mg/dL)	0.70±0.16	0.94±0.54	2.41±0.89	>0.05 (NS)	< 0.01	< 0.01
Serum ALT (IU/L)	39.82±10.3	55.5±21.8	73.5±33.2	0.02	< 0.01	< 0.01
Serum AST (IU/L)	73.6±20.45	102.58±49	156±26.7	< 0.01	< 0.01	< 0.01
Serum ALP (IU/L)	247±111	330±124	352±136	< 0.01	< 0.01	>0.05 (NS)
Serum Albumin (g/dL)	3±0.24	2.63±0.5	2.34±0.57	< 0.01	< 0.01	< 0.01
Prothrombin Time (SEC)	12.2±1.13	18±4.8	20.8±7.3	<0.01	< 0.01	< 0.01

Table 6. Mean Values of Biochemical Parameters with Severity of Birth Asphyxia

*p value: ANOVA and followed by post-hoc test applied.

This table depicts the statistically significance of all the biochemical parameter.

Outcomes	HIE-1 No. (%)	HIE-2 No. (%)	HIE-3 No. (%)	Total No. (%)	P value* HIE-1 vs HIE-2	P value* HIE-1 vs HIE-3	P value* HIE-2 vs HIE-3
Mortality	0	2 (2.3)	27 (65.9)	29 (19.3)	0.4604	<0.0001	<0.0001
Recovery without abnormal movement/ FND and without AED	23 (100)	66 (76.7)	0	89 (59.3)	0.0241	<0.0001	<0.0001
Recovery with abnormal movement/ FND and with AED	0	18 (21)	14 (34.1)	32 (21.4)	0.0371	0.0043	0.1087
Total	23	86	41	150			

Table 7. Outcomes with Severity of Birth Asphyxia

*p value: Chi-square test applied.

Mortality was more in severe degree of asphyxia as compared to mild and moderate variety and it was statistically significant (p < 0.01). The chance of favourable outcome diminishes with severity of asphyxia (p < 0.05). Bad recovery was more in moderate-to-severe degree as compared to the mild variety of asphyxia and they were statistically significant (p < 0.01).

Parameters	Level	Survival	Death	Total	P value***
Sodium	Normal	86(71%)	2(7%)	88(58.7%)	0.000
	Low	35(29%)	27(93%)	62(41.3%)	
Potassium	Normal	41(34%)	0(0%)	41(27.33%)	0.000
	High	80(66%)	29(100%)	109(72.67%)	
Calcium Ionised	Normal	32(26%)	0(0%)	32(21.3%)	0.000
	Low	89(74%)	29(100%)	118(78.7%)	
Urea	Normal	60(49.6%)	2(7%)	62(41.3%)	0.000
	High	61(50.4%)	27(93%)	88(58.7%)	
Creatinine	Normal	43(35.5%)	1(3%)	44(29.3%)	0.000
	High	78(64.5%)	28(97%)	106(70.7%)	
ALT	Normal	70(58%)	9(31%)	79(53%)	.000
	High	51(42%)	20(69%)	71(47%)	
AST	Normal	68(56%)	10(34%)	79(53%)	0.000
	High	53(44%)	19(66%)	71(47%)	
ALP	Normal	60(49.6%)	13(45%)	73(49%)	>0.05
	High	61(50.4%)	16(55%)	77(51%)	
Albumin	Normal	68(56%)	9(31%)	77(51%)	.000
	Low	53(44%)	20(69%)	73(49%)	
Prothrombin Time	Normal	69 (57%)	6 (21%)	75 (50%)	.000
	High	52 (43%)	23 (79%)	75 (50%)	
Total		121	29	150	

Table 8. Different Biochemical Level with Outcomes

***p value: Chi-square test applied with the significance observed.

This table depicts the statistically significance of all the biochemical level at outcome.

