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Original Articles

Predictors of Mortality in Ventilated Neonates in Intensive Care Unit

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Abstract

Background: A large number of neonates in intensive care unit require mechanical ventilation due to various conditions and have a high mortality. To reduce the high mortality in this group of neonates, identification of risk factors is important.

Objective: This study was undertaken to find out the predictors of mortality in ventilated neonates in the Intensive Care Unit.

Methods: This study was carried out in the Intensive Care Unit of Dhaka Shishu Hospital from March 2006 to November 2006. Neonates consecutively put on mechanical ventilation during the study period were enrolled. The enrolled neonates were divided into two groups; neonates who died after putting to the ventilator were in group-I and neonates who survived after receiving mechanical ventilation were in group-II. Clinical, biochemical and ventilator parameters were analyzed to find out the predictors of mortality of ventilated neonates.

Results: During the study period total 51 out born very critically sick neonates were ventilated due to different causes. Out of these 51 neonates, 58.8% were male with a male to female ratio 1.42:1. Mean age, weight and gestational age were 5.3±6.5 days, 2171±796.2 gm and 34.8±4.1 weeks respectively. Out of 51 mechanically ventilated neonates enrolled for this study, 70.6% died. Factors significantly different in non-survivors were mean weight, mean gestational age, initial arterial pH and duration of hospital stay ($p<0.05$). Weight <2500gm, gestation <34weeks, initial pH <7.1, $PaCO_2$ >60 mmHg, serum sodium <130 mmol/l, serum potassium <3.5 mmol/l and FiO_2 >60% were significantly associated with mortality in neonates requiring mechanical ventilation ($p <0.05$). Significant relation with mortality was found in those neonates who developed complications during ventilation ($p=0.01$).

Conclusion: Among the analyzed factors weight <2500gm, gestation <34weeks, initial arterial pH <7.1, O_2 saturation<80%, $PaCO_2$ >60mmHg, FiO_2 >60%, hyponatremia, hypokalemia and complications during ventilation were the significant predictors of mortality in ventilated neonates in the intensive care unit.

Key words: *Neonates, mechanical ventilation, predictors of mortality.*

Introduction

In all critically ill patients, the immediate objective is to preserve life and prevent reserve or minimize damage to vital organs such as the brain and the kidneys. Intensive care medicine is concern predominantly with the management of patients with acute life threatening conditions[1]. Intensive care medicine and neonatal intensive care service is now on an advancing stage in Bangladesh. With the improvement of health service facilities especially for neonates, more critically ill neonates are reaching to the health facilities but many of them are in very critical condition and mortality of these neonates is still very high. Mortality rate of critically ill babies in ICU of Dhaka Shishu Hospital was 491/1000 admission[2] during July 1995 to June 1996, 530/1000 admission[3] during 1997 to 1999. An unpublished data from the same unit revealed that mortality rate was 408/1000 admission from January to December 2005 and no improvement regarding mortality reduction has been evident over the last 10 years.

The widespread introduction of mechanical ventilation into neonatal intensive care units during 1960s and

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1970s improved the survival of sick newborn[4]. Actually assisted ventilation has revolutionized the outcome of sick newborn in NICUs[5]. It is one of the important advancement in neonatal medicine which reduces neonatal mortality. A large number of neonates in neonatal intensive care unit require mechanical ventilation. These mechanically ventilated neonates have a high fatality[6-7]. One study was conducted in ICU of Dhaka Shishu Hospital during 1998 showed that the survival rate of ventilated neonates was only 24.5%[8]. Trotman et al[9] found 64% and Karthikeyan et al[10] found 67.9% survival rate, though less than that quoted for developed countries (91%)[11] compares favourably with figures quoted for other developing countries (46-54%)[12,13]. Differences in mortality of ventilated neonates between developed and developing countries may be related to the ready availability of surfactant and parenteral nutrition in developed countries as compared to developing countries. Limited technical expertise and technological advances in developing countries may also be an added factor.

