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Factors Associated with the Outcome of Ventilated Neonates in the Intensive Care Unit

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Abstract **Original Research Article**

Introduction: Despite significant reductions in overall neonatal mortality in Bangladesh, outcomes among mechanically ventilated neonates remain suboptimal. Mortality in this high-risk population is influenced by multiple interrelated clinical and biochemical factors. Identifying these determinants is critical for risk stratification and targeted interventions in resource-constrained healthcare settings. ***Aim of the Study:*** This study aimed to determine the clinical and biochemical factors associated with outcomes in mechanically ventilated neonates admitted to the neonatal intensive care unit. ***Methods:*** This case-control study included 60 outborn neonates [0–28 days] who required mechanical ventilation between June 2007 and March 2008. Neonates who died following ventilation were classified as cases [n=37], while those who survived were controls [n=23]. Demographic, clinical, ventilatory, and biochemical parameters were collected at admission. Bivariate analysis and multivariate logistic regression were used to identify factors independently associated with mortality. ***Results:*** Overall mortality was 61.7%. Deceased neonates had lower birth weight [1970 ± 735 g vs 2509 ± 752 g, p=0.01] and more frequent gestational age <28 weeks [29.7% vs 4.3%, p=0.02]. Septicemia [48.6% vs 21.7%, p=0.04] and delayed ICU admission >12 hours [64.9% vs 21.7%, p<0.01] were significantly more common among deaths. Severe metabolic acidosis [pH <7.1] increased mortality risk [OR 7.50], as did base excess ≤–10 [OR 7.56], hyponatremia [OR 6.39], and hypokalemia [OR 7.16]. Higher initial ventilator settings, including peak inspiratory pressure [22.1 vs 20.8 cmH_2O, p=0.01] and FiO_2 [82.5% vs 72.2%, p<0.001], were also associated with mortality. Multivariate analysis identified septicemia [aOR 219.6], respiratory distress syndrome/pneumonia [aOR 111.3], base deficit [aOR 1.79 per unit decrease], and delayed ICU admission [aOR 8.29] as independent predictors of death. ***Conclusion:*** Mortality among mechanically ventilated neonates was strongly influenced by underlying sepsis or respiratory illness, delayed ICU admission, severe metabolic acidosis, electrolyte imbalance, and high ventilatory requirements. Early recognition of these high-risk features and prompt escalation of care may improve survival in resource-limited neonatal ICUs.

Keywords: Mechanical ventilation, Neonatal, Mortality, Intensive care unit.

INTRODUCTION

Newborn survival is a critical indicator of a nation's healthcare quality, yet mortality among mechanically ventilated neonates remains unacceptably high in many low- and middle-income countries, including Bangladesh. Over the last few decades, neonatal services in Bangladesh have improved significantly, with better infrastructure, trained personnel, and modern equipment, but critically ill neonates requiring intensive care still face disproportionately poor outcomes [1,2]. Despite reductions in overall neonatal mortality—from approximately 78 per 1,000 live births in the early 1990s to 42 per 1,000 live births in recent years the rates among high-risk neonates remain alarming. Major contributors include perinatal asphyxia, prematurity, low birth weight, and neonatal infections such as sepsis, pneumonia, and meningitis [2]. Intensive care interventions, including mechanical ventilation, have substantially improved survival in selected cases, yet mortality among ventilated neonates continues to exceed

