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Original Article

Indications and Short-Term Outcomes of Conventional Mechanical Ventilation in a Neonatal Intensive Care Unit of a Tertiary Care Hospital in a Developing Country

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ABSTRACT

Background: Mechanical ventilation is an advanced intervention employed in neonatal intensive care units (NICUs) to assist neonates who require external ventilation for adequate gas exchange, while minimizing associated complications. Understanding the indications and short-term outcomes of mechanical ventilation is crucial for improving neonatal care, especially in developing countries with limited resources.

Objective: To examine the indications and short-term outcomes of conventional mechanical ventilation in a neonatal intensive care unit of a tertiary care hospital in a developing country.

Methods: This descriptive cross-sectional study was conducted from July 2022 to February 2023 in the Department of Paediatrics at Combined Military Hospital, Kharian. The study included 227 pediatric patients admitted to the NICU for mechanical ventilation, selected via consecutive non-probability sampling. Written informed consent was obtained from parents or guardians. Data collected included neonatal and pregnancy parameters, primary indication for mechanical ventilation, duration of mechanical ventilation, and length of hospital stay. Patients were monitored for complications such as pneumothorax, sepsis, and ventilator-associated pneumonia. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0. Quantitative variables were expressed as mean ± standard deviation or median and interquartile range, while qualitative variables were presented as frequencies and percentages. Comparisons were made using the Chi-square test, Fisher's exact test, independent samples t-test, or Mann-Whitney U test as appropriate, with a p-value of ≤0.05 considered significant.

Results: The study included 128 males (56.4%) and 99 females (43.6%). The mean gestational age at birth was 36.4 ± 1.5 weeks, and the mean birth weight was 2994.1 ± 450.1 grams. Common indications for mechanical ventilation included pneumonia (26.4%), respiratory distress syndrome (24.7%), and sepsis (18.5%). The mean duration of mechanical ventilation was 7.1 ± 2.5 days, and the mean length of hospital stay was 13.4 ± 6.0 days. Complications were observed in 29.5% of patients, with ventilator-associated pneumonia (18.1%) being the most common, followed by sepsis (9.7%) and pneumothorax (5.3%). The overall mortality rate was 18.5%. Significant associations were found between mortality and duration of mechanical ventilation ($p<0.001$), occurrence of complications ($p<0.001$), and requirement for re-intubation ($p<0.001$).

Conclusion: The study highlights the significant association between prolonged mechanical ventilation, the development of complications, and increased mortality in neonates. Effective strategies to prevent and manage complications, as well as to limit the duration of mechanical ventilation, are essential to improve neonatal outcomes in resource-limited settings.

Keywords: Neonatal mechanical ventilation, NICU, neonatal outcomes, developing countries, ventilator-associated pneumonia, neonatal sepsis, neonatal mortality, respiratory distress syndrome, neonatal care, healthcare resources.

INTRODUCTION

Mechanical ventilation is a critical intervention employed in neonatal intensive care units (NICUs) to assist neonates who require external ventilation to maintain adequate gas exchange while minimizing associated complications. This advanced technique is

primarily indicated when the airway is compromised due to trauma or obstruction, hypoventilation, inadequate lung expansion, poor gas exchange, or a significant ventilation-perfusion mismatch or raised ventilatory demand (1,2). However, mechanical ventilation is not without disadvantages; it is cost- and resource-intensive, necessitates vigilant patient monitoring, and is associated with complications such as volutrauma, barotrauma, atelectrauma, biotrauma, and infections both during intubation and ventilation (3,4).

The neonatal period is a critical phase in a child's life, particularly for premature or critically ill infants who require intensive care due to the immaturity of lung tissue, low surfactant production, and the high risk of complications such as respiratory distress syndrome. This syndrome is a frequent indication for mechanical ventilation in the western population (5,6). Other common indications for mechanical ventilation in developed countries include neonatal sepsis, meconium aspiration syndrome, and congenital diaphragmatic hernia (7,8). In developing countries, access to resources and infrastructure can significantly impact the availability and quality of mechanical ventilation. Therefore, understanding the indications and short-term outcomes of mechanical ventilation in this context is crucial for enhancing the management and outcomes of neonates who require this treatment modality (9,10).