The benefits of intensive care including mechanical ventilation are clear but provision of these intervention are labour intensive and require a major financial expenditure that is not entirely recoverable. Also morbidity and mortality of the neonates who received mechanical ventilation till now is high. For reduction of fatality in this group of neonates, identification of risk factors is important. Recent evidence indicates that weight and gestational age are the major determinant of neonatal mortality along with severity of illness on admission has some influence on outcome[8]. pH, $PaCO_2$, base excess and FiO_2 have long been identified as critical risk factor in ventilated neonates[6]. Incidence of complications related to ventilatory techniques and strategies also has impact on outcomes[8]. Maximum data regarding ventilated sick neonates were from developed countries. In a developing country like Bangladesh, where budgetary constraints limit technological advances, the policy of implementation of mechanical ventilation needs to be line-up in such a way that could be helpful in reduction of morbidity and mortality. So, the present study was designed to find out the predictors of mortality in mechanically ventilated neonates in intensive care unit in Bangladesh in order to institute appropriate resource planning and management to improve their survival.

Materials and Methods

This prospective study was conducted from 1st March 2006 to 30th November 2006 in the Intensive Care Unit (ICU) of Dhaka Shishu (Children) Hospital (DSH). In DSH all the neonates were out born, either referred from other hospitals or born at home and transported to this hospital directly by relatives. Fifty one neonates consecutively put on mechanical ventilation during the study period were enrolled. Neonates who required ventilation with multiple congenital anomalies were excluded from the study. The enrolled neonates were divided into two groups; neonates who died after putting to the ventilator were in group-I and neonates who survived after receiving ventilation were in group-II.

For each ventilated neonate, information included age, sex, date and time of birth, admission weight (recorded by electronic weighing machine), gestational age (determined from maternal records) and primary diagnosis were recorded.

The indications for initiation of mechanical ventilation were (1) pH <7.25, (2) $PaCO_2$ >55 mm of Hg, (3) PaO_2 <50 mm of Hg, (4) Intractable apnoeic spell, (5) Retraction and/or gasping respiration, (6) Recurrent apnoeic spells with bradycardia and/or cyanosis, (7) O_2 saturation <80% in head box. Pressure limited time cycled ventilator was used and observations at the time of initiation of ventilation include peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), fraction of oxygen in inspired air (FiO_2), inspiratory time (Ti) and arterial blood gas analysis (ABG). Oxygen saturation (SaO_2) was monitored and maintained between 92% and 95%. Complications encountered during ventilation and duration of ventilation was also noted. Finally, outcome and duration of hospital stay were recoded. Relevant investigations including serum electrolytes, blood urea, serum creatinine, random blood sugar and CXR were done.

Written consent was taken in each cases and permission of ethical review committee of Bangladesh Institute of Child Health and Dhaka Shishu Hospital was also taken. After proper cleaning the collected data were analyzed thoroughly. In addition to descriptive statistics chi-square (χ^2) test, Fisher exact test and 't' test were applied accordingly to determine statistically significant differences. For data entry and analysis SPSS version 12 was used.

Results

This study included 51 very sick out born neonates who required mechanical ventilation in ICU of DSH. Among the ventilated neonates, 30 (58.8%) were male and 21 (41.2%) were female and male female ratio was 1.42:1. Mean age, weight and gestational age were 5.3±6.5days, 2171±796.2gm and 34.8±4.1 weeks respectively (Table-I). Among the enrolled neonates, 28 (54.9%) were admitted within first 3 days of life, 9 (17.6%) were 4-7 days of age and remaining 14 (27.5%) were admitted after 7 days of age.

