

Research Article

Neonatal Mechanical Ventilation: Predictors of Mortality and Outcomes

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Abstract

Introduction: A large number of neonates in neonatal intensive care unit require mechanical ventilation and they have high fatality rate. Early identification of complications and factors influencing the outcome is important to improve the survival of ventilated neonates.

Aims: To determine the predictors of fatality in ventilated neonates.

Settings and Design: This prospective cohort study was conducted among the ventilated neonates in the department of Neonatal Intensive Care Unit (NICU), BSMMU. To identify factors affecting fatality clinical, biochemical and ventilator parameters were followed. The final outcome was recorded as “survivor” and “non-survivor” at discharged or death. Quantitative variables were compared by unpaired t-test; categorical variables were compared by chi-square test. To determine predictors of fatality, multivariate logistic regression analysis was performed.

Results: A total 74 neonates were included, among them 23(31.1%) were survivors and 51(68.9%) were non-survivors. Mean gestational age (30.90 ± 5.20 weeks Vs 33.91 ± 2.52 weeks, $p=0.010$) and mean birth wt (1501 ± 623.38 g Vs 1873.04 ± 481.76 g, $p=0.013$) were significantly lower in non-survivor group. Shock (84.3% Vs 34.8% ; $p<0.001$), pulmonary hemorrhage (15.7% Vs 0.00% ; $p=0.044$), acute kidney injury (58.8% Vs 30.4% ; $p=0.024$), hyperglycemia (56.9% Vs 21.7% ; $p=0.005$), hyponatremia (41.2% Vs 17.4% ; $p=0.045$) were significantly higher in non-survivor group. Mean initial arterial pH (7.20 ± 0.117 Vs 7.31 ± 0.065 ; $p<0.001$), highest PIP (16.51 ± 1.91 Vs 14.96 ± 1.33 ; $p=0.001$), highest FiO₂ (0.93 ± 0.07 Vs 0.58 ± 0.083 ; $p<0.001$), mean age of initiation of ventilation (8.53 ± 6.49 Vs 5.70 ± 4.15 ; $p=0.027$) were also significantly higher in non-survivor group than survivor group. Multivariate logistic regression analysis indicated the predictors of mortality were low birth weight (OR-0.997, 95% CI 0.995-1.00, $p=0.00$), AKI (OR-0.393, 95% CI 0.090-10.563, $p=0.035$), shock (OR-0.507, 95% CI 0.1717-52.639, $p=0.010$),

hyponatremia (OR-4.202, 95% CI 1.071-16.495, $P=0.040$), high FiO₂ (OR-1.545, 95% CI 2.927-8.158, $p=0.045$) and high PIP (OR-2.122, 95% CI 1.273-3.537, $p=0.004$).

Conclusion: The frequency of mortality in ventilated neonates was 68.9%. Low birth weight, shock, acute kidney injury, requirement of high PIP, high FiO₂ and hyponatremia were associated with increased mortality.

Keywords: Fatality; Neonatal Mortality; Mechanical Ventilation; NICU

Introduction

Mechanical ventilation supports oxygenation and ventilation in critically ill neonates and has become an indispensable part of neonatal intensive care [1,2]. This innovative technology has reached to a significant level in the affluent nation, but due to its high cost, expert skill requirements, has limited its use in developing countries [3]. Bangladesh is a resource-limited developing country in Southeast Asia with a neonatal mortality rate 30 per 1,000 live births [4]. Intensive care medicine and neonatal intensive care services are now in an advancing stage in Bangladesh with the improvement of health service facilities. Especially for neonates, more critically ill babies are reaching the health facilities but many of them are in very critical condition and the mortality of these neonates is still very high [5]. Bangladesh has made tremendous progress towards millennium development goal [4]. Sustainable development goal targets to reduce neonatal mortality to at least as low as 12 per 1,000 live births by 2030 [6]. Improving intensive care facilities for neonates in the country could be one of the effective interventions to achieve this goal. A large number of neonates in neonatal intensive care units require mechanical ventilation, and these ventilated neonates have a high fatality [7]. Recent evidence shows that weight and gestational age are the major determinants of neonatal mortality along with the severity of illness on admission having some influence on the outcome. pH, PaCO₂, base excess and FiO₂ have long been identified as critical risk factors in ventilated neonates. Incidence of complications related to ventilator techniques and strategies also has an impact on outcomes [5]. For the reduction of fatality in this group of neonates, early identification of complications and factors influencing the outcome is important. This study was conducted to find out the predictors of mortality in mechanically ventilated neonates in a tertiary intensive care unit in Bangladesh in order to institute resource planning and management to improve their survival.

