

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCE
SCHOOL OF NURSING AND MIDWIFERY
DEPARTMENT OF NURSING AND MIDWIFERY**

**SURVIVAL STATUS AND PREDICTORS OF MORTALITY AMONG
NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT IN
DESSIE REFERRAL HOSPITAL, NORTH EAST ETHIOPIA, 2021. A
RETROSPECTIVE COHORT STUDY**

BY: MOHAMMED KEBEDE (BSCN)

ADISOR: Dr.GIRUM SEBSIBE (MSC, PHD)

FEVEN MULUGETA (BSC, MSC)

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Name of principal investigator	Mohammed Kebede (BSC)
Name of advisors	Dr. Girum Sebsibe (MSC, PHD) Cell phone: +251-920856732 E-mail: girumseb@gmail.com
	Mrs. Feven Mulugeta (BSC, MSc) Mobile: +251910712396 Email: fevishome@gmail.com
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Address of investigator	Telephone: +2519 13803674 E-mail: mohama26.mk@gmail.com

Approval sheet by the board of examiners

I, the undersigned MSc student, declare that I have submitted my original work entitled with Survival status and predictors of mortality among neonates admitted to neonatal intensive care unit in Dessie Referral Hospital, Northeast Ethiopia, 2021 for examination.

Submitted by:

Mohammed Kebede (BSc) _____

Name of student Signature Date

This thesis by Mohammed Kebede is accepted in its present form by the board of examiners as satisfying thesis for degree of masters in pediatrics and child health nursing.

Approved by

EXAMINER: _____

Nigusie Tadele (Assistant Professor) Signature Date

ADVISORS:

Dr. Girum Sebsibe (MSC, PHD) _____

Name of major advisor Signature Date

Mrs. Feven Mulugeta (BSc, MSc) _____

Name of co -Advisor Signature Date

DEPARTMENT HEAD

Name _____

Nigusie Tadele (Assistant Professor) Signature Date

STATEMENT OF DECLARATION

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INVESTIGATOR

Name	Signature	Date
Mohammed Kebede	_____	_____

ADVISORS:

Dr.Girum Sebsibe (MSC, PHD)	_____	_____
-----------------------------	-------	-------

Name of major advisor	Signature	Date
Mrs. Feven Mulugeta (BSc, MSc)	_____	_____

Name of co -Advisor	Signature	Date
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ABBREVIATIONS AND ACRONYMS

AHR - Adjusted Hazard Ratio

AIDS - Acquired Immune Deficiency Syndrome

ANC - Antenatal Care

AOR - Adjusted Odds Ratio

APGAR - Appearance, Pulse, Grimace, Activity and Respiration

DM - Diabetic Miletus

EDHS - Ethiopian Demographic and Health Survey

EVLBW - Extremely Very Low Birth Weight

HIV - Human Immunodeficiency Virus

HMD – Hyaline Membrane Diseases

HSTP - Health Sector Transformation Plan

IDMs – Infant from Diabetic Mothers

MDG4 – Millennium Development Goal 4

MAS – Meconium Aspiration Syndrome

NICU - Neonatal Intensive Care Unit

NBW – Normal Birth Weight

NMR - Neonatal Mortality Rate

PNA – Prenatal Asphyxia

RDS – Respiratory Distress Syndrome

SDG – Sustainable Developmental Goal

SVD – Spontaneous Vaginal Delivery

U5MR – Under Five Mortality Rate

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ABSTRACT

Background: The first 28-days of life, particularly the day of birth, are the most challenging and vulnerable time for a child's survival and health. Neonatal deaths as a share of under-five deaths decreased more slowly than mortality among children aged 1–59 months and accounted for 47 percent of all under-five deaths. Moreover, Ethiopia is still on the 4th and 2nd rank of global and sub-Saharan Africa neonatal mortality rate, respectively, which indicates neonatal death is a critical problem which needs farther studying of the underline predictors. Even though, some studies were conducted on predictors and determinants of neonatal mortality in Ethiopia, little is known about the time to neonatal death and its predictors. Therefore, this study aimed to assess the survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital. **Objectives:** To determine the survival status and predictors of mortality among neonates admitted to NICU from 01/01/2018-31/12/2020 in Dessie Referral Hospital, Northeast Ethiopia, 2021. **Methods:** An institution-based retrospective cohort study was used among 542 neonates admitted from 2018-2020 in NICU of Dessie Referral Hospital, Northeast Ethiopia. Medical record numbers were obtained from patient register logbooks. Then data was collected from patient cards by using a systematic sampling method with pretested checklist. Data was entered using Epi-data 4.6 and analyzed using STATA 16. Kaplan Meier was used to estimating median survival time and cumulative probability of survival, and the log-rank test was used to compare survival curves. The Cox proportional hazard regression model was used to analyze the relationship between independent and outcome variables. **Results:** Out of 542 eligible participant neonates, 104 (19.19%) died with an overall incidence rate of 35.54 (95%CI: 29.33, 40.08) deaths/1000 neonate-days observations. The overall median survival time was 14 days, with an overall cumulative survival probability of 36.10%. Low birth weight (AHR: 3.03, 95%CI: 1.53, 6.00), prolonged labor (AHR: 3.32, 95%CI: 1.46,7.53), primiparous mother (AHR: 2.23, 95%CI: 1.44, 3.45), preeclampsia (AHR: 2.17, 95%CI: 1.10, 4.25), Diabetic mother (AHR: 3.74, 95%CI: 1.57, 8.90), PNA (AHR: 2.61, 95%CI: 1.11, 6.13), and neonatal anemia (AHR: 9.14, 95%CI: 3.33, 25.08) were independent predictors of death. **Conclusion:** The incidence of death was 35.54 per 1000 neonate-day and LBW, primipara mother, prolonged labor, preeclampsia, maternal DM, PNA, neonatal anemia were identified as independent predictors of time to death of neonates. **Keywords:** Neonate, Survival Status, Neonatal Mortality, Predictors, Time to Death

1. INTRODUCTION

1.1 Background

In the first 28 days of life, infants are known as neonates and are the most critical age for child survival. The death of infants within the 28 days of life is called neonatal mortality and is stated as neonatal deaths/1000 live births. It is estimated that worldwide, 2.5 million neonatal death occur each year, contributing 47% of under-five mortality. Among deaths, close to three-quarters of all neonatal deaths occur in the first week after birth, and 36% die on the day they are born (1).

Globally, an estimated 19 million newborn babies suffer from preterm birth, intrapartum-related brain insults, severe bacterial infection, and pathological jaundice, which causes mortality and survival with long-term complications every year (2). In developing countries, prematurity (39.8%), perinatal asphyxia (20.8%), neonatal sepsis (17.1%), and congenital malformation (15.7%) were the major cause of neonatal deaths (3).

In sub-Saharan Africa, infections, birth asphyxia, complications of preterm birth, and low birth weight are the most common cause of neonatal mortality. Five countries shared 50% of neonatal death in this region; Nigeria, the Democratic Republic of Congo, Ethiopia, Tanzania, and Uganda (4). Moreover, in East Africa, a study showed that home births, mothers without an education and mothers whose husbands decided on contraceptive practices, and rural residency are predictors of neonatal mortality (5).

Between 1990 and 2017, the estimated global neonatal death fell by half from 5 million to 2.5 million and the mortality rate decreased from 37 deaths/1,000 live births to 18 (6). Despite decreasing neonatal mortality globally, marked differences exist across regions and countries. For example, in 2017, the highest neonatal mortality was found in sub-Saharan Africa, with 27 deaths/1,000 live births. Neonates born in this region had 9 times the risk of death in the first month than neonates in high-income countries. Likewise, the neonatal mortality rate ranged from 1 death per 1,000 live births to 44 deaths across countries. (1).

Ethiopia is the sixth among ten countries with highest neonatal death numbers with 87800 deaths annually and showed slow progress in reducing neonatal mortality rate (NMR) (2). According to the 2019 Ethiopia Mini Demographic and Health Survey (2019 EMDHS) report, Ethiopia's

neonatal mortality rate is 30 per 1000 live birth (7). Moreover, a study done in Amhara Regional State Referral Hospitals investigated that NMR per 1000 live birth was 27 (8).

In Ethiopia, studies showed that parental residency, the length of stay in NICU, low birth weight, prematurity, respiratory distress syndrome (RDS), perinatal asphyxia (PNA), congenital malformations, meconium aspiration syndrome (MAS), low 5min Apgar score, time of initiation of breastfeeding, and hyperthermia, were predictors of neonatal mortality in the neonatal intensive care unit (NICU) (9,10).

1.2 Statement of the Problem

The first 28-days of life, particularly the day of birth, are the most challenging and vulnerable time for a child's survival and health. Every day, an approximated 7,300 newborns die globally from complications of prematurity, intrapartum related deaths, and neonatal infections, and most of these causes are preventable and treatable (11). Worldwide around 2.4 million neonates died in 2019, with the highest neonatal mortality rate in sub-Saharan Africa and South Asia (12,13). Among those deaths, 99000 were from Ethiopia, which holds the 4th rank globally next to India, Nigeria, and Pakistan (13).

According to Ethiopia demographic and health survey (EDHS 2016) report, in Ethiopia, 1 in 35 children dies in the first month of life. This report also found that shorter intervals between births (< 2 years gap between birth), being a boy newborn, being small or very small newborn at birth, born from women age 34 or older, born from women of age less than 18, and born from mother of high parity (birth order higher than three) were the contributed factors of those deaths (14).

Despite the declining global child mortality rate, Sub-Saharan Africa remains with the highest under-five mortality rate (U5MR), and 39 percent of global newborn deaths occurred in this region (1,15). Two-thirds of neonatal mortality is reported from 12 countries, six of which are in sub-Saharan Africa with a rate of 30 or more deaths per 1 000 live birth (16). Also, there is a difference in neonatal survival between the poorest and the wealthiest regions and countries. In sub-Saharan Africa (1 in 37) and in Europe and Northern America (1 in 333) child die in the neonatal period (1). Moreover, neonatal deaths as a share of under-five deaths decreased more slowly than mortality among children aged 1–59 months and accounted for 47 percent of all under-five deaths (1,17).

Ethiopia has well achieved its target for MDG 4, reducing child mortality by two-thirds, before three years to the target year 2015; however, its achievement in reducing neonatal mortality remains unchanged (30 per 1000 live births) (7,18) and is still on the 4th and 2nd rank of global and sub-Saharan Africa neonatal mortality rate, respectively, which indicates neonatal death is a critical problem which needs farther studying of the underline predictors (13). The Ethiopian government showed its effort to improve neonate's survival by including pronounced life-saving interventions in its national strategy for Newborn and Child Survival and Health Sector

Transformation Plan (HSTP) (19,20). Regardless of these efforts, neonatal mortality is still high and needs further investigation of the root causes.

In the era of Sustainable developmental goal (SDG), decreasing neonatal mortality is an integral part of goal 3 to end preventable deaths of newborns and under-five children to reduce neonatal death to at least 12/1,000 live births by 2030 (1,6,11,17). However, with the current neonatal death rate trend, Ethiopia needs to accelerate at least 2 times the current reduction rate of progress to meet the NMR targeted by SDG 2030 (6,17). Therefore investigating the predictors of time to neonatal death is the key to attain the goal.

In Ethiopia, some studies were conducted on the predictors and determinants of neonatal mortality. However, little is known about the time to deaths of neonates and its predictors. This study will also find the median survival time of neonates and their predictors. Moreover, no published study is found on a similar topic in the study area as my literature review. Therefore this study is important to show the incidence density rate of neonatal mortality and its predictors in the study area. Furthermore, maternal medical condition predictors are added in detail in this study as compared to other studies conducted in Ethiopia. Currently, reducing neonatal mortality is the global as well as an Ethiopian priority health issue. Therefore, this study aimed to assess the survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital.

1.3 Significance of the Study

At this time, studying of neonatal mortality and its predictors is very important because, reducing neonatal mortality is a prioritized issue in the world as well as in Ethiopia as part of the third Sustainable Development Goal (SDG), to end preventable child deaths. Therefore to achieve this goal, an understanding of the predictors of neonatal mortality will require (6).

This study will contribute to the implementation of global and national intended strategies and programs towards reducing NMR by providing data that is essential in forwarding planning, especially budgeting and facilities, staffing, and training with the aim of improving the outcome of neonates in the healthcare settings.

This study will use as baseline-information for future researchers who will be interested to do their research on related topics. It will also useful for health policymakers to design appropriate policies, strategies, and interventions.

Findings from this study in the study area will also offer input to decision-makers, program implementers, monitors, and evaluators, to advance better maternal and newborn care. It also improves mothers' awareness about predictors of neonatal mortality and the importance of early care-seeking behavior and birth preparedness.

The study results will be useful for health professionals in identifying predictors of time to death of neonates and to take intervention accordingly. This study will also increase the nursing knowledge and nursing practice, and promote nursing education and research.

2. LITERATURE REVIEW

2.1. The Magnitude of Neonatal Mortality in NICU

Worldwide, an estimated 2.5 million newborns, approximately 7,000 every day, died in the first 28 days of life in 2017 (1). Among these deaths, 98% occur in low-resource countries, including Ethiopia (21). Thus, around three-quarters of all newborn deaths is early neonatal death in the first week of life. In addition, the shared neonatal mortality among under-five deaths increased from 40 percent in 1990 to 47 percent in 2017 (1), indicating that currently, around half of under-five death occurred in the neonatal period.

A systematic and meta-analysis study in the NICU of Iran showed that 11.4 percent of neonates died (22). Another Hospital-based prospective and retrospective study in India revealed that the overall neonatal mortality rate was 9.73 percent (23) and 10.4 percent (24). UNICEF's report in 2015 showed that the incidence of neonatal mortality in Afghanistan was 36 per 1000 live birth (25). Different studies in Africa reported that neonatal mortality rate was 22% in rural Ugandan NICU (26), 14.2% in Nigeria Enugu State University Teaching Hospital (27), 10.7 % in Northern Tanzanian neonatal care unit (NCU), in which 56.7% of those deaths occurred in the first 24 hours, and 91.6% within the first week of life (28). Similarly, a study done in Mauritania revealed that 34.7% of neonates died, and among those deaths, 71.3% were during the first six days of life (29). The incidence of NM in the Democratic Republic of Congo was 94 per 1000 live births (30).

