ORIGINAL ARTICLE

Analysis of Consequences of Birth Asphyxia in Infants: A Regional Study in Southern Punjab, Pakistan

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Abstract

Objective: To evaluate the biochemical consequences and platelet counts of birth asphyxia in neonates.
Study Design: Cohort study.
Place and Duration of Study: Department of Child Health, Nishter Medical College and Hospital, Multan, from September to November 2015.
Methodology: The data of 50 (50%) asphyxiated neonates and 50 (50%) non-asphyxiated neonates, with age range less than 1 month, was collected from Children Ward of Nishtar Hospital, Multan, Pakistan. Data on platelet count in blood, kidney function tests (creatinine, urea), liver function tests (bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST)) and cardiac enzyme test (lactate dehydrogenase (LDH)) were analysed by paired sample t-test by SPSS software. Sociodemographic data of those neonate's mothers was also collected.
Results: In asphyxiated neonates LDH, ALT, AST, creatinine, bilirubin, urea levels were higher than healthy infants, while the platelet count was smaller in asphyxiated neonates than healthy infants.
Conclusion: There was a higher rate of alteration in platelet count, levels of LDH, AST, ALT, urea creatinine and bilirubin in asphyxiated infants. These alterations may be correlated with damage of vital organ of asphyxiated neonates.

Key Words: *LDH. ALT. AST. Creatinine. Bilirubin. Urea. Platelet count. Birth asphyxia.*

INTRODUCTION

Birth asphyxia is an insult to the fetus or newborn due to failure to breath or breathing poorly, leading to decrease oxygen perfusion to various organs.[1] According to World Health Organization (WHO), 4 million deaths occur due to birth asphyxia yearly, representing 38% of all deaths of children fewer than 5 years of age.[1] Asphyxia is a condition that occur when there is an impairment of blood-gas exchange, resulting in hypoxemia (lack of oxygen) and hypercapnia (accumulation of carbon dioxide). The combination of the decrease in oxygen supply (hypoxia) and blood supply (ischemia) results in a cascade of biochemical changes inside the body, whose events lead to neuronal cell death and brain damage. The main cause of perinatal asphyxia is the interruption in placental blood flow, leading to brain cell ischemia anoxia triggering anaerobic condition. This in turn results in high consumption of ATP reserves and accumulation of lactic acid.[2]

Some define birth asphyxia in terms of fetal metabolic acidosis and a pH of less than 7.2 as generally accepted to be abnormal. Others define it in terms of APGAR score and make the diagnosis if the score is less than five at five minutes. Therefore, abnormalities in the fetal heart rate are essential,[3] if the hypoxia continues; blood will be redistributed from non-vital organs (liver, kidney) to brain. The fetal brain can metabolize in the absence of oxygen to form lactic acid (hence the metabolic acidosis). When the degree of hypoxia becomes so severe then the heart can no longer produce an output, and brain damage rapidly follows.[4] Most of the neonatal deaths (99%) arise in low- and middle-income countries and over half occur at home, where the bulk of deliveries take place.[5]

Hypoxia can damage almost every tissue and organ. In response to hypoxic-ischemic insult to the fetus, a series of protective reflexes, called diving sea reflexes,[6] get initiated to prevent damage to more vital organs at the expense of lesser vital organs by an attempt to redistribute available blood flow. Liver receives nearly three-fourths of its blood supply from the portal vein and the rest through the hepatic artery.[7] Liver cell injury commonly occurs after perinatal asphyxia, and is similar to shock liver syndrome. Hepatic injury is commonly assessed using serum levels of enzymes which are released from injured hepatocytes, namely alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH), which are commonly referred as the liver enzymes.[8] Blood urea and serum creatinine are significantly higher in asphyxiated babies compared to the normal babies.[9]

One of the most common causes of early-onset thrombocytopenia (<72 hours of birth) in term neonates is prenatal asphyxia. Thrombocytopenia, defined as a platelet count below 150 x 10^9/L, occurs in 1 - 5% of

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healthy term neonates. The prevalence of thrombocytopenia is reported to be much higher in sick neonates, ranging from 22 to 35%. In thrombocytopenia, the major concern is an increased risk of bleeding.[10]

Considering the high incidence of asphyxia and its adverse consequences, the present study was conducted to evaluate the major biochemical consequences and prognosis of the vital organ damage with maternal factors affecting the asphyxiated infants.

METHODOLOGY

This study was carried out on neonates born in Nishtar Medical College and Hospital, Multan, Punjab, Pakistan, which belonged to Multan as well as other regions of south Punjab. The approval for study was taken from the Head of Child Health Department, Nishtar Medical College and Hospital as well as parents also gave their written reported approval for their conscription in the study. All the neonates were below the age of one month. They were born and admitted at the Department of Child Health from September till November, 2015. The operational definition of birth asphyxia was failure or delayed onset of unprompted breathing after delivery or when there was need of positive pressure ventilation for >1 minute. Severity of asphyxia was assessed by APGAR scoring, consisted of the 5 physical signs: heart rate, respiratory effort, reflex irritability, muscle tone, and color. Birth asphyxia rigorousness in infants falls between 0 and 10, where babies were classified as severe asphyxia with APGAR score less than 3.