acceptable thresholds. Survival in mechanically ventilated neonates is strongly associated with gestational age and birth weight, with very low birth weight [<1500 g] and extreme prematurity being consistently linked to higher mortality, while neonates weighing ≥2500 g or born at later gestational ages demonstrate comparatively better outcomes [3]. The nature and severity of the underlying condition also influence prognosis. Neonates with sepsis, pneumonia, or severe perinatal complications often require prolonged ventilatory support and experience higher fatality rates than those with respiratory distress syndrome or moderate asphyxia [4]. Ventilator-related factors, including hypercapnia [$PaCO_2$ >60 mmHg], hypoxemia, high oxygen requirements, and prolonged ventilation, are associated with adverse outcomes, emphasizing the importance of optimal ventilator settings and close monitoring [5,6]. Other factors affecting survival include the place of birth and transport status. Outborn neonates transferred to tertiary care centers face higher mortality, likely due to delayed resuscitation, inadequate stabilization during transport, and late initiation of mechanical ventilation [7]. Biochemical imbalances such as dyselectrolytemia, hypoglycemia, and disturbances in fluid homeostasis further compromise survival and are common in critically ill neonates [8,9]. These findings indicate that mortality among mechanically ventilated neonates is not determined solely by respiratory failure but by a combination of clinical status at admission, underlying disease, ventilator requirements, biochemical derangements, and quality of perinatal and intensive care support. Given the persistent burden of neonatal mortality in Bangladesh despite improvements in ICU capacity, identification of routinely measurable parameters that influence outcomes is crucial for early risk stratification and improved management. Birth weight, gestational age, primary diagnosis, disease severity, $PaCO_2$, SpO_2, duration of mechanical ventilation, blood glucose, and electrolyte disturbances represent such parameters and may guide targeted interventions to optimize survival. In this context, the present study aims to determine the association of these clinical and biochemical variables with outcomes among mechanically ventilated neonates admitted to the ICU of Dhaka Shishu Hospital, providing evidence to improve neonatal care strategies and reduce mortality in this high-risk population.

METHODS

This case-control study was conducted in the Intensive Care Unit [ICU] of Dhaka Shishu Hospital, a tertiary care pediatric centre, from June 2007 to March 2008. All outborn sick neonates requiring mechanical ventilation during the study period were consecutively enrolled, totaling 60 patients. Neonates who died following mechanical ventilation were categorized as cases, while those who survived were taken as controls. For each participant, detailed demographic and clinical information, including age, sex, gestational age, admission weight, time of ICU entry, and relevant perinatal history, was collected from parents or attendants using a structured questionnaire and hospital records. Mechanical ventilation was initiated based on predefined criteria: intractable or recurrent apneic spells with bradycardia/cyanosis, PaO_2 <50 mmHg or SaO_2 <85% with FiO_2 >60%, pH <7.25, or PCO_2 >60 mmHg. Pressure-limited time-cycled ventilators were used, and initial ventilator settings [PIP, PEEP, inspiratory time, and FiO_2] along with arterial blood gas values were recorded at initiation. Oxygen saturation was maintained between 92–95%. Weaning was attempted upon clinical, radiological, and blood gas improvement, with ventilator settings reduced to a rate of 10–15/min, PIP of 12–15 cm H_2O, PEEP of 2–4 cm H_2O, and FiO_2 of 0.4–0.5, followed by extubation to an oxygen hood. The outcome was documented as death [case] or improvement [control]. Ethical approval was obtained from the institutional review board.

Inclusion Criteria

- Neonates aged 0–28 days
- Outborn sick newborns requiring mechanical ventilation

Exclusion Criteria

- Age >28 days
- Neonates ventilated solely for surgical procedures
- Presence of multiple congenital anomalies

RESULTS

Table 1: Baseline Characteristics and Clinical Profile of Ventilated Neonates [N=60]

Characteristic	Total [N=60]	Improved [N=23]	Died [N=37]	p-value
Demographics				
Gestational Age [weeks], Mean ± SD	35.60 ± 4.31	36.91 ± 3.45	34.78 ± 4.61	0.06
Gestational Age <28 weeks, n [%]	12 [20.0]	1 [4.3]	11 [29.7]	**0.02**
Birth Weight [grams], Mean ± SD	2176.96 ± 798.76	2508.70 ± 752.12	1970.27 ± 734.89	**0.01**
Birth Weight <2500g, n [%]	41 [68.3]	12 [52.2]	29 [78.4]	**0.03**
Male Sex, n [%]	37 [61.7]	16 [69.6]	21 [56.8]	0.33
Primary Diagnosis, n [%]				
Septicemia	23 [38.3]	5 [21.7]	18 [48.6]	**0.04**
Perinatal Asphyxia	28 [46.7]	11 [47.8]	17 [45.9]	0.89
Pneumonia	9 [15.0]	1 [4.3]	8 [21.6]	0.07

