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Original Research Article.

Clinical Profile and Outcome of Neonates Requiring Mechanical Ventilation

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ABSTRACT

Background: Mechanical ventilation is one of the important advancement which has contributed to the decline of neonatal mortality in the various parts of the world. Many sick neonates admitted to neonatal intensive care unit (NICU) require mechanical ventilation for different clinical conditions but it is associated with various complications and the outcome of these neonates is unpredictable.

Objective: To find out the clinical conditions and immediate outcome of neonates requiring mechanical ventilation.

Methods: This prospective observational study was conducted in Neonatal Intensive Care Unit (NICU), Department of Neonatology of Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of August 2015 to July 2016. Neonates required to put on mechanical ventilation were consecutively enrolled. All babies were monitored for clinical profile and outcome as well as complications. The enrolled neonates were divided into two groups. Neonates who remained successfully extubated for >48 hours and did not require re-intubation were grouped as survivors and who died during mechanical ventilation or within 48 hours of extubation were grouped as non-survivors. Clinical, biochemical, ventilator parameters and occurrence of complications were analyzed to find out the factors associated with mortality of ventilated neonates.

Results: During the study period 53(8.6%) of admitted neonates in NICU received mechanical ventilation. Out of these 53 neonates 69.8% were male with male to female ratio 2.3:1.Inborn babies were more (58.5%) than out born (41.5%). Mean age, gestational age and birth weight were 3.58±5.45days 33.34±3.40 weeks and 1852.55±513.48g respectively. Commonest condition for initiating mechanical ventilation was refractory apnea (35.8%) followed by severe respiratory distress with Downe score >6 (20.8%) and SpO2< accepted level (17.0%). Disease pattern were sepsis (35.8%), RDS (20.8%), congenital pneumonia (18.9%), perinatal asphyxia (15.1%), meconium aspiration syndrome (3.8%), TTN (1.9%) and Meningitis (3.8%). The survival rate was 35.8%. Factors significantly different in non-survivors were mean gestational age, mean birth weight, initial arterial p^H, age at admission and age at initiation of ventilation ($p<0.05$). The mean maximum PIP requirement was significantly higher in non-survivors ($p<0.05$). Hospital acquired sepsis (67.9%) was the most common complication during mechanical ventilation followed by tube block (52.8%) and ventilator associated pneumonia (26.4%). Shock (64.2%) was the commonest co-morbidity followed by dyselectrolytemia (52.8%), sepsis (35.8%) and DIC (28.3%). Hospital acquired sepsis, shock and DIC were associated with mortality ($p<0.05$). Shock was found independent predictor of mortality ($p=0.001$).

Conclusion: The most common condition for initiating mechanical ventilation was refractory apnea. Sepsis was the commonest disease for which ventilation required. The survival rate of ventilated neonates was 35.8% and percentage of survival was more in babies with RDS. Hospital acquired sepsis was the major complication of ventilated neonates. Presence of hospital acquired sepsis, shock and DIC was significantly high in non-survivors. Shock was found as independent predictor of mortality.

Keywords: Complications, Mortality, Outcome, Neonates, Mechanical Ventilation.

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INTRODUCTION

Among the global birth scenario, nearly 3.5 million neonates are born each year in Bangladesh accounting for 2.7%.[1] Out of this number of neonates, 74000 die before initial four weeks of their life.[2] The number of neonatal mortality in developed region 3 per 1,000 live births, Pakistan 42 per 1,000 live births, India 29 per 1,000 live births.[3] Bangladesh is a resource limited developing country in South-East Asia with neonatal mortality rate 24.40 per 1000 live births (World Health Statistics. 2013). Neonatal deaths now account for more than two –thirds of all deaths in the first year of life and for about half of all deaths in under five children. Bangladesh has achieved millennium development goal in reduction of child mortality. Sustainable Development Goals target to reduce neonatal mortality to at least as low as 12 per 1000 live births by 2030.Improving intensive care facilities for the neonates in the country could be one of the effective interventions to achieve the global target of reducing under five mortality by two thirds. The descending trend of mortality has been even more impressive so far specially for very low birth weight infant whose birth weight is <1500gm.[4] Increased availability and proper utilization of mechanical ventilation in the hands of skilled manpower are the prerequisites of giving appropriate care to the high risk neonates.[5] It has been observed recently that the introduction of surfactant and TPN are also attributable factors for reduction of mortality.[6] There factors are only ensured in a modern neonatal intensive care unit (NICU). Mechanical ventilation is a part and parcel of modern NICU care.[7]

