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Original Research Article

Demographic, clinical profile and short-term outcome of neonates referred for mechanical ventilation: experience in a referral neonatal intensive care centre in Southern Nigeria

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ABSTRACT

Background: The use of mechanical ventilation (MV) in NICU is not widespread in Nigeria. Although a life-saving tool in neonates, MV is associated with potentially high morbidity and mortality rate. There are various factors which impact the outcome of MV in neonates. The aim of this study is to assess outcome, demographics and clinical profile of babies who received MV in the region.
Methods: This was a retrospective study, involving 20 infants, who were all referred from other Health care centres.
Results: The overall survival rate of ventilated babies in this study was 30.0%; however, relative survival rate compared to non-survival group was 53.8%. Although, the mean weight and mean gestational age (GA) of those who survived were higher than that in those who did not survive, this difference was not statistically significant. However, a significantly higher proportion (87.3%) of those who were ventilated for 1-3 days survived, compared to those ventilated for less than 24 hours or more than 3 days.
Conclusions: The survival of neonates referred for MV in our study was comparable to that seen in other developing countries. Duration of MV (DMV) was the only significant factor affecting the outcome of MV in our study.

Keywords: Neonatal mechanical ventilation, Newborn intensive care unit, Level III neonatal units in Southern Nigeria, Assisted ventilation in neonates

INTRODUCTION

Mechanical ventilator is a lifesaving procedure, which is commonly used in newborn intensive care units in developed countries.[1] Indications for its use include: severe respiratory distress, perinatal asphyxia, meconium aspiration syndrome, and intraventricular haemorrhage.[2] MV has improved newborn survival significantly.[3] A study by Richardson et al showed that due to introduction of MV, surfactant and pressors, neonatal intensive care unit mortality declined from 17.1% to 9.5%, and total mortality declined from 31.6% to 18.4% over a period of 5 years.[4] Compared to developed countries, in many low to medium income countries, including Nigeria, the use of MV in NICU is not widespread.[5] Although a life-saving tool in neonates, MV is associated with potentially high morbidity and mortality rate, which is higher in developing countries, with fatality rate of upto 75.5% compared to developed countries, where survival is upto 91%.[4] There are various factors which impact the outcome of MV in neonates; smaller babies with extreme low birth weight and extreme prematurity have been known to have a poorer outcome compared to bigger babies delivered at older GA.[6] Other factors include age at presentation, male sex, indication of MV, and mechanical ventilator set parameters. In Nigeria, these factors and their impact on the outcome of MV have not been well studied in our region. Thus, the aim of this study is to assess the outcome, demographics and clinical profile of babies who received MV in the region.

METHODS

This was a retrospective study, involving 20 infants, who were all referred from other health care centres for advanced care in our facility. This study was conducted at Med-Vical medical centre, which has a 9-bedded neonatal intensive care unit. Data was collected between January to December, 2023. Med-Vical medical centre is located in Benin City, which is the Capital of Edo State, in the South-South geopolitical zone of Nigeria. The medical centre, receives referral from the whole of the city, other parts of the State, and from neighboring states, including Delta State.

All neonates (0-28 days) who required MV were recruited into the study. All neonates involved in the study, were referred from other Health care facilities, including tertiary and secondary health care facilities. The indications for initiation of MV were: i) intractable or recurrent apnea, (ii) gasping or poor respiration, (iii) oxygen (O_2) saturation <85% on supplemental oxygen, (iv) humidified high flow failure and/or continuous positive airway pressure (CPAP) failure, defined as worsening respiratory distress, oxygen saturation <85% despite high flow rate of 6-8L/min and/or CPAP pressure of 7-8 cm H_2O at fractional inspired oxygen (FiO_2) of 0.8 or recurrent episodes of apnea.[7] Assist control-synchronized intermittent mandatory ventilation mode was the main mode of ventilation in the neonates in our study. Pressure limited time cycled ventilation was used and the different ventilator parameters were varied based on each patient's condition and the lung mechanics and compliance. In general, the set parameters used were: positive end-expiratory pressure (PEEP) 5-7 mmHg, peak inspiratory pressure (PIP) 18-30 mmHg, tidal volume: 6-10 ml/kg, inspiratory time 0.25-0.5 s, and the FiO_2 0.40-0.80.