Age at Death	HIE-2 No. (%)	Mean X±SD day	HIE-3 No. (%)	Mean X±SD day	Total No. (%)	Mean X±SD day
< 1 day	0	3.5±0.5	1(3.7)	3.8±1.2	1(3.4)	3.8±1.19
1-3 day	1(50)		10(37)		11(38)	
4-7 day	1(50)		15(55.6)		16(55.2)	
>7 day	0		1(3.7)		1(3.4)	
Total	2		27		29	

Table 9. Age at Death with Severity of Birth Asphyxia

Most of the babies from HIE-3 group expired within 1 - 3 days (37%) and 4 - 7 days (55.6%). Mean age at death of babies with moderate asphyxia was 3.5 ± 0.5 day, severe asphyxia was 3.8 ± 1.2 day and as a whole was 3.8 ± 1.19 day.

Severity of Asphyxia	Age at Discharge in Days				Mean Age at Discharge X±SD day	*P value HIE-1 vs HIE-2	*P value HIE-2 vs HIE-3	*P value HIE-1 vs HIE-3
	1-3	4-7	8-14	>14				
HIE-1 (%)	11(47.8)	12(52.2)	0	0	3.8±0.8	<0.05	<0.05	<0.05
HIE-2 (%)	0	24(28.6)	59(70.2)	1(1.2)	9.1±2.4			
HIE-3 (%)	0	0	3(21.4)	11(78.6)	17.2±3.5			

Table 10. Age at Discharge with Severity of Birth Asphyxia

*p value: ANOVA and followed by post-hoc test applied.

Mean age at discharge of HIE-1, HIE-2 and HIE-3 babies were 3.8 ± 0.8 day, 9.1 ± 2.4 day, 17.2 ± 3.4 day respectively. Duration of hospital stay increased with severity birth asphyxia as 'p' value < 0.05.

DISCUSSION

The present study was undertaken to analyse the biochemical parameters of perinatal asphyxia and their relationship with the outcome.

In the present study mild, moderate and severely asphyxiated babies constituted 15.33%, 57.33% and 27.34% respectively (Table 1). Chiabi A and Nguetack S et al (2013)^[10] that out of total number of asphyxiated babies 51% were HIE-1, 26% were HIE-2 and 23% were HIE-3. Mukesh Choudhary et al (2015)^[7] in their study observed 14.28% were HIE-1; 25.73% were HIE-2; 11.42% were HIE-3. Hassan Boskabadi et al (2015)^[11] in their study found HIE-1 were 11.86%; HIE-2 were 45.76%; HIE-3 were 42.37%. Variation in incidence might be due to most of the cases admitted to our hospital as referred cases sent from other peripheral hospitals of Orissa, where most of the mild cases were managed and some of the mild cases stay with their mother at SCB Medical College and Hospital. Males outnumbered females (77.3% vs 22.7%) in the present study, even in three different degrees of asphyxia (mild- 56.5%, moderate- 84.9%, severe- 73.2%). Male: Female ratio was 3.4: 1. This study is well comparable with the results of Yvonne W. Wu et al (2004)^[12] who documented the association of ethnicity, male gender and low socio-economic status with increased incidence of birth asphyxia. Another study with similar outcome was found by Asad Nauman Kiyani et al (2014)^[13] with males (64%) outnumbering females (36%). Similar result was observed by Mahmoud H Ibrahim et al (2016)^[14] with male sex accounting for 71.3%. This difference may be due to more number of male asphyxiated babies who were brought to the hospital.

Incidence of severity of birth asphyxia increased with post maturity in HIE-2 and HIE-3 (HIE-1: 13%, HIE-2: 45.3%, HIE-3: 53.7%), which was statistically significant (p < 0.01) (Table 2). A study by Sithivuddhi Futrakul et al (2006)^[15] reported that inappropriate antenatal care, post-term gestation, vacuum extraction, male, prolapsed cord and low 1

and 5-minute Apgar scores were significant risk factors for HIE.

The present study showed that maximum number of birth asphyxia cases were seen in birth weight between 2500 - 3000 gm as evidenced by 87%, 61.6%, 58.5% in HIE-1, HIE-2 and HIE-3 respectively (Table 4). Similar result was observed by Asad Nauman Kiyani (2014)^[13] with mean weight of the newborn was calculated as 2621.37 (± 74.21) grams. Another study by Mahmoud H Ibrahim et al (2016)^[14] found the mean weight to be 2.9 ± 0.5 kg.