Subjects and Methods

This prospective cohort study was conducted in Neonatal Intensive Care Unit (NICU), Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. from October 2017 to September 2018. Term and Preterm neonates who received mechanical ventilation in the NICU of BSMMU were included consecutively. Neonates with major congenital anomalies and neonates on ventilator for surgical causes were excluded from the study.

After taking written informed consent from the parents, baseline characteristics of each ventilated neonate, such as gestational age (determined from maternal record), birth weight, sex, place of delivery, postnatal age of initiation of ventilation and primary diagnosis were recorded in a pre-designed data collection form. Diagnosis of underlying condition were made using standard clinical, laboratory and/or radiological criteria.

All babies were treated according to existing institutional management protocol. ABG analysis was done within 1 hour of initiation of mechanical ventilation and as preset protocol of NICU. E.g.: 12 hourly in stable babies and more frequently in unstable babies and with changes of ventilator settings. The indications for initiation of mechanical ventilation were set as protocol of NICU of BSMMU.

Time cycled, Pressure limited, continuous flow ventilator was used with aim to maintain normal oxygen saturation with normal blood gases with minimal work of breathing. (Model of Puritan Bennett 840 ventilator system was used in this study).

Observation during ventilation were included, (1) Peak Inspiratory Pressure (PIP), (2) Positive End Expiratory Pressure (PEEP), (3) Fraction of Oxygen in inspired air (FiO₂). Oxygen saturation by pulse oximetry, maximum ventilator parameters for each neonate and duration of mechanical ventilation were also recorded. The initial setting was varied with underlying disease/clinical condition and subsequent setup were changed upon ABG analysis.

All babies were monitored for any complication like air leak, pneumonia, sepsis, PDA, IVH etc. Relevant investigations including sepsis workup, serum electrolytes, serum creatinine, random blood sugar, chest X-ray, ECHO were done as per requirement. Neonates who survived after receiving mechanical ventilation were termed as survivor group and neonates who died while on ventilator were in non-survivor group. Clinical, biochemical and ventilator parameter were compared to find out the factor associated with mortality between survivors and non-survivors'. Neonates were observed up to death or discharged.

Statistical consideration and data analysis: Data were analysed using the Statistical Package for Social Sciences (SPSS) version 20.0. Quantitative data were expressed as mean $\pm$ SD and categorical data were presented as proportion. All quantitative

variables (between the groups of survivors and non-survivors) were compared by unpaired-t test or student-t test. Categorical variables were compared by Chi-square tests. p-value <0.05 were considered significant. To determine independent predictors of outcome multivariate logistic regression analysis were performed. Odds ratios and 95% confidence intervals were calculated.

Results

During the study period, a total 82 neonates received mechanical ventilation. Among these 82 neonates, 8 neonates were excluded; 3 neonates were excluded due to major congenital anomalies, 2 neonates were excluded due to postsurgical intubation and 3 patients were Left Against Medical Advice (LAMA). Finally, 74 neonates were analysed. Out of them 23 (31.1%) were in survivor group and 51 (68.9%) were in non-survivor group (Fig. 1).