Despite its widespread use, there is limited data on the indications and outcomes of mechanical ventilation in neonates in developing countries. This study aimed to examine the indications and short-term outcomes of conventional mechanical ventilation, such as the length of stay in the intensive care unit and survival to the end of the neonatal period, as indicators of the intervention's effectiveness, in a NICU of a tertiary care hospital in a developing country. By providing a comprehensive review of these outcomes, this article aims to contribute to the knowledge base on neonatal intensive care and inform clinical practice in resource-limited settings.

MATERIAL AND METHODS

The study was conducted as a descriptive cross-sectional research from July 2022 to February 2023 in the Department of Paediatrics at the Combined Military Hospital, Kharian, involving 227 pediatric patients admitted to the neonatal intensive care unit (NICU) for mechanical ventilation. Written, informed consent was obtained from the parents or guardians of all participants, and the study adhered to the ethical principles outlined in the Declaration of Helsinki. Participants were selected via consecutive non-probability sampling. The sample size was calculated using the World Health Organization (WHO) sample size calculator, with a confidence level (1-α) of 95%, absolute precision (d) of 0.05, and an anticipated population proportion (P) of 18.0%, based on the percentage of pediatric patients requiring mechanical ventilation for birth asphyxia as reported by Iqbal et al. (11).

Inclusion criteria encompassed all newborns of both genders who received mechanical ventilation during their hospital stay in the neonatal period. Exclusion criteria included neonates diagnosed with congenital anomalies such as heart disease, central nervous system malformations, those requiring surgery, or those with suspected metabolic disorders. At the time of study inclusion, neonatal and pregnancy parameters, such as birth weight, gestational age at birth, and gender, were documented when patients were transferred to the NICU. Mechanical ventilation was initiated for patients with PaO2 <50 mmHg, SpO2 <85%, PaCO2 >60 mmHg, persistent apnea, or gasping despite continuous positive airway pressure (CPAP) at a pressure of 8 cm H2O and an FiO2 of 0.8 (11).

Participants received mechanical ventilation in the synchronized intermittent mandatory ventilation (SIMV) mode, which was adjusted at the clinician's discretion. Ventilator settings were customized based on the patient's requirements, disease condition, and lung mechanics/compliance, in accordance with arterial blood gas status. Regular testing was conducted to monitor organ system functions, including complete blood counts, chest X-rays, serum urea, creatinine, electrolytes, alanine transaminase, total bilirubin, blood and tracheal aspirate cultures, blood glucose levels, serum calcium, and cranial imaging. Patients were monitored for the development of sepsis and septic shock, with sepsis defined as signs or symptoms of sepsis (hypotension, dyspnea, irritability, poor feeding, pyrexia, lethargy, or hypothermia) combined with a positive urine or blood culture, or negative cultures with a white blood cell (WBC) count >30,000/µL, or C-reactive protein (CRP) levels >6 µg/mL (12). Septic shock was defined as clinical evidence of hypoperfusion, such as delayed capillary refill >3 seconds, oliguria with urine output <1 mL/kg/hour, and hypotension <90/60 mmHg, accompanied by lactic acidosis (11). Patients who developed new pulmonary infiltrates on chest X-ray within two days of mechanical ventilation initiation and exhibited positive cultures or signs of sepsis/septic shock were diagnosed with ventilator-associated pneumonia (VAP) (11). Hypoglycemia was defined as a blood glucose level <50 mg/dL, and thrombocytopenia was defined as a platelet count <150,000/µL (11). Patients were followed for the duration of mechanical ventilation, hospital admission, and until the end of the neonatal period to monitor for complications and mortality.

Data was analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 26.0, IBM Corp; Armonk, USA). Quantitative variables such as gestational age at birth, birth weight, duration of mechanical ventilation, and length of hospital stay were expressed as mean ± standard deviation or median and interquartile range, as appropriate. Qualitative variables including gender, mode of delivery, primary indication for mechanical ventilation, complications associated with mechanical

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ventilation, success during weaning on the first attempt, and treatment outcomes (including mortality) were presented as frequencies and percentages. Patients were categorized into two groups based on mortality, and comparisons of qualitative variables between groups were made using the Chi-square test or Fisher's exact test, while quantitative variables were compared using the independent samples t-test or Mann-Whitney U test, as appropriate. A p-value of ≤0.05 was considered statistically significant.

