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Department of Pediatric and Child Health

Outcome and associated factors of mechanically ventilated Neonates among selected hospitals in Addis Ababa, Ethiopia; Cross -sectional Multi-center study

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ADDIS ABABA ETHIOPIA

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILDHEALTH

I, the undersigned Pediatrics and Child health resident declare that I have submitted my original thesis on the title Outcome and Associated Factors of Mechanically Ventilated Neonates among Selected hospitals in Addis Ababa, Ethiopia 2024 in partial fulfillment ofthe specialty program.

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Abstract

Background: Neonatal mortality has a significant impact on global mortality, morbidity, economic cost, and hospitalization worldwide. Improving neonatal health through innovations in healthcare, such as mechanical ventilation, is vital for improving the well-being and lowering mortality rates among newborns. The most common indication for MV in NICUs was respiratory distress syndrome.

Objective: To assess the outcome and associated factors of mechanically ventilated neonates admitted in three NICUs at selected hospitals in Addis Ababa, Ethiopia 2023

Methods: A cross-sectional study was conducted to examine the outcomes and contributing factors for mechanically ventilated neonates admitted to Girum Hospital, Addis Hiwot Hospital, and Myungsung Christian Medical Center (MCM). Three private hospitals were chosen through a simple random sampling method, where a total of 160 mechanically ventilated neonates were identified during the study period. A univariate and multivariate binary logistic regression analysis was performed to examine the factors associated mortality of mechanical ventilated neonates. The results of logistic regression reported as adjusted odds rations (OR) with 95% confidence intervals and p-value < 0.05 are considered statistically significant

Results: An analysis of 160 neonates requiring mechanical ventilation that 61.3% were male and 63.7% displayed preterm gestational age. The primary reasons for mechanical ventilation (MV) in this study was respiratory distress syndrome (RDS) being the most prevalent at 51.9%, followed by meconium aspiration syndrome (MAS) at 12.5%, and neonatal sepsis at 11.9%. The overall mortality rate of mechanical ventilated neonates was 24.4%. Moving to associated factors requirement of resuscitation(AOR=9.9(1.7, 58.5),p=0.011),extreme prematurity (AOR=61.7(3.3,1150.1),p=0.0006),DIC(AOR=13.1(1.6, 104.5), p=0.015),AKI (AOR=13.1(2.24, 76.9), p=0.004), MOF (AOR=246.9(14.4, 4242.8), p=0.0000) and pulmonary hemorrhage (AOR=16.7(1.9,145.9), p=0.011) emerged as the most statistically significant variables determining mortality of neonates on mechanical ventilator

Conclusion: The commonest indication for mechanical ventilation in was RDS. Prematurity and disease-related complications were among the preventable factors contributing to mortality. Although the mortality rate of mechanically ventilated neonates is lower compared to similar studies in low and middle-income countries,.

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Contents

List of tables and figure Acronyms and abbreviations

ARDS	Acute respiratory distress syndrome
CPAP	Continuous positive airway pressure
ETT	Endotracheal tube
GA	Gestational Age
IVH	Intraventricular hemorrhage
MAS	Meconium aspiration syndrome
MOF	Multiorgan failure
MV	Mechanical ventilation
NICU	Neonatal Intensive care unit
RDS	Respiratory distress syndrome
SIMV	synchronized intermittent mandatory ventilation
PS	Pressure support
SPSS	statistical package for social sciences
VAP	Ventilator associated pneumonia
WHO	World health organization

CHAPTER ONE: INTRODUCTION

1.1. Background

Neonatal health stands as a critical global public health issue, intricately intertwined with various facets of societal well-being(1). According to a report by the World Health Organization (WHO) in 2020, nearly half (47%) of all deaths among children under the age of five occurred during the neonatal period, within the first 28 days of life(2). This critical time frame is marked by vulnerabilities to various health challenges, with preterm birth, intrapartum-related complications such as birth asphyxia, infections, and birth defects being identified as the primary causes of neonatal mortality(2). The Sustainable Development Goal (SDG) 3.2 underscores the urgency to eradicate preventable deaths among newborns and children under the age of five by 2030. This ambitious goal sets specific targets, aiming for a reduction in neonatal mortality to at least 12 per 1,000 live births and under-five mortality to at least 25 per 1,000 live births(3). The most common cause of newborn death frequently involves respiratory problems that needs higher standard of care and faster advancements in respiratory support. Improving neonatal health through advancements in healthcare, such as mechanical ventilation, is essential for enhancing the well-being of newborns and decreasing mortality rates among children under five years.

Mechanical ventilation (MV) is one of the most common lifesaving respiratory interventions and the essential components in the neonatal Intensive Care Unit (NICU) care, despite its important role it may exacerbate, or even initiate lung injury and inflammation which leads to significant morbidity. Neonates, being highly vulnerable due to unique physiological characteristics in their early development, are particularly prone to respiratory distress. Factors such as their elevated metabolic rate, reduced lung compliance, increased airway resistance, and insufficient surfactant levels in preterm infants contribute to this susceptibility. Consequently, common indications for mechanical ventilation in neonates include respiratory distress syndrome (RDS), perinatal asphyxia, meconium aspiration syndrome, sepsis, prematurity-related apnea, among others(4, 5). The prognosis of neonates receiving mechanical ventilation depends on various factors, including the severity of their condition, advancements in mechanical ventilation technology, the expertise of the neonatal healthcare team, and the effective management of complications associated with both mechanical ventilation and the underlying disease The death

rate among ill neonates in the NICU is high; however, death among mechanically ventilated neonates is considerably higher. (4)

1.2. Statement of the problem

Neonatal age group mortality and morbidity is an indirect predictor for growth and development of a specific country. Neonatal mortality disproportionately impacts low and middle-income countries. Sub-Saharan Africa bears the highest burden of neonatal mortality(1) According to a study published in 2020 by the World Health Organization (WHO), Ethiopia ranks fourth among the top 10 countries in terms of the number of newborn deaths (2,3). In doing so based on Health Sector Transformation Plan (HSTP)-II the target is to reduce neonatal mortality to 21 per 1000 live birth by the end of the plan period 2024/25 but unfortunately proportion of neonatal deaths from the total under-five deaths increased from 43% in 1990 to 55% in 2019.So that by all measures the achievement so far is unsatisfactory. Respiratory arrest is the commonest mode of death so that Mechanical ventilation serves as a crucial life-saving intervention to enhance the survival chances of neonates in the aspect of respiratory support ,Although mechanical ventilation is crucial for saving lives, multiple studies have shown that the survival rate of neonates receiving mechanical ventilation varies significantly, ranging from 24.5% to 67.9% in developing countries and around 91% in developed countries that shows disparity in outcome of mechanical ventilated neonates (4, 8, 9)

However in our country Ethiopia the experience of neonatal ventilation is so limited .Even though there are no published data yet on the outcome of mechanical ventilated neonates , it's evident that this problem is even more pronounced in our setting and observed gaps includes shortage of Mechanical ventilator, delayed diagnosis and presentation for intubation and shortage of human power ,sedation and analgesics for neonates on MV , lack of knowledge on mechanical ventilation and poor supportive care of neonates on mechanical ventilation are some of the various challenges we are facing during our day to day stay in NICU.

