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Clinical Profile and Outcome of Mechanically Ventilated Neonates: Evidence from a Prospective Study

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ABSTRACT

Background: Mechanical ventilation (MV) is a vital life-support intervention widely used in NICUs (NICUs) to assist newborns with respiratory distress or failure. We aimed to explore the clinical profile, complications and survival rate of neonates undergoing MV.

Methods: A prospective observational research design was followed in this study. Descriptive statistics using frequency and percentage were used to describe the maternal and newborn factors related to MV. Pearson's Chi-squared test was used to determine the level of significance.

Results: In this study total of 1548 NICU admitted cases were enrolled out of which 216 were mechanically ventilated during the study period. The major outcomes of the study are improvement (24.9%) and mortality (75.1%) Three main causes of MV were sepsis (58%), prematurity (58%) and perinatal asphyxia (52%). Preterm babies at (aOR 2.603(1.452-4.666), 95% CI) are almost 3 times more likely to require MV. Similarly, neonates who needed bag and mask resuscitation were almost 2.5 times more likely to be mechanical ventilated (2.494(1.275-4.876), 95% CI.

Conclusion: Prematurity, neonatal sepsis and Birth asphyxia were found to be the major burden among the sick newborns needing MV. Clinical parameters and metabolic abnormalities should be monitored for better survival among the babies under MV.

Keywords: *Birth asphyxia (BA), Mechanical ventilation (MV), neonatal morbidity, prematurity, sepsis.*

INTRODUCTION

In low-income countries, due to limited access to quality healthcare, inadequate maternal and newborn care, poor nutrition, infectious diseases, and other socio- economic disparities the neonatal mortality rate (NMR) is often higher compared to high-income countries.[1] Addressing NMR in low-income countries have been a major focus of global health initiatives and development organizations {World Health Statistics 2016 [OP]}. The adoption of the Sustainable Development Goals (SDGs) from 2016-2030 expected to result in a significant decline in global neonatal mortality, as–the number of deaths is observed to be decreasing from 5.0 million to 2.4 million from 1990 in 2019 {World Health Statistics 2016 [OP]}. SDGs established by the United Nations in 2015, comprises specific targets aimed at reducing NMR and improving maternal and child health. These goals are focused on strengthening healthcare infrastructure, increasing access to essential medical services, enhancing nutrition, and promoting maternal education and awareness. To achieve these goals, a range of interventions has been implemented, including the

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promotion of antenatal care (ANC), skilled birth attendance (SBA), postnatal care, immunization programs, and community-based initiatives, in low-income countries.[2]

MV is a vital life-support intervention widely used in NICUs (NICUs) to assist newborns with respiratory distress or failure.[3] This advanced medical technique provides essential respiratory support by delivering oxygen and maintaining adequate ventilation for infants with compromised lung function. Despite its life-saving potential, MV is not without risks, and understanding its indications and outcomes is critical for optimizing neonatal care.

The present study aims to investigate two key aspects concerning MV in neonates, to identify indicators for the use of MV and explore the potential link between underlying medical conditions and neonatal outcomes, including complications, while undergoing MV. The significance of this research lies in its potential to enhance the understanding of neonatal respiratory care and improve neonatal outcomes. Unraveling the common indication for MV can streamline the initial management of critical neonatal conditions thereby minimizing unwarranted delays in delivering vital support. Moreover, establishing connections between underlying medical conditions and clinical results can assist in categorizing risk and shaping personalized care strategies ultimately improving prognosis and reducing complications during the MV phase. To achieve these objectives, the study conducted a thorough review of medical records for clinical information from neonates receiving MV at the study site. By examining a substantial dataset, the study aims to identify the risk factors, signs and symptoms, potential clinical diagnosis and outcomes of neonates undergoing MV.

This study holds the promise of shedding light on the common indicators for MV in neonates and illuminating the intricate interplay between underlying disorders, survival rates, and complications during this critical intervention. The findings derived from this research endeavor have the potential to drive positive changes in neonatal respiratory care, ultimately improving the outcomes and well-being of the tiniest neonates in the NICU of Propmaker Maternity Hospital of Kathmandu, Nepal.

