TIME TO PRETERM NEONATE MORTALITY AND RISK FACTORS AMONG THOSE ADMITTED TO JIMMA MEDICAL CENTER, JIMMA, SOUTHWEST ETHIOPIA, 2023: SURVIVAL ANALYSIS

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Abstract

Background: preterm birth is one of the highest global challenges in the 21st century and accounts for about 1 million neonatal deaths worldwide. Despite many strategies and interventions being implemented to reduce preterm neonatal mortality, the rate of neonatal mortality in Ethiopia is unacceptably high and not reduced as expected. In addition, little is known about the time to preterm mortality and its risk factors. Therefore, this study aimed to assess time to mortality and risk factors among preterm neonates admitted to the neonatal intensive care unit of Jimma Medical Center from 2018-2022, Jimma, Southwest Ethiopia, 2023

Methods: Institution-based retrospective follow-up study was conducted at Jimma Medical Center from May to June, 2023. All preterm neonates admitted to the Neonatal Intensive Care Unit at Jimma Medical Center from [2018-2022] were taken. A total of 476 samples were recruited by applying Computer-generated random sampling technique to select eligible medical records. Data were collected by record review method with pre-tested structured checklist and entered using Epi-data version 4.6, and analyzed using STATA 17. Kaplan-Meier and log-rank tests were used to estimate the survival time and compare survival curves. Descriptive statistics, bivariable, and multivariable analyses were done in a Cox- regression model. Adjusted Hazard Ratios with 95% Confidence Intervals (CI) was used to assess the relationship between risk factors associated with time to death. Finally, variables with P-value of <0.05 were considered statistically significant in predicting preterm mortality.

Objective:

Result: A total of 456 preterm neonates included in this study, 111 (82.2%) of deaths occurred during the first week after admission with the overall incidence rate of 34(95%CI:28.72,40.24) per 1000 neonate-day. Not initiating breastfeeding within one hour of birth (AHR=1.96(95%C:1.18,3.23), low 1st and 5th minute APGAR score(AHR=1.77(95%C1:1.06,2.94),and (AHR=2.49(95%C1:1.54,4.02) respectively, respiratory distress syndrome(AHR=1.9(95%CI:1.15,3.14),lack of kangaroo-mother care(AHR=2.61(95%CI:1.65,4.12), low birth weight (AHR=0.52 (95% CI:0.32,0.83) were found to be significantly associated with the time to preterm neonate mortality.

Conclusion: The first week after admission was the hazardous time to death. Neonates who were not breastfed within 1 hour of birth, low 1st and 5th minute APGAR score, respiratory distress syndrome, and lack of kangaroo-mother care were found to be independent risk factors of preterm neonatal mortality. On the other way being born with low birth weight prolong time to death. Therefore, emphasis should be given to neonates during the first week after admission and with identified risk factors to prolong time to death and reduce preterm mortality.

Keywords: Preterm, mortality, risk factors, incidence, survival analysis

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ABBREVIATION AND ACRONYMS

AHR: Adjusted Hazard Rate

ANC: Ante Natal Care

AOR: Adjusted odd ratio

APGAR : Appearance, Pulse, Grimace, Activity and Respiration

CHR: Crude Hazard Rate

CI: Confidence interval

CPAP: Continuous positive airway pressure

DM: Diabetes mellitus

EDHS: Ethiopian Demographic and Health Survey

FMOH: Federal Ministry of Health

GA: Gestational Age

HIV/AIDS: Human immunodeficiency virus/ acquired immunodeficiency syndrome

HIV: Human Immune deficiency Virus

HMD: Hyaline Membrane Disease

HSDP: Health sector development program

IHRERC : Institute of health research ethics review committee

JMC: Jimma Medical center

KMC; Kangaroo mother care

LBW: Low birth weight

LMICs: low and middle-income countries

MOH; Ministry of Health

MRN; Medical registration number

NEC: Necrotizing enterocolitis

NICU: Neonatal Intensive Care Unit

NMR: Neonatal Mortality Rate

PI :Principal investigator

PNA: Prenatal Asphyxia

PPROM: preterm Premature Rupture of Membrane

PTB: preterm birth

RDS: Respiratory distress Syndrome

SD: Standard devasion

SDG3: sustainable development goal 3

SPSS: Statistical Package for Social Science

SSA: sub- Saharan Africa

VIF: Variance inflation factors

VLBW: Very low birth weight

WHO: World Health Organization

Chapter one: Introduction

1.1 Background

The World Health Organization (WHO) defines preterm neonate as a baby delivered alive before 37 completed weeks or 259th day of gestation, counting from the first day of the last normal menstrual period(1). Those preterm neonates born before reaching maturity are fragile, weighing less than full term neonates, and who are at greater risk of death than those born at full term(2). Preterm birth may happen spontaneously or may be initiated by a provider (3).

Preterm birth can be further sub-divided based on gestational age: Extremely Preterm(EPTN), Very Preterm (VPTN), and moderate to late preterm (born in <28, 28-<32, and 32-<37 weeks of Gestational Age (GA) respectively (4), and by birth weight: Extremely Low Birth Weight (ELBW)), Very Low Birth Weight (VLBW), and Low Birth Weight (LBW) (<1000g,1500-2500 g,<2500 g respectively) (5).

Preterm neonatal mortality is the death of preterm newborns within the first 28 days of life (6), which is a significant public health problem throughout the world in general and predominantly affect low-income countries(7). The time elapsing from born with prematurity to the occurrence of the death is called time to preterm neonate mortality (8). Globally, out of more than 15 million preterm neonates, majority were found in Africa and South Asia, more than 1.1 million deaths occur due to preterm birth (9). The survival in Africa is the poorest in the world (10, 11). Likewise, the magnitude of preterm mortality in Ethiopia lies between 8.1 and 28.8%(12).

As different studies conducted so far in the different area reported, there are multiple risk factors that affect the time to death of neonates with prematurity, factor such as being in rural residency, maternal age (13), primipara, pregnancy complications (14),GA, asphyxia, and Respiratory Distress Syndrome(RDS) are among the few variables that contribute for neonatal mortality (15).

Prematurity is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health (16). The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs. Moreover, Those Preterm neonates require prolonged hospital stay after birth, frequent hospital admissions, and increased risk of chronic disease (17), putting the parents in social and financial crisis.

Despite different local and international initiatives and implementations that have been implemented to prevent neonatal death, it is still high and not reduced as expected in developing countries including Ethiopia.

1.2 Statement of the problem

Preterm mortality is a significant public health problem throughout the world in general and more predominantly affect low-income countries (18). Globally, 2.3 million children died in the first month of life, approximately 6,500 neonatal deaths every day. Of those, about a third of all neonatal deaths occurred within the first day after birth, and three-quarters occurring within the first week of life, and more than third of these babies were preterm(19, 20)

In 2021, Children face the highest risk of dying in their neonatal period at an average global rate of 18 deaths per 1,000 live births. Despite a declining neonatal mortality rate, there are still noticeable differences across regions, and nations(21). Regionally, the highest neonatal mortality reported in Sub-Saharan Countries(SSA) which was 27 deaths per 1,000 live births with 43% of global newborn deaths, followed by central and southern Asia which was 23 deaths per 1,000 live births with 36% of global newborn deaths (21, 22).

In Africa 50% of the neonatal deaths are from preterm babies caused by only preterm complications and SSA countries loses approximately 290,000 neonates in each year due to preterm complication (23). More than 50% of newborn deaths in East Africa are related to preterm births(24). In Ethiopia 23,100 children under five die due to direct preterm complications(25). As the Ethiopia Mini Demographic and Health Survey (EDHS) 2019 report , neonatal mortality increased by 30 deaths per 1000 live births, up from 29 deaths per 1000 in 2016(26).

According to the study conducted in Iran the overall median survival time of preterm and LBW infants' was 76 days(27). Another study done in Brazil revealed that 29% preterm neonates died within the first 0–6 days of life. Of these, 33% died within the first 24 hours of life (28).

Study also conducted in Africa reported different survival time of preterm birth, According to the study done in Zambia the overall median survival time of the infants was 98 hours (IQR, 34-360) (29). Similar study undertaken in Uganda revealed that 65.8% of deaths occurring within 72 hours from admission (30). Likewise, Study done in Ethiopia, Adiss Abeba showed that 84% neonates died in the first 7 days after admission with the median time to death of 6 days (23), in Gondar among the deaths 11.4% died within first 24 hours of life, and 85.23% were an early neonatal death occurring in the first 7 days of life (31), and in Jimma among all death, 81.1% of deaths occurred within 7 days of life (32).

Different available evidence indicated that being rural residency, sex of neonate, mother's age, lower income, RDS, necrotizing enterocolitis, asphyxia, hospital-acquired infection, GA, place of delivery, delivered from antepartum hemorrhage mother, lack of Kangaroo-mother care(KMC), unable to start

feeding within a hour of birth, lower APGAR score, sepsis, pneumonia, meningitis, not having Anti-Natal Care(ANC), having previous bad obstetric history, Hyaline Membrane Disease(HMD), jaundice, hypoglycemia and hypothermia were the identified socio-demographic, maternal, and neonatal-related risk factors, which were significantly associated with time to death of preterm neonates (12, 14-16, 23, 31, 33-36),

Many survivors are facing a lifetime of disability, including cerebral palsy, impaired learning, and visual impairments, and an increased risk of chronic disease in adulthood. Preterm birth has a substantial monetary cost due to the necessity for neonatal intensive care as well as continuous medical care and educational expenses. The social cost is also high, with many families experiencing the sudden loss of a preterm baby or a stressful hospital stay, sometimes for months(37).

Ethiopian Ministry of Health developed the first comprehensive National Child Survival Strategy (2005–2015), and also revised child survival and the long-term strategy (2015–2020), with the goal of eliminating all preventable child deaths by 2030(38). The country has been adopted the new WHO recommendations for improving preterm birth outcomes in the clinical standard (33). In addition to this the country developed different policies and initiatives including expanding Neonatal Intensive Care Unit (NICU), integrated management of neonatal and childhood illness, and quality improvement program to tackle newborn death by controlling major neonatal complications(39). Despite many international and local efforts, the rate of neonatal mortality among preterm neonates is unacceptably high in developing countries including Ethiopia.

Progress in reducing neonatal mortality attributable to prematurity has stagnated and premature deliveries have been on the rise over the past 20 years (40). Although there was a similar decrease in Neonatal Mortality Rates (NMR), majority of them caused by preterm birth, it was slower than the decline in child mortality rates. To achieve a Sustainable Development Goal-3 (SDG3) in decreasing child mortality, investigating data from different geographical areas of Ethiopia and recognizing risky time to preterm neonatal mortality is crucial. Knowing the particular time which is risk for preterm neonate death is vital for policymakers and other stakeholders to intervene accordingly. In addition, risk factors of mortality should be identified concerning time for prevention and management of preterm problems. To do so, further studies should be conducted. As far as my knowledge, even though several studies are conducted on prevalence of preterm infants' mortality and associated factors so far, but little is known about the time to death of preterm neonatal mortality and contributing factors. Study also done with short year of observation, and limited variable, especially in the study area. Therefore, this study was conducted to assess Time to mortality of preterm neonates and contributing risk factors among preterm neonates

admitted to NICU at Jimma Medical Center(JMC), Jimma, Southwestern Ethiopia from January 2018 to December 2022.

1.2 Significance of the study

The finding of this study will have a significant contribution to different stakeholders first for JMC, and other health institutions that help to provide useful information about the hazard time to death and factors that hinder reduction of preterm neonatal mortality, forcing them to consider designing a new program or improving the quality and effectiveness of the current intervention programs to decrease preterm neonatal mortality.

Second, it is hoped that this study will help health care providers to know the hazard time and the major risk factors contributing to preterm neonatal mortality and enhance evidence-based practice implementation to reduce preterm neonatal mortality. Third, preterm newborns and their mothers will be directly benefited from the finding of the study.

Finally, evidence obtained from this study will supports the achievement of Sustainable Development Goal number 3 #3.2(SDG3) (Newborn and child mortality: By 2030, end preventable mortality of neonates and children under 5 years of age**)**. Furthermore, the study will also be an important addition to the existing literature to estimate time to mortality, and the identification of risk factors associated with preterm neonatal mortality. The result of this study will be also a source for further investigations, and systematic review that will further have input to policy makers, and care planners.

Chapter two: literature review

2.1 Magnitude and time to mortality among preterm neonates admitted to NICU

Globally, an estimated 13 million infants are born before 37 completed weeks of gestation annually. Rates are generally highest in low and middle-income countries and increasing in some middle and high-income countries. More than 1 in 10 of the world's babies were born prematurely, making an estimated 15 million premature births, of which more than 1 million died as a result of their prematurity (41). Worldwide, out Of the 15 million preterm births every year, more than 84% occur at 32–36 weeks of gestation. Only about 5% of birth are ELBW (<28 weeks) and the other 10% are born at 28–32 weeks of gestation(37).

Different studies have been done in developed as well as in developing countries to determine the survival among preterm neonate that are admitted to NICU. A retrospective study conducted in the USA showed that the mortality rate of preterm newborn was 26.48% (42). Another study done in Netherland showed that extremely preterm infants survival was (13%–34%)(43). A retrospective follow-up study done in China; eastern, central and western regions revealed that preterm infant death were 51.3%, 42.0% and 44.5% respectively.