In Ethiopia, the neonatal mortality rate has fallen from 39 to 29 deaths /1,000 births between 2015 and 2016 but has remained constant since 2016-2019 (7). A study conducted in NICU at Arba Minch General Hospital discovered that the IDR of neonatal mortality was 31.6/1,000 neonate days. The 1st day of survival probability was 96.1%. This study also showed that survival probability at the 7th, 14th, and 21st day was 75%, 69.9%, and 66.2%, respectively, with an overall median survival time of 6 days (31). Also, a study in Jimma University Medical center showed that the incidence of NM was 30 deaths per 1,000 institutional live births (10) and 27 per 1000 neonates-days (32). A study done in the University of Gondar Comprehensive Specialized Hospital (UoGCSH) revealed that 14% of the neonatal death was in the first 24 hrs, 60% in the first 3 days, and almost 84% in the first 1 week of life. Also, the failure probability was 13.79%, 59.77%, 83.91%, and 97.70% in the 1st, 3rd, 7th, and 14th days of hospital stay

with an incidence rate of 23.81, 33.92, 31.48, and 28.90 deaths per 1000 neonate-days observation, respectively (33). Another study conducted in the Tigray region revealed that the neonatal mortality incidence was 62.5 per 1000 live birth. Similarly, studies done in the NICU of Arba Minch General Hospital and Debre Markos Referral Hospital discovered 20.8% and 21.3% deaths, respectively (31,34). The failure probability at the 1st, 3rd, and 7th, days of hospital stay was 19.4%, 58.2%, and 91%, respectively, and there was no failure after 16 days(31). All the above findings indicated that NM incidence in Ethiopia is far from the united nations SDG targeted to achieve 12 or fewer neonatal death per 1000 live birth by2030 (35).

Studies done in Ethiopia showed that survival time significantly differed among the covariates of neonatal age at admission, 1st and 5th minute APGAR score, breastfeeding initiation, place of delivery, prolonged Labor, residence, PROM, and birth weight with log-rank test (p-value<0.05). However, there was no survival time difference between categories of sex, maternal age, ANC follow-up, mode of delivery, GA, number of parity, and multiple pregnancies with a p-value >0.05 (31,36).

2.2 Predictors of Mortality in Neonates

2.2.1 Socio demographic factors

Different findings revealed that low birth weight, gestational age, maternal age at birth, and residence were the most common Socio-demographic predictors of neonatal mortality (24,28,31,37–40). For example, studies showed that neonatal survival was significantly associated with low birth weight (< 2500 gm) (9,24,29,37,38,40–44).

A study in the Democratic Republic of Congo revealed that neonates born from mothers age less than 18 and more than 35 years had a high risk of death (OR=9.65) (45). A meta-analysis study showed that Nulliparous/age <18 years (AOR: 2.07) (46). In Ethiopia, newborns from mothers less than or equal to18 years old accounts for most of the neonatal death compared to babies born from mothers aged 35 years or above (AHR: 12.6) (47). Another study showed that neonates born from mothers of advanced age were a higher risk of death (AHR=2.60) (8).

Regarding gestational age, the risk of death in preterm (before 34) was 4.5% higher than babies born after 34 weeks, and the risk becomes higher at 32 weeks (10.17 times) (P<0.0001) (24). In another study, the deaths of preterm babies were higher (24.5%) than deaths of term babies (7.1%) (38). Research done in South Africa reported that being preterm delivery (OR=2.975)

was a significant predictor of neonatal mortality (43). Similarly, a study showed that neonatal mortality tends to occur with gestational age lower than 37 weeks ($p = 0.000$) than gestational age greater than 37 weeks (37). In other findings being preterm was significantly associated with increasing time to neonatal death (Pooled Hazard Ratio (PHR): 3.78) (48).

A study conducted in sub-Saharan Africa revealed that rural residence was a significant predictor of time to neonatal death (PHR: 1.91) (48). Neonatal death was high both in the early and late neonatal periods in rural areas than in urban area (44). Research done in South Africa reported that being male babies (OR=1.633) was a significant predictor of NM (43). But research conducted in Nigeria showed that gender was not a significant predictor of neonatal mortality ($p > 0.05$) (37).

2.2.2 Obstetrics and gynecologic factors

Different studies in different countries discovered many causes of neonatal mortality and survival and obstetrics and gynecology predictors were among the major predictor that contribute to neonatal death. A study conducted in Northwestern rural China on predictors of neonatal death revealed that neonatal death was higher among multiparous women (OR= 2.77) (49). A Study done in Sub-Saharan Africa revealed that multiple births (being twins or triplets or more) was independent predictors of time to neonatal death (48). Similarly, studies in Ethiopia showed that multiple pregnancies increased neonatal death risk as compared to a single pregnancy with (AHR=3.96) (8,32).

Concerning Antenatal care (ANC), NMR was higher among mothers who did not receive ANC in the first trimester of pregnancy (OR= 2.49) (49). A Study in the Democratic Republic of Congo also showed that being born from mothers with ANC follow-up <4 was a predictor of NM (OR=9.59) (45). A study in NICU at Referral Hospital in Southern Ethiopia discovered that having no ANC visits during pregnancy significantly increases neonatal deaths with AHR=6.02 (32) and a study done in NICU at Debre Markos Hospital with AHR: 1.9 (34). Research done in Assosa zone and Ayder comprehensive hospital (Mekele) revealed that neonatal mortality was high among primipara mothers neonate (50,51). Another study showed that prolonged rupture of the membrane increases the risk of time to neonatal death with AHR:2.6 (31).

A study from middle-income countries reported that cesarean section was a significant predictor of NM with OR = 1.8 (42). Similarly, a study done in Afar Region Public Hospitals found that

NM was high among those delivered by cesarean section than those delivered by spontaneous vaginal delivery (SVD) with AOR=3.52 (52). However, Southern Ethiopia research revealed a 66% protective effect on neonatal death compared with SVD (32). Besides, a study done in NICU at the University of Gondar Hospital showed that instrumental delivery had a high risk of neonatal mortality with AOR: 2.99 (53). Also, another study showed that NM was higher in assisted delivery compared to SVD (AOR=3.28, P<0.05) (52).

A study conducted in Afghanistan investigated that ANC by a skilled provider (AOR: 0.7), and institutional delivery (AOR: 0.7), had reduced NM (54). Research done in East and West Africa (Mozambique (OR = 1.4), and Niger (OR=2.6),) found that home delivery had a higher risk of neonatal mortality (5). A study done in the NICU of the UoGCSH showed that home delivery (AHR: 2.43) was a statistically significant predictor of time to death of neonates at a p-value \leq 0.05 (33).

2.2.3 Neonatal medical conditions

As investigated by different studies, neonatal medical problems are the primary cause of neonatal mortality. For example, a systematic Review and Meta-Analysis study done in Iran on neonatal mortality in NICU found that (RDS) (31.93%), septicemia (12.66%), and asphyxia (7.58%) were the most common predictors of neonatal mortality (22). Other studies in India and Bangladesh also revealed that RDS (33.6%) (24), PNA (25.3% and 24.3%), and sepsis (25.3% and 21.9%) were predictors of neonatal death, respectively (24,40). Also, research done in Vietnam found that infection (38%), cardio/respiratory disorders (27%), and congenital abnormalities (20%) were the main causes of neonatal deaths (55).

Research done in sub-Saharan Africa discovered that sepsis (PHR: 1.94), PNA (PHR: 2.03), and RDS (PHR: 2.49) were independent predictors of time to neonatal death (48). PNA was an independent predictor of mortality (AOR =5.817) in the study done in tertiary care hospitals of Addis Ababa (56). Likewise, a study done in Dessie Referral Hospital on determinants of NM discovered that RDS (AOR = 3.61), PNA (AOR = 2.27), MAS (AOR = 2.35), and infection (AOR = 2.26) were significantly associated with NM (57).

Low first and 5th minute Apgar score (PHR: 3.47) and neonates who did not initiate breastfeeding within one hour of birth (PHR: 3.77) were independent predictors of time to neonatal death in the study found in sub-Saharan Africa (48). Moreover, neonates for whom breastfeeding was not

initiated within the first 24hours were also more likely to die (AOR=12.16) (9). Studies conducted in public General hospitals of Eastern Ethiopia and Arba Minch General Hospital revealed that the fifth minute APGAR scores ≤ 5 had a higher risk of neonatal death with AHR: 5.2 (9,47).

A study done in NICU of UoGCSH showed that neonates born before 34 weeks had a higher hazard of death (AHR: 3.25) (33). Furthermore, resuscitated neonates had a higher hazard of death than the counterparts with AHR 2.28 (32). Studies showed that fever on admission (AOR=6.68) (9) and hypothermia ($<35.5^{\circ}\text{c}$) on admission (AHR= 1.58) (32) were significantly associated with time to death of neonates.

2.2.4 Maternal medical conditions

Different studies discovered that neonates born to mothers with the medical problem had a low survival rate. In addition, neonatal mortality was higher among neonates born from mothers with a history of illness than neonates born from mothers without a history of illness during pregnancy.

A study in Mozambique found that the prevalence of maternal anemia (49.4%), severe anemia (4.1%) at $p<0.001$, and syphilis (6.6%) were higher in HIV- infected women than in those HIV-uninfected women (40.6% and 1.8%, $p = 0.004$) and (1.8%, $p<0.001$). Likewise, new born anemia was higher among neonate born from HIV-infected mothers (10.6% vs 7.3%, $p = 0.022$) (58). A study done in Amhara Region revealed that the risk of death of neonates born from HIV-positive mothers was higher than those neonates born to HIV-negative mothers (AHR =6.57) (8).

Regarding maternal hypertension and neonatal outcome, a study conducted on 60 mothers with their baby revealed that 73.33% of babies were born as preterm, 76.66% were born as low birth weight, 50% had respiratory distress, 13.33% had PNA with seizure, 20% had meconium aspiration syndrome (MAS), and 38.33% had suspected sepsis (59). All these conditions are the most predictors of neonatal mortality. A study done in Rwanda found that babies born from hypertensive mothers had low birth weight (75.4%), were preterm (59.6%), had intrauterine growth restriction (32.4%).

Research done in India on neonatal outcome in infants born to diabetic mothers found that their neonates had hypoglycemia (54%),RDS (16%), Congenital anomalies (40%), out of which cardiac anomalies (85%) (60). All of these problems are the most predictors of neonatal morbidity and mortality. A study conducted in Nigeria found that hypoglycemia (63.8%) and hyperbilirubinemia (57.4%) were significantly higher in IDMs than non-IDMs (61).

2.3. Conceptual Frameworks

After reviewing different literatures (5, 9, 21, 23, 29-31, 33, 38, 40, 42, 44-51) about predictors of neonatal mortality, the following conceptual frame work is adapted and showing the interaction between sociodemographic, maternal medical condition, obstetrics and gynecological, neonatal medical predictors, and institutional factors and association between dependent and independent variables.

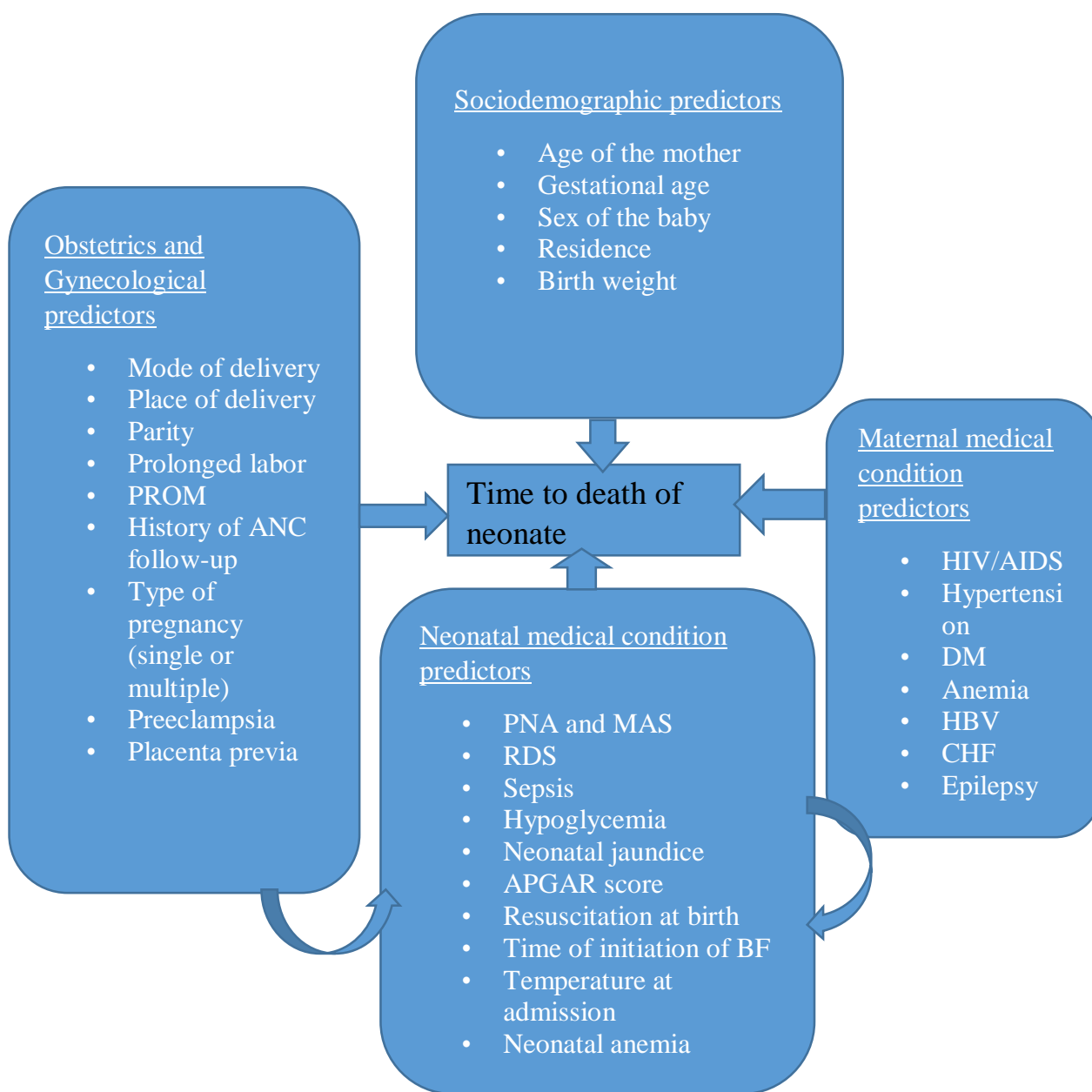


Figure 1: Conceptual framework for the survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital, Northeast Ethiopia, 2021

3. OBJECTIVES

3.1. General Objective

To determine survival status and predictors of mortality among neonates admitted to NICU from 01/01/2018-31/12/2020 in Dessie Referral Hospital, Northeast Ethiopia, 2021.

3.2. Specific Objectives:

To determine survival status of neonates admitted to NICU from 2018-2020 in Dessie Referral Hospital, Northeast Ethiopia, 2021.