METHODS

The study was conducted in selected NICU of Paropakar Maternity and Women's Hospital, Kathmandu which serves approximately 23000 deliveries per year and 2400 sick newborns. This hospital is a tertiary hospital with 40 bedded Neonatal Care Unit with trained consultants and other necessary health workers. All medical information, including diagnosis, treatment, investigation, and outcomes pertaining to newborns admitted to the Neonatal Unit for the period of 12 months, from Chaitra 1, 2078 to Falun 30 2079 were reviewed by utilizing the admission register patient's medical records, electronic medical records from the center's laboratories. All newborns who were mechanical ventilated were included in the study.

Subsequently, all the gathered data underwent a rigorous cleaning process and were then exported to Statistical Package for the Social Sciences version 25 for in-depth data analysis. Various types of single and cross tabulations were employed to scrutinize the data, and when necessary, charts, graphs, and relevant diagrams were utilized to condense the information. The neonatal outcomes, encompassing improvements and fatalities were elucidated through bi-variate analysis, specifically Pearson's Chi-Squared test.

To establish the relationship between clinical, socio-demographic and laboratory factors and the use of MV, a multivariate analysis was conducted employing logistic regression. The regression coefficient (b1) was estimated to reflect the change in the log odds of the outcome MV with each unit increase in the value of the exposure (predictors).

TERMINOLOGIES USED

Neonatal sepsis: The term neonatal sepsis is used to designate a systemic condition of bacterial, viral, or fungal (yeast) origin that is associated with hemodynamic changes and other clinical manifestations and results in substantial morbidity and mortality. Sick babies were classified as having any of the following morbidity

Preterm: Babies born before 37 weeks of gestation (Child Health Division. Department of Health Services, Ministry of Health and Population: National Newborn Clinical Protocol. In. Kathmandu; 2016.)

Perinatal asphyxia: Perinatal asphyxia is a lack of blood flow or gas exchange to or from the fetus in the period immediately before, during, or after the birth process.

MV is a life-saving strategy for ill infants suffering from respiratory failure. The purpose of MV is to oxygenate the newborn and eliminate carbon dioxide while attempting to minimize lung damage.

Low birth weight: babies born with birth weight less than 2500gm.

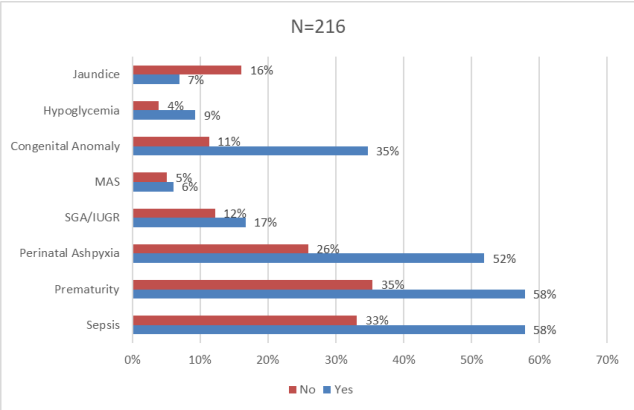
Continuous positive airway pressure (CPAP): is a type of positive airway pressure that is used to deliver a set pressure to the airways that is maintained throughout the respiratory cycle, during both inspiration and expiration.

APGAR Score: The Apgar score provides an accepted and convenient method for reporting the status of the newborn infant immediately afterbirth and the response to resuscitation if needed

RESULTS

In this study total of 1548 neonates were admitted in NICU, out of which 216 were mechanically ventilated during the study period. Among which 140 (64.8%) male babies and 76 (35.2%) females were intubated.

The three main indication of mechanical ventilation were sepsis (58%), prematurity (58%) and perinatal asphyxia (52%) as shown in (Figure 1).



The major outcomes of the study are improvement (24.9%) and mortality (75.1%) indicating significant proportion of patients died despite receiving the mechanical ventilation. All extremely preterm neonates with gestational age < 28 weeks, severe respiratory distress (SRDS) and recurrent apnea were provided CPAP therapy and those who had failure of CPAP therapy were ventilated.

In Multivariate analysis involving socio-demographic categorical variables, the percentage of cases requiring mechanical ventilation were higher among the (20-35 year) of the respondent's maternal age and with regards to ethnicity the percentage of cases of mechanical ventilation were higher among Janajati (52.3%). Nonetheless, no overall significant association was seen. Contrary to these findings, parity, obstetric complications and sex of the respondent had significant association with mechanical ventilation as shown in (Table1a) but after adjustment of other predictor variables the association was found to be non-significant.