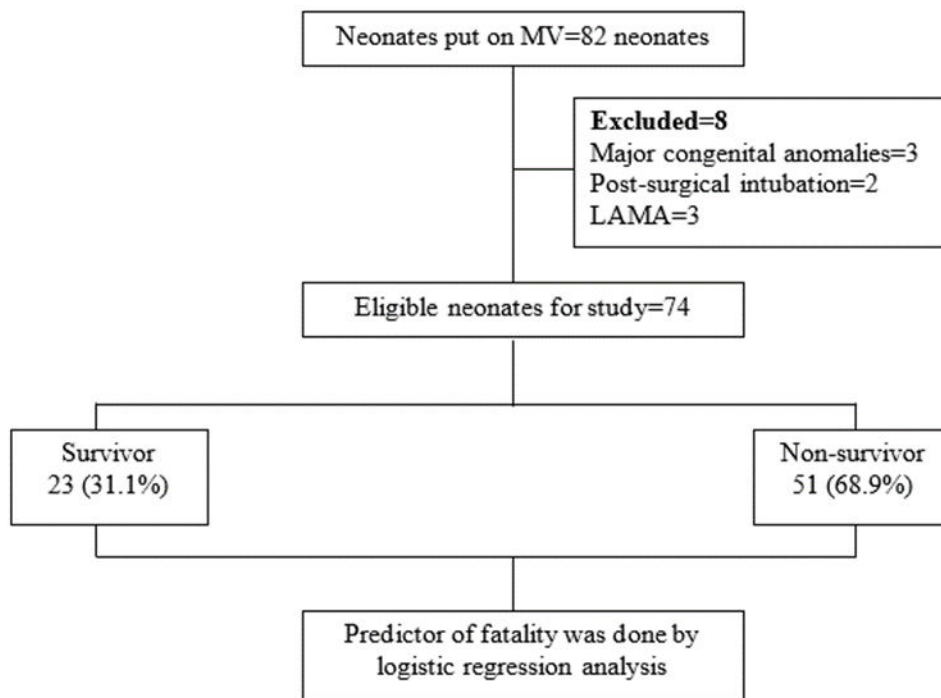


Figure 1: Flow chart of enrolled patients and their outcome.

Baseline characteristics of the studied infants are presented in Table 1. The highest percentage (58.1%) of neonate had gestational age of 28-<34 weeks. Only 9.5% neonates had gestational age of < 28 weeks. According to birth weight classification, highest percentage (45.9%) of neonate were very low birth weight (1000-<1500 g). Only 12.2% of neonates were of normal birth weight. Gender distribution reflected male preponderance in enrolled neonates; 67.6% were male and 32.4% were female. Delivery by LUCS (67.6%) was twice then delivery by NVD (32.4%). Among the enrolled neonates, outborn babies were 54.1%.

Characteristics	No. of Neonates (n=74)	Percentage (%)
Gestational age (wk)		
<28 wk	7	9.5%
28-<34 wk	43	58.1%
34-<37 wk	14	18.9%
≥37 wk	10	13.5%
Birth weight(g)		
<1000 g	8	10.8%
1000 - <1500 g	34	45.9%
1500 - <2500 g	23	31.1%

≥2500 g	9	12.2%
Sex		
Male	50	67.6%
Female	24	32.4%
Place of delivery		
Inborn	34	45.9%
Outborn	40	54.1%
Mode of delivery		
NVD	24	32.4%
LUCS	50	67.6%
NVD-Normal Vaginal Delivery, LUCS-Lower Uterine Caesarean Section. Categorical data are presented as number and percentage (%)		

Table 1: Distribution of demographic characteristics among the enrolled neonates (n=74).

Among the total 74 mechanically ventilated neonates, 23 (31.1%) were in survivor group and 51 (68.9%) were in non-survivor group as shown in Table 2.

