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Predictors of Mortality among Ventilated Young Infants in Intensive Care Unit of a Tertiary Care Hospital

Dr. Johora Akter[1*], Prof. Dr. M Monir Hossain[2], Dr. Abdullah Al Mamun[3]

[1]Register, Department of Paediatric Respiratory Intensive Care Unit, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh
[2]Professor & Head, Department of Neonatology, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh
[3]Associate Professor, Department of Paediatric Cardiology, Bangladesh Shishu Hopital & Institute, Dhaka, Bangladesh

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***Corresponding author:** Dr. Johora Akter
Department of Paediatric Respiratory Intensive Care Unit, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh

Abstract **Original Research Article**

Introduction: The management of children with invasive ventilation in developing countries with limited resources is challenging. A large number of infants in intensive care unit require mechanical ventilation due to various conditions and have a high mortality. ***Aim of the study*:** To identify the predictors of mortality among ventilated young infant up to 2 months age in Intensive Care Unit of Bangladesh Shishu Hospital & Institute. ***Methodology*:** The prospective observational study was conducted in the Department of Intensive Care Unit of Bangladesh Shishu Hospital & Institute, from January 2020 to December 2020. Critically ill young infants upto 2 months age who required mechanical ventilation in Intensive Care Unit were included in this study. Data was collected on a structured proforma and included the basic demographic profile, presenting complaints, preliminary diagnosis, investigation results, mode of ventilation and initial ventilator parameters & hospital stay and outcome. Permission from ethical review committee of the hospital was taken. ***Results*:** From 50 critically ill patients, mortality rate was 74.0%. Mean age was 14±10.1 days. Significant relation was found between the ventilated patients having FiO_2, PIP, PEEP, HCO_3, BE, serum sodium level, duration of ventilation and outcome respectively. Severe respiratory distress before death was found significantly related with outcome. Metabolic acidosis was found significant in death patients before ventilation and before death (75.7% & 51.4%). ***Conclusion:*** The rate of mortality in the ICU was high. Initial high PIP, low HCO_3, severe respiratory distress and prolong duration of ventilation (>5days) were significant independent predictors of mortality.

Keywords: Mechanical Ventilation, Young Infants, Mortality, Predictors.

INTRODUCTION

The infant mortality rate is a crucial indicator of a society's general health in addition to providing essential information regarding maternal and baby health [1]. Mortality in infants remains disproportionately high, representing over one-thirds of under-5 deaths in children [2]. Nearly all (90%) of them occur in low-income and middle-income countries [3]. Critically ill children generally have a disease process that affects more than one organ system. These children are managed in paediatric intensive care unit with the aim of achieving a better outcome [4]. Intensive care medicine is concerned predominantly with the management of patients with acute life threatening conditions [5]. Intensive care medicine is now on an advancing stage in Bangladesh [6]. Mechanical ventilation, a life supporting device, invasive technology of intensive care unit, mimic the respiratory physiological function at the time of either impending or acute respiratory failure [7]. The percentage of children receiving mechanical ventilation in intensive care units ranges from 17-64% in developed countries [8-11]. Mechanical ventilation is becoming widespread in PICUs throughout the world as a central strategy, not only in the management of patients with acute and chronic respiratory failure but also as an adjuvant therapy of patients with normal healthy lungs e.g. patient with neurological disease or following general anaesthesia for elective procedures and operation [12]. The objectives of mechanical ventilation are primarily to decrease the work of breathing and to reverse life threatening hypoxemia or acute progressive respiratory acidosis. Several reports mention respiratory failure due to respiratory illnesses as most common reason for mechanical ventilation in paediatric patient as well as young infants up to 2 months age [8-14]. Age, weight clinical condition along with severity of illness has

