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Status of Serum bilirubin, Serum Proteins and Prothrombin time in babies with Perinatal Asphyxia

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Abstract:

Background and Objectives: Because of hypoxemia, different organ systems of the body are affected in perinatal asphyxia. This study was carried out to see the status of Serum bilirubin, Serum Proteins and Prothrombin time in asphyxiated babies and to know any correlation existing between hepatic dysfunction 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 & Sarnat stages of HIE as stage I, II & III (Sarnat & Sarnat' 1976). Babies who are small for gestational age, having severe jaundice, sepsis or congenital anomalies of the hepatobiliary system were excluded from the study. A total of 50 healthy newborns were also studied as reference group. Two c.c. of venous blood were taken both from asphyxiated and healthy babies between 2nd and 5th day of life to estimate Total serum bilirubin (TSB), Serum Total protein (STP), Serum Albumin and Prothrombin time (PT). 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 at $P < 0.05$ the results were considered significant.

Results: The mean TSB, STP & S. Albumin of asphyxiated babies were 5.52 ± 2.01mg/dl, 55.74 ± 8.84 & 32.60 ± 5.48 g/L respectively and those of normal babies were 4.51 ± 1.19 mg/dl, 66.30 ± 10.36 & 40.90 ± 6.45 g/L 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 PT showed a significant positive correlation with the severity of perinatal asphyxia. On the other hand STP, S. Albumin & TSB showed no significant correlation.

Conclusion: This study concludes that TSB, STP & S. Albumin significantly elevated and this elevation was proportional to the severity of perinatal asphyxia. On the other hand no significant changes were noted in prothrombin time.

Recommendation: A large scale multi-centre study is recommended to establish this finding.

Key words: *Serum bilirubin, Newborn, Perinatal asphyxia*

. Introduction :

Perinatal asphyxia is a major cause of death and disability among the newborns in less developed countries like Bangladesh.[1] The outcome of asphyxiated babies totally depend on severity of hypoxemia which adversely affects the liver, kidney, heart, brain and other organs. The liver may be so damaged (Shock liver) that it may not provide its basic functions.[2] Researchers found changes in different liver function tests including Serum bilirubin and Prothrombin time among the asphyxiated babies. They also found a correlation

between the hepatic dysfunction and the severity of hypoxia.[3] Recent studies suggest the determination of plasma proteins for assessment of hepatic function.[4] In Bangladesh, we do not have any information on this issue. Therefore, this study was designed to see the status of Serum bilirubin, Serum Proteins and Prothrombin time among the asphyxiated babies and to know any correlation existing between hepatic dysfunction and the severity of perinatal asphyxia.

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 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) (Sarnat & Sarnat' 1976) 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, severe jaundice, sepsis or congenital anomalies of the hepatobiliary system were excluded from the study. Two c.c. of venous blood were taken both from asphyxiated and healthy babies between 2nd and 5th day of life to estimate Total serum bilirubin (TSB), Serum Total protein (STP), Serum Albumin and Prothrombin time (PT).

Serum bilirubin was estimated by Colorimetric Method, Serum Total protein by Biuret method & Serum albumin by Bromocresol Green method. Prothrombin time was measured mechanicaly (Berktow, Robert, et al, 2004). Data were analyzed by computer software SPSS version 15. Unpaired student's 't' test was used to measure the level of significance and at $P < 0.05$ the results 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 (38.57%) were in HIE Stage-I, 30 (42.86%) in HIE Stage-II & 13 (18.57%) in HIE Stage-III.

The mean TSB, STP & S. Albumin of asphyxiated babies were 5.52 ± 2.01mg/dl, 55.74 ± 8.84 & 32.60 ± 5.48 g/L respectively and those of normal babies were 4.51 ± 1.19 mg/dl, 66.30 ± 10.36 & 40.90 ± 6.45 g/L 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 PT showed a significant positive correlation with the severity of perinatal asphyxia. On the other hand STP, S. Albumin & TSB showed no significant correlation.

Table: 1. Comparative study of different Hepatic function tests between study group and reference group:

Hepatic function test's	Study group (N=70) Mean ± SD	Reference group (N=50) Mean ± SD	P* value
TSB (mg/dl)	5.52 ± 2.01	4.51 ± 1.19	0.002
STP (g/L)	55.74 ± 8.84	66.30 ± 10.36	<0.001
S. Albumin (g/L)	32.60 ± 5.48	40.90 ± 6.45	<0.001
PT (seconds)	15.17 ± 1.79	14.78 ± 1.53	0.213

*t test was done to measure the level of significance.

