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Predictors of mortality in ventilated neonates

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Abstract--In all critically ill patients, the first objective should always be to preserve life and prevent or minimize damage to vital organs such as the brain and kidneys. The introduction of mechanical ventilation into neonatal intensive care units improved the survival of sick newborn. Assisted ventilation has revolutionized the outcome of sick newborn in NICUs. It is one of the most important advancements in neonatal medicine which achieves reduction in neonatal mortality. The aim of this study is to study the predictors that influence the mortality rates among mechanically ventilated neonates with the objectives to study the various predictors of mortality of mechanically ventilated neonates and to determine the various complications associated with ventilation and their effect on outcome of neonates. Results : Out of the 83 neonates who were included in the analysis, 50(60.25%) expired and 33 survived(39.75%). Factors which showed significance among those died were mean age, weight, mean gestational age, initial arterial pH, PaO₂, PaCO₂, duration of ventilation and duration of hospital stay. Among those who died, 43 had weight <1250 grams, 45 had gestation <32 weeks, 39 had Ph >7.1, 36 had PaO₂ >50, 32 had paCO₂ >60, 40 had sodium <130, 46 had Potassium <3.5, 35 had glucose >45, 31 had urea >12, 26 had S.creat <1.2 and all had FiO₂ >60.

Keywords---patients, ventilated neonates, predictors mortality.

Introduction

Critical care medicine and NICU services are now on an advancing stage in India. Advances in technology and government interventional programmes have helped in the improvement of healthcare services and facilities thus aiding more critically ill neonates to reach the health facilities. However, many of them are in very critical condition on arrival and mortality of these neonates remains very high.

Study Design

Materials and Methodology

It was a retrospective study of neonates put on ventilator in Neonatal ICU of tertiary care hospital, Karad, identified from NICU database.

Study Area

The study was carried out in Paediatrics department at a tertiary care hospital.

Source of Data

All the data including Gestational age, Birth weight, Primary diagnosis, Indication for ventilation, Duration of ventilation, Ventilator settings, Complications associated with ventilation, Duration of hospital stay and Outcome was collected from Medical Records.

Study Period

The study duration was conducted for 18 months after clearance from departmental committee and ethics.

Study Design

It was a retrospective study where predictors of mortality were studied in ventilated neonates.

Sample Size

The sample size for the study was calculated using following formula
 $n = 4pq/L^2$; $n = 83$

Inclusion Criteria

Any babies having any of the following were included in the study:

1. Birth Asphyxia
2. Prematurity
3. Intractable apnoeic spell
4. Gasping respiration
5. Recurrent apnoeic spells

6. O₂ saturation <80% on CPAP

Exclusion Criteria

Any babies with any of the following were excluded from the study:

1. Multiple Congenital Anomalies
2. Term Gestation

Results

Out of the 83 neonates who were included in the analysis, 50(60.25%) expired and 33 survived (39.75%). Mean age in days was 6.17+ 7.9, mean weight in grams was 1160.96+344.84 and mean gestational age in weeks was 30.6+2.12. 33 had perinatal asphyxia and among them 18 died and 15 survived. 19 had recurrent apnoea among them 13 died and 6 survived. 12 had sepsis among them majority 11 died and only 1 survived. Statistical significance was seen between sepsis and outcome. Meconium aspiration syndrome and pneumonia also had significance ($p<0.05$). Factors which showed significance among those who died were mean age, weight, mean gestational age, initial arterial pH, PaO₂, PaCO₂, duration of ventilation and duration of hospital stay. Among those who died, 43 had weight <1250 grams, 45 had gestation <32 weeks, 39 had Ph >7.1, 36 had PaO₂ >50, 32 had paCO₂ >60, 40 had sodium <130, 46 had Potassium <3.5, 35 had glucose >45, 31 had urea >12, 26 had S.creat <1.2 and all had FiO₂ >60. Indications for mechanical ventilation among enrolled neonates were recurrent apnoea in 23, gasping respiration in 18, asphyxia in 15 cases, oxygen saturation <80% after giving oxygen via bubble CPAP in 25 and intractable apnoea in 2. Among 15 asphyxia cases, 7 survived and 8 died. Among 25 oxygen saturation <80% after giving oxygen via bubble CPAP cases, 12 survived and 13 died. Among 18 gasping respiration cases 8 survived and 10 died. Among 2 Intractable Apnoea, cases both died. Among 23 Recurrent Apnoea cases, 6 survived and 17 died. 26 cases had complications and 57 had no complication. Among 26 having complication 9 survived and 17 died. Among 57 having no complications 24 survived and 33 died. ETT block was commonly seen followed by accidental extubation, pneumothorax and Ventilator Associated Pneumonia. 14 cases had CRP positive and 69 had negative CRP. Among 14 cases having CRP positive 3 survived and 11 died. 13 had positive blood culture and among them 6 had Klebsiella Pneumoniae, 5 had Pseudomonas Aeruginosa, 1 each had Burkholderia Cepacia and Staphylococcus Hemolyticus respectively. 43 were females and 40 males. Among males, 28 died and among females 22 died.