some influence on outcome of mechanical ventilation. Longer length of PICU stay and invasive procedures has led to an increase of nosocomial infection and high mortality with respiratory disorders [13-15]. Paediatric intensive care units (PICUs) are essential areas of service to save the lives of children with acute neurological deterioration, respiratory distress, cardiovascular compromise, severe infections, accidental poisoning as well as other life-threatening conditions [16,17]. Most studies done on predictors of mortality in the PICUs are from high-income countries and are dependent on clinical and laboratorial characteristics which are not readily available in low-income countries [18]. So, as a developing country to find out the risk factors of mortality among children especially young infants up to 2 months age admitted to the PICU becoming the crying need for the most fruitful practice based on the prediction of patient outcomes. This study aims to identify the predictors of mortality among ventilated young infant up to 2 months age in Intensive Care Unit of Bangladesh Shishu Hospital, Dhaka, Bangladesh. It will add to the knowledge of mortality and its predictors. However, hoping to plan the most efficient method of intervention for those at higher mortality risk may contribute to the recovery & making the assessment of the performance of the services delivered in PICU.

OBJECTIVES

General Objective

To identify the predictors of mortality among ventilated young infant up to 2 months age in Intensive Care Unit of Bangladesh Shishu Hospital & Institute.

Specific Objectives

1. To find out the frequency of mortality among ventilated patients.
2. To determine the factors influencing the mortality of ventilated patient.

MATERIALS & METHODOLOGY

This observational study was conducted in the Department of Intensive Care Unit of Bangladesh Shishu Hospital & Institute, Sher-e-Bangla Nagar, Dhaka from January 2020 to December 2020. The study was carried out on patients who required ventilation on various indications according to ICU protocol after taking informed written consent from the patient's guardian/attendant. Fifty young infants up to 2 months age consecutively put on mechanical ventilation during the study period were enrolled. Informed written consent was taken confidentially from all patients who fulfilled the inclusion and exclusion criteria. Infants more than 2 months age, with congenital heart disease, congenital malformations & requiring surgical intervention were excluded from this study. Permission from ethical review committee of the hospital was taken. Young infants were monitored clinically (Heart rate, Respiratory rate, Temperature, CRT) along with regular cardiac monitor and pulse Oximetry. The initial parameter (Rate, PIP, PEEP, FiO_2 Inspiratory time) was set according to need of patients and adjusted according to clinical variables, chest X-ray and ABG. Sedation was applied if indicated. After 2 hours of ventilation ABG was done to adjust the parameters. Then subsequent parameters (PIP, PEEP, Rate of ventilation, FiO_2) on mechanical ventilation were modified according to need of oxygenation and ventilation through SpO_2 and blood gas analysis. Along with this, biochemical (Serum Electrolytes, Creatinine, Urea, CRP, Random blood sugar) and haematological profiles were checked according to patient's clinical condition. All infants were monitored for complications. Pneumothorax was identified by daily clinical examination & when suspected confirmed by chest radiographs. VAP was diagnosed when ventilation more than 48 hours with new & persistent infiltrate on chest X-ray. Patients were extubated when clinically stable both haemodynamically & neurologically, having self-respiration, maintaining oxygen saturation, normal chest X-ray & with low ventilator parameters or after gradual weaning. Patient was followed up till death or extubation. All the data were collected by researcher herself to avoid errors. After collection, data editing and clearing was done manually and prepared for data entry and analysis by using SPSS-25 & MS Excel-2016.

RESULTS

Almost three fourth (74.0%) patients were dead and 13(26.0%) were survived. [Figure-1] About 27(73%) patients were belonged to age ≤15 days in death group and 7 in survival group. [Figure-2] Majority patients were male; in death group 22(59.5%) and 10(76.9%) in survival group. Then, 30(81.1%) patients were found gestational age>34 weeks in death group and 12(92.3%) in survival group. Majority 20(54.1%) patients were found weight <2500gm in death group and 4(30.8%) in survival group. The difference was not statistically significant (p>0.05) between two groups [Table-1]. Regarding clinical diagnosis, 21(56.8%) patients had sepsis in death group and 6(56.2%) in survival group.20 (54.1%) patients were low birth weight in death group and 4(30.8%) in survival group found in this study [Figure-3]. 43.2% patients developed complication during ventilation in death group and 4(30.8%) in survival group [Table-2]. ET tube blocked, re-intubation and VAP were higher in death group than survival group but pneumothorax and accidental extubation lower in death group than survival group [Figure-4].Thirty-six(97.3%) patients were found FiO_2 >80 percent in death group and 6(46.2%) in survival group. Then 32(86.4%) patients were found PIP >18 cmH_2O in death group and 11(84.6%) in survival group. About 26(70.3%) patients were found PEEP >5.0 cmH_2O in death group and 2(15.4%) in survival group. After those 26(70.3%) patients had HCO_3 level<15mmHg in death group and 3(23.1%) in