In the present study, maximum number of birth asphyxia was more common in forceps/ ventouse delivery (46.3%) which was statistically significant (p < 0.01). LSCS was mostly associated with mild degree of asphyxia and it was statistically significant (p < 0.01) (Table 3). Itoo BA et al (2003)^[16] study showed that incidence of birth asphyxia was more in normal vaginal delivery (40%) and instrumental delivery (30%) as compared to breech (9%), emergency LSCS (21%) and elective LSCS. Asad Nauman Kiyani et al (2014)^[13] observed spontaneous vertex delivery in most commonly associated with birth asphyxia (44.39%) followed by emergency caesarean section in 32.14% and 23.47% instrumental delivery. Also similar results were found in studies conducted by Gupta P et al (1997)^[17] and AS Daga et al (1990).^[18]

The prolonged labour (87.8%) and meconium stained liquor (63.4%) were more commonly seen in severe degree of birth asphyxia and they were statistically significant (p < 0.01). NH and MRC (National Health and Medical Research Council) shows that the incidence of asphyxia to be higher in complicated pregnancies like PET, IUGR, APH, malpresentation and meconium stained liquor.^[19] D Kaye et al (2003)^[20] study showed that antepartum hospitalisation, antepartum/ intrapartum anaemia, APH, severe pre-eclampsia/ eclampsia, PROM, MSAF, vacuum extraction, LBW and malpresentation are significantly associated with birth asphyxia.

Chiabi A et al (2013)^[10] observed prolonged labour, arrest of labour, prolonged rupture of membrane, non-vertex presentation. Abnormal amniotic fluid (foul smell, meconium stained, yellowish) are strongly associated with higher incidence of birth asphyxia. Similar study result was found by Asad Nauman Kiyani in the year 2014.^[13]

In the present study though birth asphyxia cases were more in primigravida mothers, but it was not significantly associated with the severity of birth asphyxia. Similarly, Sithivuddhi Futrakul MD et al (2006)^[15] and Tayyaba Khawar Butt et al (2008)^[21] found no correlation between parity and HIE.

In the present study, incidence of severity of birth asphyxia increased with delivery outside the hospital (HIE-1: 8.7% vs HIE-3: 48.8%) as compared to the hospital delivery and it was statistically significant as 'p' value was < 0.01 (Table 5). Similar study were conducted by Rahana Majeed et al (2007)^[22] and they have shown that incidence of birth asphyxia was more in home deliveries (56%) as compared to hospital/ maternity home deliveries (40%).

The mean values of different biochemical parameter with severity of asphyxia was statistically significant (Table 6). Basu et al (2010)^[22] study showed that among the cases, hyponatraemia and hypocalcaemia developed early and simultaneously the decrease in their serum levels was directly proportional to each other and to the degree of asphyxia. Though, mean potassium level was within the normal limit, the value was higher among cases than controls and directly proportional to asphyxia. The outcome of present study was similar to Basu et al study, except the serum K⁺ level. Serum K⁺ was towards the higher side in this study, whereas it was within normal limit in the study conducted by Basu et al.

Jajoo et al (1995)^[23] study showed that asphyxiated full-term (AGA) as well as full-term (IUGR) infants had significantly lower serum calcium level than control infants. Similar result was found by BK Jain, Daljit Singh et al (2000)^[24] and Seema Rai et al (2015).^[25] Najaf Masood et al (2016)^[26] observed low sodium and low calcium level in asphyxiated group and concluded that hyponatraemia and hypocalcaemia showed linear co-relation with severity of birth asphyxia.

Similar result was observed by Rahman F and Siddique MAB et al^[27] in the year 2017. Study by G Joag et al (2017)^[28] showed similar result of decreased mean value of serum sodium, serum calcium and serum glucose in asphyxiated newborns, which had positive correlation with the severity of birth asphyxia.

Mishra et al (1991)^[29] study has shown that decreased serum sodium and increased serum potassium, creatinine and blood urea nitrogen were consistently found in all cases of moderate-to-severe degree of birth asphyxia. The outcome of present study was similar to their study.

