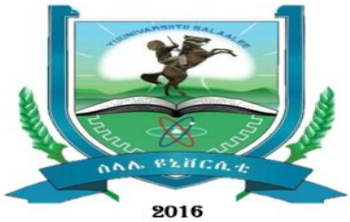

TIME TO RECOVERY AND ITS PREDICTORS AMONG NEONATES ADMITTED WITH DIAGNOSIS OF RESPIRATORY DISTRESS IN NEONATAL INTENSIVE CARE UNIT OF SELECTED PUBLIC HOSPITALS IN NORTH SHOA, ETHIOPIA, 2024: A RETROSPECTIVE COHORT STUDY.

INVESTIGATOR: AHMED MOSSA (BSC)

A THESIS TO BE SUBMITTED TO SALALE UNIVERSITY, COLLEGE OF HEALTH SCIENCES, MIDWIFERY DEPARTEMENT IN PARTIAL FULFILLMENT OFTHE REQUREMENT FOR THE DEGREE OF MASTERS OF SCIENCE IN MATERNAL AND NEONATAL HEALTH.

DECEMBER, 2024

FITCHE, ETHIOPIA

Declaration sheet

I declare that this research thesis entitled “Time to recovery and its predictors among Neonates Admitted with respiratory distress in NICU of North Shoa Zone Selected Public Hospitals” is my own work that have note been indicated and acknowledged as a complete reference.

Name of investigator: Ahmed Mossa (BSC) Signature: _____Date_____

I hereby certify that I have read and evaluated this thesis entitled “Time to recovery and its predictors among Neonates Admitted with respiratory distress in NICU of North Shoa Zone Selected Public Hospitals” is prepared under my guidance by Ahmed Mossa. I recommend that is be submitted as fulfilling a thesis requirement.

Major Advisor:Mr.Dejene Edosa (MSc, Assistant Professor)

Signature:_____Date :28/12/2024

Co-advisor: Mr. Mukemil Awol. (MSc)Signature: _____ Date:_____

As the member of the Board of the examiners of the MSc thesis open Defense Examinations, I certify that I have read and evaluated the thesis prepared by Ahmed Mossa examined the candidate. I recommend that the thesis be accepted as fulfilling the thesis requirements for Degree of Master of Maternity and Neonatal Health.

Chair Person :Signature:_____ Date:_____

Internal Examiner: Signature:_____Date:_____

External Examiner :Signature: _____date :_____

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ABSTRACT

Background:Neonatal Respiratory distress is a major cause of Neonatal Morbidity and Mortality, particularly in Developing Countries. Time to recovery is an indicator of the severity of respiratory distress and risk factors are wide-ranging significantly according to study population and settings.However,North Shoa still lacks appropriate data on time to recovery from respiratory distress.

Objective: The aim of the study was to assess the Time to recovery and its predictors among Neonates admitted with Respiratory Distress in Neonatal Intensive Care Unit at North Shoa Zone Selected public Hospitals 2024.

Method: An institution-based retrospective cohort study design was conducted among 702 Neonates with respiratory distress. A structured and pre-tested check list was used for data collection. The median time to recovery, Kaplan Meier curve, and adjusted survival curve were computed. Both bi-variable and multi-variable Cox regression models were applied to analyze the data. P-value of 0.25 was used to transfer from bi to multi-variable analysis. P-value of < 0.05 consider as significant

Results: Of all respiratory distress neonates, 433 were successfully recovered. They were followed for a total of 4,498- Neonate day's observation and the median time to recovery was 8 days (IQR=5–11 days). After adjusting for covariates,Antibiotics (AHR=1.8,95%CI:0.5,6.5),Direct Oxygen (AHR = 2.3, 95% CI: 1.31, 5.73), PROM (AHR=1.32,95%CI:1.07,1.62),PNA(AHR=2.56,95%CI:1.27,5.12),Hypoglycemia(AHR = 0.28, 95%CI: 0.13, 0.59), and C/S (AHR = 2.31, 95%CI: 1.53, 3.48) were independently associated with the time to recovery .

Conclusion: The study's results were moderately comparable to earlier findings. Identifying key factors can help detect neonates at risk of prolonged respiratory distress, guiding timely referrals in primary health sectors and providing prognostic insights for clinicians and families. **Keywords**: respiratory distress, recovery time, neonate.

ACRONYMS AND ABBREVIATIONS

AHR	Adjusted Hazard Ratio
CHR	Crude Hazard Ratio
APGAR	Appearance,Pulse,Grimace,Activity, Respiratory
C/S	Caesarean Section
DM	Diabetes Mellitus
HIV	Human Immune Deficiency
HR	Hazard Ratio
NICU	Neonatal Intensive Care Unit
NRD	Neonatal Respiratory Distress
PROM	Premature Rupture Of Membrane
RD	Respiratory Distress
RDS	Respiratory Distress Syndrome
SUCSH	Salale University Comprehensive Specialized Hospital
WHO	World Health Organization

1. INTRODUCTION

1.1. Background

Neonatal Respiratory Distress (NRD) refers to breathing difficulties in newborns up to 28 days of age (Sweet, Carnielli et al. 2023). Clinically, it is characterized by tachypnea, nasal flaring, grunting, chest retraction, and cyanosis (Mwipopo and Manji 2023).NRD is a leading cause of neonatal morbidity and mortality globally (Gebreheat, Tadesse et al. 2022). It is categorized into mild, moderate, and severe forms based on its severity (Okolo, Emeagui et al. 2023).

Premature infants are particularly vulnerable to NRD due to inadequate surfactant, fluid absorption issues, and other anatomical or physiological challenges (Walsh 2018, Madar, Roehr et al. 2021).

Management of NRD depends on severity and underlying causes, including airway stabilization, oxygen therapy, CPAP, mechanical ventilation, and specific treatments such as Surfactant for RDS or Antibiotics for infections (Sweet, Carnielli et al. 2019). Continuous monitoring is essential for improvement (Desalew, Sintayehu et al. 2020).

Recovery time is influenced by factors such as Preterm Delivery, Sepsis, PROM, and Maternal Diabetes Mellitus (Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022, Tochie, Sibetcheu et al. 2023). NRD can lead to complications like Multi-Organ dysfunction, Motor and Cerebral delays, death, severe neuropathic developmental delays, and Hospital-Acquired Infections (Qari, Alsufyani et al. 2018, Tochie, Sibetcheu et al. 2023, Girma,Tesf ahun et al. 2024). Identifying predictors can optimize management, improve survival rates, and allocate resources effectively (Getaneh, Moges et al. 2024).

In Wealthier Nations, advancements in surveillance, Treatments, and early NICU interventions have improved outcomes, with shorter recovery times (5–7 days) (Qari, Alsufyani et al. 2018, Girma, Tesfahun et al. 2024). In contrast, developing Nations face higher mortality rates and prolonged recovery times (7–33 days) due to limited

resources (Abou- Zambrano, Garcés et al. 2022, Chekole, Fetene et al. 2023, Girma, Tesfahun et al. 2024).

Reducing Neonatal Morbidity and Mortality is critical to achieving Sustainable Development Goals (Lee, Kjaerulf et al. 2016, Tochie, Sibetcheu et al. 2023).Timely management of NRD significantly reduces related complications, and the ability to predict recovery times benefits Families, Clinicians, and Health care systems (Getaneh, Sebsbie et al. 2022, Girma, Tesfahun et al. 2024, Moretti, Gizzi et al. 2024).

Identifying factors influencing recovery time is vital to designing preventive measures, improving intervention strategies, and reducing Hospital stays, Morbidity, and Mortality (Yismaw, Gelagay et al. 2022).

1.2. Statement of the problem

Globally, The incidence rate of NRD ranging from 5 % to 50% (Moretti, Gizzi et al. 2024). With higher incidence rates found in Asia, the Middle East, and Africa (Desalew, Sintayehu et al. 2020). It also increased with decreasing Gestational Age (Carniellib, Hallmand et al. 2023). Across Europe, France 18.5%,7.3-9.3 cases/100,000 in Australia, and 8% in German (Shalish, Lakshminrusimha et al. 2020). Asia ranges from 4.24% to 20.5% % Pakistan and China respectively (Chen and Chen 2022), the Middle East from 1.64% to 2.74% (Moretti, Gizzi et al. 2024), and Africa from 42.9 % to 47.5 % (Moretti, Gizzi et al. 2024).

In Ethiopia 42.9% incidence rate of Neonatal Respiratory Distress (Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022). In Eastern Ethiopia, it is the primary cause of death (66%) and the second cause of neonatal admission (43.8%) (Desalew, Sintayehu et al. 2020, Ab-ou-Faddan and Abdelaziz 2018, Tochie, Sibetcheu et al. 2023).

The incidence of Neonatal Respiratory Distress recovery ranging from 2.83% in resource limiting area to 90-95% in high resource setting area ,where surfactant therapy is available (Carniellib, Hallmand et al. 2023). Incidence of recovery in India: 12.6% (Gaurav and Ahmad 2023), 2.83% in Kampala (Magondu 2023) Sudan: 4.83% (Aljawadi and Ali 2019); Nigeria: 10%;(Okolo, Emeagui et al. 2023) ;Egypt 13.9% (Hegazy, Metawie et al. 2024), Ethiopia: 11.5% (Enyew, Bitew et al. 2022) .

The recovery duration for NRD changes by region, influenced by NICU technology and gestational age at birth (Ekhaguere, Okonkwo et al. 2022). Recovery time takes five days in developed nations (Shalish, Lakshminrusimha et al. 2020), 9–14 days in Nepal (Suwal, Katwal et al. 2024), 10–21 days in Kampala (Magondu 2023), over seven days in Egypt (Baseer, Mohamed et al. 2020), and 7–12.4 days in Ethiopia (Enyew, Bitew et al. 2022). Longer recovery times are associated with poor clinical outcomes, including complications such as Nosocomial infections and increased mortality (Gaurav and Ahmad 2023, Tochie, Sibetcheu et al. 2024).

Globally, 2.5 million Neonatal deaths occur Annually, with NRD contributing 19.5% in the USA (Murphy, Kochanek et al. 2021), 15.5% in China (Cao, Jiang et al. 2021), and 12.8% in Poland (Sartorius, Philibert et al. 2024). Long recovery time significantly contributes for these deaths (Stylianou-Riga, Boutsikou et al. 2021). Additionally, over 200,000 treatment failures and 1 million procedural complications, including Adverse Drug Reactions, are reported yearly (Yismaw, Gelagay et al. 2022). Most undesirable outcomes are linked to respiratory distress and prolonged recovery time (Baseer, Mohamed et al. 2020; Shah, Fabres et al. 2022; Sisay, Mengistu et al. 2022; Suga, Kyono et al. 2022; Sabry, Bastawy et al. 2023).

In Africa, more than 2 million Neonatal deaths occur Annually (Baseer, Mohamed et al. 2020). NRD accounts for 49.6% of Neonatal deaths in Nigeria, 19.2% in East Africa, and 49.5% in Ethiopia, largely due to delayed recovery times (Sabry, Bastawy et al. 2023).

Delayed recovery from NRD leads to poor clinical outcomes, increased rates of Nosocomial infections (neonatal sepsis), Cardiopulmonary arrest, Respiratory arrest, and Death (Derese, Belay et al. 2020). It also results in higher Bed occupancy rates and imposes significant Psychological, Social, and Economic burdens on Families, including increased Costs, Time, and Stress (Derese, Belay et al. 2020). Prolonged recovery increases adverse events, such as Medical errors, and leads to undesirable treatment outcomes, including Complications, referrals to higher Facilities, Treatment failures, and Death (Yismaw, Gelagay et al. 2022).

Contributing factors-include Socio demographic factors like,Sex, residence,Age of the Neonate and the Mother (Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022,Suga, Kyono et al. 2022, Sabry, Bastawy et al. 2023).Mothernal medical disorder like,Human Immune Deficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), Maternal Diabetes Mellitus and Chronic Hypertension

(Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022,Singh, Shrikhande et al. 2018, Savchuk, Morvan et al. 2019,).

Neonatal outcome and Health care service related like, Meconium Aspiration, Hypoglycemia, Hypothermia, Jaundice, Sepsis, Apgar Score, Birth Asphyxia, Congenital Anomaly, CPAP, Direct Oxygen, KMC, Antibiotic (Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022,Sahiledengle, Tekalegn et al. 2020, Shalish, Lakshminrusimha et al. 2020, Sauer, Peukert et al. 2021), and Obstetric and related factors like,Multiple pregnancy, Parity, PROM, Pre-eclampsia, Abruptio Placenta, Place of Delivery and Mode of Delivery (Aynalem, Mekonen et al. 2020, Enyew, Bitew et al. 2022,Sahiledengle, Tekalegn et al. 2020, Shalish, Lakshminrusimha et al. 2020,).

