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Original Article

Integrative Analysis of Hematological and Biochemical Markers Related to Ventilation Outcomes in Critically Ill Infants

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ABSTRACTs

Background: *Critically ill infants often require mechanical ventilation, and identifying predictors of outcomes in this vulnerable population remains a clinical priority.* ***Objective:*** *To evaluate the relationship between hematological and biochemical markers and ventilation outcomes in infants up to 2 months of age.* ***Methods & Materials:*** *This prospective observational study was conducted in the Department of Intensive Care Unit of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh, from January 2020 to December 2020. This study included 50 critically ill young infants up to 2 months of age who required mechanical ventilation. Of these infants, 37 (74.0%) died during the study period, while 13 (26.0%) survived.* ***Results:*** *The study found no statistically significant differences between the two groups regarding age, gestational age, birth weight, or sex. Hematological markers, including WBC count, hemoglobin, and platelet count, showed no significant differences between the two groups before ventilation and before extubation or death ($p > 0.05$). Similarly, RBS, CRP, serum creatinine, and blood urea levels did not demonstrate a statistically significant association with outcome ($p > 0.05$). However, hypernatremia (serum sodium >145 mmol/L) was significantly more prevalent in the death group (89.2%) compared to the survival group (61.5%) and was the only parameter that showed a statistically significant correlation with mortality ($p = 0.039$).* ***Conclusion:*** *In this study, most hematological and biochemical markers, including WBC count, platelet count, hemoglobin, RBS, CRP, serum creatinine, and blood urea, did not show a significant association, while elevated serum sodium levels were significantly associated with mortality in ventilated infants.*

Keywords: *Mechanical ventilation, Ill infants, Hemoglobin, CRP, Electrolyte*

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INTRODUCTION

Critically ill children often present with multi-organ dysfunction and require special care in pediatric intensive care units (PICUs) to improve outcomes [1]. Intensive care medicine primarily focuses on managing acute, life-threatening conditions [2]. In recent years, both pediatric and neonatal intensive care services have seen significant advancements in Bangladesh [3].

Neonatal mortality remains a significant global health concern, with the majority of deaths occurring in low-income countries. Nearly one million of these deaths are attributed to infectious causes such as neonatal sepsis, meningitis, and pneumonia [4]. The World Health Organization (WHO) reports that approximately four million neonates die annually within the first 28 days of life, with 75% of these deaths occurring during the first week postpartum [5,6]. Globally, the primary causes of neonatal mortality have been estimated to include infections (35%), complications of preterm birth (28%), intrapartum-related events (24%), and perinatal asphyxia (23%) [7]. Among these, sepsis is considered the most prevalent cause, accounting for 30–50% of neonatal deaths in developing regions [7].

In addition to infectious causes, respiratory complications are common among preterm neonates, particularly those born at <28 weeks of gestation. These infants frequently require assisted ventilation due to immature pulmonary function. The evolution of neonatal respiratory support has been central to advancements in neonatal-perinatal medicine and has significantly improved the survival rates of infants who previously had a very little chance of survival. Mechanical ventilation is a critical life-saving intervention in neonatal intensive care units (NICUs), which is employed for critically ill neonates experiencing respiratory failure [8].

A substantial proportion of neonates admitted to NICUs require mechanical ventilation and this subgroup is associated with a notably high mortality rate. Reported survival rates among mechanically ventilated neonates vary, with studies by Trotman and by Karthikeyan and Hossain indicating survival rates of 64% and 67.9%, respectively [9,10]. These figures remain lower than those reported in high-income settings [11].

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Despite its life-saving potential, mechanical ventilation is also associated with several complications, including nosocomial infections, bronchopulmonary dysplasia, brain injury, retinopathy of prematurity, and long-term neurodevelopmental impairments [8,12]. Moreover, studies from developing nations indicate mortality rates among ventilated neonates ranging from 40% to 60% [13,14]. Previous studies reported that VAP associated mortality in neonates ranges from 13% to 55% [15]. In Bangladesh, Hossain et al. reported a higher mortality of 70.6% among ventilated neonates[3].

Factors such as age, weight, clinical condition and illness severity influence the outcomes of mechanical ventilation. Prolonged PICU stays and invasive procedures increase the risk of nosocomial infections, further elevating mortality, particularly in those with respiratory disorders [16,17].