Definition of terms

Ventilator-associated pneumonia (VAP): this is defined as pneumonia that occurred within 48-72 hours or beyond following commencement of MV; and characterized by the presence of a new or progressive infiltrate; symptoms and signs of infection; changes in sputum/endotracheal aspirate characteristics; and detection of a causative agent.[9] Extubation success is defined as sustained oxygen saturation at 88%-95% or more (for term neonates) on HHHFNC at FiO_2 of 0.4 and without the need for any other mode of non-invasive ventilation.

Extubation failure is defined as: the need for re-intubation within 7 days of extubation.

Data collection

Data collected include: age at admission, gender, weight at admission, type of gestation (multiple or singleton gestation), duration of pregnancy (preterm or term), GA at delivery, duration of illness, DMV, set ventilator parameters (PIP, PEEP, FiO_2), indication for MV and complications of MV.

Statistical analysis

Data was entered into SPSS, version 22 (IBM Corp., Armonk, NY, USA). Continuous variables were analysed using the t test. Chi-square test and Fischer's exact test were used to analyse categorical variables. $P<0.05$ was considered significant. Independent t test was used to compare mean of continuous variables (such as GA, weight at presentation, positive inspiratory pressure and positive end expiratory pressure) between neonates that survived and those that died.

RESULTS

A total of 20 neonates were recruited for the study. There were more males in the study (66.7%), most of the study participants were preterm neonates (55.0%), only one neonate was a product of multiple gestation (Table 1). Majority of infants weighed between 1000-2400 g (60%), with the mean weight of 2.200±0.837 kg. Half (50%) of the neonates in the study, were admitted within 24 hours of birth (Table 1). Mean GA was 34.400±4.684 weeks and a higher proportion (55%) were delivered at <36 weeks GA compared to those delivered at >36 weeks GA. Duration of illness in about 60% of them was under 24 hours. Mean duration of MV was 2.373±2.476 days, with most of the infants ventilated between 1 to 3 days. Most of the mothers of infants in this study had at least secondary level of education (LOE) (Table 1).

Most common indications for MV were severe respiratory distress syndrome (RDS) (55.0%) and perinatal asphyxia (33.0%) (Table 2). VAP and extubation failure occurred in 20.0% and 10.0% respectfully of all ventilated babies (Table 3).

The overall survival rate of ventilated babies in this study was 30.0%; however, relative survival rate compared to those who expired (did not survive) was 53.8% (Table 4). Comparing survived and non-survived neonates only (n=13), according to measured continuous variables on neonatal baseline characteristics, there was no significant difference between the two groups (Table 5). The mean weight and mean GA of those who survived were higher than that in those who did not survive, while the mean age at presentation, and mean duration of illness were higher in those who expired, compared to those that survived (Table 5). A significantly higher proportion (87.3%) of those who were ventilated for 1-3 days survived, compared to none survival in those ventilated less than 24 hours or more than 3 days (Table 6).

More male infants (60.0%) than female infants (33.3%) survived (Table 6). Comparable proportion of term and preterm infants survived. The only product of multiple gestation did not survive; none of the infant weighing under 1000 g and delivered before 28 weeks survived, while only 25.0% and 50.0% of those weighing more than 2.4 kg and delivered after 36 weeks survived; and 75.0% and 80% of those weighing 1-2.4 kg and delivered at 28-36 weeks survived (Table 6). Majority (62.5%) of those that presented within 24 hours of birth survived compared to the others. Concerning duration of illness, majority (55.6%) of those who presented within 24 hours of onset of illness survived compared to others. None of the infants delivered to mothers with less than secondary LOE survived, while all babies (100%) who survived belong to mothers with at least a secondary LOE.

Indication for MV had no impact on survival rate of all ventilated babies, with an equal proportion (50%) having severe RD and perinatal asphyxia respectively in both groups (Table 7). In comparing survived and non-survived babies by ventilator parameters, mean PIP, PEEP and FiO_2 settings were higher in those who expired than in those who survived (Table 8). However, this difference was not statistically significant.