Policies, Strategies, and Programs, including the Sustainable Development Goals, aim to reduce and prevent long recovery times for NRD world wide (Sisay, Mengistu et al. 2022). The WHO and its partners Collaborate with Ministries of Health to strengthen care and reduce Neonatal Mortality and Morbidity associated with delayed recovery (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022; Girma, Tesfahun et al. 2024).

Despite these efforts, little is known about the Time to recovery and its predictors among NRD in Ethiopia (Derese, Belay et al. 2020, Enyew, Bitew et al. 2022, Girma). Limited studies in Resource-Constrained Settings and most studies conducted in single Institutional-Level (Girma and Nigussie 2021) .

Filling up the Gaps and figuring out the rate of recovery, duration of recovery time, and factors that influence variation in recovery time are the goals of this study for Neonates with Respiratory Distress admitted to NICU of North Shoa Zone Selected Public Hospitals.

1.3. Significance of the study

This study aimed to identify the Time to recovery and its predictors among Neonates with Respiratory Distress. The findings will help Hospitals and Health offices to address RDS by identifying high-risk Neonates requiring extended monitoring, guiding NICU resource allocation, and developing targeted interventions to accelerate recovery. Additionally, it will provide Parents with informed expectations about outcomes.

The results will also assist Policymakers, including the Ministry of Health, Governmental, and Non-Governmental Organizations, in making evidence-based decisions for Neonatal Health Programs. Improved program implementation and efficient resource use are crucial for enhancing Neonatal survival.

2. LITRATURE REVIEW

2.1. Incidence and time to recovery of RD neonates

Prospective cohort observational data research on RD in active newborns in India using meconium-stained amniotic fluid reveals that the incidence rate of RD in active newborns was 39.6%, and the incidence rate of recovery is 17.5 per 100 newborn days, which is a high rate of recovery compared to 11.5 per 100 newborn days in Ethiopia (Enyew, Bitew et al. 2022).

According to a different study conducted in India, the recovery proportion of RD in NICUs is 88.84%, which is higher than the recovery proportion found in an Ethiopian study 68.6% (Kshirsagar, Kshirsagar et al. 2019). An Indian study on early neonatal respiratory distress found that 2.83% of newborns in NICUs had respiratory distress (Bamehrez 2023) .

The incidence of RD among preterm babies was found to be 14.6% in a prospective cohort research study on incidence, prognosis, and predictors of death in RDS conducted in a tertiary care institution in Nepal. 12.7% of all newborn admissions are related to RD. The incidence recovery rate was 5.5 per 100 neonates per day, and the median length of recovery time was 14 days (range 4–14 days) (Basnet, Aryal et al. 2022).

According to a cross-sectional study conducted in Kampala, the typical recovery time for neonates with low birth weight and preterm infants is more than 21 days (Namiiro, Mugalu et al. 2012).

The length of recovery time for RDS was 30.555% and 33.25 days, respectively, and hospital-born patients had an incidence rate of 66.38%, while out-born patients had 33.61%, according to an Egyptian study on the incidence, causation, and outcome of RD. MAS recovery time ranged from 8.25 to 9.25 days, while TTN recovery ranged from 3 to 5 days (Ali 2019).Research on respiratory distress in term and post-term neonates conducted at the Yaoundé (Cameroon) tertiary health center showed that the

rate of RD in the NICU was 8%, which is lower than the findings of a study in Nigeria (30%). The length of recovery time was more than seven days, slightly longer than the global average of 5 to 7%. Data from level III NICUs in Baghdad and Saudi Arabia also showed that the rate of RD was 1.64–2.78% (Kue, Nanfack et al. 2020).

Results from the Gondar University Comprehensive Specialized Hospital showed that the cumulative proportion of recovery among preterm neonates with RD is 60.9%. The overall length of recovery time was 7 days, and the median length of recovery time was 11 per 100 neonate days. These results are higher than those of a study conducted at Jima University Specialized Hospital (42.78%), a referral hospital in southern Ethiopia (34.04%), and Assuit University Children Hospital in Egypt (30.5%) (Yismaw, Gelagay et al. 2022).

Among RD neonates admitted to the neonatal intensive care unit, a retrospective cohort study at Gondar University Comprehensive Hospital on incidence, time to recovery, and predictors revealed an incidence rate of recovery of 11.5 per 100 person-days, a median recovery time of 7 days, and a cumulative proportion of recovery of 68.6%. This is a low recovery incidence proportion compared to India (88.84%) and an unacceptably higher median recovery time than the WHO report, which is 72 hours (Enyew, Bitew et al. 2022).

The overall incidence rate of RD is 8.1 per 100 neonate days, according to data from a retrospective cohort study on the incidence and predictors of newborn respiratory distress among neonates hospitalized to the neonatal intensive care unit at Tikur Anbessa Specialized Hospital. The RD neonates' overall median recovery time was 9 days, which is unacceptable compared to reports from Egypt, India, and Nepal (Aynalem, Mekonen et al. 2020). The median survival recovery time for newborns admitted to the NICU was 7 days , according to a retrospective cohort study done to evaluate recovery times and related factors in Diredawa study (Derese, Belay et al. 2020).The average length of recovery time in the NICU at the Southern Ethiopian referral hospital was 6.1 days, according to a retrospective cohort research on the

factors that predict infant mortality in the unit (Orsido, Asseffa et al. 2019). Another Study conducted Diredawa public hospital show that overall survival time of neonate admitted to public hospital was 7 days short as short reported from Brazil average length of recovery time 19 days (Derese, Belay et al. 2020).

The median life duration for an asphyxiated infant is 9 days, and the overall survival rate (occurrence density) was 9.9 per 100 neonates observed throughout the observation period, according to research conducted at Debre Birhan Comprehensive Specialized Hospital (Girma, Tesfahun et al. 2024). According to a study conducted at Black Lion Specialty Comprehensive Hospital, neonates with RD had a median recovery time of 9 days and an overall hospital stay of 28 neonatal days (Aynalem, Mekonen et al. 2020).

Research on survival and determinants in asphyxiated neonates is presented in a dissertation. During 100 neonatal days of observation, a survival rate of overall density among asphyxiated neonates was discovered, with a median survival time of 9 days (Derese, Belay et al. 2020).

2.2. Predictors of time to recovery

2.2.1 socio-demographic factors

According to a Chinese study, neonates with RD born to mothers older than 35 but younger than 20 take longer to recover than their counterparts (Mu, Li et al. 2021). Findings from Gondar University Specialized Hospital indicate that the recovery time for NRD neonates born to mothers aged >34 and <20 is delayed by 65% and 55%, respectively, compared to their counterparts (Enyew, Bitew et al. 2022). A report from the Ethiopian Health Demographic Mini Survey and a retrospective cohort study conducted at Gondar University show that male neonates are more likely to develop RD and take longer to recover than female neonates (Enyew, Bitew et al. 2022).

Research conducted at Gondar University Specialized Hospital revealed that twins recover faster than singletons, and neonates with a birth weight of 2000 grams or

more have a 2.12 times higher recovery rate compared to their counterparts (Yismaw, Gelagay et al. 2022). A study in Dire Dawa shows that neonates admitted 1-6 days after birth have a 0.5 higher probability of recovery than those admitted 7-28 days after birth (Derese, Belay et al. 2020). A retrospective cohort study conducted in Eastern Ethiopia on the causes and predictors of neonatal mortality among neonates admitted to public hospitals shows that neonates with a hospital stay of >7 days have a 39% slower recovery than their counterparts (Desalew, Sintayehu et al. 2020).

2.2.2 Obstetric and related factors

Scoping review data on the worldwide, regional, and national burden reveal that during placenta previa and placental abruptio, RDS and recovery time increase by 4.21–5 times (Tochie, Sibetcheu et al. 2023). Premature infants are more likely than term neonates to acquire NRD and have a longer recovery period, according to a report from a systematic review and modeling study on preterm delivery in WHO member states (Chawanpaiboon, Vogel et al. 2019). According to a study conducted at Black Lion Hospital, the risk of extended recovery time for neonates with RD who were delivered at home is 2.9 times higher than for neonates delivered in a hospital (Aynalem, Mekonen et al. 2020).

Research from Black Lion Hospital showed that factors that lengthen the recovery period for RD newborns include multiple pregnancies, lack of prenatal follow-up, home birth, C/S, maternal diabetes, and PROM (Aynalem, Mekonen et al. 2020). A retrospective study carried out at Debre Birhan University Comprehensive Specialized Hospital found that 58% of babies admitted with NRD had longer recovery times due to mothers who had protracted labor (Girma, Tesfahun et al. 2024; Yismaw, Gelagay et al. 2022).

2.2.3 Medical disorder of the mother

Evidence from a scoping review on global, regional, and national trends shows that hypertensive disorders of pregnancy are 1.12–17 times more likely to be associated with a longer hospital stay, and HELLP syndrome is associated with an incidence of NRD in neonates of 5.7–40% (Tochie, Sibetcheu et al. 2023).

A retrospective cohort study conducted at Black Lion Specialized Hospital revealed that neonates delivered by mothers with diabetes mellitus were 2.3 times more likely to take longer to recover than those delivered by non-diabetic mothers. This finding is supported by evidence from China, where neonates delivered by HIV/AIDS-infected mothers were 1.5 times more likely to experience prolonged recovery than their counterparts (Aynalem, Mekonen et al. 2020).

Another study from Black Lion Specialized Hospital revealed that maternal DM and HIV/AIDS were significantly associated with time to recovery among neonates admitted with RD (Aynalem, Mekonen et al. 2020)

2.2.4 Neonatal outcome condition and health care service related factors

Multicenterd prospective study on the relationship between admission hypothermia and outcomes in very low birth weight infants in China found that RD neonates have a five-fold increased risk of moderate/severe hypothermia and a three-fold increased risk of mild hypothermia, respectively, requiring a longer recovery period than their counterparts (Yu, Wang et al. 2020).

A prospective study on hypothermia during birth and the issues it causes for newborns was carried out at IMAM Hospital in Tehran, Iran. The study found that newborns with hypothermia are twice as likely to require a lengthy recovery period (Nayeri and Nili 2019). An observational prospective study on the incidence, prognosis, and mortality of RDS neonates in Nepal reveals that neonates with sepsis have longer hospital stays than newborns without sepsis (Basnet, Aryal et al. 2022).

According to a systematic review and meta-analysis in East Africa on the impact of respiratory distress and asphyxia on preterm survival, neonates with RD and asphyxia have a higher risk of prolonged recovery time than their counterparts (Chanie, Alemu et al. 2021).

A study examining the effects of respiratory distress on neonates admitted to As Suit University Children Hospital in Egypt's NICU showed that the mean survival times for HMD, MAS, pneumonia, PPHTN, and congenital anomalies were 23.1 to 31.54, 9.84 to 14.94, 25.65 to 32.65, and 6.73 to 9.33 days, respectively (Abou-Faddan and Abdelaziz 2018).

A study on the survival and outcomes of RDS with neonatal hypoxia showed that neonatal seizures occurring after 24 hours slow recovery time by 31%, and thrombocytopenic neonates require twice as long to recover as those with normal platelet counts (Getaneh, Sebsbie et al. 2022).

Research on the survival of preterm newborns reveals an inverse relationship between gestational age and both neonatal respiratory distress and recovery time. According to a study, preterm neonates both very preterm and late preterm have a higher risk of developing RD and require longer recovery times than term newborns (Kue, Nanfack et al. 2020).

According to a retrospective cohort study in Dire Dawa, newborns who are not intubated or receiving oxygen have a longer risk of lengthy recovery (hazard ratio of 6.725 and 1.336) than their counterparts, and neonates weighing less than or equal to 2500 grams have a higher risk (1.648) than those weighing more than or equal to 4000 grams (Derese, Belay et al. 2020). Very low birth weight, low birth weight, very preterm birth, sepsis, and hypothermia had, in comparison to their counterparts, 83%, 50%, 58%, 50%, and 39% of the risk of a protracted recovery period, according to study results from Gondar University Hospital (Enyew, Bitew et al. 2022).

