Clinical Profile and Outcomes of Preterm Neonates Requiring Mechanical Ventilation: A 7-Year Review in a Tertiary Private Hospital

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ABSTRACT

Background: Mechanical ventilation is one of the important advancements in neonatal intensive care that improves survival. Many unwell preterm newborns admitted to the neonatal intensive care unit (NICU) require mechanical ventilation for a variety of clinical problems, but this is fraught with complications, and the outcome is unpredictable.

Objective: The research aimed to determine the clinical profile and outcomes of preterm neonates who required mechanical ventilation in a tertiary private hospital in Quezon City.

Methods: A descriptive study was conducted in a tertiary private hospital in Quezon City on preterm neonates who required mechanical ventilation from the year 2016-2022 using chart review. Frequency distribution and proportions, mean and standard deviations were used to describe the profile and outcomes of the preterm neonates.

Results: A total of 147 preterm neonates were included in the study. Most preterm neonates were 30-33 weeks age of gestation (42.2%), male (63.3%), inborn (95.9%), and t delivered via cesarean section (65.3%). There were 27 preterm neonates (18.4%) who were treated with surfactant therapy. The most common indications for mechanical ventilation were respiratory distress syndrome (n=75, 51%) followed by pneumonia (n=43, 29%). The survival rate of neonates who had mechanical ventilation was 81.6%. The mean duration of mechanical ventilation was 14.4 (± 10.12) days, and mean hospital stay was 24.4 (±21.18) days. Ventilator-associated pneumonia (40%) was identified as the most common complication in preterm neonates on mechanical ventilation.

Conclusion: Majority of the preterm neonates requiring mechanical ventilation are early preterm, low birth weight, male and delivered via cesarean section. They usually have respiratory distress syndrome and majority of them survive. Ventilator-associated pneumonia is a common complication of mechanical ventilation among preterm neonates.

Key words: Neonates, mechanical ventilation, respiratory distress syndrome

Preterm birth refers to a childbirth that occurs before 37 weeks age of gestation.[1] Worldwide, an estimated 15 million preterm births occur yearly, which is about 1 out of 10 deliveries.[2] It is one of the leading causes of mortality and morbidity in childhood. It accounts for approximately 1 million deaths of babies annually.[3] The 2017 health survey in the Philippines, showed that the country's preterm birth rate was 3.0%.[4]

Preterm birth is associated with a lot of complications such as infection, breathing difficulties, feeding problems, anemia, neurodevelopmental disabilities, and other chronic conditions that may present later in life. Preterm neonatal mortality is higher in developing countries than in developed countries. Mechanical ventilation and surfactants therapy have been shown to improve the overall respiratory status, reduce hospitalization, and improve overall outcome.

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Mechanical ventilation has evolved into an essential component of neonatal intensive care. One of the new major inventions in neonatology was the launch of mechanical ventilation during 1960s to 1970s, which provided extensive life-saving support for neonates with respiratory problems and failure.[5] The need for mechanical ventilation is usually determined by a number of factors, including the gestational age, diseases, birth weight, and other clinical factors. Since the introduction of mechanical ventilation, neonatal mortality and morbidity remains high.[9] Several studies identified that gestational age and weight of the sick neonate are the major contributory factors to neonatal mortality.[6] Several studies reported the severity of the illness at the time of admission, difficulties related to ventilator techniques and strategies, and the incidence of co-morbid disorders such as coagulopathy, sepsis, multiorgan dysfunction, and congenital abnormalities as risk factors.[7] In order to reduce these numbers among mechanically ventilated sick neonates, describing their profile and outcomes could help significantly in identifying possible factors associated with survival.

To date, there are limited local data on the profile and outcomes of these premature neonates. The current study aimed to determine the clinical profile and outcomes of premature neonate patients who required mechanical ventilation in a tertiary hospital. Identification of the following data will provide probable factors that could help improve the overall survival outcomes, improve overall care in the intensive care unit, and lessen severe morbidities of preterm neonate patients who would require mechanical ventilation in the future.

