

Identifying Risk Factors Associated with Mortality in Critically Ill Ventilated Infants at a Tertiary Care Setting

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ARTICLE INFO

Received: 21 Feb 2026
Accepted: 26 Feb 2026
Published Online: 27 Feb 2026

DOI: 10.5281/zenodo.18814728

Volume: 9, Number: 1, Page: 35-40

e-ISSN: 2789-5912
ISSN: 2617-0817

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ABSTRACT

Background: Critically ill infants requiring mechanical ventilation face a high risk of mortality, especially in resource-limited settings. Identifying modifiable risk factors is crucial to improving survival outcomes. **Objective:** To evaluate risk factors associated with mortality among ventilated infants in a tertiary care hospital. **Methods & Materials:** This 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. Among these infants, 37 (74.0%) died during the study period, while 13 (26.0%) survived. **Results:** The study showed no significant differences in age, gestational age, birth weight, or sex distribution between the two groups. Higher initial ventilatory settings, including $\text{FiO}_2 > 80\%$, PIP > 18 cmH₂O, and PEEP > 5 cmH₂O, were significantly associated with death ($p < 0.01$). Hyponatremia ($\text{Na}^+ > 145$ mmol/L) also showed a significant association with mortality ($p = 0.039$). However, severe respiratory distress before extubation and ventilation duration > 5 days were significantly associated with poor outcomes. Multivariable regression analysis confirmed initial high PIP, low bicarbonate, severe respiratory distress, and prolonged ventilation as independent predictors of mortality. **Conclusion:** Infants on mechanical ventilation with high initial settings, metabolic acidosis, severe respiratory distress, and prolonged ventilation have increased mortality risk. Early recognition and management of these factors may improve survival outcomes.

Keywords: Neonatal Mortality, Mechanical Ventilation, Respiratory Distress, NICU, Risk Factors.

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INTRODUCTION

Infant mortality remains a major global health concern, especially in low- and middle-income countries. Infant mortality rate defined as the probability of dying between birth and age one, is a key indicator of child health progress [1]. Globally, infant mortality has declined significantly dropping from an estimated 8.9 million deaths in 1990 to approximately 4.5 million in 2015 [2].

In Bangladesh, although progress has been made, reduction in infant mortality has not kept pace with the decrease in under-five mortality. From 1993 to 2014, infant mortality dropped from 87 to 38 deaths per 1,000 live births [3,4]. However, this decline is slower than the reduction in under-five mortality which dropped from 133 to 46 per 1,000 over the same period [3].

A large population-based survey across 56 countries from 1990 to 2002 highlighted key factors that contribute to infant mortality worldwide. These include being a firstborn child, having a short birth interval, male sex, multiple gestation, and living in rural settings. Additionally, infants born to mothers with lower levels of education or those living far from health services are at a greater risk of dying in their first year [5,6]. Neonatal mortality is a significant

contributor to infant deaths. According to the Health Bulletin 2017 of the Directorate General of Health Services (DGHS), the neonatal mortality rate in Bangladesh was reported as 19 per 1,000 live births (SVRS 2016) and 28 per 1,000 live births (BDHS 2014) [4]. Globally, the leading causes of neonatal mortality include preterm birth, birth asphyxia, sepsis, and pneumonia [7,8]. Although the exact causes of neonatal deaths are sometimes unclear, studies consistently identify sepsis, asphyxia, birth injuries, neonatal tetanus, prematurity, congenital anomalies, and undetermined factors as major contributors [9]. In developing countries, preterm birth, infections, and birth asphyxia remain the predominant causes, with mortality rates ranging between 40% and 60% [10,11].

Mechanical ventilation (MV) is commonly used in the management of critically ill infants, especially those with severe respiratory infections. Although MV itself is not a direct cause of complications, it is an essential intervention in cases of severe respiratory failure, which can be associated with multiple organ dysfunction [12,13]. While MV can increase the risk of secondary complications such as ventilator-associated pneumonia, these are often consequences of the underlying illness rather than the ventilation itself [14,15]. MV

remains a vital therapy that provides crucial respiratory support to critically ill infants and is not a cause of additional infections that might complicate the clinical course [16].