Table-I

Distribution of the ventilated neonate by baseline characteristics (n=51)

Baseline characteristic	Mean	SD	Range
Age (days)	5.3	±6.5	1-27
Weight (gm)	2171	±796.1	650-3120
Gestation (weeks)	34.8	±4.1	27-41

Out of 51 mechanically ventilated neonates enrolled in this study, 36 (70.6%) died (Fig.-1). Disease pattern among the ventilated neonates were perinatal asphyxia (37.3%), preterm LBW with refractory apnoea or respiratory failure (29.4%), neonatal sepsis (15.7%), RDS (5.9%), meconium aspiration syndrome (MAS) (5.9%), pneumonia (3.9%) and meningitis (1.9%). Among the neonates with perinatal asphyxia 68.4%, preterm low birth weight 80.0% and neonatal sepsis 75% died (Table-II). There was no significant relation between mortality and perinatal asphyxia [$\chi^2_{\{df=1\}}$=.069, p=0.51], preterm low birth weight [$\chi^2_{\{df=1\}}$=.907, p=0.27] and neonatal sepsis [$\chi^2_{\{df=1\}}$=.089, p=0.56].

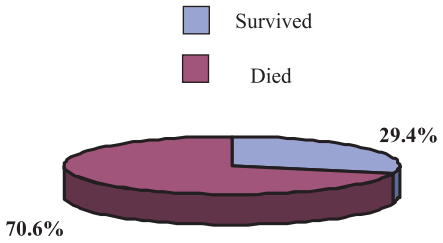

Fig.-1: *Distribution of outcome of ventilated neonates*

Table-II

Distribution of outcome of neonates who were ventilated by diagnosis (n=51)

Diagnosis	Total N (%)	Survived N (%)	Died N (%)
Perinatal Asphyxia	19 (37.3)	6 (31.6)	13 (68.4)
Preterm LBW with refractory apnea or respiratory failure	15 (29.4)	3 (20)	12 (80)
Neonatal Sepsis	8 (15.7)	2 (25)	6 (75)
RDS	3 (5.9)	1 (33.3)	2 (66.7)
MAS	3 (5.9)	1 (33.3)	2 (66.7)
Pneumonia	2 (3.9)	2 (100)	0
Meningitis	1 (1.9)	0	1 (100)
Total	51 (100)	15 (29.4)	36 (70.6)

Factors significantly different in non-survivors were mean weight, mean gestational age, initial arterial pH and duration of hospital stay ($p < 0.05$). However, age, PaO_2, $PaCO_2$, HCO_3, duration of ventilation, PIP, PEEP and rate were not associated with fatality (Table-III). Weight <2500gm, gestation <34weeks, initial pH <7.1, $PaCO_2$ >60 mmHg, serum sodium <130 m mol/l, serum potassium <3.5 mmol/l and FiO_2 >60% were significantly associated with mortality in neonates requiring mechanical ventilation ($p<0.05$) (Table-IV).

Table-III

Predictors of mortality in ventilated neonates (n=51)

Parameters	Non-survivors Mean±SD	Survivors Mean±SD	p value*
Age (days)	5.3±6.7	5.2±6.02	0.95
Weight (gm)	1827±697.2	2715.9±864.7	0.04**
Gestation (weeks)	33.1±4.2	36.4±2.7	0.006**
Initial arterial pH	7.14±0.15	7.25±0.17	0.04**
PaO_2 (mm of Hg)	62.8±29.8	67.4±36.7	0.64
$PaCO_2$ (mm of Hg)	44.6±22.8	42.3±18.5	0.73
HCO_3 (mmol/l)	18.4±7.1	19.9±7.3	0.49
Duration of ventilation (hours)	54.4±32.3	50.9±21.9	0.69
PIP (cm of H_2O)	22.3±2.8	23.1±2.5	0.34
PEEP (cm of H_2O)	3.5±0.5	3.4±0.5	0.41
Rate (/min)	41.1±12.5	40±11.5	0.76
Duration in hospital (days)	3.7±2.7	10.8±8.2	0.00**