A study undertaken in India demonstrated that among the preterm newborns admitted to NICU, 7.5% died (44). A retrospective study done in Bangladesh showed that late preterm mortality was 1.4%(45). Similar study carried out in Nepal in 2018 showed that among preterm newborns Hospitalized to NICU 24.74% were died (13). A prospective population-based cohort study done in Pakistan found that the 28-day neonatal mortality rate was 47.3 per 1000 live births. Some 45% of the deaths occurred within 48 hours and 73% within the first week (46). A retrospective cohort study done in Iran showed that 39% and 63.7% were died within the first 24 hours and the first 48 hours, respectively, 84.3% in early neonatal period (the first week). Survival rate at first 24 hours, 48 hours, one week, 2 weeks and 4 weeks were 95%, 93%, 87%, 83%, and 79% respectively. The mean survival time was estimated 43.008±2.10 days (14).

Generally, higher estimates have been reported in varies studies conducted in Africa particularly in sub-Saharan Africa region. A study in South Africa showed that VLBW infant mortality rate was 22.6% (47). A prospective cohort study also conducted in western Uganda in 2019 reported 31.6% death and 65.8% of deaths occurring within 72 hours from admission (30). Another investigation done in Nigeria, found that the overall survival rate was 24.3% (48). According to the study done in Zambia revealed that

the cumulative median time to death of the infants was 98 hours (29). A ten-years review done in Ghana showed that 67.6% were discharged alive, and 27.6% preterm neonate were died. The average length of hospital stay was 8.3 (±9.88) days (49).

Ethiopia is the 4th ranked country in the world which has highest neonatal mortality next to India, Nigeria and Pakistan(2). Almost 90% of neonatal deaths in the country are due to preterm birth complications (37%), intra partum related complication (28%), and infection (24%)(50).

Different retrospective and prospective cohort studies have been conducted in Ethiopia. From which Perspective follow up study done in Addis Ababa, Public Hospital revealed that out of 686 preterm neonates admitted to NICU, 36.1% were died, with incidence rate of 36.4/1000 person-day. The first 7 days of admission was the hazard time to death with median time of 6 days (23). Another study done in Tikur Anbessa Specialized Hospital; 29.7% preterm neonates died during the follow-up period with the incidence rate of 39.1 per 1000-person day. The overall Kaplan Meier estimate showed that preterm neonates had a higher chance of surviving on the first day of admission, and increased failure to survive throughout the follow-up period. The cumulative median survival time was found to be 21 days (51).

A retrospective follow-up study conducted in northern Ethiopia found that out of 1017 preterm neonates 14.6% were died. Moreover, among the newborns Hospitalized to NICU, 11.7% died in the first 5 days of their life. The overall probability of survival at the first 24 hours, the first and second weeks of life was 97.9%, 82.9% and 77.2%, respectively. The average time to death of premature neonates was 47.0 days (12). A retrospective cross-sectional study done in Bahir Dar; Felege Hiwot Specialized Hospital showed that 36.1% preterm neonates were died. The survival rate was 0%, 19.4%, 46.7% and 75% for gestational age <28weeks, 28–31+6weeks, 32–33+6weeks and 34–36+6weeks, respectively. And 16.6% of preterm neonatal death occurred in first 24h of life (15). Another study done in University of Gondar Hospital showed that the overall probability of survival at the end of the first 24 hours was 96s.71%, at 5 to 6 days was 74.62%, and at 20–32 days was 57.14% (31).

A study done in Hawassa University Comprehensive Specialized Hospital found that the probability of survival of preterm neonates during the 1st, 7th and 10th days were 25.6%, 55.6%, and 78.4% respectively. The maximum survival was observed at 27th day which was 83.3% (52). According to retrospective cohort study conducted in Mizan Tepi Hospital revealed the cumulative probability of survival at the end of 1, 7, and 28-day period of follow-up were 88.03%, 59.37% 35.90% respectively. with median survival time of 15 days(34). A study done in Jimm on preterm neonates Admitted to NICU found that 34.9% preterm neonates were died (53).

2.2. Risk factors of preterm neonates' mortality

2.2.1 Scio-demographic characteristics of preterm neonates and their mothers

A finding in Florida revealed that maternal age < 18 with HR of 1.13 and greater than 35 with HR of 0.99 were higher risks than 18-35 for premature mortality(42). In Africa ,A study conducted in western Uganda showed that preterm neonates whose mothers were aged 35 years and above were 4.5 (AOR:4.5) times more likely to die, than those aged between 25-34 years(30). But Another study done in Ghana revealed that no association was found for maternal age (49). With regard to Residence, A study done in Tikur Anbessa Specialized Hospital found that the neonates who came from rural area had 1.45 times high increased risk of death (AHR: 1.45) compared to its counter parts (51). Another study done in Jimma showed that neonates who came from addresses outside the city had 1.89 times higher increased risk of mortality (AOR 1.89) compared to neonates who came from the city(54).

A study done in Ghana (49)and Uganda(30) revealed that place of delivery were significantly associated with preterm neonatal mortality. A study done in University of Gondar comprehensive specialized hospital showed that preterm neonate who had home delivery were 2.25(AHR = 2.25) times higher risk of death than hospital delivery (31). Neonates born in Tikur Anbesa hospital had 79% lesser risk of death compared to the neonates born outside [OR=0.21)(55).

A finding in Florida revealed that males sex have at higher risk of death (42). Similarly study done in Brazil showed that male preterm neonate had 2-time higher hazard of death compared to its counter parts (HR,2.01) (28). Another prospective Cohort Study done in Western Uganda found that being male sex (AOR=2.0) were significantly associated with preterm mortality (30). However, A ten-year review conducted in Ghana found that no association was found for sex of the baby(49). Conversely, in Ethiopia , Tikur Anbessa Specialized Hospital study showed that HR for death was 1.51 times (AHR: 1.51,) higher in male patients(51).

2.2.2. Obstetric and/ or gynecological characteristics

As different studies stated, causes of preterm neonate mortality vary from country to country and obstetrics and/or gynecology factors was among the major contribute factors of premature death. A study conducted in Iran showed that previous dead neonate, non-cephalic presentation and, multiple pregnancy was significantly associated with preterm neonatal mortality (P <0.001)(14). A study in Brazil found that absence of antenatal steroids (HR 1.59) was associated with premature mortality (28).

A study conducted in western Uganda at tertiary Hospital showed that no antenatal care, >4 ANC visits, singleton pregnancy were predictor of preterm neonatal mortality(30). Another study done in Ghana revealed that mode of delivery (p <0.001) was significantly associated with preterm neonatal

mortality(49). A study in Tanzania also found that preeclampsia ,placenta previa ,and abruption placenta were risk factors of premature mortality (56).

Finding in University of Gonder Hospital showed that gravidity of (6-10) statistically associated with time to death of premature infants(41). A study in Gonder found that the hazard of death among preterm neonates who delivered at home was 2.3 times higher as compared to those who were delivered in the hospital (AHR = 2.29) (31). According to study conducted in Mizan Tepi University Hospital showed that preterm neonate who delivered by Vaginal mode of delivery and born from mothers with no ANC follow-up were significantly associated with time to preterm neonatal mortality (34). Another similar prospective follow up study done in Addis Ababa public Hospital showed that Born from antepartum hemorrhage mother (AHR=3.1) were significantly associated with preterm mortality (23) A Retrospective Cohort Study done in Hawassa University revealed that, recent multiple pregnancies (AHR=1.66) were significantly associated predictors of preterm neonatal mortality. Another study done in Jimma found that Antenatal steroid use (AHR=0.55) was a significant predictor of preterm neonatal mortality(32)

2.2.3. Medical disorder in mother

Various studies revealed that premature neonates born to mothers with the medical disorder were high mortality rate. A population-based retrospective cohort study in Australian indicted that preterm neonate born from mother with no hypertensive were found to be preventive of death with AOR of 0.93(57). A study conducted in Nigeria showed that maternal febrile illness reduce the odd of preterm neonatal survival by 75%(OR = 0.25,) as compared to not have maternal febrile illness so, adversely affected neonatal survival (58).

A study conducted in Tikur Anbessa Specialized Hospital, revealed that neonates born from mothers who were non-diabetic at baseline of admission had a longer survival time than those born from mothers with DM and among the total mothers enrolled in the study 13.3% had HIV/ADIS, and 9.8%had DM (51). According to study done in Hawassa University Comprehensive Specialized Hospital Around 37.8% of the mothers were anemic and only 1% had kidney problem(52). Finding in University of Gonder Hospital showed that HIV states of the mother and anemia statistically associated with time to death of premature infant (41).

2.2.4 Preterm neonate-related characteristics

As different finding in developed and developing nations showed that preterm neonate medical problem and other related factors were the major risk factors of death in preterm neonate .A study conducted in

western Uganda Hospital showed that RDS, apnea, hypothermia, and small for gestational age were significantly associated with preterm neonatal mortality(30).

Institution-based prospective follow up study done in Addis Ababa public Hospital showed that lack of Kangaroo mother care, unable to start feeding within 24 hour of admission, apnea, and dehydration were significantly associated with preterm neonate mortality(23). A study conducted in Tikur Anbessa Hospital, showed that neonatal sepsis (AHR:1.62), respiratory distress (AHR:1.54), extreme prematurity (AHR:2.87), and low APGAR score (AHR:3.11) were found to be associated risk factors (51). Another study conducted in Mizan Tepi University Hospital revealed that fifth minute APGAR score <7 (AHR: 1.87), RDS (AHR: 1.74), didn't receive KMC (AHR: 1.45), did not cry immediately after birth (AHR: 2.81)), VLBW (AHR: 2.67), LBW (AHR: 2.24,), and hypothermia (AHR: 1.36) were significantly associated with preterm mortality (34).

A study done at Felege Hiwot comprehensive specialized hospital, Bahir Dar in 2020 showed that RDS (AHR:1.77), necrotizing enterocolitis (AHR:1.84), asphyxia, hospital-acquired infection(AHR:1.8), birth weight, and gestational age were significantly associated with time to death of preterm neonates (15). Similar study undertaken two year later at the same hospital, showed that presence of neonatal RDS (AHR:2.55), perinatal asphyxia (AHR: 4.26), and jaundice (AHR: 3.25), However, admission weight of 1,500–2,499 g (AHR: 0.23) ,and ≥2,500 g (AHR: 0.12), early breastfeeding (AHR= 0.44) and kangaroo mother care (AHR:0.11) were protective factors of preterm mortality(33).

A cohort study conducted retrospectively at Tigray region revealed that perinatal asphyxia ,RDS, 1-minute APGAR score, and birth weight were found to be significant predictors of time to preterm neonatal mortality(12). According to a study conducted at University of Gondar Hospital showed that preterm neonates with hyaline membrane disease, gestational age, cry immediately at birth, kangaroo mother care, presence of jaundice, and hypoglycemia at admission were found to be significant predictors of time to death for preterm neonates (31).

2.2.5 Conceptual Framework

The conceptual framework illustrated below suggests how various risk factors interact with time to preterm neonatal mortality among preterm neonates admitted to NICU. The model broadly includes Sociodemographic factors, Obstetric and/ or gynecological characteristics, medical disorder in mother, and Preterm neonate-related characteristics. These factors may be inter-related and may contribute to preterm neonate mortality among preterm neonate. This conceptual model adapted from different literature, and slightly modified(12, 15, 23, 31, 32, 52).

Figure 1: Conceptual frame work for time to mortality and Risk factors among preterm neonate admitted to NICU of JMC,

Chapter three: Objectives

3.1 General objective

- To assess time to preterm neonate mortality and risk factors among those admitted to Jimma Medical Center from January 2018 to December 2022, Jimma, Southwest Ethiopia, 2023.

3.2 Specific objectives

- To determine time to preterm neonate mortality among those admitted to Jimma Medical Center from January 2018 to December 2022, Jimma, Southwest Ethiopia, 2023.
- To identify risk factors of time to preterm neonate mortality among preterm neonates admitted to Jimma Medical Center from January 2018 to December 2022, Jimma, Southwest Ethiopia, 2023.

Chapter four: Methods and materials

4.1 Study area and period

The study was conducted in NICU of Jimma Medical Center, Jimma town, south west of Ethiopia. Jimma town is located 357 km towards the southwest of Addis Ababa, the capital of Ethiopia. JMC is the only biggest tertiary and referral teaching hospital in the southwestern part of the country and currently provides different services for approximately 15 million people in the catchment area(32). This hospital provides in-patient and outpatient services across various departments and wards. The neonatal ICU is one of the ICU services that the hospital is currently running. The unit has separate 18 neonatal beds and two KMC room with 10 beds each .The unit also has incubators, radiant warmers, Continuous Positive Airway Pressure (CPAP), phototherapy, and oxygen concentrator machines and other equipment. . Advanced procedures such as exchange transfusion, and Lumber punctures are performed at the center. The unit is staffed with pediatricians, pediatric residents, and neonatal nurses, and located adjacent to the labor ward to receive high-risk newborns from this unit. In addition, the unit receives referrals from nearby health facilities and homes. The study was conducted from May to June, 2023.