survival group. As well as 28(75.7%) patients had BE <-10 in death group and 5(38.5%) in survival group. Significant relation was found in initial FiO_2, PIP, PEEP, HCO_3, BE and outcome of ventilation patients [Table-3]. Before ventilation metabolic acidosis was found 28(75.7%) and 5(38.5%) in death and survival group respectively, that was significant [p=0.019, OR=4.07 (1.09-15.20)]. Before extubation/death metabolic acidosis was 19(51.4%) in death group and 2(15.4%) in survival group, that was significant [p=0.024, OR=5.81 (1.13-28.89)] [Table-4]. Regarding respiratory distress and outcome in this study, before ventilation, majority patients had moderate respiratory distress in both groups, that was 24(64.9%) in death group and 9(69.2%) in survival group. Before extubation/death, severe respiratory distress was found in death group 16(43.2%) and in survival group1 (7.7%), that was significant [(p=0.04, OR 9.14 (1.07-77.80)] [Table-5]. The serum creatinine level of 4(10.8%) patients was found <40 µmol/L in death group 3(23.1%) in survival group. There was no relationship between serum creatinine level and outcome [p=0.283, OR=2.47(0.47-12.96)] [Table-6]. Sixteen (43.2%) patients were found duration of ventilation >5 days in death group and 1(7.7%) in survival group [Table-7]. Initial high PIP, initial HCO_3, severe respiratory distress and duration of ventilation (>5 days) were found to be significantly (p>0.05) associated with death but other variables were not found to be significantly (p>0.05) associated with death [Table-8].

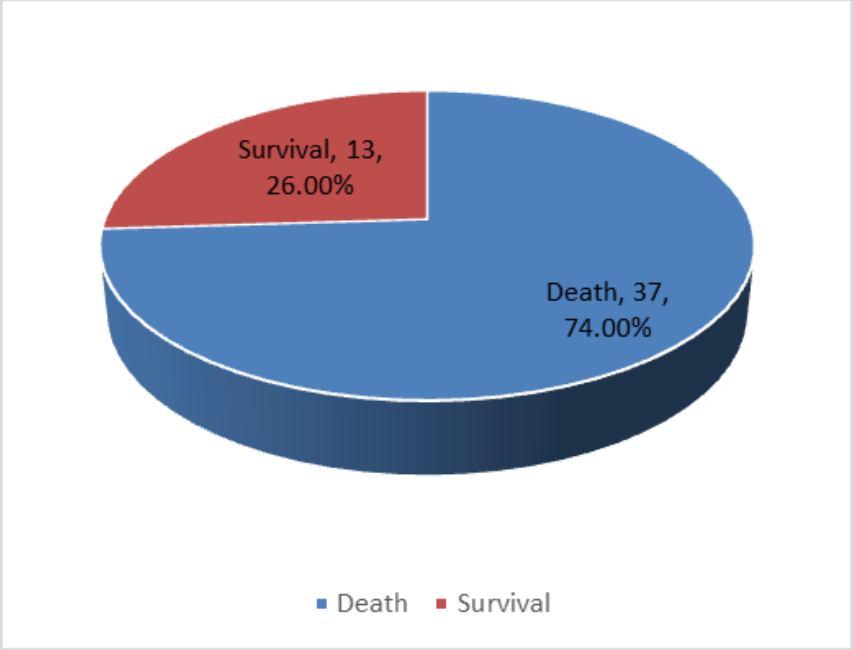

Figure 1: Distribute the study patients according to the outcome (N=50)