In addition, haematological and biochemical markers can be described as potential indicators of disease severity and prognosis in critically ill patients. Parameters such as white blood cell (WBC) count, hemoglobin, platelet count, random blood sugar (RBS), C-reactive protein (CRP), serum creatinine and blood urea are routinely measured in clinical settings and they may reflect underlying inflammatory, infectious or metabolic disturbances. Electrolyte imbalances are also common among critically ill pediatric patients and significantly affect prognosis [18]. Abnormal levels of sodium, potassium, calcium, magnesium, and phosphorus can impair cellular function, leading to increased mortality [19,20].

However, the association between these markers and ventilation outcomes in critically ill infants under two months of age remains poorly defined. Understanding the prognostic value of these laboratory parameters may aid in early risk stratification and clinical decision-making.

OBJECTIVES

This study aimed to evaluate the relationship between selected hematological and biochemical markers and the outcomes of mechanical ventilation in critically ill infants.

METHODS & MATERIALS

This prospective observational study was conducted in the Department of Intensive Care Unit of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh, from January 2020 to December 2020. In this study, we included 50 critically ill young infants up to 2 months of age who required mechanical ventilation in the Intensive Care Unit of Dhaka Shishu Hospital.

These are the following criteria to be eligible for enrollment as our study participants:

Inclusion criteria

a) All critically ill young infants aged ≤2 months
b) Infants who received mechanical ventilation in the Intensive Care Unit of Dhaka Shishu Hospital

Exclusion criteria

a) Infants more than 2 months old
b) Young infants who required ventilation for surgical intervention
c) Young Infants with cyanotic congenital heart disease
d) Infants with congenital malformations.

Data Collection Procedure: Legal guardians or parents of infants were asked to be included in the present study. A written consent was obtained after an explanation of the study procedure. The study included fifty young infants consecutively placed on mechanical ventilation during the study period. Before initiating ventilation, relevant investigations such as arterial blood gas (ABG) analysis, chest X-ray, and other necessary tests were performed and documented. The infants were continuously monitored clinically, assessing heart rate, respiratory rate, temperature, and capillary refill time (CRT) using a cardiac monitor and pulse oximetry. The initial parameters, including respiratory rate, peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2) and inspiratory time were set according to the needs of patients and adjusted based on clinical findings, chest X-ray results and ABG values. Sedation was administered when necessary.

After 2 hours of ventilation, ABG was done to adjust the parameters. Then, subsequent parameters (PIP, PEEP, Rate of ventilation, FiO2) on mechanical ventilation were modified according to the need for oxygenation and ventilation through SpO2 and blood gas analysis. Throughout ventilation, biochemical parameters including serum electrolytes, creatinine, urea, C-reactive protein (CRP) and hematological profiles (complete blood count), were monitored based on the clinical status of each infant. All infants were observed for complications and were followed until the time of extubation or death.

Statistical Analysis: Quantitative data was expressed as mean and standard deviation, and qualitative data was expressed as frequency distribution and percentage. The Odds ratio, chi-square test and student "t" test were used to analyze. P-value <0.05 was considered significant. Statistical analysis was performed by using SPSS 25 (Statistical Package for Social Sciences) for Windows version 10. This study was ethically approved by the Institutional Review Committee of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.

RESULTS

In this study, we initially enrolled 50 critically ill young infants up to 2 months of age who required mechanical ventilation. During the study, nearly three-fourths of the patients, 37 (74.0%) died, while 13 infants (26.0%) survived. Therefore, the study aimed to evaluate the relationship between hematological and biochemical markers and ventilation outcomes in the death and survival groups.

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Table – I: Demographic characteristics of the study patients (*n*=50)

Demographic Variables	Death (n=37) n (%)	Survival (n=13) n (%)	P-value
Age			
≤15 days	27 (73)	7 (53.8)	
16-30 days	7 (18.9)	2 (15.4)	
31-45 days	2 (5.4)	3 (23.1)	
>45 days	1 (2.7)	1 (7.7)	
Mean±SD (days)	14.2±10.1	20.2±18.2	0.145
Gestational age			
<34 weeks	7 (18.9)	1 (7.7)	0.321
>34 weeks	30 (81.1)	12 (92.3)	
Weight			
<2500 gm	20 (54.1)	4 (30.8)	0.148
>2500 gm	17 (45.9)	9 (69.2)	
Sex			
Male	22 (59.5)	10 (76.9)	0.216
Female	15 (40.5)	3 (23.1)	