The purpose of the study is to identify indications of ventilation, determine whether mechanically ventilated newborns survived or not and also to investigate the associated factors responsible for poor outcome in ventilated neonates. In addition to Evaluate the association between delayed ventilation initiation following indication and outcome, for which our setup has no published data till now.

1.3. Significance of the study

Since there are no published data on the outcomes of mechanically ventilated neonates in our country, This study sheds light on the critical outcomes and associated factors in neonates requiring mechanical ventilation so that by evaluating these features and their predictions that could help to identify any management practice gaps, differentiating and avoiding characters of the patients with poor outcome which is essential for early intervention and enhancing the quality of newborn respiratory support, and decrease prolonged hospital stays and economic costs.

Second, it will assist in realizing and understanding the significance of mechanical ventilation as well as its drawbacks, which will help to expand the availability of mechanical ventilator devices in our nation, resulting in adequate ventilator therapy that can lead to reduction in neonatal mortality.

Additionally, it will add an input to baseline data for any intervention that will be carried out in Ethiopian hospitals with NICUs. This study can also serve as a starting point for any high scale study to be done at a university level. Finally, it will also be a bridge for further prospective studies and aids in implementing additional protocols, guidelines in NICU. Therefore, this study aims to serve as a foundational piece of research that will provide valuable evidence for various stakeholders in the healthcare sector, neonatal health advocates, policymakers, and researchers.

CHAPTER TWO: LITERATURE REVIEW

2.1. Burden of Neonatal mortality

Neonatal mortality indeed poses a significant global challenge, as it not only affects mortality rates but also has profound implications for disability and economic loss(1, 10). The analysis of the global burden of disease revealed a staggering 2.42 million neonatal deaths worldwide in 2019(1). Furthermore, this comprehensive assessment highlighted a gradual reduction in the global neonatal mortality rate, which decreased from 28·0 deaths per 1000 live births in 2000 to 18 in 2019(1). Remarkably, findings from a similar study indicated that 133 countries, accounting for 65% of the global population, had achieved or surpassed the SDG 3.2 threshold for neonatal mortality rates (1). In 2021, approximately 2.3 million children died within the first month of life, equating to around 6,400 neonatal deaths daily(11). The risk of neonatal mortality is highest during this critical period, with a global average rate of 18 deaths per 1,000 live births(11). This issue is particularly prevalent in low and middle-income countries, where disparities in neonatal mortality rates persist despite a global decline. Geographically, regions such as sub-Saharan Africa and South Asia bear the highest burden of neonatal deaths, with rates estimated at 27 and 23 deaths per 1,000 live births respectively in 2021(1, 2, 10, 11). Children born in these regions face significantly higher risks of mortality compared to those born in high-income countries, with a child in sub-Saharan Africa being over 10 times more likely to die within the first month than a child in a high-income country. Similarly, a child born in South Asia is nine times more likely to face the same fate(11). In a 2020 report from the World Health Organization (WHO), it was revealed that almost half (47%) of deaths in children under five years old were neonatal fatalities(2). Over 70% of these deaths in the early neonatal period were attributed to conditions that could have been avoided or managed with access to basic and cost-effective interventions(12). With less than ten years left until the SDGs target date, Ethiopia reported a neonatal mortality rate of 33 deaths per 1000 live births in 2019(6). This rate in Ethiopia surpasses the global target for 2019 and surpasses the estimates for sub-Saharan Africa (27 deaths per 1000 live births) and the global average (18 deaths per 1000 live births) for the same year(2, 11). Neonatal conditions, including complications from preterm birth, neonatal encephalopathy, birth trauma, and infections like sepsis, accounted for 41% of under-five deaths in Ethiopia(13).

2.2. Indication of mechanical ventilation for Neonates

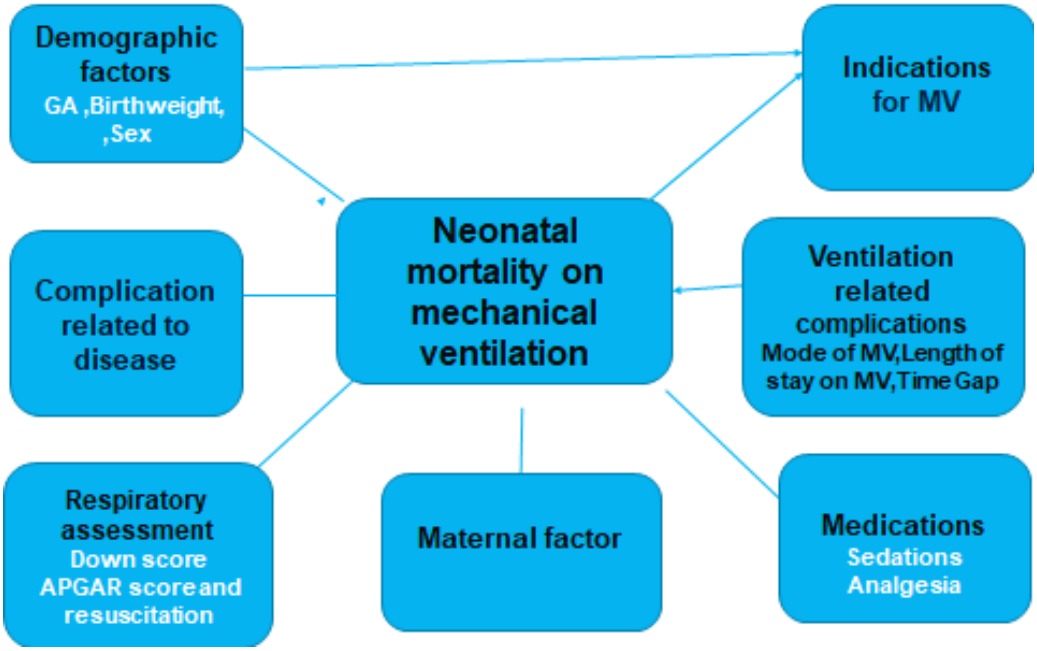
According to global data, the majority of neonatal fatalities (75%) occur within the initial week of life, with approximately 1 million newborns passing away within the first 24 hours in 2019. Preterm birth, childbirth-related complications such as birth asphyxia, infections, and birth defects were the leading causes of neonatal deaths that year(2). Multiple prior studies have highlighted various factors that contribute to neonatal mortality, with preterm birth (28%), sepsis (26%), and asphyxia (23%) being significant predictors. In developing nations, sepsis emerges as the leading cause of neonatal deaths, likely accounting for 30–50% of total neonatal fatalities annually(14, 15). In South Africa, the primary factors contributing to neonatal mortality are preterm birth (36%), intrapartum hypoxia (20%), and infection (14%)(15, 16). Mechanical ventilation is a critical lifesaving procedure that carries a significant risk of causing damage to the lungs, brain, and other organs, potentially leading to severe complications. Improvements in perinatal and neonatal healthcare have notably decreased neonatal morbidity and mortality rates. A study of 300 neonates undergoing mechanical ventilation identified respiratory distress syndrome (RDS) (31.1%), sepsis (22.7%), and birth asphyxia (18%) as the leading reasons for ventilation(17). In a study of 50 neonates, the primary reason for mechanical ventilation was identified as hyaline membrane disease (HMD), with sepsis and perinatal asphyxia following as the next most common indications(18). Examination of 141 neonates in Iran requiring mechanical ventilation identified respiratory distress syndrome (RDS) as the most prevalent reason for ventilation at 58.9%, with neonatal surgery and asphyxia following as other common indications(5). In a recent study on 110 newborns needing mechanical ventilation in Egypt, it was reported that the leading reason for requiring ventilation was respiratory distress syndrome (RDS) at 30%, with congenital pneumonia and sepsis following closely behind at 16.4% each, and apnea at 9%(4).Another study on 53 newborns in Bangladesh requiring Mechanical Ventilation found that most common reason for starting mechanical ventilation was refractory apnea at 35.8%, with respiratory distress syndrome at 20.8%, congenital pneumonia at 18.9%, and perinatal asphyxia at 15.1%(9). In a study involving 130 neonates requiring ventilation in Nepal, it was revealed that neonatal sepsis (33.6%) was the most frequent reason for ventilation, followed by bronchiolitis (24.3%), respiratory distress syndrome (16%), apnea of prematurity (16%), and meconium aspiration syndrome (10.1%)(7)