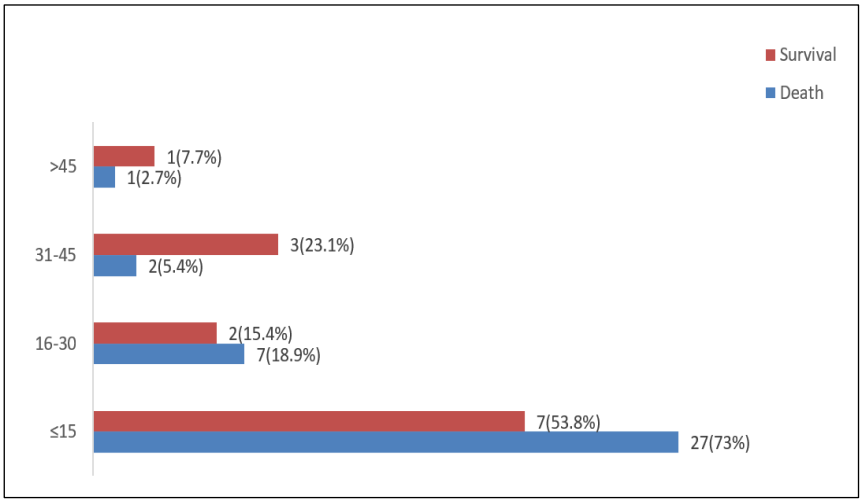

Figure 2: Age distribution of the study patients (N=50)

Table 1: Demographic characteristics of the study patients (N=50)

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

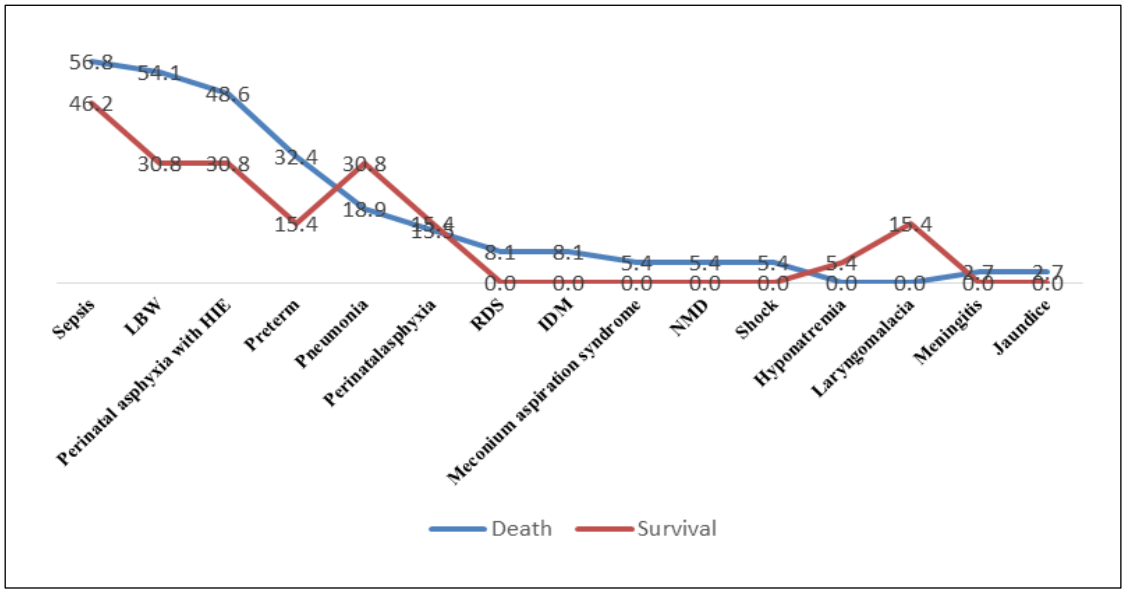

Figure 3: Bar diagram showing clinical diagnosis of the study patients (N=50)

