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ORIGINAL ARTICLE

Clinico-Biochemical Profile in Neonates with Birth Asphyxia

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ABSTRACT

Objective: To study the biochemical derangements in neonates with asphyxia having different clinical presentation.

Patients and Methods: This cross-sectional study was conducted at Neonatal Intensive Care Unit, Federal Govt. Polyclinic (PGMI) Hospital, Islamabad from 1st November 2016 to 30th April 2017. All neonates with history suggestive of birth Asphyxia were inducted in study. Complete history, examination and laboratory investigation (Complete blood count, Blood Sugar, Serum Calcium, Serum Electrolytes, Serum Urea, Serum Creatinine, Liver function tests, Cardiac Enzymes) were done. The data was entered in SPSS version 23 for further analysis.

Results: Out of 39 babies, 66.7% had moderate and 33.3% had severe birth asphyxia. Severity of birth asphyxia was associated with lower APGAR Scores. Multi-organ involvement was observed with increasing severity of birth asphyxia as; respiratory system 71.8%, cardiovascular system (shock) 25%, central nervous system (convulsion)15.4%, renal tract (acute renal failure) 12.8% and gastro intestinal tract 5.1%. Significant mortality was noted with shock, convulsion and hypoglycemia. Cardiac and liver enzymes were deranged and were significantly related to severity of birth asphyxia.

Conclusion: Multi-organ dysfunction is common in birth asphyxia. Early assessment of clinical and biochemical profile will help in managing disease, reducing severity and improving the outcome of illness.

Key words: Birth asphyxia, Clinico-biochemical profile, Multiorgan dysfunction, Neonates,

Author`s Contribution
[1] Conception, synthesis, planning of research and writing of manuscript, [2] Active participation in methodology, interpretation and discussion, review of manuscript, [3] Review of literature [4] Statistical data analysis, [5,6] Data collection, data entries and data analysis

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Article info.
Received: April 19, 2017
Accepted: May 20, 2017

Cite this article: *Ashraf N, Butt N, Munir S, Zahid M, Fatima K,Minhas A. Clinico-Biochemical Profile in Neonates with Birth Asphyxia. JIMDC. 2017; 6(2):64-68.*

Funding Source: *Nil*
Conflict of Interest: *Nil*

Introduction

Despite of important advances in perinatal care, asphyxia remains a severe condition leading to significant mortality & morbidity. Prevalence of Hypoxic Ischemic Encephalopathy (HIE) ranges from 0.1%-0.5% of total live births.[1] According to WHO, in Pakistan 49% deaths occur in first 28 days of life out of total mortality under five years of age. Birth Asphyxia and birth trauma together are the second most common cause of neonatal deaths and contribute to approximately 23% of total neonatal deaths.[2] Birth asphyxia results in damage to multiple organs including brain, heart, lungs, kidney, liver and GIT.[3,4] The common complications of birth asphyxia are hypoxic ischemic encephalopathy, persistent pulmonary hypertension, hypotension, cardiogenic shock or heart failure and renal tubular necrosis.[3] A number of metabolic derangements coexists with the above mentioned complications like acidosis, hypoglycemia, hypocalcaemia, hyponatremia, raised liver enzymes, raised cardiac enzymes, which may alter the outcome of the disease process.[4] Due to involvement of different

organs in birth asphyxia, a number of metabolic derangements have been analyzed to estimate quick and reliable markers of tissue damage for diagnostic and prognostic purpose respectively. This study was conducted to identify different clinical manifestations and biochemical changes in neonatal birth asphyxia, in order to make early interventions, so that asphyxia related morbidity and mortality could be reduced.

Patients and Methods

This cross-sectional study was conducted at NICU, Pediatrics department, Federal Govt. Polyclinic Hospital, Islamabad from 1st November 2016 to 30th April 2017. The study was approved by ethical committee of the hospital. All neonates admitted and managed for birth asphyxia during the study period, with gestational age of ≥ 38 weeks and APGAR score of < 7 at 1 minute were inducted in the study. Informed consent from parents was taken. Neonates with respiratory distress syndrome, prematurity, Low birth weight, neonatal sepsis, congenital anomalies, syndromes, tumors, trauma and maternal history of drug addiction or analgesia were excluded from the study. The diagnostic criteria jointly released by American College of Obstetricians and Gynecologists (ACOG) and American Academy of Paediatrics (AAP) was: (i) umbilical cord pH of < 7 (mixed or metabolic) (ii) APGAR score of 0-5 for longer than 5 mins (iii) Neurological complications including hypotonia, convulsion, coma (iv) Multiorgan failure.[5]

