

## Disease pattern and Biochemical profile as a predictor of outcome of Critically sick neonates in a Neonatal Intensive Care Unit

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### Abstract

**Background :** Neonatal Intensive Care Unit (NICU) is predominately concerned with the management of critically sick neonates having acute life threatening conditions. Usually neonates having respiratory distress, acute neurological deterioration, severe infection and prematurity contribute the major admission in a NICU.

**Objective :** To find out the disease pattern and biochemical profile as a predictor of outcome of critically sick neonates in NICU.

**Methods :** This observational prospective study was carried out at NICU of Dhaka Shishu (Children) Hospital from January 2015 to July 2015. Total 121 neonates were enrolled according to inclusion criteria and analyzed some important biochemical profile specially electrolyte and blood gas status as a part of proper management as well as to predict their outcome.

**Results :** Among critically sick neonates, perinatal asphyxia was common disorder followed by sepsis. Biochemical profile specially electrolyte and acid-base disruption play important role to the outcome of critically sick neonates. Low pH, low potassium and high base-deficit level were found to have worse outcome.

**Conclusion :** Perinatal asphyxia constitute major cause of admission of critically sick neonates. Early detection of electrolyte and acid-base status is helpful to care and overall survival of these neonates. Mortality was the highest among neonatal sepsis followed by perinatal asphyxia. Metabolic acidosis and hypokalemia were the predictor of outcome of such critically sick neonates.

**Keywords :** Admission pattern, perinatal asphyxia, critically sick, acid-base-electrolyte status

DOI: <https://doi.org/10.3329/nimcj.v10i2.45433>

Northern International Medical College Journal Vol. 9 No. 2 January 2018, Page 381-385

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### Introduction

NICU is predominantly concerned with acute life threatening disease conditions of critically sick neonates in a specialized unit having a very high level of monitoring, especially vital signs and other body functions. Neonates with respiratory distress, acute neurological deterioration, ventilation-perfusion compromise, severe infections and prematurity constitute major admission to a NICU.<sup>1</sup> These occur in a variety of pathological conditions and may remain unrecognized leading to morbidity and mortality irrespective of the primary disease. Hence caring of critically sick neonates remain one of the most demanding and challenging aspects of the field of Paediatrics.

Disease pattern in early age group is a sensitive indicator of the availability, utilization and effectiveness of mother and child health services in the community. Therefore, regular review of the disease pattern and their consequence events in any particular setting is important for providing better health services, as well as overall survival.

Critically sick neonates are admitted in a NICU because of they may need mechanical ventilation, invasive intravascular procedures and frequent attention by both nursing and medical staffs.<sup>2</sup> These neonates commonly have electrolyte and acid-base disorder, a valuable predictor to a Paediatrician about patient assessment, therapeutic decision and ongoing

prognosis of the patient.<sup>3</sup> Blood gas measurements permitted the diagnosis of metabolic and respiratory acidosis or alkalosis associated with birth process and postnatal adaptation to air breathing.<sup>3</sup>

Perinatal asphyxia and neonatal sepsis both are common occurrence in neonates, major health problems in Bangladesh like other developing countries and devastating cause of mortality.

Marked structural and functional difference is present in children in comparison to adults, so atelectasis develops quickly resulting in rapid-onset of hypercarbia and hypoxia. Chest wall is compliant and respiration is less efficient; the respiratory center is immature, hypoxia and hypercarbia lead to decreased respiratory drive. In addition, they have reactive vascular bed to maintain blood pressure until late, therefore one cannot rely on hypotension to diagnose shock as in adults.<sup>4</sup> Identify the presence of metabolic acidosis, the categorization ends with a broad differential of anion gap (4-12mEq/L). This includes essential electrolytes e.g. Cation ( $\text{Na}^+$ ,  $\text{K}^+$ ) and Anion ( $\text{Cl}^-$ ,  $\text{HCO}_3^-$ ).<sup>5</sup> Hence both acid-base and electrolyte status provide essential information about critically ill neonates and predict their consequences.

Sodium and potassium are major electrolyte regulate voltage of action potentials in skeletal muscles, nerves and myocardium, maintenance of acid-base and fluid balance in the ECF through osmolality. Bicarbonate is an important electrolyte acts as a buffer to maintain the normal level of acidity (pH) in the blood and other fluids in the body.<sup>6</sup>

In perinatal asphyxia and neonatal sepsis, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a common problem where severe hyponatremia and hyperkalemia can occur. Hyperkalemia results from ischemic insult reflected cellular changes leading to diminished oxidative phosphorylation and ATP production. This energy failure impairs ion pump function resulting in accumulation of intracellular  $\text{Na}^+$  and extracellular  $\text{K}^+$ .<sup>7</sup> If inappropriate fluid-electrolyte and acid-base are replaced serious morbidity can result. Excessive sodium-bicarbonate, improper preparation of formula feeds, increased insensible water loss specially in premature babies kept under radiant warmers can cause hypernatremia in neonates.<sup>8</sup>