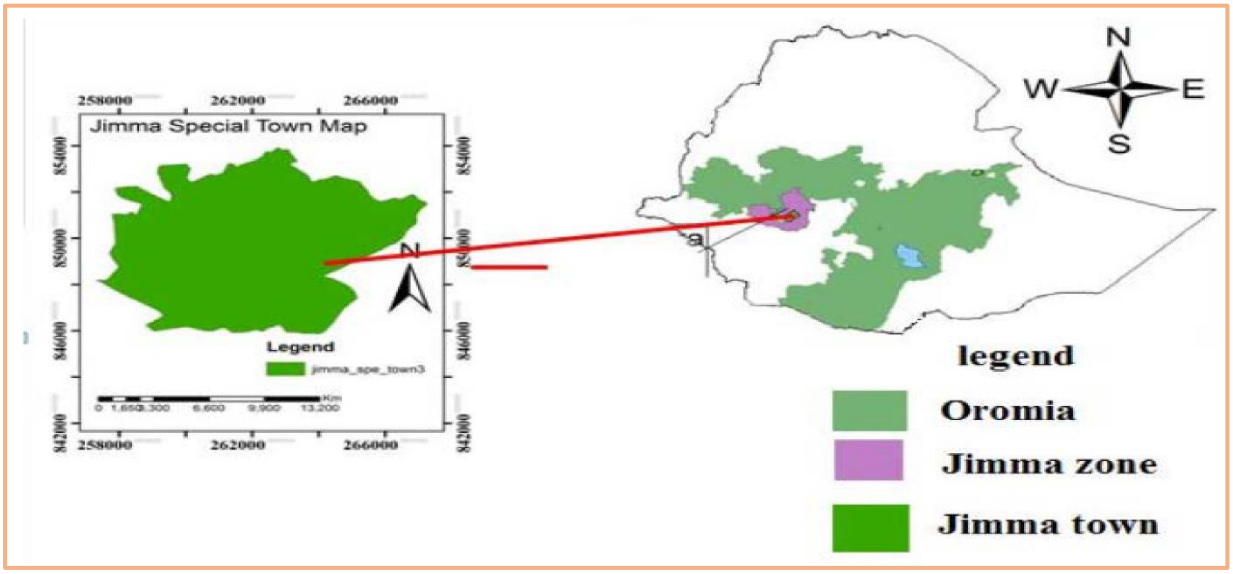

Figure 2:Map of Jimma Town (source: Jimma town administrative office, online)

4.2. Study design

An institutional-based retrospective cohort study was conducted among preterm neonates admitted at the NICU at JMC from January 1, 2018 to December 31, 2022

4.3. Source population

All preterm neonates admitted to the neonatal intensive care unit at JMC with a gestational age of less than 37 completed weeks were considered as a source population. The gestational age was determined by first-trimester ultrasound results for mothers with available reports or from the first day of the last menstrual period for those mothers without the reports.

4.4. Study population

All preterm neonates admitted to the NICU at JMC from a period of January 1, 2018 to December 31, 2022, were the study population.

4.5. Study unit

Each selected preterm neonate medical chart from the hospital's NICU registry log book.

4.6. Inclusion and exclusion criteria

4.6.1 Inclusion criteria

All alive neonates admitted to the NICU at JMC by the diagnosis of preterm birth from January 1, 2018 to December 31, 2022.

4.6.2 Exclusion criteria

Preterm neonates admitted at NICU with incomplete charts (cards that missed to register at least the following data: date of admission, date of the last contact, status of the neonates and other major risk factors) and records which are not available at the time of data collection were considered under exclusion criteria.

4.7. Sample size determination

Schoenfeld DA formula(59), was used to determine the sample size; by RDS, 5th minute APGAR score, very low birth weight, non-vertex presentation, Cry immediately at birth, and ANC follow up as the major risk factors, furthermore, Cry immediately at birth was considered as the independent risk factors since it give the maximum sample size.

$E = (z\alpha + z\beta)2 \ / (\ln \text{HR})^2 \text{Pq}$

n =E/Pr (E)

Where: -

E: the number of events required to be observed

P: the proportion of exposed to the event (28.8% or 0.288from the previous study)(31).

q: is the proportion of non-exposed to the event (71.2% or 0.712 from the previous study).

Zα: is the critical value for the test at the specified type 1 error (e.g., 1.96 for a 2-sided test at α=0.05)

zβ: Power is the upper standard normal quantile at the desired power (0.842 for 80% power).

Ln (HR) = the natural logarithm of the hazard ratio.

HR =the hazard ratio

n= total sample size

Pr (E) = probability of the event (the occurrence of death) observed (0.288)(31)

Table1: sample size calculation to assess time to mortality and risk factors among preterm neonates admitted to NICU from[2018-2022] in JMC, Jimma, Southwest Ethiopia, 2023

S.NO	Variable	AHR	P(E)	Event(E)	Total sample size	After adding 10%
1.	Respiratory distress syndrome	1.74	0.35	113	323	355 (34)
2.	5th minute APGAR score<7	1.87	0.35	88	251	276(34)
3.	Very low birth weight	2.67	0.35	36	103	113(34)
4.	Non-vertex presentation	1.8	0.35	100	286	314(34)
5.	Cry immediately at birth	1.74	0.288	125	433	476(51)
6.	ANC follow up	1.9	0.35		239	262(34)

4.8. Sampling technique and procedure

First, the Medical Registration Number (MRN) of all preterm neonates admitted to the NICU at JMC during the previous five years from a period of January 1, 2018 to December 31, 2022, was taken from the NICU log-registration book. The total number of preterm neonates admitted to the NICU of JMC from

[2018-2022] were 2519. The sample was proportionally allocated for each year. A sampling frame was prepared from the logbook of preterm neonates that were admitted in NICU from [2018-2022] for each year by numbering the units of each year on the frame from 1 to N (N=total number admission for each year), A computer-generated simple random sampling technique was applied to select a total of 476 study participants proportionally from each year. Then Medical chart of the eligible preterm neonate's charts was reviewed.

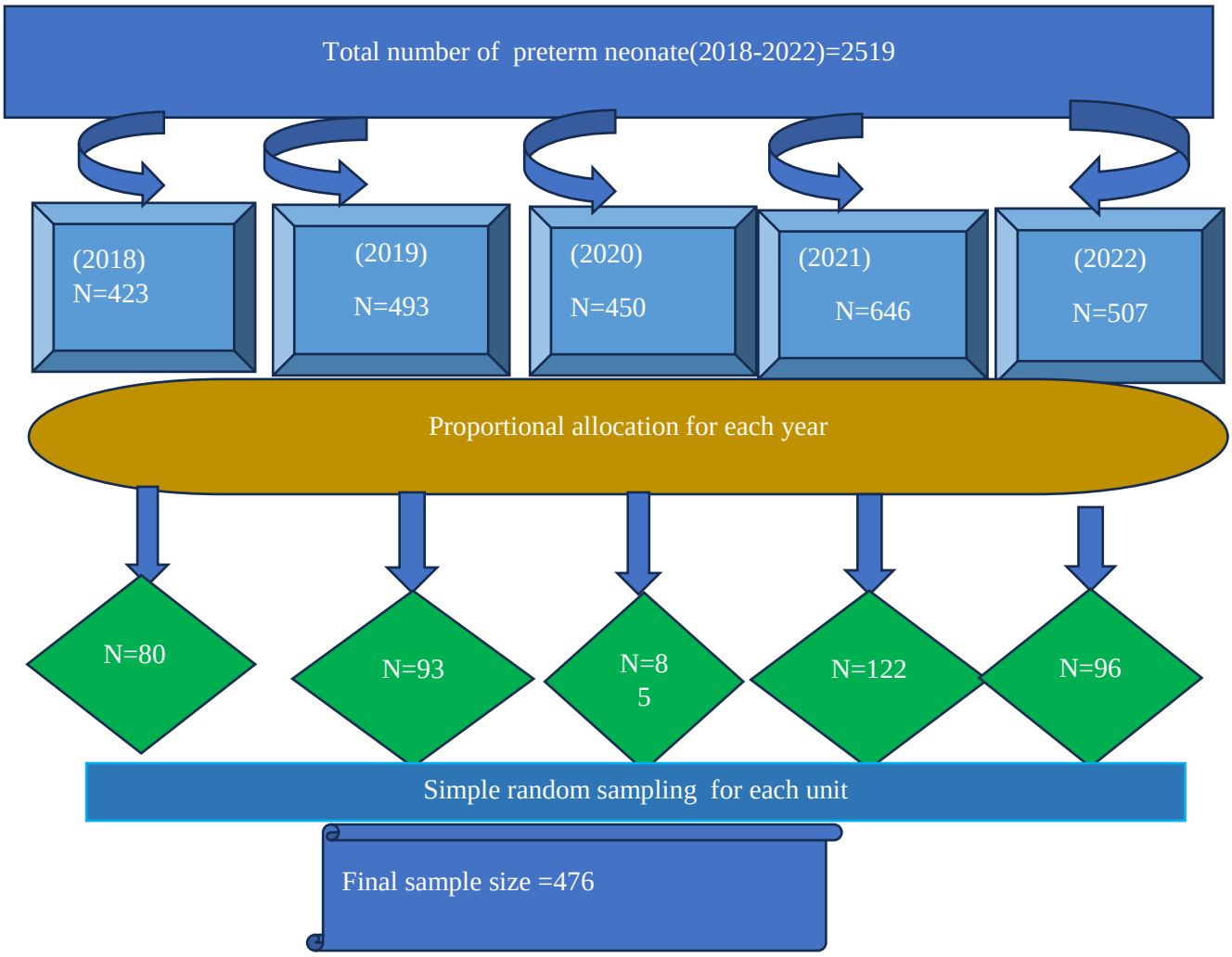

Figure 3: schematic presentation of sampling procedure to assess time to mortality and risk factors among preterm neonates admitted to NICU from [2018-2022] in JMC, Jimma, southwest Ethiopia, 2023

4.9. Study Variable

4.9.1. Dependent variable

Time to preterm neonatal mortality

4.9.2. Independent variable

Socio-demographic Characteristics: Age of mother, residency, sex of neonate, place of delivery, Age at admission, Date of NICU, admission and discharge.

Obstetric and/ or gynecological characteristics: Such as ANC visit, parity, types of pregnancy, mode of delivery, PROM, preeclampsia, abruption placenta, and steroid administration.

Medical disorder in mother: Like hypertension, diabetes mellites, HIV/AIDS, anemia, and maternal febrile illness.

Neonatal related characteristics: - Such as gestational age, birth weight, APGAR score, KMC, initiation of breast feeding within one hour of birth ,RDS, sepsis, jaundice ,PNA, hypothermia, and hypoglycemia.

4.10. Operational and variable Definitions

4.10.1. Operational definition

Time to death: it is the time elapsing from admission at NICU of JMC to the occurrence of the event(death), which can be computed by subtracting the date of death from the date of admission.

Low APGAR SCORE: A neonate with an Apgar score of <7

The Time Origin: Admission of preterm neonates to NICU at Jimma medical center

Follow-Up Time: From the time of admission until either an event or censorship occurs

Event; preterm neonate who died during the follow-up

Death: preterm neonate who died during the follow-up time and had death summery.

Censored: preterm neonates who left the follow up without event (transferred to another institution, left against medical advice, discharged and preterm stays more than 28 days).

Bad obstetric history: mothers who had history of abortion, stillbirth, and early neonatal death.

Having ANC follow up: If the mother has a follow up of at least four times at her pregnancy period.

Type of pregnancy: women were assigned to type of pregnancy (single versus multiple).

Fetal presentation: classified as vertex and non-vertex. The first used as the reference category.

Mode of delivery: grouped into spontaneous vaginal, cesarean section and instrumental delivery (forceps and vacuum). Spontaneous vaginal used as reference group.

perinatal asphyxia: profound metabolic or mixed acidemia, persistence of an Apgar score of 0–3 for longer than 5 min, neonatal neurologic sequelae (e.g., seizures, coma, hypotonia, and inability to suck/cry).

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

Neonatal complications; are considered if the neonate had one or more of the following problems such as Perinatal Asphyxia (PNA), Necrotizing Enterocolitis (NEC), jaundice, hypothermia, sepsis, hypoglycemia, RDS, and HMD)

Time scale: Days from the admission of preterm neonate

4.10.2. Definition of Variables

Multigravidas: Recorded gravida of >2.

Multiparty: Recorded parity of >2.

Preterm neonatal mortality: Death of preterm neonates within 28 days of admission or at discharge, whichever comes first.