Outcome	No(n)	Percentage (%)
Survivor	23	31.1%
Non-survivor	51	68.9%
Categorical data are presented as number and percentage (%)		

Table 2: Outcome of the ventilated neonates (n=74).

In comparison to the survivor group, the non-survivor group had substantially lower mean gestational age (30.90 ± 5.20 weeks vs. 33.9 ± 12.52 weeks, $p=0.010$) and birth weight (1501 ± 623.38 g vs. 1873.04 ± 481.76 g, $p=0.013$). Regarding the place of birth, mode of delivery, and distribution of sexes among the enrolled neonates, there was no significant difference between the non-survivor and the survivor group (Table 3).

Characteristics	Survivor (n=23)	Non-Survivor (n=51)	p-value
Gestational age (wks) Mean ± SD	33.91 ± 2.52	30.90 ± 5.20	0.010
Birth wt (g) Mean ± SD	1873.04 ± 481.76	1501 ± 623.38	0.013
Place of delivery			
Inborn	10(43.5%)	24(47.1%)	0.775
Outborn	13(56.5%)	27(52.9%)	
Mode of delivery			
NVD	6(26.1%)	18(35.3%)	0.434
LUCS	17(73.9%)	33(64.7%)	
Sex			
Male	17(73.9%)	33(64.7%)	0.434
Female	6(26.1%)	18(35.3%)	
NVD-Normal Vaginal Delivery; LUCS-Lower Uterine Caesarean Section. Continuous data are presented as mean ± SD and categorical data as number and percentage (%) Statistical test: Chi square test			

Table 3: Comparison of baseline characteristics among the survivor and non-survivor group (n=74).

Among the 74 mechanically ventilated neonates, the most common indication of mechanical ventilation was sepsis 45 (60.8%) followed by perinatal asphyxia 15 (20.3%). According to the outcome of ventilated babies, most of the non survivors are in the group of sepsis 32 (62.7%), followed by perinatal asphyxia 9 (17.6%) and RDS 4 (7.8%) (Fig. 2). Regarding the clinical condition, shock (84.3% Vs 34.8%; $p<0.001$), pulmonary haemorrhage (15.7% Vs 0.00%; $p=0.044$), acute kidney injury (58.8% Vs 30.4%; $p=0.024$) found more in non-survivors' group than survivor group. In Comparison of biochemical parameters, hyperglycaemia (56.9% vs 21.7%; $p=0.005$) and Hyponatremia (41.2% vs 17.4%; $p=0.045$) were found to be significant in non-survivors' group when compared with survivor group of ventilated neonates as shown in Table 4.