A high index of suspicion, prompt recognition and through understanding of blood gas and common electrolyte abnormalities are necessary to ensure their total correction as well as reduce mortality of critically sick neonates admitted in ICU.<sup>9</sup>

This study was carried out in neonates with various ailments attending ICU at a tertiary care hospital of Dhaka, Bangladesh. We concluded this study to document the disease pattern and important biochemical marker (especially acid-base and electrolyte status in critically sick neonates) and its association with primary illness and their consequence output. This may help to assist doctors, health workers and planners to pay due attention for better utilization of health care facilities because exact understanding of situation leads to better management.

### Materials and Methods

This observational prospective study was conducted at the NICU, Dhaka Shishu (Children) Hospital during the period of January 2015 to July 2015. The selection was unbiased. The data may therefore be generalized on a population of sick neonates seeking ICU care.

Before enrollment parent of each child was given a detail explanation about nature and purpose of the study. One hundred twenty-one (121) neonates were analyzed for electrolyte, blood gas as well as baseline investigations for proper management.

Total 161 neonates admitted during this period among these 40 were excluded from this study due to any congenital anomalies (medical or surgical), Jaundiced due to blood group incompatibilities or received LAMA (Left against medical advice).

For each neonate, a detailed history from mother or other caregiver was recorded in a questionnaire. Then with all aseptic precaution, blood sample was collected in the disposable syringe. Electrolyte analyzer (Rapid lab-1265) based on the principle of potentiometry analyzed  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ . Blood gas analyzer (Gastat-600) based on the principle of potentiometry analyzed pH,  $\text{PCO}_2$  respective electrodes. Base excess (BE) and  $[\text{HCO}_3^-]$  were calculated parameters from pH and  $\text{PCO}_2$  were provided by the analyzer. Anion gap was calculated from the following formula<sup>5</sup>  $\text{AG} = [\text{Na}^+ + \text{K}^+] - [\text{Cl}^- + \text{HCO}_3^-]$ .

Each case was thoroughly examined and follow-up regularly. Definite neonatal septicemia was diagnosed by positive blood culture and probable septicemia was diagnosed by a scoring system or positive CRP.<sup>10</sup> Relevant investigations for diagnosis and follow-up included complete blood count, blood culture, serum electrolyte, blood gas analysis, blood grouping, serum bilirubin and chest X-ray were done.

Hyponatremia and hypernatremia were defined as serum sodium concentration  $<130\text{mmol/L}$ <sup>11</sup> and  $>150\text{mmol/L}$ <sup>12</sup> respectively. Hypokalemia and hyperkalemia were defined as serum potassium level  $<3.5\text{mmol/L}$ <sup>12</sup> and  $>6\text{mmol/L}$ <sup>13</sup> respectively.

Normal range of pH(7.35-7.45), PCO<sub>2</sub>(35-45 mmHg), [HCO<sub>3</sub><sup>-</sup>] (23-27mmol/L), Base excess (<10mmol/L) were considered.<sup>14</sup>

Unpaired t-test was used to test the significance of difference of electrolyte and acid-base status of critically sick neonates among survivors and non-survivors.

**Results**

This study was carried out on the neonates suffering from a wide variety of ailments attending ICU care over a period of six months. Among 121, male predominance was found, 84 neonates were male and 37 were female. Male: Female ratio were 2.27:1. Most of the neonates were up to 2 days of age (Table I).

**Table I : Age and Sex distribution of Critically sick neonates admitted in NICU**

Age	Male N (%)	Female N (%)	Total
0 – 2 days	49 (40.50)	24 (19.84)	73 (60.34)
3 –7 days	22 (18.18)	08 (6.61)	30 (24.79)
8 – 28 days	13 (10.74)	05 (4.13)	18 (14.87)
	84 (69.42)	37 (30.58)	121 (100)

On admission blood gas derangement(Acid-Base imbalance) was seen in 78 (64.46%) critically sick neonates, among them 33(42.30%) died (Table II). We found that Perinatal asphyxia was the common disorder 43(35.54) in this group of neonates and majority 27(22.31%) of them had acid-base imbalance. Also they had the highest 12(44.44%) mortality (Table II).

**Table II : Disease profile with Acid-Base imbalance (on admission) and percentage of the non-survival among them**

Primary disease	No. of patient (%)	Acid-Base imbalance no (%)	Non-survival among Acid-Base imbalance patients no (%)
Perinatal asphyxia	43(35.54)	27(22.31)	12(44.44)
Neonatal sepsis	39(32.23)	23(19.01)	9(39.13)
Preterm LBW	19(15.70)	15(12.40)	7(46.66)
Others	20(16.53)	13(10.74)	5(38.46)
Total	121(100.00)	78(64.46)	33(42.30)

On admission total 121 neonates were analyzed for electrolyte. Among them 30 (24.79%) babies had normal electrolyte, of which 8 (24.79%) died. Rest 91 (75.2%) babies had electrolyte abnormalities, of which 42 (46.15%) died (Table III).