A study carried out at Debre Birhan University Comprehensive Specialized Hospital reveals that newborns with normal consciousness and normal Moro reflex recover from RD with asphyxia 2.5 and 2.4 times faster than their counterparts. HIE stage increases also contribute to this recovery time, with stage 1 HIE patients recovering 5.1 times faster than their counterparts. Direct oxygen and amonophyline also shorten the recovery period by 4.2 and 2 times, respectively (Girma, Tesfahun et al. 2024). A study on a discrepancy in neonatal asphyxia indicates that newborns receiving intravenous fluid and calcium gluconate within 24 hours had a somewhat faster median recovery time than those not receiving fluid (Getaneh, Sebsbie et al. 2022).

According to a retrospective study in Gondar, 46% of preterm infants with RD who use a bag and mask ventilation system had a slower recovery than those who do not (Yismaw, Gelagay et al. 2022).

2.3. Conceptual frame work

A conceptual framework revised from different articles show that Generally,there are four factors that affect recovery time of neonatal respiratory distress.

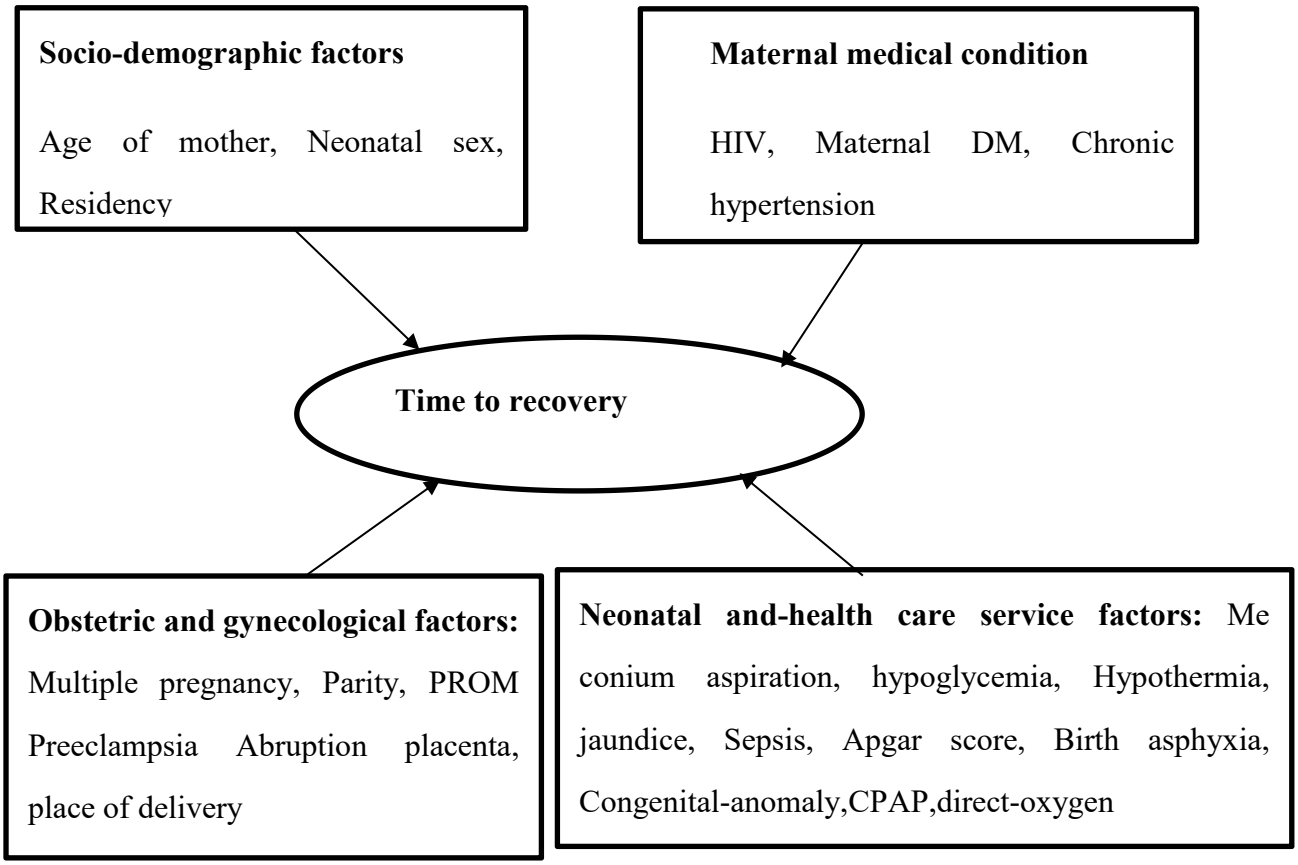


Figure 1: A conceptual framework describing predictors of time to recovery among neonates admitted with respiratory distress (source: researcher own construction (2024) based on review of literature (Aynalem, Mekonen et al. 2020, Bacha, Hailu et al. 2022, Enyew, Bitew et al. 2022, Girma, Tesfahun et al. 2024).

3. OBJETIVES

3.1 General Objectives

- To assess Time to recovery and its predictors among neonates admitted with diagnosis of Respiratory Distress in NICU at North Shoa Zone Selected public Hospitals, North Shoa zone, Oromia, Ethiopia 024.

3.2 Specific Objectives

- To assess incidence of recovery among neonates admitted with diagnosis of respiratory distress in NICU at North Shoa Zone Selected public Hospitals.
- To identify Time to recovery among neonates admitted with diagnosis of respiratory distress in NICU at North Shoa Zone Selected public Hospitals.
- To assess predictors associated with time to recovery among neonates admitted with diagnosis of RD in NICU at North Shoa Zone Selected public Hospitals.

4. METHODS

4.1 Study area and period

4.1.1 Study setting

The study was conducted at NICU of North Shoa Zone Selected public Hospitals. Oromia Regional state of Ethiopia. North Shoa Boarder on the South by Adiss Ababa, on the South West by West Shoa, on the North by Amhara Region, and on the South East by East Shoa. The Zone has a total popullation of about 1,639,586, of which 717,552 and 922,034 were Men and Women (Reference -North Shoa Zone health office). There are five Public Hospitals in North Shoa Zone. They are Chan co Primary Hospital, Muke turi Primary Hospital, Salale University Comprehensive Specialized Hospital, Kuyu General Hospital and Dera District Hospital which is deliver service for Chan-co, Muke turi, Kuyu, Fiche town and Dera woreda population respectively. The last two hospitals were selected based on data criteria.

4.1.2 Study Period

This study was conducted from June to July 2024.

4.2. Study design

The Multi Centered Institution-based Retrospective Cohort study was conducted among cohort of Neonates admitted with Respiratory Distress in Neonatal Intensive Care Unit at selected public Hospitals of North Shoa Zone.

4.3 Population

4.3.1 Source population

All Neonates admitted with Respiratory Distress in Neonatal Intensive Care Unit at public Hospitals of North Shoa Zone during the study period .

4.3.2 Study population

All Neonates admitted with Respiratory Distress during the study period at selected public Hospitals of North Shoa Zone and meet the studies eligibility criteria.

4.3.3 Study unit

Each Neonate admitted with Diagnosis of Respiratory Distress during study period and selected through sampling technique at selected public Hospitals of North Shoa Zone.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All Neonates admitted with the diagnosis of RD in clinical or other diagnostic criteria in NICU and had complete medical record at selected public Hospitals of North Shoa Zone In the study period was included in the study.

4.4.2 Exclusion criteria

Neonates with RD and incomplete data or missing critical data and record at the date of admission /date of discharge .

4.5 Sample size determination

The sample size was calculated using Schonfield formula and single proportion formula.

4.5.1. For objective One

For estimating proportion of recovery by using simple proportion population formula from previous study proportion of recovery Gondar university Hospital (Enyew, Bitew et al. 2022). P = 0.686

$$n = \frac{(z_{a/2})^2 p\, q}{d^2}$$

$$n = \frac{(1.96)2(0.686)\,(0.314)}{0.0025} = 331$$

P=proportion of recovery from previous study

Q=proportion of cases no develop an event

D=standard error

$Z = Z_{a/2}$ =critical value of normally distributed variable at 5% significance level (1.96)

4.5.2. For the Second Objective

The sample size was determine by power approach using sample size formula for survival analysis (Enyew, Bitew et al. 2022).

$A = (Z_{a/2-} + B)^2$

$B = (\log(RH)^2 p_1 p_2$

$N_{total} = A/B$

Where N_{total} =total sample size

$Z_{a/2}$ =critical value of normally distributed variable at 5% significance level (1.96)

Z_B =critical value of normally distributed variable at 20% significant level (0.8416) or type two error

RH=is the log (hazard ratio)

P_1=proportion of patients in the first category

P_2=proportion of patients in the second category (Enyew, Bitew et al. 2022)

The proportion of recovered RD neonate in this case is P = 0.686.Based on previous study conducted on Gondar University Comprehensive Specialized Hospital (Enyew, Bitew et al. 2022).

By considering predictors significantly associated with time to recovery of RD neonates from previous studies sample size is calculated using schoenfeld formula or STATA software version 15.

$E = \frac{(Z_{A/2} + Z_B)^2}{\text{Log (HR)}^2 P1P2}$ $n = \frac{E}{P(E)}$

E= number of required event

n =sample size

HR =hazard ratio of selected covariates

P1 =proportion of subjects under exposed group

P2 =1-p1

P (E) =probability of an event from previous study

Assuming probability of type I error or alpha 0.05, power of the study 80%

Probability of card incompleteness 0.1

Table 1. minimum sample size for excoriates associated with time to recovery of RD neonates

Variable		AHR	P-event	Event	Sample size	Reference
SEPSIS		0.50	0.686	393.96	574	(Enyew, Bitew et al. 2022)
Apgar score <7	The 1st minute	0.35	0.686	243.47	354	(Enyew, Bitew et al. 2022)
Apgar score < 7	5th minute	0.45	0.686	437.98	638	(Enyew, Bitew et al. 2022)
Very low birth weight		0.17	0.686	133.3	194.31	(Enyew, Bitew et al. 2022)

Finally the sample size is calculated by considering the above covariates very low birth weight, Apgar score less than seven the first one minute, Apgar score less than seven the first five minute and sepsis. Maximum sample size taken from Apgar score of less than seven the fifth minute =638.Non response rate (card incompleteness) = 10%. Final sample size =638+63.8=702

4.6 Sampling technique and procedure

Among five hospitals found in North Shoa Zone, the two of them, 25-30%, (Dera Hospital and SUCSH) were selected due to the criteria of Data availability. Then, all neonates who met the inclusion criteria during the study period were included in the study in each proportionally allocated Hospitals.

Then with systemic random sampling the study participants of each year was selected as-follows: first numbering the units of each year on the frame from 1to N (N=total admission of each year), then determine sampling fraction (k=6) by dividing the number of units in the population by desired sample size of each year (n=sample size of each year). The number between was select randomly,this number was called random start(2). The other was selected every k^{th} interval from the first number .

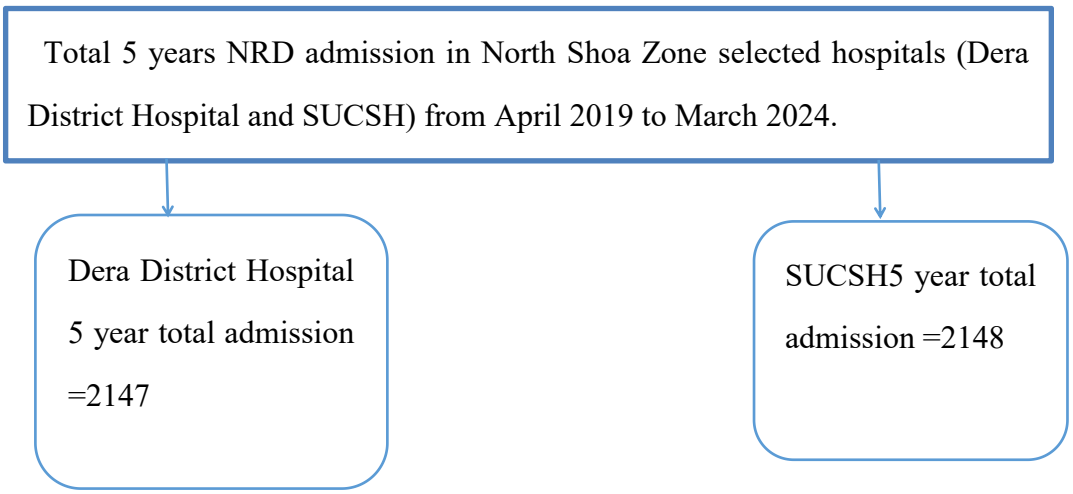
Hint for the below sampling technique scheme

Among five hospitals in North shoa zone two of them selected based on criteria. The average annual neonatal admission at Dera Hospital and Salale university comprehensive specialized-hospital was 429 and 430 respectively per year. Total admission 859 per year and 4295 per 5 years.

