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Indications And Outcomes In Neonates Requiring Mechanical Ventilation In Level III Neonatal Intensive Care Unit, Wah Cantt, Pakistan

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Abstract

Objective: This study was carried out in resource-restricted settings receiving patients predominantly from middle- or lower-income classes, to highlight the indications, outcomes, and multiple factors affecting the outcome of mechanical ventilation in neonates.

Materials and Methods: A retrospective study was conducted in level 3 NICU. Neonates ventilated from January 2018 to July 2021 were included in this study. Primary disease as an indication of ventilation along with outcomes in comparison to various parameters (clinical and laboratory) was listed as predictors of mortality. Thrombocytopenia was defined as platelet count<150,000/ µl and thrombocytopenia present was recorded as positive and negative for normal platelet count. C Reactive Protein levels of > 6 mg/dl were taken as positive.

Results: A total of 320 ventilated neonates were included in the study. Among them 65.6% were males and 41.3% survived. Respiratory distress syndrome (RDS) (28.7%), Hypoxic Ischaemic Encephalopathy (HIE) (26.6%), and Neonatal sepsis (NNS) (14.1%) were the three most indications for ventilation. The disease-specific outcome shows mortality was 64.4% in NNS, 64% in RDS, and 56.4% in HIE. Out of the total enrolled babies for the study, 62.1% were received outdoors and 37.8 % were indoors 74.4% of babies with HIE were received outdoors. Low birth weight, prematurity, mode of admission, first CRP at the time of presentation, thrombocytopenia, and duration of ventilation were portending factors of mortality

Conclusion: Prematurity associated with RDS, HIE and NNS were the major indications for ventilation. Outdoor babies have poor survival due to late referrals and late presentations. Thrombocytopenia and early sepsis were found to be bad prognostic factors.

Keywords: Ventilation, Neonates, Mortality, Prematurity

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1. Introduction

Mechanical ventilation (MV) is integral to any intensive care setting. MV is a life-supporting device, the goal of which is to oxygenate blood and remove carbon dioxide with minimal lung damage.[1] Originally main objective of MV was to restore the patient's ventilation but the concept expanded as other variables of gas exchange were understood. In the last few decades with the widespread use of mechanical ventilation, non-invasive ventilator support, antenatal steroids, surfactant, total parenteral nutrition, and caffeine there has been an exponential reduction in neonatal mortality in developed countries.[2,3,4]Contrary to this, developing countries are still at a nascent stage where the term mechanical ventilator is a scary proposition that comes with fear of severe morbidity and mortality. Moreover, it is a dismal fact that factors like high cost, maintenance, and expertise limits mechanical ventilator use in developing countries.[5]

World Health Organization (WHO)2020 data shows that 2.4 million children had died globally in the first month of life.[6] About one-third of all neonatal deaths occurred on the first day of life and around three-quarters within the first week of life. The most common causes were sepsis, prematurity, and birth asphyxia.[6]

Pakistan is one of the most populous countries in the world with a population of 220 million. According to the UNICEF data, Pakistan has neonatal mortality of 75 deaths per 1000 live births in 1970 which has reduced to 40.3 deaths per 1000 live births in 2020.[7]There is an apparent improvement in statistics but progress has been very slow as per 2000 Millennium Developmental Goals (MDG) .[8]In comparison, neighbouring countries facing similar obstacles have almost achieved their targets.[7]

From the perspective of developing countries, a myriad of factors contributes to high neonatal mortality. The most common factors in Pakistan are prematurity 39.3%, birth asphyxia, birth trauma 20.9%, and sepsis 17.2%.[7, 9,10,11] Respiratory distress

syndrome (RDS) is the most common indication for mechanical ventilation.[12]

There are a few important factors related to pre-hospital and hospital care of newborns which are directly or indirectly related to the high mortality of ventilated neonates and need special attention in our part of the world. Pre-hospital factors include scarcity of Neonatal Resuscitation Program (NRP) trained professionals at referring healthcare facilities, late referrals, referrals without prior contact with the NICU team, lack of an organized transport facility in terms of equipment and trained neonatal transport team, referring without thermoregulation and respiratory support.[2] Whereas intra-hospital factors include difficulty in the availability and administration of surfactant, Total Parental Nutrition (TPN), CPAP, and ventilators due to high cost.[5]

Although ventilatory support in Neonatal Intensive Care Unit (NICU) is being used in Pakistan for the last few decades with variable outcomes. But unfortunately, there are a handful of published articles on neonatal mortality and mechanical ventilation. Therefore, it is not only difficult to get a clear picture of the true incidence of mortality on ventilators but also to get a meaningful understanding of different variables affecting the outcome.