Table I summarizes the demographic characteristics of the study population, comparing infants who died (n=37) with those who survived (n=13) following mechanical ventilation. The majority of infants in both groups were ≤15 days old accounting for 73.0% in the death group and 53.8% in the survival group. The mean age was slightly higher in the survival group (20.2 ± 18.2 days) compared to the death group (14.2 ± 10.1 days). In terms of gestational age, 81.1% of infants in the death group and 92.3% in the survival group were born after 34 weeks of gestation. Low birth weight (<2500 g) was observed in 54.1% of infants in the death group and 30.8% in the survival group, while the remaining had birth weights ≥2500 g. Regarding sex distribution, males constituted a higher proportion in both groups with 59.5% in the death group and 76.9% in the survival group. None of the demographic variables showed statistically significant differences between the two groups.

Table – II: Relation between hemoglobin and outcome (*n*=50)

Hemoglobin (g/dl)	Death (n=37)		Survival (n=13)		OR (95% CI)	P value
	n	%	n	%		
Before ventilation						
<11.5	9	24.3	4	30.8	0.72 (0.18-2.92)	[a]0.453[ns]
>11.5	28	75.7	9	69.2	0.72 (0.18-2.92)	[a]0.453[ns]
Mean±SD	12.8 ±1.9		12.3±1.8			[b]0.435[ns]
Before Extubation/ death						
<11.5	15	40.5	3	23.1	2.27 (0.53-9.66)	[a]0.216[ns]
>11.5	22	59.5	10	76.9	2.27 (0.53-9.66)	[a]0.216[ns]
Mean±SD	12.0 ±1.5		12.9 ±1.6			[b]0.056[ns]

ns = not significant, [a]P value reached from chi-square test, [b]P value reached from unpaired t-test

Table II shows that before ventilation, the mean hemoglobin level was 12.8 ± 1.9 g/dL in the death group and 12.3 ± 1.8 g/dL in the survival group. Before extubation or death, the mean hemoglobin level was 12.0 ± 1.5 g/dL in the death group and 12.9 ± 1.6 g/dL in the survival group. The differences between the two groups were not statistically significant (p > 0.05).

Table – III: Relation between hematological markers (WBC, platelet) and outcome (*n*=50)

Hematological markers	Death (n=37)		Survival (n=13)		Odds ratio (95% CI)	P value
WBC (/cumm)						
Before ventilation						
<11000	8	21.6	6	46.2	0.32 (0.08-1.23)	[a]0.093[ns]
>11000	29	78.4	7	53.8	0.32 (0.08-1.23)	[a]0.093[ns]
Mean±SD	16135.1 ±8271.6		12892.3±4007.4			[b]0.183[ns]
Before Extubation/ death						
<11000	21	56.8	10	76.9	0.39 (0.09-1.67)	[c]0.170[ns]
>11000	16	43.2	3	23.1	0.39 (0.09-1.67)	[c]0.170[ns]

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Mean±SD	11459.5±9476.9		9476.9 ±3545.7			[b]0.453[ns]
Platelet (/cumm)						
Before ventilation						
<150000	19	51.4	5	38.5	1.69 (0.46-6.14)	[a]0.424[ns]
>150000	18	48.6	8	61.5	1.69 (0.46-6.14)	[a]0.424[ns]
Mean±SD	134110.8±78216.0		175230.8±91676.2			[b]0.125[ns]
Before Extubation/ death						
<150000	20	54.1	5	38.5	1.88 (0.52-6.84)	[a]0.333[ns]
>150000	17	45.9	8	61.5	1.88 (0.52-6.84)	[a]0.333[ns]
Mean±SD	131567.6 ±96817.9		165230.8±53511.9			[b]0.241[ns]

ns = not significant, [a]P value reached from chi-square test, [b]P value reached from unpaired t-test, [c]P value reached from Fisher's exact test

Table III shows that before ventilation, the mean white blood cell (WBC) count was 16,135.1 ± 8,271.6 /cumm in the death group and 12,892.3 ± 4,007.4 /cumm in the survival group. Before extubation or death, the mean WBC count decreased to 11,459.5 ± 9,476.9 /cumm in the death group and 9,476.9 ± 3,545.7 /cumm in the survival group. These differences were also not statistically significant (p > 0.05). Regarding platelet counts, the mean value before ventilation was 134,110.8 ± 78,216.0 /cumm in the death group and 175,230.8 ± 91,676.2 /cumm in the survival group. Before extubation or death, the mean platelet count was 131,567.6 ± 96,817.9 /cumm in the death group and 165,230.8 ± 53,511.9 /cumm in the survival group. Again, no statistically significant difference was found between the groups (p > 0.05).