After the APGAR infants were divided into two groups: Group A (control) consisting of 50 (50%) non-asphyxiated infants, and group B (test) including 50 (50%) newborn babies who were ill with birth asphyxia. Then complete case histories of those 100 neonates (50% control and 50% asphyxiated) were taken. Laboratory tests of all neonates were performed in Nishtar Clinical Laboratory, to check platelet count, serum creatinine, blood urea level, bilirubin, ALT, AST, and LDH levels in blood. The physical appearance (i.e. feeding habits, tone, convulsions, laziness etc.) of all asphyxiated children was also observed. Socio-demographic data of maternal factors of all asphyxiated infants during pregnancy was also collected.

Biochemical analysis of platelet count, serum creatinine, blood urea, bilirubin, ALT, AST was done to evaluate the consequences of vital organ damage due to asphyxia in neonates. Platele count, serum creatinine, urea bilirubin, ALT, LDH and AST were estimated by standard methods.

The obtained data of platelet count, serum levels of creatinine, urea, bilirubin, LDH, AST, ALT were analysed by using SPSS statistical software version 20.0 (SPSS Inc, Chicago), and percentages with frequencies are also mentioned. Paired sample t-test was performed to check the significance of values obtained. P-values <0.05 was taken as significant.

RESULTS

The range of APGAR score on healthy infants was 7-9, while in asphyxiated infant it had fallen between 0 and 2. The serum levels of creatinine, urea, bilirubin, LDH, AST, ALT and platelet count in blood in asphyxiated and non-asphyxiated subjects were showed as serum creatinine ($t = -10.108$, $df = 49$, $p < 0.0001$, CI = 95%), urea ($t = -29.078$, $df = 49$, $p < 0.0001$, CI = 95%), bilirubin ($t = -24.547$, $df = 49$, $p < 0.0001$, CI = 95%), LDH ($t = -13.193$, $df = 49$, $p < 0.0001$, CI = 95%), ALT ($t = -40.365$, $df = 49$, $p < 0.0001$, CI = 95%) and AST ($t = -120.045$, $df = 49$, $p < 0.0001$, CI = 95%), were significantly increased. While platelet count ($t = 477.199$, $df = 49$, $p < 0.0001$, CI = 95%) was significantly decreased in asphyxiated neonates than normal infants (Table II).

Twenty-eight (56%) newborns had poor feeding and 20 (40%) newborns were totally incapable to get food or suck milk. Sluggishness or immobility was found in 26 (52%), whereas irritability was found in 18 (36%) children, respiratory distress was present in 23 (46%). Seizures were seen in 14 (28%), while cyanosis was found in 21 (42%) newborns. Reduced pitch was noticed in 22 (44%), whereas amplified pitch was created in 13 (26%) of newborns.

Table II shows the sociodemographic data of asphyxiated neonates' mothers. Only 6 (12%) mothers had appropriate antenatal appointments to skilled medical specialists (doctors or eligible paramedics). Ten (20%) went to inexpert birth helpers, or not fully trained midwives, lady health visitors (LHV) or a nurse. Major fraction of study population mothers, i.e. 32 (64%), did not go to any medical professional. Most of the mothers, i.e. 23 (56%), had home deliveries. Fourteen (28%) had deliveries at private clinics and maternity homes, while only 6 (12%) newborns came at tertiary care centres. A severe danger was linked with expanded breakage of membranes 12 (24%). Ten (20%) were delivered by optional caesarean section. Severe intra-partum difficulties were more common among obstructed labour,

Table I: Descriptive biochemical parameters of non-asphyxiated (A) and asphyxiated (B) groups.

Biochemical parameters	Group A (n=50), (Mean ± S.D)	Group B (n=50) (Mean ± S.D)
Platelet count	$2.141x10^{11}$/L ± 3172843957^{+}	91733.600/µL ± 168275.252*
Creatinine level	0.644 U/L ± 0.029^{+}	1.312 U/L ± 0.469*
Urea level	29.640 mg/dL ± 3.088^{+}	67.007 mg/dL± 9.286*
Bilirubin level	0.4916 mg/dL ± 0.031^{+}	7.596 mg/dL ± 2.045*
LDH level	294.160 U/L ± 3.203^{+}	1782.560U/L ± 797.900*
AST level	32.960 U/L ± 3.630^{+}	158.914 U/L ± 6.310*
ALT level	33.560 U/L ± 4.941^{+}	84.596 U/L ± 6.226*

LDH=Lactate dehydrogenase; AST=Aspartate aminotransaminase; ALT=Alanine Aminotransaminase.
*Values are Mean ± SD. Differences in *vs+ are significant (p < 0.05).*

Table II: Sociodemographic data of asphyxiated neonates' mothers.