This study was carried out in a resource-restricted setting, receiving patients predominantly from the middle- or lower-income class where patients must bear all expenses. A study was conducted to highlight the indications, outcomes, and multiple factors affecting the outcome of mechanical ventilation in neonates.

2. Materials & Methods

This retrospective study was conducted from January 2018 to July 2021 in the Neonatal intensive care unit (NICU) of Izzat Ali Shah Hospital Wah Cantt, Pakistan. It is a level III referral centre receiving babies from large geography including rural and urban areas. The turnover is approximately 1100 babies per year.

Inclusion criteria: Neonates with a gestational age of 28 weeks and above requiring mechanical ventilation

Exclusion criteria: Neonates with congenital malformations**,** complex cardiac congenital disease, an inborn error of metabolism, neonates requiring surgery or ventilated for less than 24 hours, and newborns beyond the 28th Day of life.

A total of 362 neonates were included who had conventional invasive ventilation. Out of these, 42 babies were excluded from the study according to exclusion criteria. All babies were intubated via oral route with an appropriate size un-cuffed Endotracheal Tube (ETT). The ETT position was confirmed by a chest radiograph. Humidified mechanical ventilation was provided by Babylog 8000 Plus. Synchronized Intermittent Mechanical Ventilation (SIMV) with Volume Guarantee (VG) was used in all cases. High-Frequency Oscillatory Ventilation (HFOV) mode was not used in any neonate.

Babies born with prematurity and early features of RDS, not requiring any resuscitation and breathing spontaneously were given early rescue NCPAP trial with caffeine (loading dose of 20mg per kg per dose followed by a daily maintenance dose of 5mg per kg). Babies who deteriorate in spite of the above interventions were intubated.

Intubations were done according to unit neonatal ventilation guidelines. Indications for mechanical ventilation were:

1. Poor respiratory effort
2. Multiple episodes of apnea
3. Respiratory acidosis
4. Persistent hypoxemia
5. Bi-level CPAP /CPAP failure

Some of the neonates presented with RDS were given surfactant via Intubate -Surfactant- Extubate technique (INSURE)while others were given surfactant while on a mechanical ventilator. Blood gases were done routinely, and other investigations like blood counts, X-rays, liver function tests, renal function tests, and cerebrospinal fluid analysis were done as needed. Point-of-care echocardiography and cranial ultrasounds were done in all babies by an onsite Paediatric Cardiologist and Neonatologist. All diagnoses were made on the basis of clinical information, laboratory and radiological evidence. To study the relationship between sepsis and neonatal ventilation outcome we recorded platelet count and quantitative C-reactive proteins (CRP) at the time of admission, as they were easily available. Thrombocytopenia was defined as platelet count<150,000/ µl and it was recorded as positive when it was less than this level. C Reactive Protein levels of > 6 mg/dl were taken as positive. Study approval was taken from the local ethical committee of the hospital. Neonatal record of ventilated babies was retrieved from

the NICU database and case notes. Parameters like age, gender, mode of admission, weight, gestational age, primary diagnosis, mode of admission, and duration of hospital stay were recorded. Data were coded and analyzed using IBM SPSS version 23. A p-value of<0.05 was considered significant. After applying the exclusion criteria, a total of 320 critically ill neonates requiring mechanical ventilation were included in this study, which includes both indoor (born in side Izzat Ali Shah Hospital) and outdoor (born in some other hospital) babies.

3. Results

Males were predominant, 210(65.6%), and females were 110 (34.4%). The mean age of presentation was 2.76±5 days of life. Table 1 shows the frequency of indications requiring ventilator support. RDS, 92(28.7%), Hypoxic Ischemic Encephalopathy (HIE) 85 (26.6%) and Neonatal sepsis (NNS) 45 (14.1%) were the three most common conditions.

Table-1 Frequency of indications requiring ventilation.