Preterm [<37 weeks]	22 [36.7]	11 [47.8]	11 [29.7]	0.17
Admission Factor				
ICU Admission >12 hours after hospital admission, n [%]	29 [48.3]	5 [21.7]	24 [64.9]	**<0.01**

A total of 60 ventilated neonates were included in this study. The mean gestational age was 35.60 ± 4.31 weeks, with neonates who died showing a lower mean gestational age [34.78 ± 4.61 weeks] compared to those who improved [36.91 ± 3.45 weeks, p=0.06]. Gestational age below 28 weeks was significantly associated with mortality [29.7% vs 4.3%, p=0.02]. The mean birth weight was 2176.96 ± 798.76 g, with the lowest values observed in deceased neonates [1970.27 ± 734.89 g vs 2508.70 ± 752.12 g in survivors, p=0.01]. Low birth weight [<2500 g] was more frequent among deaths [78.4% vs 52.2%, p=0.03]. Sex distribution was not associated with outcome [male: 56.8% deaths vs 69.6% improved, p=0.33]. Regarding primary diagnoses, septicemia was significantly more common among neonates who died [48.6% vs 21.7%, p=0.04], while perinatal asphyxia [45.9% vs 47.8%, p=0.89] and pneumonia [21.6% vs 4.3%, p=0.07] did not reach statistical significance. Preterm birth [<37 weeks] was observed in 29.7% of deceased neonates and 47.8% of those who improved [p=0.17]. Delayed ICU admission [>12 hours after hospital admission] was strongly associated with mortality [64.9% vs 21.7%, p<0.01].

Table 2: Biochemical and Ventilatory Parameters Associated with Mortality [Bivariate Analysis]

Parameter	Improved [N=23]	Died [N=37]	p-value	OR [95% CI]
Blood Gas [Mean ± SD]				
pH	7.20 ± 0.09	7.06 ± 0.11	<0.001	-
pH < 7.1, n [%]	5 [21.7]	25 [67.6]	<0.001	7.50 [1.97 - 30.43]
Base Excess [BE] ≤ -10, n [%]	12 [52.2]	33 [89.2]	<0.01	7.56 [1.74 - 35.53]
HCO_3 [mmol/L]	17.55 ± 4.91	12.17 ± 4.83	<0.001	-
Electrolytes, n [%]				
Hyponatremia [<130 mmol/L]	2 [8.7]	14 [37.8]	0.01	6.39 [1.16 - 46.28]
Hypokalemia [<3.5 mmol/L]	2 [8.7]	15 [40.5]	<0.01	7.16 [1.30 - 51.67]
Initial Ventilator Settings [Mean ± SD]				
Peak Inspiratory Pressure [PIP, cmH_2O]	20.78 ± 1.67	22.11 ± 2.05	0.01	-
Fraction of Inspired Oxygen [FiO_2, %]	72.17 ± 6.88	82.54 ± 8.41	<0.001	-

Bivariate analysis of biochemical parameters showed significant differences between the groups. Blood pH was lower in deceased neonates [7.06 ± 0.11 vs 7.20 ± 0.09, p<0.001], with pH <7.1 increasing the odds of death [67.6% vs 21.7%; OR 7.50, 95% CI 1.97–30.43]. Base excess ≤ -10 was observed in 89.2% of deaths versus 52.2% of survivors [OR 7.56, 95% CI 1.74–35.53, p<0.01], and bicarbonate levels were also significantly lower in the deceased group [12.17 ± 4.83 vs 17.55 ± 4.91 mmol/L, p<0.001]. Electrolyte disturbances were more frequent in neonates who died, including hyponatremia [37.8% vs 8.7%, OR 6.39, 95% CI 1.16–46.28, p=0.01] and hypokalemia [40.5% vs 8.7%, OR 7.16, 95% CI 1.30–51.67, p<0.01].