2.3. Outcomes and attributable factors

An analysis of 300 neonates revealed that the mortality rate among mechanically ventilated neonates was 43%. Disease-specific mortality rates were 33.3% for perinatal asphyxia, 44.7% for respiratory distress syndrome (RDS), 26.7% for meconium aspiration syndrome (MAS), 60% for pneumonia, 64.7% for sepsis, and 54.5% for meningitis(17). Another study involving 50 neonates receiving mechanical ventilation revealed a mortality rate of 60%. The study identified high mortality rates in cases of septic shock, pulmonary hemorrhage, air leak syndrome, and intraventricular hemorrhage (IVH), with IVH showing a 100% mortality rate(18). A study of 67 neonates in Pakistan who underwent mechanical ventilation revealed a mortality rate of 52.23%, with higher mortality observed in cases of preterm birth, low birth weight, and severe hypoxic-ischemic encephalopathy (HIE)(19). A study of 141 neonates in Iran who needed mechanical ventilation revealed an overall mortality rate of 42.8%. High mortality rates were observed in cases of congenital disease, fulminant sepsis, culture-positive infections, and complications with pneumothorax(5). In a recent study involving 110 newborns requiring mechanical ventilation in Egypt, it was reported that the mortality rate was 40.9%(4). A comprehensive data analysis encompassing 240 neonates requiring mechanical ventilation in Egypt revealed that the incidence of complications linked to mechanical ventilation was 43.3% and Ventilator-Associated Pneumonia (VAP) was 20%. Additionally, complications associated with specific disease patterns were noted at 56.7% and 22.5% for sepsis and septic shock. Shockingly, it was found that 48.3% of the subjects faced mortality, coinciding with a significant rise in VAP(8). In a study conducted on 130 neonates requiring ventilation in Nepal revealed a mortality rate of 51.3%. The study observed a particularly high mortality rate as high as 95% in septic shock with multiple organ failure (MOF), while neonates developing pulmonary hemorrhage and intraventricular hemorrhage (IVH) had a 100% mortality rate(7).

A study involving 300 neonates who required mechanical ventilation revealed that factors such as low birth weight (<2500 g), premature birth (<34 weeks gestation), low initial pH (<7.1), presence of sepsis, apnea, shock, pulmonary hemorrhage, hypoglycemia, neutropenia, and thrombocytopenia were significantly linked to mortality(17). A thorough analysis of 240 neonates requiring mechanical ventilation revealed a significant association between Ventilator-Associated Pneumonia (VAP) and mortality.

Conceptual framework



CHAPTER THREE: OBJECTIVE

3.1. General objectives

- To assess the outcome and associated factors of mechanically ventilated neonates in NICU at selected hospitals in Addis Ababa, Ethiopia.

3.2. Specific objectives

- To identify the common indications for mechanical ventilation for neonates in NICU from three selected hospitals at Addis Ababa, Ethiopia.
- To identify the outcome of mechanically ventilated neonates in NICU from three selected hospitals at Addis Ababa, Ethiopia.
- To identify associated factors related to neonatal mechanical ventilation outcome in NICU from three selected hospitals at Addis Ababa, Ethiopia.

CHAPTER FOUR: METHODOLOGY

4.1. Study area and period

The research was carried out in three private hospitals in Addis Ababa that operate as Neonatal Intensive Care Units (NICU) and are equipped with advanced mechanical ventilators for neonatal intubation. These hospitals have experienced neonatologists and pediatricians on staff. Girum Hospital, established in 2002, offers specialized care for preterm and critically ill newborns, treating an average of 320 patients annually in the NICU. The hospital has ten years of experience in newborn mechanical ventilation and currently operates four ventilators. Addis Hiwot General Hospital, established in 2000G.C (1993E.C), is renowned for its high-quality care and services, with top physicians and modern equipment. The hospital sees an average of 220 NICU patients annually, with eight years of experience in newborn mechanical ventilation using three ventilators. Myungsung Christian Medical Center (MCM) Comprehensive Specialized Hospital, a Korean hospital in Addis Ababa founded in 2004, provides quality healthcare and training for Ethiopian medical professionals. The hospital treats an average of 180 NICU patients annually, with eight years of expertise in newborn mechanical ventilation using three ventilators. Data was collected from Jan 1 2022- Dec 30, 3023

4.2. Study design

The hospital based cross-sectional study was employed to investigate outcomes and factors associated with neonates on mechanical ventilation with admitted different indications.