Figure 1: Outcome of the total 83 neonates

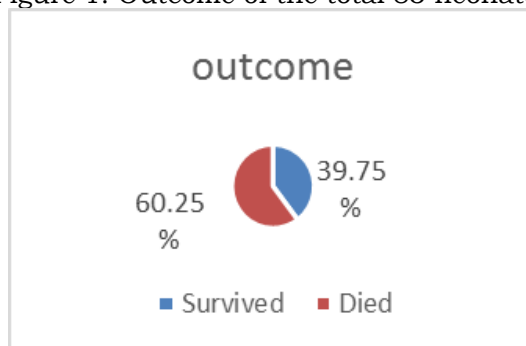


Figure 2: Distribution of outcome of neonates who were ventilated by diagnosis

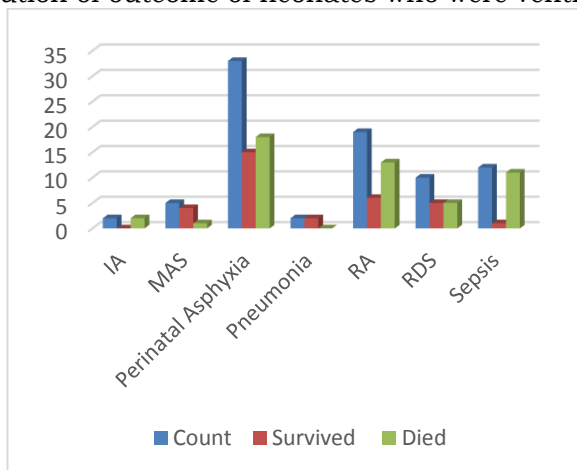


Table 1: Distribution of outcome in neonates ventilated by diagnosis

Diagnosis	Count	Survived	Died	P value
Sepsis	12	1	11	0.008*
Meconium aspiration syndrome	5	4	1	0.02*
Perinatal Asphyxia	33	15	18	0.19
Pneumonia	2	2	0	0.03*
Recurrent apnoea	19	6	13	0.2
Respiratory distress syndrome	10	5	5	0.2
Intractable apnoea	2	0	2	0.24
Total	83	33	50	-

Table 2: Predictors of mortality

Parameters	Died Mean + SD	Survivors Mean + SD	P value
Age in days	7.78+9.03	3.72+4.85	0.02*
Weight in gram	996.1+235.1	1410.7+334.3	<0.0001*
Gestation week	29.82+1.69	31.78+2.17	<0.00001*
Initial Arterial pH	7.18+0.11	7.3+0.09	<0.00001*
PaO ₂	53.9+6.14	67.15+5.8	<0.00001*
Pa CO ₂	55.92+8.24	43.69+6.79	<0.00001*
HCO ₃	18.78+2.51	19.24+2.13	0.32
Duration of ventilation in hours	50.96+30.6	33.3+22.3	0.005*
PIP	15.82+1.3	16.24+1.74	0.06
PEEP	4.86+0.34	4.81+0.38	0.47
Rate	51.8+2.4	51.21+2.14	0.49
Duration in hospital in days	10.28+9.64	27.12+23.03	<0.00001*

Applying 't' test, p value <0.05 shows statistical significance

Figure 3: Distribution of outcome by indication for ventilation

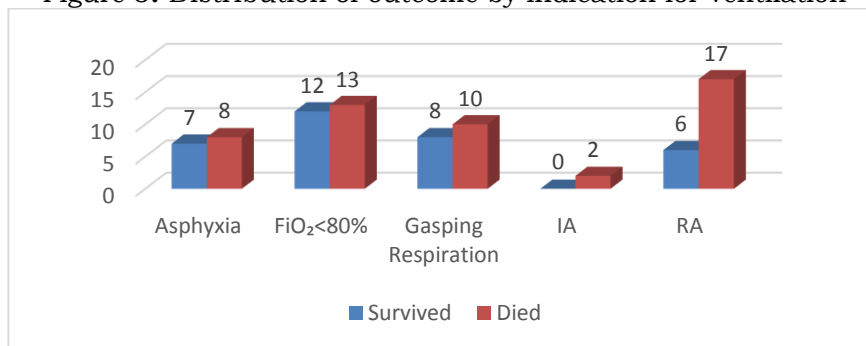


Figure 4 : Distribution of outcome of neonates by ventilated neonates by Complications