*t test; **statistically significant

Table-IV

Correlation of variables with outcome in mechanically ventilated neonates

Parameters	Group-I	Fatality N (%)	Group-II	Fatality N (%)	p value*
Weight (gm)	<2500	22 (88.0)	>2500	14 (53.8)	0.01 **
Gestation (wks)	<34	13 (92.8)	>34	23 (62.2)	0.04 #**
Initial pH	<7.1	17 (89.5)	>7.1	19 (59.4)	0.04 **
PaO_2 (mm of Hg)	<50	16 (72.7)	>50	20 (68.9)	0.7
$PaCO_2$ (mm of Hg)	>60	16 (94.1)	<60	20 (58.8)	0.02 **
BE	>-10	17 (80.9)	<-10	19 (63.3)	0.29
Sodium (mmol/l)	<130	16 (94.1)	>130	20 (58.8)	0.02 **
Potassium (mmol/l)	<3.5	17 (89.5)	>3.5	19 (59.4)	0.04 **
Blood Glucose (mmol/l)	<3	8 (61.5)	>3	17 (70.8)	0.71 #
Blood Urea (mg/dl)	>12	1 (50.0)	<12	19 (76.0)	0.18 #
S. Creatinin (mmol/l)	>120	1 (50.0)	<120	18 (81.8)	0.13 #
FiO_2 (%)	>60	26 (81.2)	<60	10 (52.6)	0.03 **

*Chi-square (χ^2) test; #Fisher exact test; **statistically significant

Indications of starting mechanical ventilation among the enrolled neonates were recurrent apnoea in 17 (33.3%), intractable apnoea in 10 (19.6%), gasping respiration in 17 (33.3%) and oxygen saturation <80% after giving oxygen by oxygen hood in 36 (70.6%) cases. Among 17 neonates with recurrent apnoea 11 (64.7%) were died, 8 (80.0%) died among 10 intractable apnoea cases, among 17 neonates with gasping respiration 14 (82.4%) died and out of 17 cases had O_2 saturation <80%, 11 (64.7%) died (Fig.-2). Among the indications, only significant relation was found between the neonates had O_2 saturation <80% and mortality [$\chi^2_{\{df=1\}}$=16.409, p=0.00].

Twenty (39.2%) neonates developed complication during ventilation and complications encountered were blockage of ET tube in 8 (40.0%) cases, accidental extubation in 6 (30.0%) cases, intrventricular haemorrhage (IVH) in 3 (15.0%) cases, pneumonia in 1 (5.0%) case and pneumothoarx in 2 (10.0%) cases. Among them, 10% survived and 90% died (Fig.- 3). Significant association was found in between mortality and development of complication related to ventilation [$\chi^2_{\{df=1\}}$=5.972, p=0.01].

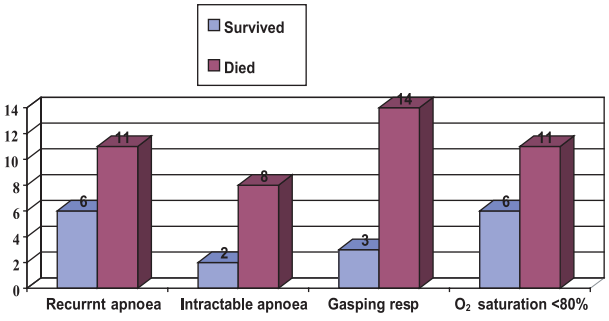

Fig.-2: *Indications of ventilation in neonates and their outcome*

Fig.-3: *Outcome of ventilated neonates by complications*

Discussion

Mortality among the very sick neonates in ICU is high[2,3], but the mortality among the mechanically ventilated neonates in ICU is still higher. In this study mortality among the ventilated neonates were found

in 70.6%. Hossain et al[8] in Bangladesh found 75.5% mortality and Mathur et al[14] in India found 74% mortality among the ventilated neonate. Some centers had better survival rate ranged from 41.3% to 68.3%[5].