Table 3: Indications for Mechanical Ventilation and Association with Outcome

Indication for Ventilation	Total [N=60] n [%]	Improved [N=23] n [%]	Died [N=37] n [%]	OR [95% CI]
Recurrent Apnea	31 [51.7]	8 [34.8]	23 [62.2]	3.08 [0.92 - 10.60]
Intractable Apnea	9 [15.0]	2 [8.7]	7 [18.9]	2.54 [0.45 - 21.23]
Gasping Respiration	23 [38.3]	4 [17.4]	19 [51.4]	5.01 [1.26 - 21.63]
O_2 Saturation <80%	7 [11.7]	4 [17.4]	3 [8.1]	0.42

Initial ventilator settings were also significantly different. Deceased neonates required higher peak inspiratory pressure [22.11 ± 2.05 vs 20.78 ± 1.67 cmH_2O, p=0.01] and higher fraction of inspired oxygen [82.54 ± 8.41% vs 72.17 ± 6.88%, p<0.001]. Among indications for mechanical ventilation, gasping respiration was associated with the highest mortality [51.4% vs 17.4% improved; OR 5.01, 95% CI 1.26–21.63], while recurrent apnea and intractable apnea showed a trend toward increased risk but were not statistically significant.

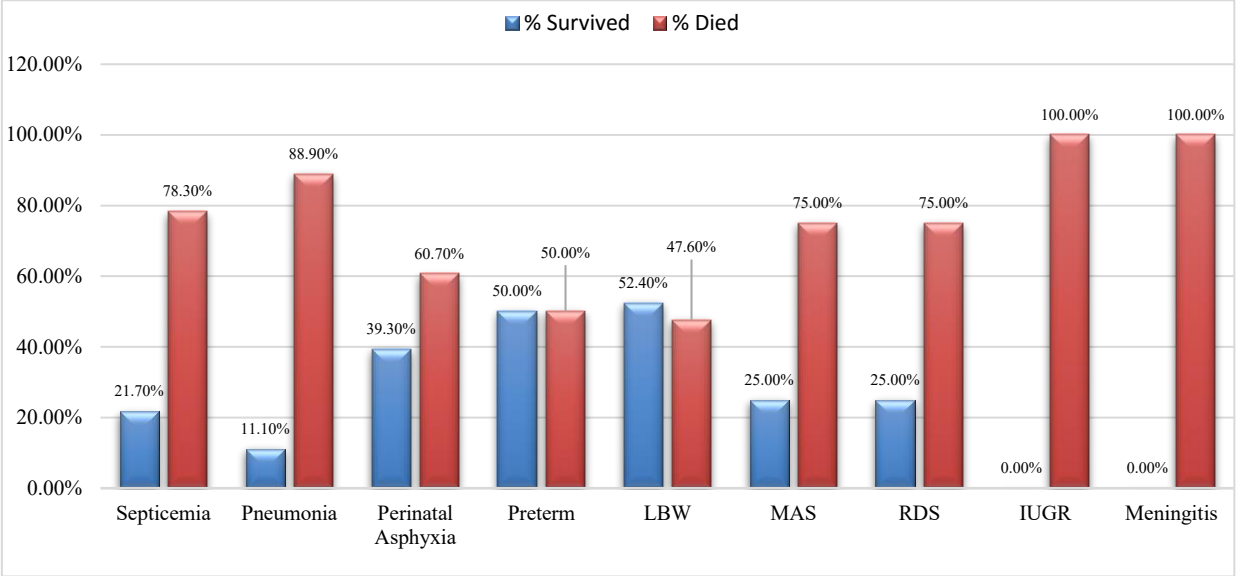

Figure 1: Bar Chart of Mortality by Primary Diagnosis

In this figure, septicemia and pneumonia were associated with the highest mortality burdens, with 78.3% [18/23] and 88.9% [8/9] of affected neonates dying, respectively. Other severe diagnoses, like respiratory distress syndrome [RDS] and meconium aspiration syndrome [MAS], also had high mortality rates of 75%. In contrast, a designation of prematurity or low birth weight without another primary diagnosis was associated with a lower mortality rate of 50.0% and 47.6%, respectively, highlighting that superimposed severe illness significantly worsens prognosis.

Table 4: Multivariate Logistic Regression of Factors Independently Associated with Mortality

Predictor	Adjusted Odds Ratio [aOR]	95% Confidence Interval	p-value
Septicemia	219.59	1.15 - 448.80	0.044
RDS & Pneumonia	111.28	1.20 - 138.50	0.044
Base Deficit [per unit decrease]	1.79	1.11 - 2.80	0.018
Time to ICU Admission [>12 hours]	8.29	1.20 - 23.50	0.024
Perinatal Asphyxia	50.26	0.19 - 132.00	0.169
LBW	0.05	0.01 - 3.60	0.168

Nagelkerke $R^2 = 0.769$