Table 1a: Background Characteristics

Indicators	Mechanical Ventilation		P-value	aOR(95%CI)	P-Value
Maternal Age*	No	Yes	0.431		
20-35	1067(85.2%)	135(82.3%)			
15-19	105(8.4%)	14(8.5%)			
>35	81(6.5%)	15(9.1%)			
Parity*			0.026		
Primipara	473(44.2%)	49(33.1%)		ref	
Nullipara	426(39.9%)	67(45.3%)		1.385 (0.889-2.157)	0.149
Multipara	170(15.9%)	32(21.6%)		1.580 (0.910-2.746)	0.104
Ethnicity*			0.253		
Dalit	129(9.7%)	15(6.9%)			
Janajati	677(50.8%)	113(52.3%)			
Madhesi	53(4.0%)	9(4.2%)			
Muslim	15(1.1%)	6(2.8%)			
Brahmin/Chhetri	458(34.4%)	73(33.8%)			
Sex*			0.032		0.116
Male	760(57.1%)	140(64.8%)		ref	
Female	572(42.9%)	76(35.2%)		0.716 (0.473-1.086)	

Further indicators included in the multivariate analysis involving socio-demographic categorical variables is shown in (Table 1b) the percentage of cases requiring mechanical ventilation were higher with 111 (51.4%) among the newborn's delivered through c-section and 58 (44.3%) among women having obstetric complications, an overall significant association was seen but after adjustment of other predictor variables the association was found to be non-significant.

Table 1b: Obstetric Characteristics

Indicators	Mechanical Ventilation		P-value	aOR(95%CI)	P-Value
	No	Yes			
Mode of Delivery			0.057		
Normal	740(55.6%)	105(48.6%)		ref	
C-Section	594(44.4%)	111(51.4%)		1.27 (0.843-1.918)	0.251
Obstetric Complication*			0.032		
No	606(65.3%)	73(55.7%)		ref	
Yes	322(34.7%)	58(44.3%)		1.183 (0.782-1.790)	0.425

As shown in (Table 2a), Among the mechanically ventilated cases clinical parameters such as preterm, low birth weight, obstetric complication was included, then multivariate analysis was carried out. Later on, the findings revealed preterm babies at (aOR 2.603(1.452-4.666), 95% CI) are almost 3 times more likely to require MV thus indicating significant association even after adjusting other predictor variables. In regards to other predictors, LBW neonates, obstetric complications were more likely to require MV. However, after adjustment of other variables the association was found to be non-significant.

As shown in (Table 2b), among the MV cases resuscitation parameters such as bag and mask, APGAR were included with the clinical parameters presented at (Table 2a), then multivariate analysis was completed, the findings showed neonates who needed bag and mask resuscitation were almost 2.5 times more likely to be mechanical ventilated [2.494(1.275-4.876), 95% CI]. In regards to other predictors, APGAR at 1-minute scoring 0 to 3 were more likely to require MV. However, after adjustment of other variables the association was found to be non-significant. Nevertheless, low APGAR at 5 minutes scoring 0 to 3 were 9 times [9.017(3.144-25.866, 95% CI)] more likely to require MV showing significant association even after adjustment of other predictor variables.

Table 2a: Logistic regression analysis among clinical Parameters of the cases requiring MV

Indicator	Mechanical Ventilation		cOR(95%CI)	p-value	aOR(95%CI)	p-value
	No	Yes				
Preterm						
No	865 (64.9%)	91 (42.1%)	ref		ref	
Yes	467 (35.1%)	125 (57.9%)	2.544 (1.899-3.409)	0.0000	2.603 (1.452-4.666)	0.001
Low Birth Weight (LBW)						
No	755 (56.7%)	74 (34.3%)	ref		ref	
Yes	576 (43.3%)	142 (65.7%)	2.511 (1.858-3.393)	0.0000	1.511(0.837-2.728)	0.171
Obstetric Complication*						
No	606(65.3%)	73(55.7%)	ref		ref	
Yes	322(34.7%)	58(44.3%)	1.495 (1.033-2.165)	0.0330	1.152(0.751-1.768)	0.517