Table 2 Relation between ventilator related complications and outcome (N=50)

Complications	Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
With Complications	16 (43.2)	4 (30.8)	1.71(0.45-6.58)	0.430
Without Complications	21 (56.8)	9 (69.2)		

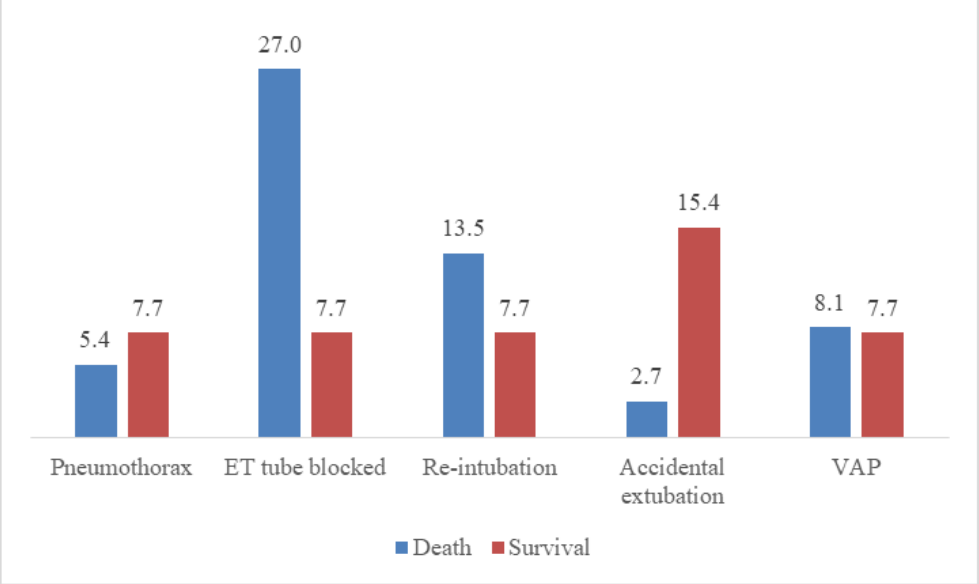

Figure 4: Bar diagram showing ventilator related complications of the study patients (N=50)

Table 3: Relation between initial FiO_2, PIP, PEEP, HCO_3, BE and outcome of ventilated patients (N=50)

Initials		Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
FiO_2(%)	>80	36 (97.3)	6 (46.2)	42 (4.35-405.14)	0.001
	<80	1 (2.7)	7 (53.8)		
PIP (cmH_2O)	>18.0	32 (86.4)	2 (15.4)	35 (5.95-208.14)	0.001
	<18.0	5 (15.6)	11 (84.6)		
PEEP (cmH_2O)	>5.0	26 (70.3)	2 (15.4)	13 (2.46-68.60)	0.002
	<5.0	11 (29.7)	2 (84.6)		
HCO_3(mmHg)	<15	26 (70.3)	3 (23.1)	7.88 (1.81-34.28)	0.003
	>15	11 (29.7)	10 (76.9)		
BE	<-10	28 (75.7)	5 (38.5)	4.98 (1.30-19.31)	0.019
	>-10	9 (24.3)	8 (61.5)		

Table 4: Relation between acidosis & outcome (N=50)

Parameter	Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
Before ventilation				
Metabolic acidosis	28 (75.7)	5 (38.5)	4.07 (1.09-15.20)	0.019
Respiratory acidosis	3 (8.1)	1.(7.7)	1.06 (0.10-11.18)	0.725
Before extubation/ death				
Metabolic acidosis	19 (51.4)	2 (15.4)	5.81 (1.13-29.89)	0.024
Respiratory acidosis	5 (13.5)	1.(7.7)	1.88 (0.20-17.74)	0.503

Table 5: Relation between respiratory distress and outcome according to Downe's score (N=50)

