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Alteration of Hepatic Function: Helpful to Diagnose and Assess Severity of Perinatal Asphyxia

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Abstract

Background and Objectives: Diagnosis of perinatal asphyxia is mostly established retrospectively. But it is difficult to diagnose perinatal asphyxia retrospectively in the absence of perinatal records. As because of hypoxaemia, different organ systems of the body are affected in perinatal asphyxia, this study was done to assess the hepatic function for the diagnosis of perinatal asphyxia and to find out any correlation existing between hepatic enzyme change and the severity of perinatal asphyxia.

Methods: A total of 70 full-term asphyxiated newborns (study group) were studied during January 2008 to December 2008 in the department of Paediatrics, Mymensingh Medical College Hospital. After enrolment these babies were grouped according to Sarnat and Sarnat stages of HIE as stage I, II and III. Another 50 healthy newborns were also studied as reference group. Venous blood was analyzed between 2nd and 5th day of life to estimate serum AST, ALT and alkaline phosphatase (ALP), serum total bilirubin (STB), serum total protein (STP), serum albumin and prothrombin time (PT). Unpaired student's 't' test and Spearman's rank correlation was used for data analysis and P value of <0.05 were considered significant.

Results: The mean AST, ALT, ALP, STP, S. albumin and TSB of asphyxiated babies were 76.3±37.4 U/L, 82.2±48.08 U/L, 369.6±123.05 U/L, 55.7±8.8 U/L, 32.6±5.5 g/L & 5.5±2.01mg/dL respectively and those of normal babies were 23.5±8.5 U/L, 26.5±7.8 U/L, 208.2±46.9 U/L, 66.3±10.4 g/L, 40.9±6.5 g/L and 4.5±1.2 mg/dl respectively and these differences were statistically significant (P <0.001). On the other hand no significant changes were noted in prothrombin time. The rise of AST, ALT, ALP and PT also showed a significant positive correlation with the severity of asphyxia and the stages of HIE.

Conclusion: It is concluded that estimation of hepatic enzymes can be used to diagnose perinatal asphyxia and also to assess its severity.

Key words: Alanine aminotransferase, aspartate aminotransferase, newborn, perinatal asphyxia.

Introduction

Perinatal asphyxia is a major cause of death and disability among the newborns in less developed countries like Bangladesh[1]. According to WHO between four and nine million newborns develop birth asphyxia each year. Of those, an estimated 1.2 million die and at least the same number develop severe consequences, such as epilepsy, cerebral palsy, and developmental delay[2]. Diagnosis of perinatal asphyxia is mostly established retrospectively[3]. But in our country, it is difficult to retrospectively diagnose perinatal asphyxia in the absence of perinatal records[4].

The outcome of asphyxiated babies depend on severity of hypoxemia which adversely affects the liver, kidney, heart, brain and other organs (multi-system insult)[5,6]. The liver may be so damaged (Shock liver) that it may not provide it's basic functions[7]. Previous studies revealed elevated hepatic enzymes that was correlated with degree of hypoxia. Knowledge of the behavior of

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AST and ALT activity may have important implications in the diagnosis and early treatment of perinatal asphyxia[8]. Therefore, this study was designed to find out any correlation existing between hepatic dysfunction and the severity of perinatal asphyxia and to see if this hepatic dysfunction can be useful as a diagnostic tool in cases of perinatal asphyxia.

Materials and Methods

This cross-sectional study was conducted in the department of Paediatrics, Mymensingh Medical College and Hospital (MMCH) from January 2008 to December 2008. A total of 70 full term neonates whose age were 1-5 days and having one of the following: I) history of failure to breath spontaneously immediately after birth, II) history of delayed crying or not crying at all after birth, III) APGAR score ≤6 at 5 minutes, IV) history of undertaken resuscitation procedures to sustain life after birth; followed by evidence of hypoxic-ischemic encephalopathy (HIE) were enrolled as 'Study group'.

Another 50 age and sex matched healthy neonates from Obstetrics and Gynecology department of MMCH were enrolled as 'Reference group'.

Full term newborn babies having birth weight <2.5 kg, having severe jundice, sepsis or congenital anomalies of the hepatobiliary system were excluded from the study. 2 mL of venous blood were taken both from asphyxiated and healthy babies between 2nd and 5th day of life to estimate serum AST, ALT, alkaline phosphatase (ALP), total serum bilirubin (TSB), serum total protein (STP), albumin and prothrombin time (PT). AST and ALT were estimated by Kinetic ultraviolet method, ALP was estimated by optimal standard method, serum bilirubin by colorimetric method, serum total protein by biuret method and serum albumin by Bromocresol Green method. Prothrombin time was measured mechanicaly. Data were analyzed by computer software SPSS version 15. Unpaired student's 't' test was used to measure the level of significance and Spearman's rank correlation was done to see the correlation and P value of <0.05 were considered significant.

Results

Average gestational age of the study group was 38.99 weeks and that of the reference group was 39.12 weeks. Birth weight ± SD of the study group was 2.78±0.2 Kg and that of the reference group was 2.82±0.2 Kg. Among the 70 asphyxiated patients 27 (38.6%) were in HIE Stage-I, 30 (42.9%) in HIE Stage-II and 13 (18.6%) in HIE Stage-III.