To assess survival time difference between groups of variables among admitted neonates to NICU from 2018-2020 in Dessie Referral Hospital, Northeast Ethiopia, 2021.

To identify predictors of time to death among admitted neonates in NICU from 2018-2020 in Dessie Referral Hospital, Northeast Ethiopia, 2021.

4. METHODOLOGY

4.1. Study Area and Period

The study was carried out in Dessie Town, a South Wollo Zone major city under Ethiopian's Amhara Regional State. Dessie Town is located 401km away from Addis Ababa, the capital city of Ethiopia, and 480 km from Bahir Dar, the capital city of Amhara Regional State. It has one governmental and three nongovernmental hospitals. Dessie referral Hospital is the only governmental Hospital with 597 beds in medical, gynecological and obstetrics, surgical, pediatrics, emergency and outpatient department (OPD), and NICU. It serves approximately 7,000,000 population and has 246 nurses, 12 Anesthesiologists, 103 General Physician (GP), 24 surgeons, 34 midwives, and 48 laboratory technicians.

The NICU of Dessie Referral Hospital ward has a maximum of 35 beds with average of 6 patient's daily admission. There are on average 1900-2200 annual admissions of neonates and averagely 32% of admissions are from referrals of other birth centers.

The study was conducted from February 08-March 08/ 2021.

4.2. Study Design

An institution-based retrospective cohort study was conducted among neonates admitted at NICU at Dessie Referral Hospital, Northeast Ethiopia.

4.3. Populations

4.3.1. Source of populations

This study's source of populations were all neonates admitted to NICU at Dessie Referral Hospital.

4.3.2. Study population

The study populations were all selected neonates admitted at NICU from the first of January 2018- the end of December 2020 at Dessie Referral Hospital.

4.3.2. Sample population

All neonates admitted to NICU at Dessie Referral Hospital, from January 2018- December 2020 and neonates who fulfilled the inclusion criteria.

4.4. Eligibility Criteria

4.4.1. Inclusion criteria

All admitted neonates during the study period (01/01/2018-31/12/2020) in NICU at Dessie referral hospital.

4.4.2. Exclusion criteria

Incomplete records of registered neonates, lost record of registered neonates, and registered neonates with an outcome beyond the 28 days of age during the follow-up period.

4.5. Sample Size Determination and Sampling Procedure

4.5.1. Sample size determination

A single population proportion formula was used to estimate the sample size for the survival status (outcome) of neonates, by using:

P = the proportion of neonatal mortality among neonates admitted in NICU, 21.3% from a study done in Debre Markos, Ethiopia (34)

Z $\alpha/2$ = the resultant Z score of 95% CI and $\alpha=0.05$

d= a tolerable margin of error (5%) and N= the minimum sample size required

$$N = \frac{(Z\alpha/2)^2 \times P(1-P)}{(d)^2}$$

$N = (1.96)^2 \times 0.213 \times 0.787 / (0.05)^2 = 258$. After taking a 10 % non-response rate, the final sample size will be 284.

For predictors of neonatal mortality, the double population proportion formula was used to estimate the sample size by using the weight of neonate, RDS, congenital malformation, prematurity, and multiple pregnancies as the major predictor variables. Then, a variable gives the largest sample is used as the independent predictor, which is prematurity (to decrease the role of chance) (Table1). The sample size is calculated by using Epi info version 7.2.3.1 statistical package.

$$\frac{\left[\frac{Z\alpha}{2} \sqrt{\left(1 + \frac{1}{r}\right) P1(1 - P1)} + Z\beta \sqrt{P1(1 - P1) + \frac{P2(1 - P2)}{r}} \right]^2}{(P1 - P2)^2}$$

Table 1: Sample size calculation to assess the survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital, Northeast Ethiopia, 2021

Variable	Assumption	Total sample size	After adding 10% non - response rate
Weight of neonate (low birth weight)	P1=0.312 P2= 0.087	114 (32)	125
RDS	P1= 0.40 P2= 0.165	130 (34)	143
Congenital malformation	P1= 0.06 P2= 0.204	198 (32)	218
Prematurity	P1= 0.286 P2= 0.18	536 (34)	590
Multiple birth	P1= 0.48 P2= 0.12	60 (32)	66

Where:

P1 = is the percent of exposed with the outcome

P2 = is the percent of non-exposed with the outcome

Z $\alpha/2$ = is taking 95% CI, which is 1.96.

ZB = 80% power

And r is the non-exposed to the exposed ratio (1:1)

Finally, the sample size selected for this study was 590.

4.5.2. Sampling technique and procedures

There were 6336 patients admitted to NICU from January 2018-December 2020 when obtaining the number of admission for each year. The medical record number (MRN) of the neonate was used as a sampling frame. The sample was proportionally allocated for each year. Study participants were selected using a systematic random sampling method until obtained the required sample size during the actual data collection period. The study participant neonates of each year were chosen as follows. First, determine the sampling interval (K) value by dividing the total admitted neonate in the study period by the total sample size, which gives $10.74 \approx 11$. Then, each year's desired sample size was calculated by dividing the number of admission within each year by the sampling interval (K). Finally, one number was selected between 1 and 11 at random to start sample selection, and the number is included in the sample (in this case, 9 was selected). Then, the next selection was continued every 11th unit after 9th.

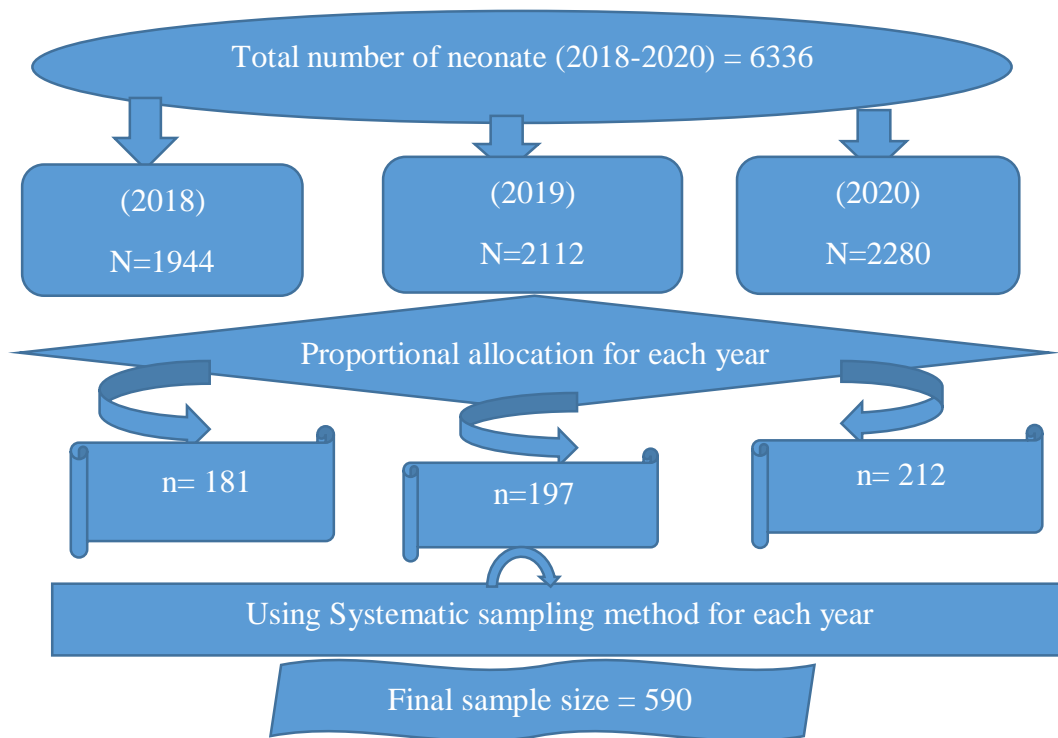


Figure 2: Schematic presentation of sampling procedure to assess the survival status and predictors of neonatal mortality among neonates admitted to NICU in Dessie Referral Hospital, Northeast Ethiopia, 2021

4.6 Study Variables

4.6.1 Dependent variable

Time to death of neonate

4.6.2. Independent variable

Sociodemographic factors: Birth weight, Sex, GA, Maternal age, Residence

Obstetrics and gynecological factors: Mode of delivery, delivery attendant, Place of delivery, Parity, PROM, prolonged labor, preeclampsia, placenta previa, ANC, Multiple Pregnancy, and Place of delivery

Neonatal medical condition factors: PNA, MAS, RDS, HMD, Sepsis, Hypoglycemia, Low Apgar score, having Resuscitation, Temperature at admission, Time of initiation of BF, Neonatal anemia

Maternal medical condition factors: HIV/AIDS, Hypertension, DM, Anemia, HBV, CHF, Epilepsy

4.7 Operational Definitions

Censored: The neonate's outcome during the study period discharge to home (recovered), discharged against medical advice, or transfer out to other health institutions with an unknown outcome.

Follow-up time- The time from admission until either death or censorship occurs.

Survival status: outcome of the neonate; either death or censored

Survival time: Measures the follow-up of time from admission to the occurrence of the outcome (death or censorship).

4.8 Conceptual Definitions

Early neonatal period: The baby considered that after birth, the first 7 days of life

Having ANC follow up- Mother who has a follow up of ≥ 4 times during her pregnancy.

Medical disorders in the mother: Any registered medical diagnosis history of the mother on the neonate's medical record.

Multiparty: Documented maternal parity of >2 on the neonate's medical record.

Late neonatal period: Neonate after 7 days of life after birth

Low APGAR SCORE: A neonate who have an Apgar score of <7 .

Preterm (premature) birth: Neonate born before 37 weeks of gestational age.

Premature rupture of membrane: the rupture of membrane 12 hrs before the onset of labor

Prolonged labor: labor continuing beyond 18 hrs without delivering the baby

4.9 Data Collection Tools and Procedures

The tools were adapted from different literature and modified according to the Ethiopian context (8,10,32–34,44,48). The questionnaire was prepared as a checklist in the English language. The tool consists of sociodemographic characteristics neonates and mothers, maternal and neonatal medical disorders, gynecologic and obstetric factors, date of admission, date of discharge, and

outcome of the neonate. Two BSc nurse data collectors retrospectively reviewed the neonate's medical records that fulfill the inclusion criteria admitted to NICU at Dessie Referral Hospital during the study period. The survival status of patients and predictors were obtained from the medical record. Survival time was obtained by considering the time between the dates of admission to date of discharge (the date of death or censored).

4.10. Data Quality Control

The checklist was pre-tested among 5% of the study participants in the study area (Dessie Referral Hospital) to assure the data quality. The necessary modifications and corrections were made to standardize and ensure its validity. The data collectors and supervisor were senior experienced BSc nurses who are working in NICU (one supervisor and two data collectors were selected). One day, training was given on the purpose of the study, the data collection tool (checklist), data collection methods, and ethical concerns during data collection. The supervisor had monitored the data collection process of the data collectors. The Principal investigator and supervisor had done spot-checking and reviewing the complete checklist by the data collectors to ensure the completeness and consistency of the collected information (data). Consistency was examined through a random selection of cards by the principal investigator.

4.11. Data Processing and Analysis

Data were entered using Epi-Data version 4.6.0 and analyzed by STATA 16 statistical software. Data were cleaned and edited before analysis. Neonates' cohort characteristics of continuous data were described by mean and standard deviation. Categorical data were calculated using frequency distribution. Then, the outcome of each participant neonate was dichotomized into censored or death. Incidence density rate (IDR) was estimated for the entire study period and specified day intervals of hospital stay. Consequently, the NMR within the study period was divided by the total neonate day at hazard on follow-up and reported per 1000 neonate day. Kaplan Meier was used to calculating median survival time cumulative probability of survival. The log-rank test was used to compare survival curves after admission to NICU. Cumulative survival probability at certain time intervals was estimated using a life table. The Cox proportional hazard regression model was used to analyze the relationship between independent and outcome variables. Bivariate analysis was done for all variables and, variables with a p-value ≤ 0.25 (62) were transferred to multivariable analysis. Before multivariate analysis,

multicollinearity was tested using the VIF command to check variable inflation factor (mean VIF=1.62) (table 9). Then proportional hazard assumptions were checked using both Schoenfeld residual test (global test) with a value of $P > \chi^2 = 0.4655$ (table 8) and concordance probability test (Harrell's $c = 0.8286$), which means that the predictive ability of the survival time model for pair of data was 82.86%. Also, Cox proportional hazard model fitness to the data was checked using cox Snell residuals, in which the hazard function follows the 45-degree baseline (figure 13). In conclusion, the final model was fitted the data successfully. In multivariate analysis, any statistical test with a $p < 0.05$ was considered statistically significant. Then, associations were summarized using an adjusted hazard ratio and statistical significances tested at 95% CI. Lastly, the results were presented using texts, tables, and graphs.

4.12. Ethical Considerations

Ethical clearance was obtained from research and ethical review board of Nursing Department, School of Nursing and Midwifery, College of Health Sciences, Addis Ababa University. A formal letter of cooperation from the University was submitted to the hospital administrative body for data collection (Dessie Referral Hospital). Permission was obtained from all concerned bodies in the hospital. Next to these, searching and getting the chosen samples' medical record was managed with the data collectors. Care was taken from disclosing patient's records and confidentiality was maintained by omitting their name and personal identification from the data collection format. Finally, all collected informations was coded and locked in an isolated room before entering the computer and locked by password after entering the computer.

4.13. Dissemination of the Result

The result will be submitted to Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery. Also, the result will be submitted to Dessie Referral Hospital. Further effort will be made to present it at a workshop and conference and publish it on a trustworthy journal.

5. RESULTS

Among 590 neonatal cards, 542 records met the inclusion criteria in the final analysis with a response rate of 91.86%.

5.1. Socio-Demographic Characteristics of the Study Participants

Of 542 study participants, 316 (58.3%) of them were males. More than half of the participants (310 (57.2 %) came from rural areas. Most neonates (401 (73.99%) were admitted to the NICU within 24 hrs of age. The cohort's mean neonatal age at admission to NICU was 2.05 ± 0.12 SD days (95%CI: 1.81, 2.27). The majority of mothers (451(83.21%) were belonging to 20-35 years. Among admitted neonates, 45 (8.3%) of them were in the GA group of very premature (28-32 weeks), of which 33 (73.33%) died, which was more than 3 and 5 times higher than premature (21.25%) and mature neonate (12.95%), respectively. The mean GA was 37.55 ± 0.123 SD weeks (95%CI: 37.3, 37.9). The minimum birth weight was 800 gram and the maximum was 4500 gram with a mean weight of 2651.11 ± 32.56 SD gm (95%CI: 2587.15, 2715.06). Among 542 neonates, 181 were born with <2500 grams of birth weight, which contributes more than half (61 (58.65%) of the total neonatal death.