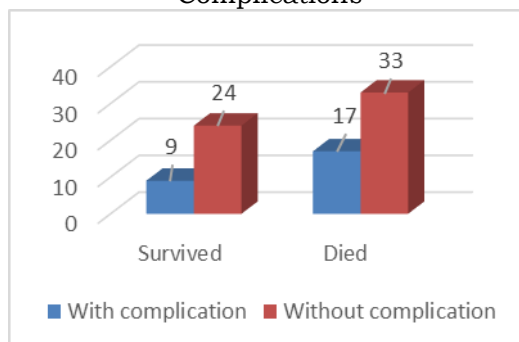


Figure 5 : Outcome of ventilated CRP

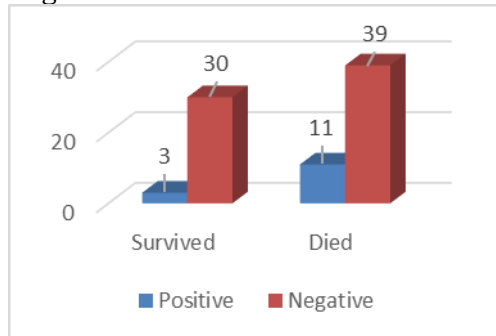


Figure 6 : Outcome of ventilated neonates by Blood culture

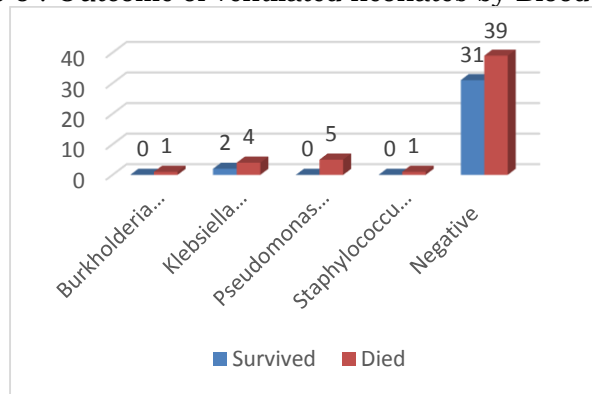


Figure 7: Complications in ventilated neonates and outcome

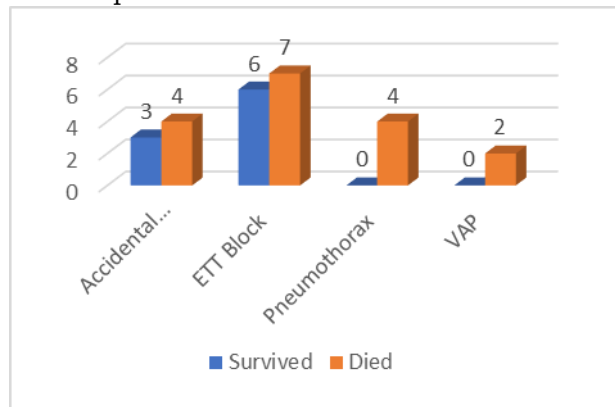
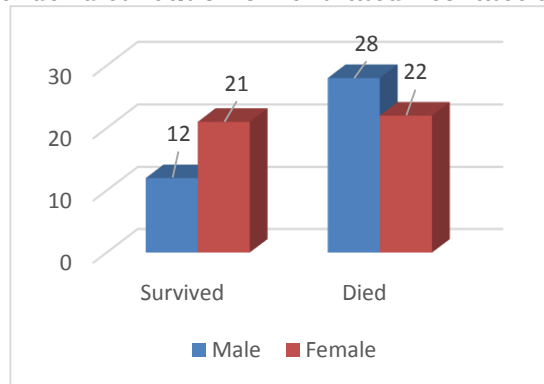


Figure 8: gender distribution of ventilated neonates and outcome



Discussion

Baseline characteristics

Mean age in days was 6.17 ± 7.9 , mean weight in gram was 1160.96 ± 344.84 and mean gestational age in weeks was 30.6 ± 2.12 . Study by Hossain MM et al ⁽¹⁾ showed that Mean age, weight and gestational age were 5.3 ± 6.5 days, 2171 ± 796.2 gm and 34.8 ± 4.1 weeks respectively.