Mechanical ventilation may be defined as the movement of gas into and out of the lungs by an external source connected directly to the patient by way of a tracheostomy or an endotracheal tube.[8] Mechanical ventilation of newborn has been practiced for several years with several advances made in the way. It was introduced in the West in 1960s to support the infants with respiratory failure.[9] This innovative technology have reached to significant level in affluent nation, but due to its high cost, expert skill requirements has limited its use in developing countries.[10]

Babies with perinatal hypoxia & birth asphyxia as well as critically sick babies who developed life threatening apnea, progressive respiratory distress with impending respiratory failure or cardiovascular collapse need mechanical ventilation. So, mechanical ventilation has become a must to enhance newborn survival in those situations.[11] The survival of sick neonates have improved significantly with the widespread use of mechanical ventilation in NICUs.[12]

The benefits of intensive care including mechanical ventilation are clear but provision of these intervention are labor intensive and require a major financial expenditure that is not entirely recoverable.[13] Also morbidity and mortality of neonates who received mechanical ventilation till now is high. For reduction of fatality in this group of neonates, early identification of complications and factors influencing the outcome is important. Maximum data regarding ventilated sick neonates were from developed countries. In a developing country like Bangladesh, where budgetary constraints, limited 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.[14] It is hoped that, this study can identify the clinical profile and outcome of critically ill babies requiring ventilator care in NICU.

The main aim of this study was to observe the clinical profile and outcome of the neonates required mechanical ventilation.

MATERIALS AND METHODS

This prospective observational study was carried out in Neonatal Intensive Care Unit (NICU), Department of Neonatology of Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of August 2015 to July 2016.

Neonates required to put on mechanical ventilation were consecutively enrolled. Neonates with multiple congenital anomalies, surgical conditions and who died within 12 hours of initiation of ventilation were excluded. Clinical management was given according to standardized unit protocol. All babies were monitored for complications. The enrolled neonates were divided into two groups. Neonates who remained successfully extubated for >48 hours and did not require re-intubation were grouped as survivors. Those neonates who died during mechanical ventilation or within 48 hours of extubation due to same disease for which they received mechanical ventilation were grouped as non-survivors. Clinical, biochemical, ventilator parameters and occurrence of complications were recorded by a pre structured, peer reviewed, interview and observation based data collection sheet.

All data were entered, managed and analyzed a software named Statistical Package for social science (SPSS) version 23 (Ilinois; Chicago: USA). The continuous variables were analyzed by student's t test and the categorical variables were analyzed by chi square test. P-value was significant at <0.05. Besides, all the variables were expressed in frequency, percentages and mean with standard deviation.

Table 1: Distribution of demographic characteristics among enrolled neonates (N=53)

Demographic characteristics	n	%
Sex		
Male	37	69.8
Female	16	30.2
Gestational age (weeks)		
28-31	17	32.1
32-34	19	35.8
35-36	6	11.3
≥ 37	11	20.8
Birth weight (g)		
<1000	1	1.9
1000-<1500	17	32.1
1500-<2000	15	28.2
2000-<2500	9	17.0
≥ 2500	11	20.8

Table 2: Mode and place of birth history of enrolled neonates (N=53)

Birth history	n	%
Place of birth		
Inborn	31	58.5
Outborn	22	41.5
Mode of delivery		
NVD	15	28.3
Cesarean section	38	71.7

Table 3: Profile of ventilated neonates

Variable	Mean±SD	Range
Age(days)	3.58±5.45	1-27
Gestation(weeks)	33.34±3.4	28-40
Birth weight(g)	1852.55±513.48	950-2650
Initial arterial P^H	7.21±0.96	6.91-7.35
Age at initiation of ventilation(hours)	54.08±82.17	1-480
Duration of ventilation (hours)	152.87±9.14	70-506

Table 4: Outcome of enrolled neonates in relation to baseline characteristics.