Table 2: Socio-demographic characteristics of neonate and their mother in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	Total (%)	Survival Status	
			Died (%)	Censored (%)
Sex	Male	316 (58.30)	60 (57.7)	256 (58.45)
	Female	226 (41.70)	44 (42.3)	182 (41.55)
Residency	Rural	310 (57.20)	63 (60.58)	247 (56.39)
	Urban	232 (42.80)	41 (39.42)	191 (43.61)
Maternal age	<20 years	56 (10.33)	12 (11.54)	44 (10.05)
	20-35 years	451 (83.21)	84 (80.77)	367 (83.79)
	>35 years	35 (6.46)	8 (7.69)	27 (6.16)
Neonatal age at admission	<24 hrs.	401 (73.99)	82 (78.85)	319 (72.83)
	1-7	114 (21.03)	17 (16.34)	97 (22.15)
	>7 day	27 (4.98)	5 (4.81)	22 (5.02)
GA in weeks	28-32	45 (8.30)	33 (31.73)	12 (2.74)

	33-36	80 (14.76)	17 (16.35)	62 (14.15)
	≥37	417 (76.94)	54 (51.92)	363 (82.88)
Birth weight in gram	<1000	7 (1.29)	6 (5.77)	1 (0.23)
	1000-1499	35 (6.46)	25 (24.04)	10 (2.28)
	1500-2499	139 (25.65)	30 (28.84)	109 (24.89)
	≥2500	361 (66.61)	43 (41.35)	318 (72.60)

5.2. Obstetric and Gynecological Characteristics of the Study Participants

In this study, 420 (77.49%) of neonates were born through SVD, which contributed 78 (75%) to the total neonatal death. More than half 346 (63.84%) of the study participants had delivered in Hospital. Most (528 (97.42%) of the deliveries were conducted by health professionals. Regarding maternal obstetric and gynecological factors, 104 (19.19%) had PROM, 25 (4.61%) had prolonged labor, and 31 (5.72%) had preeclampsia. More than half 20 (64.52%) of neonates born from preeclampsia mothers died during the follow-up period. Among 104 dead neonates, 60 (57.69%) died from their mother's parity of less than 2. Of the total neonates enrolled in this study, 49 (9.04%) were twin pregnant. This study also showed that neonates born from mothers who had no ANC follow-up were more vulnerable to death (33.33%) than their counterparts (19.03%). (See Table 3).

Table 3: Obstetric and gynecological characteristics of the study participant in NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	Total (%)	Survival Status	
			Died (%)	Censored (%)
Mode of delivery	SVD	420 (77.49)	78 (75)	342 (78.08)
	Instrumental	36 (6.64)	10 (9.62)	26 (5.94)
	Caesarian section	86 (15.87)	16 (15.38)	70 (15.98)
Place of delivery	Hospital	346 (63.84)	62 (59.61)	284 (64.84)
	Health center	182 (33.58)	38 (36.54)	144 (32.88)
	Home	14 (2.58)	4 (3.85)	10 (2.28)
	Health professional	528 (97.42)	100 (96.15)	428 (97.72)

Delivery conducted by	Traditional birth attendance	2 (0.37)	1	1
	Other	12 (2.21)	3 (2.88)	9 (2.05)
PROM	Yes	104 (19.19)	24 (23.08)	80 (18.26)
	No	438 (80.81)	80 (76.92)	358 (81.74)
Prolonged labor	Yes	25 (4.61)	12 (11.54)	13 (2.97)
	No	517 (95.39)	92 (88.46)	425 (97.03)
Preeclampsia	Yes	31 (5.72)	20 (19.23)	11 (2.51)
	No	511 (94.28)	84 (80.77)	427 (97.49)
Placenta Previa	Yes	3 (0.55)	2	1
	No	539 (99.45)	102 (98.08)	437 (99.77)
Number of parity	<2	217 (40.04)	60 (57.69)	157 (35.85)
	2-4	281 (51.85)	40 (38.46)	241 (55.02)
	>4	44 (8.12)	4 (3.85)	40 (9.13)
Multiple pregnancies	Yes	49 (9.04)	13 (12.5)	36 (8.22)
	No	493 (90.96)	91 (87.5)	402 (91.78)
ANC follow-up	Yes	536 (98.89)	102 (98.08)	434 (99.09)
	No	6 (1.11)	2 (1.92)	4 (0.91)

5.3 Maternal Medical Diagnosis of the Study Participants

Among the total mothers enrolled in this study, 14 (2.85%) mothers had HIV/AIDS, and 10 (1.85%) had hepatitis B virus (HBV), but no death was recorded among those mothers neonate. Besides, 10 (1.85%) of mothers had DM, in which 7 (70%) of their neonates died. Furthermore, 2 (0.37%) of mothers had epilepsy, of which all of their neonates died. (See table 4)

Table 4: Maternal medical diagnosis in NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	Total (%)	Survival status	
			Died (%)	Censored (%)
HIV/AIDS	Yes	14 (2.58)		14 (3.17)
	No	528 (97.42)	104(100)	424 (96.80)

Hypertension	Yes	4 (0.74)		4 (0.91)
	No	538 (99.26)	104 (100)	434 (99.07)
Maternal anemia	Yes	2 (0.37)	1 (0.96)	1 (0.23)
	No	540 (99.63)	103 (99.04)	437 (99.77)
DM	Yes	10 (1.85)	7 (6.73)	3 (0.68)
	No	532 (98.15)	97 (93.27)	435 (99.32)
HBV	Yes	10 (1.85)		10 (2.28)
	No	532 (98.15)	104 (100)	428 (97.72)
CHF	Yes	2 (0.37)		2 (0.46)
	No	540 (99.63)	104 (100)	436 (99.54)
Epilepsy	Yes	2 (0.37)	2 (1.92)	
	No	540 (99.63)	100 (98.08)	437 (100)

5.4 Common Medical and Other Diagnosis of Neonates Admitted to NICU

The significant admission medical problems documented among neonates admitted to NICU during the follow-up period were low APGAR score (1st and 5th minute APGAR score <7, 242 (44.65%) and, 128 (20.66%) respectively), sepsis 143 (26.38%), PNA 68 (12.73%), Jaundice 36 (6.83%), MAS 42 (7.75%), and RDS 43 (7.93%). Among admitted neonates with RDS, 32 (74.42%) died, and RDS was the leading cause of death. In this study, sepsis was among a minor killer medical problem, in which 10 (6.7%) of neonates died from 143 neonates. Other common causes of admissions were Bag and mask resuscitation at birth, hypothermia, hypoglycemia, anemia, congenital malformation. (See Table 5)

Table 5: Common medical and other diagnoses of neonates that were admitted to NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	Total (%)	Survival Status	
			Died (%)	Censored (%)
RDS	Yes	43 (7.93)	32 (30.77)	11 (2.51)
	No	499 (92.07)	72 (69.23)	427 (97.49)
Jaundice	Yes	36 (6.83)	8 (7.69)	28 (6.39)
	No	507 (93.17)	96 (92.31)	410 (93.61)

PNA	Yes	68 (12.73)	23 (22.12)	45 (10.27)
	No	473 (87.27)	81 (77.88)	393 (89.73)
MAS	Yes	42 (7.75)	7 (6.73)	35 (7.99)
	No	500 (92.25)	97 (93.27)	403 (92.01)
Sepsis	Yes	143 (26.38)	10 (9.62)	133 (30.37)
	No	399 (73.62)	94 (90.38)	305 (69.63)
Hypothermia	Yes	70 (12.92)	6 (5.77)	64 (14.61)
	No	472 (87.08)	98 (94.23)	374 (85.39)
Hypoglycemia	Yes	46 (8.49)	1 (0.96)	45 (10.27)
	No	496 (91.51)	103 (99.04)	393 (89.73)
Anemia	Yes	18 (3.32)	8 (7.69)	10 (2.28)
	No	524 (96.68)	96 (92.31)	428 (97.72)
Congenital malformation	Yes	33 (6.09)	4 (3.85)	29 (6.62)
	No	509 (93.91)	100 (96.15)	409 (93.38)
Birth trauma	Yes	16 (2.95)	5 (4.81)	11 (2.51)
	No	526 (97.05)	99 (95.19)	427 (97.49)
Bag and mask resuscitation	Yes	106 (19.56)	39 (37.5)	67 (15.30)
	No	436 (80.44)	65 (62.5)	371 (84.70)
Fist minute APGAR score	<7	242 (44.65)	71 (68.27)	171 (39.04)
Fifth minute APGAR score	≥7	300 (55.35)	33 (31.73)	267 (60.96)
Initiation of BF within 1 hr	<7	128 (20.66)	52 (50)	76 (17.35)
	≥	414 (79.34)	52 (50)	362 (82.65)
Initiation of BF within 1 hr	Yes	226 (41.70)	18 (17.31)	208 (47.49)
	No	316 (58.3)	86 (82.69)	230 (52.51)

5.5. Survival Status of Neonate

A total of 542 neonates that were admitted to NICU had been followed from 0 to 28 days. The overall mean hospital stay was 5.631 (95%CI: 5.316, 5.946) with a minimum and maximum follow-up time of 1 and 20 days. In this finding, 104 (19.19%) of the study participant died during the follow-up period. And from this male accounts more than half of the death 60 (57.69%). From neonates included in the analysis, 438 (80.81%) were censored (recovered, discharged for left against medical advice, and referred to other health facilities) at the end of the follow-up. (See figure 3 below).

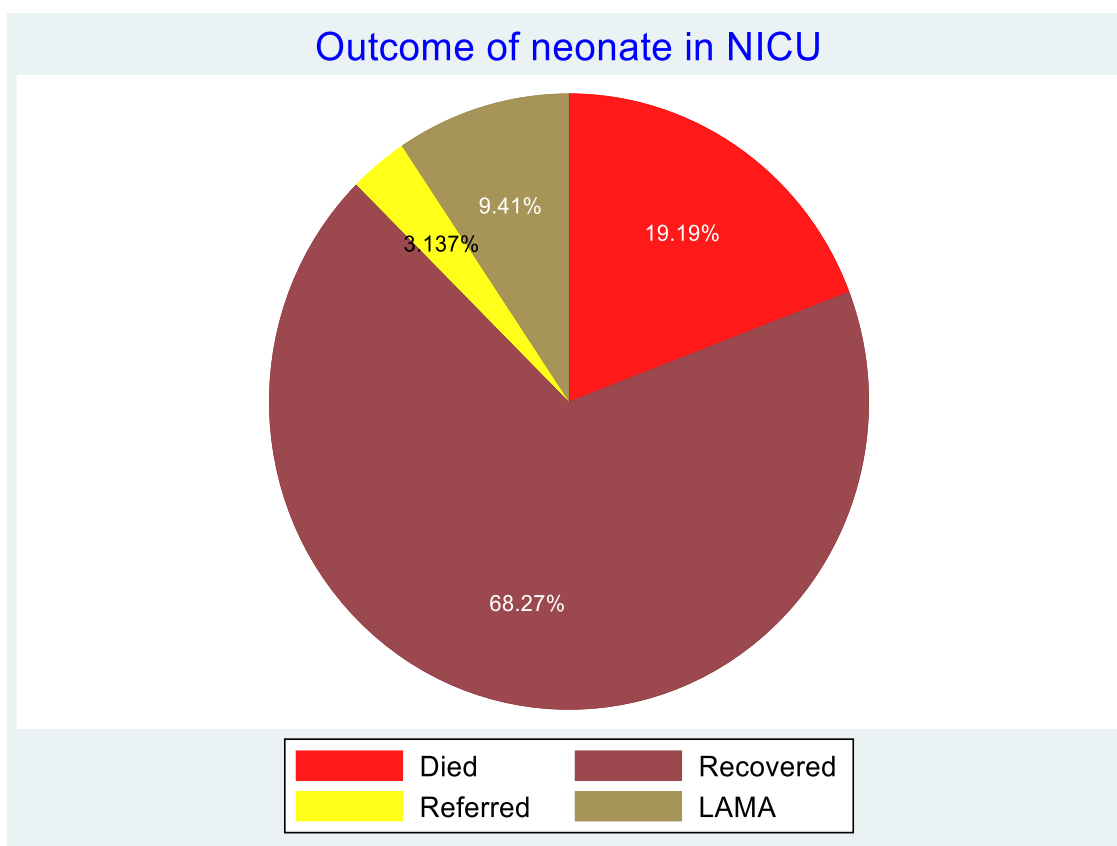


Figure: 3 Outcome of neonates admitted to NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

N.B*LAMA=Left against medical advice

5.5.1. Death/Failure of neonates and overall Kaplan- Meier failure function

The total follow-up was 2926 person-day in this study, with an incidence rate of 35.54 deaths per 1000 person-day observations (95%CI: 29.33, 40.08). Neonates admitted in the first 24 hrs were more likely to die with an incidence rate of 39.61/1000 person-time observations (95%CI: 30.87, 47.60). Incidence of neonatal death was higher in neonates born as very premature (28-32 weeks of GA) with an incidence rate of 107.74/1000 neonate-days observations (95%CI=76.19, 152.36), which is more than three and four times compared to neonates born as premature (33-36 weeks of GA) and mature (>37 weeks) with an incidence rate of 34.29/1000 neonate-days (95%CI: 21.60, 54.42) and 24.22/1000 neonate-days observations (95%CI: 18.55, 31.62), respectively. Similarly, EVLBW and VLBW neonates had a high incidence of neonatal death with 127.66/1000 neonate-days (95%CI: 57.35, 284.15) and 100.04/1000 neonate-days (95%CI: 67.84, 148.59), respectively compared to LBW 37.83/1000 (95%CI: 26.45, 54.11) and NBW 21.91/1000 (95%CI: 16.25, 29.54).

On the 1st day of hospital stay, the hazard probability of neonates was 11 (10.58%) with an incidence rate of 20.29 death per 1000 neonate-days observations (95%CI: 11.24, 36.65). Similarly, the failure probability of neonates at 3rd, 7th, and 14th days of hospital stay were 39 (37.5%), 83 (79.81%), and 103 (99.04%) with an incidence rate of 27.66 (95%CI: 20.21, 37.86), 32.79 (95%CI: 26.45, 40.66), and 35.56 (95%CI: 28.35, 42.21) deaths per 1000 person-days observations, respectively. As shown in the figure below, the Kaplan Meier failure curve increases stepwise during the hospital stay, and there is no death after 16 days of hospital stay. (Figure 4).