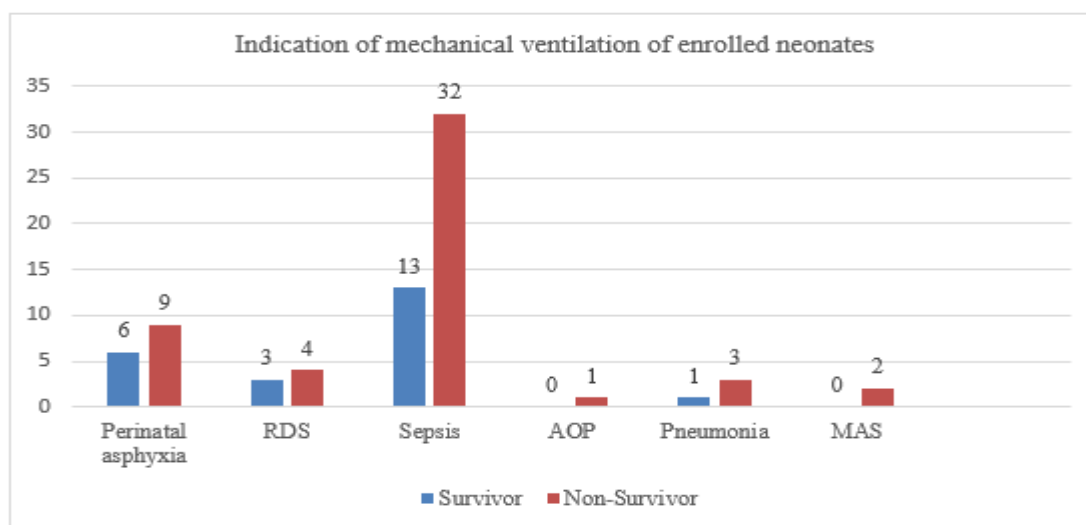


Figure 2: Indication of mechanical ventilation of the enrolled neonates (n=74).

Variable	Survivor n=23 (%)	Non survivor n=51 (%)	p-value
Clinical conditions			
Hypothermia	1 (4.3%)	3 (5.9%)	0.787
Hyperthermia	0 (0.00%)	2 (3.9%)	0.336
Shock	8 (34.8%)	43 (84.3%)	<0.001
PPHN	2 (8.7%)	6 (11.8%)	0.694
AKI	7 (30.4%)	30 (58.8%)	0.024
PDA	3 (13.0%)	8 (15.7%)	0.767
NEC	2 (8.7%)	5 (9.8%)	0.880
Pulmonary Hg	0 (0.00%)	8 (15.7%)	0.044
Biochemical Parameter Hyperglycemia	2 (8.7%)	12 (23.5%)	0.132
Hyperglycemia	5 (21.7%)	29 (56.9%)	0.005
Hyponatremia	4 (17.4%)	21 (41.2%)	0.045
Hypernatremia	0 (0.00%)	3 (5.9%)	0.235
Hypokalemia	5 (21.7%)	17 (33.3%)	0.313
Hyperkalemia	1 (4.3%)	4 (7.8%)	0.579
Statistical test: Chi-square test, PPHN-Persistent pulmonary hypertension of newborn, AKI-Acute kidney injury, PDA-Patent ductus arteriosus, NEC-Necrotizing enterocolitis			

Table 4: Outcome of ventilated neonates according to clinical conditions and Biochemical parameters (n=74).

Complication associated with ventilation showed, ET tube block was significantly more in non-survivor group 16 (31.4%), compared to survivor 2 (8.7%) group (Table 5).

Variable	Survivors n=23 (%)	Non survivors n=51 (%)	p-value
ET tube block	2 (8.7%)	16 (31.4%)	0.035
Air leak	2 (8.7%)	2 (3.9%)	0.401
VAP	2 (8.7%)	6 (11.8%)	0.694
Tracheal colonization	4 (17.4%)	6 (11.8%)	0.512
Statistical test: Chi-square test; VAP: Ventilator Associated Pneumonia			

Table 5: Outcome of ventilated neonates according to complication of ventilation (n=74).

Table 6 showing the outcome of ventilated neonates according to ABG parameters, ventilator parameters and duration of ventilation between survivor and non-survivor group. ABG parameter of the ventilated neonates showed, the mean initial arterial pH and the mean lowest arterial pH were significantly lower in non survivors group and. Mean maximum BE was significantly higher in non survivors group then the survivors group. Regarding the ventilator parameter, mean highest PIP and highest FiO₂ is significantly higher and mean age of initiation of ventilation (days) is also significantly higher in non-survivor group then the survivor group.

Variable	Survivor (n=23)	Non-survivor (n=51)	p-value
Initial pH	7.31 ± .065	7.20 ± .117	<0.001
Lowest pH	7.26 ± .063	7.15 ± .112	<0.001
Lowest paO ₂	63 ± 30	55 ± 21	0.230
Highest paCO ₂	54 ± 11	57 ± 16	0.380
Maximum BE	-6.70 ± 5.47	-11.97 ± 5.94	0.001
Highest PIP	14.96 ± 1.33	16.51 ± 1.91	0.001
Highest FiO ₂	0.58 ± .083	0.93 ± .070	<.001
Maximum PEEP	5.09 ± 0.29	5.21 ± 0.559	0.357
Age at initiation of ventilation(days) mean ± SD	5.70 ± 4.15	8.53 ± 6.49	0.027
Duration of MV (days)	5.13 ± 3.27	3.90 ± 2.85	0.106
BE: Base Excess; MV: Mechanical Ventilation; PIP: Peak Inspiratory Pressure. PEEP: Peak End Expiratory Pressure; Statistical test: Independent Sample t test			