Table: 2. Correlation between different stages of HIE with different parameters of liver function tests in study group.

Stage of HIE vs.	r value	p value
• STB	0.136	0.263
• STP	-0.152	0.210
• S. Albumin	-0.183	0.129
• PT	0.265*	0.026

Spearman's rank correlation was done to measure the correlation

Figure: 1. Correlation of serum total Protein level within different stages of HIE

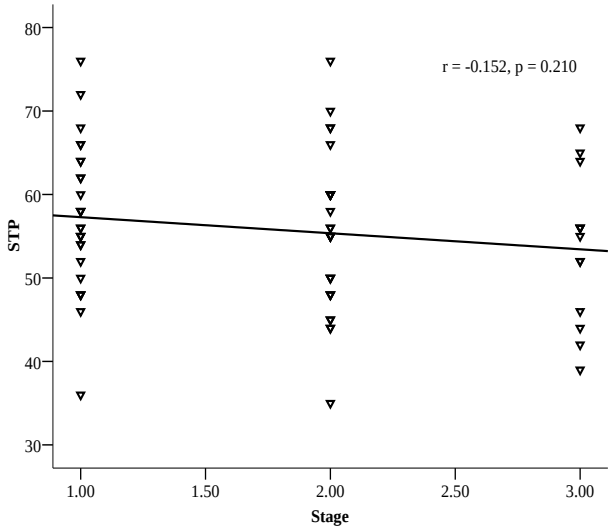

Fig. 1 shows, serum total protein level is negatively correlated with stages of HIE and this correlation is statistically not significant (p =0.21).

Figure: 2. Correlation of prothrombin time within different stages of HIE

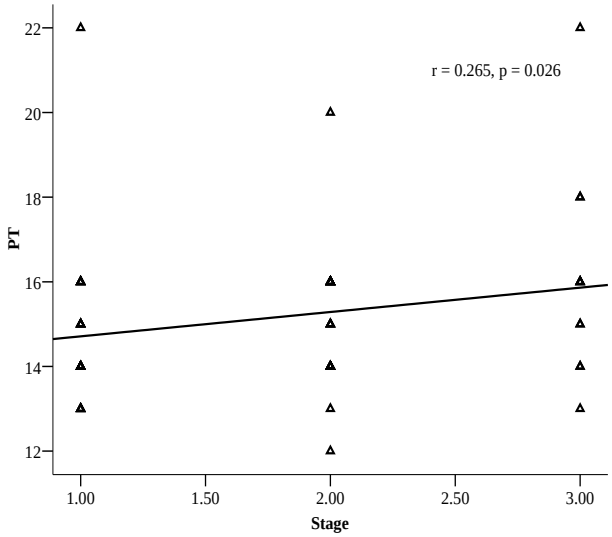

Fig. 2 shows, prothrombin time is positively correlated with stages of HIE and this correlation is statistically significant (p =0.026).

Discussion :

Birth asphyxia is a multisystem disorder.[5] It can cause hepatic hypoxic injury in newborns.[3,6]

Some recent studies suggest the determination of plasma proteins for assessment of hepatic function in adults. Because no corresponding data have been published for neonates, J Becett, AJ Hussey & co-workers accessed the use of measuring plasma protein in birth asphyxiated newborns.[4] Prevalence of hypoproteinemia noted by SV Godambe and co-workers were 34% and others reported 44% in asphyxiated newborns.[1,7] In this study only similar assessment was done and the difference between study group and reference group was statistically significant ($p<0.001$). Karlsson M et al sowed that albumin was decreased ($p<0.001 – 0.008$) in the asphyxiated infants. It was described by other workers also.[8]

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[9] and in another study, peak levels of total bilirubin ranged from 170 – 220 µmol/L.[10] In our study bilirubin was within normal limit probably due to treatment with anticonvulsants including the bilirubin conjugating enzyme.

S.V. Godambe et al have shown that Prothrombin index (PI) reduced in all grades of asphyxia.[7] 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.[11,12] 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 showed that PT positively correlated with different stages of HIE and this correlation was statistically significant. On the other hand STP, S. Albumin & TSB showed no significant correlation.

Conclusion :

This study concludes that TSB, STP & S. Albumin significantly elevated and this elevation was proportional to the severity of perinatal asphyxia. On the other hand no significant changes were noted in prothrombin time. A large scale multi-centre study is recommended to establish this finding.

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