Factors	Number	Percentage (%)
No antenatal visit	32	64
Antenatal visit to LHV, Dai or other health worker	10	20
Antenatal visit to qualified doctor	6	12
Vaginal bleeding	17	34
Fever at a time of delivery	12	24
Anemia	30	60
Oedema	23	46
Hypertension	10	20
Age greater than 35	7	14
Age less than 18	8	16
Age between 18-35	35	70
Home delivery	28	56
Delivered at private clinic or maternity home	14	28
Delivered at tertiary care hospital	6	12
Mode of delivery NVD	40	80
Mode c-section	10	20
Meconium stained liquor	5	10
Extend break of membrane greater than 18 hours	12	24
Presentation other than cephalic	10	20
Numerous birth	5	10

LHV=Lady Health Visitor; NVD=Normal Vaginal Delivery

resulting in a prolonged second stage; normal vaginal delivery was in 14 (80%). Maternal hypertension was found in 10 (20%). Meconium stained liquor, especially thick (particulate) meconium, was mainly linked with encephalopathy 5 (10%). Multiple births were observed in 5 (10%) cases. Most of the mothers were between 18 - 35 years of age. Seven (14%) were older than 35 years, whereas 8 (16%) were of 18 years and younger. A noteworthy risk factor was that 30 (60%) mothers were anemic.

DISCUSSION

The basic goal of our research was to evaluate the consequences in neonate asphyxia. The important findings of the present study shows that serum concentration of bilirubin, urea, creatinine, ALT, ASP and LDH were increased and blood platelet counts were decreased in asphyxiated neonates than normal infants. On the other hand, APGAR score and physical appearance of neonates put them in the category of asphyxiated infants. Similarly, sociodemographic data of asphyxiated infants' mothers reveal that all the causes discussed in the Table II are also associated with the future pathologic problems, such as neonatal encephalopathy.

The levels of LDH in the heart and liver have been increased following birth asphyxia, which indicate that the anaerobic respiration instead of the aerobic has been taken place in case of neonate asphyxia, which leads to mental retardation and neurophysiological disorders. While due to deficiency of oxygen, multiple organ damages take place,[11] it can cause severe lifelong pathologies. The metabolic changes can cause energy depletion. Due to this, acidosis occurs which follow high lactate level because of high LDH level.[12] The present results also show an increase in serum LDH level (Table I), which may be associated with future life-threatening problems including liver disease, heart attack, anemia, muscle trauma, bone fracture, cancer, and infections such as meningitis, encephalitis, and HIV.

Extensive studies have reported that in neonate asphyxia, hepatic injury occurred due to increase in enzymatic secretions, i.e. AST and/or ALT.[13] The present study is also consistent with previous study and indicates that the elevated levels of AST and ALT (Table I) could be prominent sign for the development of hepatic injury in neonate asphyxia.

Many studies stated that abnormal increase in the levels of blood urea and creatinine is associated with malfunctioning of kidney. Renal tubular cells demand and consume large amount of energy due to high metabolic rate. In asphyxia, the energy production is low so the renal requirements do not fulfill and renal injury occurs.[19] Results of the present study also exhibited increase levels of creatinine and urea in serum (Table I), which may also contribute in abnormal functioning of kidney in asphyxiated neonate.

The prevalence of thrombocytopenia was almost three-fold higher (OR 2.75) than in the control group with perinatal asphyxia.[14] Therefore, the decreasing levels of platelets as in the present study (Table I) in asphyxiated pediatrics are the side effect of asphyxia due to hypoxic condition. While degradation of RBCs also affected in neonates asphyxia, which has been revealed by increasing bilirubin level in liver (Table I).

Results of sociodemographic data (Table II) were consistent with other studies, which revealed that higher incidence of asphyxia was related with lack of antenatal care, poor nutritional status, antepartum hemorrhage, and maternal toxemia.[15] Female growth and nutrition improvement ought to be a lasting aim in the public health of women. Enhanced antenatal and perinatal care could decrease such high mortality.[16]

Perinatal asphyxia is an inclusive problem causing morbidity and death. Perinatal mortality rate was 111/1000 live births in non-booked cases as compared to 17/1000 in booked cases.[17] Perinatal and neonatal mortality by perinatal asphyxia reflect social, educational and economical principles of a society. In developing countries, like Pakistan where health facilities are restricted to urban areas, prevalence of asphyxia is greater; though the topic with restricted local data has been widely studied and reviewed all-inclusive. Trained staff availability and pediatric supervision are lacking at home deliveries in our community, while 80% deliveries are at home in our society.[18,19] In this study, 64%

(Table II) had no antenatal visit, which is vital risk for birth asphyxia along with home and untrained delivery.

CONCLUSION

In birth asphyxia, multiple organ systems are damaged in neonates due to increase in the levels of LDH, AST, ALT, urea, creatinine and bilirubin in blood, and decrease in platelet counts. The harshness of dysfunction relates well with increasing harshness of asphyxia and relates well with poor APGAR score. Furthermore, maternal factors are also significantly associated with birth asphyxia. The slight parenchymal damage and alterations at molecular level may affect organ functions in future life, which require continuous long-term follow-up of these neonates for various pathological outcomes.

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