4.3. Study Period

The study was conducted at NICU at Girum, Addis Hiwot and Myungsung Christian Medical Center (MCM) Comprehensive Specialized Hospital Jan 1, 2022 to Dec 30, 2023

4.4. Population

4.4. 1. Source population:

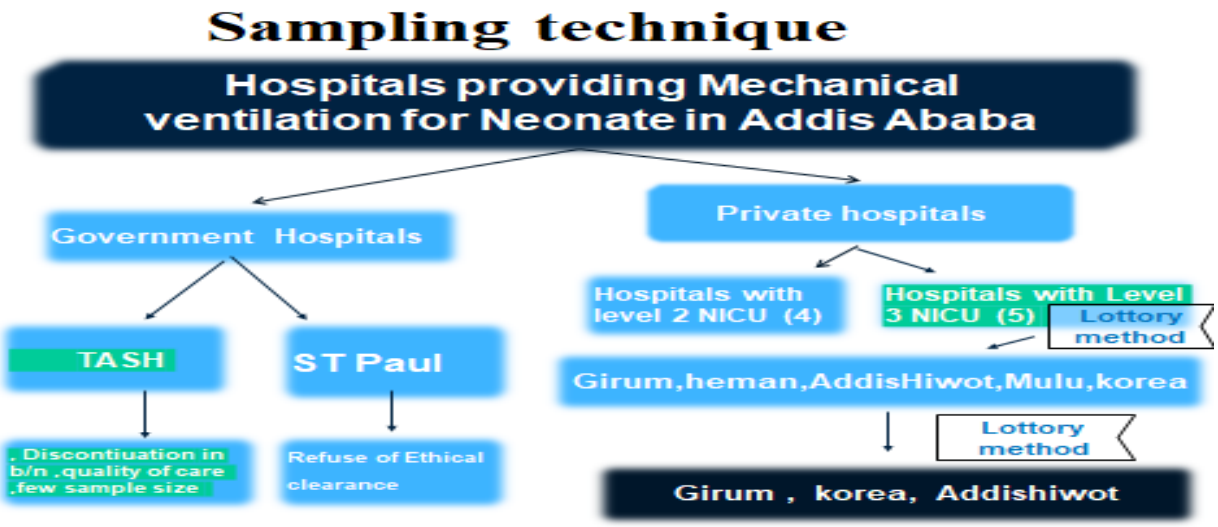
- All neonates admitted to NICU during the study period

4.5 Study Population

- All selected neonates admitted to NICU and requiring mechanical ventilation during the study period

4.6. Sampling method:

The research employed a cross- sectional design to investigate outcomes and risk factors associated mortality for mechanical ventilated neonates. The medical records of neonates who required mechanical ventilation and were admitted to the NICU during the study period for various indications were reviewed. Three private hospitals were selected using a convenient sampling technique, primarily focusing on their high-volume neonatal centers



4.7. Sample size determination

With the general assumption that this study will be presented with a level of confidence of 95% and 5% precision, I will use single population proportion formula to calculate the minimum sample size for this study. Based on proportion of the numbers of mechanically intubated neonates was 234 (N=the total number of mechanical ventilated neonates over 2 yrs. time period

) was taken from HMIS of the three selected hospital including Girum Hospital, MCM Comprehensive Specialized Hospital, and medical college and Addis Hiwot General Hospital

Sample size: $n=Z^2P(1-P) = 1.96^2 * 0.5*(1-0.5) = 384$ $d^2 \quad 0.05^2$

where: n=

minimum

sample size

p= Estimated sample proportion

d= the level of precision (margin of error)

z= the value at 95% confidence level

$$n = \frac{n_0}{\left(1 + \frac{n_0}{N}\right)}$$

Finale Corrected Sample size + 10% =n

145+10% =160

Sample size =160

Adding 10% of the calculated value for missing and incomplete data makes the final sample size required 160. To obtain the required sample size it will be based on the proportion of neonates on mechanical ventilation in each specific hospital based on their baseline patient load.

4.8. Inclusion and exclusion criteria

4.8.1. Inclusion criteria

- ✓ Neonates in NICU who need conventional mechanical ventilation of all GA.
- ✓ Neonates on mechanical ventilation for at least more than 6 hrs.

4.8.2. Exclusion criteria

- ✓ Neonates with Major congenital anomalies
- ✓ Post-surgical neonates requiring mechanical ventilation

4.9. Data collection and measurement

The structured questionnaire utilized in the study was crafted based on existing literature with same research topic and setup and encompassed sections on sociodemographic data, clinical profiles, and obstetrics history**.**. Prior to the primary data collection, the questionnaire underwent a pretest with 5% of the sample size to ensure the clarity and relevance of the questions. ODK version 1.25.2 software and Kobo Toolbox server were used to collect the data & to store the data respectively Data collection was done by trained two general practitioner and the principal investigator checked the data consistency and completeness in each day.

4.10. Study Variables

4.10.1. Independent Variables

Neonatal factors

- Age
- Sex
- Gestational age
- Birth weight
- APGAR Score
- Downes Score
- Maternal obstetrics cases
- Maternal chronic illness
- Requiring resuscitation
- Complication related to underlining disease
- Bleeding
- Shock
- Seizure
- DIC
- AKI
- MOF

Ventilation factors

- Indication to mechanical ventilation
- Complication associated with MV
- Sedation
- Analgesia
- Length of mechanical ventilation stay
- Time gap between intubation and decision

4.10.2. Dependent Variables

- Death of mechanical ventilated neonates in the selected hospitals

4.11. Data Analysis

The analysis was made with SPSS software with version 25. The categorical variables in the study were presented with using frequency, percentage, and compared between groups using the chi-square test. The normal distribution of continuous variables was assessed using Shapiro-Wilk test. The mean and standard deviation calculated for normality distributed data while median and interquartile range calculated for skewed data. Multicollinearity test performed for categorical, continuous and binary variables. Multicollinearity measured by variance inflation factor (VIF) and tolerance. When a VIF was below five and tolerance was above 0.1, variables were forwarded to multivariable binary logistic regression analysis. Variables with a VIF score of ≥ 5 to 10 and tolerance below 0.1 were excluded from the final model. A univariate and multivariate binary logistic regression analysis was performed to examine the factors associated mortality of mechanical ventilated neonates. Backward variable selection multivariable binary logistic model was employed to adjust cofounder factors. The results of logistic regression reported as adjusted odds rations (OR) with 95% confidence intervals and p-value < 0.05 are considered statistically significant.

4.12. Ethical Consideration

Ethical clearance to conduct this study was obtained from the pediatrics and child health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, and Addis Ababa University. Confidentiality has been fully maintained during Data collection and further analysis and dissemination of results. Participants will be anonymous during dissemination of results.