K=4295/702=6.11

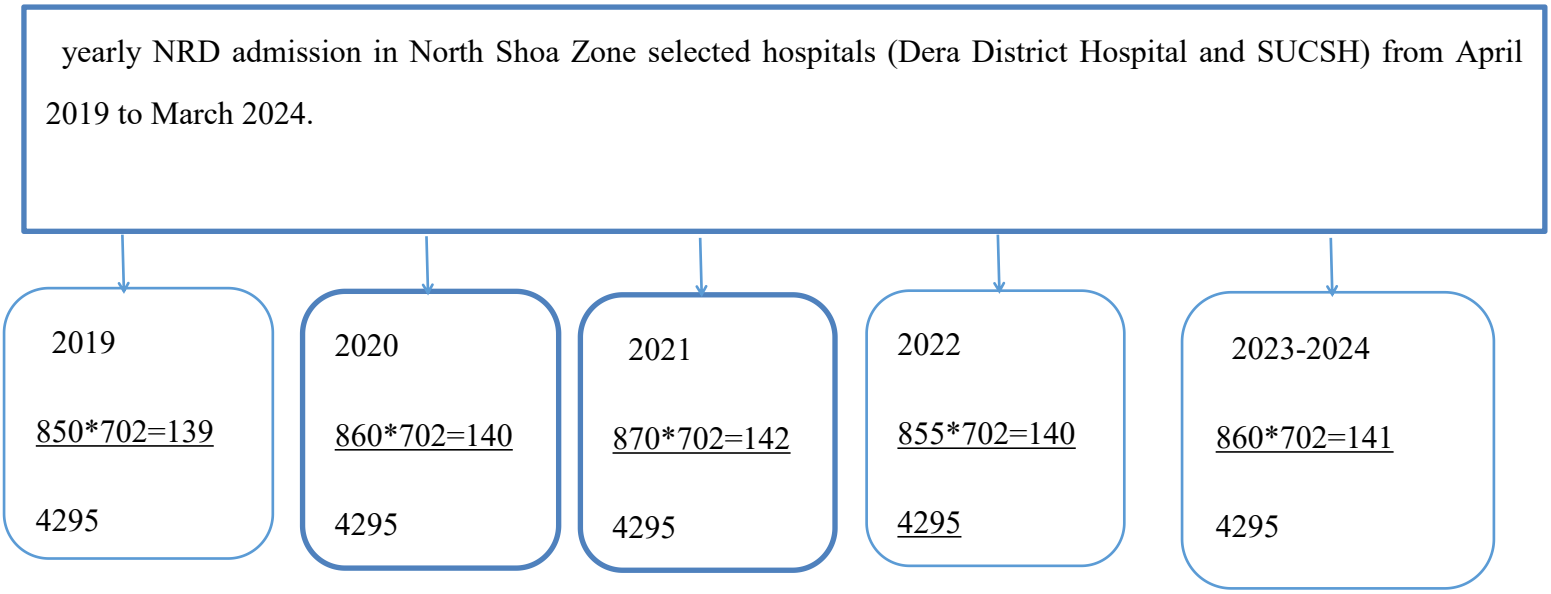
.

Sampling technique proportionally allocated for each Hospital



✓ From each hospital proportionally 351 data was collected

Sampling technique proportionally allocated for each year



FINAL N =702 total sample size

Figure 2 Schematic presentation of sampling technique and sample size proportional allocation from 2019 to 2024.

4.7. Data collection tool,technique and procedure

Data were collected using check list of adapted from RD neonatal charts and similar studies (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022; Girma, Tesfahun et al. 2024). It was written in English. The tool was hold the following information like Maternal and Neonatal Socio Demographic condition, Neonatal and Maternal medical condition and Obstetric and Gynecologic predictors .

The questionnaire was constructed after the review of relevant literature in order to maintain the standards of the questionnaire (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;). Then, the validity was established by doing expert discussions (Pediatricians and Public Health experts) and pre-test study. As a result, changes were made based on both a pre-test and expert opinion to make the questionnaire measure what is intended to measure. After data were collected using a pre-test study, it was assessed for suitability of the content, clarity, sequence, and flow of the questionnaire.

To diagnose NRD, the World Health Organization Integrated Management of Neonatal and Childhood Illness (IMNCI) guideline was considered, in addition to physician diagnosis and NRD was suggested with the presence of any one or more of the clinical signs and one investigation criteria. These include the presence of difficulty of breathing, nasal flaring, Grunting , chest retractions, chest in drawing, respiratory rate 60 breaths per minute and x-ray result shows confirmed case (Okolo, Emeagui et al. 2023).

Four BSC NICU Nurses as data collectors and two BSC Midwives as supervisors were collected the data after giving one day training.

4.8. Study variable

4.8.1. Outcome variable

Time to recovery from RD in (days).

4.8.2 Exposure variable

4.8.2.1 Socio demographic factors

Sex, Residence and age of the Neonate and the Mother (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022; Suga, Kyono et al. 2022, Sabry, Bastawy et al. 2023).

4.8.2.2 Maternal medical disorder,

Human Immune Deficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), Maternal Diabetes Mellitus and Gestational Hypertension (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;Singh, Shrikhande et al. 2018, Savchuk, Morvan et al. 2019,).

4.8.2.3 Condition of neonatal outcome and health care service related variables

Meconium Aspiration, Hypoglycemia, Hypothermia, Jaundice, Sepsis, Apgar Score, Birth Asphyxia, Congenital Anomaly, CPAP, Direct Oxygen, KMC, Antibiotics (Sahiledengle, Tekalegn et al. 2020, Shalish, Lakshminrusimha et al. 2020, Sauer, Peukert et al. 2021,Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

4.8.2.4 Obstetric and related factors

Multiple Pregnancy, Parity, PROM, Pre-eclampsia, Abruptio Placenta, Place of Delivery and Mode of Delivery (Sahiledengle, Tekalegn et al. 2020, Shalish, Lakshminrusimha et al. 2020,Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

4.9 Operational definition

Defaulter. Refers to neonate left (or stops treatment) the treatment unit against medical advice or the treatment (Shalish, Lakshminrusimha et al. 2020, Sauer, Peukert et al. 2021, Singh, Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

Death. A neonate died by RD during the treatment or at the treatment unit (Aynalem, Mekonen et al. 2020;).

Recovery: If a neonate was recovered from the Respiratory distress after completing the treatment according to physician diagnosis (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

Event: Means neonates recover from RD (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

Censored: RD neonates refereed to other facility, those neonates admitted with RD but that have death summery sheet, against medical advice or defaulter (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

Time to recovery: a time period between neonates admission with RD and neonates discharge while recover. It will calculate by subtracting date of discharge from date of admission (no of days until discharge /recovery) or free from clinical feature of RD(measured by incidence density rate and median recovery time) (Aynalem, Mekonen et al. 2020; Derese, Belay et al. 2020; Enyew, Bitew et al. 2022;).

Admission: neonates with respiratory distress with formally registered, initiation of care and clinical decision (Stylianou-Riga, Boutsikou et al. 2021, Shah, Fabres et al. 2022,)

Transition period: a period of time fetal circulation transforms in to neonatal type, it stars when the umbilicus clamped (Stylianou-Riga, Boutsikou et al. 2021, Shah, Fabres et al. 2022, Sisay, Mengistu et al. 2022).

4.10 Data quality assurance

First designing appropriate data abstraction tool was ensured data quality .Then check list was evaluated by experience researcher to check, appropriateness of the tool and necessary amendment was taken. Pretest was conducted on 5% sample. One day intensive training was provided for data collector and supervisor. The supervisor and principal investigator was closely monitored to check data is consistent and complete. Daily evaluation was done for any difficulty occur during data collection and solve accordingly. During data management, storage and analysis all collect data was double checked for completeness and consistency.

4.11 Data processing and analysis

The data was collected using Kobo data collection tool with structured check list and export STATA version 15 statistical analysis. Missing value was be handled and data was cleaned by revising the original code.Kaplan mi ere curve, Adjusted survival curve and Median time recovery was computed. By using Graphically and Sch on field Residual Global test the proportional hazard assumption was verified.

Which is the-graph is-parallel-and global test found to be met ($\chi 2 = 10.00$, df = 9 P-value = 0.3502). To describe the association between dependent and independent variable bi-variable and multi variable cox regression model Analysis was conducted. Multi co-linearity was checked thorough VIF and the result was 1.40. P-value 0.25 was selection criteria to entered from Bi variable to Multi variable regression analysis to control confounding effect .

To check General models goodness of fit, Cox Snell residual test was used and it shows-that,the hazard function follows the 45 closest to the baseline, indicating that th e model was appropriate. To assess the strength of association between dependent variable and independent variable, used Crude Hazard Ratio (CHR) and Adjusted Hazard Ratio (AHR), with their respective 95% confidence interval, p-value 0.05 was consider significant.

4.12 Ethical consideration

Ethical clearance was obtained from the institutional health research ethics review com mite (IRE) of colleague of health and medical science, of Salale University (Ref No/SLU-IRERC-264/2016).

Following the approval, official letter of cooperation was written to Salale University Comprehensive Specialized Hospital, North Shoa Zone. Informed voluntary written and signed consent was obtained from the head of the hospitals. The neonates was not harmed because of the study was carried out by using information from their medical registration.

The identifying information including name was not recorded on the checklist, and the information obtain from the chart was strictly confidential and kept in a secure location. Following this correction, access to the medical charts was granted, and we were done our best to maintain confidentiality by storing charts in a file cabinet and keeping them in keyed and locked. In addition Confidentiality of the patient was ensured using anonymous data collection procedure throughout research process.

4.13 Dissemination of the result

The results of the study were submitted to Selale University College of Health Science department of Midwifery as a partial fulfillment of the MSc in Neonatal and Maternal Health, Selale University Comprehensive Specialized Hospital and Dera District Hospital. Effort was made to present the result in a Local or International Workshops and Conferences. For the publication purpose, the abstract of the thesis was submitted to National or International Peer Reviewed Publisher.

5. Results

5.1. Socio-demographic and clinical characteristics of the neonates

A total of 702 NRD charts were examined and among the study participants 479 (68.23%) were Males. More than 90% of Neonates were admitted with in the first weeks of life. Based on gestational age 477(67.95%) were term, 195 (27.78%) were late preterm,13(1.85%) were extremely preterm and 17(2.42%) were post term. Similar to this, more than half (52.28%) of Neonates had normal birth weight,39 (5.56%) Neonates had extremely low birth weight,269 (38.32%) Neonates had low birth weight and 27(3.85%) Neonates had over weight.In total, 291 (41.45%) and 107(15.24%) of them had Apgar score of less than seven in the 1^{st} and 5^{th} minutes respectively.The manifestations that are found in Neonates with RD Neonatal Sepsis 405 (57.69%), Jaundice 102 (14.53%), Hypoglycemia 303 (43.16%), PNA 212 (30.16%), MAS 209 (29.77%).

5.2 TREATMENT RELATED FACTORS

Among the study subjects, 357 (50.85%) Neonates were ventilated using a Bag and Mask system,420 (59.85%) neonates were heated with a Radiant Warmer, 168 (23.95%) infuse with Calcium Gluconate (IV); 503 (71.65%) neonates were on Continuous Positive Airway Pressure (CPAP), 469 (66.80%) neonates were treated with Antibiotics ,189(26.92%) neonates were Assisted with Direct Oxygen, 65(9.26%) neonates were treated with KMC.

Table 2.Socio-demographic, clinical and intervention-al characteristics of neonates admitted to the NICU in North Shoa selected Public Hospital, 2024(n = 702).