Parameters	Total No.	Outcome	
Sex		**Survived No. (%)**	**Expired No. (%)**
Male	37	15(40.5)	22(59.5)
Female	16	4(25.0)	12(75.0)
Place of birth			
Inborn	31	15(48.4)	16(51.6)
Out born	18	4(22.2)	14(77.8)
Gestational age (weeks)			
28-31	17	4(23.5)	13(76.5)
32-34	19	4(21.1)	15(78.9)
35-36	6	2(33.3)	4(66.7)
≥37	11	9(81.8)	2(18.2)
Birth weight (g)			
<1000	1	1(100)	0(0.0)
1000-<1500	17	2(11.8)	15(88.2)
1500-<2000	15	4(26.7)	11(73.3)
2000-<2500	9	4(44.4)	5(55.6)
≥2500	11	8(72.7)	3(27.3)

Table 5: Disease pattern of ventilated neonate and Outcome

Variables	Total No.(%) 53(100)	Outcome	
		Survived No (%) 19 (35.8)	**Expired No (%) 34 (64.2)**
Perinatal asphyxia	8(15.1)	4(50)	4(50.0)
RDS	11(20.8)	6(54.5)	5(45.5)
Congenital Pneumonia	10(18.9)	5(50.0)	5(50.0)
Sepsis	19(35.8)	4(21.1)	15(78.9)
MAS	2(3.8)	0(0.0)	2(100)
TTN	1(1.9)	0(0.0)	1(100)
Meningitis	2(3.8)	0(0.0)	2(100)

Table 6: Comparison of profile between survivors and non-survivors

Variables	Survivors (n=19) Mean±SD	Non-survivors (n=34) Mean±SD	p value
Gestational age (wks)	34.6±4.10	32.6±2.84	0.041*
Birth-weight (g)	2114.7±559.0	1706.0±428.2	0.004*
Age at admission(days)	1.58±1.30	4.71±6.51	0.044*
Initial arterial P^H	7.28±0.04	7.17±0.10	<0.001*
Initial PO2	76.9±15.4	65.5±23.1	0.059^{ns}
Age at Ventilation(hrs)	23.52±33.07	71.14±95.94	0.042*
Duration of ventilation (hrs)	131.3±78.9	164.9±100.8	0.215^{ns}

*=Significant, ns=Not significant; Independent sample t-test were done

Table 7: Comparison of ventilator parameters between survivors and non-survivors

Variables	Survivors (n=19) Mean±SD	Non-Survivors (n=34) Mean±SD	p value
Maximum PIP (cm of H_2O)	16.52±1.12	18.06±1.18	`<0.001*
Maximum PEEP (cm of H_2O)	5.47±0.51	5.59±0.61	0.491^{ns}
Maximum FiO_2	0.69±0.10	0.75±0.13	0.091^{ns}

Independent sample t-test were done; *=Significant, ns=Not significant

Table 8: Association of hospital acquired sepsis and outcome of ventilated neonates

Hospital acquired sepsis	Ventilated neonates: Survived Freq. (%)	Ventilated neonates: Not-survived Freq. (%)	Total Freq. (%)	X^2	p Value
Yes	9(25)	27(75)	36(100)	5.77	0.017*
No	10(58.8)	7(41.2)	17(100)		
Total	**19(35.8)**	**34(64.2)**	**53(100)**		

*=Significant

Table 9: Association of shock and outcome of ventilated neonates

Had Shock	Ventilated neonates: Survived Freq. (%)	Ventilated neonates: Not-survived Freq. (%)	Total Freq. (%)	X^2	p Value
Yes	6(17.6)	28(82.4)	34(100)	13.66	0.0002*
No	13(68.4)	6(31.6)	19(100)		
Total	**19(35.8)**	**34(64.2)**	**53(100)**		

*=Significant

Table-10: Association of DIC and outcome of ventilated neonates

Had DIC	Ventilated neonates: Survived Freq. (%)	Ventilated neonates: Not-survived Freq. (%)	Total Freq. (%)	X^2	p Value
Yes	2(13.3)	13(86.7)	15(100)	4.611	0.032*
No	17(44.7)	21(55.3)	38(100)		
Total	**19(35.8)**	**34(64.2)**	**53(100)**		