CHAPTER FIVE: RESULTS

5.1. Result

An analysis of 160 neonates requiring mechanical ventilation revealed intriguing insights into the population studied. Among them, 61.3% were male, showcasing a male gender predominance within the study. When considering gestational age, 36.3% displayed normal gestational age, while a significant portion consisted of preterm neonates, with 15.6% extremely preterm, 20% very preterm, 14.4% moderate preterm, and 12.5% late term neonates. Interestingly, 43.8% of neonates requiring mechanical ventilation necessitated resuscitation after delivery, with varying APGAR scores indicating the condition upon birth—moderate and severe scores were recorded in 23.1% of cases. Cesarean section (C/S) delivery was the primary mode in 76.9% of cases, highlighting a prevalent method of birth within the cohort, and 57.5% of neonates were born outside the hospital. Furthermore, a notable proportion of mothers experienced 25% had Preeclampsia and premature rupture of membranes (PROM) , accounting for 24.4% of cases, while, indicating potential maternal health complexities that could impact neonatal outcomes.

Table 1:Sociodemography characteristics of mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

Variables	Response	Frequency	Percentage
Sex	Female	62	38.8
	Male	98	61.3
GA	Extremely	25	15.6
	Very	32	20.0
	Moderate	23	14.4
	Late	20	12.5
	Post	2	1.3
	Normal	58	36.3
APGAR	Sever	2	1.3
	Moderate	35	21.9
	Normal	123	76.9
Required Resuscitation	No	90	56.3

	Yes	70	43.8
Down score	Mild	1	.6
	Moderate	53	33.1
	Sever	106	66.3
Mode of ventilation	AC	147	91.9
	SIMV	13	8.1
	Inborn	68	42.5
	Out born	92	57.5
Mode of delivery	C/S	123	76.9
	Vaginal delivery	37	23.1
PROM	Yes	39	24.4
	No	121	75.6
Preeclampsia	Yes	40	25
	No	120	75

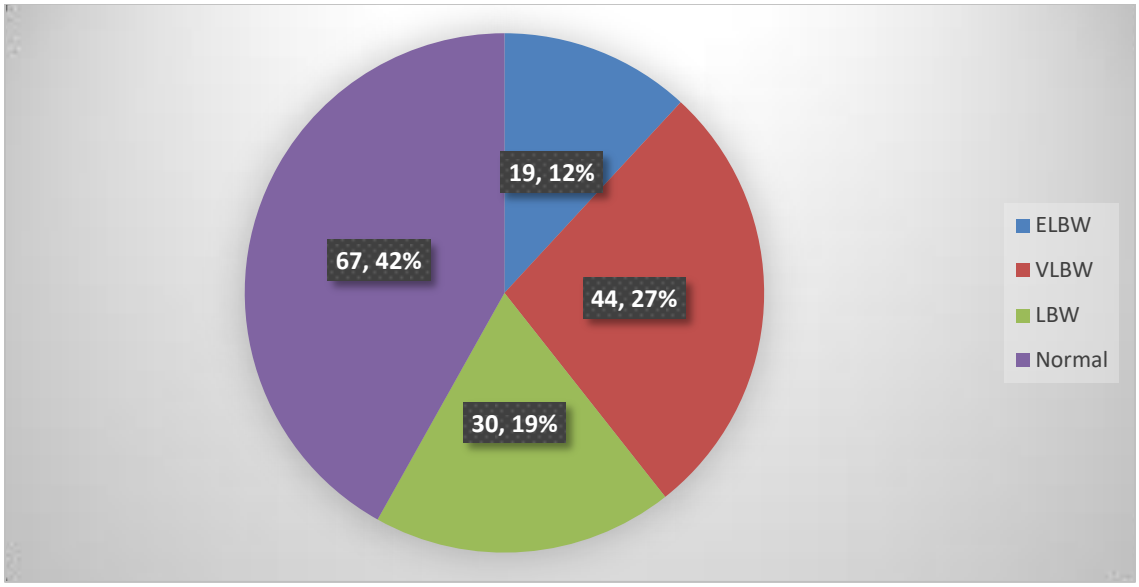


Figure 1: Birth weight classifications among mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

During the study, it was found that the median age at intubation for neonates was 12 hours (±IQR=22.75 hours). The primary reasons for mechanical ventilation (MV) among the neonates studied varied, with respiratory distress syndrome (RDS) being the most prevalent at 51.9%, followed by meconium aspiration syndrome (MAS) at 12.5%, and neonatal sepsis at 11.9%. Complications arising from mechanical ventilation were observed in 41.9% of the neonates, highlighting the challenges faced during ventilation support. Concerning device-related issues, blood-borne infections associated with devices affected 26.3% of the neonates, while ventilator-associated pneumonia (VAP) was reported in 19.4% of cases, and pneumothorax occurred in 6.9% of intubated neonates, making them the prominent mechanical ventilator-related complications in this cohort. Surfactant was administered for 64 ventilated neonates, 62 was given for indication of RDS and 2 given for Meconium aspiration syndrome.

Analgesia was not administered to 76(48%) neonates on mechanical ventilator .Sedation was not used for 50% of the intubated neonates, however from sedation used, diazepam comprises of 38% and fentanyl 12%.Among the neonates who underwent mechanical ventilation, a substantial 59.4% experienced complications related to their underlying conditions post-ventilation. These complications varied, with nosocomial infections being a significant factor in 47.5% of cases, followed by bleeding complications in 37.8% of neonates. Additionally, pulmonary hemorrhage was noted in 13.8% of cases, while seizures occurred in 11.9% of neonates. Moreover, a proportion of neonates experienced multi-organ failure (MOF) as a complication, affecting 7.5% of the ventilated neonate.

Table 2: Admission medical profile, complications and outcomes of mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

Variables	Response	Frequency	Percentage
Age of intubation (hr.)	Median ±IQR	12(±IQR=22.75)	
Primary indication of MV	RDS	83	51.9
	PNA	16	10.0
	Sepsis	19	11.9

	Congenital pneumonia	18	11.3
	Apnea	4	2.5
	MAS	20	12.5
Overall diagnosis	RDS	92	57.5
	MAS	32	20.0
	PNA	24	15.0
	Sepsis	27	16.9
	Congenital pneumonia	43	26.9
	Apnea	10	6.3
Mechanical related complication	Yes	67	41.9
VAP	Yes	31	19.4
Devices associated blood born infection	Yes	42	26.3
Pneumothorax	Yes	11	6.9
BPD	Yes	3	1.9
Extubation failure	Yes	9	5.6
Disease related complication	Yes	95	59.4
Nosocomial infection	Yes	76	47.5
Pulmonary hemorrhage	Yes	22	13.8
MOF	Yes	12	7.5
Apnea	Yes	29	18.1
Bleeding	No	100	62.5
	Yes	60	37.5
Seizure	No	141	88.1
	Yes	19	11.9
Shock	No	146	91.3
	Yes	14	8.8
Median time between diagnosis and intubation	Median ±IQR	2((±IQR=)	