Mechanical ventilation is one of the life-saving treatments for patients with severe illness in a hospital's intensive care unit. Despite advancements in mechanical ventilation to improve recovery and survival, short and long-term complications still occur such as bronchopulmonary dysplasia, brain injury, retinopathy of prematurity, and poor neurodevelopmental outcome, with some other preterm infants requiring respiratory support at birth.

In an observational study of Mannan et. al. (2017)[8] on preterm neonates who required mechanical ventilation, out of the 50 neonates who were mechanically ventilated, 34 (68%) survived. The survival rate of 34-37 weeks Gestational Age (GA) group was higher (77%), and gradually dropped in the 30-34 weeks (71%) and 27-30 weeks (56%) GA groups. The neonates with birth weight of >2500 grams had a 100% survival rate, while the neonates with birth weight 1000-1499 grams (68%) and 800-999 grams (33%) had lower survival rates. Inborn neonates (68%) had marginally higher survival rates than outborn neonates (66%). Preterm female babies (72%) had higher survival rates than male (65%). Respiratory distress syndrome (62%) was the most common reason for mechanical ventilation, followed by neonatal sepsis (14%), perinatal asphyxia (10%), congenital pneumonia (8%) and pneumothorax (6%). RDS (77%) had higher survival rates than other indications such as pneumothorax (66%), PNA (60%), sepsis (57%), and pneumonia (50%). Respiratory distress syndrome treated with surfactant therapy (n=14) recovered 7 days earlier (71.43%) than those non-surfactant therapy neonates who required prolonged ventilator support for 7 days (82.35 %).

In another prospective observational study of Sultana, et al. (2020)[9], mechanical ventilation was used by 53 (8.6%) of the newborns admitted to the NICU. Out of these 53 neonates, 69.8% of which were male, with a male to female ratio of 2.3:1. Most of the neonates were delivered via cesarean section (71.7%). Refractory apnea (35.8%) was the most common reason for starting mechanical ventilation, followed by severe respiratory distress. 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%) were the disease patterns. The overall survival rate was 35.8%.

In a retrospective study by Regmi, et al. (2018)[10] at Chitwan Medical College (CMC) in Nepal, there were 130 mechanically ventilated patients among the 1306 total NICU admissions. Of the 119 out of the 130 neonates requiring mechanical ventilation, 71.4% were male. More than half (51.3 %) were preterm and outborn (58%). Sepsis was the most common reason for mechanical ventilation, followed by birth asphyxia, respiratory distress syndrome/hyaline membrane disease, and meconium aspiration syndrome. The overall survival rate was 45 (37.8 %). The best survival rate observed during the study period was in birth asphyxia. The most common complications that were encountered during mechanical ventilation were shock and disseminated intravascular coagulation. Individual predictors of outcome included shock, multi-organ dysfunction, and ventilator-associated pneumonia.

In a descriptive cross-sectional study by Manandhar (2019)[11], 63 neonates were identified with

respiratory distress syndrome. Majority were males (n=45, 71%). The average birth weight of neonate who received Bubble Continuous Positive Airway Pressure was 2661.75 +/-84 grams, and the gestational age was 36.67 +/-3.4 weeks. Bubble Continuous Positive Airway Pressure was initiated at 8.05+/-2 hours of life, and the duration of Bubble Continuous Positive Airway Pressure required to resolve respiratory distress was 95.71+/-3 hours. 39 (61%) improved their respiratory distress with Bubble Continuous Positive Airway Pressure, while 24 (39 %) required mechanical ventilation and other modalities.