4.11, Data collection procedures

4.11.1 Data Collection tool

Information on the patient medical chart was first observed and structured data abstraction checklist was prepared in English. Data collection checklist for this study was adapted from a similar study conducted in Felege hiwot specialized Hospital, Bahir Dar, and Modification made on the checklist based on the NICU registration format, and through reviewing other relevant related literature(12, 15, 23, 31, 32, 52). The checklist also comprises socio-demographics characteristics of both mothers, and preterm neonates, obstetric and/or gynecological characteristics, medical disorder in mother, and neonatal related characteristics

4.11.2. Data collection and data collectors

Data was collected by record review methods after pre-test was done on 5% of sampled population in Agaro hospital one week before the actual data collection for the applicability and consistency of relevant variables. Variables like gravidity, birth trauma, and birth interval were removed from the checklist after pre-test because those variables were not available on patient medical chart. The starting point for retrospective follow-up was the time from first day of admission and the endpoint was date of death and censored till the last neonatal period. Death was confirmed by reviewing medical death certificate in the hospital. All charts of preterm neonates, admitted to the NICU at JMC from a period of

January 1, 2018 to December 31, 2022, were reviewed from neonatal log registries book. Each sampled record that met the eligibility criteria preterm neonate's medical charts was retrieved from NICU card room by JMC main card room worker. Then abstractors were used a structured checklist form to retrieve the required information from medical charts. The data was collected by trained three BSC nurses, one card room worker to retrieve medical chart and supervised by one bachelor's degree holder senior nurse for 28 days. Training on objective of the study, the contents of the questionnaire, selection of study participants chart, techniques of data extraction, and data quality management by the principal investigator was given for data collector and supervisor for two days. Intensive supervision was done by the principal investigator and supervisors.

4.12. Data quality control

Before data collection: Data quality was assured by careful designing of the data abstraction checklist. The adopted and prepared data collection format was evaluated by experienced researchers. The data collection tool was pretested on 5% of sampled population in Agaro hospital one week before the actual data collection. Required modification was made after pretest by principal investigator under the guidance of supervisors. proper training was given for data collectors and supervisors for two days about the objective of the study, confidentiality of information and techniques of data extraction.

During data collection: close supervision and monitoring was carried out by supervisors and principal investigator to ensure that the data was complete and consistent. Daily evaluation of the data for completeness and encountered difficulties on the time of data collection was attended accordingly. Principal investigator has checked the consistency of the extracted data.

During entry and analysis: The collected data were entered into Epi data 4.6 software, which includes control mechanisms such as range, must enter, and jump. Thereafter, STATA software version 17 was used to re-code, clean the data and a crosstab was performed to check the frequency of explanatory variable with the dependent variable in order to test the assumptions.

4.13. Data processing and analysis procedure

Before analysis, data was checked for completeness, edited, and coded. Thereafter data was entered into Epi-data version 4.6 and exported to STATA version 17 for further cleaning, and analysis. Any identified error at this time was corrected after review of the original data using the code numbers. Descriptive data was presented using text, tables and figures to see the distribution of study variables, and frequencies, percentages, and rates was used. The mean with standard deviation and median with interquartile range were used to summarize normally and non-normally distributed continuous variables, respectively. The

overall neonatal mortality rate (incidence density) was calculated by dividing the number of preterm neonates who died during the follow-up period by the total neonate-days at risk of observation and reported per 1000pd. The Kaplan-Meier curve was used to estimate median survival time, cumulative probability of survival, and compare survival difference between the different covariates. The log-rank test was used to compare survival curves between groups of explanatory variables. Cox regression model was used to identify the independent predictors of preterm mortality. Hazard Ratios (HRs) with 95% Confidence Intervals (CI) was used to assess the relationship between factors associated with the time to death of preterm neonatal mortality. Those variables having P-value <0.2 in the bivariable analysis was transferred to the multivariable analysis and those variables having P-value <0.05 at 95% confidence level were considered as independent predictors of preterm mortality.

Multicollinearity of each independent variable was checked using Variance Inflation Factor (VIF) and the highest observed VIF-value was 1.84 with the mean value of 1.37, assuring that there was no multicollinearity threat. Proportional hazard assumption was tested by martingale residuals and deviance residuals were used to check the linearity of the test and the presence or absence of extreme observations or outliers respectively. Schoenfeld residuals test for each variable and overall model of the cox proportional hazard (Global test. P-Value=0.5951> 0.05) was satisfied. The goodness of model fitness was checked by using cox-Snell residual test.

4.14. **Ethical consideration**

In this study, it was impossible to get informed consent from the neonates' family because there was no contact either with the neonates or families and the data was collected from neonates' medical chart after they were discharged or died. But Ethical clearance was obtained from the Institutional Health Research Ethics Review Committee (IHRERC), Institute of Health, Faculty of public health, Jimma University with Ref No: JUIH/IRB/370/23. Thus, an official letter confirming Ethical clearance to conduct the study was written from the department to Jimma medical center and then permission letter obtained from hospital medical director to department of Pediatrics and child Health, NICU staffs and main card room to co-operate during data collection. The purpose of the study was informed for those stakeholders prior to the commencement of actual data collection. Any neonatal personal identification wasn't utilized in the study. All data was kept strictly confidential and used only for those study purpose.

4.15. Dissemination Plan

The findings of the study will be submitted and presented to the Jimma university institute of health, faculty of public health, department of epidemiology for partial fulfillment for the degree of master's public health in epidemiology. Likewise, the result will also be submitted to JMC to enable them take recommendations in to consideration during development of their interventional strategic plan and the

finding will also be presented in both local and international seminars, conferences and meetings. Publication in peer reviewed, national or international journals will also be considered.

Chapter Five: Results

5.1. Socio-demographic characteristics of the study participants

In this study, a total of 476 preterm neonates medical records were reviewed, and 456(95.8%) records met enrollment criteria in the final analysis. Of them, about three-fourths, 343 (75.2 %) of preterm neonates were admitted on the first day of their life, which contributed, 112(83.0%) of the death. Out of all study participants (456), more than half, 250 (54.8%) of them were males. The average age of mothers was 27.9±6.03 SD years old. The youngest and the oldest mother found in this study were 17 and 45 respectively. The mean age of the cohort at the time of admission to NICU was 1.1±2.09 SD days (Table 2).

Table 2: Socio-demographic characteristics of preterm neonates and their mothers in JMC, Jimma, Southwest Ethiopia, 2023(N=456)

Variables	Category	Status		Total (%)
		Death (%)	Censored (%)	
Neonatal age at admission	<24 hours	112(83.0)	231(72.0)	343(75.2)
	1-6 days	20(14.8)	85(26.5)	105(23)
	≥7days	3(2.2)	5(1.5)	8(1.8)
Sex	Male	78(57.7)	172(53.6)	250(54.8)
	Female	57(42.3)	149(46.4)	206(45.2)
Maternal age	<20	6(4.4)	15(4.7)	21(4.6)
	20-34	99(73.3)	245(76.3)	344(75.4)
	≥35	30(22.3)	61(19)	91(20)
Residence	Rural	71(52.6)	204(63.6)	275(60.3)
	Urban	64(47.4)	117(36.4)	181(39.7)

5.2 Obstetric and/or gynecologic and, Maternal medical-related characteristics

Among the total mothers who participated in the study, around half, 206(45.2%) of the mothers delivered in JMC(inborn) and only 18(3.9%) neonates were born at home. Around half,231(50.7%) of the mothers had two up to four births, and about 56(12.3%) of the mothers had bad obstetric history. Almost all, 436 (95.6%) of mothers enrolled in the study had ANC follow-up. The majority, 377 (82.7%) of the mothers had spontaneous onset of labor and 327(71.7%) of the mothers had four up to eighteen-hour duration of labor. Three hundred eighteen (69.7%) of neonates were born via Spontaneous Vaginal Delivery (SVD) and 135(29.6%) of them were via Caesarian Section (C/S), and 158(34.6%) of the mothers had multiple pregnancies. Medical disorder in mothers were also identified (Table 3).

Table 3: Obstetrics and/or gynecological and maternal medical characteristics of mothers who had neonate admitted to NICU of JMC, Jimma, Southwest Ethiopia, 2023(N=456)

Variables	Category	Status		Total (%)
		Death (%)	Censored (%)	
Place of delivery	Inborn	61(45.2)	145(45.2)	206(45.2)
	Other Hospital	40(29.6)	73(22.7)	113(24.8)
	Health center	29(21.5)	80(24.9)	109(23.9)
	Home	1(0.7)	17(5.3)	18(3.9)
	Others	4(3.0)	4(1.9)	10(2.2)
Parity	I	46(34.1)	111(34.6)	157(34.4)
	II-IV	69(51.1)	162(50.5)	231(50.7)
	≥V	20(14.8)	48(14.9)	68(14.9)
Bad obstetric history	Yes	22(16.3)	34(10.6)	56(12.3)
	No	113(83.7)	287(89.4)	400(87.7)
ANC follow up	Yes	129(95.6)	307(95.6)	436(95.6)
	No	6(4.4)	14(4.4)	20(4.4)
Onset of labor	Spontaneous	108(80.0)	269(83.8)	377(82.7)
	Induced	19(14.1)	29(9.0)	48(10.5)
	Caesarian section	8(5.9)	23(7.2)	31(6.8)
Duration of labor(hours)	<4	23(17.0)	46(14.3)	69(15.1)
	4-18	93(68.9)	234(72.9)	327(71.7)
	>18	11(8.1)	18(5.6)	29(6.4)
	No labor	8(6.0)	23(7.2)	31(6.8)
Presentation	Vertex	106(78.5)	262(81.6)	368(80.7)
	Non-vertex	29(21.5)	59(18.4)	88(19.3)
Mode of delivery	Spontaneous	94(69.6)	224(69.8)	318(69.7)

	vaginal			
	C/S	40(29.6)	95(29.6)	135(29.6)
	Instrumental	1(0.8)	2(0.6)	3(0.7)
Pregnancy type	Single	90(66.7)	208(64.8)	298(65.4)
	Multiple	45(33.3)	113(35.2)	158(34.6)
		Death	Censored	
Antenatal steroid	Yes	65(48.1)	150(46.7)	215(47.1)
	No	70(51.9)	171(53.3)	241(52.9)
Obstetric complications	Yes	56(41.5)	103(32.1)	159(34.9)
	No	79(58.5)	218(67.9)	297(65.1)
PROM	Yes	20(14.8)	43(13.4)	63(13.8)
	No	115(85.2)	278(86.6)	393(86.2)
Preeclampsia	Yes	30(22.2)	27(8.4)	57(12.5)
	No	105(77.8)	294(91.6)	399(87.5)
Eclampsia	Yes	4(3.0)	10(3.1)	14(3.1)
	No	131(97.0)	311(96.9)	442(96.9)
Placenta previa	Yes	8(5.9)	12(3.7)	20(6.2)
	No	127(94.1)	309(96.3)	436(93.8)
Abruption placenta	Yes	4(2.9)	10(3.1)	14(3.1)
	No	131(97.1)	311(96.9)	442(96.9)
Chorioamnionitis	Yes	2(1.5)	9(2.8)	11(2.4)
	No	133(98.5)	312(97.2)	445(97.6)
Other obstetric complication*	Yes	5(3.7)	17(5.3)	22(4.8)
	No	130(96.3)	304(94.7)	434(95.2)
Medical disorder in mothers	Yes	13(9.6)	21(6.5)	34(7.5)
	No	122(90.4)	300(93.5)	422(92.5)
Maternal febrile illness	Yes	1(0.7)	6(1.9)	7(1.5)
	No	134(99.3)	315(98.1)	449(98.5)
Anemia	Yes	1(0.7)	5(1.6)	6(1.3)
	No	134(99.3)	316(98.4)	450(98.7)
Dm	Yes	2(1.4)	3(0.9)	5(1.1)
	No	133(98.6)	318(99.1)	451(98.9)
RVI	Yes	4(3.0)	4(1.2)	8(1.8)
	No	131(97.0)	317(98.8)	448(98.2)
Chronic hypertension	Yes	4(2.9)	5(1.6)	9(2.0)
	No	131(97.1)	316(98.4)	447(98.0)
Other medical disorders in mothers**	Yes	2(1.5)	2(0.6)	4(0.9)
	No	133(98.5)	319(99.4)	452(99.1)

*Nonreassurance fetal heart pattern, oligohydramnios, polyhydramnios, postpartum hemorrhage, fetal distress, and Cord prolapse.

**Renal disease, cardiac disease, and UTI.

5.3 Preterm neonate-related characteristics

Two hundred seventy-five (60.3%) of the preterm neonates had LBW (1500-<2500 g) with a mean birth weight of 1686.39 ±442.54g, and 172(37.7%) of the neonates belonged to late preterm (34-<37) category with the average gestational age of 32.98±2.01 weeks ranged 27 to 36 weeks. Almost half,65(48.1%) of the death contributed by VPNT(28-<32) category of gestational age. The median admission temperature was 36c^{o} (IQR=35.4 c,36.6^{o}). Ninety-one (20%) premature neonates didn't cry immediately after birth and around two-thirds, 313(68.6%) neonates were not initiated breastfeeding within one hour of birth.

Concerning the APGAR score, 205(44.9%) of neonates had <7 first-minute APGAR score, and nearly quarter, 104(22.5%) of them also had <7 fifth-minute APGAR score. Out of the cohort, more than half 241(52.9%) of neonates were diagnosed with hypothermia followed by hyaline membrane disease [231(50.7%], neonatal sepsis [171(37.5%)], jaundice [150(32.9%)], hypoglycemia [63(13.8%)], and RDS [37(8.1%)]. Among the study subjects, 361(79.2%) of them were treated by antibiotics. Near to two-fifths 194(42.5%) neonates received Kangaroo-mother care and almost one-third 156(34.2%) received nasal CPAP (Table 4).