The mean AST, ALT, ALP, STP, S. Albumin and TSB of asphyxiated babies were significantly different from the reference group (P <0.001). On the other hand no significant changes were noted in prothrombin time (Table-I).

The rise of AST, ALT, ALP and PT also showed a significant positive correlation with the severity of asphyxia and the stages of HIE. The fall in STP, s. albumin and rise in TSB did not have any significant correlation with increasing severity of HIE (Table-II).

Table-I

Comparison of different hepatic function tests between study group and reference group

Hepatic function test	Study group (N=70) Mean ± SD	Reference group (N=50) Mean ± SD	P* value
AST (U/L)	76.3 ± 37.4	23.5 ± 8.5	<0.001
ALT (U/L)	82.2 ± 48.08	26.5 ± 7.8	<0.001
ALP (U/L)	369.6 ± 123.05	208.2 ± 46.9	<0.001
STP (g/L)	55.7 ± 8.8	66.3 ± 10.4	<0.001
S. Albumin (g/L)	32.6 ± 5.5	40.9 ± 6.5	<0.001
TSB (mg/dl)	5.5 ± 2.01	4.5 ± 1.2	0.002
PT (seconds)	15.2 ± 1.8	14.8 ± 1.5	0.213

*t test

Table-II
Correlation between different stages of HIE with different parameters of liver function tests in study group

Stage of HIE vs.	r value	p value
AST	0.562**	0.001
ALT	0.616**	0.001
ALP	0.531**	0.001
STP	-0.152	0.210
S. Albumin	-0.183	0.129
STB	0.136	0.263
PT	0.265*	0.026

Spearman's rank correlation was done to measure the correlation

Discussion

It is well known that birth asphyxia in newborn infants can cause hepatic hypoxic injury[8,9]. The serum activity of AST and ALT is one of the more specific parameters of liver cell injury both in adults and pediatric age group[8].

This study showed that serum AST, ALT and ALP increased more than the reference group and the difference's were statistically significant (p<0.001). Among the asphyxiated newborns 52.9% showed rise in AST, 87.1% showed rise in ALT and 32.9% showed rise in ALP. Hepatic dysfunction based on raised aminotransfereses was present in 75-85% of the asphyxiated babies in different studies[4,5,10-12]. Saili A, Sarna MS found deranged liver function in 64.5% babies[13]. Some other authors also noted similar results[14]. According to them rise in transaminases indicative of liver cell dysfunction is either due to hepatocyte necrosis or due to changes in cell permeability.

Goldberg et al[15] showed ALT ranged from 446-3050 IU/L in asphyxiated babies[15]. Elevated ALT of more than 40 IU/L was observed by other authors[8]. In this study the mean±SD of AST level was 76.3 ± 37.4 IU/L, that of ALT was 82.2 ± 48.08 IU/L and ALP was 369.6 ± 123.05 IU/L respectively.

In a study done in Edinburgh in 1989, there was no significant change in ALT during initial 24 hours period but after 24 hours, ALT increased significantly (p<0.01) reaching peak median values of 2.1 times the upper limit of reference interval by 48 hrs postpartum[14]. The plasma half life of ALT is ~ 48 hrs and after hepatic damage has ceased, ALT remains increased[16]. Keeping this in mind, in this study blood samples were taken after 24 hours of life upto 120 hours.

J Becett and co-workers accessed the use of measuring plasma protein in birth asphyxiated newborns[16]. Prevalence of hypoproteinemia noted by SV Godambe and co-workers were 34% and others reported 44% in asphyxiated newborns[1,5]. Karlsson M et al showed that albumin was decreased (p<0.001 – 0.008) in the asphyxiated infants[10]. It was described by other workers also[17]. In this study similar assessment was done and the difference between study group and reference group was statistically significant (p<0.001).

In this study the rise of TSB in asphyxiated newborns was statistically significant when compared with the study group; though total serum bilirubin was found to be within normal limit (1.80-11.80) in asphyxiated babies. One study noted, TSB concentration ranged from 1.1-14.3 mg/dl[15] and in another study, peak levels of total bilirubin ranged from 170-220 µmol/L[18]. In our study bilirubin was within normal limit probably due to treatment with anticonvulsants including the bilirubin conjugating enzyme.

Godambe et al have shown that prothrombin index (PI) reduced in all grades of asphyxia[5]. Another study showed that INR (International normalized ratio) increased during the first 2 days of life in the asphyxiated group. Some other study also showed similar results[19,20]. But in our study, the rise of PT in asphyxiated babies was not statistically significant when compared with reference group.

Correlation between different stages of HIE with different parameters of liver function tests in study group shows that serum AST, ALT, ALP, TSB and PT levels were positively correlated with different stages of HIE and all these correlations were statistically significant except for TSB. STP and S. albumin shows negative correlation within different stages of HIE and their correlations were statistically not significant. Similarly Karlsson et al[10] suggests that there is a correlation existing between the magnitude of elevation of ALT, AST and the severity of the hypoxic event.

Conclusion

This study suggests that estimation of hepatic enzymes can be useful as a diagnostic tool as well as to detect the severity of perinatal asphyxia and

thus early treatment can be provided on the basis of liver function tests particularly whose birth details are not well recorded.

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