There is a paucity of data on mechanical ventilation in out born neonates and the number of units catering to these neonates is grossly inadequate. In our study all the ventilated neonates were out born. Mathur et al[14] also observed similar situation in one centre in India where all the neonates put on mechanical ventilator were out born and had high mortality (74%). Causes of high mortality among the out born ventilated neonates may be due to damages that already occurred in utero or at birth or delay in transport to intensive care unit. To reduce mortality in these neonates a proper network of neonatal services, referral and transport system need to be established in our country.

This study found similar trend of disease pattern for which the neonates were transferred to ICU and subsequently put on mechanical ventilation reported by Hossain et al[8]. Mortality in this study among preterm low birth weight (80%) is higher; neonatal sepsis (75%) is similar and perinatal asphyxia (68.4%) is lower than their findings. Singh et al[5] found similar survival rate in asphyxia. Severe perinatal asphyxia associated with irreversible brain damage may go into respiratory failure due to central cause and responsible for poor outcome. We found higher survival rate in pneumonia (100%) as reported by Hossain et al[8].

This study tried to find out the predictors of mortality in mechanically ventilated neonates. Age and sex of the neonates did not play any significant role in outcome ($p>0.05$), similar findings reported by Kollef[15]. Mortality was significantly higher in cases had weight <2500 gm and gestational age <34 week ($p<0.05$). Similar findings reported by Mathur et al[14]. p^H before ventilation was also found to be an important predictor of poor outcome. Mathur et al[14] had found relation between p^H below 7.3 and mortality, Hossain et al[8] reported significant relation in pH <7 with poor outcome where as we found significant relation between pH <7.1 and case fatality. 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. Early identification of acid-base disturbances might prevent organ damage and improve the outcome. This study found no significant role of PaO_2 on poor outcome ($p>0.05$) but FiO_2 was found significantly related with outcome ($p<0.05$). But Mathur et al[14] found significant relation of PaO_2 and FiO_2 with outcome. Initial high FiO_2 required maintaining O_2 saturation reflected the severity of respiratory failure and subsequently poor outcome.

We found significant relation between hyponatraemia and hypokalaemia with outcome ($p<0.05$). Majority of the neonates were admitted due to perinatal asphyxia and neonatal sepsis which along with mechanical ventilation may developed SIADH, subsequently electrolyte abnormalities and poor outcome. Hossain et al[16] also found significant relation between hyponatraemia, hypokalaemia and poor outcome of neonates in ICU.

Hossain et al[8] found significant relationship between apnea and mortality, but among the parameters used for initiation of ventilation in this study, only unstable oxygen saturation (saturation <80%) was found statistically significant ($p<0.01$). The mean duration of ventilation was less in this study in comparison to finding reported by Mathur et al[7]. No relation between duration of ventilation and poor outcome was found in this study where as he found significant relation in duration of ventilation and outcome.

Ventilation related complications are common among the ventilated neonates which influence the outcome. We found complications in 39.2% cases, which was significantly related to poor outcome ($p<0.05$). Rate of ET tube block (15.7%) and accidental extubation (11.8%) was high in the present study compared to lower rate founded by Hossain et al[8] and Mathur et al[7]. As accidental extubation is a hazardous complication, special attention should be given to reduce these preventable complications. By improving monitoring facility like use of Nellcor Stat Cap[17] by which position of ET tube can be accurately recognize and early detection of these preventable complications are necessary for better outcome. In this study ventilator associated pneumonia was present in a very low rate (only 5%) with low mortality compared to higher mortality, 29.4% and 28.3% founded by Petdachai[18] and Apisarnthanarak[19] respectively. Incidence of barotraumas evident by pneumothorax, pneumomediastinum, pneumoperitoneum was lower in this study compared to the findings of Wilson[20].

Conclusion

Among the analyzed factors weight <2500gm, gestation <34 weeks, initial arterial pH <7.1, O_2

saturation<80%, $PaCO_2$ >60mmHg, FiO_2 >60%, hyponatremia, hypokalemia and complications during ventilation were the significant predictor of mortality in ventilated neonates in the intensive care unit.

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