Table 4: Neonatal related characteristics of premature neonates that were admitted to NICU of JMC, Jimma, Southwest Ethiopia, from[2018-2022],(N=456)

Variables	Category	Status		Total (%)
		Death (%)	Censored (%)	
Birth weight(gram)	<1000	13(9.6)	2(0.6)	15(3.3)
	1000-<1500	71(52.6)	79(24.6)	150(32.9)
	1500-<2500	50(37.1)	225(70.1)	275(60.3)
	≥2500	1(0.7)	15(4.7)	16(3.5)
Gestational age	<28	3(2.2)	1(0.3)	4(0.9)
	28-<32	65(48.1)	62(19.4)	127(27.9)
	32-<34	39(28.9)	133(41.4)	172(32.7)
	34-<37	28(20.8)	125(38.9)	153(33.5)
Weight for gestational age	AGA	129(95.6)	303(94.4)	432(94.7)
	LGA	1(0.7)	6(1.9)	7(1.6)
	SGA	5(3.7)	12(3.7)	17(3.7)
Temperature at admission	<36.5	91(67.4)	206(64.2)	297(65.2)
	36.5-37.5	38(28.1)	103(32.1)	141(30.9)
	>37.5	6(4.5)	12(3.7)	18(3.9)
Immediately cry after birth	Yes	82(60.7)	283(88.2)	365(80.0)
	NO	53(39.3)	38(11.8)	91(20.0)
Initiation of breastfeeding within one hour of birth	Yes	21(15.6)	122(38..0)	143(31.4)
	No	114(84.4)	199(62.0)	313(68.6)
1st minute APGAR score	<7	100(74.1)	104(32.4)	205(44.9)
	≥7	35(25.9)	217(67.6)	252(55.1)
5th minute APGAR score	<7	69(51.1)	35(10.9)	104(22.8)
	≥7	66(48.9)	286(89.1)	352(77.2)
Neonatal sepsis	Yes	53(39.3)	118(36.8)	171(37.5)
	No	82(60.7)	203(63.2)	285(62.5)

RDS	Yes	23(17.0)	14(4.4)	37(8.1)
	No	112(83.0)	307(95.6)	419(91.9)
Hypoglycemia	Yes	17(12.6)	46(14.3)	63(13.8)
	No	118(87.4)	275(85.7)	393(86.2)
Anemia	Yes	15(11.1)	32(10.0)	47(10.3)
	No	120(88.9)	289(90.0)	409(89.7)
Hospital acquired infection	Yes	8(5.9)	13(4.0)	21(4.6)
	NO	127(94.1)	308(96.0)	435(95.4)
Jaundice	Yes	47(34.8)	103(32.1)	150(32.9)
	No	88(65.2)	218(67.9)	306(67.1)
Hyaline membrane disease	Yes	91(67.4)	140(43.6)	231(50.7)
	No	44(32.6)	181(56.4)	225(49.3)
Perinatal asphyxia	Yes	13(9.6)	9(2.8)	22(4.8)
	No	122(90.4)	312(97.2)	434(95.2)
Apnea of prematurity	Yes	9(6.7)	8(2.5)	17(3.7)
	No	126(93.3)	313(97.5)	439(96.3)
NEC	Yes	5(3.7)	3(0.9)	8(1.8)
	No	130(96.3)	318(99.1)	448(98.2)
Hypothermia	Yes	77(57.0)	164(51.1)	241(52.9)
	No	58(43.0)	157(48.9)	215(47.1)
Other medical neonatal problems*	Yes	6(4.4)	14(4.3)	20(4.4)
	No	129(95.6)	307(95.7)	436(95.6)
Treated by antibiotics	Yes	110(81.5)	245(76.3)	361(79.2)
	No	19(18.5)	76(23.7)	95(20.8)
Feeding practice	Brest sucking	47(34.8)	131(40.8)	178(39.0)
	NPO	21(15.5)	65(20.2)	86(18.8)
	NGT tube	62(45.9)	116(36.2)	178(39.1)
	Cup feeding	5(3.8)	9(2.8)	14(3.1)
Neonates who received kangaroo mother care	Yes	25(18.5)	169(52.6)	194(42.5)
	No	110(81.5)	152(47.4)	262(57.5)
Received CPAP	Yes	43(31.9)	113(35.2)	156(34.2)
	No	92(68.1)	208(64.8)	300(65.7)
Resuscitated with bag and mask	Yes	44(32.6)	111(34.6)	155(34.0)
	No	91(67.4)	210(65.4)	301(66.0)
Phototherapy	Yes	34(25.2)	99(30.8)	133(29.2)
	No	101(74.8)	222(69.2)	323(70.8)
Hated with radiant warmer	Yes	73(54.1)	154(48.0)	227(49.8)
	NO	62(45.9)	167(52.0)	229(50.2)
Intra nasal oxygen	Yes	76(56.3)	146(45.5)	222(48.7)
	NO	59(43.7)	175(54.5)	234(51.3)

*Meconium aspiration syndrome, Meningitis, Intraventricular hemorrhage, Neonatal seizure, Ophthalmic neon trim, congenital malformation, Cranocenthesis, DIC

5.4 Time to mortality of preterm neonates

A total of 456 premature neonates that were admitted to NICU have been followed up to 28 days of age starting from admission up to the occurrence of outcome. The minimum follow-up period observed in this cohort was 1 day and the maximum was 28 days. The overall mean of the entire Hospital stay period was 8.71(95%CI:8.00,9.42) with the median of 6(IQR=11,13). During the follow-up,135(29.61%)

(95%CI:25.58,33.97) of the neonates died. Among death, most of neonates (82.2%) died in the first 7 days after admission, 27.41%, 40.74%,82.22%, and 94.81% died during the first 24 hours, 48 hours, in the early neonatal period (the first week), and two weeks of life respectively. Out of the cohort, 321(70.39%(95%CI:66.03,74.41) were censored, from which 291(63.82%) were discharged with improvement, 11(2.41%) left against medical advice, and the remaining 19(4.17%) were referred to other hospitals at the end of the follow- up (Fig.4).

Totally the participants were assessed for 3972 neonates-days observation retrospectively, with the incidence rate of 34(95%CI:28.72,40.24) deaths per 1000 neonate-day observations. The incidence death rate of preterm neonates was 81, 47, 40, 15, and 11 per 1000 neonate-day observation in the first 24hr, 48hr,first week, second week, and greater than two weeks after admission respectively.

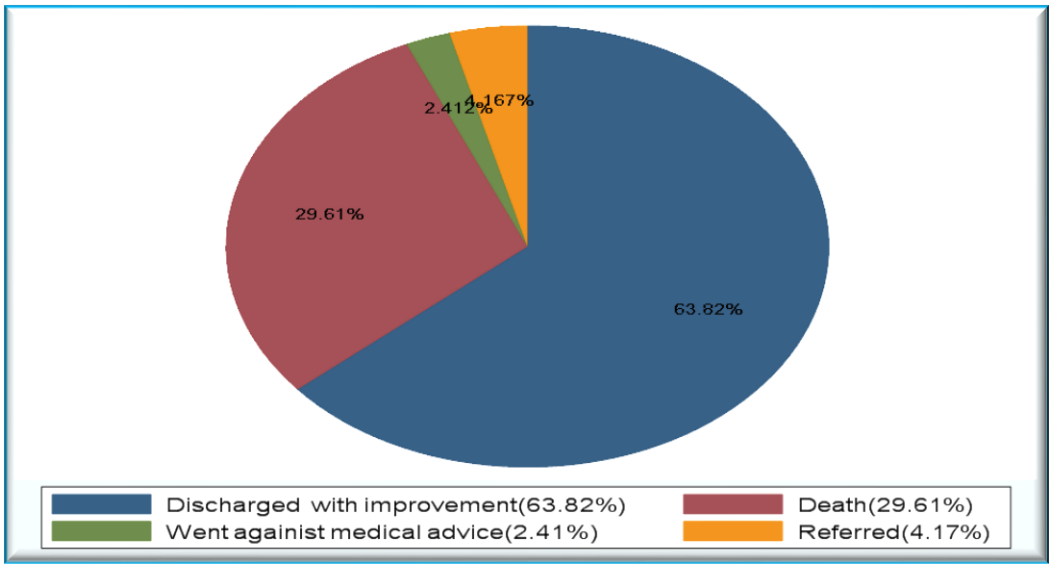

Figure 4: Overall outcomes of preterm neonates admitted to the neonatal intensive care unit of JMC, Southwest Ethiopia, from [2018-20122],2023

5.4.1. Overall Survival Function

Premature neonates were followed for different follow-up periods. Throughout the follow-up the probability of survivorship was different according to their exposure. The survivors observed in the cohort of less than 28 weeks of gestational age were only one out of four preterm neonates. The survivors of those preterm neonates having less than 1000 g were only two from a total of 15 preterm neonates. The cumulative Survival rate at the end of the first 24 hours, 48 hours, one week, and two weeks were 91.89%, 87.52%, 71.40%, and 64.01%, respectively. The overall probability of survival of preterm neonate was 52.66% throughout the follow-up period. The cumulative survival of preterm neonates was high in the first day after admission, which decreased as follow-up time increased up to 28 days. The median survival time was not identified since to

estimate median survival time at least 50% of the preterm neonates have to experience the event of interest during the follow-up period. But, only 29.61%% of neonates had experienced death in this study.

As has been seen in the graph below the left side, the overall survival probability of preterm neonates during the follow-up period was illustrated by a step-down Kaplan-Meier survival curve. The graph went down increasingly over the first seven days, showing a lower probability of preterm neonatal survival. However, in the remaining days of the follow-up time, the graph fell down slowly indicating that the likelihood of preterm neonatal death decreased (Fig.5).

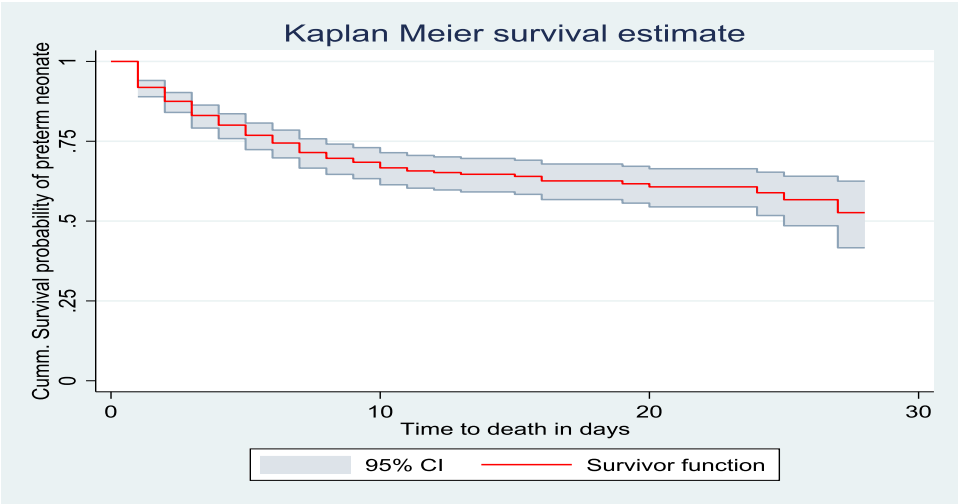

Figure 5: Overall Kaplan-Meier survival estimate of preterm neonate admitted to NICU of JMC, Jimma, Southwest Ethiopia from [218-2022], 2023.

5.4.2. Survival function and Comparison of Survivorship Function between different categorical variables

The Kaplan-Meier estimator survival curve gives the estimate of survivor function among different groups of a variable to make comparisons. Separate graphs of the estimates of the Kaplan-Meier survivor functions were constructed for different categorical variables as described below. In general, the pattern that one survivorship curve lying above another means the group defined by the upper curve has better survival than the group defined by the lower curve or had a longer survival experience than the group defined by the lower curve. In contrast, for failure curve the vice versa is true. However, the statistical question is whether the observed difference seen on the plot is significant or not. This can be shown by log- rank test.

In this study, preterm neonates who initiated breastfeeding within one hour of birth had favorable survival probability than their counterpart with overall survival function of 81.3%(95%CI:72.43,87.62), and

43.4%(95%CI:31.98,54.33) at 28 days of the follow-up period respectively, (X^2=19.6, P-value<0.001)(see fig. 6).