Table – IV: Relation between biochemical markers (RBS, CRP, serum creatinine, blood urea) and outcome (*n*=50)

Biochemical markers	Death (n=37)		Survival (n=13)		Odds ratio (95% CI)	P value
RBS (mmol/L)	**n**	**%**	**n**	**%**		
<3	13	35.1	3	(23.1	1.80(0.42-7.74)	0.421[ns]
>3	24	64.9	10	76.9		
CRP (mg/L)						
Prolonged (>5)	31	83.8	9	69.2	2.29(0.52-9.95)	0.266[ns]
Normal (<5)	6	16.2	4	30.8		
Serum creatinine (µmol/L)						
>110	33	89.2	10	76.9	2.47(0.47-12.96)	0.283[ns]
<110	4	10.8	3	23.1		
Blood urea (mmol/L)	n	%	n	%		
>5.8	10	27.0	6	46.2	0.43(0.11-1.60)	0.209[ns]
<5.8	27	73.0	7	53.8		

ns = not significant, P-value reached from Fisher's exact test

Table IV shows that elevated random blood sugar (RBS) levels (>3 mmol/L) were observed in 24 patients (64.9%) in the death group and 10 patients (76.9%) in the survival group. However, this difference was not statistically significant (p > 0.05). C-reactive protein (CRP) levels were elevated in 31 patients (83.8%) in the death group and 9 patients (69.2%) in the survival group. However, this difference was not statistically significant (p > 0.05). The table also indicates that low serum creatinine levels (<40 µmol/L) were observed in 4 patients (10.8%) in the death group and 3 patients (23.1%) in the survival group. No significant association was found between serum creatinine levels and outcomes [p = 0.283, OR = 2.47 (95% CI: 0.47–12.96)]. Additionally, blood urea levels <5.8 mmol/L were recorded in 27 patients (73.0%) in the death group and 7 patients (53.8%) in the survival group. This difference, too, was not statistically significant (p > 0.05).

Table – V: Relation between Electrolytes (sodium, potassium, calcium) and outcome (*n*=50)

Electrolytes	Death (n=37) n (%)	Survival (n=13) n (%)	Odds Ratio (95% CI)	P-value
Serum sodium (mmol/L)				
>145	33 (89.2)	8 (61.5)	0.19 (0.04–0.89)	0.039[s]
<135	4 (10.8)	5 (38.5)		
Serum potassium (mmol/L)				
>5.5	34 (91.9)	11 (84.6)	2.06 (0.30–13.97)	0.389[ns]
<3.5	3 (8.1)	2 (15.4)		
Serum calcium (mmol/L)				
>3.0	31 (83.7)	7 (53.8)	3.16 (0.20–11.68)	0.218[ns]
<1.2	6 (16.2)	6 (46.1)		

s=significant, ns = not significant, P-value reached from Fisher's exact test

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Table V shows that among the infants who died, 89.2% had hypernatremia (serum sodium >145 mmol/L), compared to 61.5% in the survival group. Regarding potassium levels, hyperkalemia (serum potassium >5.5 mmol/L) was noted in 91.9% of the death group and 84.6% of the survival group. Hypercalcemia (serum calcium >3.0 mmol/L) was observed in 83.7% of patients who died compared to 53.8% of survivors. Among the electrolytes analyzed, only serum sodium levels showed a statistically significant relationship with patient outcomes (p = 0.039).

DISCUSSION

In the present study, the mean age was slightly higher in the survival group (20.2 ± 18.2 days) compared to the death group (14.2 ± 10.1 days). This finding aligns with observations from various global studies. For instance, the reported median age at death was 4 days in Australia [21], 4.4 days in Nigeria [22] and 10.5 days in Portugal [23]. Musooko et al. reported that 45.9% of infants with early neonatal deaths in Uganda died within the first day of life[24].