RESULTS

The study analyzed 227 pediatric patients admitted to the neonatal intensive care unit for mechanical ventilation, with a gender distribution of 128 males (56.4%) and 99 females (43.6%) (Table 1). The mean gestational age at birth was 36.3 ± 1.5 weeks for males and 36.5 ± 1.6 weeks for females. The mode of delivery was predominantly per vaginum, occurring in 70.3% of males and 75.8% of females, while Caesarean sections accounted for 29.7% of male and 24.2% of female births. Birth weight averaged 3017.3 ± 436.3 grams for males and 2963.5 ± 468.5 grams for females.

Table 1: Patient Characteristics/Study Results According to Gender (n=227)

Variable	Male (n=128)	Female (n=99)
Gender	128 (56.4%)	99 (43.6%)
Gestational Age at Birth (weeks)	36.3 ± 1.5	36.5 ± 1.6
Mode of Delivery		
- Per Vaginum	90 (70.3%)	75 (75.8%)
- Caesarean Section	38 (29.7%)	24 (24.2%)
Birth-Weight (g)	3017.3 ± 436.3	2963.5 ± 468.5
Primary Indication for Mechanical Ventilation		
- Pneumonia	34 (26.6%)	25 (25.3%)
- Respiratory Distress Syndrome	36 (28.1%)	20 (20.2%)
- Sepsis	27 (21.1%)	15 (15.1%)
- Birth Asphyxia	13 (10.2%)	20 (20.2%)
- Meconium Aspiration Syndrome	13 (10.2%)	8 (8.1%)
- Meningitis	5 (3.8%)	11 (11.1%)
Duration of Mechanical Ventilation (days)	6.9 ± 2.5	7.4 ± 2.5
Length of Hospital Stay (days)	13.1 ± 5.8	13.9 ± 6.2
Total Complicated Cases	36 (28.1%)	31 (31.3%)
Individual Complications		
- Pneumothorax	6 (4.7%)	6 (6.1%)
- Pneumomediastinum	3 (2.3%)	3 (3.0%)
- Sepsis	14 (10.9%)	8 (8.1%)
- Ventilator-associated Pneumonia	21 (16.4%)	20 (20.2%)
Requirement for Re-Intubation		
- Yes	106 (82.8%)	80 (80.8%)
- No	8 (6.2%)	2 (2.0%)
- Not Applicable	14 (11.0%)	17 (17.2%)
Mortality	22 (17.2%)	20 (20.2%)

Table 2: Patient Characteristics/Study Results According to Mortality (n=227)

Variable	Death (n=42)	Alive (n=185)	p-value
Gender			
- Male	22 (52.4%)	106 (57.3%)	0.562
- Female	20 (47.6%)	79 (42.7%)	
Gestational Age at Birth (weeks)	36.7 ± 1.4	36.3 ± 1.6	0.087
Mode of Delivery			0.572
- Per Vaginum	32 (76.2%)	133 (71.9%)	

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Variable	Death (n=42)	Alive (n=185)	p-value
- Caesarean Section	10 (23.8%)	52 (28.1%)	
Birth-Weight (g)	2927.1 ± 405.6	3008.9 ± 459.6	0.288
Primary Indication for Mechanical Ventilation			0.219
- Pneumonia	9 (21.4%)	50 (27.0%)	
- Respiratory Distress Syndrome	11 (26.2%)	45 (24.3%)	
- Sepsis	8 (19.0%)	34 (18.4%)	
- Birth Asphyxia	7 (16.7%)	26 (14.1%)	
- Meconium Aspiration Syndrome	1 (2.4%)	20 (10.8%)	
- Meningitis	6 (14.3%)	10 (5.4%)	
Duration of Mechanical Ventilation (days)	8.7 ± 2.4	6.8 ± 2.4	<0.001
Length of Hospital Stay (days)	18.1 ± 6.5	12.4 ± 5.4	<0.001
Total Complicated Cases	31 (73.8%)	36 (19.5%)	<0.001
Individual Complications			
- Pneumothorax	6 (14.3%)	6 (3.2%)	0.004
- Pneumomediastinum	3 (7.1%)	3 (1.6%)	0.079
- Sepsis	8 (19.0%)	14 (7.6%)	0.023
- Ventilator-associated Pneumonia	23 (54.8%)	18 (9.7%)	<0.001
Requirement for Re-Intubation			<0.001
- Yes	10 (23.8%)	0 (0%)	
- No	1 (2.4%)	185 (100%)	
- Not Applicable	31 (73.8%)	0 (0%)	