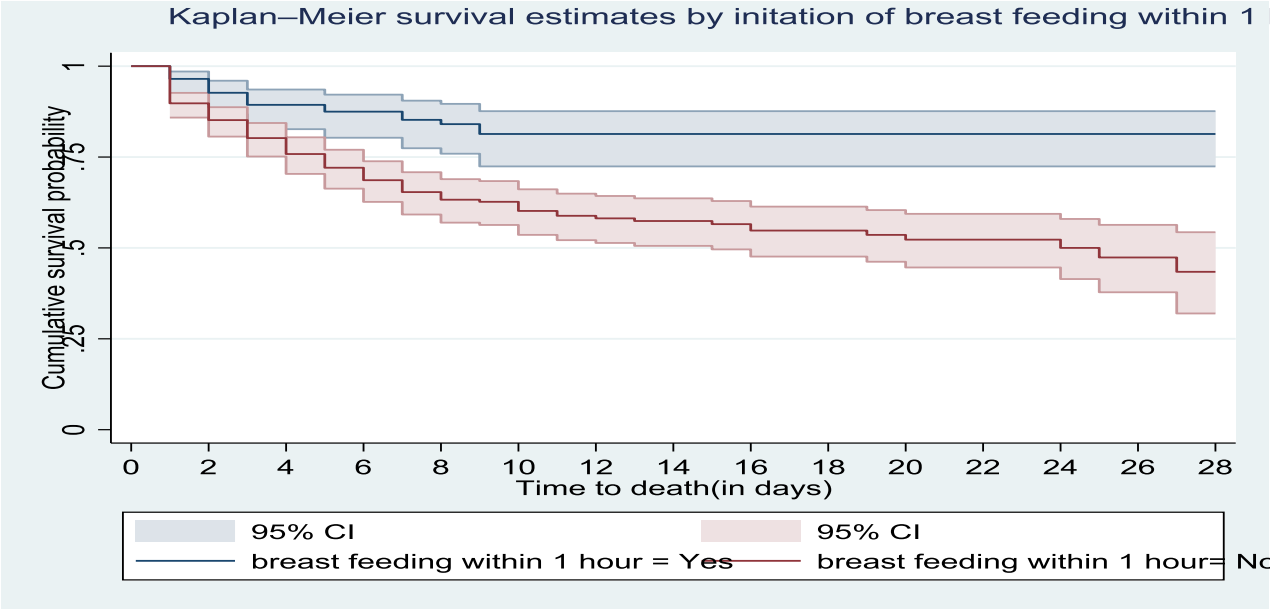

Figure 6: Kaplan-Meier survival curves compare survival time of premature neonates with categories of breastfeeding within one hour of birth at NICU, JMC, Jimma, Southwest Ethiopia, 2023

This study also revealed that, neonates having the APGAR score of<7 at 1st minute after birth had lower survival experience than neonates having APGAR score ≥7 at 1st minute with the overall survivorship of 29.78% (95%CI: 17.99,42.52) and 79.82%(95%CI:71.95,85.69) respectively, at the end of the follow-up period. This difference was statistically significant (X 2=63.39, P-value<0.001) (see Fig. 7).

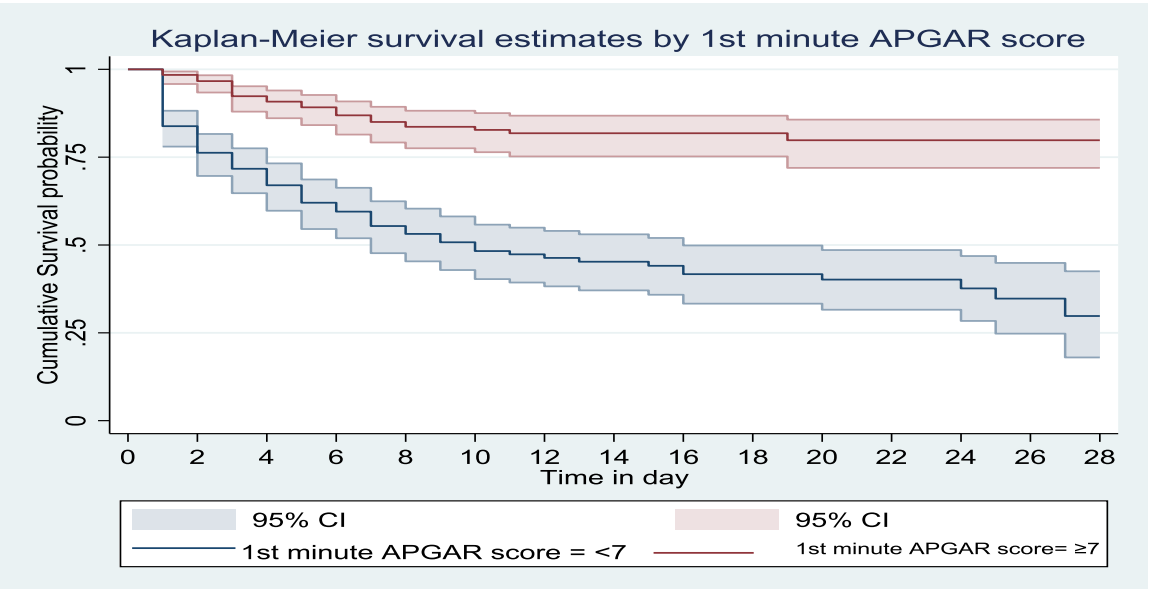

Figure 7: Kaplan-Meier survival curves compare survival time of premature neonates with categories of 1st minute APGAR score at NICU, JMC, Jimma, Southwest Ethiopia from [2018-2022], 2023

In this study, neonates having the APGAR score of <7 at the 5th minute had lower survival time than neonates having an APGAR score of ≥7 at the 5th minute of birth, and the overall survivorship found to be 16.72%(95%CI:7.71,28.71) for 5th minute Apgar score<7 at 26 days of follow-up and 64.7%(95%CI:50.55,75.76) for ≥7 at the end of follow-up period (X^2=110.65, P-value<0.001) (Fig. 8).

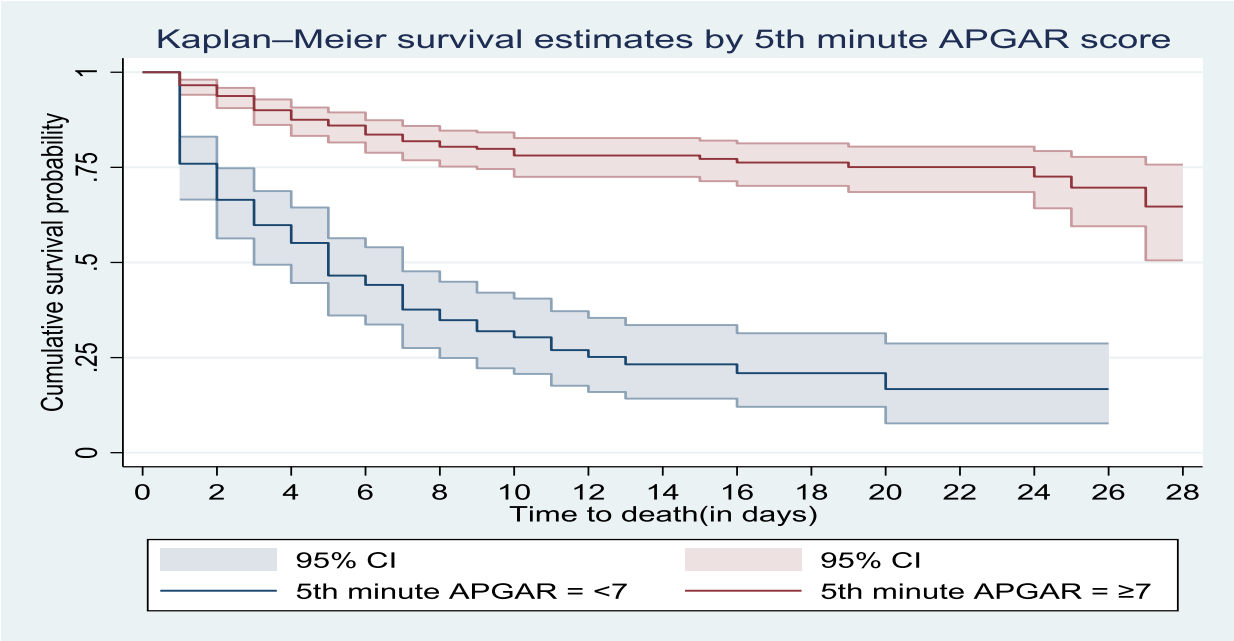

Figure 8: Kaplan-Meier survival curves compare survival time of premature neonates with categories of 5th minute APGAR score at NICU, JMC, Jimma, Southwest Ethiopia from [2018-2022], 202

Neonates having RDS during follow-up times had higher hazard than those neonates without RDS. The cumulative hazard of those neonates at the end of the follow-up period found to be 74.61% with RDS and 45.14% without RDS. The incidence rate was 101/1000 for neonates with RDS and 30/1000 neonates without RDS. This was statistically significant with (X 2=27.4, P-value<0.001) (see Fig.9).

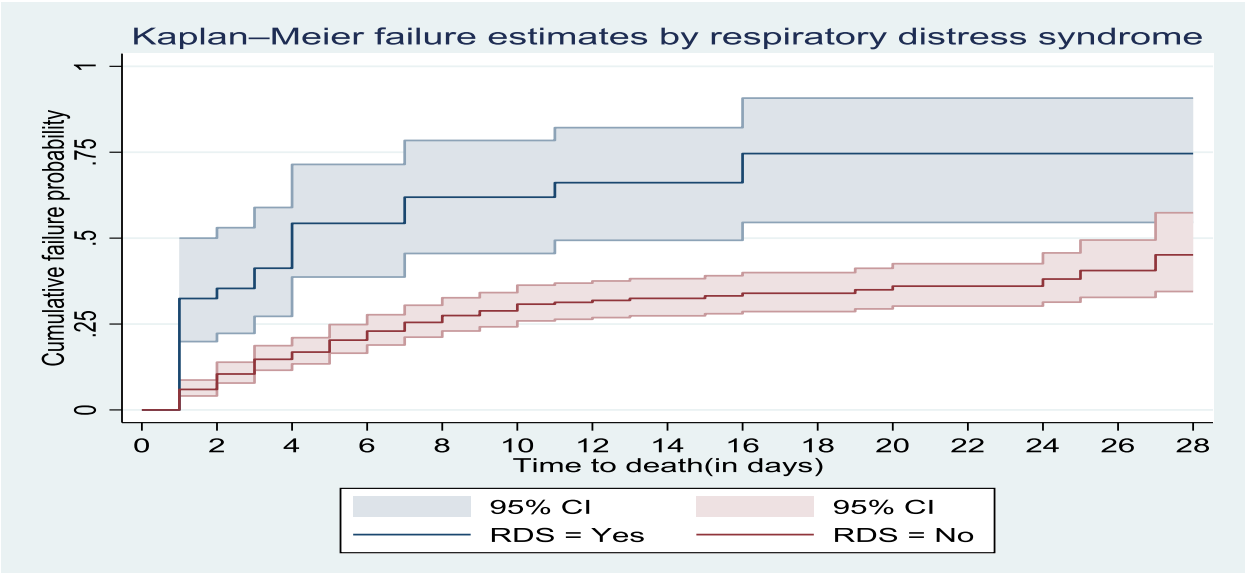

Figure 9: Kaplan-Meier hazard curves compare survival time of premature neonates with categories of RDS at NICU, JMC, Jimma, Southwest Ethiopia from [2018-2022], 2023

In this cohort, preterm neonates who received KMC had lower failure probability than those who hadn't with the overall hazard of 20.58% and 66.61% for those who obtained KMC and not obtained KMC respectively ($X^{2=}$ 43.18, P-value<0.001) (Fig. 10).

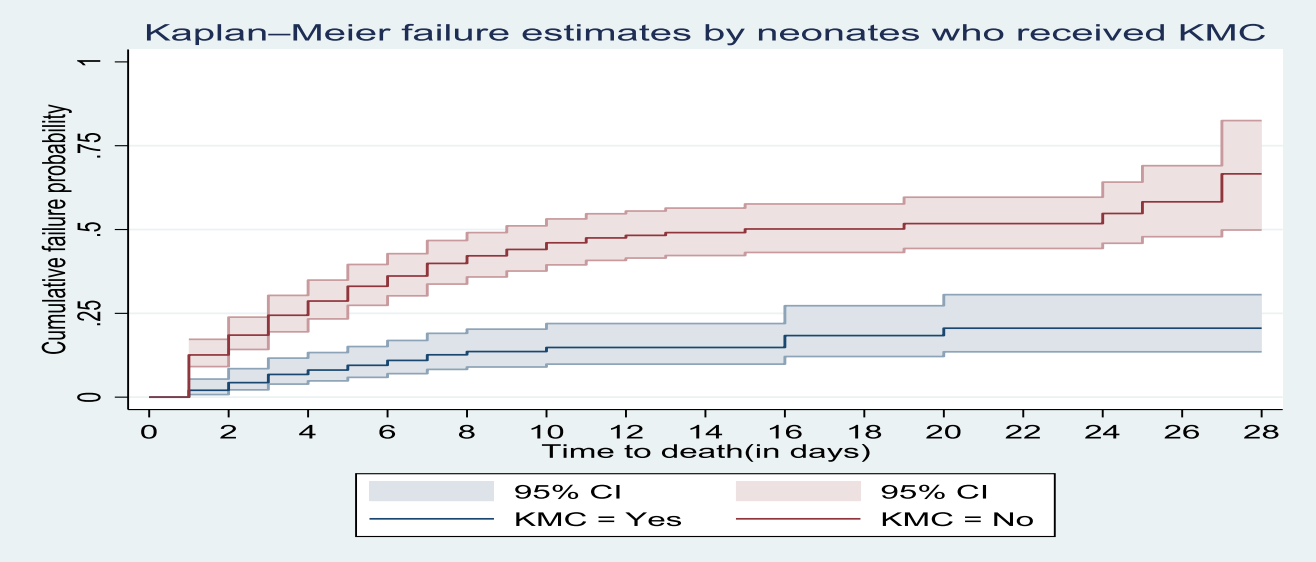

Figure 10: The Kaplan-Meier hazard curves compare the survival time of premature neonate with categories of KMC at NICU, JMC, Jimma, Southwest Ethiopia from [2018-2022], 2023

5.5. Test of proportional hazard assumption

Testing the proportional hazard assumption is essential for the interpretation and use of fitted proportional hazard models. Therefore, all risk factors variables were checked with graphical method of Kaplan-Meier curves and log-log plot curves among different groups of categorical variables. In this study Goodness-of-Fit (GOF) particularly the Schoenfeld residuals proportional hazard assumption test for the individual variable and global tests was used. Each variable (P-Value > 0.05) and all of variable simultaneously (Global test =0.5951> 0.05) met the proportional hazard assumption.