*=Significant

Table 11: Multivariate regression analysis for predicting mortality of ventilated babies

Variables	Total no of neonates	Survived No. (%)	Odd ratio	95% CI	p value
Shock	34	6(17.6)	53.72	5.691-507.228	0.001*
Hospital acquired sepsis	36	9(47.4)	2.263	0.402-12.746	0.354
DIC	13	2(15.4)	2.285	0.304-17.191	0.422

*=Significant; Multivariate logistic regression analysis was done

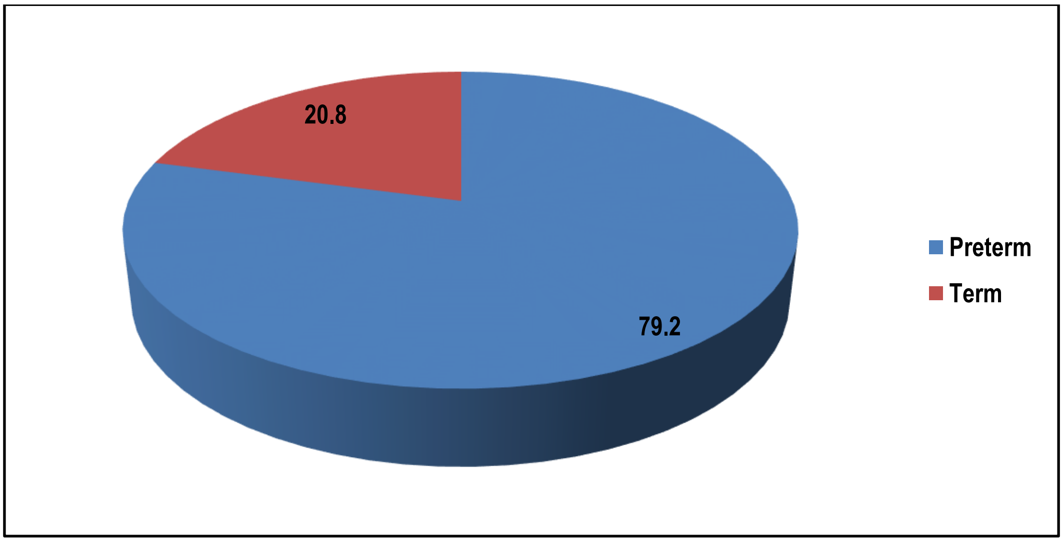


Figure 1: Distribution of enrolled neonates by their maturity status (N=53)