Several studies have reported that respiratory failure from respiratory illnesses is the most common indication for mechanical ventilation in pediatric patients, including infants up to two months of age. [17-19] Factors such as age, weight, clinical condition, and severity of illness all influence the outcomes of mechanical ventilation. Extended stays in the pediatric intensive care unit (PICU) and the need for invasive procedures can increase the risk of nosocomial infections, contributing to higher mortality rates, particularly in those with respiratory disorders [17,20].

Despite significant advancements in healthcare, infant mortality remains shaped by a complex interplay of risk factors. Understanding these risk factors is essential for designing effective interventions to reduce infant mortality and improve child health outcomes worldwide.

Objectives

The objective of this study was to evaluate the risk factors associated with mortality among ventilated infants in a tertiary care hospital.

METHODS & MATERIALS

This 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.

Inclusion criteria

- All critically ill young infants (age 0 day to 2 months)
- Infants who received mechanical ventilation in the Intensive Care Unit of Dhaka Shishu Hospital
- Infants whose parents or guardians were willing to participate

Exclusion criteria

- Young infants who required ventilation for surgical intervention
- Young Infants with cyanotic congenital heart disease
- Infants with congenital malformations were excluded from our study.

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 who were consecutively placed on mechanical ventilation. Before initiation, investigations such as ABG, chest X-ray, and other relevant tests were performed. Infants were

continuously monitored using clinical assessments and devices like cardiac monitors and pulse oximetry. Ventilator parameters, including respiratory rate, PIP, PEEP, FiO₂, and inspiratory time, were set according to each patient and adjusted based on clinical signs, chest X-rays, and ABG results. 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 20 oxygenation and ventilation through SpO₂ and blood gas analysis. Patients were extubated when clinically stable, both hemodynamically & neurologically, having self-respiration, maintaining oxygen saturation, normal chest X-ray & with low ventilator parameters or after gradual weaning. All infants were observed for complications and followed until extubation or death.

Ethical Considerations

Ethical approval was obtained from the Ethical Review Committee of Bangladesh Shishu Hospital & Institute. Informed consent was taken from patients or their legal guardians before enrollment. Confidentiality of patient information was strictly maintained and data were used solely for research purposes.

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, student “t” test, and multiple logistic regressions were used to analyze the data. A p-value <0.05 was considered significant. Statistical analysis was performed by using SPSS 25 (Statistical Package for Social Sciences) for Windows version 10.

RESULTS

In the present 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. The present study was done to identify risk factors associated with mortality in critically ill ventilated infants.

Table 1 shows that 27 patients in the death group and 7 in the survival group were aged ≤15 days. Most patients in both groups had a gestational age >34 weeks, 30 (81.1%) and 12 (92.3%) in the death and survival groups, respectively, with no statistically significant difference between the groups (p > 0.05). Low birth weight (<2500 g) was observed in 20 (54.1%) patients in the death group and 4 (30.8%) in the survival group, again showing no significant difference (p > 0.05). Male infants were predominant in both groups, comprising 59.5% of the death group and 76.9% of the survival group; however, the difference was not statistically significant (p > 0.05).

Table 1
Demographic characteristics of the study patients (n=50).

Demographic Variables	Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	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 ^{ns}
Gestational age				
<34 weeks	7 (18.9)	1 (7.7)	2.8(0.31-25.26)	0.321 ^{ns}
>34 weeks	30 (81.1)	12 (92.3)		
Weight				
<2500 gm	20 (54.1)	4 (30.8)	2.6(0.69-10.15)	0.148 ^{ns}
>2500 gm	17 (45.9)	9 (69.2)		
Sex				
Male	22 (59.5)	10 (76.9)	0.44 (0.10-1.87)	0.216 ^{ns}
Female	15 (40.5)	3 (23.1)		

ns= non-significant, ^aP value reached from unpaired t-test, s= significant, ^bP value reached from Fisher's exact test