Table 6: Outcome of ventilated neonates according to ABG parameters, ventilator parameters and duration of ventilation between survivor and non-survivor group(n=74).

Multivariate logistic regression analysis showed, the independent predictors of mortality were, mean low birth wt (p=0.002), presence of shock (p=0.010), AKI (p=0.035), high FiO₂ (p=0.045) and high PIP (p= 0.004) and hyponatremia (p=0.040) (Table 7).

Predictors	Mortality		
	B	OR (95% CI)	p-value
Low Birth weight	-0.003	0.997 (.995-1.000)	0.002
Low Gestational age	-0.250	0.779 (.533-1.137)	0.195
Sepsis	0.642	1.901 (.416-8.686)	0.407
Shock	2.252	9.507 (1.717-52.639)	0.010
ET tube block	1.371	3.940 (0.691-22.47)	0.123
AKI	1.22	3.393 (1.090-10.563)	0.035
Highest PIP	0.752	2.122 (1.273-3.537)	0.004
Highest FiO ₂	44.184	1.54 (2.92- 8.15)	0.045
Maximum BE	-0.021	0.97 (.671-1.429)	0.913
Hyperglycaemia	1.703	5.488 (0.856-35.168)	0.072
Hyponatremia	1.436	4.202 (1.071-16.495)	0.040
Age at initiating of MV	0.122	1.130 (0.983-1.299)	0.086

Table 7: Factors associated with mortality in ventilated neonate by multiple binary logistic regression.