Prodhan MS, Moniruzzaman A, Majumder B, Rahman MJ, Suja-Ud-Doula A, Nabi SN and Mostakim MA (2017)^[30] observed that babies with perinatal asphyxia developed hyponatraemia, hyperkalaemia, significant rise of serum creatinine and blood urea which was proportionate to the severity of asphyxia.

All the above biochemical parameters were affected in an increasing pattern from mild-to-severe degree of birth

asphyxia, as their 'p' values were statistically significant. This is similar to the findings observed by Basu et al,^[22] Gupta et al^[31] and Mishra et al^[29] study.

Our study for mean values of biochemical parameters with severity of birth asphyxia is similar to the findings observed by Mukesh Choudhry et al,^[8] Karlsson M, Wiberg-Itzel E et al,^[32] Tariqul I, Seikh AH et al in 2010^[33] and Chaitali et al in 2016.^[34]

Mortality was more in severe degree of asphyxia as compared to mild and moderate variety and it was statistically significant (p < 0.01). The chance of favourable outcome diminishes with severity of asphyxia (p < 0.05). Bad recovery was more in moderate-to-severe degree as compared to the mild variety of asphyxia and they were statistically significant (p < 0.01) (Table 9). Out of total 150 cases 19.3% cases expired, 59.3% cases discharged with no abnormal movement, FND or AED use and 21.4% cases developed abnormal movement, FND and discharged with AED use (Table 7).

C Robertson and N Finer et al (1985)^[35] studied outcome of 291 full-term infants with hypoxic-ischaemic encephalopathy as a function of severity of neonatal neurological syndrome and found that all cases of mild HIE had normal neurological outcome, whereas moderate and severe degree developed neurological sequelae in 24% and 20% of cases respectively. Mortality was 5% in moderate, but 80% in severe degree of birth asphyxia. Hassan Boskabadi et al (2006)^[11] found in their study that statistically significant association between HIE severity and long-term prognosis, i.e. with increase in severity of HIE incidence of developmental delay increases. The outcome of the present study was similar to their study.

The present study showed that hyponatraemia, hypocalcaemia, hyperkalaemia, high serum urea and creatinine levels were more in death group and were all statistically significant as 'p' value was < 0.05 (Table 8). It was similar to the findings observed by Mishra et al,^[29] Najaf Masood et al,^[26] Rahman F et al^[27] and Prodhan et al^[30] in their studies.

Gupta et al (2005)^[31] in their study has shown that severity of renal function abnormality correlates well with degree of asphyxia. Oliguria, hyponatraemia and abnormal sonographic scan are bad prognostic signs in renal failure secondary to birth asphyxia.

S Nouri et al (2008)^[36] studied 87 cases of full-term neonates with perinatal asphyxia and found that neurologic examination was abnormal in 36 out of 72 (50%) neonates without renal failure and in 9 of the 12 (75%) survivors with renal failure. Among the 12 neonates with renal failure, 7 had abnormal neurologic features at discharge. Renal function assessment using plasma creatinine level seems to be correlated with neurologic outcome.

The present study showed that the increased level of serum ALT, AST, hypoalbuminaemia and prolonged prothrombin time were associated more with death groups (69%, 66%, 55, 69%, 79%) as compared to survival group (42%, 44%, 50.4%, 44%, 43%) and they were statistically significant as 'p' value was < 0.001 (Table No. 8). This study is similar to the findings observed by Mukesh Choudhary,^[7] Tariqul I et al^[33] and Chaitali Patra et al.^[34]

The Table 9 depicts that 2 babies from HIE-2 group died, one within 1 - 3 days and the other one within 4 - 7 days.

Most of the babies from HIE-3 group expired within 1 - 3 days (37%) and 4 - 7 days (55.6%). Mean age at death of babies with moderate asphyxia was 3.5 ± 0.5 days and severe asphyxia was 3.8 ± 1.2 days.

Table 10 shows that 11 (47.8%) and 12 (52.2%) cases of HIE-1 were discharged within 1 - 3 days and 4 - 7 days respectively. Most of the cases of HIE-2 (70.2%) were discharged within 8 - 14 days. 11 (78.6%) cases of HIE-3 were discharged after day 14.