Multivariate logistic regression identified septicemia [aOR 219.59, 95% CI 1.15–448.80, p=0.044], RDS & pneumonia [aOR 111.28, 95% CI 1.20–138.50, p=0.044], base deficit per unit decrease [aOR 1.79, 95% CI 1.11–2.80, p=0.018], and ICU admission delay >12 hours [aOR 8.29, 95% CI 1.20–23.50, p=0.024] as independent predictors of mortality. Perinatal asphyxia and low birth weight were not significant in multivariate analysis. The model demonstrated good predictive power with a Nagelkerke R^2 of 0.769.

DISCUSSION

In this study of 60 mechanically ventilated neonates, the overall mortality was 61.7%. Several clinical, biochemical, and ventilatory parameters were associated with poor outcomes. We observed that deceased neonates had a lower mean gestational age [34.78 ± 4.61 weeks] compared to survivors [36.91 ± 3.45 weeks, p = 0.06], and gestational age <28 weeks was significantly associated with mortality [29.7% vs 4.3%, p = 0.02]. Similarly, mean birth weight was lower among deaths [1970 ± 734.9 g vs 2508 ± 752.1 g, p = 0.01], and low birth weight [<2500 g] was more frequent among non-survivors [78.4% vs 52.2%, p = 0.03]. These findings align with Saleem et al. [2020] and Jańczewska et al. [2023], who also reported higher mortality in very low birth weight and preterm neonates [10,11]. However, in our multivariate model, low birth weight and gestational age lost significance, suggesting that acute illness factors, such as sepsis and metabolic derangements, exerted a stronger influence on survival. This differs from some large multicenter studies where prematurity remained an independent predictor, likely due to differences in case-mix and the availability of advanced neonatal care. Septicemia was significantly associated with mortality [48.6% vs 21.7% in survivors, p = 0.04], while RDS/pneumonia also contributed to deaths. This finding is consistent with Chaurasia et al. [2019] and Das et al. [2021], who reported sepsis as a leading cause of death in ventilated neonates in South Asia [1,12]. Mortality among pneumonia cases [88.9%] in our study is similar to observations by Meshram et al. [2025] [13]. Unlike in high-income settings, where