Outcome

Majority of neonates died 60.25% and only 39.75% survived. Study by Hossain MM et al ⁽¹⁾ showed that 70.6% died. Mathur et al ⁽²⁾ in India found 74% mortality among the ventilated neonate. Some centers had better survival rate ranged from 41.3% to 68.3%. ⁽³⁾ Iqbal Q et al ⁽⁸⁾ showed that 43.3% neonates died, whereas in study by Sangeeta et al ⁽⁹⁾ 46% neonates died. Singh et al ⁽³⁾ found that mortality in ventilated neonates were 44.5%.

Outcome of neonates who were ventilated on the basis of diagnosis

Majority had perinatal asphyxia (33) and among them 18 died and 15 survived. 19 had recurrent apnoea among them 13 died and 6 survived. 12 had sepsis among them majority 11 died and only 1 survived. Statistical significance was seen between sepsis and outcome. Meconium aspiration syndrome and pneumonia also had significance ($p < 0.05$).

Study by Hossain MM et al ⁽¹⁾ showed that out of 51 mechanically ventilated neonates enrolled in this study, 36 (70.6%) died. 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.

Petdachai⁽⁴⁾ and Apisarnthanarak ⁽⁵⁾ showed 29.4% and 28.3% mortality among ventilated associated pneumonia.

Predictors of mortality in ventilated neonates

Factors which showed significance among those died were mean age, weight, mean gestational age, initial arterial pH, PaO₂, PaCO₂, duration of ventilation and duration of hospital stay (p <0.05). Factors which were not associated with fatality were HCO₃, PIP, PEEP and rate. Study by Hossain MM et al ⁽¹⁾ showed that mean weight, mean gestational age, initial arterial pH and duration of hospital stay (p <0.05). However, age, PaO₂, PaCO₂, HCO₃, duration of ventilation, PIP, PEEP and rate were not associated with fatality. Kiruthika D et al ⁽⁶⁾ showed that mean gestational age and mean birth weight of babies who survived were significantly higher in comparison to babies who expired but not statistically significant.

Correlation of variables with outcome in mechanically ventilated neonates

Majority among those who died, 43 had weight <1250 grams, 45 had gestation <32 weeks, 39 had Ph >7.1, 36 had PaO₂ <50, 32 had paCO₂ >60, 40 had sodium <130, 46 had Potassium <3.5, 35 had glucose >45, 31 had urea >12, 26 had Sr. creat <1.2 and all had FiO₂ >60. Mathur et al ⁽²⁾ in India found that mortality was significantly higher in cases that had gestational age <34 weeks and weight <2.5kgs (p<0.05). Hossain et al ⁽¹⁾ reported significant relation in pH <7 with poor outcome whereas in our study, we found a significant relation between pH <7.1 and mortality. Kiruthika D et al ⁽⁶⁾ showed that the babies having a pH of >7.3 had a better survival than those with a pH of <7.299, with significant p value.

Indication for ventilation

Indications for mechanical ventilation among enrolled neonates were recurrent apnoea in 23, gasping respiration in 18, asphyxia in 15 cases, oxygen saturation <80% after giving oxygen via bubble CPAP in 25 and intractable apnoea in 2. Among 15 asphyxia cases, 7 survived and 8 died. Among 25 oxygen saturation <80% after giving oxygen via bubble CPAP cases, 12 survived and 13 died. Among 18 gasping respiration cases 8 survived and 10 died. Among 2 Intractable Apnoea, cases both died. Among 23 Recurrent Apnoea cases, 6 survived and 17 died.

Study by Hossain MM et al⁽¹⁾ showed that 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 O₂ saturation <80%, 11 (64.7%) died. Among the indications, only significant relation was found between the neonates had O₂ saturation <80% and mortality [χ^2 {df=1}=16.409, p=0.00]. The study by Malik et al. ⁽¹⁴⁾ revealed that about 43.94% of babies were admitted with birth asphyxia, which was one of the major causes of mortality, and 50.32% of them developed convulsion. Shrestha P et al ⁽⁷⁾ showed that most common indication for mechanical ventilation was severe respiratory distress (gasping respiration /

respiratory distress score >5 / SpO₂ <80% with oxygen via CPAP) seen in 36 neonates (70%) while it was birth asphyxia in 6 neonates (12%). Other indications were recurrent apnea in 4 (8%), recurrent seizures in 2 (4%), diaphragmatic hernia in 1 (2%) and failure to extubate following a major surgery in 2 neonates (4%).