Variables and Categories	Frequency	Percent (%)
Sex of the neonate		
Male	479	68.23
Female	223	31.77
Age of neonate at admission in days		
0-6	654	93.16
7-28	48	6.84
Gestational age in weeks		
Very preterm	13	1.85
Late Preterm	195	27.78
Term	477	67.95
Post term	17	2.42
Birth weight in grams		
Very low birth weight	39	5.56
Low birth weight	269	38.32
Normal birth weight	367	52.28
Over birth weight	27	3.85
Sepsis		
No	297	42.31
Yes	405	57.69
Meconium-aspiration Syndrome		
No	493	70.23
Yes	209	29.77
Prenatal asphyxia		
No	491	69.84
Yes	212	30.16
Hypoglycemia		
No	303	43.16
Yes	399	56.84
Jaundice		
No	600	85.47
Yes	102	14.53
Hypothermia		
No	554	78.92
YES	148	21.08
Apgar score at first minute		
<7	291	41.45

>=7	411	58.55
Apgar score at fifth minute		
<7	107	15.24
>=7	595	84.76
Bag and mask ventilation		
No	345	49.15
Yes	357	50.85
Heated with radiant warmer		
Yes	420	59.83
No	282	40.17
Iv fluid with Ca gluconate		
Yes	168	23.93
No	534	76.07
On CPAP		
Yes	503	71.65
No	199	28.35
On Anti biotic		
Yes	669	95.30
No	33	4.70
Direct oxygen		
Yes	189	26.92
No	513	73.08
KMC		
Yes	65	9.26
No	637	90.74

Key:KMC:kangaroo mother care CPAP: continuous positive air way pressure IV: intra venous

5.3 Socio-demographic and obstetric and gynecologic characteristics of mothers

The median age of the Mothers was 28 years with IQR (23,32).The majority of Mothers 541(77.07%) participate in the study were between the age of 20 and 34 years. (54.56%) Mothers were urban resident. The majority of Mothers had a spontaneous onset of labor, (90%), 574 (81.88%) Mothers had a parity one up to four, 458 (65.15%) Mothers had a Spontaneous Vertex Delivery, over 90 % mothers had delivered at the same Health Institutions, 349 (62.32%) had four ANC visits. Of all, 24 (3.42%) Mothers had twin pregnancies, 50 (7.12%) Mothers had PIH, 31 (4.41%) Mothers had an Ante part-um Hemorrhage,54 Mothers had PROM. In relation to Medical Health 14 Mothers Had HIV/AIDS,23 Mothers had Diabetes Mellitus ,31 Mothers had Chronic Hypertension.

Table 3.Socio-demographic, medical and obstetric characteristics mothers of neonates admitted to the NICU in North Shoa selected public Hospital 2024(n=702)

Variables and categories	frequency	Percent (%)
Age of the mother		
<20	38	5.41
20-34	541	77.07
>=35	123	17.52
Residency		
Urban	383	54.56
Rural	319	45.44
Parity		
1-4	574	81.88
>4	127	18.12
ANC follow up		
Yes	560	79.77
No	142	20.23
How many time follow ANC		
One times	22	3.93

Two times	55	9.82
Three times	134	23.93
Four and above	349	62.32
Pregnancy related problem		
Yes	142	20.23
No	560	79.77
Types of pregnancy related problem		
pre-eclampsia	50	34.97
Abruptio placenta	31	21.68
PROM	54	37.76
others	7	4.59
Pregnancy status		
single	678	96.58
multiple	24	3.42
Corticostroid		
Yes	128	18.23
No	574	81.77
Magnesium sulphate		
yes	51	7.26
no	651	92.74
Precipitated labour		
yes	93	13.25
no	609	86.75
Onset of labor		
spontaneous	627	89.32
induce	75	10.68
Place of birth		
Other facility	65	9.26
The same facility	637	90.74
Mode of delivery		
SVD	458	65.15
C/S	153	21.76
INSTRUMENTAL DELIVERY	92	13.09
Maternal medical problem		
Yes	72	10.26
No	630	89.74
Type of medical problem		
HIV/AIDS	14	19.72
DIABETUS MELITU	23	32.39
CHRONIC HYPERTENSION	31	43.66
OTHERS	3	4.23

Key: ANC: antenatal care, PIH: pregnancy-induced hypertension, PROM: premature rupture of membrane, HIV/AIDS: human immune virus/acquired immune diseases syndrome SVD: spontaneous vaginal delivery C/S: cesarean delivery

5.4. The incidence rate of recovery and the median time to recovery

The Neonates with RD were followed for a total of 4498-neonate day observations. 433 (61.68%), developed the Event (Recovered), while 269(38.32%) Neonates were Censored and 57(7.69%) Died. The overall RD recovery rate was 9.62 per 100-person day (95% CI: (8, 9). The overall median recovery time from RD (IQR) was 8 days (5, 11 days).

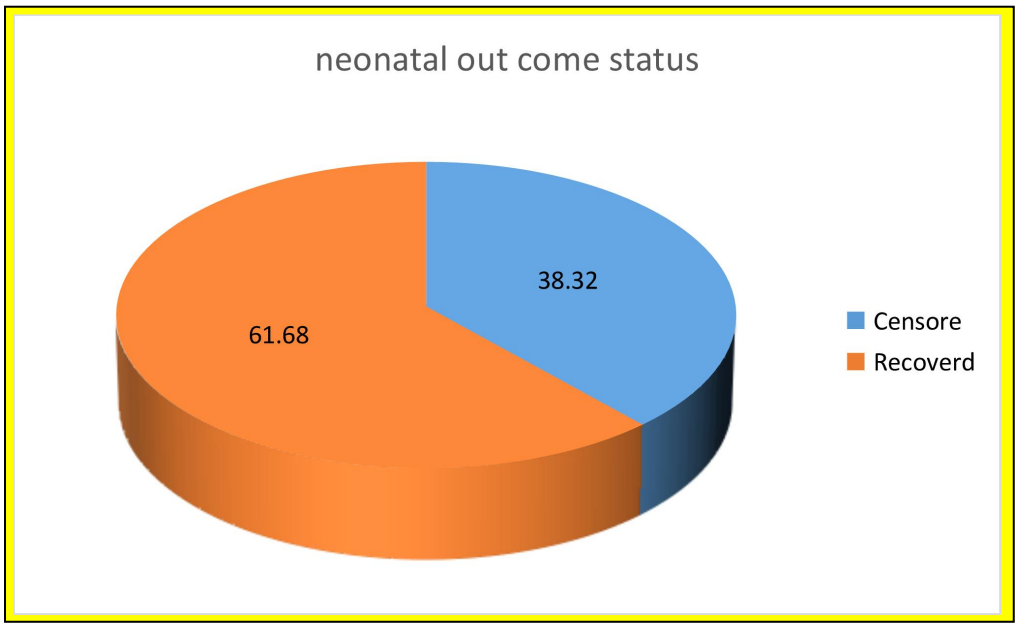


Figure 3.Pie chart shows neonatal out come status of neonates admitted to the NICU in North Shoa selected public Hospital 2024(n=702

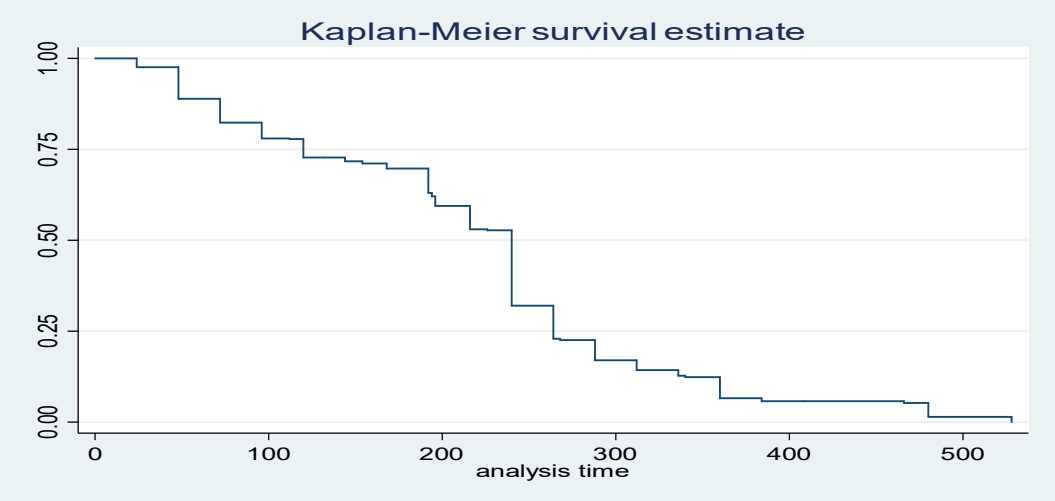


Figure 4. Kaplan– Meier survival estimates of the median time to recovery from RD of neonates admitted to the NICU in north Shoa zone selected public hospitals, 2024.

5.5 Comparison of survival status for different factors with adjusted survival curve and Kaplan mier curve and how to draw adjusted survival curve

The two primary quantities desired from a survival analysis point of view are estimated Hazard ratios and estimated survival curves. Understanding to estimation of survival curves using the Cox model. Recall that if no model is used to fit survival data, a survival curve is better to estimated using a Kaplan–Meier method.But this data is fitted with Cox model. So,Below the way how to change from-Cox model hazard function to adjusted survival curve is draw:

Cox model hazard function: h (t, **x**) =ho (t) exponential of [∑Bi Xi]

Changed in to Cox model survival function

Cox model survival function: S (t, **x**) =So (t) exponential of [∑Bi Xi]

Then estimated survival function: S (t, **x**)=So(t)exponential of [∑Bi Xi].

The-adjusted-survival curve-and-Kaplan mier curve was used to assessed the over all survival status of the new borns with RD based on several variables.

Using PNA , Mode of Delivery , Direct Oxygen, Hypoglycemia and Antibiotics .The study found roughly parallel graphs for the length of follow up when plotting the Adjusted-survivalcurve.This indicates that the proportional hazard assumption was m et and significant difference between groups.

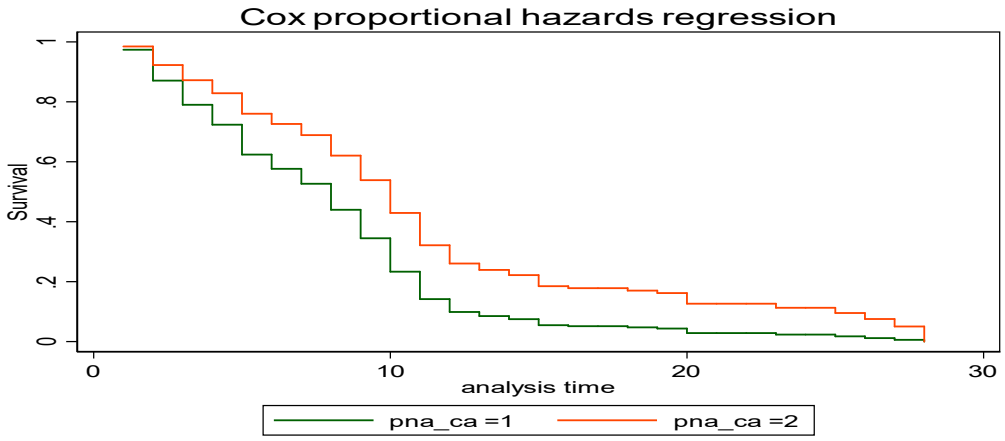


Figure 5. Proportional hazard survival regression model of neonates with RDS admitted in NICU by Prenatal asphyxia North Shoa Zone selected public hospitals, 2024

