Enzymatic Evidence of Multi Organ Dysfunction in Perinatal Asphyxia

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Perinatal asphyxia is one of the major causes of death and disability among newborn in less developed countries like Bangladesh. Serum enzymes (ALT, AST and LDH) activities are significantly elevated in asphyxiated newborns within first days of life. Objective of the study was to evaluate the enzymatic evidence of multi-organ dysfunction in perinatal asphyxia. It was a cross-sectional study, done at neonatal ward, Department of Paediatrics, Rangpur Medical College Hospital, Rangpur from 1st May, 2014 to 30th October, 2014. Total 100 asphyxiated newborn were included. With all aseptic measure 2 ml of blood from antecubital vein was taken and sent to the laboratory at Department of Biochemistry for measuring serum enzymes ALT, AST and LDH. All data were collected in individual predetermined case record form. P<0.05 was used as the minimum level of significance. This study showed among the asphyxiated 100 newborn 65(65%) were in HIE stage-2 followed by 25(25%) and 10(10%) in stage-3 and stage-1 respectively. Of total subjects, 63% demonstrated rise in ALT, 79 % in AST and 70% in LDH. Mean ±SD of ALT was 207.1±201.043 IU/L, AST 186.30±173.817 IU/L and LDH 369.6±123.05 IU/L respectively. Serum enzymes AST, ALT and LDH are elevated in perinatal asphyxia with MOD.

[Dinajpur Med Col J 2017 Jan; 10 (1):102-106]

Key words: LDH (Lactate dehydrogenase), ALT (Alanine aminotransferase) AST (Aspartate aminotransferase), Hypoxic Ischemic Encephalopathy (HIE), Multi Organ Dysfunction (MOD)

Introduction

American Academy of Pediatrics defines perinatal asphyxia as umbilical cord artery pH <7.0 with base deficit of >10meq/L, neonatal neurological manifestations suggestive of hypoxic ischemic encephalopathy (HIE) and evidence of multi organ dysfunction (cardiovascular, renal, gastrointestinal, and pulmonary system).[1] Global incidence of perinatal asphyxia has been reported to be 1% to 1.5%.[2] According to WHO estimates in the developing countries, 3% of all infants suffer from moderate to severe birth asphyxia, of them 23% eventually succumb.[3] Approximately same percentage develops serious consequences, such as developmental delay, cerebral palsy, and epilepsy etc.[4] The systems involved in MOD are the renal, hepatic, intestinal, pulmonary and cardiovascular system. MOD is evident with varying severity in all infants with HIE. MOD most frequently affects lungs and liver (86%and 85% respectively) followed by the renal (70%) and the cardiovascular system (62%)' Within 24 hours of a hypoxic ischemic episode, MOD becomes apparent.[5] In HIE once injured, the cells leak intracellular enzymes Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and

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Lactate dehydrogenase (LDH) signaling multi organ dysfunction.[6] LDH is widely distributed in tissue, particularly in the heart, liver, muscles and kidney.[7] AST is an intra-cellular enzyme found in hepatic, myocardial, and muscle and kidney tissue.[8] ALT is present predominantly in the liver but also in other tissues. ALT is considered as liver specific enzyme.[9,10] Previous studies reveal level of LDH, ALT and AST rise substantially after organ damage in perinatal asphyxia which is evident in cord blood soon after birth.[11, 6, 7,9]

Methods

This was a cross sectional descriptive study done in the department of Paediatrics in Rangpur Medical College Hospital from 1st May, 2014 to 30th October, 2014. Total 100 newborns of 1 to 5 days old who had features of perinatal asphyxia based on inclusion and exclusion criteria were enrolled in this study where inclusion criteria were history of delayed cry or failure to breath spontaneously immediately after birth and history of resuscitative measures undertaken to sustain life and exclusion criteria were- birth weight <2.5 Kg, severe jaundice involving palms and soles, sepsis evidenced by raised CRP and increased total leukocyte count, Shock (septic and haemorrhagic), congenital anomalies. After all aseptic precautions 2 ml of venous blood was taken by using 19g baby needle and 3cc disposable syringe from antecubital vein and sent for estimation of serum LDH, ALT, AST, CRP and total leukocyte count. Serum LDH, ALT and AST were analyzed by kinetic ultraviolet method.

Results

In this study it was revealed that out of 100 asphyxiated neonates, majority 62(62%) were male, 38 (38%) were female (Fig-1), 52(52%) newborn attended within 24-48 hours of age followed by 48(48%) between 48-120 hours of age (Table-I), 80(80%) asphyxiated neonates were within 38 completed weeks and 20(20%) were more than 38 weeks (Table-II). About the staging of asphyxia of neonates, it was observed that among 100 asphyxiated newborn majority 65(65%) were in stage-2 followed by 25(25%) and 10(10%) in stage-3 and stage-1 respectively (Table-III). Among 100 asphyxiated newborn serum LDH, AST and ALT levels were raised in 70(70%), 79(79%) and 63(63%) respectively (Table-IV). Study revealed that serum AST was raised and statistically significant in all stages but more marked in HIE stage-II. Serum LDH was raised and statistically highly significant in all stages but more marked in HIE stage-II, and serum ALT was raised and statistically significant in all stages but more marked in HIE stage-II.