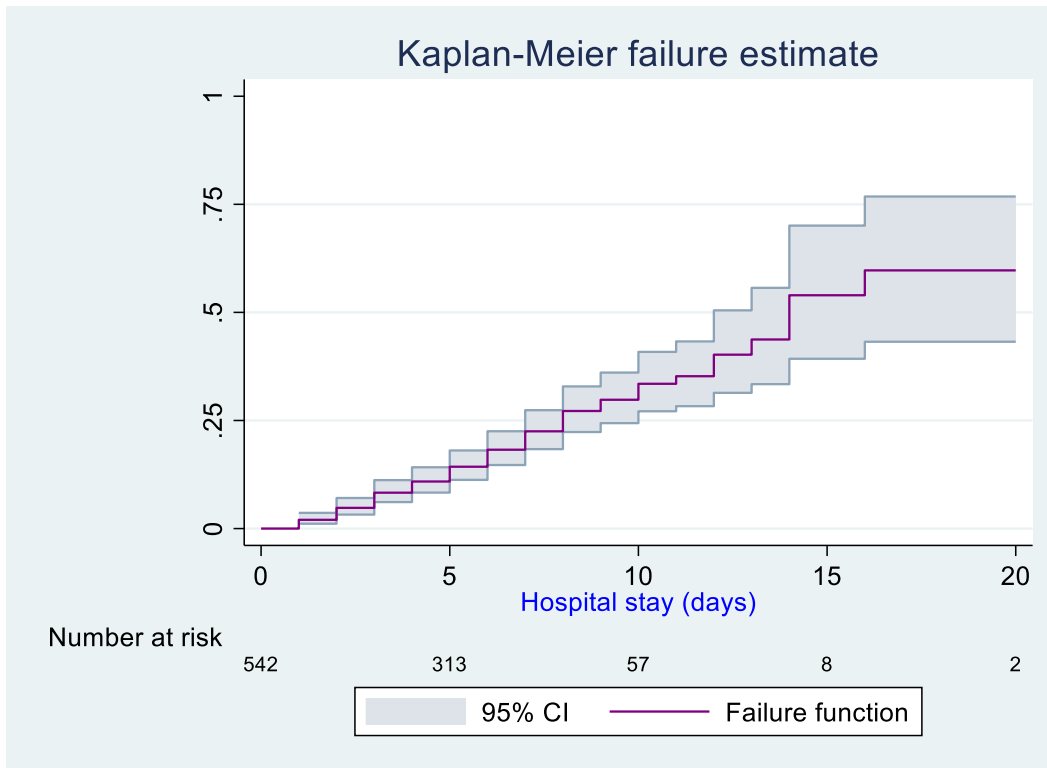


Figure 4: Overall Kaplan-Meier failure estimate of neonate admitted to NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

5.5.2. Overall Kaplan- Meier Survival Function

The overall Kaplan- Meier estimate showed that the probability of survival of neonates was high on the 1st day of admission, which comparatively decreases as follow-up time increases (see figure 5). During the 1st day of hospital stay, a maximum (97.83%) (95%CI: 96.12, 98.80) probability of survival was observed with a standard error of 0.65. The overall median survival time of neonates admitted to NICU in the study was 14 days (95%CI: 12,) with a standard error of 1.511. This study also showed that the probability of neonatal survival at the 7th and 14th day of hospital stay was 75.75% (95%CI: 70.49, 80.20, SD = 2.47) and 42.12% (95%CI: 26.36, 57.08, SD = 8.05), respectively. At the 20 days of hospital stay, the overall survival probability of neonates was 36.10% (95%CI: 19.51, 52.98) with a standard error of 8.87. (See figure 5).

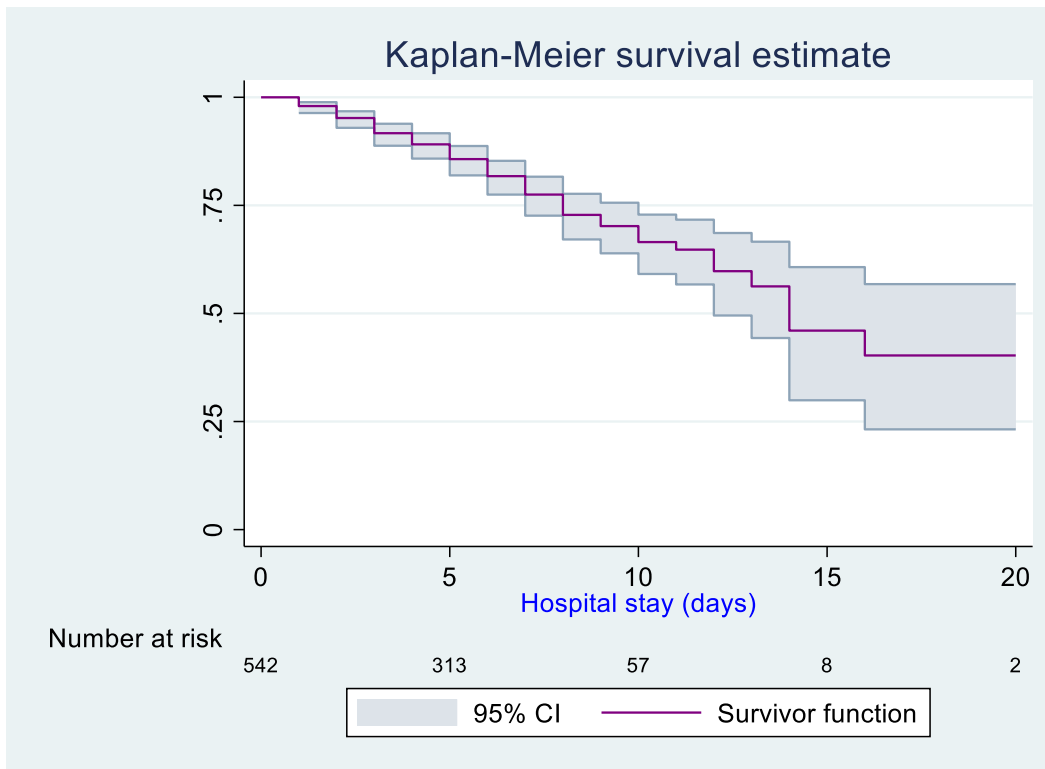


Figure 5: Overall Kaplan-Meier survival estimate of neonate admitted to NICU of Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

5.5.3. Comparison of survival time for different groups of variables

The Kaplan-Meier estimator is a non-parametric statistic used to estimate the survival function (the probability of survival) of right-censored data. Separate graphs Kaplan-Meier survivor functions are used to compare the probability of survival among different categories of variables, and it was constructed as described below. In general, the category defined by the upper curve has a better survival probability than the category defined by the lower curve. The same for the Kaplan-Meier failure (hazard) function is that the category defined by the upper curve has a higher hazard probability than the category defined by the lower curve.

However, the statistical question is whether the observed difference seen on the graph is significant or not. The Cochran-Mantel Haenszel Log-rank test can solve this. The Log-rank test was performed to test the equality of survival curves of different categorical explanatory variables (Table 6). The test statistics with a p-value <0.05 showed that there is a significant difference in survival time for different categorical variables. These variables include neonatal

age at admission, GA, birth weight, number of parity, prolonged labor, preeclampsia, placenta previa, maternal DM, maternal epilepsy, RDS, PNA, sepsis, neonatal anemia, Bag and Mask resuscitation, 1st and 5th minute APGAR score, and time of initiation of breastfeeding.

As showed from the figure plotted below, the Kaplan Maier survival function for prolonged labor had a lower survival time (median survival time of 7 days, 95% CI: 3,) than the counterparts (median survival time of 14 days, (95% CI: 13,) with overall survival probability of 28.71% and 37.19% at the end of the study period respectively. The difference was statistically significant at p-value = 0.0001 (See figure 6)

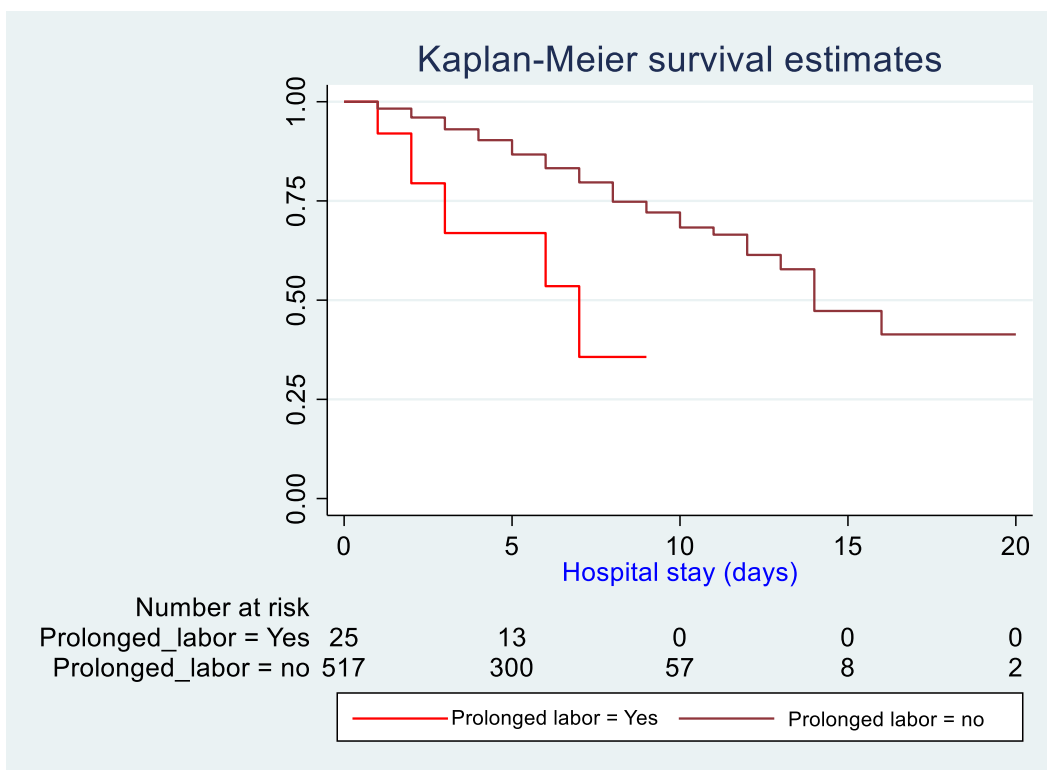


Figure 6: The Kaplan-Meier survival curves compare survival time of neonate with groups of prolonged labor at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020

Likewise, neonates diagnosed with RDS had a lower survival time with 7 days (95% CI: 4, 8) of median survival time compared to those who had not been diagnosed with RDS. At the 20 days of hospital stay, the overall survival of neonates with RDS and without RDS was 14.29% and 39.37%, respectively (Figure 7). This survival time difference was statistically significant with a p-value = 0.0000 (see Table 7).

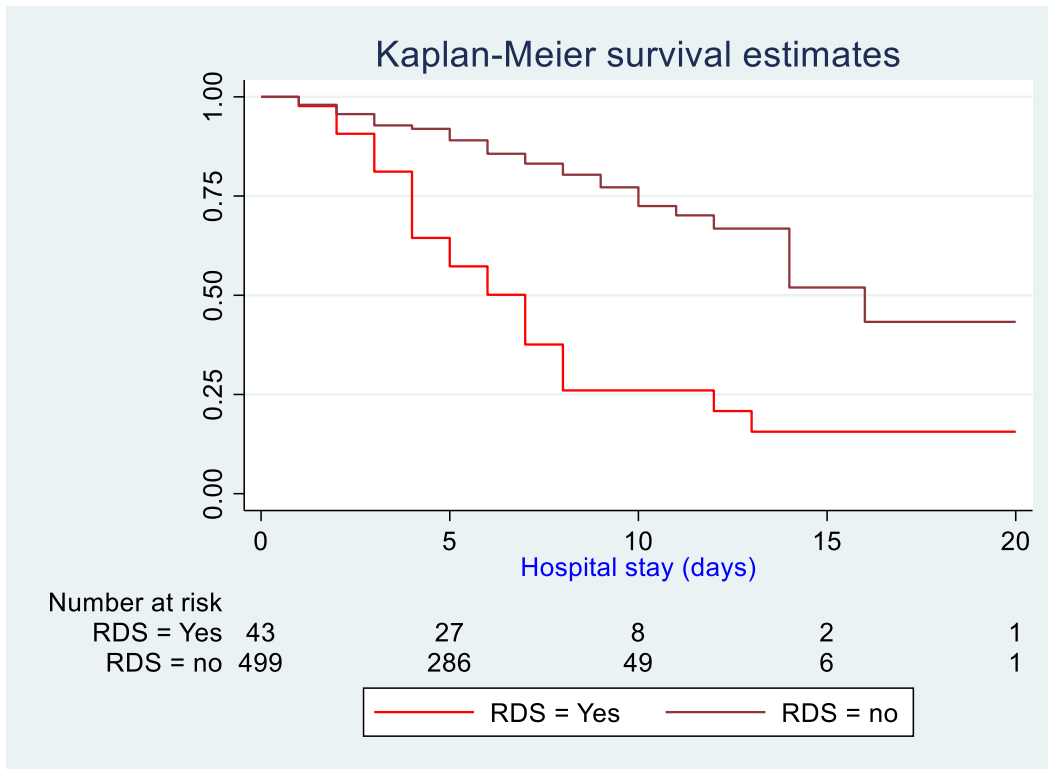


Figure 7: The Kaplan-Meier survival curves compare survival time of neonate with groups of RDS at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

On the contrary, neonates diagnosed with sepsis had a longer survival time compared to those who hadn't sepsis, with overall survival status of 64.63% and 25.97% at the end of the follow-up period. P-value = 0.0000 (See Figure 8).