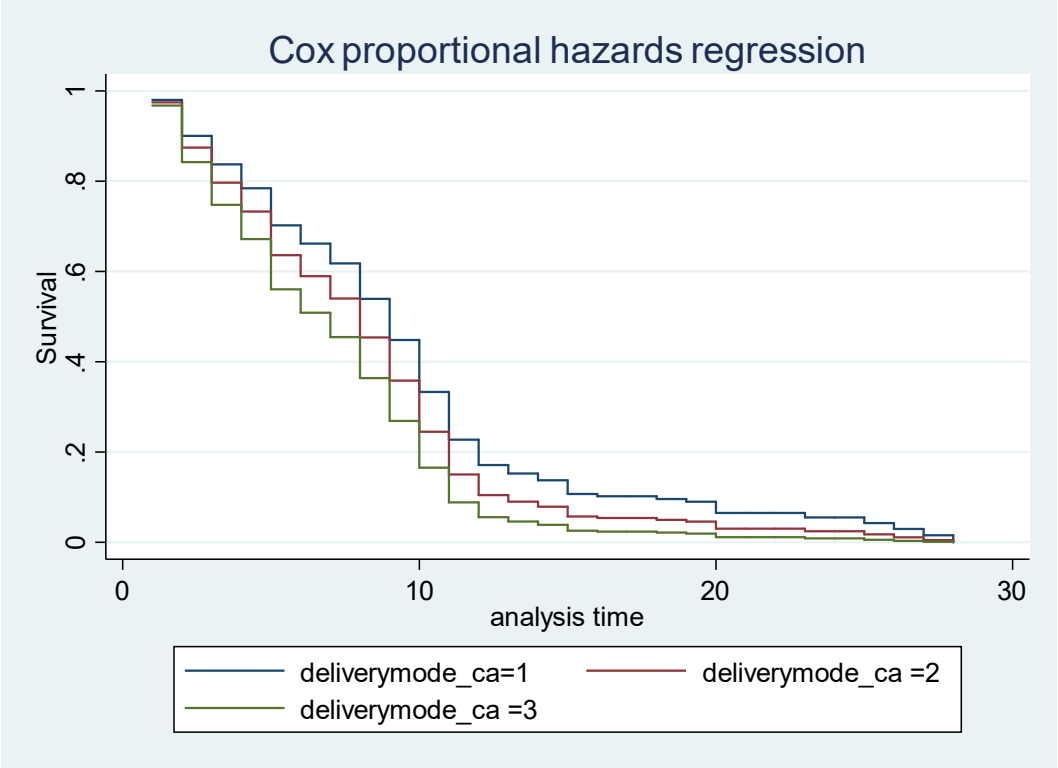


Figure 6. Proportional hazard survival regression model of neonates with RDS admitted in NICU by mode of delivery North Shoa Zone selected public hospitals, 2024

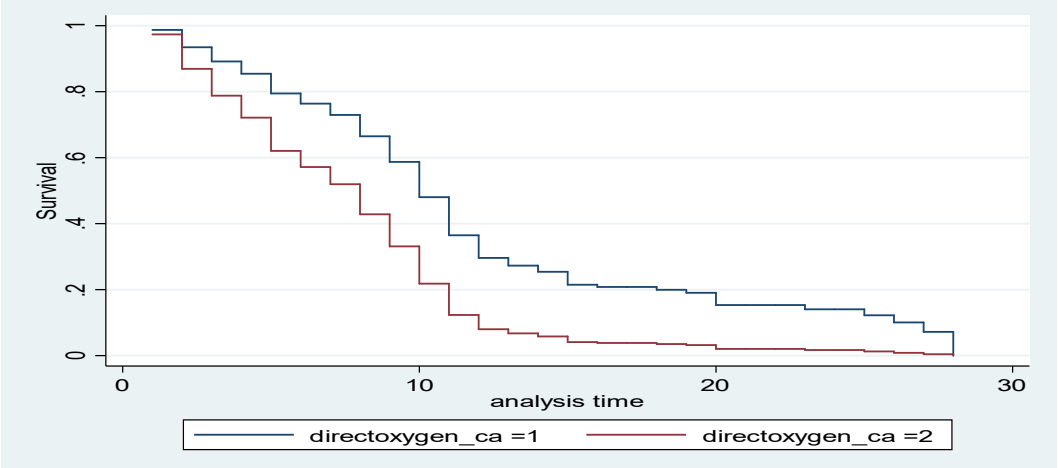


Figure7.proportional hazard survival regression model of neonates with RDS

admitted in NICU by direct oxygen , North Shoa Zone selected public hospitals, 2024

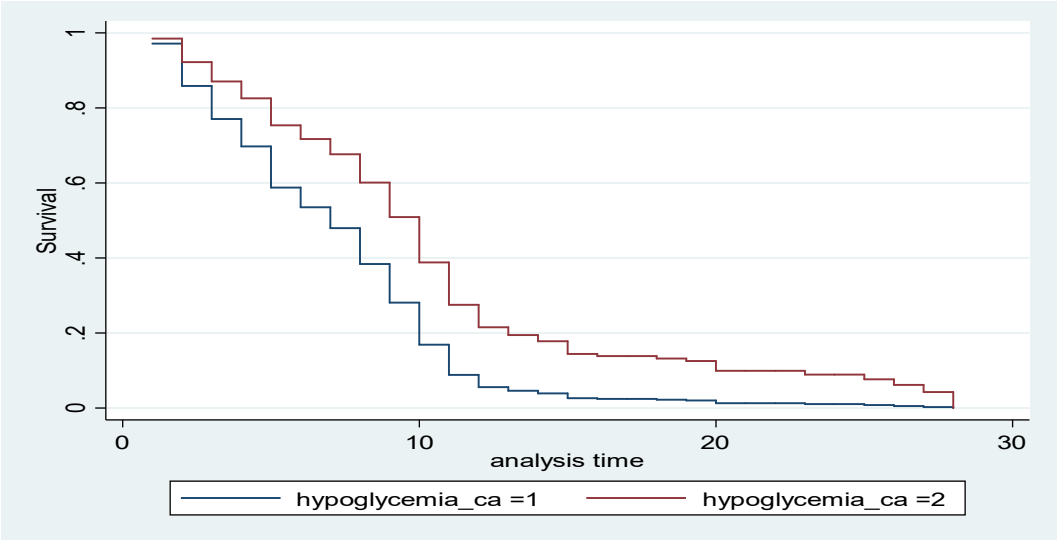


Figure 8. proportional hazard survival regression model of neonates with RDS admitted in NICU by hypoglycemia, North Shoa Zone selected public hospitals, 2024.

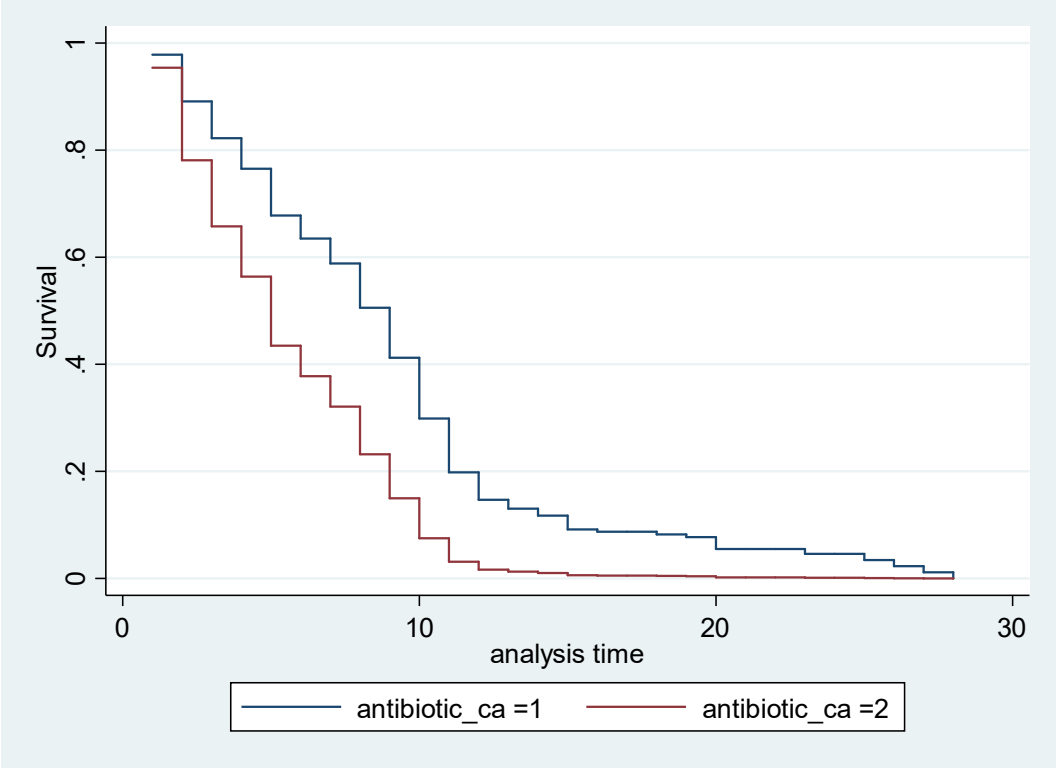


Figure 9. Proportional hazard survival regression model of neonates with RDS admitted in NICU by Antibiotics, North Shoa Zone selected public hospitals, 202

5.4. OVER ALL MODEL OF FITNESS

Using graphical &Schoenfeld residual global test, the proportional hazard assumption was verified in the entire model global-test found to be met ($\chi 2$ 10.00, df = 9 P-value = 0.3502).The graphs were parallel,this indicates proportional hazard assumption was met.

Additionally, The Cox-Snell Residual Test was performed to assess the fitted model's goodness of fit.The Cox-Snell Residual Graph for the goodness of model fitness showed that the hazard function follows the 45 closest to the baseline, indicating that the model was appropriate.

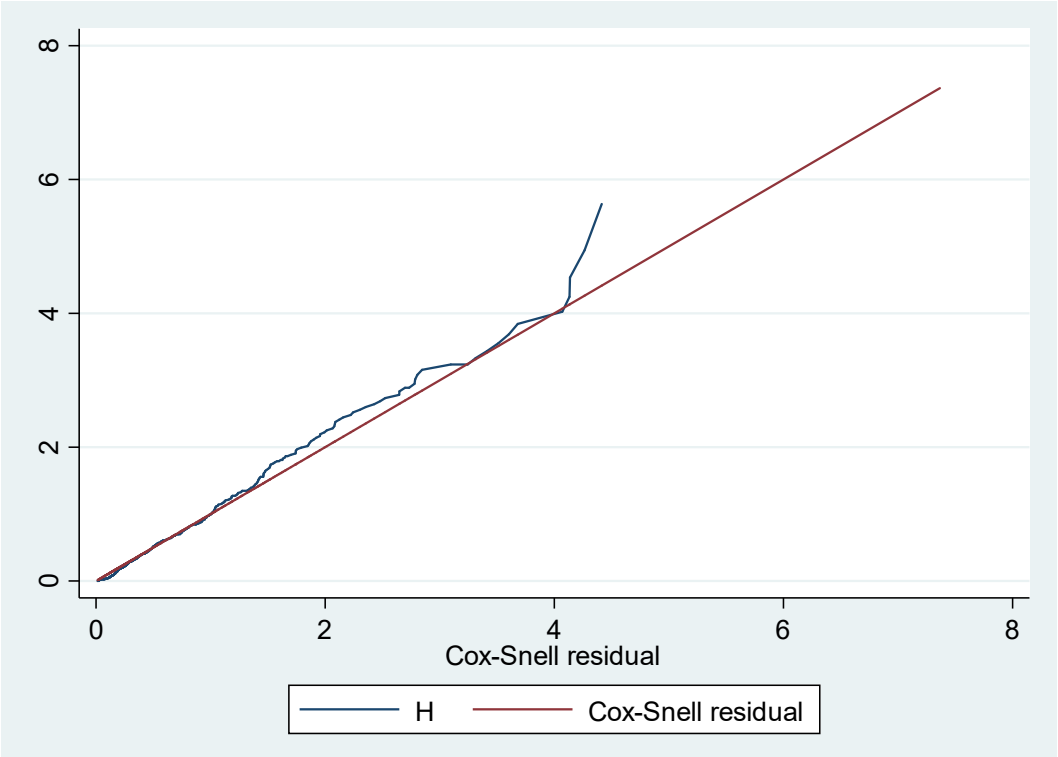


Figure 10.Cox-Snell Residual Graph for the goodness of model fitness that shows the hazard function follows the 45° closed to the baseline, in North Shoa selected public hospital,2024.

5.7 Predictors of time to recovery respiratory distress

In the bi variate analyses, the following variables were significantly associated with time to recovery of NRD: very low birth weight, low birth weight, taking calcium gluconate, antibiotic treatment, CPAP, direct oxygen, jaundice, hypoglycemia, hypothermia, APGAR scores at the first and fifth minutes, prenatal asphyxia, bag-and-mask ventilation, use of a radiant warmer, mode of delivery, sex of the neonate, and types of pregnancy complications.

The final Multi-variable Cox regression analysis revealed that the following variables were significantly Associated with the time to recovery of RD: Antibiotics (AHR=1.8,95%CI:0.5,6.5),Direct Oxygen (AHR = 2.3, 95% CI: 1.31, 5.73), PROM (AHR=1.32,95%CI:1.07,1.62),PNA(AHR=2.56,95%CI:1.27,5.12),Hypoglycemia (AHR = 0.28, 95%CI: 0.13, 0.59), and C/S (AHR = 2.31, 95%CI: 1.53, 3.48) were independently associated with the time to recovery .

Table 4. A table show variable and multi-variable analysis of neonates admitted to the NICU in North Shoa selected Public Hospital , 2024(n = 702).