The mean age at discharge of HIE-1, HIE-2 and HIE-3 babies were 3.8 ± 0.8 days, 9.1 ± 2.4 days, 17.2 ± 3.4 days respectively. The above findings can clearly conclude that duration of hospital stay increased with severity of birth asphyxia ($p < 0.05$).

Summary

Out of 150 cases, moderate asphyxia constitutes majority 86 (57.33%) of cases. Male babies outnumbered (77.3%) female babies in all the three grades of birth asphyxia. The incidence of severity of birth asphyxia increases with post maturity ($p < 0.01$). Maximum number of birth asphyxia cases [97(64.7%)] were seen in the birth weight between 2500 - 3000 gm. Severe degree of birth asphyxia was more common in forceps/ ventouse delivery (46.3%) and it was statistically significant as 'p' value was < 0.01 . Prolonged labour and meconium stained liquor were more commonly seen in severe degree of birth asphyxia and they were statistically significant (p value < 0.01). Incidence of severity of birth asphyxia increased with delivery outside the hospital as compared to the hospital delivery and it was statistically significant (p value < 0.01). All the biochemical parameters like serum Na⁺, K⁺, Ca²⁺, Urea, Creatinine, ALT, AST, ALP, Albumin and Prothrombin time were affected in an increasing pattern from mild-to-severe degree of birth asphyxia, as their 'p' values were statistically significant. Mortality was more in severe degree of asphyxia as compared to mild and moderate variety and it was statistically significant ($p < 0.01$). The chance of favourable outcome diminishes with severity of asphyxia ($p < 0.05$). Bad recovery was more in moderate-to-severe degree as compared to the mild variety of asphyxia and they were statistically significant ($p < 0.01$). Cases of hyponatraemia, hypocalcaemia, hyperkalaemia, high serum urea and creatinine levels were more in death group (93%, 100%, 100%, 93%, 97%) as compared to the group with survival group (29%, 74%, 66%, 50.4%, 64.5%) and they were all statistically significant (p value < 0.001).

The present study showed that the increased level of serum ALT, AST, hypoalbuminaemia and prolonged prothrombin time were associated more with death groups (69%, 66%, 55, 69%, 79%) as compared to survival group (42%, 44%, 50.4%, 44%, 43%) and they were statistically significant as 'p' value was < 0.001 .

Mean age at death of babies with moderate asphyxia was 3.5 ± 0.5 days and severe asphyxia was 3.8 ± 1.2 days.

Mean age at discharge of HIE-1, HIE-2 and HIE-3 babies were 3.8 ± 0.8 days, 9.1 ± 2.4 days, 17.2 ± 3.4 days respectively. Duration of hospital stay increased with severity of birth asphyxia ($p < 0.05$).

CONCLUSION

It can be concluded that babies with perinatal asphyxia develop hyponatraemia, hypocalcaemia, hyperkalaemia, high serum urea and creatinine, high serum ALT, AST, ALP, decrease in serum albumin, increase in prothrombin time in proportion to the severity of asphyxia. Grossly asphyxiated babies may develop severe derangement of the above biochemical parameters, which may require immediate medical interventions. There is a definite correlation between the severity of birth asphyxia with dyselectrolytaemia, deranged renal function parameters, deranged hepatic enzymes, serum albumin and prothrombin time.

A significant number of babies with birth asphyxia and deranged biochemical parameters either died or discharged with severe neurological sequelae. It can be concluded that deranged biochemical parameters are early indicators of poor outcome.

Studies should be held on the effects of early correction of these metabolic derangements with their outcomes, so that it may invent a new horizon of treatment for birth asphyxia babies.

Timely and prompt resuscitation of newborn babies at birth, active and early management by therapeutic hypothermia in asphyxiated babies is highly essential to reduce the severity of birth asphyxia which can minimise the mortality and future neurological complications.

It is further recommended that the obstetricians, paediatricians as well as the paramedical workers need 'Neonatal Resuscitation Training,' which will definitely prevent birth asphyxia and indirectly help reducing IMR of the state.

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