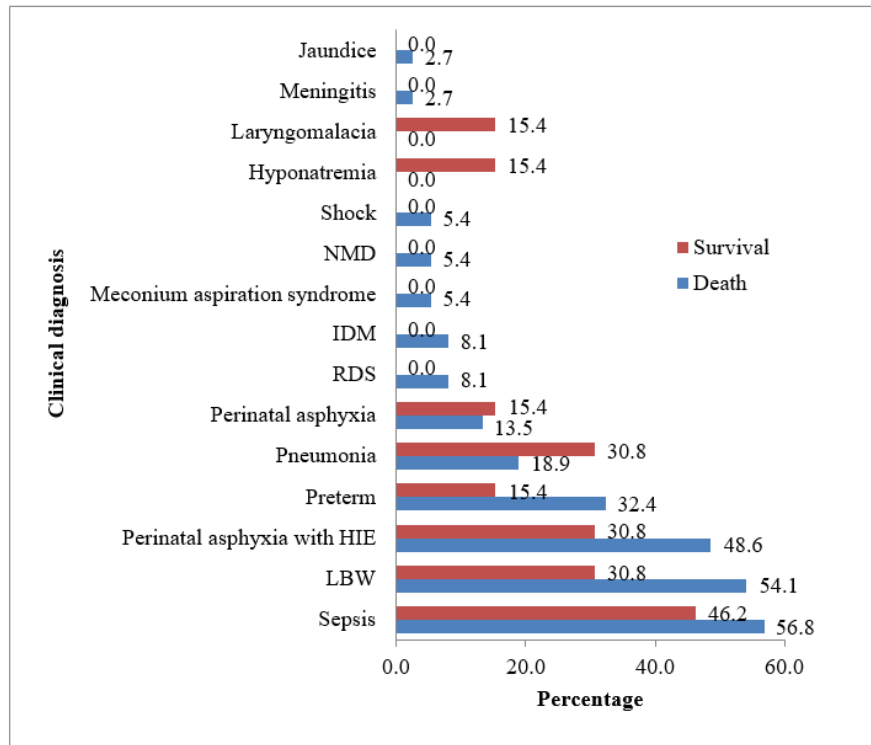


Figure 1 Clinical diagnosis of the study patients (n=50).

Figure 1 shows that the majority of 21(56.8%) patients had sepsis in the death group and 6(56.2%) in the survival group. Twenty (54.1%) patients were low birth weight in the death group and 4(30.8%) in the survival group, followed by 48.6% & 30.8% had perinatal asphyxia in the death and survival group, respectively. Clinical diagnoses were not statistically significant (p>0.05) between the two groups.

Table II shows that among the ventilated infants, several initial clinical and

biochemical parameters were significantly associated with mortality. A higher initial fraction of inspired oxygen (FiO₂ >80%) was observed in 97.3% of deaths compared to 46.2% of survivors (OR: 42, 95% CI: 4.35–405.14; p = 0.001). Similarly, peak inspiratory pressure (PIP >18 cmH₂O) and positive end-expiratory pressure (PEEP >5 cmH₂O) were significantly higher among non-survivors, both showing strong associations with mortality (PIP OR: 35, p = 0.001; PEEP OR: 13, p = 0.002). Infants with bicarbonate (HCO₃) levels <15 mmHg

and base excess (BE) values <-10 had significantly higher mortality (HCO₃ OR: 7.88, p = 0.003; BE OR: 4.98, p = 0.019), reflecting a correlation between metabolic acidosis and adverse outcomes. Furthermore, hyponatremia (serum sodium >145 mmol/L) was significantly more common among those who died (89.2% vs. 61.5%), and was associated with reduced odds of survival (OR: 0.19, 95% CI: 0.04–0.89; p = 0.039).

Table II

Relation between initial FiO₂, PIP, PEEP, HCO₃, BE, serum sodium and outcome of ventilated patients (n=50).

Parameters	Death (n=37) n (%)	Survival (n=13) n (%)	Odds Ratio (95% CI)	P-value
FiO₂ (%)				
>80	36 (97.3%)	6 (46.2%)	42 (4.35–405.14)	0.001 ^s
<80	1 (2.7%)	7 (53.8%)		
PIP (cmH₂O)				
>18.0	32 (86.4%)	2 (15.4%)	35 (5.95–208.14)	0.001 ^s
<18.0	5 (13.6%)	11 (84.6%)		
PEEP (cmH₂O)				
>5.0	26 (70.3%)	2 (15.4%)	13 (2.46–68.60)	0.002 ^s
<5.0	11 (29.7%)	11 (84.6%)		
HCO₃ (mmHg)				
<15	26 (70.3%)	3 (23.1%)	7.88 (1.81–34.28)	0.003 ^s
>15	11 (29.7%)	10 (76.9%)		
BE				
<-10	28 (75.7%)	5 (38.5%)	4.98 (1.30–19.31)	0.019 ^s
>-10	9 (24.3%)	8 (61.5%)		
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)		

^s= significant, P value reached from Fisher's exact test.