Variables	Recovered from NRD		CHR(95%CI)	AHR(95%CI)	P-CHR	P-AHR
	Censored(%)	Event(%)				
Types of pregnancy problem						
Other	2(0.28)	3(0.42)	1			
pre-eclampsia	17(2.42)	34(4.84)	2.36(0.7-7.1)	2.25(0.5-9.1)	0.157	0.255
Abruptio placenta	16(2.27)	16(2.27)	1.61(0.4-5.6)	1.13(0.26-4.8)	0.449	0.866
PROM	31(4.41)	24(3.41)	1.12(0.4-5.1)	1.32(1.07,1.62)	0.003	0.002
Delivery mode						
SVD	218(31.05)	239(34.04)	1			
C/S	19(2.70)	134(19.08)	1.7(1.4-2.1)	2.31(1.53-3.4)	0.000	0.000
Instrumental delivery	32(4.55)	60(8.54)	1.38(1.0-1.83)	4.1(2.1,10)	0.025	0.31
Sex of neonate						
female	92(13.1)	131(18.6)	1			
male	177(25.2)	302(43.01)	1.14(0.9-1.4)	0.66(0.37-1.1)	0.21	0.151
Birth Weight						
Normal birth weight	55(7.83)	312(44.44)	1			
Very low birth weight	38(5.41)	1(0.14)	0.03(0.004-0.21)	0.82(0.6-0.89)	0.000	0.43
Low birth weight	172(24.50)	97(13.81)	0.36(0.29-0.46)	0.38(0.20-0.75)	0.000	0.702
Over birth weight	4(0.56)	23(3.27)	1(0.65-1.54)	2.37(0.51-11)	0.964	0.268
PNA						
NO	154(21.93)	336(47.86)	1			
YES	115(16.38)	97(13.81)	0.58(0.46-0.72)	2.63(1.41-4.8)	0.000	0.002
HYPOTHERMIA						
NO	173(24.64)	381(54.27)	1			
YES	96(13.67)	52(7.40)	0.43(0.32-0.58)	0.97(0.46-2)	0.000	0.950

JAUNDICE						
NO	204(29.05)	396(56.41)	1			
YES	65(9.25)	37(5.27)	0.58(0.41-0.81)	1.4(0.71-3)	0.002	0.288
HYPOGLYCEMIA						
NO	151(21.50)	248(35.32)	1			
YES	118(16.80)	185(26.35)	0.53(0.43-0.64)	0.28(0.13-0.59)	0.000	0.001
BAG AND MASK						
YES	176(25.07)	181(25.78)	1			
NO	93(13.24)	252(35.89)	1.46(1.20-1.77)	1.2 (0.68-2.2)	0.000	0.484
RADIANT WARMER						
YES	204(29.05)	216(30.76)	1			
NO	65(9.25)	217(30.91)	2.03(1.6-2.4)	0.71(0.36-1.4)	0.000	0.338
CAGLUCONATE						
YES	82(11.68)	86(12.25)	1			
NO	187(26.63)	347(49.43)	1.36(1.07-1.72)	1.3(0.7-2.6)	0.010	0.298
CPAP						
YES	163(23.21)	340(48.43)	1			
NO	106(15.09)	93(13.24)	0.51(0.40-0.64)	3.4(0.7-16.54)	0.000	0.76
ANTIBIOTIC						
YES	265(37.74)	404(57.54)	1			
NO	4(0.56)	29(4.13)	2.14(1.46-3.13)	1.8 (0.5-6.5)	0.000	0.041
DIRECT OXYGEN						
YES	104(14.81)	85(12.10)	1			
NO	165(23.50)	348(49.57)	2.07(1.63-2.63)	2.3(1.31-5.73)	0.000	0.002
First Min Apgar						
>=7	206(29.34)	85(12.10)	1			
<7	63(8.97)	348(49.57)	2.69(2.12-3.42)	0.83(0.41-1.6)	0.000	0.623
Fifth min APGAR						
>=7	175(24.92)	420(59.82)	1			
<7	94(13.39)	13(1.85)	4.56(2.62-7.94)	2.5(0.31-19)	0.000	0.382

KEY: P-CHR:p-value of crude hazard ratio P-AHR:p-value of adjusted hazard ratio

RD recovery duration were 1.8 times shorter in infants receiving Antibiotic treatment than their counterpart.In PNA neonates compared to their counterparts, the risk of a longer recovery period from RD was 2.56 times higher.

The time it took for RD recovery in newborns born to women with PROM was 1.32 ti mes longer than the newborns delivered to mothers without PROM. In a similar vein, neonates admitted with hypoglycemia had a 72% longer recovery pe riod from RD than their contemporaries.

Neonates who received direct oxygen recovered 2.3 times faster than their-counterpart s.According to the study's findings, neonates delivered via C/S experienced a 2.31-fol d delay in recovery compared to their counterparts.

6.Discussion

This study assessed the incidence and predictors of recovery time for Neonatal Respiratory Distress (NRD) among neonates admitted to Selected Public Hospitals in the North Shoa Zone. The study followed 433 neonates with NRD for a total of 4,498 neonate-days. Of these, 433 (61.68%) were recovered, while others were censored. The median recovery time was 8 days (IQR = 5–11 days). The NRD recovery incidence rate was 9.62% (95% CI: 8, 9).

The recovery proportion of this study (61.68%).The result is lower than studies conducted in Dire Dawa (84.4%) (Derese, Belay et al. 2020), Gondar-university Comprehensive Specialized Hospital (68.68%) (Enyew, Bitew et al. 2022), Woldia (78.63%) (Ambaye, Yimer, et al. 2024), and Debre Birhan (81.8%) (Yehouala, Tesfahun et al. 2024). This discrepancy may be due to variations in newborn screening, study population, the availability of advanced NICU care, and resource scarcity caused by the Northern Shoa conflict.

However, this study's recovery proportion was higher than that of studies in Addis Ababa (56.1%) (Sisay, Mengistu et al. 2022), and Northwest Ethiopia (45.37%) (Bonger, Mamo et al. 2023). The difference could be attributed to variations in study population demographics, sample size, and the inclusion of both preterm and term neonates in this study.

The incidence rate of NRD recovery in this study (9.62%).The result is higher than that of reported in Addis Ababa (6%) (Getaneh, Moges et al. 2024), India (2.83%) (Murki, Vardhelli et al. 2020), Nepal (4.6%) (Shakya, Shrestha et al. 2014), and Saudi Arabia (1.64%) (Bamehrez 2023), which may reflect differences in study settings,

maternal and newborn care services sophistication, sample size, and socio-demographic characteristics. Conversely, the incidence was lower than studies conducted in Debre Birhan (9.9%) (Yehouala, Tesfahun et al. 2024) and Gondar University Comprehensive Specialized Hospital (11.5%) (Enyew, Bitew et al. 2022). Potentially due to variations in study design, population, comorbidity, and NICU resources.

The median recovery time for NRD in this study was 8 days (IQR = 5–11), which aligns with studies conducted in China (Xie, Shu et al. 2022) and Brazil (Campanha, Magalhães-Barbosa et al. 2024), both of which reported a similar recovery time.Those studies are similar feature like, follow up period, sample size,study setting and popullation. The slight difference compared to a study at Tikur Anbesa Comprehensive Specialized Hospital (8.92 days) (Sisay, Mengistu et al. 2022).The difference may be due to sample size and population differences.

This study's recovery time was slightly higher than studies in Gondar University Comprehensive Specialized Hospital (7 days) (Enyew, Bitew et al. 2022), Gobba Referral Hospital (7 days) (Sahiledengle, Tekalegn et al. 2020), and Southern Ethiopia (7 days) (Gedefaw, Abuhay et al. 2024).The difference which could be due to variations in study design, patient age, and technological advancements.

The recovery time was slightly lower than studies in Gondar University comprehensive Specialized Hospital (11 days) (Yismaw, Gelagay et al. 2022), Addis Ababa (10 days) (Sisay, Mengistu et al. 2022), Debre Birhan (9 days) (Yehouala, Tesfahun et al. 2024), India (9 days) (Murki, Vardhelli et al. 2020), and China (9 days) (Xie, Shu et al. 2022). Differences in sample size,study popullation, and study settings could explain this discrepancy.

The time to recovery-from NRD mainly influenced by-Direct Oxygen, PNA, PROM, Hypoglycemia, Antibiotics and C/S .

In this study neonates taking antibiotics were 1.8 times fast to heal than their counter parts.This result is supported by studies conducted in Saudi Arabia (Al-Matary, Al Sulaiman et al. 2022) and Taiwan (Huang, Yan et al. 2020). Those studies reported that, Neonates treated with Antibiotics recoverd with short period of time than their counter parts.

Antibiotics are Anti inflammatory agents that reduce Cytokines, Inflammation and other inflammatory agents treat causing or exacerbating of RD (Simeoli, Cairoli et al. 2022). So it reduces time to recovery by treating comorbidity like sepsis and other infection or protect the occurrence of infection as prophylaxis and prevent complication of NRD (Huang, Yan et al. 2020).

Neonates with PNA at admission had a 2.56-fold longer recovery period than those without PNA, consistent with findings from Debre Birhan University Comprehensive Specialized Hospital (Yehouala, Tesfahun et al. 2024) and India (Singh, Shrikhande et al. 2018). PNA, especially if it begins before delivery, delays recovery. Its multi organ involvement effect and mixed causes cause to prolong recovery time (Ambaye, Yimer et al. 2024).

Neonates with Hypoglycemia had a 72% longer recovery time compared to their counterparts. This is supported by studies in Hawasa (Tadele, Jembere et al. 2024) and Saudi Arabia (AlJohani, Qaraqei et al. 2020). Hypoglycemia affects respiratory muscle function, the central nervous system, surfactant production, and metabolic acidosis, all of which prolong recovery (Gupta, Walker et al. 2022).

Neonates born to mothers with PROM recovered 1.32 times slower than those whose mothers did not have PROM. This is supported by studies in Iran (Asgarian, Sourani et al. 2019) and Saudi Arabia (Alfarwati, Alamri et al. 2019). PROM increases the risk of infection, preterm birth, and respiratory distress, which prolong recovery time (Sultana, Ishtiaq et al. 2019).

Neonates receiving direct oxygen recovered 2.3 times faster than their counterparts. This is consistent with studies from Debre Birhan (Yehouala, Tesfahun et al. 2024), Dire Dawa (Derese, Belay et al. 2020), and Taiwan (Lin, Wu et al. 2022). Direct oxygen therapy improves tissue oxygenation and lung function, relieving signs of respiratory distress (Sweet, Carnielli et al. 2019).

Neonates delivered via C/S experienced a 2.31-fold longer recovery time than their counter parts. This finding is supported by studies in Gondar University Comprehensive Specialized Hospital (Yismaw, Gelagay et al. 2022), China (Xie, Shu et al. 2022), and Saudi Arabia (Alfarwati, Alamri et al. 2019). C/S delivery impairs lung fluid clearance, surfactant production, and increases the risk of respiratory complications, all of which extend recovery time (Yeganegi, Bahrami et al. 2024).

This study highlights the lack of information on the Time to recovery and its predictors among neonatal respiratory distress. The results can help predict recovery times based on prenatal history and clinical care, aiding decision-making in healthcare facilities and informing the management of neonatal respiratory distress.

7. Strength and Limitations of the study

Since the data were collected from secondary sources, some important predictors, such as socioeconomic factors such as nutritional status of mother, educational level,House hold income,Cultural and social practice and birth interval, might be missed, which may have a significant effect on recovery time from RD.

Despite those draw backs, the current study used relatively a large sample and relatively muti scope level from other study conducted in Ethiopia and using Kobo plate form for data collection.

8. Conclusion

The time to recovery of this study was moderately comparable as compared to the previous studies. The determinants that were independently associated with time to recovery of respiratory distress were,Hypoglycemia,PNA,C/S delivery and PROM-were being in critical conditions and delay in recognition of such illness at health care level follows further damage.The aforementioned predictors could be used to identify neonates with respiratory distress who are at risk of developing a long-term illness and guide prompt referral to hospitals.

Direct oxygen, and Antibiotics have helping effect during management of NRD because of shorten recovery period.This will also provide clinicians with prognostic information, as longer recovery times have economic and social implications in resource limited countries like Ethiopia.