Respiratory distress	Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
Before ventilation				
Severe	13 (35.1)	4 (30.8)	1.21(0.31-4.73)	0.775
Moderate	24 (64.9)	9 (69.2)		
Before extubation/ death				
Severe	16 (43.2)	1 (7.7)	9.14(1.07-77.80)	0.04
Moderate	21 (56.8)	12 (92.3)		

Table 6 Relation between serum sodium and outcome (N=50)

Serum sodium (mmol/L)	Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
<135	4 (10.8)	5 (38.5)	0.19 (0.04-0.89)	0.039
>135	33 (89.2)	8 (61.5)		

Table 7: Relation between duration of ventilation and outcome (n=50)

Duration of staying		Death (n=37) n (%)	Survival (n=13) n (%)	Odds ratio (95% CI)	P value
Duration of ventilation (days)	>5	16 (43.2)	1 (7.7)	9.14(1.0744-77.803)	0.04
	<5	21 (56.8)	12 (92.3)		

Table 8: Multivariable regression analysis for prediction of death (n=50)

Predictors	Adjusted OR	95% CI		P value
		Lower	Upper	
Initial PIP (>18)	10.09	5.133	96.029	0.003
Initial PEEP (>5)	15.274	0.925	69.638	0.056
Initial FiO_2(>80)	17.068	0.747	39.177	0.076
Initial HCO_3(<15)	6.855	1.012	46.407	0.049
Initial Be (<-10)	1.444	0.229	9.092	0.695
Metabolic acidosis	0.746	0.137	4.059	0.737
Severe respiratory distress	10.031	1.053	95.557	0.045
Hyponatraemia	0.227	0.042	1.215	0.083
Duration of ventilation (>5 days)	11.919	1.333	86.573	0.027

DISCUSSION

Mortality among the sick children in ICU is high, but mortality among the mechanically ventilated children in ICU is still higher. In this study mortality among the ventilated infants up to 2 months age were found in 74.0%. Hossain *et al.,* [6] in Bangladesh found 75.5% mortality.

In this study, among the ventilated infants 86% were neonates and they were out born. In developed countries overall mortality was less than 2%. [8]. The high mortality is due to many of the sick neonate were ventilated as a last attempt at the eleventh hours of life. As all the neonates were out born, high case fatality of ventilated neonates may also be contributed by the damages that already occurred in utero or at birth or during transport to Intensive Care Unit. Disease pattern for which the infants were transferred to ICU and subsequently needed mechanical ventilation were low birth weight (54.1%) in death group and (30.8%) in survival group, perinatal asphyxia (13.5%%) in death group and (15.4%) in survival group, neonatal sepsis (56.8%) in death group and (46.2%) in survival group, RDS (8.1%) in death group, meconium aspiration syndrome (8.1%) in death group and pneumonia (18.9%) in death group (30.8%) in survival group. Shirly *et al.,* [19] documented 51.4% respiratory failure for invasive ventilation. Sing *et al.,* [20] found similar survival rate in asphyxia. Survival rate was higher in pneumonia (100%).