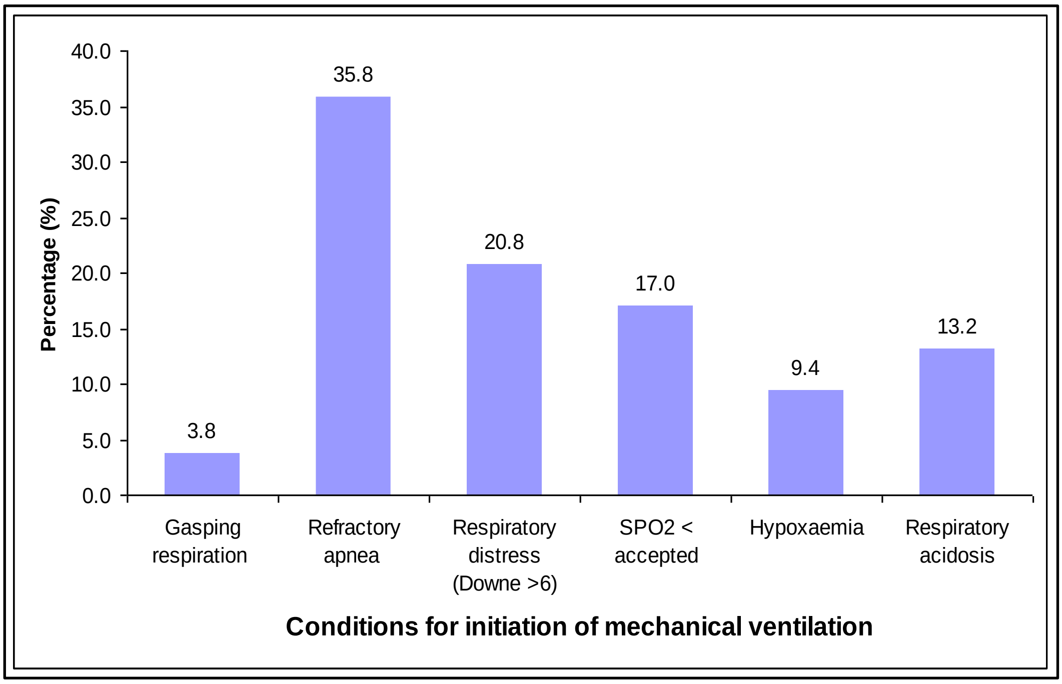


Figure 2: Conditions for initiation of mechanical ventilation in enrolled neonates

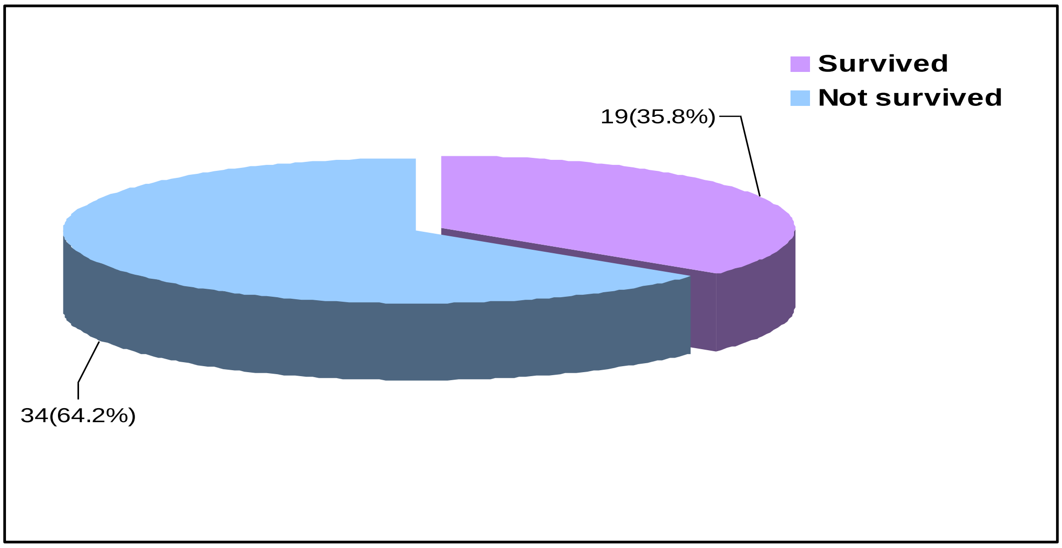


Figure-3: Distribution of outcome of ventilated neonates (N=53)