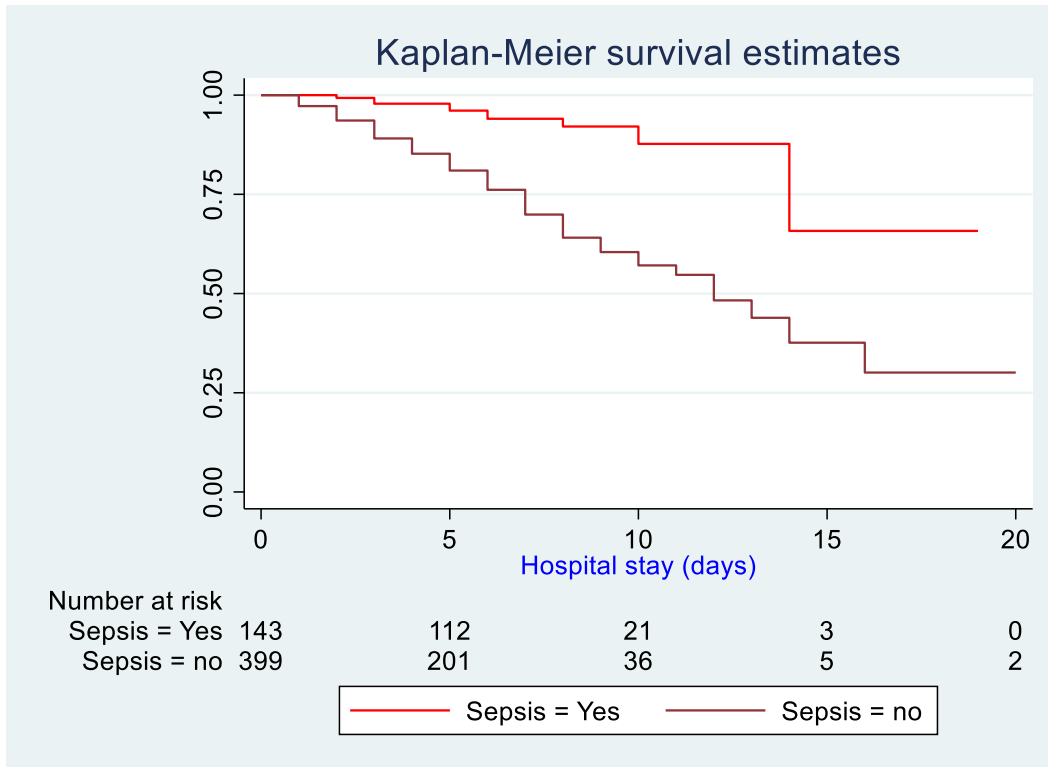


Figure 8: The Kaplan-Meier survival curves compare survival time of neonate with groups of sepsis at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Also, neonates who had Anemia had a lower survival time with a median survival time of 7 days of age (95%CI: 3,) compared to the counterparts (median survival day 14, 95%CI: 13,) with 29.03% and 36.73% of survival probability at the end of the follow-up period. The difference was statistically significant at p-value=0.0000 (see figure 9)

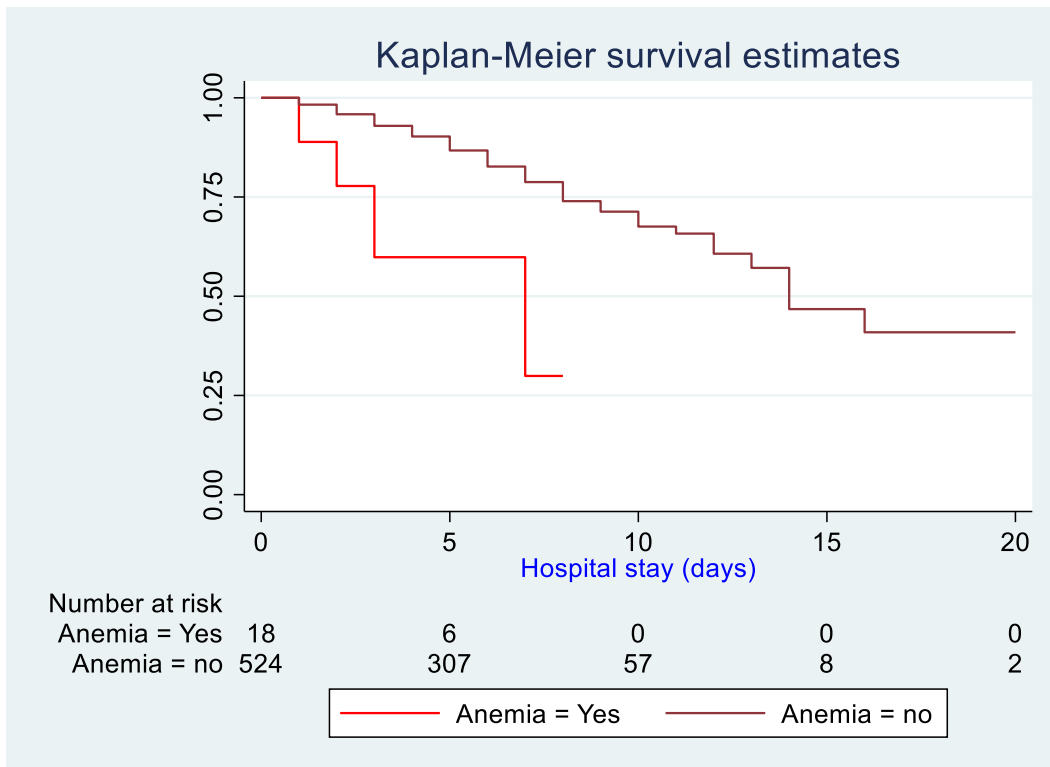


Figure 9: The Kaplan-Meier survival curves compare survival time of neonate with groups of anemia at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

The median survival time of neonates who had a Bag and Mask resuscitation at birth was 12 days, but it was 14 days for neonates who had no Bag and Mask resuscitation at the time of birth. The variation was significant at p-value =0.0001) (see fig 10).

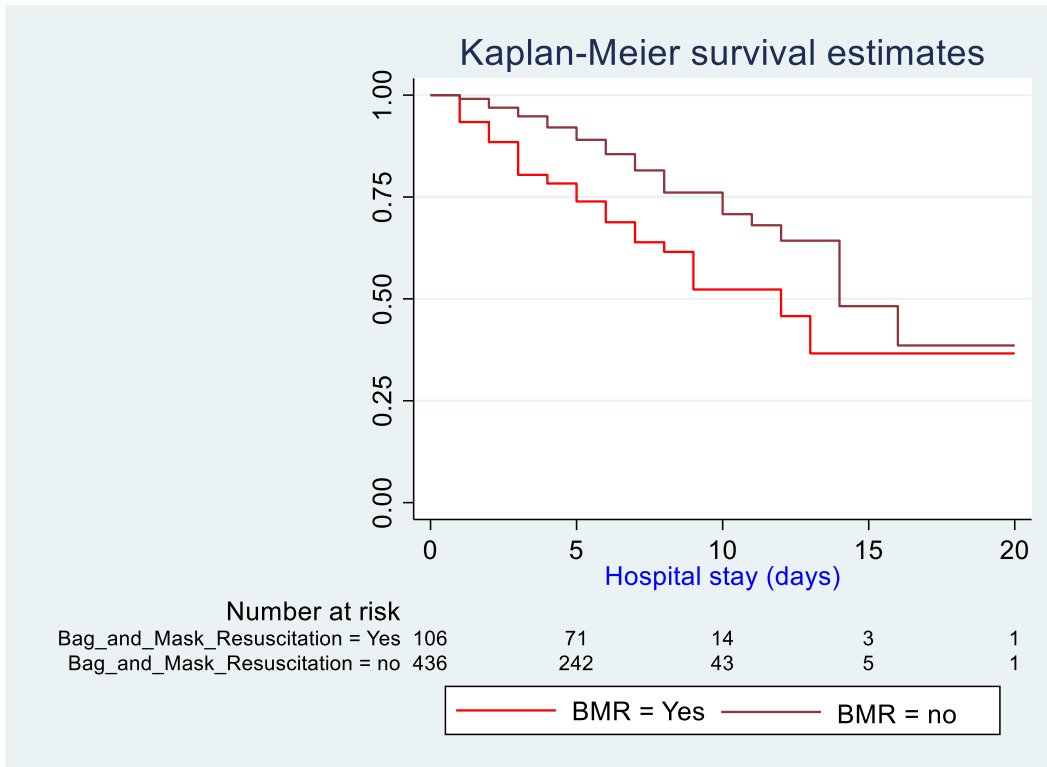


Figure 10: The Kaplan-Meier survival curves compare survival time of neonate with groups of bag and mask resuscitation at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

The result of this study showed that neonates with a 1st minute APGAR scores of ≥ 7 had good survival probability (median survival time of 16 days, 95%CI: 14,) than neonates with a 1st minute APGAR scores of < 7 (median survival time of 13 days, 95%CI: 12,). At the end of the follow-up period, the overall survival probability of neonates with 1st minute APGAR score ≥ 7 and < 7 was 38.00% and 33.06%. The difference was significant at P-value=0.0002. (See figure 11 below)

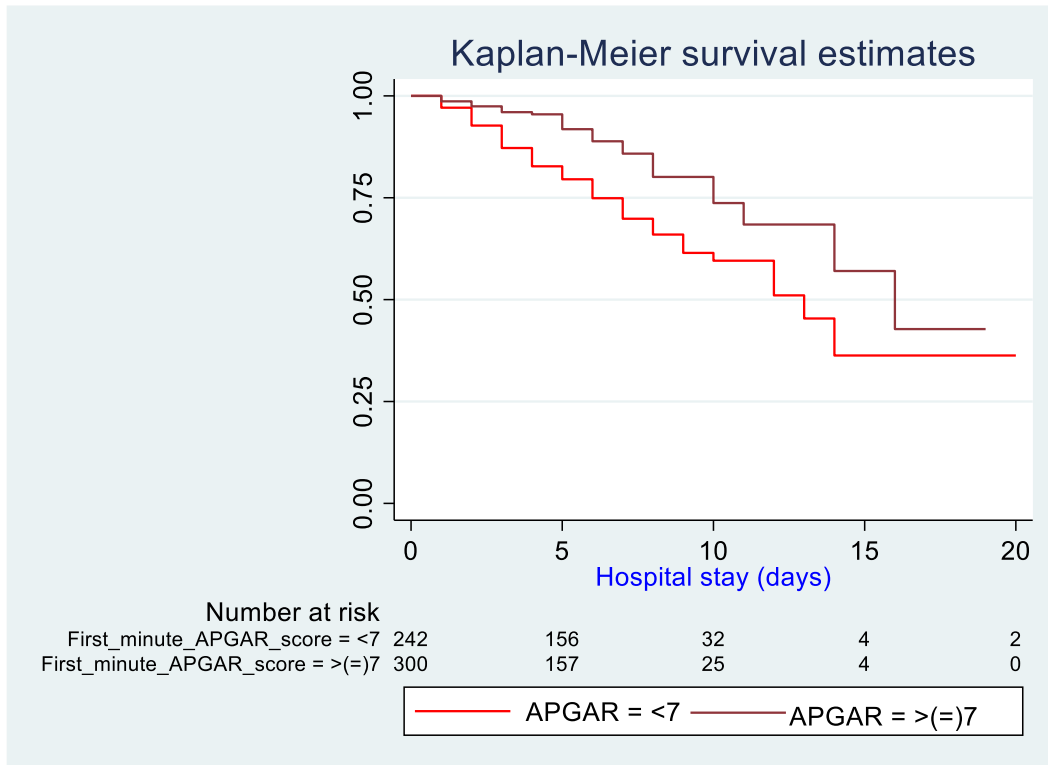


Figure 11: The Kaplan-Meier survival curves compare survival time of neonate with groups of first minute APGAR score at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020

Similarly, neonates with a 5th minute APGAR score of ≥ 7 had a longer survival time (median survival time of 14 days, 95%CI: 14,) than neonates with a 5th minute Apgar score of <7 (median survival time of 9 days, 95%CI: 7.). The difference was statistically significant at p-value = 0.0000 (see Figure 12)

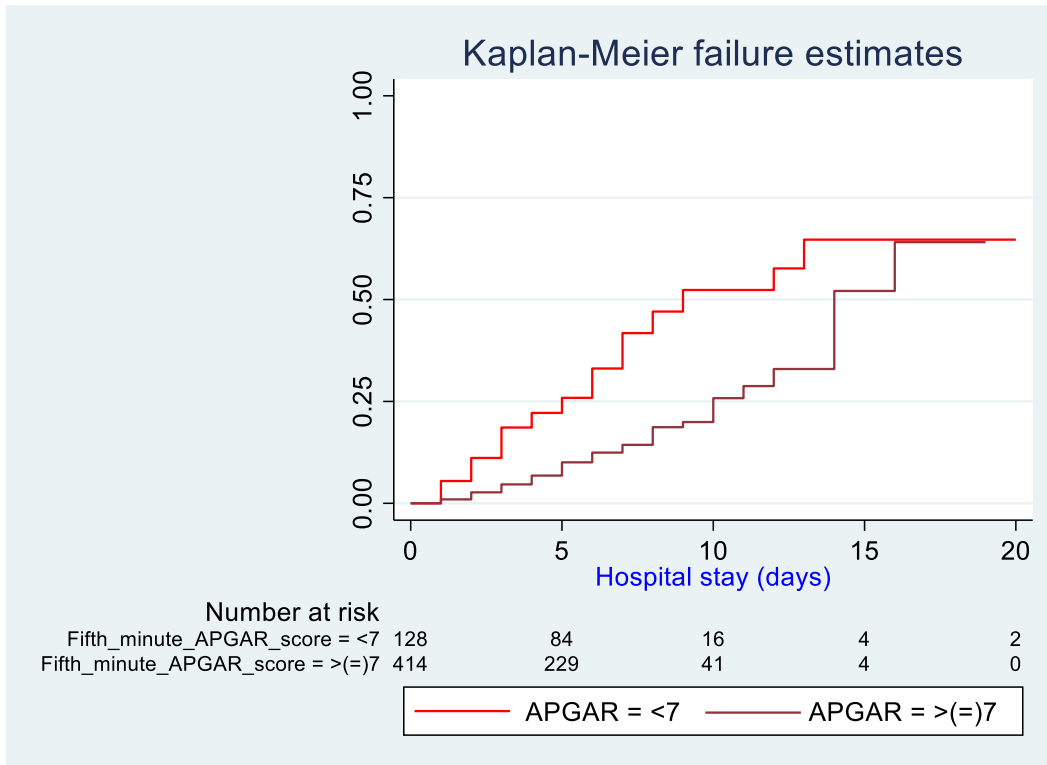


Figure 12: The Kaplan-Meier failure curves compare survival time of neonate with groups of fifth minute APGAR score at NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020

Table 6: Median survival time and log-rank test for equality of survivor functions among neonate admitted to NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	Median survival time (95%CI)	Log-rank test (χ^2)	P-value
Maternal age	<20 years	(8,)	0.28	0.8702
	20-35 years	14 (12,)		
	>35 years	10 (8,)		
Residence	Rural	14 (12,)	0.79	0.3741
	Urban	(11,)		
Sex	Male	16 (12,)	0.02	0.9017
	Female	14 (11,)		
ANC follow up	No	(2,)	1.34	0.2464
	Yes	14 (12,)		
Multiple pregnancies	No	14 (12,)	1.53	0.2159
	Yes	16 (7,)		
Neonatal age at admission	<24 hrs	13 (12,)	6.24	0.045
	1-7 days	16 (14,)		
	>7 days	(6,)		
Mode of delivery	SVD	14 (12,)	1.22	0.5434
	Instrumental	9 (7,)		
	C/S	(9,)		
Place of delivery	Hospital	16 (14,)	2.23	0.3279
	Health center	12 (10,)		
	Home	(4,)		
GA in weeks	<37	11 (8, 14)	20.15	0.0000
	\geq 37	----(14,)		
Birth weight in gram	<2500	11 (8, 16)	23.02	0.0000
	\geq 2500	----(14,)		