Primary indications	Frequency	(%)
RDS	92	28.7
HIE	85	26.6
NNS	45	14.1
Others*	38	11.9
MAS	32	10.0
aspirational Pneumonia	9	2.8
idiopathic PPHN	4	1.3
congenital pneumonia	15	4.7
Total	320	100

*Others include opioid and other poisons, tetanus, pneumothorax, pulmonary hemorrhage, status epilepticus, Meningitis, etc

Table 2 shows that 41.3% (132) of ventilated babies were extubated successfully and discharged home. The disease-specific outcome shows mortality was 29 (64.4%) in NNS, 59 (64%) in RDS, and 48(56.4%) in HIE.

Out of the total enrolled babies for the study 199(62.1%) were received outdoors and 121 (37.8 %) were indoor. Of the total 92 babies having RDS, 43 (53.6%) were outdoors and 42(46.7%) were indoors. In the case of NNS 40 (86.6%) babies were admitted form outdoors and 5(13.3 %) cases were indoors, as shown in Table 3

Table-2 Primary Indication vs Outcome

Primary indication	Outcome	
	Survivor	Non-survivors
RDS	33(35.8%)	59(64%)
HIE	37(43.5%)	48(56.5%)
NNS	16(35.5%)	29(64.4%)
Other	19(50%)	19(50%)
MAS	14(43.7%)	18(56.2%)
aspirational Pneumonia	4(44.4%)	5(55.5%)
Idiopathic PPHN	4(100%)	0
Congenital pneumonia	5(33.3%)	10(66.7%)
Total	132 (41.2)	188 (58.7)
p-value	0.23	

The percentage of mortality was higher in outdoor patients, 127(63.8%) than indoor (P value 0.001), especially in HIE babies with mortality of 74.4% and 38% respectively (Table 3).

Multiple factors which contributed to the outcome were analyzed. Low birth weight, prematurity, mode of admission, first CRP at the time of presentation, thrombocytopenia, and duration of ventilation were the most significant (Table 4).

5. Discussion

The importance of mechanical ventilation in neonatal critical care has been emphasized through numerous articles published in last decade.

In spite of promising benefits, mechanical ventilation still carries substantial risks.

Comparing the different variables, there is 58.8% mortality of ventilated babies in present study which is higher than quoted percentage for Western countries[13], whereas it is comparable to the mortality of Eastern countries which is 52%, 51%, 43.3% and 48% reported by Khushdil[14], Dutt[5], Iqbal[15] and Mokhtar[16] et al respectively.

Males were the predominant gender out of the total neonates enrolled in the current study which is consistent with results of Wesam et al and other studies.

The variance in gender of neonates however did not have statistically significant association with the outcome as was found in Iqbal et al.[15] Age at time of presentation was also not statistically significant.

Table-3 Primary Diagnosis and Outcome vs Mode of Admission

Primary diagnosis			Mode of admission		P values
			Outdoor	Indoor	
RDS	outcome	Survivors	18(36.7%)	15(34.8%)	
		Non-Survivors	31(63.2%)	28(65%)	0.853
	Total		49	43	
HIE		Survivors	11(25.5%)	26(61.9%)	
		Non-Survivors	32(74.4%)	16(38%)	
	Total		43	42	0.001
NNS		Survivors	13(32.5%)	3(60%)	
		Non-Survivors	27(67.5%)	2(40%)	
	Total		40	5	0.226
Other		Survivors	15(55.5%)	4(36.3%)	
		Non-Survivors	12(44.4%)	7(63.6%)	0.283
	Total		27	11	
MAS		Survivors	6(33.3%)	8(57%)	
		Non-Survivors	12(66.7%)	6(42.8%)	
	Total		18	14	0.178
Aspirational Pneumonia		Survivors	4(44.4%)	0	
		Non-Survivors	5(55.5%)		-
	Total		9	0	
Idiopathic PPHN		Survivors	3	1	
		Non-survivors	0	0	-
	Total		3	1	
congenital pneumonia	outcome	Survivors	2	3	
		Non-Survivors	8	2	
	Total		10	5	0.121
Total		Survivors	72	60	0.18
		Non-Survivors	127	61	
	Total		199 (62.1%)	121 (37.8%)	

Most common indication for ventilation were RDS, NNS and HIE. Mortality was highest in RDS and NNS. We saw high mortality in RDS of 64% which is higher when compared to other studies, that is 44.6%, 28.3%,46.7%.[15,16, 5] In addition to late presentation, one possible contributory factor for high mortality in RDS in this study was, the lack of use of surfactant in significant number of babies due to non-affordability.