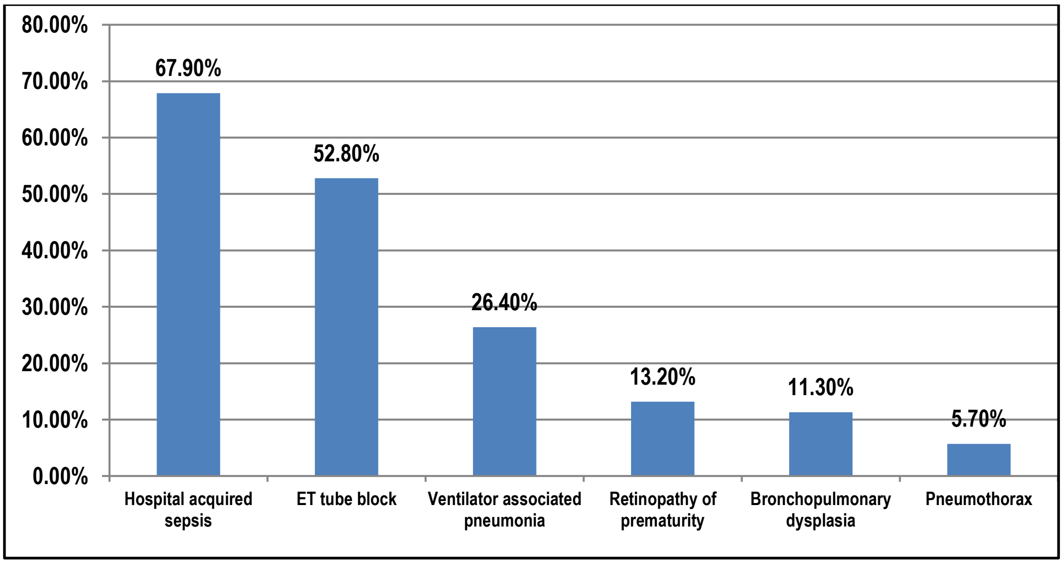
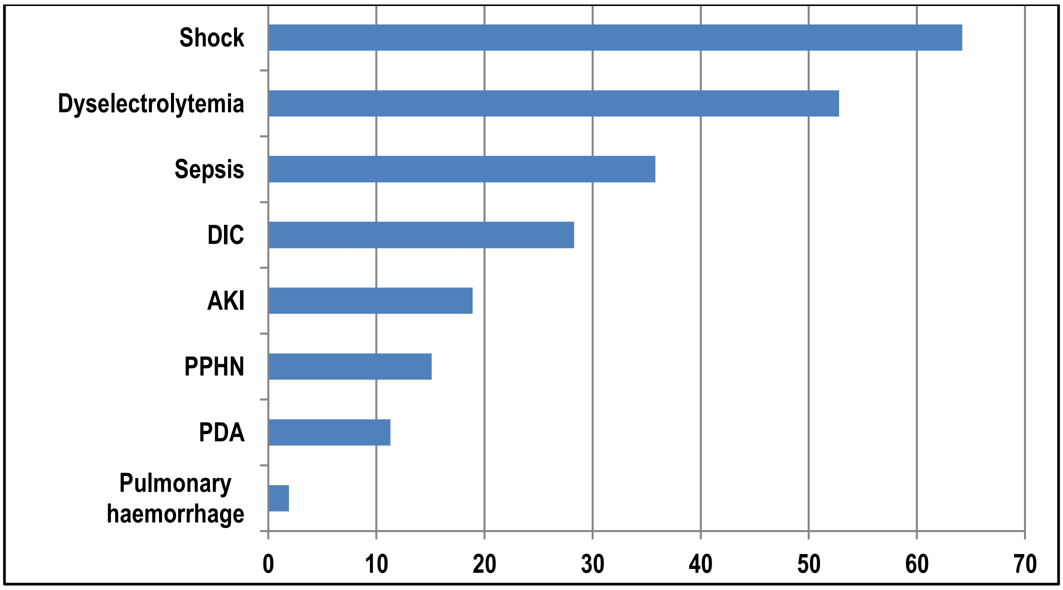


Figure 4: Complications during mechanical ventilation



(Percentage of co-morbidities were expressed in X axis)

Figure-5: Co-morbidities of Ventilated Neonates

RESULTS AND DISCUSSION

Neonatal morbidity and mortality rates are the reflection of a country's socioeconomic appearance. Besides the performance a good health of a care service can also be expressed by these indications.[15] The survival rate of neonates on mechanical ventilation in the low income countries (LICs) ranges from 25%-64%.[16] In this study, among the NICU admitted neonates received ventilatory treatment approximately one third (35.88%) were survived. Like other previous studies, the outcome of the neonate required mechanical ventilation was better with increasing birth weight and gestational age.[17]

In this study, total 53 neonates (8.6%) out of 615 admissions in one year were enrolled who required mechanical ventilation. This figure was in line to some previous studies where they reported 5.6%, 6.81%, 6.83% and 10.6% neonates of total admission required ventilatory support.[16] These variations may be due to several factors including inclusion and exclusion criteria, service availability, infrastructure and different admission policies of the NICU.