Table 1: Neonatal demographic characteristics, (n=20).

Neonatal demographic characteristics	N	Percentage (%)
Gender		
Male	14	66.7
Female	7	33.3
Duration of pregnancy		
Preterm	11	55.0
Term	9	45.0
Type of gestation		
Singleton	19	95.0
Multiple	1	5.0
Weight		
<1000 g	1	5.0
1000-2400 g	12	60.0
>2400 g	7	35.0
Mean weight	2.200±0.837	
Age at presentation		
<24 hours	10	50.0
1-3 days	4	20.0
>3 days	6	30.0
Mean age at presentation	2.783±4.928	
GA		
<28 weeks	3	15.0
28-36 weeks	8	40.0
>36 weeks	9	45.0
Mean GA	34.400±4.684	
Duration of illness (DOI)		
<24 hours	12	60.0
1-3 days	4	20.0
>3 days	4	20.0
Mean DOI	12.00±9.967	
Duration of MV (DMV)		
<24 hours	3	15.0
1-3 days	10	50.0
>3 days	7	35.0
Mean DMV	2.373± 2.476	
Mother's LOV		
None/primary	3	15.0
Secondary	13	65.0
Tertiary	4	20.0

Table 2: Clinical indication of MV, (n=20).

Clinical indication	N	Percentage (%)
Severe RDS	11	55.0
Perinatal asphyxia	6	30.0
Meconium aspiration syndrome	1	5.0
Severe acute bilirubin encephalopathy	1	5.0
Congenital heart disease	1	5.0

Table 3: Complications from ventilator, (n=20).

Ventilator complications	N	Percentage (%)
VAP	4	20.0
Extubation failure	2	10.0

Table 4: Outcome of ventilated neonates, (n=20).

Outcomes	N	Percentage (%)
Discharged	7	35.0
Expired	6	30.0
LAMA	4	20.0
Re-intubated	2	10.0
Referred	1	5.0

LAMA: Leave against medical advice

Table 5: Comparison between survived and non-survived neonates only (n=13) according to some continuous variables (neonatal baseline characteristics).

Neonatal demographic characteristics	Survived, (n=7) (%)	Non survived, (n=6) (%)	P value
Mean weight	2.314±0.647	2.067±0.869	0.568
Mean age at presentation	1.208±1.365	1.347±1.180	0.849
Mean GA	35.570±2.637	34.170±6.494	0.609
Mean duration of illness	1.430±0.787	1.500±0.837	0.877
Mean DMV	1.430±0.535	2.000±1.095	0.246

Table 6: Comparison between survived and non-survived neonates (n=20) according to all neonatal baseline characteristics.

Variables	Survived, (n=7) (%)	Not survived, (n=6) (%)	Total, (n=13)	T value	P value
Gender					
Male	6 (60.0)	4 (40.0)	10	-	0.559
Female	1 (33.3)	2 (66.7)	3		
Term/preterm					
Preterm	4 (57.1)	3 (42.9)	7	-	1.000
Term	3 (50.0)	3 (50.0)	6		
Type of gestation					
Singleton	7 (58.3)	5 (41.7)	12	-	0.462
Multiple	0 (0)	1 (100.0)	1		
Weight					
<1000 g	0 (0)	1 (100)	1	3.946	0.139
1000-2400 g	6 (75.0)	2 (25.0)	8		
>2400 g	1 (25.0)	3 (75.0)	4		
Age at presentation					
<24 hours	5 (62.5)	3 (37.5)	8	0.761	0.684
1-3 days	1 (33.3)	2 (66.7)	3		
>3 days	1 (50.0)	1 (50.0)	2		
GA					
<28 weeks	0 (0)	2 (100.0)	2	3.745	0.154
28-36 weeks	4 (80.0)	1 (20.0)	5		
>36 weeks	3 (50.0)	3 (50.0)	6		
Duration of illness					
<24 hours	5 (55.6)	4 (44.4)	9	0.034	0.983
1-3 days	1 (50.0)	1 (50.0)	2		
>3 days	1 (50.0)	1 (50.0)	2		
Duration of mv					
<24 hours	0 (0)	2 (100.0)	2	10.769	0.009
1-3 days	7 (87.5)	1 (12.5)	8		
>3 days	0 (0)	3 (100.0)	3		

Continued.