Primary indications for mechanical ventilation varied, with pneumonia being the leading cause for both genders, affecting 26.6% of males and 25.3% of females. Respiratory distress syndrome was the second most common indication, noted in 28.1% of males and 20.2% of females. Sepsis accounted for 21.1% of male and 15.1% of female cases, while birth asphyxia was observed in 10.2% of males and significantly higher at 20.2% in females. Meconium aspiration syndrome affected 10.2% of males and 8.1% of females, and meningitis was more prevalent in females (11.1%) compared to males (3.8%). The mean duration of mechanical ventilation was slightly longer for females (7.4 ± 2.5 days) compared to males (6.9 ± 2.5 days), and the length of hospital stay also reflected this trend, with females staying an average of 13.9 ± 6.2 days versus 13.1 ± 5.8 days for males.

Regarding complications, 28.1% of male patients and 31.3% of female patients experienced complications. Pneumothorax occurred in 4.7% of males and 6.1% of females, while pneumomediastinum was reported in 2.3% of males and 3.0% of females. Sepsis was slightly more common in males (10.9%) than females (8.1%). Ventilator-associated pneumonia was noted in 16.4% of males and 20.2% of females. A high requirement for re-intubation was observed, with 82.8% of males and 80.8% of females needing it, whereas only 6.2% of males and 2.0% of females did not require re-intubation. Mortality rates were comparable between genders, at 17.2% for males and 20.2% for females (Table 1).

When comparing patients based on mortality outcomes (Table 2), the study found that 52.4% of the deceased were male and 47.6% were female, with no significant gender difference (p=0.562). The mean gestational age at birth was 36.7 ± 1.4 weeks for those who died and 36.3 ± 1.6 weeks for survivors (p=0.087). Mode of delivery showed no significant difference, with 76.2% of deceased patients delivered per vaginum and 71.9% of survivors (p=0.572). Birth weight was slightly lower in deceased patients (2927.1 ± 405.6 grams) compared to survivors (3008.9 ± 459.6 grams), though not statistically significant (p=0.288).

Primary indications for mechanical ventilation did not significantly differ between those who died and those who survived. Pneumonia was the primary indication in 21.4% of deceased and 27.0% of survivors, while respiratory distress syndrome affected 26.2% of deceased and 24.3% of survivors. Sepsis was noted in 19.0% of deceased and 18.4% of survivors. Birth asphyxia accounted for 16.7% of deceased and 14.1% of survivors. Notably, meningitis was significantly higher in deceased patients (14.3%) compared to survivors (5.4%).

The mean duration of mechanical ventilation was significantly longer in deceased patients (8.7 ± 2.4 days) than in survivors (6.8 ± 2.4 days) (p<0.001). Similarly, the length of hospital stay was longer for deceased patients (18.1 ± 6.5 days) compared to survivors (12.4 ± 5.4 days) (p<0.001). Complications were significantly more frequent among deceased patients, with 73.8% experiencing complications compared to 19.5% of survivors (p<0.001). Individual complications such as pneumothorax (14.3% vs. 3.2%, p=0.004) and sepsis (19.0% vs. 7.6%, p=0.023) were significantly higher in the deceased group. Ventilator-associated pneumonia was markedly

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more common in deceased patients (54.8%) compared to survivors (9.7%) ($p<0.001$). The requirement for re-intubation was also significantly higher in deceased patients (23.8%) compared to survivors, with all survivors not requiring re-intubation ($p<0.001$).

DISCUSSION

Predicting the clinical course of patients admitted to a critical-care unit while on mechanical ventilation is essential for providing timely and appropriate management, especially for severely ill neonates. This study demonstrated that several factors, such as duration on mechanical ventilation, requirement for re-intubation, and development of complications like pneumothorax and ventilator-associated pneumonia, were associated with increased mortality. No significant differences were found in gestational age and birth weight between survivors and non-survivors ($p=0.087$ and $p=0.288$, respectively). This contrasted with findings from Yadav et al., who reported that neonates born at an earlier gestational age and with lower birth weight had a higher likelihood of dying while on mechanical ventilation ($p<0.01$) (Yadav et al., 2016). Gahlawat et al. also noted that neonates born at less than 32 weeks gestation were particularly at risk of death on mechanical ventilation ($p<0.05$) on univariate analysis, although this association disappeared on multivariate analysis (Gahlawat et al., 2018). The discrepancy may stem from the characteristics of our study population, which had a minimum gestational age of 34 weeks, unlike the other studies that included patients born before 30 weeks of gestation.