Additionally, we have observed overall survival rate of ventilated neonates as 35.8% which was strongly supported by some previous studies where the reported the overall survival of neonates as 33.3% and 35.48%.[9]

Among the study participants, 69% were male baby and 30.2% were female baby. The sex distribution revealed that male babies had better survival rate (40.5%) in comparison to female babies (25%). This trend was supported by a previous study where male vs female neonates survival were reported as 51.1% vs 40%.[18]

In this study, the mode of delivery revealed cesarean section (71.7%) was mostly chosen approach which was subsequently followed by NVD (28.3%). The increased rate of babies born by caesarian section was due to increased number of high risk pregnancies being referred to this hospital.

Out of 53 neonates, 79.2% were preterm and rest 20.8% were term which was also similar to a previous study.[19] The more number of preterm in this study was probably because of greater chance of development of respiratory distress syndrome at birth and require mechanical ventilator support in preterm babies.

Nearly sixty percent babies were inborn when compared to out born (58.5% vs 41.5%) and outcome was much better in intramural babies compared to extramural babies (48.4% vs 22.2%). These statistics were also observed in some other Indian studies.[19] These findings remind the importance of regionalization of newborn care to improve the overall outcome by the implementation of early intervention for high risk and sick inborn babies.

The most common condition of initiating mechanical ventilation in the present study was refractory apnea in 19 (35.8%) followed by respiratory distress with Downe score >6 in 11(20.8%), SPO2 less than accepted level in 9 (17.0) % cases. Other indications were respiratory acidosis in 7(13.2%), hypoxaemia in 5(9.4%) and gasping respiration in 2(3.8%) of enrolled neonates. In another Bangladeshi study, almost the same indications of starting mechanical ventilation were observed where recurrent apnea in 17(33.3%), gasping respiration in 17(33.3%), intractable apnea in 10(19.6%), oxygen saturation <80% with oxygen hood in 36(70.6%).[14] A Nepalese study reported that severe respiratory distress as their commonest condition for starting mechanical ventilation.[20]

In our study, mean gestational age of enrolled infants was 33.34 ± 3.41weeks and mean gestational age was significantly higher in survivors than that of non-survivors (34.6 ± 4.10 vs 32.6 ± 2.84weeks, p value< 0.05). Survival rate was 81.8% in term, 33.3% in 35-36weeks, 21.1% in 32-34 weeks and 23.5% below 32 weeks of gestational age. A recent study claimed similar results where the survival was better in term newborn. Mean birth weight of enrolled neonate was 1852.55 ± 513.48g and mean birth weight was significantly higher in survivors than that of nonsurvivors (2114.7 ± 559.0g vs 1706.0 ± 428.2 g, p value<0.004). At least, two previous studies shown significantly higher mean gestational age and mean birth weight of the survivors than that of non-survivors which is comparable to our study.[14]

Mean age of enrolled babies at admission of ventilated babies was 3.58±5.45 days in this study and significant delay in mean age at admission was observed in non survivors than that of survivors (4.71± 6.51Vs1.58±1.30days,p value <0.05)). Another Bangladeshi study shown mean age of ventilated babies at admission were 5.3±6.7Vs 5.2±6.02 days but no statistical significant difference was found between survivors and non survivors.[14] This low mean age of admission among survivors is probably due to our inborn babies admitted within first few hours of life at early part of illness before occurring metabolic changes and multiorgan damage.

In this study, mean initial arterial PH was significantly low in non-survivors than that of survivors (7.17±0.10Vs7.28±0.04, p value <0.001) which is supported by the results of an Indian study where the author reported low mean initial arterial pH in non survivors than survived newborn but the difference was not statistically significant.[21] 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 was significantly higher in non survivors than that of survivors (16.5±1.1 Vs 18.0±1.1cm of H2O, p value<0.001). They also shown significantly higher mean of the maximum PIP requirement of non survivors than that of the survivors which is comparable to the present study. In this study we have found that the non survivors required a greater mean maximum PEEP and maximum FiO2 than survivors, but the difference was not statistically significant. Similar findings were observed in some previous studies where the authors shown no statistical significant difference of mean maximum PIP, maximum PEEP and maximum FiO2 requirement between survivors and non-survivors.[21]

In the present study, mean age at initiation of ventilation of enrolled newborn was 54.08±82.17 hours. Mean age at initiation of ventilation was significantly higher in non survivors than that of survivors (71.14±95.94 Vs 23.52±33.07 hours (p value<0.05). It may also be compared to the results of a previous study where it was shown the significantly higher age at initiation of ventilation in non survivors than that of survivors.[19]