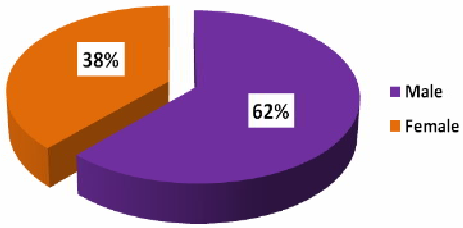

Fig-1. Distribution of sex of the asphyxiated newborn

Table I: Distribution of age of the asphyxiated newborn

Age in Groups	Frequency (n)	Percentage (%)
24-48 hours	52	52%
49-120	48	48%

Table I shows that among 100 asphyxiated newborn 52(52%) attended within 24-48 hours of age followed by 48(48%) between 49-120 hours of age.

Table II: Distribution of asphyxiated neonates according to their gestational age

Gestational age	Frequency (n)	Percentage (%)
38 weeks	80	80%
More than 38 weeks	20	20%

Table II shows gestational age of 80 (80%) asphyxiated neonates were within 38 completed weeks and 20(20%) were more than 38 weeks.

Table III: Distribution of perinatal asphyxia as per sarnat and sarnat HIE staging

Sarnat and Sarnat Staging	Frequency	%
Stage 1	10	10.0
Stage 2	65	65.0
Stage 3	25	25.0

Table III shows that among 100 asphyxiated newborn majority 65(65%) were in stage-2 followed by 25(25%) and 10(10%) in stage-3 and stage-1 respectively.

Table IV: Alteration of Serum enzyme assay of the asphyxiated newborn

Serum Enzyme Status		Frequency	%
Serum ALT Status	Normal	37	37.0
	Raised	63	63.0
Serum AST Status	Normal	21	21.0
	Raised	79	79.0
Serum LDH Status	Normal	30	30.0
	Raised	70	70.0

Table IV shows among 100 asphyxiated newborn serum LDH, AST and ALT levels were raised in 70(70%), 79(79%) and 63(63%) respectively.

Discussion

Perinatal asphyxia is a multisystem disorder.[12] In this study, of total 100 neonates, 62(62%) were male and the rest 38(38%) were female with a male to female ratio of 1.63:1. The male predominance may be explained by the male dominant neonatal admission statistics of this hospital.[13] This is similar to a study conducted in Health and Diseases Training and Research Hospital, Ankara, Turkey where among 94 asphyxiated newborns 57.4% were male and 42.22% female with male to female ratio 1.35:1.[4] In the present study, majority 65(65%) were in HIE stage-2 followed by 25(25%) and 10(10%) in stage-3 and stage-1 respectively. These findings are consistent with the findings of other authors. Islam et al showed in their study out of 70 asphyxiated patients majority 30 (42.9%) were in HIE Stage II 27, (38.6%) were in HIE Stage-I, and 13 (18.6%) in HIE Stage-III.[12] Beken S et al showed in their study out of 94 asphyxiated neonates 29 (30.9%) patients were in stage I, 36 (38.3%) in stage II and 29 (30.9%) in stage III of HIE.[14] In the current study, serum ALT, AST and LDH were increased more than the reference value. Out of 100 cases 63(63%) showed rise of ALT, 79(79%) had elevated AST and 70(70%) raised LDH. This finding is almost similar to the findings of Islam et al except serum LDH level. They showed 87.1% rise of ALT & 52.9% rise in AST.[12] A retrospective cohort study conducted by Sha P et al at the Hospital for Sick Children, Toronto, Canada revealed among 144 asphyxiated newborns 133 neonates had features of multi-organ dysfunction.[15] In this study, Mean ± SD of ALT level was 207.1 ± 201.043 IU/L, that of AST was 186.30± 173.817 IU/L and LDH was 226.51 ± 86.22IU/L respectively. Our findings are almost consistent with the findings of Islam, et al and Paliwal P et al except serum level of LDH. Islam et al showed mean ± SD of ALT 82.2 ±48.08 IU/L, AST 76.3±37.3 IU/L and ALP 369.6 ± 123.05 IU/L respectively.[12]

Paliwal P et al, found mean AST and ALT of 70 asphyxiated babies 80.3±47.4 U/L and 88.8±43.5 U/L, respectively and those of normal babies were 20.5±8.5 U/L and 27.5±8.5 U/L respectively.[16.] In the present study the median value of serum AST, ALT and LDH were 107, 95.3 and 202.50. Reddy S et al observed similar findings in a study where they observed 25 asphyxiated newborn had a median value of LDH 965 U/L. Raised LDH had 100% sensitivity.[17]

Limitations of the study

1. This study was conducted in a single tertiary care hospital. Therefore, the findings may not reflect the exact scenario of all other health facilities that cater care to sick newborn admitted with similar ailment.
2. The current study was conducted among 100 patients, not a large sample to draw a definite conclusion.
3. In Bangladesh, studies on perinatal asphyxia in the perspective of objective of current study are scant. Hence, elaborate & precise comparison & contrast with similar studies could not be delineated in spite of tantalizing efforts.
4. Samples were taken by purposive method in which the question of personal biasness might arise.

Conclusion

Considering all above findings it may be concluded that serum enzymes AST, ALT and LDH are elevated in newborns suffering from perinatal asphyxia with MOD.

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