Sepsis was the other most common indication for ventilation and respiratory failure in septic neonate is a bad prognostic factor.[15]It was observed that 88% babies were received from outside with late onset neonatal sepsis requiring ventilatory support, and had variable outcome which could be due to delayed presentation and mostly multi drug resistant organism. Two other studies conducted in our setup in relation to mortality in NNS showed MRSA has the highest mortality and it was the most common isolated pathogen in neonate with late onset sepsis.[17, 18]

Table-4 Factors affecting mechanical ventilation outcome

Factors	Outcome		P-value
	survivors	Non-survivors	
Gender			0.570
Male	89(42%)	121(57.6%)	
Female	43(39%)	67(60.9%)	
Birth Weight categories, kg			0.010
Extremely low birth weight <1 kg	2(17%)	10(83%)	
Very low birth weight 1-1.5kg	8(25%)	24(75%)	
Low birth weight 1.5 to <2.5kg	45(38%)	75(62.5%)	
Normal birth weight >2.5 to <4 kg	77(49%)	79(50.6%)	
Gestational age categories, weeks			0.052
Extremely preterm (<28weeks)	1(12.5%)	7(87.5%)	
Very preterm (28 to 31+6 weeks)	8(24.2%)	25(75.7%)	
Preterm (32 to 36+6 weeks)	37 (45.6%)	44(54.3%)	
Term (≥37 weeks)	86(43.3%)	112(56.5%)	
Age at presentation (day of life)			0.590
<3 days	112(40.2%)	166(59.7%)	
4 to 7 days	5(45.5%)	7(63.6%)	
More than 7 days	15(50%)	15(50%)	
Mode of admission			0.012
Indoor	60(49.5%)	61(50%)	
Outdoor	72(36.1%)	127(63.8%)	
CRP			0.026
Positive	75(47.4%)	83(52.5%)	
Negative	57(35%)	105(64.8%)	
Thrombocytopenia			0.001
Positive	29(28.1%)	74(71.8%)	
Negative	103(47.4%)	114(52.5%)	

As far as primary indication and outcome versus mode of admission is concerned total number of babies intubated due to HIE were 26.6% (50.5% were outdoor

and 49.5% were indoor). Two third of the babies (74.4%) with HIE requiring intubation were received from outside did not survive, while survival rate was much better in babies with HIE born indoor. (61.9%). The high number of indoor babies with HIE in this study had significant percentage of babies born to non-booked mothers who were received in active labour. Current study showed statistically significant relationship ($p < 0.05$) between HIE outcome versus mode of admission whereas no statistically significant relationship found in other diagnoses. There is no single study found which compared the disease specific mortality in babies born indoor versus outdoor. Thrombocytopenia and Positive CRP had a statistically significant correlation with mortality in our study. Positive CRP and Thrombocytopenia at time of admission was seen to be a bad prognostic factor, the mortality seen was 71% which is also recognized by others as well like in Iqbal et al .[15]

This study also shows an association between low birth weight, prematurity, and high mortality as shown by many studies.[5,12, 19] 75% mortality was observed in very preterm and very low birth weight babies.

The key elements associated with better outcomes on mechanical ventilators in neonates have been addressed by multiple studies. There is a consensus that one-to-one skilled nursing, stringent Infection control, better staff expertise in the use of equipment, and preference for noninvasive methods of ventilation where indicated can improve the outcome.[20,21,22]
Ventilator-related complications have been one of the most emphasized areas for research in recent years. This has been an important limiting factor in this study along with other factors.

5. Conclusion

Prematurity associated with RDS, HIE, and NNS were the major indications for ventilation. Outdoor babies have poor survival due to multiple factors, the most important of which are late referrals and late presentations. Thrombocytopenia and early sepsis were found to be bad prognostic factors. The strong association between prematurity, birth weight, and mortality are reconfirmed by our study.

CONFLICTS OF INTEREST- None

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Contributions:

M.A, S.N, S.H - Conception of study
M.A, S.N, S.H, H.S - Experimentation/Study conduction
M.A, S.N, S.H -Analysis/Interpretation/Discussion
M.A, H.S - Manuscript Writing
S.H - Critical Review
M.A, S.N, S.H - Facilitation and Material analysis

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