Median time to MV stay(hr)	Median ±IQR	72(±IQR=65.25)	
Surfactant supplementation	Yes	64	40.0
Analgesia on MV	Fentanyl	23	14.4
	Morphine	61	38.1
	None	76	47.5
MV length	Below 24	22	13.8
	24.1-72	75	46.9
	72.1-144	44	27.5
	above 144.1	19	11.9
Time gap	below 1hr	75	46.9
	1-6hr	71	44.4
	6-24	10	6.3
	above 24	4	2.5
Outcome	Death	39	24.4
	Alive	121	75.6

Table 3: Comparison of alive and dead mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

Diagnosis	Number	Alive	Death
RDS	83(51.9%)	60(72.3%)	23(27.7%)
PNA	16(10%)	12(75%)	4(25%)
Sepsis	19(11.9%)	14(73.7%)	5(26.3%)
Congenital pneumonia	18(11.3%)	17(94.4%)	1(5.5%)
Apnea	4(2.5)	1(25%)	3(75%)
MAS	20(12.5)	17(85%)	3(15%)

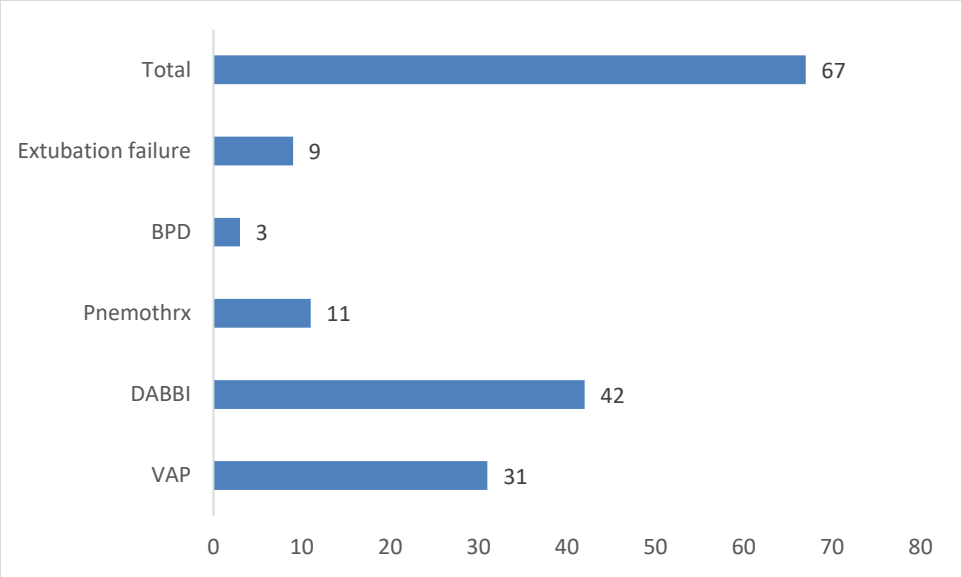


Figure 2:Mechanical ventilation associated complications among mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

The overall mortality rate of mechanical ventilated neonates was 24.4%. A comprehensive analysis, comprising both univariate and multivariate approaches, was undertaken to pinpoint the critical determinant factors contributing to neonatal mortality following mechanical ventilation. In the univariate analysis segment, several key factors stood out significantly in relation to neonatal mortality during mechanical ventilation. Notably, extremely preterm birth (COR=6.4(2.3, 18.0), p=0.000), extremely low birth weight (ELBW) (COR=9.8(3.1, 30.8), p=0.000), presence of shock (COR=26.4(5.6, 125.1), p=0.000), incidents of bleeding (COR=6.0(2.73, 13.2), p=0.000), disseminated intravascular coagulation (DIC) (COR=5.0(2.3, 10.9), p=0.000), acute kidney injury (AKI) (COR=6.2(2.5, 15.6), p=0.000), multi-organ failure (MOF) (COR=47.1(5.8, 380.4), p=0.000), and pulmonary hemorrhage (COR=17.9(5.9, 53.6), p=0.000) were identified as statistically significant factors associated with neonatal mortality during mechanical ventilation. Moving on to the multivariate analysis, employing a backward variable selection method, it was revealed that certain factors emerged as notably influential in predicting neonatal mortality post-mechanical ventilation. Factors such as the requirement of resuscitation (AOR=9.9(1.7, 58.5), p=0.011), extreme prematurity (AOR=61.7(3.3, 1150.1), p=0.0006), DIC (AOR=13.1(1.6, 104.5), p=0.015), AKI (AOR=13.1(2.24, 76.9), p=0.004), MOF

(AOR=246.9(14.4, 4242.8), p=0.0000) and pulmonary hemorrhage (COR=17.9(5.9, 53.6), p=0.000) emerged as the most statistically significant variables determining neonatal mortality subsequent to mechanical ventilation. These findings provide crucial insights into the factors influencing neonatal outcomes during mechanical ventilation, underscoring the importance of early identification and targeted interventions to improve survival rates and enhance neonatal care practices.

Table 4:Univarite and multivariate binary logistic regression analysis to identify attributable risk factors for mortality among mechanical ventilated Neonate at Girum Hospital, Addis Hiwot, and Myungsung Christian Medical Center (MCM), Addis Ababa, Ethiopia 2024

Variable	Response	Death	Alive	COR	P	AOR	P
Sex	Female	17	45	1.3(0.63,2.7)	0.48		
	Male	22	76	1			
Age at intubation(hr.)	Below 24hr	28	92	1			
	24-72hr	6	27	0.7(0.3,1.95)	0.5		
	Above 72	5	2	8.2(1.5, 44.7)	0.015		
Place of delivery	Inborn	20	48	1.6(0.77,3.31)	0.2*		
	Out born	19	73	1			
Mode of delivery	C/S	28	95	1			
	Vaginal delivery	11	26	1.4(0.63, 3.3)	0.39		
Gestational age	Extremely	14	11	6.4(2.3, 18.0)	0.000**	61.7(3.3,1150.1)	0.006*
	Very	11	21	2.6(0.97,7.1)	0.058	1.3(0.3,6.3)	0.76
	Moderate and late	4	39	0.5(0.15,1.76)	0.28	0.48(0.1,3.3)	0.45
	Normal	10	50	1		1	
Birth weight	ELBW	12	7	9.8(3.1,30.8)	0.000		
	VLBW	12	32	2.1(0.8,5.5)	0.11		
	LBW	5	25	1.14(0.35	0.83		