Table III shows that metabolic acidosis before ventilation was significantly associated with mortality, with 75.7% of deaths occurring in infants with this condition compared to 38.5% of survivors (OR: 4.07, 95% CI: 1.09–15.20; p = 0.019). A similar pattern was observed

before extubation/death, where metabolic acidosis was present in 51.4% of those who died versus 15.4% of survivors (OR: 5.81, 95% CI: 1.13–29.89; p = 0.024). Before ventilation, severe respiratory distress was present in 35.1% of those who died and 30.8% of survivors, showing no significant

difference (OR: 1.21; p = 0.775). In contrast, severe respiratory distress before extubation/death was more common in non-survivors (43.2%) than in survivors (7.7%), and this difference was statistically significant (OR: 9.14, 95% CI: 1.07–77.80; p = 0.04).

Table III
Relation between acidosis, respiratory distress, and outcome (n=50).

Acidosis	Death (n=37)		Survival (n=13)		Odds ratio (95% CI)	P value
	n	(%)	n	(%)		
Before ventilation						
Metabolic acidosis	28	(75.7)	5	(38.5)	4.07 (1.09-15.20)	^a 0.019 ^s
Respiratory acidosis	3	(8.1)	1	(7.7)	1.06 (0.10-11.18)	^b 0.725 ^{ns}
Before extubation/ death						
Metabolic acidosis	19	(51.4)	2	(15.4)	5.81 (1.13-29.89)	^b 0.024 ^s
Respiratory acidosis	5	(13.5)	1	(7.7)	1.88 (0.20-17.74)	^b 0.503 ^{ns}
Respiratory Distress						
Before Ventilation						
Severe	13	(35.1)	4	(30.8)	1.21 (0.31-4.73)	^b 0.775 ^{ns}
Moderate	24	(64.9)	9	(69.2)		
Before Extubation/Death						
Severe	16	(43.2)	1	(7.7)	9.14 (1.07-77.80)	^b 0.04 ^s
Moderate	21	(56.8)	12	(92.3)		

s= significant, ns= not significant, ^aP value reached from Chi square test, ^bP value reached from Fisher's exact test.

In Table IV, a heart rate >130 bpm was observed in 45.9% of neonates who died, compared to 30.8% of survivors. However, this difference was not statistically significant (OR: 1.91, 95% CI: 0.49–7.33; p = 0.344). Only 13.5% of non-survivors had HR >130 bpm before death, while just

7.7% of survivors had elevated HR at extubation. Again, this difference was not statistically significant (OR: 1.87, 95% CI: 0.19–17.74; p = 0.583). Delayed CRT (>3 seconds) was found in 27.0% of deaths and 15.4% of survivors (OR: 2.03, 95% CI: 0.38–10.84; p = 0.404), showing no

significant association. Delayed CRT was more frequent in the death group (32.4%) than in survivors (7.7%). However, this association did not reach statistical significance (OR: 5.76, 95% CI: 0.66–49.59; p = 0.111).

Table IV
Relation between heart rate, CRT, and outcome of ventilated patients (n=50).

Heart Rate (bpm)	Death (n=37) n (%)	Survival (n=13) n (%)	Odds Ratio (95% CI)	P Value
Before Ventilation				
>130	17 (45.9%)	4 (30.8%)	1.91 (0.49-7.33)	^a 0.344 ^{ns}
<130	20 (54.1%)	9 (69.2%)		
Before Extubation/Death				
>130	5 (13.5%)	1 (7.7%)	1.87 (0.19-17.74)	^a 0.583 ^{ns}
<130	32 (86.5%)	12 (92.3%)		
CRT (sec)				
Before Ventilation				
Delayed (>3 sec)	10 (27.0%)	2 (15.4%)	2.03 (0.38-10.84)	^b 0.404 ^{ns}
Normal (<3 sec)	27 (73.0%)	11 (84.6%)		
Before Extubation/Death				
Delayed (>3 sec)	12 (32.4%)	1 (7.7%)	5.76 (0.66-49.59)	^b 0.111 ^{ns}
Normal (<3 sec)	25 (67.6%)	12 (92.3%)		

ns= not significant, ^aP-value reached from chi-square test, ^bP-value reached from Fisher's exact test.