This study tried to find out the predictors of fatality in mechanically ventilated infants. Mean age was 14.2±10.1 days in death group and 20.2±18.2 days in survival group, more than two third (73.0%) belonged to age<15 days in death group and 53.8% in survival group. Age did not play any significant role in outcome. Kollef [20] found similar result in their study. A study done in India by Dave *et al.,* [21] also found similar result in their study. Mortality was higher in cases having weight <2500 gm but not significant (p=0.148). In this study gestational age was found to be an important predictor of fatality in ventilated neonate. Mortality was higher in cases having gestational age more than 34 weeks but not significant (p=0.321). In premature neonate all physiological systems are immature particularly the respiratory system. Moreover, premature neonates stop respiration when become hypoxic. Again, the immaturity of respiratory tract, poor mucocilliary clearance and poor immunity guard the prognosis of ventilated premature neonate. Acid base disturbance in the form of acidosis before ventilation was found to be an important predictor of poor outcome. In this study significant relation was found between metabolic acidosis & outcome. Among the ventilated infants, metabolic acidosis was found 75.7% & 38.5% before ventilation in death & survival group respectively (p=0.019) whereas metabolic acidosis before death was 51.4% in death & 15.4% in survival group (p=0.024). Among the ventilator parameters PIP and PEEP were found significantly related with poor outcome of ventilated neonate. Rate of ventilation had no significant relation with poor outcome of ventilated neonates. FiO_2 was found significantly related with outcome (p=0.001). Hossain *et al.,* [6] also found significant relation of FiO_2 with outcome (p< 0.05). This study showed significant relation between serum sodium level and outcome of ventilated patients (p=0.039). The presence of dysnatremias (either hypo or hypernatremia) in ICU has been reported to be around 30%.[22,23] Most of the study has reported hyponatremia to be more prevalent than hypernatremia 23.2% vs. 16.7%[24], 27.43% vs. 3.5%[24], 50.5% vs. 9.4%[25]. Sachdev A noted hyponatremia in 19.3% [26]. But it might vary due to institutional policy of maintenance intravenous fluid. Ventilation related complications were common among ventilated infants. 16(43.2%) patients developed complications during ventilation in death group and 4(30.8%) in survival group. The difference was not statistically significant (p>0.05) between two groups. ET tube blocked, re-intubation and VAP were higher in death group than survival group but pneumothorax and accidental extubation lower in death group than survival group in this study compared to lower rate found in Hossain *et al.,* [6]. Special attention should be given to reduce these preventable complications. Ventilator associated pneumonia was present in a very low rate 8.1% in death group and 7.7% in survival group in this study. Higher mortality in pneumonia cases was found in Petdachai *et al.,* [27] and Apisamthanarak *et al.,* [28] (29.4% and 28.3% respectively) compared to this study. Incidence of barotraumas evident by pneumothorax, pneumomediastinum, pneumoperitoneum was lower in this study compared to the findings of Wilson *et al.,* [29]. Adequate ventilation along with short length of ventilation may be the cause of lower incidence of these complications. Significant relation between duration of ventilation and poor outcome was found in this study. Wilson *et al.,* [29] f also found significant relation between duration of ventilation and outcome. Mean duration of ventilation was also less in this study compared to Bejersten *et al.,* [30]. Before death severe respiratory distress was statistically significant P >0.05. An increasing respiratory rate or tachypnoea is used as one of the most important signs of illness in infants. As lower respiratory tract infections are one of the reasons of morbidity and mortality in the first year of life. [31]. The sign of tachypnoea is taught as an important indicator of respiratory failure, bronchiolitis, pneumonia or heart failure in infants. [32].

In multivariable regression analysis prediction for mortality among ventilated neonates found that initial high PIP >18, initial low HCO_3 <15mmHg, severe respiratory distress and duration of ventilation (>5 days) were found to be significant (p<0.05). Mukhtar *et al.,* [33] also tried to find out the predictors of mortality in mechanically ventilated children in

PICU. Acute cardiac failure ($p<0.001$) and prolonged mechanical ventilation (10 days) ($p<0.05$) were significantly important predictor of mortality in mechanically ventilated children in the PICU. Another study done by Mathur *et al.*, [34] reported that initial arterial pH<7.1 O_2 saturation <80%, $PaCO_2$> 60 mmHg, FiO_2>60%, hyponatremia, hypokalemia and complications during ventilation were the significant predictors of mortality in ventilated neonates in the intensive care unit.

LIMITATIONS OF THE STUDY

This observational study was conducted in only one selected hospital in Dhaka city, so the results of the study may not reflect the exact picture of the country. As well as small sample size was also a limitation of the present study due to covid-19 pandemic situation.

CONCLUSION

The rate of mortality in the ICU was high. Initial high PIP, low HCO_3, severe respiratory distress and prolong duration of ventilation (>5 days) were significant independent predictors of mortality. Repeated assessment of these parameters will help in better management of critically ill children. A favorable outcome requires repeated monitoring of ventilator & biochemical parameters & meticulous management of those abnormalities.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) had given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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