Case fatality rate was highest in those with hypokalaemia. Among those 8 (100%) patients 6 (75%) died, which was followed by hyponatremia (62.5%), hypernatremia (50%), mixed (47.62%), hyperkalemia(34%) and lowest with normal electrolyte (26.67%) (Table III).

Hypokalaemia was found to have a significantly higher mortality (p=.001) when compared to those with normal electrolyte values and similar underlying disorders (Table III).

**Table III : Disease pattern with electrolyte status at admission and mortality statistics (n=121)**

Electrolyte status	Survival	Non-survival	Total	Case Fatality No (%)	Statistics
<b>Normal electrolyte</b>					
Perinatal asphyxia	3	2	5	40.00	
Neonatal sepsis	9	4	13	30.76	
Preterm LBW	8	1	9	11.11	
Others	2	1	3	33.33	
Total	22	8	30	26.67	
<b>Hyponatremia</b> p= .032					
Perinatal asphyxia	1	6	7	85.71	
Neonatal sepsis	3	2	5	40.00	
Preterm LBW	0	2	2	100.00	
Others	2	0	2	00.00	
Total	6	10	16	62.50	
<b>Hypernatremia</b> p= 0.744					
Perinatal asphyxia	0	1	0	00	
Neonatal sepsis	0	1	1	100	
Others	1	0	1	00	
Total	1	1	2	50	
<b>Hypokalemia</b> p= .001					
Perinatal asphyxia	0	1	1	100	
Neonatal sepsis	1	2	3	66.67	
Preterm LBW	0	1	1	100.00	
Others	1	2	3	66.67	
Total	2	6	8	75	
<b>Hyperkalemia</b> p= 0.251					
Perinatal asphyxia	14	6	20	30.00	
Neonatal sepsis	7	2	9	22.22	
Preterm LBW	4	3	7	42.86	
Others	4	4	8	50.00	
Total	29	15	44	34.09	
<b>Mixed</b>					
Perinatal asphyxia	7	3	10	30.00	
Neonatal sepsis	2	6	8	75.00	
Preterm LBW	0	1	1	100.00	
Others	2	0	2	00.00	
Total	11	10	21	47.62	
GRAND TOTAL	71	50	121	100.00	

Comparative observation of acid-base-electrolyte parameter was done in our study population of critically sick neonates (perinatal asphyxia and neonatal sepsis). On admission initial pH and Na<sup>+</sup> were found low, K<sup>+</sup> level was high in PNA than sepsis (statistically significant) (Table IV).

**Table IV : Acid-Base-Electrolyte parameters in Perinatal Asphyxia and Sepsis (on admission)**

	PNA(n=43) Mean±SD	Sepsis(n=39) Mean±SD	p value
pH	7.33± 0.122	7.38± 0.12	0.042 <sup>s</sup>
PCO <sub>2</sub> (mm of Hg)	32.67± 15.74	29.85± 11.71	0.364 <sup>ns</sup>
HCO <sub>3</sub> <sup>-</sup> (mmol/L)	16.83±4.91	19.31 ±10.09	0.155 <sup>ns</sup>
BE(mmol/L)	-7.14±5.17	-8.3±17.55	0.681 <sup>ns</sup>
Na <sup>+</sup> (mmol/L)	135.76 ±7.41	140.03 ±9.44	0.026 <sup>s</sup>
K <sup>+</sup> (mmol/L)	5.26 ±1.40	4.7 ±1.0	0.016 <sup>s</sup>
Cl <sup>-</sup> (mmol/L)	98.86 ±10.29	102.79 ±15.3	0.176 <sup>ns</sup>
Anion Gap (AG)	25.5±10.25	21.81±14.82	0.193 <sup>ns</sup>

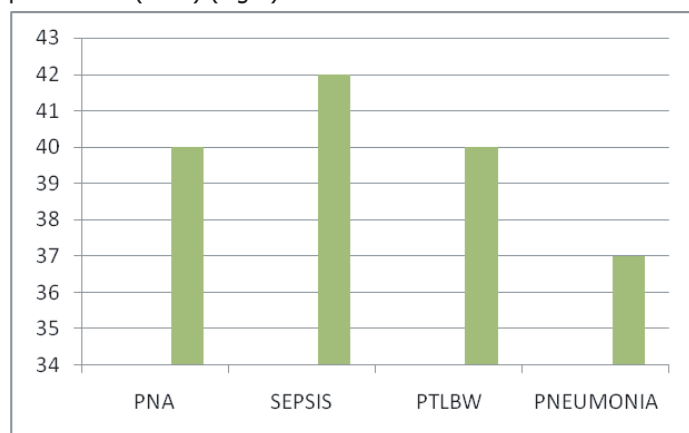
A comparative observation of blood gas status among survivors and non-survivors of critically sick neonates showed that Non-Survivors had low pH and more BE level than survivors, which was statistically significant (Table V).