According to NNPD (National Neonatal Perinatal Database) moderate birth asphyxia was defined as APGAR Score between 4-6 at 1 minute of age or slow gasping breathing at 1 minute of age and Severe birth asphyxia was defined as APGAR Score 3 or less at 1 minute of age or no breathing at 1 minute of age.[6]

In our study, we have used history suggestive of birth asphyxia, APGAR Score at 1 minute of age and clinical evidence of hypoxic ischemic encephalopathy. Detail history and examination was done by trained paediatricians.

Organ dysfunction was defined as follows: [4, 7,8,10]

CNS: Evidence of hypoxic ischemic encephalopathy as Sarnat & Sarnat classification.

Respiratory system: Respiratory distress with respiratory rate >60/min or hypoxia needing O2 to maintain Oxygen saturation (SpO_2) >92% for >24 hours or requirement for CPAP / mechanical ventilation.

Renal failure: Oliguria <1ml/kg/hr for > 24 hours or Serum Creatinine of >1.5mg/dl.

Cardiac dysfunction: Signs of poor perfusion in terms of increased capillary refill time, poor pulses, tachycardia H/R >160/min, with or without hypotension, need of ionotropic support or raised cardiac enzymes than normal (CPK upto 325U/L, CKMB upto 25U/L and LDH 230-460U/L). [4, 10]

Gastrointestinal disturbance: Evidence of Necrotizing Enterocolitis (NEC) in the form of GI bleed, abdominal distension, or X ray abdomen suggestive of NEC.

Hepatic dysfunction: Elevation of alanine amino transferase (ALT) or aspartate amino transferase (AST) of more than two times of its normal value (ALT upto 40U/L and AST upto 37U/L).

Metabolic derangements: Hypoglycemia <40 mg/dl, Hyponatremia <135 meq/L, Hypokalemia <3.5 meq/L and Hypocalcemia <8mg/dl.

Laboratory investigations included were CBC, Blood sugar, Serum Calcium, Serum Electrolyte (Na^+& K^+), Urea, Creatinine, Liver enzymes and Cardiac enzymes. Venous sample of 2ml was sent to measure Serum Ca+ by direct complexometric method, Serum electrolyte by ISE method, liver enzymes and cardiac enzymes by Kinetic IFCC method.

All the babies were monitored and treated according to their clinical condition as standard protocol of NICU. The data was entered in SPSS version 23. Continuous data was expressed as mean and median along with standard deviation values. Categorical data was expressed as number & percentages. Different groups of continuous variables were compared by using independent samples student's t-test or Mann-Whitney test while categorical variable groups were compared by applying chi-square test and Fisher's exact test.

Results

A total of 39 neonates were included in the study. All of the neonates were full term and were admitted in hospital within 24 hours after birth. Out of 39 neonates, 23 were

males and 16 were females. There were increased number of spontaneous vaginal deliveries (SVD's) followed by cesarean sections and assisted vaginal deliveries (AVD's) (Table 1).

Table 1: Demographic characteristics of participants (n=39)

Variable	Number	Percentage
Gender		
Male	23	59
Female	16	41
Mode of deliveries		
Spontaneous vaginal deliveries	17	43.6
Assisted vaginal deliveries	3	7.7
Cesarean sections	19	48.7

Distribution of moderate and severe birth asphyxia was 26(66.7%) and 13(33.3%) respectively. Severe birth asphyxia was observed to be more common in combined vaginal deliveries (61.54%) as compared to caesarean sections (38.46%) but the difference was not statistically significant. A statistically significant difference was observed in the mean APGAR score of moderately and severely asphyxiated neonates at I minute and 5 minutes. Single organ system involvement was observed in 11 (28.2%) neonates. Multiorgan dysfunction with two organs and more than two organs were found in 17 (43.6%) and 11 (28.2%) cases respectively. Incidence of multiorgan dysfunction was more frequently observed among severely asphyxiated neonates as compared to moderately asphyxiated neonates (Table 2).