Table V shows that neonates ventilated for more than 5 days had a significantly higher mortality rate (43.2%) compared to survivors (7.7%). This association was

statistically significant (OR: 9.14, 95% CI: 1.07–77.80; p = 0.04). Although a greater proportion of deaths (67.6%) occurred in those with ICU stays longer than 7 days

compared to survivors (46.2%), the association was not statistically significant (OR: 2.43, 95% CI: 0.66–8.82; p = 0.177).

Table V
Relation between duration of ventilation and ICU stay and outcome (n=50).

Duration of Ventilation (days)	Death (n=37) n (%)	Survival (n=13) n (%)	Odds Ratio (95% CI)	P-value
>5	16 (43.2%)	1 (7.7%)	9.14 (1.0744-77.803)	0.04 ^s
<5	21 (56.8%)	12 (92.3%)		
Duration of ICU Stay (days)				
>7	25 (67.6%)	6 (46.2%)	2.43 (0.66-8.82)	0.177 ^{ns}
<7	12 (32.4%)	7 (53.8%)		

s= significant, ns=non-significant, P-value reached from Fisher's exact test

Table VI shows that initial high PIP, low bicarbonate, severe respiratory distress, and duration of ventilation (>5 days) were identified as significant independent

predictors of mortality in neonates ($p < 0.05$). These factors may serve as important markers for early identification of high-risk patients and tailoring of

intensive care strategies. Other variables were not found to be significantly ($p > 0.05$) associated with death in patients.

Table VI
Multivariable regression analysis for prediction of death ($n=50$).

	Adjusted	95% CI		P value
	OR	Lower	Upper	
Initial PIP (>18)	10.090	5.133	96.029	0.003 ^s
Initial PEEP (>5)	15.274	0.925	69.638	0.056 ^{ns}
Initial FiO ₂ (>80)	17.068	0.747	39.177	0.076 ^{ns}
Initial HCO ₃ (<15)	6.855	1.012	46.407	0.049 ^s
Initial BE (<-10)	1.444	0.229	9.092	0.695 ^{ns}
Hyponatraemia	0.227	0.042	1.215	0.083 ^{ns}
Metabolic acidosis	0.746	0.137	4.059	0.737 ^{ns}
Severe respiratory distress	10.031	1.053	95.557	0.045 ^s
Duration of ventilation (>5 days)	11.919	1.333	86.573	0.027 ^s

s= significant, ns= not significant, p value reached from multivariate analysis by binary logistic regression analysis, OR=Odds Ratio.

DISCUSSION

In the present study, a total of 50 infants were included during the study period, and male predominance was observed among the participants. This finding is consistent with similar studies conducted in other developing countries, which reported male predominance of 63% in Pakistan, 57.8% in South Africa, 63.3% in India, and 58.3% in Ethiopia [21-25].

Globally, the leading contributors to neonatal morbidity and mortality include preterm birth, perinatal asphyxia, and neonatal infections [26,27]. In our cohort, the disease patterns for which infants were transferred to the ICU and subsequently required mechanical ventilation included low birth weight (54.1% in the death group vs. 30.8% in the survival group), perinatal asphyxia (13.5% in the death group vs. 15.4% in the survival group), neonatal sepsis (56.8% in the death group vs. 46.2% in the survival group), respiratory distress syndrome (8.1% in the death group), meconium aspiration syndrome (8.1% in the death group), and pneumonia (18.9% in the death group vs. 30.8% in the survival group). These findings are partially aligned with a study by Demisse et al., where the most frequently observed complications were hypothermia (71%) and neonatal sepsis (67.9%) [25]. Notably, our sepsis rates are significantly higher compared to studies in Pakistan (20.3%) [20] and South Africa (21%) [22], as well as Nigeria (16.9%), Nepal (34.5%), and another study from Ethiopia conducted at SPHMMC (22.7%) [24,28,29].