DM	Yes	6 (3,)	15.53	0.0001
	No	14 (13,)		
Epilepsy	Yes	1 (1,)	11.51	0.0007
	No	14 (12,)		
RDS	Yes	7(4,8)	51.18	0.0000
	No	16 (14,)		
PNA	Yes	12 (9,)	4.76	0.029
	No	14 (13,)		
Sepsis	Yes	----(14,)	28.61	0.0000
	No	12 (10,16)		
Anemia	Yes	7 (3,)	17.59	0.0000
	No	14 (13,)		
Bag and Mask resuscitation	Yes	12 (8,)	14.81	0.0001
	No	14 (14,)		
First minute APGAR score	<7	13 (12,)	13.73	0.0002
	≥7	16 (14,)		
Fifth minute APGAR score	<7	9 (7,)	29.60	0.0000
	≥7	14 (14,)		
Initiation of BF within 1 hr	Yes		13.42	0.0002
	No	13 (12, 16)		
Number of parity	<2	11 (8,14)	15.82	0.0001
	≥2	16 (14,)		
Prolonged labor	Yes	7 (3,)	20.95	0.0001
	No	14 (13,)		
PROM	Yes	(10,)	0.35	0.5528
	No	14 (12,)		
Placenta previa	Yes	5 (5,)	5.84	0.0156
	No	14 (12,)		
Preeclampsia	Yes	7 (5,8)	29.01	0.0000
	No	16 (13,)		

5.6. Predictors of Time to Death among Neonates Admitted to NICU

The relationship between the independent and outcome variables was analyzed using Cox proportional hazard regression model. In the bivariate Cox proportional regression analysis, the number of parity, prolonged labor, preeclampsia, placenta previa, epilepsy, GA, birth weight, RDS, PNA, neonatal anemia, bag and mask resuscitation, 1st and 5th minute APGAR score, and time of initiation of breastfeeding were statistically significant predictors of time to death of neonates (p-value < 0.05). Furthermore, to find independent predictors of time to death of neonates and survival, multivariate cox regression analysis was done for all predictors with a p-value <0.25 in the bivariate analysis. Nevertheless, the strong predictors of time to death in the multivariate analysis were found that the number of parity, prolonged labor, preeclampsia, DM, birth weight, PNA, and neonatal anemia.

Neonates born from primipara mothers had approximately 2 times more likely to die (AHR 2.231 (95%CI: 1.442, 3.451) than neonates born from multiparous mothers. The hazard ratio for neonates born with prolonged labor was more than 3 times more likely than those neonates born without prolonged labor (AHR: 3.317 (95%CI: 1.462, 7.526). The hazard ratio for death was 2.165 times higher among neonates born from mothers who have preeclampsia during their pregnancy as compared to their counterparts (AHR: 2.165 (95%CI: 1.102, 4.253). Neonates born from diabetic mothers were approximately 4 times more likely to die than those born from mothers without DM (AHR: 3.738 (95%CI: 1.569, 8.904). The hazard of neonatal mortality was 3.026 times higher for those neonates born with low birth weight as compared to neonates born with normal birth weight (AHR: 3.026 (95%CI: 1.526, 5.999). Similarly, neonates admitted to NICU with PNA at baseline had 2.613 times the risk of death than those admitted to NICU without PNA (AHR: 2.613 (95%CI: 1.114, 6.126). The hazard of death was 9.139 times higher among neonates admitted with the diagnosis of neonatal anemia than those neonates admitted without anemia (AHR: 9.139 (95%CI: 3.329, 25.084), at P-value=0.000.

Table 7: Results of bivariate and multivariate analysis using Cox regression model for predictors of time to death among neonate admitted to NICU, in Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

Variable	Category	CHR (95%CI)	P-value	AHR (95%CI)	P-value
Number of parity	<2	2.042 (1.383, 3.017)	0.000	2.231 (1.442,3.451)	0.000
	≥2	1			
ANC follow up	Yes	1			
	No	2.437(0.599, 9.915)	0.213	1.234 (0.262, 5.812)	0.790
Prolonged labor	Yes	3.070(1.661, 5.553)	0.000	3.317 (1.462,7.526)	0.004
	No	1			
Preeclampsia	Yes	3.747(2.292,6.127)	0.000	2.165 (1.102,4.253)	0.025
	No	1			
Placenta previa	Yes	5.021(1.229,20.512)	0.025	0.562 (0.100, 3.160)	0.513
	No	1			
Place of delivery	Hospital	1			
	Health center	1.316 (0.879, 1.972)	0.182	1.082 (0.682, 1.717)	0.738
	Home	2.444(0.888, 6.731)	0.084	1.488 (0.469, 4.728)	0.500
Maternal anemia	Yes	4.106(0.570,29.564)	0.161	2.855(0.356,22.881)	0.324
	No	1			
DM	Yes	3.363(1.555, 7.270)	0.002	3.738 (1.569,8.904)	0.003
	No	1			
Epilepsy	Yes	5.724(2.099,15.609)	0.001	4.422(0.791,24.726)	0.091
	No	1			
GA at birth in weeks	<37	2.457 (1.671, 3.614)	0.000	1.112 (0.462, 2.677)	0.813
	≥37	1			
Birth weight in gram	<2500	2.553 (1.727, 3.775)	0.000	3.026 (1.526, 5.999)	0.002
	≥2500	1			
RDS	Yes	4.010 (2.638,6.097)	0.000	2.017 (0.931,3.759)	0.075

	No	1			
PNA	Yes	1.656 (1.041,2.635)	0.033	2.613 (1.114, 6.126)	0.027
	No	1			
Sepsis	Yes	0.204 (0.106,0.392)	0.000	0.659 (0.297, 1.462)	0.305
	No	1			
Neonatal anemia	Yes	4.467 (2.142, 9.316)	0.000	9.139(3.329,25.084)	0.000
	No	1			
Birth trauma	Yes	1.823 (0.741, 4.482)	0.191	1.889 (0.551,6.483)	0.312
	No	1			
Bag and mask resuscitation	Yes	2.132 (1.432,3.173)	0.000	1.510 (0.758, 3.003)	0.241
	No	1			
1 st minute APGAR score	<7	2.209 (1.460,3.341)	0.000	0.967 (0.484, 1.931)	0.924
	≥7	1			
5 th minute APGAR score	<7	2.789 (1.898,4.099)	0.000	1.243 (0.605, 2.555)	0.554
	≥7	1			
Initiation of BF within 1 hr	Yes	1			
	No	2.538 (1.524, 4.225)	0.000	0.852 (0.394, 1.844)	0.685

Those bold numbers above showed significantly associated predictors of time to death.

CHR: Crude Hazard Ratio; AHR: Adjusted Hazard Ratio; CI: Confidence Interval

P-value: level of significance at <0.05

5.7. Multicollinearity Test

Predictor variable in a multiple Cox-regression Model can linearly predict from the others with a considerable degree of accuracy. Multicollinearity occurs when predictor covariates in the Cox-regression model are correlated. This correlation is a problem because the relationship between each predictor variable with the outcome variable should be independent. Multicollinearity can be checked by calculating variance inflation factor (VIF) for each predictor variable (based on binary cox-regression outcome). According to some guidelines, a VIF value less than 10 is considered as an acceptable collinearity level. However, a VIF value greater than 4 needs further investigation. In this study the maximum VIF value was 3.08 with a mean VIF of 1.62. Therefore, there was no multicollinearity, and we can interpret the results of this study. (See table 9).

Table 9: Multicollinearity check for each variable based on binary outcome (p-value<0.25) to neonates admitted in NICU at Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020

Variable	VIF	1/VIF
5 th minute APGAR score	3.08	0.324580
Bag and Mask resuscitation	3.06	0.326814
GA at birth in weeks	2.80	0.357054
PNA	2.16	0.462119
Birth weight	2.09	0.477332
RDS	2.02	0.494866
1 st minute APGAR score	1.97	0.508196
Initiation of BF within 1 hr	1.69	0.591746
Preeclampsia	1.44	0.694875
Sepsis	1.23	0.810378
Neonatal anemia	1.20	0.833318
Prolonged labor	1.18	0.845737
Birth trauma	1.15	0.871025
Place of delivery	1.10	0.908991
Number of parity	1.07	0.936072

Epilepsy	1.06	0.942373
ANC follow up	1.06	0.946078
Placenta previa	1.03	0.968156
Maternal anemia	1.03	0.974988
DM	1.02	0.980894
Mean VIF	1.62	

5.8. Test of Proportional Hazard Assumption

Based on binary and multicollinearity outcomes, testing proportional hazard assumption is vital to interpret, use fitted proportional hazard models, and accept multivariate analysis results. In this study, Schoenfeld residuals proportional hazard assumption test for the individual covariates was done and global tests were used. If P-value < 0.05, then the proportional hazard assumption is rejected. (See table 7). Also, a concordance probability test was performed (Harrell's c=0.8286).

Table 8: Schoenfeld Residuals test for Cox-Proportional Hazard Regression model assumption (estat, phtest) of each variable for neonates admitted in NICU at Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020.

VARIABLES	RHO	CHI² (X²)	P-VALUE
Parity	-0.02547	0.07	0.7926
ANC follow up	-0.01834	0.03	0.8699
Prolonged labor	0.01415	0.02	0.8784
Preeclampsia	0.10112	1.21	0.2717
Placenta previa	0.02558	0.09	0.7656
Within 1 hr BF initiation	0.13377	1.42	0.2333
Place of delivery (HC)	0.04399	0.20	0.6539
Place of delivery (Home)	0.08676	0.56	0.4534
Maternal anemia	0.12809	1.70	0.1928
DM	0.06052	0.44	0.5059
Epilepsy	-0.01076	0.01	0.9164
GA	0.00997	0.01	0.9230
Birth weight	0.00162	0.00	0.9867

RDS	-0.08130	0.78	0.3756
PNA	-0.04986	0.34	0.5572
Sepsis	0.02364	0.05	0.8230
Neonatal anemia	-0.12699	1.46	0.2270
Birth trauma	-0.02825	0.06	0.8064
Bag and mask resuscitation	-0.10275	1.13	0.2869
1st minute Apgar score	-0.14225	2.07	0.1501
5th minute Apgar score	0.01955	0.04	0.8363
GLOBAL TEST		20.89	0.4655

5.9. Cox-Snell residuals Test

Cox-Snell residuals test is used to assess the overall goodness of fit in survival models. It is done graphically with the usual graphs of Cox-Snell, and it is observed that residuals from a correctly fitted model follow exponential unite distribution along the 45 degree of slope (baseline). It is used to identify extreme observations that need additional investigation. In this study, the hazard function follows the 45-degrees line closed to the baseline. It showed that the multivariate cox-regression model is fitted for the analysis and interpretation of the results of this study.

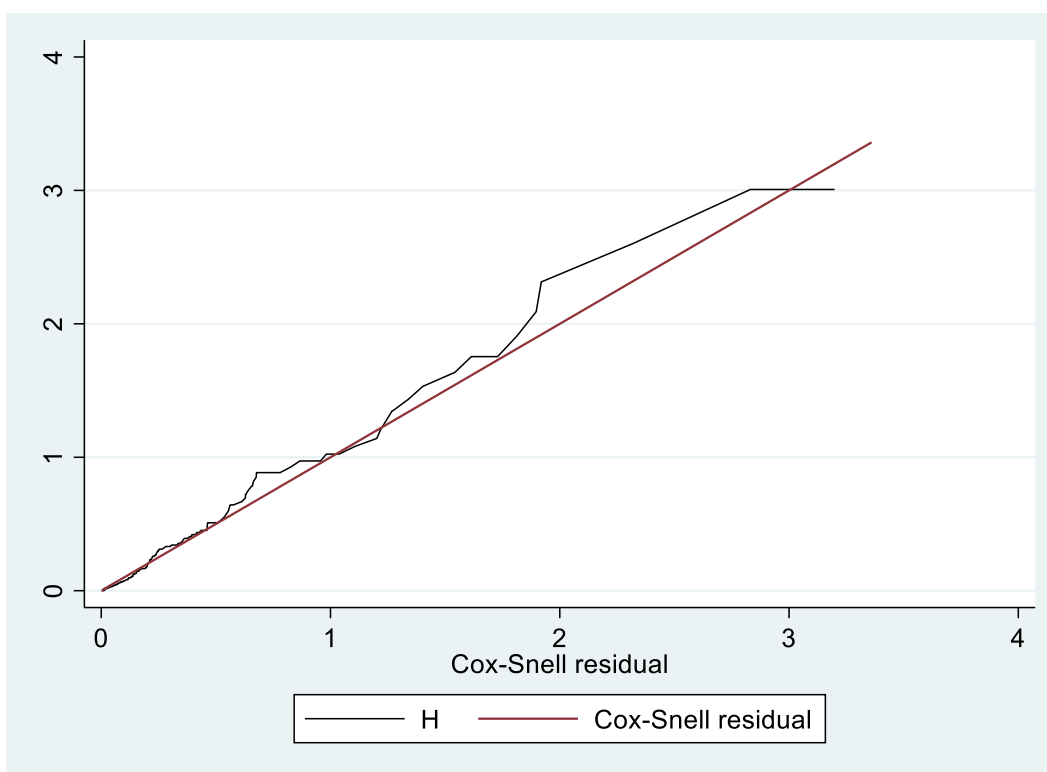


Fig 13: Cox-Snell residual cumulative hazard graph on neonates admitted in NICU at Dessie Referral Hospital, Northeast Ethiopia, January 1st, 2018 – December 31th, 2020

6. DISCUSSION

This retrospective follow-up study was aimed to determine the survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital. This study shows that the overall neonatal mortality (NMR) in NICU of Dessie Referral Hospital in the study period was 104 (19.19%), which is equivalent to the NMR of 192/1000 admitted neonates (95%CI: 160, 228). This finding was more than three times higher than the study done in Ethiopia, Tigray region (5.90% (62.5/1000 live birth) (63) and slightly in line with a study conducted in Arba Minch General Hospital (20.8%) (31) and Debre Markos Referral Hospital (21.3%) (34). Also, the finding was higher than a study done in northern Tanzania which was 10.7% (28) and Nigeria (14.2%) (27), but lower than the study conducted in Mauritania (34.7%) (29). Similarly, the neonatal mortality rate of this study was higher than studies conducted in Iran (11.4%) (22) and India (10.4%) (24). These different results might be due to different reasons. The possible reason may be different in methodology and study period. The other justification could be the difference in availability of medical equipment and other resources in NICU, and the difference in availability of trained human resources (difference in care).