In another study in Dhaka by Das, et al. (2022)[12], 30 newborns were included. 22 (73.3%) were preterm neonates, and 25 (83.3%) had a birth weight of 2500 grams. The most common reason for mechanical ventilation was respiratory distress syndrome (n= 11, 36.7%). Other indications were perinatal asphyxia (7(23.3%), septicemia (6 (20.0%), congenital pneumonia (5 (16.7%), and meconium aspiration syndrome (1 (3.3%). Average duration of mechanical ventilation was 4.1 ± 2.61 days and average duration of hospitalization was 13.1 ± 5.77 days. Septicemia (40.0%), acute renal failure (16.7%), pneumonia (16.7%), pulmonary hemorrhage (10.0%), intraventricular hemorrhage (6.7%), pneumothorax(10.0%), and heart failure (6.7%) were the most common problems during the ventilation period. 17 newborns (56.7%) survived, while 13 (43.3%) expired. Perinatal asphyxia 4 (57.1%), septicemia 3 (50.0%), respiratory distress syndrome 5 (45.5%), and ventilator associated pneumonia 1 (20.0%) were the top complications that majority of the neonates expired.

In a retrospective chart review of Jahan et. al. (2017)[13], survival rate was 67.24 % (n= 39) with a male to female ratio of 1.9:1. The average birth weight was 2264 gm (range 800-3900 grams), and the gestational age was 34 weeks (range 27-39 weeks). A total of 39 (67.24%) babies were inborn, and 29 (80.55%) survived. Outborn babies had a low survival rate (n= 10, 52.61%). The survival rate was higher when the birth weight was greater than 2500gm (76.19%) and the gestational age was between 34 and 37 weeks (88.88%). Survival rates in neonates born at 30 weeks age of gestation were 69.23% and 60% in those with birthweight of 1000 grams. Most neonates were on mechanical ventilatory support for 1-7 days (46%). The most common indication for mechanical ventilation was respiratory distress syndrome (32.75%) followed by perinatal asphyxia (18.96%), pneumonia (13.79%), neonatal sepsis (13.79%), meconium aspiration syndrome (10.16%), and pneumothorax (10.16%). Pneumonia (12.06%) was the most common complications of mechanical ventilation.

There were no published research on the clinical profile and outcomes of preterm neonates who required mechanical ventilation in HERDIN and Acta Medica Philippina.

The objective of the study was to determine the clinical profile and outcomes of preterm neonates on mechanical ventilation in a tertiary private hospital in Quezon City

MATERIALS AND METHODS

Research Design

The study is a descriptive study on preterm neonates who required mechanical ventilation from the year 2016-2022 using chart review.

Sampling Population

They were preterm neonates who required mechanical ventilation in a tertiary private hospital in Quezon City.

Sample Size

Sample size was calculated based on the estimation of the population proportion of survival among preterm neonates who required mechanical ventilation. Assuming the proportion of survival among these preterm neonates was 77%[1], with a maximum allowable error of 5% and reliability of 80% the minimum sample size calculated was 118.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Preterm neonates: <37 weeks age of gestation
- Who required mechanical ventilation

Exclusion Criteria

- Preterm neonates having major surgeries and congenital anomalies
- Incomplete medical chart information

Data Collection

Data collection was done through review of medical records. Medical charts of all preterm neonate patients who required mechanical ventilation admitted at a tertiary hospital in Quezon City from 2016-2022 that met the eligibility criteria were reviewed. Data collected were gestational age, birthweight, sex, mode of delivery, place of delivery, surfactant therapy, reasons for ventilation, duration of ventilation, duration of hospital stay, complications and outcomes.

Data Analysis

Data were encoded using Microsoft Excel 16.54 for tabulation and analysis. Descriptive analysis was done with the use of frequency and percentage for the following categorical variables: gestational age, birthweight, sex, mode of delivery, place of delivery, surfactant therapy, reasons for ventilation, and outcomes. Mean with SD was used for the duration of hospital stay and duration of ventilation.

Limitation of the Study

The study was limited to preterm neonate patients delivered in a tertiary private hospital in Quezon City. Since this was a review of records, only those with complete information were included. Furthermore, this was a single-center study in a private hospital, hence generalizability is limited to those with the same characteristics as the included patients.