advanced ventilation and surfactant therapy reduce mortality in RDS, in our cohort, RDS remained highly fatal, likely reflecting limited access to antenatal corticosteroids and surfactant therapy. A delay of more than 12 hours before ICU admission was strongly associated with mortality [64.9% vs 21.7%, $p < 0.01$; aOR 8.29]. This result mirrors findings from Hossain et al. [2009], where delayed admission and outborn status significantly increased the risk of death [14]. Early ICU admission is critical to prevent progression of shock, hypoxia, and sepsis. Our data reinforce the importance of timely referral and transfer in resource-limited settings. Deceased neonates had significantly lower blood pH [7.06 ± 0.11 vs 7.20 ± 0.09, $p < 0.001$] and bicarbonate levels [12.17 ± 4.83 vs 17.55 ± 4.91 mmol/L, $p < 0.001$], with base excess ≤ -10 strongly associated with death [OR 7.56, 95% CI 1.74–35.53]. Each unit decrease in base excess increased mortality odds by 1.79. These results are consistent with Hossain et al. [2009] and Ahmad et al. [2015], who identified severe acidosis as a strong predictor of mortality among ventilated neonates[14,15]. The similarity suggests that metabolic derangements are a universal marker of illness severity, independent of geographic setting. Hyponatremia and hypokalemia were significantly more frequent in deceased neonates [37.8% vs 8.7%, OR 6.39; 40.5% vs 8.7%, OR 7.16, respectively]. This aligns with Naseem et al. [2019], who reported that electrolyte imbalances, particularly hyponatremia, correlate with poor outcomes in critically ill neonates [16]. In contrast, some high-resource centers report lower rates of electrolyte-related mortality due to rigorous monitoring and early correction protocols, highlighting resource limitations in our context. Deceased neonates required higher peak inspiratory pressure [22.11 ± 2.05 vs 20.78 ± 1.67 cmH_2O, $p = 0.01$] and higher FiO_2 [82.5% vs 72.2%, $p < 0.001$]. This finding is consistent with Schulzke et al. [2022], who suggested that higher initial ventilatory support reflects greater underlying disease severity [17]. However, in developed countries, early use of lung-protective strategies reduces the predictive value of initial ventilator settings, explaining differences in effect magnitude. Our adjusted model identified septicemia [aOR 219.6], RDS/pneumonia [aOR 111.3], base deficit [aOR 1.79 per unit decrease], and delayed ICU admission [aOR 8.29] as independent predictors. Perinatal asphyxia and low birth weight were not significant. The very high adjusted odds ratios reflect the small sample size and strong imbalance of outcomes, but are directionally consistent with other regional studies. Similar studies in India and Pakistan report high odds of death associated with sepsis, severe respiratory illness, and delayed ICU care, though effect sizes are more modest [aOR 4–8][18,19]. Mortality among neonates with prematurity or low birth weight without severe infection was lower [47–50%], highlighting that superimposed critical illness drives poor outcomes. This pattern is consistent with Lianou et al. [2022], emphasizing that infection and respiratory compromise, rather than prematurity alone, are primary determinants of mortality in low-resource ICUs[20].

Limitations of the Study:

This study was conducted in a single tertiary care center with a relatively small sample size, limiting the generalizability of the findings.

CONCLUSION

This study demonstrates that mortality among mechanically ventilated neonates is driven primarily by severe infection, respiratory compromise, metabolic acidosis, electrolyte imbalance, and delays in receiving intensive care. While low birth weight and prematurity were common among non-survivors, they were not independent predictors once critical illness factors were accounted for. These findings suggest that early illness severity and treatment timeliness have a stronger impact on survival than baseline demographic characteristics.

RECOMMENDATIONS

Improving outcomes in resource-limited neonatal ICUs will require earlier referral and faster initiation of ventilation, particularly for neonates presenting with sepsis or respiratory distress. Routine monitoring and rapid correction of acid-base imbalance and electrolytes should be made standard practice. Strengthening infection control protocols, optimizing transport stabilization for outborn neonates, and establishing risk-based triage systems could further reduce preventable deaths. Future studies with larger cohorts are recommended to validate these predictors and develop practical scoring tools for early risk stratification.

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