Regarding birth weight, 54.1% of neonates in our study were classified as LBW (<2500 g), which is comparable to reports from Pakistan (37.7%) and Tanzania (29%), though slightly lower than South Africa (52.5%) and India (60%) [21-24]. The prevalence of LBW in developing countries is closely linked to multiple maternal and socioeconomic factors,

including poverty, inadequate prenatal care, maternal infections, malnutrition, and anemia [30].

In the present study, the overall infant mortality rate was notably high at 74%. In comparison, Demisse et al reported a significantly lower neonatal mortality rate of 14.3% (95% CI: 11.9–16.9) [25], which aligns with findings from studies conducted in South Africa (13.8%) and Nigeria (14.2%) [22,29]. However, this rate is higher than those reported from SPHMMC in Addis Ababa (23.2%) and Bangladesh (20.6%) [27,31]. In contrast, even lower mortality rates were observed in studies from Pakistan and Nepal, at 6.2% and 4.6%, respectively [28,32].

More than half (56.8%) of the deaths in our study occurred within the first five days of admission. While Demisse et al. noted that 62.7% of neonatal deaths took place within 24 hours of admission [25], and this trend is consistent with studies from Nigeria (55%) and Tanzania (56.7%) [29,33]. These early fatalities underscore the importance of immediate and aggressive neonatal care, as the initial hours after birth are critical for survival. Lamberti et al., in a study involving older neonates (mean age 6 months), reported a mortality rate of 2.3%, including a death in a 1.7-kg neonate with perinatal asphyxia (PA) [34]. Similarly, Williams et al., in a large series of 2000 Blalock-Taussig shunt cases over six decades, documented an overall mortality rate of 14% [35].

In this study, multivariable regression analysis identified several factors that were independently and significantly associated with increased risk of mortality. These included an initial peak inspiratory pressure (PIP) >18 cmH₂O, low serum bicarbonate (<15 mmol/L), severe respiratory distress, and a duration of mechanical ventilation exceeding five days ($p < 0.05$). These parameters can serve as early warning indicators for clinicians to

identify neonates at elevated risk and intervene accordingly. A study by Demisse et al identified hypothermia, sepsis, and perinatal asphyxia as significant predictors of neonatal mortality through multivariate analysis [25]. Another study by Iqbal et al. conducted a multiple regression analysis on ten variables that were found to be significant in univariate analysis, including gestational age <34 weeks, birth weight <2500 g, shock, apnea, sepsis, pulmonary hemorrhage, neutropenia, thrombocytopenia, and pH <7.1. The analysis identified gestational age <34 weeks, presence of shock, neutropenia, pulmonary hemorrhage, and a pH <7.1 as significant independent predictors of mortality in mechanically ventilated neonates [36]. These findings are consistent with those reported in several previous studies [37-39]. Other studies have further reinforced the association between neonatal hypothermia, intraventricular hemorrhage (IVH), and mortality [40,41].

Additionally, a study from China highlighted that the majority of deaths in preterm infants occur in those with the lowest gestational age. The primary causes of mortality in this group included apnea, respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), IVH, infections, and asphyxia [42]. These findings are consistent with the multifactorial nature of prematurity-related complications that contribute to early neonatal mortality.

CONCLUSION

This study highlights several critical risk factors associated with mortality in ventilated infants in a tertiary care setting. The study findings indicate that specific ventilatory parameters, such as high initial PIP, elevated FiO₂, and increased PEEP, along with metabolic parameters, including low bicarbonate levels and metabolic acidosis, are strongly associated with poor outcomes. Additionally, clinical signs such

as severe respiratory distress before extubation and prolonged duration of mechanical ventilation emerged as significant independent predictors of mortality. These results underscore the importance of early recognition and prompt intervention targeting modifiable risk factors.

Further study with a prospective and longitudinal study design, including a larger sample size, needs to be done to validate the findings of our study.

ACKNOWLEDGMENT

I would like to express my sincere gratitude for the invaluable support and cooperation provided by the staff, participants and my co-authors/colleagues who contributed to this study.

CONFLICTS OF INTEREST

There are no conflicts of interest.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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