Table 2b: Resuscitation Characteristics

Indicator	Mechanical Ventilation		Total	p-value	cOR(95%CI)	p-value	aOR(95%CI)	p-value
	No	Yes						
Apgar at 1 minute*								
>7	118(9.0%)	10(4.7%)	124	0.000	ref		ref	
0 to 3	195(14.9%)	86(40.8%)	282	0.000	5.204 (2.601-10.413)	0.0000	0.915 (0.298-2.815)	0.877
4 to 6	1000 (76.2%)	115 (54.5%)	1115	0.177	1.357 (0.692-2.662)	0.3750	0.751 (0.322-1.751)	0.508
Apgar at 5 Minute*								
>7	929(70.9%)	89(42.8%)	1018	0.000	ref		ref	
0 to 3	26(2.0%)	33(15.8%)	59	0.000	12.985 (7.438-22.670)	0.0000	9.017 (3.144-25.866)	0.000
4 to 6	355(27.1%)	86(41.3%)	441	0.000	2.457 (1.784-3.383)	0.0000	1.427 (0.792-2.571)	0.092
Bag and Mask								
No	1067 (80.1%)	113 (52.3%)	1295	0.000	ref		ref	
Yes	265 (19.9%)	103 (47.7%)	253	0.000	3.670 (2.722-4.949)	0.0000	2.494 (1.275-4.876)	0.008

The findings regarding the laboratory parameters showing significant association of mechanical ventilation with abnormal calcium level, magnesium and sodium levels after bi-variate analysis indicating mechanical ventilation may lead to metabolic disorders, compared to creatinine levels as shown in (Table 3).

Table 3: Laboratory Parameters

Mechanical Ventilation						
Indicators	**Yes**		**No**		**Total**	**p-value**
	n	%	n	%		
Calcium (Ca)						0.036
Hypocalcemia	8	5.6%	22	2.1%	30	
Hypercalcemia	0	0.0%	4	0.4%	4	
Normal	135	94.4%	1013	97.5%	1148	
Total	143		1039		1182	
Magnesium (Mg)						0
Hypomagnesemia	7	4.9%	7	0.7%	14	
Hypermagnesemia	0	0.0%	3	0.3%	3	
Normal	136	95.1%	1025	99.0%	1161	
Total	143		1035		1178	
Creatinine (Cr)						0.743
Normal	142	96.6%	1034	97.1%	1176	
High(>1.2)	5	3.4%	31	2.9%	36	
Total	147		1065		1212	
Sodium (Na)						0.002
Normal	138	95.2%	1057	98.7%	1195	
Abnormal	7	4.8%	14	1.3%	21	
Total	145		1071		1216	
Initial ABG						0
No	5	4.2%	184	39.2%	189	
Yes	115	95.8%	285	60.8%	400	
Total	120		469		589	

Similarly, the two major outcomes of the study that is improvement (24.9%) and death (75.1%) showed significant association with mechanical ventilation as presented in (Table 4).

Table 4: Outcomes following mechanical ventilation

Indicators	Mechanical Ventilation		P- Value
	No	Yes	<0.0001
Improved	1176 (96.7%)	51 (24.9%)	
Died	40 (3.3%)	154 (75.1%)	

DISCUSSION

In this study14 % out of 1548 of the admitted neonates required MV and among them 24% survived. However, 58% of the neonates were preterm and the requirement of MV decreased with increasing gestational age and birth weight.

According to our study, the maximum number of mechanical ventilated cases are shown to be diagnosed as septicemic (58%), prematurity (58%) and perinatal asphyxia (53%) cases. Further the total mechanical ventilated cases were evaluated in terms of clinical, demographics and metabolic predictors resulting it. Similarly, A hospital-based cross- sectional study with retrospective document review done among neonates admitted to NICU at the general hospitals in Eastern Ethiopia revealed that the mechanically ventilated neonates are 5 times more likely to develop neonatal sepsis than non-ventilated cases establishing MV as a key predictor of neonatal sepsis.[4] Another study done in Tanzania among neonates with blood culture- proven sepsis at the national hospital

evaluated the risk estimate analysis of the association factors to death among septicemic babies established MV as predictor associated to death in neonates with sepsis.[5] Comparably, a prospective observational study conducted on neonates admitted in NICU of Child Health Institute at J.J.M. Medical College, Davangere who required ventilator therapy revealed birth asphyxia (37.3%) as the most common indication for ventilatory support followed by HMD (Hyaline Membrane Disease), MAS and septicemia (14.7%). Septicemia (42%) was established as the most common complication following MV.[6] One more prospective study was conducted in the NICU of A Tertiary Care Referral Hospital in North India stated sepsis (22.7%) and birth asphyxia (18%) as one of the most common indications for ventilation in neonates and gestational age or prematurity as one of the predictors of mortality in ventilated neonates.[7] A study at Chengdu Women's