5.6. The Goodness of Fit Test

As it can be seen below, the plot of the Nelson-Allen cumulative hazard function against Cox-Snell residuals close to 45^0 straight lines through the origin for the cox-proportional hazard model. This suggested that the cox-proportional hazard model provided the best fit for our data set (Figure 11).

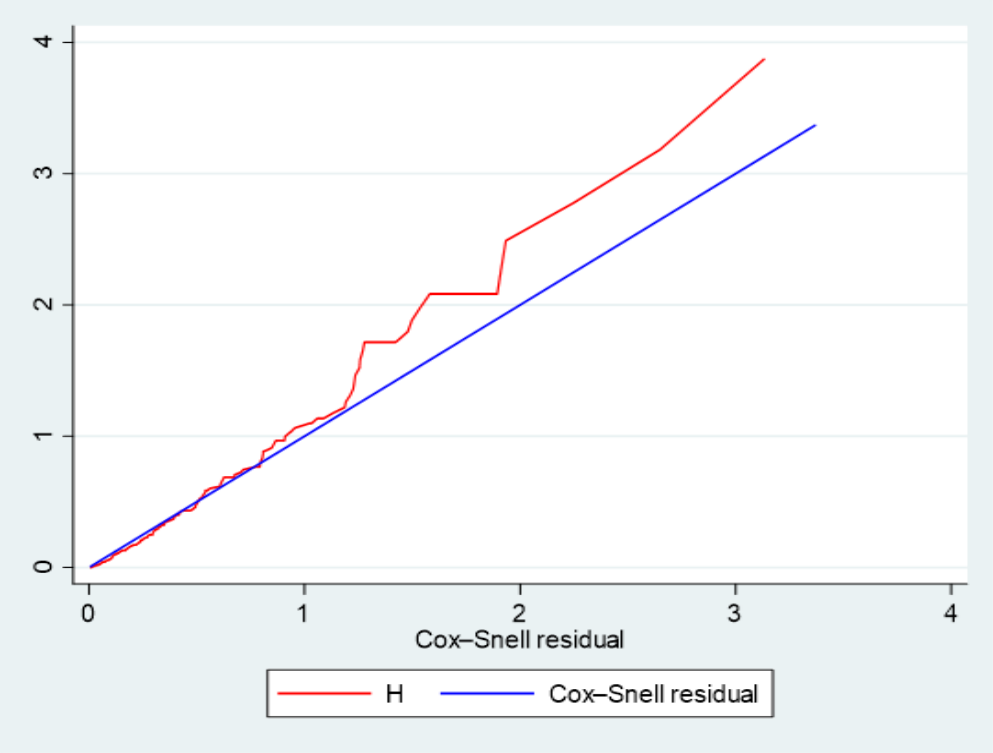

Figure11: Model fitness by using Cox-Snell residual test on preterm neonates admitted NICU, JMC, Jimma, Southwest Ethiopia from [2018-2022], 2023

5.7. Risk factors of preterm neonatal mortality

Finding from the bi-variable cox-regression analysis showed that, residence of the mother, cause of onset of labor, place of delivery, Having obstetric complication during the current pregnancy, preeclampsia, preterm birth weight, gestational age at birth, temperature at admission, neonate cried immediately at birth, initiation of breastfeeding within one hour of birth, first and fifth minute Apgar score, RDS, HMD, PNA, apnea of prematurity, NEC, hypothermia, receiving KMC, phototherapy, and heated with radiant warmer were significantly associated with time to mortality of preterm neonates at p-value<0.2. Those Significant variables with a determined p-value in bi-variate analysis were entered into multivariable Cox regression model analysis to determine risk factors for time-to-death preterm neonates.

However, after significant risk factors in the bivariate analysis entered into multi-variable cox-regression model analysis, initiation of breastfeeding within one hour of birth, first-minute Apgar score, fifth-minute Apgar score, RDS, KMC, and LBW were found to be significantly associated risk factors of preterm neonate mortality in the multivariable at p-value<0.05(Table 5).

In this study, the hazard of death among preterm neonates who didn't initiate breastfeeding within one hour of birth were 1.96-times higher as compared to their counterparts (AHR=1.96(95%CI:1.18,3.23). The risk of mortality among preterm neonates who had an APGAR score of less than seven at 1st minute were about 1.77

times faster as compared to those who had an APGAR score of greater than or equal to seven (AHR=1.77(95%C1:1.06,2.94). Preterm neonate who had an APGAR score of less than seven at fifth minute were 2.49 times more likely to die compared with those who had an APGAR score of greater than or equal to seven (AHR=2.49(95%C1:1.54,4.02). Those preterm neonates who had RDS were almost 2-times more prone to death than those without RDS throughout the follow-up period (AHR=1.9(95% CI:1.1.15,3.14). Preterm neonates who didn't receive KMC had 2.61-time shorter time to death as compared to those preterm neonates who received KMC throughout the follow-up period (AHR=2.61(95% CI:1.65,4.12). The time to death for preterm neonates born with LBW (1500-2500g) decreased by 48%, compared to those born with VLBW (1000-1500g).

Table 5: Bivariable and multivariable Cox-regression analysis of risk factors of preterm neonatal mortality in NICU of JUMC, Jimma, Southwest Ethiopia from[2018-2022], 2023 (N=456)

Risk factors	Status		CHR [95%CI]	p-value	AHR [95%CI]
	Death	Censored			
Residence					
Rural	71	204	0.73(0.52,1.02)	0.066	0.86(0.59,1.26)
Urban	64	117	1		1
Onset of labor					
Spontaneous	108	269	1		1
Induced	19	29	1.02(0.56,1.84)	0.172	1.02(0.56,1.84)
C/S	8	23	0.77(0.38,1.59)	0.492	1.56(0.69,3.51)
Place of delivery					
Inborn (JMC)	61	145	1		1
Other hospitals	40	73	1.40(0.94,2.09)	0.098	1.14(0.71,1.83)
Health center	29	80	0.90(0.58,1.41)	0.665	0.84(0.47,1.49)
Home	1	17	0.16(0.22.1.14)	0.068	0.26(0.03,1.88)
Others	4	4	2.19(0.49,6.06)	0.129	1.88(0.60,5.84)
Obstetric complication during index pregnancy					
Yes	56	103	1.26(0.89,1.78)	0.181	0.75(0.47,1.20)
No	79	218	1		1
Preeclampsia					
Yes	30	27	2.14(1.42,3.22)	<0.001	1.49(0.87,2.75)
No	105	249	1		1

Birth weight(gram)					
<1000	13	2	2.69(1.48,4.80)	0.001	1.01(0.48,2.11)
1000<1500	71	79	1		1
1500<2500	50	255	0.36(0.25,0.51)	<0.001	**0.52(0.32,0.83) ****
≥2500	1	15	0.11(0.01.0.78)		0.38(0.05,2.94)
Gestational age at birth (in weeks)			0.55(0.44,.68)	<0.001	0.95(.84,1.07)
Temperature at admission					
<36.5	91	206	1.28(.88,1.87)	.199	0.86(0.53,1.39)
36.5<37.5	38	103	1		1
≥37.5	6	12	1.24(0.52,2.92)	0.627	1.36(0.49,3.77)
Immediately cry after birth					
Yes	82	283	1		1
No	53	38	2.74(1.94,3.87)	<0.001	1.40(0.93,2.09)
Initiation of breastfeeding within one hour of birth					
Yes	21	38	1		1
No	114	122	2.68(1.68,4.28)	<0.001	**1.96(1.18,3.23) ****
1st minute APGAR score					
<7	100	104	4.9(2.79,6.02)	<0.001	**1.77(1.06,2.94) ***
≥7	35	217	1		1
5th minute APGAR score					
<7	69	55	5.03(3.57,7.08)	<0.001	**2.50(1.54,4.02) *****
≥7	66	286	1		1
Respiratory distress syndrome					
Yes	23	14	3.03(1.93,4.75)	<0.001	**1.90(1.15,3.14) ***
No	112	307	1		1
Hyaline membrane disease					
Yes	91	140	1.92(1.34,2.76)	<0.001	1.12(0.72,1.70)
No	44	181	1		1
Perinatal asphyxia					
Yes	13	9	2.44(1.37,4.33)	0.002	1.01(0.51,2.00)
No	122	312	1		
Apnea of prematurity					
Yes	9	8	1.82(0.93,3.58)	0.082	1.19(0.57,2.48)

No	126	313	1		1
NEC					
Yes	5	3	1.90(0.78,4.65)	0.158	0.54(0.19,1.49)
No	130	318	1		1
Hypothermia					
Yes	77	164	1.32(0.94,1.86)	0.108	1.25(0.79,1.95)
No	38	157	1		1
Neonates who received kangaroo mother care					
Yes	25	169	1		1
No	110	152	3.76(2.44,5.82)	<0.001	**2.61(1.65,4.12) *** **
Phototherapy					
Yes	34	99	1		1
No	101	222	1.55(1.05.2.29)	.027	1.48(0.97,2.26)
Hated with radiant warmer					
Yes	73	154	1		1
No	62	167	0.77(0.55,1.00)	0.137	0.88(.57,1.35)

NB:-CHR: crude hazard ratio, AHR: Adjusted hazard ratio, 1 are considered as reference categories.

*P-Value < 0.05, ** for p-value < 0.01 and ***for p-value<0.001

Chapter six: Discussion

This retrospective follow-up study aimed to assess time to mortality and risk factors among preterm neonates admitted at NICU of JMC. During the entire follow-up period, a total of 456 preterm neonates were followed for 3972 person-days observation. The study showed that the overall mortality proportion of preterm neonates were 29.61%(95%CI;25.58,33.97) with an overall incidence rate of 34(95%CI:28.72,40.24) deaths per 1000 neonate-days observation.

The study found that among the death, 82.22% death occurred during the first one week after admission. Initiation of breastfeeding within one hour of birth, first, and fifth-minute APGAR score, RDS, KMC, and LBW were found to be significantly associated risk factors with time to preterm neonates mortality.

The overall mortality proportions of preterm neonates admitted to JMC during the study period was 29.61%(95%CI;25.58.33.97), and highest (27.4%) proportions of death occurred on the first day of follow-up. This finding is consistent with studies conducted in Iran, Ghana, Adiss Ababa, and University of Gondar hospital with a mortality rate of 28.7%, 29.0% 29.7%, and 28.8%, respectively (27, 31, 49, 51). Nevertheless, this study is higher than a study reported from India, Cameroon, Tikur Anbesa Hospital, and Tigray with a mortality rate of 7.5%, 15.7 %, 11.1%, and 14.6% respectively(8, 12, 44, 60).

The possible discrepancy might be due to the difference in sociodemographic variation, neonatal intensive care unit set-ups: those countries unlike our NICU setups have mechanical ventilators, modern CPAP, parenteral nutrition and well-equipped health worker, while our study area which have not different sophisticated medical equipment that used to save preterm neonates. In addition, length of year of observation, study participants, level of health facility, provision of quality service, variation in health service coverage, and the difference in the study period might be the possible explanation.

Conversely, the finding of this study is lower than study done in Adiss Ababa public Hospital (34.9%),Bahir Dar(36.1%), Mizan Tepi(35%), and Jimma(34.9%) (15, 23, 34, 53). This variation might result from difference in study design, number of study site, difference in length year of observation, provision of quality services, study subject, the timing of the study, antenatal, delivery and postnatal care, institutional delivery, manner of NICU organization, the health seeking and utilization behavior of the community. Preterm neonates are still highly at risk of death, which is not acceptable and ongoing commitment and interventions need to be considered by giving due attention on identified risk factors.

At the end of cohort, the study showed the overall incidence rate was 34(95%CI:28.72,40.24) deaths per 1000 neonate-days observation. This finding is in line with the study done in Addis Abeba public hospital, and Hawassa (36.4, and 32.12 death per 1000 neonate-days observation)**(23, 52)**. However, the target of the SDG3 is to reduce neonatal mortality to 12 deaths per 1000 live births by 2030 **(61)**. But the finding of

this study was more than threefold high from the target, even if SDG3 include full term neonates, and also higher than study conducted in Adiss Ababa (19.2 mortality per 1000 neonate-day)**(8)**. Conversely, the finding was lower than study done in Pakistan, Mizan Tepi, and Sidama (47.3, 62.15, and 41 death per 1000 neonate-days observation respectively)**(34, 46, 62)**. This marked difference might be attributed to a number of factors such as neonatal care difference, difference in Sample size, length of follow up period, study period, study area and characteristics of the study participants. For instance, study conducted in Pakistan was multicenter and prospective.