At the end of the follow-up period, the overall incidence of neonatal mortality was 35.54 deaths per 1000 neonate-day observations. This result was higher than the global and sub-Saharan African incidence of neonatal mortality rate, 18 and 27 deaths per 1000 live births, respectively (1). Also, this finding was higher than the 2019 report of mini EDHS (29 per 1000 live births) (7). Likewise, the result of this study was higher than studies conducted in Ethiopia, Arba Minch General Hospital (31.6 per 1,000 neonate days) (31), and Jimma University Medical center (30 deaths per 1,000 institutional live births) (10). This finding was in line with reports in Afghanistan, which was 36 deaths/1000 live birth (25); however, it was lower than the Democratic Republic of Congo (94 deaths per 1000 live births) (30). This apparent difference could be related to several reasons, such as economic wealth difference. Developed countries might have skilled health professionals with organized personnel and equipment in the delivery room and NICU to give essential newborn care and treatment for those sick neonates. The other reason might be geographical location and climate difference, in which hot and humid day climate increases the risk of neonatal illness and mortality. Community educational level and cultural difference might also be the other reasons.

In this study, the hazard probability of neonates in the 1st, 7th, and 14th days of hospital stay was 10.58%, 73.08%, and 99.04%, with an incidence rate of 20.29, 32.79, and 35.56 deaths per 1000 neonate-days observation, respectively. This finding was similar to a study done in UoGCSH in which neonatal failure probability at the 1st, 7th, and 14th day of hospital stay was 13.79%, 83.91%, and 97.70% with an incidence rate of 23.81, 31.48, and 28.90 deaths/1000 neonate-day observations, respectively (33). Generally, the highest failure probabilities occurred among neonates admitted in the early neonatal period (99 (95.19%)) with an incidence rate of 35.59/1000 neonate-days observations. The possible scientific explanation could be the neonatal immunity system. Both their innate and adaptive immunity is functionally immature, resulting in increased neonatal morbidity and mortality in the early neonatal period. The other possible justification might be pregnancy and intrapartum-related complications, delaying early identification and treatment of those complications. But, it was higher than a study in the UoGCSH (84%) (33). The reason may be that the difference in the duration of follow-up time (year) and study area.

The overall median survival time of neonates admitted to NICU was 14 days. It was higher than a study in Arba Minch General Hospital (6 days) (31). The possible explanation for this difference could be the sample size (N=332) and the study area. The other reason could be changing (updating) of treatment modalities over time.

In the present study, the overall survival probability was 36.10% in the 20 days of the follow-up period. The survival probability at the 1st, 7th, and 14th days of hospital stay was 97.83%, 75.75%, and 42.12%. This finding was consistent in the study done at Arba Minch General Hospital in which the 1st, 7th, and 14th day of survival probabilities were 96.1%, 75%, and 69.9%, respectively, with an overall survival probability of 66.2% (31).

After adjusting the multivariate cox proportional regression model, the significant independent predictors of neonatal mortality in the NICU were low birth weight, primiparous mother, prolonged labor, preeclampsia, maternal DM, PNA, and neonatal anemia.

Birth weight was an important independent predictor of neonatal survival in which neonates with low birth weight had 3 times the hazard of death compared to neonates with normal birth weight (AHR: 3.026, P=0.002). This finding is comparable with other studies conducted in different places (9,24,29,37,38,40,41). The possible scientific justification may be that LBW

neonates are at potential risks of developing complications than normal birth weight. Secondly, in this study, most LBW neonates were also premature with many physiologic problems, especially with an immature lung leading to RDS secondary to HMD.

Being a primiparous mother was another significant predictor of the survival status of neonates. The number of parity <2 was increased the hazard of death by more than two folds than the number of parity ≥ 2 (AHR=2.231, P=0.000). This result was in agreement with other studies conducted in Assosa Zone and Ayder Comprehensive Hospital (50,51). It may be because primipara mothers are more likely to experience complications during pregnancy and birth.

Having prolonged labor was also found to increase the hazard of neonatal death (AHR: 3.317, P=0.004), which was similar to a study conducted in Arba Minch General hospital (31). The possible scientific justification might be because prolonged labor is the primary cause of neonatal infection, perinatal asphyxia, and hypoxemia, contributing to the development of neonatal morbidity and mortality.

The hazard of death for neonates born from mothers with preeclampsia was 2.165 times higher compared to those born from mothers without preeclampsia during their pregnancy (AHR: 2.165, P=0.025). This is due to preeclampsia affecting the mother's blood circulation, thereby affecting blood flow to the placenta, leading to fetal hypoxemia in the uterus. Secondly, preeclampsia can be threatening to maternal life and in this case, terminating the pregnancy is mandatory, leading to the delivery of premature babies with immature organ systems to survive.

Neonates born from diabetic mothers had close to 4 times a risk of death than neonates born from mothers without DM (AHR: 3.738, P=0.003). This might be due to complications of DM for mothers and their neonates as stated by many studies and literature (60,61). The possible scientific justification might be that neonates born from diabetic mothers are often larger than other neonates, making vaginal delivery difficult and may increase the risk of nerve injury and other trauma during delivery that increases the risk of neonatal death. The other scientific justification might be that a pregnant diabetic mother may have preeclampsia, leading to the delivery of a premature baby, which was the leading cause of neonatal mortality in this study.

Having PNA at admission was another vital predictor of time to neonatal death. Neonates who were diagnosed with PNA at admission had approximately 3 times a hazard of death than

neonates who hadn't PNA at admission (AHR: 2.613, P= 0.027). Similar results have been recorded in Ethiopia and other studies (24,40,48,56,57). The possible scientific justification could be, asphyxia contributes to the deprivation of oxygen in the body, leading to hypoxia, hypercarbia, and acidosis formation, which eventually damages vital organs leading to death.

The last significant variable that predicted the time to death of neonates in this study was neonatal anemia. Neonates who had anemia during admission were almost nine times more likely to die than neonates who hadn't anemia (AHR: 9.139, P=0.000). This might be because of the inability of RBC to deliver adequate oxygen to the tissue of the neonate.

7. LIMITATION AND STRENGTH OF THE STUDY

Strength

The data were collected by nurses who trained for neonatal care in NICU, which has an essential role in ensuring data quality.

The data were gathered from three consecutive years of admission/observations with proportional allocation, which might increase the number of events and decrease variability.

Considering censored observations was also an important strength of this study since it provides a more accurate estimation for survival analysis.

It gives an insight for researchers, especially for a prospective study.

It was easy to make a sequential association between outcome covariate (death) and predictor covariates, which were recorded at admission.

Limitations

Since the study was conducted using secondary sources, some critical covariates obtain from the mother were missing. These might be significant predictors of neonatal mortality such educational status, occupational status, nutritional status, marital status, economic status, birth interval, history of abortion, and history of stillbirth.

The study area covers only Dessie Referral Hospital. As a result, its generalizability to all hospitals of Ethiopia may be impossible.

Medical records that were incomplete or lost at the time of data collection were excluded. These possibly introduce selection bias that results under or overestimation of the findings of the study.

Unavailability of reference study for median survival time of neonates admitted in NICU and for some variables that were independent predictors of death in this study.

8. CONCLUSION

In the present study, 104 (19.19%) neonates died during the follow-up period. The overall incidence of NMR was 35.54 deaths per 1000-neonate day observation with an overall median survival time of 14 days. The incidence of death was high in the early neonatal period. Also, the overall cumulative survival probability was 36.10% at the end of the study period. This study also showed that the independent predictors of time to death of neonates admitted to NICU were low birth weight, primiparous mother, prolonged labor, preeclampsia, maternal DM, PNA, and neonatal anemia.

9. RECOMMENDATION

Even though quality of health care service expanded, especially for maternal and newborn care, neonatal mortality is still a concerning issue in all Ethiopia's study areas. Based on the findings of this study, I forwarded the following recommendations.

To the federal minister of health

Researches, including this study, showed that incidence of neonatal mortality had no reduction progress, especially since 2016 till now. Therefore, federal health policymakers should revise, particularly maternal and neonatal health policies, based on up-to-date study findings to address interventions for predictors of neonatal mortality

To Dessie Referral Hospital

The Hospital should give an early diagnosis, early intervention (care), follow-up, and regular monitoring for mothers with preeclampsia during their pregnancy since preeclampsia was an independent predictor of neonatal death in the current study.

Another emphasis should be given to prolonged labor, and delivery should be conducted within 18 hrs of the onset of labor to reduce the incidence of neonatal mortality.

The hospital should facilitate more research to find out more detailed diagnoses of predictors of neonatal mortality.

To health care providers of Dessie Referral Hospital

A special priority, monitoring and strict follow-up must be given to neonates admitted in their first 7 days of life because this study found that the highest incidence of neonatal death was in this time of neonatal age.

The health care provider should give especial attention and care for neonates born with prolonged labor, primiparous mother, having preeclampsia mother, having DM mother, low birth weight, and neonatal anemia.

It would be better to strengthen screening of DM during pregnancy

To future researchers

Upcoming researchers shall conduct a longitudinal prospective cohort study to incorporate impossible variables in retrospective study like maternal socio-economic, genetic and environmental factors.

The subsequent researchers shall also conduct a community-based study on the survival status of neonates to avoid the estimation effect due to censored data.

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APPENDIX

Appendix I Information Sheet

Title of the Research Project: Survival status and predictors of mortality among neonate admitted to NICU from (2018-2020) at Dessie Referral Hospital, Northeast Ethiopia, 2021.

Name of Investigator: Mohammed Kebede (BSc in Nursing)

Name of the Organization: Addis Ababa University College of Health Science, School of Nursing and Midwifery, Department of Pediatrics and Child Health.

Name of the Sponsor: Addis Ababa University.

Introduction: This information sheet is prepared for Dessie Referral Hospital administration and NICU coordinating office. The aim of the form is to make the above-concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To determine Survival status and predictors among neonate admitted to NICU from 2018-2020 at Dessie Referral Hospital, Northeast Ethiopia, 2021.

Procedure: In order to achieve the above objective, information which is necessary for the study was taken from neonatal medical records.

Risk and /or Discomfort: Since the information was collecting from medical charts, it will not cause any hurt on the patients. The name or any other identifying informations were not documented on the questionnaire and kept firmly private and in a safe dwelling. The information retrieved were only used for the study purpose.

Benefits: The study have no direct profit for one whose document is involved in this study. However, the indirect profit of the study for the participant in the program is obvious. The reason is that if program developers are formulating predicted strategy there is a profit for clients in the program of attaining proper care and treatment for clients survived and other newborns. In all, the study work has a principal direct profit for health care organizers and administrators.

Confidentiality: To assure privacy the informations on the charts was collected by excluding the name of the clients and the information collected from this study development was kept

private and stored in a file cabinet. In addition, it was not shown to anyone except the investigator and it have been kept in a key and locked system with computer password.

Person to contact: This study development was revised and approved by Addis Ababa University, College of Health Science, School of Nursing and Midwifery. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any the time you want.

Mohammed Kebede, Addis Ababa University, College of Health Science, Department of Pediatrics and Child Health Nursing: principal investigator

Cell phone: +251-913803674, E-mail: mohama26.mk@gmail.com

Dr.Girum Sebsibe (MSC, PHD) Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Pediatrics and Child Health Nursing: main Advisor.

Cell phone: +251-920856732

E-mail: girumseb@gmail.com

Mrs. Feven Mulugeta (BSC, MSc) Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Pediatrics and Child Health Nursing: co- Advisor.

Mobile: +251910712396

E-mail: fevishome@gmail.com

Appendix II Checklist

This checklist is organized for the gathering of socio-demographic, maternal medical and obstetrics and gynecology, neonatal medical and other key predictors and outcomes related data that are significant for the valuation of survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital. All this information was retrieved from the client's registration book and from an individual patient card without including the name of the clients from [2018-2020]. This information was collected by health care providers (BSC nurses) who are working in the NICU of the Hospital.

Contact information: Mohammed Kebede, Cell phone+251-913803674, Dr.Girum Sebsibe, Cell phone: +251-920856732, Mrs. Feven Mulugeta, Cell phone: +251-910712396

Data collection date-----month-----Year-----

Name of the Hospital -----

Name of data collector----- signature-----

Name of supervisor-----signature-----

Code no-----

Table 10: Data collection checklist for conducting of study on survival status and predictors of mortality among neonates admitted to NICU in Dessie Referral Hospital, Northeast Ethiopia, 2020

Question for the mother

1. Sociodemographic characteristics			
Question number	Question	Answer	
101	Age	1. < 20 years 2. 20-35 years 3. > 35 years	
102	Place of residence	1. Rural 2. Urban	
2. Obstetric and gynecological related factors			
201	Number of Parity	
202	Does the mother have ANC follow up?	1. Yes 2. No	
203	Was the current pregnancy multiple (twin)?	1. Yes 2. No	
204	Which among the following do you have diagnosed?	1. PROM 2. Preeclampsia 3. Placenta previa 4. Prolonged labor	
205	Mode of delivery	1. Spontaneous vaginal delivery 2. Instrumental delivery 3. Cesarean section	
206	Place of delivery	1. Hospital 2. Health center 3. Home 4. Other, specify.....	
207	Delivery conducted by	1. Health professional	

		2. Traditional birth attendance 3. Other.....	
1. Medical factor			
301	Has she been diagnosed with any medical problems	1. Yes 2. No	
302	If yes for question no 301, what was the diagnosis	1. HIV 2. Hypertension 3. Anemia 4. DM 5. STI 6. Other, specify.....	

Questions for the neonate

1. Sociodemographic characteristics			
Question number	Question	Answer	
101	ID no-	
102	Date of admission	
103	Age in day	
104	Sex	1. Male 2. Female	
105	Gestational age at birth in weeks	
106	Weight in grams at birth	
2. Neonatal medical and other related factors			
201	Mention the diagnosis of neonate	1. Respiratory distress 2. Jaundice 3. Perinatal asphyxia 3. Hypothermia 4. Hyperthermia 5. Sepsis 6. Meconium aspiration syndrome 7. Congenital malformation 8. Hypoglycemia 9. Other(specify	

202	Bag and Mask Resuscitation at birth	1. Yes 2. No	
203	APGAR score of	1. First minute..... 2. Fifth minute.....	
204	Time of initiation of breast feeding	1. Initiated within 1 hour 2. Not initiated within 1 hour	
205	Length of hospital stay	
206	Date of discharge	
207	Time of neonatal death	
208	Patient outcome	1. Died 2. Recovered 3. Referred 4. Left against medical advice	