Sepsis was the commonest disease (in 35.8% cases) among newborn requiring mechanical ventilation during hospital stay. Next to sepsis, respiratory distress syndrome 11(20.8%), congenital pneumonia 10(18.9%) and perinatal asphyxia in 8(15.1%) cases were listed as predominant disease pattern. Other conditions were meconium aspiration syndrome, meningitis and TTN in 2(3.8%), 2(3.8%) and 1(1.9%) cases respectively. Likewise, the most common disease pattern in mechanically ventilated neonates was sepsis in 19 patients (37.2%) followed by respiratory distress syndrome 9(17.6%), meconium aspiration syndrome 5(9.8%), birth asphyxia 6 (11.7%) and congenital pneumonia in 2 according to a previous Nepalese study.[21] Similar report was observed in a previous Indian study.[10] However, perinatal asphyxia was also shown as the commonest disease pattern requiring mechanical ventilation in previous two studies.[8]

In this study, complications of the ventilated babies were hospital acquired sepsis septicemia (67.9%) followed by tube block (52.8%), ventilator associated pneumonia (26.4%), ROP (13.2%), BPD (11.3%) and pneumothorax (5.7%). Hospital acquired sepsis was the commonest complication in our study, as reported in other study.[10] Sepsis is a major complication in ventilated babies due to frequent intervention like blood gases and prolonged duration of ventilation. The organism was isolated in blood culture of 14 neonates during the study period out of which 3(21.4%) survived. A previous study reported 18.7% survival of culture positive neonates which is comparable to our study.[17] In this study commonest organism was Acinetobacter spp.

Tube block was seen in 52.8% neonates which was not comparable to other studies where they shown 32.3% and 15.18% tube block cases.[10] Pnuemothorax was found in only 3(5.7 %) cases, which is comparable with other study results where they reported higher incidences of pneumothorax.[21] This lower incidence of pneumothorax in our study can probably be attributed to the judicious use of pressures and early attempts at weaning. Ventilator associated pneumonia incidence was 26.4% in our study which was contrast to low incidence (5.06%) of other study.[10] On the contrary, another study reported high incidence (55.2%) of VAP in neonates on mechanical ventilation.[22] Mechanically ventilated babies face a particular risk because artificial airways bypass the body's defenses against inhaled pathogens. Intubation associated lesions of pharynx and trachea lead to bacterial colonization by deterioration of swallowing reflex and ciliary functions. Subsequently these babies may develop pneumonia and sepsis. Hospital acquired sepsis (p value: < 0.05) was showed significantly high in non survivors.

Shock was the commonest co-morbidity (64.2%). Several other co-morbid conditions like dyselectrolytemia (52.8%), sepsis (35.8%), Disseminated intravascular coagulation 28.3% acute kidney injury (18.9%), PDA (11.3%) and PPHN (15.1%) and pulmonary haemorrhage (1.9%). Similar results (84%) were reported in an Indian study.[20] Shock and DIC were found significantly high in nonsurvivors when compared with survived newborn. Besides, a significantly higher incidence of DIC was also reported by another study which is comparable to our study.[21]

Several studies have investigated to find out the predictors or factors of mortality among ventilated newborn[20,19] and variation exist regarding findings of the studies. In the present study, regression analysis was performed with the factors those were found significant in univariate analysis to demonstrate predictors of mortality among enrolled newborn. Shock was found to be independent predictor of mortality in the present study. A previous Bangladeshi study reported shock as predictor of mortality which is comparable to our study.[14]

CONCLUSION

The most common condition for initiating mechanical ventilation was refractory apnea. Sepsis was the commonest disease for which ventilation required. The survival rate of ventilated neonates was 35.8% and percentage of survival was more in babies with RDS. Hospital acquired sepsis was the major complication of ventilated neonates. Low mean gestational age, birth weight, initial arterial P^H, delayed admission, delayed initiation of ventilation and high PIP requirement was significantly associated with poor outcome. Presence of hospital acquired sepsis, shock and DIC was significantly high in non-survivors. Shock was found as independent predictor of mortality

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