Ethical Consideration

This study was conducted in compliance with the ethical guidelines set forth in the Declaration of Helsinki. Approval was obtained from FEU-NRMF IERC prior to the conduct of the study. In compliance with Data Privacy Act of 2012, patients' information and personal data were kept confidential and secured properly by the investigator in coordination with the Data Privacy Officer and Medical Records Officer. The patients' profile was kept confidential and anonymity was maintained through encoding. The data were kept in a password-protected file accessible to the researcher only. All data collected will be permanently deleted three years after the completion of the study.

RESULTS

There were a total of 147 preterm neonates who required mechanical ventilation. The gestational age of most preterm neonates ranged from 30-33 weeks (n=62, 42.2%). Majority of the ventilated preterm were males (n= 93, 63.3%), weighed between 1500-2499 grams (54.4%), delivered within the institution (n=141, 95.9%) via cesarean section (n=96, 65.3%). There were 27 (18.4%) preterm neonates who were given surfactant therapy as adjunct to the ventilatory support. (Table 1)

Table 1. Demographic profile of preterm neonates requiring Mechanical ventilatory support at FEU-NRMF from 2016 to 2022

Demographic variable and distribution	n (%)
Gestational Age (weeks)	
• < 27 weeks	7 (4.8)
• 27 - 29 weeks	21 (14.3)
• 30 - 33 weeks	62 (42.2)
• 34 - <37 weeks	57 (38.8)
Weight	
• <1000 grams	21 (14.3)
• 1000-1499 grams	42 (28.6)
• 1500-2499 grams	80 (54.4)
• >/= 2500 grams	4 (2.7)
Sex	
• Male	93 (63.3)
• Female	54 (36.7)
Mode of Delivery	
• Normal Spontaneous Delivery	51 (34.7)
• Cesarean Delivery	96 (65.3)
Place of Delivery	
• Inborn	141 (95.9)
• Out born	6 (4.1)
Surfactant Therapy	
• With surfactant therapy	27 (18.4)
• Non-surfactant therapy	120 (81.6)

The most common reasons for mechanical ventilation were respiratory distress syndrome (n=75, 51%), pneumonia (29%), transient tachypnea of the newborn (17%). (Table 2)

Majority of the preterm neonates were on mechanical ventilation for 1- 7 days (n=85, 57.8%). Among those who survived, majority were on mechanical ventilation for 1- 7 days. Majority of the neonates who expired were either on mechanical

ventilation for < 1 day or > 7 days. The mean duration of mechanical ventilator support was 14.4 ± 10.12 days. The mean duration of hospital stay of preterm neonates who were mechanically ventilated was 24.4 ± 21.18 days. In this study, the survival rate of preterm neonates was highest on those mechanically ventilated for 1-7 days (94.1%) and lowest on those mechanically ventilated for less than one day (63.3%). (Table 3)

Table 2. Reasons for use of mechanical ventilation among preterm neonates in a tertiary private hospital in Quezon City

Reason	n (%)
Respiratory Distress Syndrome	75 (51)
Pneumonia	43 (29)
Transient Tachypnea of the Newborn	25 (17)
Perinatal Asphyxia	3 (2)
Neonatal Sepsis	1 (1)
Total	147

Table 3. Duration of mechanical ventilatory support in preterm neonates at FEU-NRMF from 2016-2022

Duration	Survival n (%)	Expired n (%)	Total n (%)
<1 day	19 (63.3%)	11 (36.7%)	30 (20.4%)
1-7 days	80 (94.1%)	5 (5.9%)	85 (57.8%)
>7 days	21 (65.6%)	11 (34.4%)	32 (21.8%)

Transient tachypnea of the newborn and neonatal sepsis (100%) were noted to have the highest survival rate among preterm neonate who required ventilation. On the hand, perinatal asphyxia (100%) had the highest mortality. (Table 4)

Table 4. Survival rate according to disease among mechanically ventilated preterm neonates admitted at FEU-NRMF from 2016-2022

Reason	Survival n (%)	Expired n (%)
Respiratory Distress Syndrome	53 (70.7%)	22 (29.3%)
Congenital Pneumonia	41 (95.3%)	2 (4.7%)
Transient Tachypnea of the Newborn	25 (100%)	0
Perinatal Asphyxia	0	3 (100%)
Neonatal Sepsis	1 (100%)	0
	120 (81.6%)	27 (18.4%)

The overall survival rate of ventilated neonates was 81.6% (n=120). The overall survival of those who acquired complications was 32%. It was highest in those preterm neonates who developed complications of ventilator associated pneumonia (40%). Acute respiratory distress, disseminated intravascular coagulation, pneumothorax, pulmonary hemorrhage and cardiogenic shock (100%) had highest number of mortalities.