Discussion

Mortality among sick neonates in NICU is high and among mechanically ventilated neonates it is even higher. Mechanical ventilation is essential tool in managing critically ill patient. Neonatal mortality is a leading cause of infant mortality and under-5 mortality in Bangladesh. Mechanical ventilation has been proved an important management strategy in neonatal care and its outcome depends on multiple factors. This study was conducted to identification of the factors for adverse outcome in ventilated neonates. In this study mortality in ventilated neonates was 68.9%. which is comparable to mortality of 70.6% reported by Hossain, et al., and 74% by Mathur, et al., [5,8]. We found most of the babies were preterm, within 28-<34 weeks followed by 34-<37 weeks. Male babies needed more assisted ventilation then female babies and mortality rate was also more in male babies in comparison to female babies. Dutt, et al., in their studies also showed similar pattern [3]. In our study, mean gestational age and mean birth weight of enrolled neonate was significantly lower among non-survivors compared to survivors. This finding is consistent with previous studies in which non-survivors had much lower mean birth weight and gestational ages than survivors [5,8,9]. Preterm low birth weight babies have a higher risk of death because they need more ventilation time and have more complications. Among the ventilated neonates, non-survivors had more proportion of sepsis 32 (62.7%), perinatal asphyxia 9 (17.6%), respiratory distress syndrome 4 (7.8%). Hossain, et al., reported 75% death of sepsis in ventilated neonates [5]. This study also reported death of perinatal asphyxia and respiratory distress syndrome are 68.4% and 66.7% respectively. It is distinct from our research. The survival equations for NICUs are evolving as more drug-resistant pathogens arises. Respiratory failure and need for mechanical ventilation in a septic neonate signify severe advanced disease and is a bad prognostic indicator. Severe prenatal asphyxia linked to irreversible brain damage may lead to respiratory failure and responsible for poor outcome. Shock had a significant impact on mortality in ventilated neonates in our study. Shock was the most frequent co-morbid condition (84%) reported by Prabha, et al., which is comparable to our study [10]. Some other studies reported shock as the common complication in ventilated neonates and also an important cause of mortality in their study [2,3,9]. The relationship of shock with mortality is understandable, as shock represents the advancement of a disease process of varied aetiologies. Pulmonary haemorrhage is a life-threatening event and it was significantly related with mortality among ventilated neonates (15.7%) in this study. Similar result was found in some other studies where ventilated neonates following pulmonary haemorrhage had very poor outcome [2,5,9]. In this study, non-survivors had more acute kidney injury when compared with survivors (58.8% vs 30.4%; $p=0.024$) among ventilated neonates. Shrestha, et al., also showed acute kidney injury as an associated factor of mortality of ventilated neonates, but was not statistically significant [11]. Ventilation related complication are common among the ventilated neonates which influence the outcome. ET tube block was significantly associated with mortality in this study. Riyas PK, et al., found similar result in their study [12]. We found pneumothorax in 5.4% cases among non-survivors which is comparable with some other studies [2,3,12]. This lower incidence of pneumothorax in our study can probably be attributed to the judicious use of pressure and early attempts at weaning. In this study it was observed that, hyperglycaemia and hyponatremia were significantly associated with mortality. Hossain, et al., in their study found significant relation between hyponatremia with outcome ($p<0.05$) which is comparable to our study [5]. Majority of the neonates were admitted due to perinatal asphyxia and neonatal sepsis may developed SIADH, subsequently electrolyte abnormalities and poor outcome. We found Initial pH, lowest pH and maximum base excess were significantly associated with mortality. Some other studies showed similar findings [2,5]. This observation suggests that the damages that have already been occurred reflected by initial acid-base disturbances before ventilation might play role in poor outcome. Mean maximum PIP and maximum FiO₂ were significantly higher in non survivors than of survivors. This observation is consistent with the findings of Mathur, et al., and Anantharaj, et al., FiO₂ requirement reflects the severity of respiratory failure and subsequently poor outcome [2]. In this present study, mean age at initiation of ventilation was significantly higher in non-survivor group than that of survivors. Prabha, et al., also shown significantly higher age at initiation of ventilation in non survivors than that of survivors which is comparable to this study [10]. We did not find any significant difference in the mean duration of ventilation which is similar to some other studies [5,10]. In this current study, the independent predictors of mortality by multivariate logistic regression analysis were low birth weight, presence of AKI, shock, hyponatremia, highest FiO₂, highest PIP. Mathur, et al., reported gestational age<34 weeks, FiO₂ > 60% are independent predictors of mortality, requirement of high FiO₂ was compatible with the findings of this study [8]. Hossain, et al., found weight<2500 g, gestation <34 weeks, Initial arterial pH <7.1, FiO₂ >60%, hyponatremia, hypokalaemia were the significant predictors of mortality [5]. Although low gestational age, initial arterial pH was significant in univariate analysis in this study, but they were not found statistically significant on multivariate analysis.

Conclusion

The frequency of mortality in ventilated neonates was 68.9% among the 74 enrolled neonate. Low birth weight, shock, acute kidney injury, requirement of high PIP, requirement of high FiO₂ hyponatraemia were independent factors associated with increased mortality.

Limitation of the Study

It was a single centered study and does not represent the whole population and sample size was small.

Recommendation

As low gestational age is one of the important predictors of mortality, so more emphasize should be given on management of the premature babies and their complication. Sepsis was the most common complication requiring mechanical ventilation, so, to prevent sepsis and sepsis related complication, strict protocol should be implemented. Early identification and optimum treatment of shock, Acute kidney injury, ventilator related complication may improve survival. Larger multicenter prospective studies should be done in order to validate the factors associated with mortality found in this study.

Conflict of Interest

The authors have no conflict of interest to declare.

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