Variables	Survived, (n=7) (%)	Not survived, (n=6) (%)	Total, n=13	T value	P value
Mother's LOE					
<secondary LOE	0 (0)	1 (100)	1	-	0.462
Secondary and above	7 (58.3)	5 (41.7)	12		

MV: Mechanical ventilation; LOE: Level of education.

Table 7: Comparison of survived and non-survived ventilated babies by indication for ventilation.

Clinical indication	Survived, (n=7) (%)	Non-survived, (n=6) (%)	Total, (n=13)	T value	P value
Severe RDS	3 (50.0)	3 (50.0)	6	6.474	0.166
Perinatal asphyxia	3 (50.0)	3 (50.0)	6		
Others	1 (100)	0 (0)	1		

Table 8: Comparison of survived and non-survived babies by ventilator parameters.

Ventilator parameters	Survived, (n=7)	Non survived, (n=6)	T value	P value
PIP	26.710±3.656	29.83±3.656	1.895	0.085
PEEP	6.140±0.690	6.670±0.516	1.525	0.155
FiO_2	52.860±11.127	64.170±10.206	1.897	0.084

PIP: Positive inspiratory pressure; PEEP: Positive end expiratory pressure; FiO_2: Fractional inspired oxygen.

DISCUSSION

All neonates in this study were referred from other health care centres, primarily for advanced respiratory support. The availability of neonatal intensive care units with advanced respiratory care services in low- and middle-income countries, like Nigeria is rare.[5] Within the period under study, there were only two centres (including our centre) with neonatal MV services and advanced respiratory support in Benin city and Edo State as a whole. This study has exposed a dearth in availability of Level III NICU centres with advanced neonatal care services in the State and Sub-region.

Majority of the neonates were males, and preterm infants; a similar pattern was found in a study in Egypt by Othman et al with 58.2% of neonates being males. Also, two studies in Bangladesh by Jahan et al and Hossain et al had 65.5% and 58.8% respectively of neonates being male.[9-11] Studies have shown that preterm male neonates tend to have more respiratory compromise than girls; this likely explains the higher proportion of boys referred for MV in this study.[12,13] Preterm infants are also known to require more ventilatory support compared to term infants due to the lack of surfactant.

The main indications for MV in this study were RDS (55.0%) and perinatal asphyxia (30.0%); this is comparable to that found by Jahan et al with RDS (32.75%), and Perinatal asphyxia (18.96%) being the most frequent reasons for MV.[10] Similar findings were found in other studies, with RDS being the most common indication for MV.[9,14-16] Concerning the outcome of neonates who received MV in this study, the overall survival rate was 35.0%, while the relative proportion of those that survived compared to those that did not survive was 53.8%. This survival rate in our study is much lower than that seen in developed countries, but comparable to that found in other low to middle income countries.[2,4,6,17] In India, studies done by Igbal et al and Marthur et al reported 35.3% and 26.0% survival rate respectively. Hossain et al and Hossain et al documented 29.4% and 24.5% survival rate respectively in Bangladesh.[6,11,16,18] Similar to our study, these studies involved out-born newborns who were referred for respiratory support. As noted by these studies, the low survival rate of these referred neonates following MV may be due to the poor mechanism and condition of referral, which includes: delay in referral, mode of referral (with poor temperature control, and oxygenation), and damages that may have already occurred at birth or in utero.[11,18] Most babies referred to our Centre, had multiple or chain referrals (presenting at 3 to 4 facilities) before finally arriving at our facility. These multiple referrals further delayed their presentation and prolonged the duration of illness and thus worsened the prognosis. Poor referral system for advanced neonatal services in the city, state and country, (due to poor network and knowledge of available NICU services in the region) is a major contributor to the poor outcome of these referred neonates who received MV.