**Table V : Pattern of Acid-Base parameters of Critically sick neonates (on admission) among Survivors and Non-Survivors(expired)**

	Survivors (n =71) Mean ± SD	Non-Survivors(n =50) Mean ± SD	p value
pH	7.36 ± 0.1	7.3 ± 0.19	0.011 <sup>s</sup>
PCO <sub>2</sub> (mm of Hg)	31.69 ± 11.54	33.63 ± 17.48	0.466 <sup>ns</sup>
[HCO <sub>3</sub> <sup>-</sup> ](mmo1/L)	18.03 ± 6.59	17.95 ± 10.4	0.961 <sup>ns</sup>
BE	-4.3 ± 6.88	-10.74 ±15.89	0.004 <sup>s</sup>

p value reached from unpaired t-test

Overall mortality was the highest among neonatal sepsis (44%) followed by perinatal asphyxia (42%), prematurity (40%), pneumonia (37%) (Fig 1)



**Fig 1 : Disease pattern(%) of Non-Survivors(expired) among Critically sick neonates**

**Discussion**

This six months’ prospective study was done to document the most common pattern of diseases with which the sick neonates were admitted in NICU of Dhaka Shishu Hospital and their biochemical profile as a predictor of outcome. The selection was unbiased. The data may therefore be generalized on a population of sick neonates seeking ICU care.

Perinatal asphyxia was common disorder in accordance with the epidemiological pattern observed in this region with the highest mortality followed by sepsis. The patterns of diseases in our study are comparable to a similar study done in Lahore, Pakistan.<sup>15</sup>

Among total number of admitted critically sick neonates’ preponderance of males in this age group consistent with other studies.<sup>16</sup>

In this study critically sick neonates have acid-base abnormalities(64.46%) and electrolyte imbalance(75%) are discussed to predict their outcome. Acid-base disorders in critically sick neonatal ICU patients were predict their survival by the presence of deranged acid-base variables.<sup>17, 18</sup>

Metabolic acidosis was one of the most frequent acid-base disorder occurring in non-survivors<sup>19</sup> more in perinatal asphyxia<sup>20</sup> as this study. An abnormal pH <7.2<sup>21</sup> and <7.2<sup>22</sup> can be used as a predictor factor for unfavorable short term outcome in newborns. In this study lower mean pH in non-survivors was around 7.3.

Consequently, the management of acid-base disorder always demands precise diagnosis and treatment of the underlying disease, it requires steps to combat the deviation to reduce mortality.<sup>23</sup>

Among electrolyte imbalance (75%) in critically sick neonates hyperkalemia was the commonest (48%). This finding was in contrast to a study in ICU admitted neonates.<sup>24</sup>

In 48.7% neonates with hyperkalemia there was concomitant metabolic acidosis, another important cause. The other possibilities of increased potassium release are tissue destruction, trauma, cephalhaematoma, hypothermia, bleeding, intravascular or extra vascular haemolysis, asphyxia, ischaemia and IVH.<sup>25</sup> Most of these condition were present in our study subjects.

Yuan et al. have found hyperkalemia in 44% of sick neonates which is consistent with the present study.<sup>13</sup>

Hyponatremia was the second most common electrolyte abnormality (13%) noted in this study. In a study conducted in a paediatric ICU, 9.5% of total admissions had hyponatremia.<sup>24</sup>

Hypokalemia was less common (8.79%) electrolyte abnormality observed in the present study. However, a significantly lower (3.6%) and two higher frequencies (14.8% and 13.9%)<sup>26,27</sup> were observed in other studies.<sup>25</sup>

The risk of mortality in our study is significantly higher in patients with hypokalemia (75%) in comparison to those with normal electrolyte values (26.6%). Higher risk of mortality was also observed in a prospective study of 727 sick children,<sup>26</sup> in

contrast lowest mortality with hypokalemia was reported by Rao et al.<sup>24</sup>

In our study hyponatremia was found to have a significantly higher mortality rate (62.5%) after hypokalemia which is consistent with other study.<sup>28</sup>

### Conclusion

Perinatal asphyxia constitutes major cause of admission of critically sick neonates. Mortality was the highest among neonatal sepsis followed by perinatal asphyxia. Metabolic acidosis and hypokalemia are valuable biochemical profile to predict the outcome of these neonates.

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