Outcome of ventilated neonates by complications

26 cases had complications and 57 had no complication. Among 26 having complication 9 survived and 17 died. Among 57 having no complications 24 survived and 33 died. ETT block was commonly seen followed by accidental extubation, pneumothorax and Ventilator Associated Pneumonia. Study by Hossain MM et al ⁽¹⁾ showed that 20 neonates developed complications. Iqbal Q et al ⁽⁸⁾ showed that patients with sepsis had the highest disease-specific mortality (67.4%), neonates developed complications like pulmonary hemorrhage, hypoglycemia, shock, VAP, IVH, and pneumothorax. Among these, pulmonary hemorrhage, shock and hypoglycemia showed significance mortality. Tayel et al. ⁽¹⁵⁾ carried out a study in Egypt to investigate the incidence of VAP during the application of preventive bundles among ventilated neonates. Assisted ventilation facilities can save neonates with perinatal hypoxia, birth asphyxia, severe apnoea, cardiovascular collapse, severe progressive respiratory distress with impending respiratory failure, and respiratory muscles fatigue.

Outcome of ventilated neonates by CRP

14 cases had CRP positive and 69 had negative CRP. Among 14 cases having CRP positive 3 survived and 11 died.

Outcome of ventilated neonates by Blood culture

13 had positive blood culture and among them 6 had Klebsiella Pneumoniae, 5 had Pseudomonas Aeruginosa, 1 each had Burkholderia Cepacia and Staphylococcus Hemolyticus respectively. Iqbal Q et al ⁽⁸⁾ showed that organisms isolated in cultures included Staphylococcus aureus, Klebsiella pneumoniae, and Candida. Shrestha P et al ⁽⁷⁾ showed that only 18.7% of blood culture positive neonates survived.

Gender and outcome

Majority were females (43) and 40 males. Among males, 28 died and among females 22 died. Study by Hossain MM et al ⁽¹⁾ showed that 30 (58.8%) were male and 21 (41.2%) were female. Studies by Iqbal Q et al ⁽⁸⁾, Haghghi et al ⁽¹²⁾ and Sankaran et al ⁽¹³⁾ showed that sex and age at admission did not have a statistically significant association with the outcome. Whereas, study by Kollef et al ⁽¹⁰⁾ and Riyas et al ⁽¹¹⁾ showed statistical significance.

Conclusion

Mean age in days was 6.17+ 7.9, mean weight in grams was 1160.96+344.84 and mean gestational age in weeks was 30.6+2.12. Majority of neonates died 60.25%

and only 39.75% survived. On diagnosis majority had perinatal asphyxia (33) and among them 18 died and 15 survived. 19 had recurrent apnoea among them 13 died and 6 survived. 12 had sepsis among them majority 11 died and only 1 survived. Statistical significance was seen between sepsis and outcome. Meconium aspiration syndrome and pneumonia also had significance ($p < 0.05$). Factors significantly different among those who died were mean age, weight, mean gestational age, initial arterial pH, PaO₂, PaCO₂, duration of ventilation and duration of hospital stay ($p < 0.05$). However, factors which were not associated with fatality were HCO₃, PIP, PEEP and rate. Majority among those who died 43 had weight < 1250 grams, 45 had gestation < 32 weeks, 39 had Ph > 7.1 , 36 had PaO₂ > 50 , 32 had paCO₂ > 60 , 40 had sodium < 130 , 46 had Potassium < 3.5 , 35 had glucose > 45 , 31 had urea > 12 , 26 had S creat < 1.2 and all had FiO₂ > 60 . Indications for mechanical ventilation among enrolled neonates were recurrent apnoea in 23, gasping respiration in 18, asphyxia in 15 cases, oxygen saturation $< 80\%$ after giving oxygen via bubble CPAP in 25 and intractable apnoea in 2. Among 15 asphyxia cases 7 survived and 8 died. Among 25 oxygen saturation $< 80\%$ after giving oxygen via bubble CPAP cases 12 survived and 13 died. Among 18 gasping respiration cases 8 survived and 10 died. Among 2 Intractable Apnoea cases both died. Among 23 Recurrent Apnoea cases 6 survived and 17 died. 26 cases had complications and 57 had no complication. Among 26 having complication 9 survived and 17 died. Among 57 having no complications 24 survived and 33 died. ETT block was commonly seen followed by accidental extubation, pneumothorax and Ventilator Associated Pneumonia. 14 cases had CRP positive and 69 had negative CRP. Among 14 cases having CRP positive 3 survived and 11 died. 13 had positive blood culture and among them 6 had Klebsiella Pneumoniae, 5 had Pseudomonas Aeruginosa, 1 each had Burkholderia Cepacia and Staphylococcus Hemolyticus respectively. Majority were females (43) and 40 males. Among males 28 died and among females 22 died.

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