Other contributing factors to low survival rate in this study include duration of illness, and age at presentation. The mean duration of illness amongst those who did not survive was slightly higher compared to those that survived; 55.6% of babies who commenced MV within 24 hours of illness survived. Although duration of illness did not have any significant association with survival, it can be assumed that babies with more prolonged illness before MV is commenced will have a poorer outcome than those with shorter duration of illness, due to late intervention and delay in commencement of MV.

In our study, a higher proportion (62.5%) of those who presented within 24 hours of life and those with male sex (60.0%) survived; however, this difference was not statistically significant. Similar findings were seen in other studies, where age and sex were not significant predictors of outcome of MV.[11,16,18,19] Mean weight and mean GA were higher in those who survived than in those who died. Weight and GA are significant determinants in the outcome of MV; Igbal et al, Mathur et al, Jahan et al and Dekate et al found that babies who survived had a higher GA and higher weight compared to those who did not survive.[10,16,18,20] Similarly, Nangia et al found that the higher the GA and birth weight the higher the survival rate.[19,21,22] Outcome of MV based on DMV, showed that those on MV for 1-3 days had a significantly higher survival rate (87.5%, p=0.009) compared to those who were ventilated for less than 24 hours or more than 3 days. Jahan et al recorded a similar pattern, where survival was higher in those ventilated between 1-7 days (70.4%) compared to those ventilated for more than one week or less than one day.[10] In contrast, Mathur et al (2005) found a higher fatality rate (88.0%) in infants ventilated under 72 hours compared to that in those (47%) ventilated for more than 72 hours.[18]

All babies (100%) who survived belonged to mothers with at least a secondary level of education. This supports the fact that maternal education plays a significant role in survival of newborn, especially with regards to seeking health care, reducing delay in referral and also in financial empowerment so as to afford health care services.

There was no difference in the survival rate in those with perinatal asphyxia and also in those with RDS as indication for MV. This is similar to that found in Dekate et al and Nangia et al.[20,21] The low survival rate of babies with RDS and those with perinatal asphyxia in this study can be attributed to the vulnerability of these infants, especially in those with severe disease (hypoxic ischemic encephalopathy stage III) and in those with RDS who did not receive surfactant due to the high cost of purchase. On the contrary, Jahan et al reported a higher fatality rate (72.7%) in those with perinatal asphyxia and a higher survival rate in those (84.2%) with RDS.[10]

Mechanical ventilator settings or parameters were compared between survivors and non- survivors; PIP and PEEP settings had no impact on outcome of neonates. This is similar to that found by Hossain et al on the other hand Dekate et al reported that compared to survivors, higher PIP (15.10 cmH_2O vs 13.48 cmH_2O) and PEEP (7.86 cmH_2O vs 6.35 cmH_2O) were required for non survivors.[11,21] FiO_2 had no impact on the outcome of MV of neonates in this study unlike that found by Dekate et al, Marthur et al and Hossain et al, where higher FiO_2 setting was used in non survivors compared to survivors.[11,18,21]

Limitations

All babies included in the study were referred; reclassification of these infants based on the severity of their illness will give more information on the impact of late presentation on the outcome of MV in referred neonates. Our study included a small number of neonates.

CONCLUSION

In conclusion, DMV was the only significant factor affecting the outcome of MV in our study. Thus, DMV can be used as a prognostic tool for MV of neonates and also guide clinical practice in determining the best time to wean-off MV. The survival rate of referred neonates commenced on MV in our study was comparable to that seen in studies done in other developing countries. The poor referral system and the poor network of neonatal intensive care units in the region are important contributing factors leading to delay in presentation, thereby causing more damage to the very ill neonate and thus poor prognosis and death.

Recommendations

The duration on MV should be used as a prognostic tool for determining the outcome of MV in neonates. In addition, weaning off MV should be done after 24 hours but less than 3 days. A good network and classification of neonatal intensive care units in Edo State and Nigeria as a nation should be created and utilized to aid proper and prompt referral. There should be upgrade of more neonatal intensive care units to offer advanced respiratory support, such as MV in the region, thereby reducing neonatal mortality in the Country.

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