Table 5. Outcome of preterm neonates who were ventilated by complications (n=25)

Complications	Survival n (%)	Expired n (%)	Total n (%)
Ventilator Associated Pneumonia	7 (70%)	3 (30%)	10 (40%)
Acute Respiratory Distress Syndrome	0	6 (100%)	6 (24%)
Disseminated Intravascular Coagulation	0	4 (100%)	4 (16%)
Pneumothorax	0	2 (100%)	2 (8%)
Pulmonary hemorrhage	0	1 (100%)	1 (4%)
Cardiogenic shock	0	1 (100%)	1 (4%)
Atelectasis	1 (100%)	0	1 (4%)
	8 (32%)	17 (68%)	25

DISCUSSION

Majority of preterm neonates who required mechanical ventilation were male, 30-33 weeks age of gestation, delivered in the institution via cesarean section, with pneumonia or respiratory distress syndrome and who survived. The widespread use of mechanical ventilation has become an integral part in the improvement of survival and recovery of ill neonates.

Preterm neonates on mechanical ventilation were mostly between 30-33 weeks of gestation. This was similar to the study by Sultana et al (2020)[9] where they reported most neonates on mechanical ventilation

to be between 32-34 weeks age of gestation. Several studies showed that prematurity were found to have a greater need for positive-pressure ventilation and supplemental oxygen than term infants[9,14] which was consistent with the findings of the present study. The lungs and their physiological function are less developed and immature in younger gestational age-neonates, hence they have increased likelihood of requiring mechanical ventilation. Most mechanically ventilated preterm neonates weighed between 1500 to 2499 grams which was in agreement with the study of Todkar & Ashtekar (2020)[15] where they also identified most neonates affected weighing between 1500-2500 grams. In the study of Nam, et al. (2020)[16], low birth weight was identified as an associated risk with postnatal disease specially respiratory failure. Most affected neonates were males consistent with the findings of Sultana, et al. (2020)[9] and Baseer, et al. (2020).[17] A higher frequency of respiratory distress syndrome associated in males than females could be explained by testosterone's effect on decreasing surfactant production. Most preterm neonates in this institution were delivered via cesarean delivery. High-risk pregnancies were referred to tertiary hospitals with indications for cesarean section. About 20% of preterm neonates were managed with surfactant administration. Surfactant, as an adjunct to treatment, improves outcome, decreases length of ventilation, and lessens complications.[18] The therapeutic efficacy of surfactant is related to its protein and lipid composition that line the alveolar surfaces of the lung, lowering surface tension and preventing atelectasis. In the study of Mannan, et al. (2017)[8], those administered with surfactant recovered earlier and had shorter ventilator support lasting < 7 days (71.43%).

The most common indication in initiating mechanical ventilation in preterm neonates was respiratory distress syndrome. It is one of the most common conditions encountered during the postnatal days of a neonate. Respiratory problems lead the cause of neonatal morbidity and mortality, as well as admission to the intensive care unit.[19] In a similar study in India by Todkar & Ashtekar (2020)[15], the top reasons for mechanical ventilation noted were respiratory distress syndrome, transient tachypnea of the newborn, and congenital pneumonia, respectively. In another study by Sultana, et al. (2020)[9], refractory apnea and respiratory distress were also noted as the most common indications for mechanical ventilation. In contrast, the study of Bhatt (2015)[20], listed perinatal asphyxia and meconium aspiration syndrome as the leading indications aside from respiratory distress syndrome.