Table 2: Association of clinical profile with moderate and severe birth asphyxia

Clinical profile	Moderate birth asphyxia (n=26) n(%)	Severe birth asphyxia (n=13)n(%)	p-value
Mode of delivery			
Combined	12(46.15)	8(61.54)	>0.05
Vaginal; n (%)	14(53.85)	5(38.46)	
C-section; n (%)			
Organ involvement			
Single; n (%)	10(38.46)	1(7.69)	0.063
Multiple; n (%)	16(61.54)	12(92.31)	
APGAR Score			
At 1 minute (mean±SD)	4.85±0.78	2.46±0.77	0.000
At 5-minutes (mean±SD)	6.62±0.63	4.92±0.76	0.000

Sarnat & Sarnat grading criteria was used to classify CNS involvement in terms of hypoxic ischemic encephalopathy (HIE). Among total of 39 neonates, 30(76.9%) were in HIE grade I, while 7(17.9%) and 2(5.1%) neonates were categorized as HIE grade II and III respectively. Among neonates with severe birth asphyxia, a significantly large proportion was HIE grade II (71.43%) and III(100%) as compared to infants with moderate birth asphyxia 28.57% and 0% respectively. Therefore, with lower APGAR score, there are more significant chances of developing HIE of higher grade. Mortality rate in this study was 10.3% (4). A large proportion of patients (50%) belonged to HIE grade III. Ventilatory support was required by 10.3% (4) of neonates. Proportion of discharged patients was high in HIE grade I (100%) as compared to grade II (57.14) and III (50%) (Table 3)

Table 3: Association of HIE grades with different variables

Variables	HIE grade I n=30	HIE grade II n=7	HIE grade III n=2	p-value
Birth Asphyxia	N (%)	N (%)	N (%)	0.004
Moderate	24(80)	2(28.57)	0(0)	
Severe	6(20)	5(71.43)	2(100)	
Outcome				
Discharge	30(100)	4(57.14)	1(50)	0.000
Expire (Mortality)	0(0)	3(42.86)	1(50)	

Percentage involvement of various organ dysfunction is shown in figure 1.

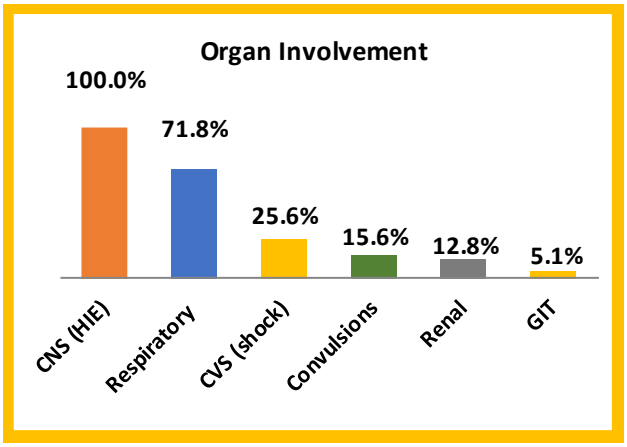

Figure 1: Percentage of organ involvement in neonates presenting with birth asphyxia

CNS involvement was present in all neonates (100%) followed by respiratory distress (71.8%) and others. Comparison of outcome with clinico-biochemical profile of neonates presenting with birth asphyxia is shown in table 4. Regarding organ dysfunction, a significant mortality was associated with convulsions and shock (p=0.001, p=0.04) respectively. Hypocalcaemia was observed in 46.2% (18) neonates, while 10.3% (4) neonates had hypoglycemia. Hyponatremia, hypokalemia and hyperkalemia were observed in 35.90% (14), 20.51% (8) and 2.56% (1) neonates respectively. Hypoglycemia was significantly associated with mortality (p = 0.045).

Cardiac enzymes were strikingly high in majority of neonates. CPK was raised (range: 342 – 5295 U/L) in 29 (74.35%) while CK MB and LDH were high (range: 26–650 U/L; 590-6001U/L) in 34 (87.17%) and 25(64.10%) neonates respectively. Median CK, Serum concentration in severe birth asphyxia was significantly higher than the moderate birth asphyxia (U=56.0, p=0.002). Similarly, median CPK MB and LDH serum concentration in severe birth asphyxia was significantly higher than the moderate birth asphyxia (U=66.0, p=0.005 and U=75.0, p=0.21 respectively). Liver enzymes were also deranged where serum ALT level was more than two times raised in 15.4% (6) (ranging from 175– 377 units/l) and serum AST level was double the normal in 41.0% (16) neonates (ranging from 82– 590 units/l) but no significance was noted with severity and mortality of birth asphyxia.