and Children's Central Hospital done to identify the risk factors for premature neonates requiring MV indicated out of 1262 premature neonates participated in the study among them (33.53%) neonates required MV.[8] In a systematic review and meta-analysis regarding risk factors of neonatal sepsis in India among neonatal risk factors male sex, out-born neonates and the need for artificial ventilation significantly increased the odds of neonatal sepsis. A meta-analysis was performed for three maternal factors gestational age <37 weeks, mode of delivery and premature rupture of membrane were also established as significant higher odds of neonatal sepsis.[9] All of the above studies clearly states the clear correlation between prematurity , neonatal sepsis and MV . In contrast to these studies one other study establishing the clinical profile, outcome and risk factors for mortality of neonates requiring MV at Tertiary Care Centre of Central Gujarat, India stated respiratory distress syndrome (RDS), Meconium Aspiration Syndrome (MAS) as the most common indication for MV.[10.]

According to the results generated in this study low APGAR score at 5 minutes was shown strong association with need for MV . Similarly, in a prospective cohort study evaluating 942 neonates admitted to a tertiary referral hospital in France indicated a low Conventional (<7) APGAR score at 5-minutes was associated with adverse neonatal outcomes including MV . In contrast after the adjustment for potential con founders such as birth weight, gestational age and many more, a depressed 5-minute conventional- Apgar score that was used in this study too lost its significant associations with all the measured adverse outcomes like IVH, mortality and ventilation.[11] A retrospective cohort and case control study in Brazil which aimed to evaluate the association between Apgar scores of less than seven at five minutes and antenatal factors and postnatal outcomes revealed late deceleration and prolong second stage of labour as predictors of low Apgar score which in return was shown to have situation association with respiratory distress, MV and hypoxic ischemic encephalopathy stating similar results of this study.[12]

In this study it is shown that bag and mask resuscitation is strongly associated with MV. Bag and mask ventilation (BMV) was initiated for all the newborns who did not initiate breathing after airway clearance as per national guidelines. Ventilation was initiated within the Golden minute and then newborn was continued with assisted ventilation (CPAP or invasive ventilation) if spontaneous ventilation does not persist.[13]

Likewise, the abnormal electrolyte levels of calcium, sodium and magnesium were shown to have a rare association with MV in this study. Though the percentage of abnormal Na, Mg and Ca level that has been affiliated with MV are very low. Alterations of Na, which is hypo or hypernatremia can be often associated with dehydration cases which should be frequently monitored. Kidneys are the principal organ of sodium homeostasis. Sodium filtered from the glomeruli is reabsorbed in proximal tubules and the remaining amount is absorbed in different locations through the nephrons by way of intra renal hemodynamics, renin-angiotensin system, vasopressin, antidiuretic hormone (ADH), and aldosterone. After sodium homeostasis is acquired water balance is constantly maintained between the ECF and ICF compartment.[14] It has been discovered through previous evidences that the neurohumoral mediators released during MV adversely affects and alters renal blood flow from cortex to medulla leading to decrease glomerular filtration rate (GFR) and eventually alter the sodium homeostasis and lead to sodium imbalance. Thus, establishing the significance of prevention of ventilator induced acute kidney injury.[15] While a study done in NICU, Fazle-Omar Hospital, Rabwah, from October 2015 to September 2016 has shown significant association between neonatal sepsis and electrolyte imbalance (hyperkalemia, hypernatremia, hypercalcemia and hypocalcemia). And as per our previous discussion sepsis being the major diagnosis in MV cases in this study. Assumption of correlative association between sepsis, MV and electrolyte imbalance can beestablished.[16] Comparably a study on Prognostic Value of Ionized Calcium Levels in Neonatal Sepsis concluded that Hypocalcemia is common in neonates with sepsis.[17] The occurrence of respiratory alkalosis from excessive MV also leads to neonatal hypocalcemia.

CONCLUSION

Our research underscores the significance of thoughtful and individualized MV management in neonates. The efficacy of non-invasive ventilation modes and early surfactant therapy in reducing the need for invasive ventilation and improving outcomes highlights the importance of staying updated with the latest evidence- based practices. While MV remains a life-saving intervention, efforts must be made to minimize its duration and associated complications, particularly concerning the long- term neurodevelopmental outcomes of neonates. Continuous research and advancements in neonatal respiratory care are essential to enhance the quality of care and improve the long-term prognosis for these vulnerable patients.

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