				,3.7)			
	Normal	10	57	1			
APGAR	Sever	1	1	3.7(0.23, 61.7)	0.36		
	Moderate	12	23	1.94(0.86,4.4)	0.11		
	Normal	26	97	1			
Required resuscitation	No	18	72	1		1	
	Yes	21	49	1.7(0.83, 3.5)	0.15	9.9(1.7,58.5)	0.011*
Down score	Moderate	11	43	1			
	Sever	28	78	1.4(0.64,3.1)	0.4		
Mode of ventilation	AC	37	110	1.8(0.39, 8.7)	0.47		
	SIMV	2	11	1			
PROM	Yes	12	27	1.5(0.69,3.46)	0.28		
	No	27	94	1			
Preeclampsia	Yes	9	31	0.87(0.37,2.04)	0.75		
	No	30	90	1			
Primary indication	RDS	23	60	2.2(0.58, 8.12)	.249		
	PNA	4	12	1.9(0.36,10.03)	.455		
	Sepsis	5	14	2.0(0.41, 9.99)	.387		
	Congenital pneumonia	1	17	0.33(0.03,3.5)	.362		
	Apnea	3	1	17.0(1.3, 223.14)	.031		
	MAS	3	17	1			
Shock	No	27	119	1			
	Yes	12	2	26.4(5.6, 125.1)	0.000		

Seizure	No	33	108	1			
	Yes	6	13	1.5(0.5,4.3)	0.48		
Bleeding	No	12	88	1			
	Yes	27	33	6.0(2.73,13.2)	0.000		
DIC	Yes	20	21	5.0(2.3, 10.9)	0.000	13.1(1.6,104.5)	0.015*
	No	19	100	1		1	
AKI	Yes	14	10	6.2(2.5,15.6)	0.000	13.1(2.24,76.9)	0.004*
	No	25	111	1		1	
MOF	Yes	11	1	47.1(5.8, 380.4)	0.000	246.9(14.4,4242.8)	0.000*
	No	28	120	1		1	
Pulmonary hemorrhage	Yes	17	5	17.9(5.9, 53.6)	0.000	16.7(1.9,145.9)	0.011*
	No	22	116	1			
Nosocomial	Yes	22	54	1.6(0.78,3.3)	0.22	5.33(0.7,38.3)	0.09
	No	17	67	1		1	
MV associated complications	Yes	19	48	1.4(0.7,2.98)	0.32		
	No	20	73	1			
Length of MV stay	Below 24	13	9	1		1	
	24.1-72	15	60	0.17(0.06,.480)	.001	0.075(0.01,0.4)	0.002*
	72.1-144	5	39	0.089(.025,0.313)	.000	0.004(0.0,0.08)	0.000
	above 144.1	6	13	0..320(.088,1.16)	.082	0.11(0.012,1.02)	0.052
Time Gap	below 1hr	22	53	1			
	1-6hr	13	58	.54(.247 1.2)	.122		
	6-24	3	7	1.03(0.24,4.36	.965		
	above 24	1	3	.80(.079 8.15)	.853		

Analgesia	Fentanyl	10	13	2.(0.87, 6.1)	0.09		
	Morphine	10	51	0.60(0.25,1.4)	0.22		
	None	19	57	1			
Sedation	None	21	57				
	Diazepam	11	52	0.6(.253 1.3)	.185		
	Fentanyl	7	12	1.58(.55, 4.561	.395		

CHAPTER SIX: DISCUSSION RECOMMENDATION

6.1. DISCUSSION

To my best of knowledge, this is the first study conducted in Ethiopia to explore the outcome of neonates on mechanical ventilation and contributing factors associate with grave outcomes. The study revealed that the primary reasons for mechanical ventilation (MV) among the neonates studied varied, with respiratory distress syndrome (RDS) being the most prevalent at 51.9%, followed by meconium aspiration syndrome (MAS) at 12.5%, and neonatal sepsis at 11.9%. A study of 300 neonates undergoing mechanical ventilation identified respiratory distress syndrome (RDS) (31.1%), sepsis (22.7%), and birth asphyxia (18%) as the leading reasons for ventilation(17). Analysis of 141 neonates in Iran requiring mechanical ventilation identified respiratory distress syndrome (RDS) as the most prevalent reason for ventilation at 58.9%, with neonatal surgery and asphyxia following as other common indications(5). In a recent study on 110 newborns needing mechanical ventilation in Egypt, it was reported that the leading reason for requiring ventilation was respiratory distress syndrome (RDS) at 30%, with congenital pneumonia and sepsis following closely behind at 16.4% each, and apnea at 9%(4). Th the main findings of these studies aligns on the consensus that respiratory distress syndrome (RDS) stands as the foremost indication necessitating mechanical ventilation among neonates. This consistent finding underscores the clinical significance of RDS in driving the need for respiratory support in neonatal care practices. The predominant reason behind this trend is the higher prevalence of respiratory distress syndrome (RDS) in premature neonates worldwide. Prematurity, a key risk factor for RDS, heightens the likelihood of neonates requiring mechanical ventilation due to the underdeveloped pulmonary function characteristic of preterm birth. Nevertheless, the subsequent indications for neonatal mechanical ventilation, including meconium aspiration syndrome (MAS), pneumonia (PNA), and sepsis, primarily stem from variances in intrapartum and neonatal care practices. These differences in management strategies reflect not only the clinical aspects but also the broader healthcare systems' capabilities and the socioeconomic conditions prevailing in individual countries. These disparities, alongside other essential factors, serve as key indicators of healthcare sophistication levels and the unique socio-economic situations characteristic of each nation. Our research revealed a mortality rate of 24.4%, a figure notably lower than those reported in various studies conducted in other low-income countries. An analysis of 300 neonates revealed that the mortality rate among mechanically ventilated neonates

was 43%. A study of 67 neonates in Pakistan who underwent mechanical ventilation revealed a mortality rate of 52.23% (19). A study of 141 neonates in Iran who needed mechanical ventilation revealed an overall mortality rate of 42.8% (5). In a recent study involving 110 newborns requiring mechanical ventilation in Egypt, it was reported that the mortality rate was 40.9%(4). Nonetheless, certain studies have indicated a lower mortality rate among mechanically ventilated neonates in specific centers. For instance, a retrospective analysis of the initial 100 neonatal ventilations conducted at Government Medical College in Ernakulam, India, documented a 25% mortality rate among ventilated neonates(20)

This disparity in mortality rates sheds light on the differences in healthcare practices, resource availability, and potentially varying factors influencing neonatal outcomes across diverse global settings. Understanding these contrasts can offer valuable insights for improving neonatal care strategies and addressing healthcare disparities to enhance survival rates among neonates in low-income regions. The research delved into various pivotal risk factors contributing to the mortality of neonates following mechanical ventilation. Among these factors, the necessity for resuscitation ($p=0.011$), extreme prematurity ($p=0.0006$), disseminated intravascular coagulation (DIC) ($p=0.015$), acute kidney injury (AKI) ($p=0.004$), and multi-organ failure (MOF) ($p=0.0000$) emerged as the most noteworthy statistically significant variables influencing neonatal mortality post-mechanical ventilation. A study involving 300 neonates who required mechanical ventilation revealed that factors such as low birth weight (<2500 g), premature birth (<34 weeks gestation), low initial pH (<7.1), presence of sepsis, apnea, shock, pulmonary hemorrhage, hypoglycemia, neutropenia, and thrombocytopenia were significantly linked to mortality(17). Numerous research investigations generate an evidence indicating that neonates requiring mechanical ventilation and subsequently developing conditions such as disseminated intravascular coagulation (DIC) and pulmonary hemorrhage are associated with alarmingly high mortality rates nearing 100%(7, 18, 20)