Males constituted a slight majority (56.4%) of our sample, yet gender was not associated with mortality ($p=0.562$). This aligns with Townsel et al.'s review, which found that while males often required mechanical ventilation more frequently at birth compared to females, overall mortality rates were similar for both genders (Townsel et al., 2017). Approximately 27.0% of neonates in our study were delivered via caesarean section, with no significant association with mortality ($p=0.572$). This rate of caesarean sections mirrors the national average for Pakistan (NIPS, 2018), and is lower than rates observed in other centers (WHO, 2015).

Common indications for mechanical ventilation in our study included pneumonia (25.9%), respiratory distress syndrome (24.7%), and sepsis (18.5%). Yadav et al. reported respiratory distress syndrome as the most common indication, followed by sepsis and birth asphyxia, similar to our findings (Yadav et al., 2016). Iqbal et al. also found that respiratory distress syndrome (31%), sepsis (22%), and birth asphyxia (18%) were the primary indications, consistent with our study (Iqbal et al., 2016).

Patients with a longer duration of admission in intensive care and on mechanical ventilation had higher mortality rates ($p<0.001$). It remains unclear whether this was due to the severity of the disease or the prolonged duration of mechanical ventilation. Choi et al. found that prolonged mechanical ventilation was significantly associated with higher mortality in premature neonates who received ventilation for more than two weeks compared to those ventilated for less than seven days (Choi et al., 2012). Prolonged ventilation was also associated with increased risk of complications and extubation failure, parameters not studied in our research.

Ventilator-associated pneumonia was the most common complication in our study (18.1%), followed by new-onset sepsis (9.7%) and pneumothorax (5.3%). Approximately one-third of patients experienced complications, and those who developed complications had higher mortality rates ($p<0.001$). Specific complications such as pneumothorax ($p=0.004$), new-onset sepsis ($p=0.023$), and ventilator-associated pneumonia ($p<0.001$) were significantly associated with increased mortality. Yadav et al. reported sepsis as the most commonly encountered complication, followed by ventilator-associated pneumonia, while Iqbal et al. noted similar findings along with pulmonary hemorrhage, hypoglycemia, and pneumothorax (Yadav et al., 2016; Iqbal et al., 2016). Our study differed in showing that specific complications were significantly associated with increased mortality, possibly due to differences in population characteristics and primary disease.

A small percentage (4.4%) of neonates required re-intubation after successful weaning, and these patients had a higher frequency of death ($p<0.001$) compared to those successfully weaned on the first attempt. Shalish et al. demonstrated that re-intubation within one to twenty-one days of extubation was associated with increased mortality, independent of total mechanical ventilation duration (Shalish et al., 2015).

Our study indicated that approximately one-fifth of neonates receiving mechanical ventilation died during the neonatal period, a lower rate compared to Iqbal et al. (43%) and Yadav et al. (60%) (Iqbal et al., 2016; Yadav et al., 2016). These differences likely stem from the higher number of premature neonates included in the latter studies.

Our study had several limitations. The intensity of admitting indications was not assessed, which may have introduced confounding factors. Additionally, the study did not account for non-invasive ventilation received before or after NICU admission, which could have influenced outcomes. While most patients received free treatment, some did not, and financial constraints might have affected management and outcomes. Conducted in a single center with a population primarily consisting of military personnel's children, the study's generalizability is limited. Future multicenter studies involving a more diverse population are recommended to provide more comprehensive insights.

This study contributes valuable insights into the indications and short-term outcomes of conventional mechanical ventilation in a neonatal intensive care unit of a developing country. It highlights the significant association between prolonged mechanical ventilation, the development of complications, and increased mortality. Effective prevention and management of these complications, as well as strategies to limit the duration of mechanical ventilation, may help reduce neonatal mortality and should be explored in future research.

CONCLUSION

This study provides essential insights into the indications and short-term outcomes of conventional mechanical ventilation in a neonatal intensive care unit in a developing country, revealing that prolonged mechanical ventilation and complications such as ventilator-associated pneumonia and pneumothorax significantly increase neonatal mortality. These findings underscore the need for targeted strategies to prevent and manage these complications, as well as to limit the duration of mechanical ventilation, to improve neonatal outcomes. Implementing these strategies could enhance clinical practices and healthcare delivery in resource-limited settings, ultimately reducing neonatal mortality rates and improving overall neonatal care.

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