Discussion

In our study, moderate birth asphyxia caused HIE grade I in 92.3% (24), HIE grade II 7.7% (2) and no case found with HIE grade III as compared to severe birth asphyxia whereas 46.2% (6), 38.5% (5) and 15.3% (2) babies had HIE grade I, II and III respectively. In our study HIE Grade I is more common than grade II and III as compared to the study conducted by Shah et al, in which 27.58% belonged to HIE grade II out of 56.8% of babies with HIE.[3]

Multiorgan dysfunction is a part of birth asphyxia due to redistribution of blood flow to the vital organs. Hypoxic ischemic injury to vital organs like brain, kidney, heart, gut and liver results in organ dysfunction and even failure, if not corrected promptly. Multiorgan involvement is 71.7% (28) in our study as compared to 80.7% (46) in study conducted by Pattar RS et al.[4] Mortality with multiorgan failure is 14.2% (4) in our study as compared to 17.3% (8) with Patter RS et al and 27.6% by Singh KS et al.[4,8]

Respiratory system was most commonly involved organ second to CNS which was 71.8% (28) and more common with severe birth asphyxia and low APGAR Score

Table 4: Comparison of Outcome with Clinico-biochemical profile of neonates presenting with birth asphyxia

Clinico-biochemical profile	Clinical outcomes (n = 39)		p- value
	Discharge n=35	Death n=4	
Organ dysfunction			
Central Nervous System (HIE) • HIE Grade I • HIE Grade II • HIE Grade III	N (%) 30 (85.7) 4 (11.43) 1 (2.86)	N (%) 0(0) 3 (75) 1 (25)	0.001
Central Nervous System (Convulsions)	2 (5.71)	4 (100)	0.001
Respiratory system	24 (68.57)	4 (100)	0.249
Cardio Vascular system (Shock)	7 (20)	3 (75)	0.045
Renal system	4 (11.43)	1 (25)	0.4
Gastrointestinal system (NEC)	2 (5.71)	0(0)	0.8
Metabolic derangements			
Hypocalcaemia (<8 mg/dl)	16 (45.71)	2 (50)	0.636
Hypoglycemia (<40 mg/dl)	2 (5.71)	2 (50)	0.045
Hyponatremia (<135 mg/dl)	14 (40)	0(0)	0.154
Hypokalemia (<3.5 mg/dl)	7 (20)	1 (25)	0.617
Hyperkalemia(>5.5mg/dl)	1 (2.86)	0(0)	0.897

(p=0.04), similar findings have been observed and reported by Shah P et al and linderkamp O et al.[3,9] Involvement of cardiovascular system is frequent involvement after respiratory distress which is 25.6% (10) with mortality of 40% (4) as compared to the that reported by Pattar RS et al, which was 54.3% (31) with mortality of 22.5% (7).[4] Renal system involvement was observed in 12.8% (5) in our study. These findings are comparable to those reported by Parkash et al[11] and Kapil Kapoor et al [12] (16 %(19) and 9.6 %(44) respectively). However almost double i.e. 29.8% (17) have been reported by Pattar RS et al.[4]

Hypoglycemia, hypocalcemia and hyponatremia were more pronounced with increasing severity of birth asphyxia, similar findings have been observed and reported by Shah et al[3] and by Pallab Basu et al.[13] We have also observed association of Hypokalemia [17.9% (7)] with severe asphyxia as well. Cardiac enzymes included CPK, CKMB, LDH and were raised in 74.35%, 87.17% and 64.10% respectively and more marked with severe birth asphyxia, findings comparable to that noted by Rajakumar PS et al and Asutosh PC et al.[10,14] Liver enzymes were raised in asphyxiated babies, however with no significance in mortality. Gurdeep SD et al and Chaitali Patra et al [16] found a significant correlation with severity and outcome of asphyxia.[15,16]

Conclusion

Birth asphyxia is associated with multiorgan dysfunction and its severity directly correlates with morbidity and mortality. Different clinical presentation and altered biochemical parameters can help us in prompt recognition, early intervention and improvement of outcome.

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