Regarding sex distribution, a male predominance was observed in both the death (59.5%) and survival (76.9%) groups. Similar trends have been reported in numerous studies. For example, a study conducted in a PICU noted a male predominance of 59.6% [25]. Hossain et al. reported that among ventilated neonates, 58.8% were male and 41.2% female[3]. Nyirasafari et al. found that males constituted 56% of non-survivors and 54% of survivors, suggesting a slight male dominance in both outcome groups [26].

In terms of hematological parameters, our findings revealed no statistically significant difference in mean hemoglobin levels between the death and survival groups. This aligns with findings by Zilberg et al., who noted that while 75% of critically ill patients had hemoglobin levels above 10 g/dL at admission, 67% still received packed red blood cell (pRBC) transfusions. Their study found 21% increase in the risk of hospital death associated with pRBC transfusion, suggesting that transfusions may serve as a marker of illness severity rather than a direct cause of mortality [27]. A study by Iqbal et al found that hypoglycemia, neutropenia, and thrombocytopenia had a statistically significant correlation with mortality in their patients [28]. The prognostic significance of these parameters has also been recognized by others [29-31].

Ye et al. identified several laboratory markers, such as procalcitonin, CRP, hemoglobin, platelet count, RDW, PDW, and lactic acid, as significantly associated with mortality. Their logistic regression analysis highlighted platelet count, lactic acid, and procalcitonin as independent predictors of death in children [32].

In this study, C-reactive protein (CRP) levels were elevated in both groups, with a higher percentage in the death group (83.8%) compared to the survival group (69.2%), although this difference was not statistically significant. Regarding the inflammatory response, Bose et al. investigated the temporal association between mechanical ventilation and systemic inflammation, revealing elevated markers such as ICAM-1, TNF-α, IL-8, and CRP in infants requiring prolonged respiratory support [33].

Increased CRP levels were associated with an increased possibility of using mechanical ventilation in premature infants. Previous studies have determined that increased CRP levels could be a useful marker of critical illness, like respiratory distress in neonates and coronavirus disease 2019 (COVID-19) in children [34,35]. A study by Yue et al found that along with elevated C-reactive protein (CRP) levels (OR = 1.044; 95% CI: 1.003–1.086; *P* = 0.036), higher respiratory rate (OR = 1.292; 95% CI: 1.238–1.355; *P* < 0.001), and the presence of patent ductus arteriosus (PDA) (OR = 2.174; 95% CI: 1.185–3.972; *P* = 0.012) were also independently associated with an increased risk of mechanical ventilation[8]. Another study found that increased CRP levels were associated with a decrease in ventilator-free days in children[36]. Herold et al also found that higher CRP levels could increase the need for mechanical ventilation in COVID-19 patients[37].

Renal function also plays a pivotal role in outcomes. Alkandari et al. found that acute kidney injury (AKI), particularly stages 2 and above, was independently associated with longer PICU stays and prolonged mechanical ventilation, regardless of the baseline serum creatinine measurement method [38]. Although our study did not find significant associations between serum creatinine or urea and survival outcomes, these findings underscore the importance of early AKI detection.

In this study, a notable finding was the significantly higher incidence of hypernatremia in the death group (89.2%) compared to the survival group (61.5%), with a p-value of 0.039. This suggests that elevated serum sodium levels may be linked to an increased mortality risk in mechanically ventilated infants. This is consistent with existing literature that reports varying incidences of dysnatremias (either hyponatremia or hypernatremia) in critical care settings. For instance, the prevalence of dysnatremias in ICU patients is approximately 30% [39,40], with hyponatremia typically being more common than hypernatremia in several studies [41,42].

Our study also observed hypocalcemia in a few cases, which does not align with the previously reported incidences of 40% and 47.5% in critically ill children [43,44]. Additionally, hyperkalemia was noted in 91.9% of the death group and 84.6% of the survival group. A study by Agarwal et al. reported that the rate of hyperkalemia was 16.12% in critically ill children [44].

LIMITATIONS OF THE STUDY

Our study was a single-center study, so it may not reflect the exact picture of the country. We took a small sample size due to the short study period. After evaluating those survived neonates, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

CONCLUSION AND RECOMMENDATIONS

The study found no statistically significant differences in hematological and biochemical markers between the death

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and survival groups. Elevated serum sodium was the only parameter significantly associated with mortality (p = 0.039). While other electrolyte abnormalities like hyperkalemia and hypercalcemia were more common in non-survivors but were not statistically significant.

Further research using a prospective and longitudinal study design with a larger sample size is needed to validate the findings of our study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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