This study revealed that the highest hazard time was the first seven days of admission in which majority of the deaths (82.22%) were encountered. This finding is consistent with the study done in Iran, Addis Ababa public hospitals, University of Gondar Hospital, Tigray, and Bahir Dar (84.3, 84%, 85.23%, 80.0%, and 85%, respectively)**(12, 14, 23, 31)**. This might be due to varies complications of premature neonates are occurred during pregnancy, at birth and transitional period of neonates from intrauterine to external environment, and abnormal intra-partum process. Lack of mechanical ventilators may also have contribution to die shortly after birth. Hence, failure in early identification and poor management of maternal medical, obstetric and /or gynecological complications, and lack sophisticated medical equipment determines mortality in the first week of neonatal life.

This study also identified risk factors of preterm neonatal mortality. Accordingly, the hazard of death among preterm neonates who didn't initiate breastfeeding within one hour of birth was almost two-times higher as compared to their counterparts. This indicated that early initiation of breast feeding is found to be a protective factor for the survival of neonates. This finding is consistent with study done, in Felege Hiwot Hospital, Bahir Dar(33). This may be due to the fact that early initiation of breastfeeding decreases the risk of hypoglycemia, hypothermia, and protects the newborn from acquiring infection. It also facilitates emotional bonding of the mother and the baby and has a positive impact on duration of exclusive breastfeeding. According to a systematic review study, newborns who initiated breastfeeding after 1 hour were 33% at risk of neonatal mortality**(63)**. For this reason, the relatively stable preterm neonate should be initiated on breastfeeding as early as possible after gut priming is once tolerated.

In the present study, first and fifth minute APGAR score were an independent significant risk factors for the time to mortality of preterm neonates. The risk of mortality among preterm neonates who had an APGAR score of less than seven at 1st minute were faster as compared to those who had an APGAR score of greater than or equal to seven. This result is supported by study done in Cameroon, Rwanda, Ghana, Tikur Anbessa Hospital, and Tigray **(12, 49, 51, 60, 64)**. Likewise, Preterm neonates who had an APGAR score of less than seven at fifth minute were more quickly to die compared with those who had an APGAR

score of greater than or equal to seven. This is in agreement with the investigation conducted in Iran, Eastern Ethiopia, Mizan Tepi, and Arba Minch **(14, 34, 65, 66)**. Clinically the first-minute APGAR score measures how well the newborn tolerated the birthing process and the need for early intervention. In the fifth-minute to assess how the newborn reacted the resuscitation effort and how well the newborn is adapting to the environment**(67)**. Effective follow-up of labor can reduce birth asphyxia, moreover, newborn resuscitation should help improve survival in preterm with low APGAR score**(64)**. This might be due to neonates who experienced the first and fifth-minute APGAR score of less than seven are those who need strictly close and critical care and support. Unless they get advanced care by skilled care providers with adequate and appropriate supply of medical equipment, they are more vulnerable to death compared to those who have first- and fifth-minute APGAR score greater than or equal to seven. This variation might be associated with a complication during pregnancy, birthing process, and neonatal resuscitation effort.

This study also demonstrated that being diagnosis with RDS also significantly influences the time to mortality. Those preterm neonates who had RDS were almost two- times faster to die than those without RDS throughout the follow-up period, This study finding is in line with the study done in Nepal, Iran, South Arica, Rwanda, Uganda, Tikur Anbessa Hospital, Debre Markos, Mizan Tepi, and Jimma**(13, 23, 30, 34, 53, 64, 68-70)**. This could be due to limited intensive facilities, inadequate perinatal care attributed to less use of surfactant and inadequate availability of ventilation methods. Bronchopulmonary sequestration, and broncho genetic cysts might be the underlined causes of RDS. Failure to diagnose and treat the underlined causes of RDS could lead to short-and long-term complications including death of neonates.

The current study showed that birth weight significantly affects the time to mortality of neonates admitted with preterm birth; preterm neonates who born with LBW had a longer time to die compared to those neonates born with VLBW. This finding is supported by study conducted in Iran, and Mizan Tepi(14, 34). This might be due to the fact that LBW neonates have relatively low body surface area to body weight ratio and better body brown fat that protect from hypothermia and hypoglycemia which will prolong time to death.

The other significant variable that predicted time to death of premature neonates in our study was KMC in which, those who didn't receive KMC had 2.61-times shorter time to death as compared to those preterm neonates who received KMC throughout the follow-up period. This result consistent with the study conducted in Tikur Anbessa Hospital, Gondar, and Mizan Tepi **(23, 31, 34)**. This finding is supported by the clinical practice that KMC is recommended for all preterm neonates until they reach term to prevent

hypothermia by reducing body surface area to the external environment. And also reduce the risk of hypoglycemia by allowing sufficient time to obtain breast feeding during their hospital stay, Furthermore, Preterm with KMC is advantageous to maintain temperature stability.

6.1 Strength and limitation of the study

6.1.1 Strength of the study

This study included study participants from a tertiary care center, which handled vast number of high-risk preterm neonates. The study comprised different years of observations with equal proportional allocation; this may increase number of events and decrease variability. Retrospective follow up study with survival analysis which consider time and censoring was used. Since the outcome was death, the approach clearly indicates the temporal sequence of the risk factors, and outcome variable

6.1.2 Limitation of the study

Since the study is retrospective, incomplete charts were excluded from the study there may be introduction of selection bias. The study was a single center study that covers only JMC and didn't address private health institutions; its generalizability to all hospitals of the region, and Ethiopia may be limited.

Chapter seven: Conclusion and recommendation

7.1. Conclusion

The finding of the study revealed that the incidence rate was unacceptably high. The first week after admission was the hazardous time to death. Didn't initiate breastfeeding within 1 h of birth, low 1st and 5th min APGAR score, RDS, and lack of KMC were found to be independent risk factors of time to preterm neonates mortality. On the other way being born with LBW prolong time to preterm neonate mortality as cox proportional hazard analysis showed.

7.2. Recommendation

Based on the finding of the study the following recommendations were forwarded:

7.2.1 To federal ministry of health and JMC

The federal ministry of health should work to increase the accessibility of NICU with infrastructures and skilled manpower at health institutions.

JMC should able to strengthen careful follow up and regular intensive monitoring for neonates during the first one week of admission to the NICU, with low Apgar score, VLBW, and RDS in order to prolong time to death and improve survival of preterm neonates. Moreover, great focus should be given to encourage early initiation of breastfeeding and KMC.

7.2.2 To health care providers of JMC

Due attention and close follow up should be given to patients in early neonatal period, The health care provider should able to give close follow-up for premature neonates particularly those identified with the risk factors of death in this study.

It would be better to diagnosis early and render proper management for patients with low APGAR score VLBW, and RDS. The health care professionals should able to strengthen early breastfeeding initiation and KMC by encouraging mothers or caregivers, because was found to be a protective factor for time to mortality of premature neonate admitted to NICU.

7.2.3 To researchers

prospective cohort study design is strongly recommended to follow premature neonates because it would be highly beneficial to avoid incomplete data, identify the long-term outcomes of premature births, and the health needs of babies who survive as prematurity.

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ANNEX -1 Abstraction checklist
Information sheet

Title of the Research Project: Time to preterm neonate mortality and risk factors among those admitted to Jimma medical center, jimma, southwest Ethiopia , 2023: survival analysis

Name of Investigator: Wondyifraw yeshitlia (BSc)

Name of the Organization Jimma university institute of health, faculty of public health, department of epidemiology

Name of the Sponsor: Jimma University.

Introduction: This information sheet is prepared for JMC 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 undertake the research.

Purpose of the Research Project: to determine time to preterm neonate mortality and risk factors among those admitted to Jimma medical center, Jimma, southwest Ethiopia, 2023:

Procedure: In order to achieve the above objective, The required information for the study will be taken from preterm neonate medical record form.

Risk and /or Discomfort: Since the stud will be conducted by taking appropriate information from Patient chart, it will not inflict any harm on the patients. The name or any other identifying information will not recorded on the checklist and all information will be taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only used for the study purpose.

Benefits: The research have no direct benefit for one whose document/ record is included in this research and already died. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services for those survived and other newly born ones. In all, the research work has a paramount direct benefit

for health care planners and managers.

Confidentiality: To reassure confidentiality the data on the chart will be collected without the name of the clients and the information collected from this research project will be kept confidential and stored in a file cabinet.

Person to contact: This research project will be reviewed and approved by Institutional Health Research Ethics Review Committee (IHRERC),Institute of Health, Faculty of public health, department of epidemiology, Jimma university. 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.

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Data collection tools

This checklist was prepared for the collection of socio-demographic , obstetrics and/or gynecology, maternal medical disorder and preterm neonatal related and other major associated and outcomes related information that are important for the time to mortality and associated factors among preterm neonates admitted to the NICU at Jimma medical center , a retrospective five year study from January1/ 2018 G.C – December,31/ 2022G.C. This checklist is adopted and modified from different literatures((12, 15, 23, 31, 32, 52).

MRN_____ Tel_____

Question Number	**Part-I Socio-demographic characteristics**	**Possible response**
1001	Date of admission	
1002	Date of discharge	
1003	Length of stay (days and/or hour	
1004	Age at admission (days and hours)	
1005	Sex of neonate	1. Male 2. Female
1006	Residence	1. Urban 2. Rural
1007	Place of birth	1. JMC 2. District hospital 3. Health center 4. Private clinic 5. Home 6. Other (specify)_____
Question numbers	**Part-II. Obstetric and/or gynecological characteristics**	**Possible response**
2001	Parity	
2002	Bad obstetric history(neonatal death, stillbirth ,abortion)	1. Yes 2. No
2003	ANC follow up	1. Yes 2. No
2004	Onset of labor	1. Spontaneous 2. Induced 3. Elective C/S
2005	Duration of labor(hours)	
2006	Presentation	1. Vertex 2. Non- vertex

2007	Mode of delivery	1. SVD 2. C/S 3. Forceps 4. Vacuum
2008	Type of pregnancy	1. Single 2. Twin 3. Triple 4. Other(specify_____
2009	Antenatal steroid	1. Given 2. Not given
2010	Obstetrics complication	1. Yes 2. No , if 2 skip to Q#3001
2011	PROM	1. Yes 2. No
2012	Preeclampsia/eclampsia	1. Yes 2. No
2013	Placenta previa	1. Yes 2. No
2014	Abruptio placenta	1. Yes 2. No
2015	Chorioaminionitis	1. Yes 2. No
2016	Other(specify)	
Question number	**Part-III .Known or diagnosed medical disorder in mother**	**Possible response**
3001	medical disorder in mothers	1. Yes 2. No, if 2 skip Q# 4001
3002	Maternal febrile illness	1. Yes 2. No
3003	Anemia	1. Yes 2. No
3004	DM	1. Yes 2. No if yes type _____
3005	RVI	1. Yes 2. No
3006	Chronic hypertension	1. Yes 2. No
3007	Other(specify)	
Question number	**Part-IV Preterm neonatal related characteristics**	**Possible response**
4001	Birth weight(gram)	
4002	Gestational age (from LNMP or early U/S)	
4003	Weight for gestational age	1. AGA 2. SGA 3.

		LGA
4004	Admission temperature(c^o)	
4005	Immediately cry after birth	1. Yes 2. No
4006	Initiation of breast feeding in one hours of birth	1. Yes 2. No
4007	1st minute APGAR score	
4008	5th minute APGAR score	
4009	Sepsis	1. Yes 2. No
4010	RDS	1. Yes 2. No
4011	Hypoglycemia	1. Yes 2. No
4012	Perinatal asphyxia	1. Yes 2. No
4013	Jaundice	1. Yes 2. No
4014	HMD	1. Yes 2. No
4015	NEC	1. Yes 2. No
4016	Hypothermia	1. Yes 2. No
4017	Does the neonate received antibiotic treatment?	1. Yes 2. No
4018	Feeding practice	1. Breast sucking 2. NPO 3,NGT tube, 4,cup feeding
4019	KMC	1. Yes 2. No
4020	Nasal CPAP	1. Yes 2. No
4021	Resuscitation with bag and mask	1. Yes 2. No
4022	Phototherapy	1. Yes 2. No
4023	Radiant warmer	1. Yes 2. No
4024	Intra-nasal oxygen	1. Yes 2. No
4025	Others(specify)	1. Yes 2. No
4026	Outcome of preterm neonate	Discharged with improvement 2. Died 3. Went against medical advice/ disappeared 4. Referred

Declaration

I, Wondyifraw Yeshitila, declare that this thesis is my original work prepared under the guidance of my advisors, Dr. Sahilu Assegid, and Mr. Addis Birhanu, and it has not been presented for a degree at any other university.

Name: Wondyifraw Yeshitila; Signature: _____Date: _____

Advisors' Approval

This thesis has been submitted for examination with our approval as university advisors in partial fulfillment of the requirements for a degree in Master of Public Health in Epidemiology

1. Dr. Sahilu Assegid (MD. Associate professor)

Signature……...Date……

2. Mr. Addis Birhanu (MPH/Epi and Bio)

Signature……...Date……