9. Recommendations

9.1 Based on the present study findings we would like to recommend the following: For government level/policymakers

Increase/create public awareness about the average length of hospital stay of neonatal respiratory distress and about identified factors that prolong the time to recovery of neonatal respiratory distress. Hopefully, this will provide prognostic information to clinicians and families as longer recovery time has economic and social implications

on the family in our country. Maintain sound referral system including transportation to avoid delay, and improve/fulfill all diagnostic facilities in all hospitals to enable early recognition of illness.

9.2 For health care providers and researchers

Factors like, Hypoglycemia, PNA, C/S delivery and PROM, are being in critical condition, and delay in recognition of illness could be used for early identification (early diagnosis and management as well) of neonates with respiratory distress at risk for protracted illness and could guide prompt referral to higher centers in primary health sectors. Health providers should arrange appropriate management and follow-ups like Antibiotics and direct oxygen which shorten recovery time and Apply. Future research should consider the time to recovery and determinant factors for preterm, term and post term neonate in a separated/isolated way since they have different characteristics in many ways. Besides, further studies in different geographical areas should be needed to recognize different factors in different ways.Time to recovery of NRD in country level with clinical trial with In specifically mild, moderate and sever form of NRD.

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11.ANNEX

SALALE UNIVERSITY

COLLEGE OF HEALTH SCEINCES

Consent form

Declaration of informed voluntary consent

I have read the participant information sheet ,I have clearly understood the purpose of the research, the procedure, the risks and benefits, issue of confidentiality, the right of participating, the contact address for any quires. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that hospital has the right to withdraw from the study at any time. I also informed that the hospital has the right to stop this study from being conducted if any unethical procedures are observed during data collection process in the hospital's premises. There for declare my voluntary consent on behalf of Selale university comprehensive specialized hospital management and Dera Primary Hospital to allow this study to be conducted in the hospital with my signature.

Nameof medical director/CEO……..signature……date……

principal investigator…….signature……..date……

Name of advisor: - DEJENE E. (BSc, MSc, Asst. professor) and Mr. MUKEMIL A.(BSc, MSc)

Name of the organization: Selale University, College of Health Sciences, School of Midwifery.

Name of the Sponsor: Oromia regional health bureau.

Title of the Research Project: - Incidence and predictors of time to recovery among neonates admitted with diagnosis of respiratory distress in NICU at Noreth Shoa Zone Selected Public Hospitals ,North Shoa,Oromia,Ethiopia 2023/24.

Confidentiality: The information collected from this research will be kept confidential, all records will be kept strictly confidential. Data collection tool will be identified by number or otherwise coded to protect any information that could be used to identify participants.

.If you have questions, complaints or concerns about this study, you can contact the principal investigator: Ahmed Moss a

Cell Phone; 0923374777

Email address :ahmedmahirk@gm ail.com

Annex: 1

1.1. Questionnaire English version

Questioners

Question-number……..name of hospital…….

Name and signature of data collector……..

Date ……

Section: I base line socio-demographic characteristics of study participants.

Table 5 base line socio-demographic characteristics of study participants

NO	question	Coding and categories	Remark
101	Age of mother(year)	……	
102	Mothernal residency	1.urban 2.rural	

.Section II Obstetric and gynecologic factors

Table 6 obstetric and gynecologic factors

No	QUESTION	Coding And Categories	REMARK

201	Had ANC in this pregnancy	1.yes 2.no	
202	Parity	1.I 2.II-IV 3.>=V	
203	Complication in this pregnancy	1.YES 2.NO	
204. If yes for 203	Types of complication	1. PROM 2. A.P 3. P.P 4. others	
205	Previous bad obstetric history	1.YES 2.NO	
206	Type of pregnancy	1.SINGLETONE 2.MULTIPLE	
207	Onset of labor	1.elective C/S 2.spontaneous 3.induce	
208	Place of birth	1.the same health facility 2.refer-from other facility	
209	Mode of delivery	1.SVD 2.C/S 3.Instrumental assisted delivery	

Section III Mothernal Medical condition

Table 7 maternal medical condition

NO	Questions	Coding and categories	Remark
301	Pre-eclampsia	1.yes 2.no	
302	DM	1.yes 2.no	
303	HIV/AIDS	1.yes 2.no	
304	PROM	1. Yes 2. no	

305	others	1.yes 2.no	

Section IV neonatal related factor

Table 8 neonatal and interventional related factor

NO	Questions	Coding and categories	Remark
401	Sex of neonate	1.male 2.female	
402	Delivery date	……..	
403	Admission date	……..	
404	Gestational age	1.Post term 2.Term 3.late Preterm 4.very preterm	
405	Weight for gestational age at birth	1.SGA 2.AGA 3.LGA	
406	Weight of neonate	1.1000-1499gm 2.1500-2499gm 3.2500-3999gm 4.>=4000gm	
407	First minute apgar score	1.>=7 2.<7	
408	Fifth minute apgar score	1.>=7 2.<7	
409	New born cry immediately after birth	1.yes 2.no	
450	Bag and mask ventilation at birth	1.yes 2.no	
451	New born temperature with in 1 hr at birth	1.<36.5 2.36.5-37.5 3.>37.5	
452	PNA diagnosed at birth	1.yes 2.no	
453	RD diagnosed at birth	1.yes 2.no	

454	Hypothermia diagnosed at admission	1.yes 2.no	
455	Hypoglycemia diagnosed at admission	1.yes 2.no	
456	jaundice	1.yes 2.no	
457	Sepsis diagnosed at admission	1.yes 2.no	
458	Breast feeding	1.yes 2.no	
459	MAS	1.yes 2.no	

Table 9 intervention and medical errors

501	heated with radiant warmer	1.yes 2.no	
502	Intravenous fluid with cagluconate	1.yes 2.no	
503	ON CPAP	1.yes 2.no	
504	Direct oxygen	1.yes 2.no	
505	On antibiotics	1.yes 2.no	

Section :V End line participant's information

Table 9.End line Respiratory distress neonate's information

NO	Questions	Coding and categories	Remark
50	Dateof/improvemet/discha	…….	

1	rg	.	
502	Length of stay(in days)	……in days	
503	Discharge status	1.died 2.transfer out 3.loss to follow up 4.recovered	

Statement of declaration

By my signature below, I declare and affirm that this thesis is my own work. I have followed all ethical principles of scholarship in the preparation and literature review. All scholarly matter that is included in the thesis has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this paper. This thesis is submitted in partial fulfillment of the requirement for a graduate degree from the Salale University at College of Health Sciences, department of Midwifery. In the preparation of thesis, I hope I was follow the same protocol that we have been used in proposal preparation such as during data collection, data analysis and completion of the thesis.

Studentname:AhmedMossa

Signature: _____ Date: _____

Place of submission: Salale University Date of submission: _____

Advisors approval

This is to certify that the research project entitled “incidence and predictors of time to recovery among Neonates Admitted with diagnosis of respiratory distress in NICU at North Shoa Zone selected Public Hospitals, Oromia, Ethiopia, 2024. Retrospective cohort Study” submitted in partial fulfilment of the requirements for the degree of Master with specialization in Maternal and Neonatal health has been carried out by Ahmed Moss a, under our supervision. Therefore, we recommend that the student has fulfilled the requirements and hence hereby can submit the research proposal to the department for defense. Approved by:

1. **Dejene Edosa** 

12/5/2024

Main Advisor Signature Date

2. _____ _____

_____

Co-Advisor Signature Date

3. _____ _____

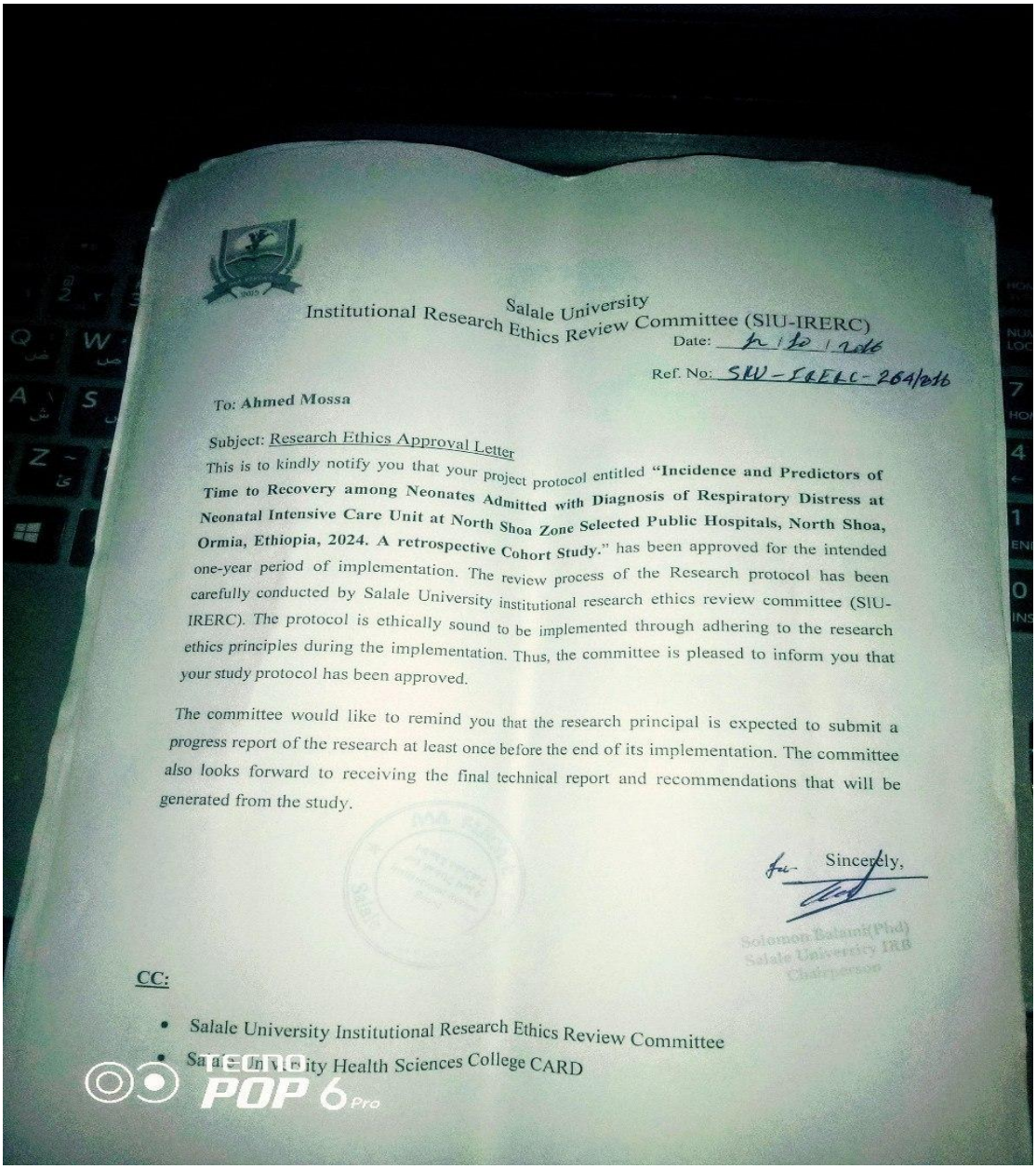
_____

Proposal Reviewer Signature

Date

Annex: 2

Research Ethics Approval Letter of Salale University Colleadge of Health Science Research Ethics Review Commite



Salale University
Institutional Research Ethics Review Committee (SIU-IRERC)

Date: 2/10/2016

Ref. No: SIU-IRERC-264/2016

To: **Ahmed Mossa**

Subject: Research Ethics Approval Letter

This is to kindly notify you that your project protocol entitled **"Incidence and Predictors of Time to Recovery among Neonates Admitted with Diagnosis of Respiratory Distress at Neonatal Intensive Care Unit at North Shoa Zone Selected Public Hospitals, North Shoa, Ormia, Ethiopia, 2024. A retrospective Cohort Study."** has been approved for the intended one-year period of implementation. The review process of the Research protocol has been carefully conducted by Salale University institutional research ethics review committee (SIU-IRERC). The protocol is ethically sound to be implemented through adhering to the research ethics principles during the implementation. Thus, the committee is pleased to inform you that your study protocol has been approved.

The committee would like to remind you that the research principal is expected to submit a progress report of the research at least once before the end of its implementation. The committee also looks forward to receiving the final technical report and recommendations that will be generated from the study.

Sincerely,

Solomon Balami(Phd)
Salale University IRB
Chairperson

CC:

- Salale University Institutional Research Ethics Review Committee
- Salale University Health Sciences College CARD