In developing nations, neonates on mechanical ventilation have a survival rate ranging from 25% to 64%.[20] In contrast, the overall survival rate of mechanically ventilated preterm in developed countries was higher at 81.6% (n=120). The survival rate in neonates with transient tachypnea of the newborn and sepsis was 100%. In neonates with perinatal asphyxia, the mortality rate was 100%. The survival rate of preterm neonates on mechanical ventilation for respiratory distress syndrome varied greatly as stated in the study of Shrestha et. al. (2016)[14] where it was reported to be 0%, and on another study of Todkar & Ashtekar (2022)[15] where it was 75%. In a study of Mannan et. al. (2017)[8], neonates with respiratory distress syndrome had the highest survival rate. Survival and recovery rates vary due to variances in underlying disorders, degree of prematurity, and quality of care. Professional and technological improvements in developing countries may also be contributing factors. Most of the preterm neonates were mechanically ventilated for a duration of 1-7 days (n=85, 57.8%) with a survival rate of 94.1% (n=80) in this study. Present study results for the mean duration of mechanical ventilation and hospital stay were higher than the study of Monsef et. al. (2019)[21] because some of the preterm where on prolonged ventilation due to associated high risk of being extremely to early preterm and extremely low to low birthweight. In comparison to Monsef, et al. study where patients were late preterm and average weight which are less likely associated with risk of respiratory failure. In contrast with the study Mannan, et al. (2017)[8], most of the neonates were ventilated for more than 7 days (82.35%) because most patients presented as early preterm with very low birthweight, presenting with respiratory distress syndrome, and were not given with surfactant as adjunct therapy.

Mechanically ventilated neonates are more vulnerable to infection because intubation process bypasses the initial body defenses. Intubation-related pharyngeal and tracheal trauma promote bacterial colonization by impairing the swallowing reflex and ciliary function. As a result, these patients may suffer complications like pneumonia and sepsis. Ventilator-associated pneumonia was identified in the present study as the most common complication associated with mechanical ventilation. A similar study with Dekate, et al. (2018)[22] also revealed that ventilator-associated pneumonia (17.8%) as the

top complication. Ventilator-associated pneumonia (VAP) is a significant consequence in neonates who are on mechanical ventilation, accounting for 6.8-32.2% of neonatal healthcare-associated infections.[23] It is usually associated with problems, particularly when ventilator treatment is prolonged, especially in developing-country intensive care units. In comparison with the studies of Bhatt, et al. (2015)[20] and Sultana, et al. (2020)[9], the predominant complication of mechanical ventilation was sepsis. Survival was highest on preterm neonates who had complications of atelectasis (100%) and pneumonia (70%). In a different study by Shrestha, et al. (2016)[6], it was those patients who had shock (46.3%) that presented with the greatest number of survivors. Mannan, et al. (2017)[8] identified sepsis as the most common associated complication but pneumonia (85.7%) has the highest survival rate.

The study was limited only to a single private tertiary hospital in Quezon City. Since, this was a chart review, only those with complete information were included. Furthermore, given this was a single-center study design in a private hospital, hence the generalized findings may have limited applicability to individuals with similar characteristics with those included in the study.

CONCLUSION AND RECOMMENDATION

Mechanical ventilation among preterm neonates is common in males, 30-33 weeks age of gestation, with birth weights between 1500 to 2499 grams, delivered via cesarean delivery and with respiratory distress syndrome. They required prolonged mechanical ventilation but with high survival rate. Respiratory Distress Syndrome was the most common indication for mechanical ventilation. Ventilator-associated pneumonia remains a major complication in ventilated preterm neonates which must be addressed.

This study shall serve as baseline data to further investigate the risk factors associated with the survival, morbidity and mortality of preterm neonates who were supported with mechanical ventilation. Furthermore, the study may serve as a bridge to the gap in the knowledge in management and care of mechanically ventilated preterm neonate patients and in improving neonatal survival. Multi-center studies are therefore, recommended for further studies to widen the information and clinical profile.

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