A thorough analysis of 240 neonates requiring mechanical ventilation revealed a significant association between Ventilator-Associated Pneumonia (VAP) and mortality(8). These findings underscore the critical importance of identifying and addressing these risk factors to improve outcomes and enhance neonatal care practices. The nuanced exploration of these factors provides valuable insights for tailored interventions and strategic enhancements in neonatal healthcare to

mitigate risk and optimize survival rates among ventilated neonates. This study uncovered a notably high mortality rate among neonates requiring mechanical ventilation within the initial 24 hours of intubation. Interestingly, significant improvements in outcomes were observed in those neonates who survived beyond the critical first 24 hours post-intubation. This observation suggests that the trauma of intubation might exacerbate the severity of the underlying condition, potentially impacting the initial outcomes but showcasing enhanced recovery with extended intubation duration.

Conclusion:

- ✓ The commonest indication for mechanical ventilation in was RDS.
- ✓ Prematurity, requirement of resuscitation and disease-related complications such as AKI, MOF, DIC and pulmonary hemorrhage were among the preventable factors contributing to mortality
- ✓ Although the mortality rate of mechanically ventilated neonates is lower compared to similar studies in low and middle-income countries, there is a crucial need for high-level efforts and an evidence-based approach to address preventable factors

6.2. Recommendation

Based on the findings of this study on mechanical ventilated neonates, we recommend healthcare providers, neonatal health equity advocates, policy makers, and researchers to do further prospective researches on both the long term and short term outcome and associated factors mechanical ventilated neonates .

The study recommended to the health care providers to the care of mechanical ventilated neonates by implementing protocols to monitor and manage disease related complications such as AKI, MOF, DIC, pulmonary hemorrhage, and nosocomial sepsis. Focus on early detection and prompt intervention to minimize the impact of these complications on neonatal outcomes.

The study also recommended to Neonatal Health Equity Advocators to advocate for improved access to quality neonatal care for all neonates, especially those at high risk due to preterm birth and low birth weight. Greater efforts should be put in to decrease the burden of premature deliveries to decrease the frequency of NICU admission and the need for MV.

Invest on mechanical ventilation machines as a resource in order to use widely in our country and training for healthcare providers to ensure optimal care for neonates requiring mechanical ventilation. By collaborating across these different sectors and implementing evidence-based recommendations, we can work towards improving the outcomes and quality of care for mechanically ventilated neonates, ultimately advancing neonatal health equity and reducing morbidity and mortality in this vulnerable population.

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Annex I: Data collecting Questionnaire

TITLE:

Outcome and associated factors of mechanically ventilated Neonates among selected hospitals in Addis Ababa, Ethiopia; Cross -sectional Multi-center study

Ababa, Ethiopia

Code number Date / / _

PART I – SOCIO- DEMOGRAPHIC DATA

1 **Sex:**

A. Male B. Female

2.**ADDRES /REGION /parents /**

A. A/A B. Oromia C. Amhara D SSNPR E. Tigray F Afar G. Benishangul-gumuz H. Dire Dawa I. Gambela

PART II GROWTH PARAMETERS

1 **GESTATIONAL AGE**

A 1 <28 weeksA2 28 to <32 weeks A3 32 to <33 weeks A4 34 0/7 to 36 6/7 weeks B 39 0/7 – 40 6/7 weeks.

C 42 0/7weeks and beyond.

2 **BIRTH WEIGHT**

A ≤ 2500gm B 2500gm – 4000 gm. C > 4000gm D <1500gm -1000gm E <1000gm

PART III RESIPARATORY ASSESMENT

1 APGAR score at five minutes

A 0-3 B 4-6 C 7- 10

2 REQUIRED RESUSCITATION

A Yes B No

3 DOWNE SCORE

A 1 – 3 B 4 –6 C >6

4 DELIVERIE

4.1PLACE OF DELIVERY

A inborn B out born

4.2MODE OF DELIVERY

A Vaginal delivery B C/S

5 MATERNAL FACTORS

5.1MATERNAL AGE

A <20 Yrs. B 20-34 Yrs. C > 35Yrs.

5.2 MATERNAL COMPLICATIONS

A Hypertension B Diabetes mellitus

C PROM D Signs of chorioamnionitis E No reported risk factor

PART IV VENTILATION FACTORS

1 INDICATION FOR MV

A Respiratory distress syndrome B Congenital pneumonia C Sepsis D Apnea

E Perinatal asphyxia F Meconium aspiration syndrome G Congenital Heart disease

2 AGE OF INTUBATION

A <24 hrs. B 24 -72 hrs. C >72 hrs.

3 Time gap between fulfillment of indication for mechanical ventilation and intubation for mechanical ventilation in Hrs.

A< 1hrs. B 6-12hrs C12-24hrs D >24hrs

4 VENTILATOR PARAMETERS

4.1 initial mode of MV

A AC B SIMV C CPAP D PSV + SIMV

5 SURFACTANT SUPLEMMENTION

A Yes B No

6 SEDATION USED……

7 ANALGESIA ON MV…….

8 LENGTH OF STAY ON MV

A 24 -72 Hrs B 72 -6 days C >7 days

9 LENGTH OF STAY IN HOSPITAL

A< 4 days B 5 -7 days C 7 15 days D16 -28 days E> 28 days

PART V COMPLICATIONS

1 COMPLICATAION RELATED TO MECHANICAL VENTIATION

A VAP B Devices associated blood born infection C Pneumothorax D Air-leak syndromes

E Extubation failure F BPD

2 COMPLICATIONS RELATED TO DISEASE PATTERN

A Nosocomial sepsis B Septic shock, MOF C DIC D NEC

E Apnea F Acute kidney injury G Pulmonary hemorrhage

Part VI-CLINICAL PROFILE

a Duration of illness in Hrs.….

b Duration of illness in Hrs before an intial visit to NICU……

c Bleeding A Yes B No

d Seizure A Yes B No

e shock A Yes B No

PART VII DIAGNOSIS

1 Diagnosis during admission to NICU

2 Diagnosis during intubation

PART IX OUTCOME

1 Outcome on mechanical ventilation

A. Alive B Death

2 Outcome at discharge

A. Alive B. Death