

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

Incidence of Mortality and Its Predictors among Preterm Neonates in Nigist Eleni Mohammed Memmorial Comprehensive Specialized Hospital, Hossana, Ethiopia: A Prospective Follow-Up Study

Lire Lemma Tirore (

 AABVwtN+AAAACXBIWXMAAA7EAAAOxAGVKw4bAAAA4EIEQVRIiWNgGAWjYNCCAhDBfABISMgQp+OAA YhkSwBp4SFFCw+EJKha3v3swccfDGyiddvPfH51o8aCh4H98NEN+LQYnsILNjhgkJa77UzuNuucY0CH8a SI3cCrpSHHTOKAweHcbQdytxnnsAG1SPCY4dfS/8b8xwGD/7nbzr95Zpzzjwgt8hI5ZkDvA624kcP80LeNC C0GEm+MJc4YJAO1PDNjzu2T4GEj5Bf5/hzDDxUVdkCHJT/+nPOtTo6f/fAx/LYcQLDZJMAkPuVgWxoQb OYPhFSPgIEwCkbByAQAP89MvqB98BAAAAAASUVORK5CYII=)

Wachemo University

Desta Erkalo

Wachemo University

Selamu Abose

Wachemo University

Lamesginew Mossie Melaku

Wachemo University

Essayas Mulugeta Tirago

Wachemo University

Abriham Shiferaw

Wachemo University

Aklilu Habte

Wachemo University

Menaseb Gebrehaweria

Adigrat University

Research Article

Keywords: Time to Death, preterm neonate, incidence, predictors

Posted Date: February 19th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3933256/v1

License: ©) This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background: Preterm birth is the leading cause of neonatal mortality accounting for 35% of all neonatal deaths worldwide, and the second most frequent cause of death for under five children. Despite different efforts, preterm neonatal mortality is still persistently high in Ethiopia. Little is known about death and its predictors among preterm neonates in the study area.

Objective: This study is aimed at estimating the incidence of mortality and its predictors among preterm neonates admitted to the NICU of NEMMCSH.

Methods and materials: A hospital-based prospective follow-up study was conducted from January to November 2022. A total of 197 preterm neonates were selected consecutively and followed. The Kaplan-Meier survival and failure curves were used to describe the proportion of deaths over time and to compare groups. The independent effects of covariates on the hazard of death were analyzed using a multivariable Cox proportional hazard model.

Results: Preterm neonates were followed for 1840 person-days. The mean time to death was 5.68 days (SD = 5.54). The incidence of mortality was 26.08 (95% CI: 19.65, 34.61) per 1000 person days. Preterm neonates of mothers with eclamsia (AHR = 3.03), preterm neonates who have not received KMC (AHR = 2.26), and preterm neonates who have not exclusively breastfed (AHR = 4.4) had higher hazards of death as compared to their counterparts.

Conclusion and recommendation: The mean time to death was 5.68 days (SD = 5.54). The incidence of mortality was 26.08 per 1000 person days. Eclamsia, KMC, and exclusive breastfeeding were significant predictors of death among preterm neonates. The role of KMC in reducing mortality rates and improving outcomes has to be emphasized for mothers and families. Caregivers have to ensure that mothers and families receive adequate support and resources to facilitate KMC, including access to lactation support, counseling, and assistance with practical aspects of caregiving. Counseling and practical support to enhance exclusive breastfeeding initiation and continuation have to be strengthened. Special attention has to be given to the preterm neonates of mothers with eclampsia.

1. Introduction

A live birth that occurs before 37 weeks of pregnancy is referred to as a preterm birth. It can occur spontaneously or be medically induced through elective cesarean birth or labor induction (1-3). A premature newborn's death during the first 28 days of life is known as preterm neonatal mortality (4). Preterm delivery is still a major global public health issue due to its substantial role in the morbidity and death of newborns (5, 6).

Preterm infants are at high risk for both short- and long-term complications, such as low birth weight, increased caloric needs, feeding difficulties, cerebral palsy, impaired brain function, developmental delay, poorer cognitive function, vision and hearing problems, perinatal asphyxia, respiratory distress syndrome

(RDS), increased risk of sudden infant death, problems controlling body temperature, heart problems, hypoglycemia, and infections (9).

Preterm infants place a heavy financial burden on families and hospitals because they require specialized medical care in a neonatal intensive care unit (NICU) and are more likely to need a prolonged hospital stay (days to months) (15–18).

An estimated 15 million (11%) preterm births worldwide (or 1 in 10 deliveries) take place each year (at a pace of 29 newborns each minute). Ninety percent of preterm deliveries take place in low- and middleincome nations. Sub-Saharan Africa and South Asia account for 12.7 million preterm births, or about 85% of all preterm births (19, 20). The majority of sub-Saharan countries are seeing an increase in preterm birth rates (21).

Various policies, and programs are implemented worldwide with the aim of preventing and treating preterm birth and lowering mortality rates (22, 23). Even so, it remains the leading cause of neonatal mortality accounting for 35% of all neonatal deaths worldwide, and the second most frequent cause of death for children under five accounting for 18% of all deaths (23–25, 28). Preterm delivery and its complications cause 1 million deaths in children under the age of five every year (26).

The likelihood of survival for a preterm baby is primarily determined by their place of residence; in lowincome nations, over 90% of extremely preterm babies pass away in the first few days of life. However, in high-income nations, the death rate is less than 10% (20). 13% of under-five deaths in sub-Saharan Africa and 25.5% in South Asia are attributed to preterm birth mortality (27).

The mortality rate for children under five has significantly decreased, but the fall in neonatal mortality has been sluggish, particularly in many low-income nations. Regretfully, families and medical professionals in many nations continue to believe that any premature baby will eventually die (29).

The trend of newborn death rates in Ethiopia stayed largely unchanged. In 2005, it was 39; in 2011, it was 37; in 2016, it was 29, and in 2019, there were 30 mortalities per 1000 live births (30). One-third of these deaths are caused by prematurity (31). Due to the prolonged hospital stays and long-term complications on the newborn's health, preterm deliveries place a strain on society's healthcare resources (5). Birth weight, gestational age, mode and place of delivery, HIV, exclusive breastfeeding (EBF), postnatal surfactant administration, presence of anomalies, multiple pregnancies, non-cephalic presentation, neonatal sepsis, respiratory distress, and a low APGAR score have all been found to be predictors of death in preterm neonatal deaths (15, 32–37).

Target #3.2 of Sustainable Development Goal 3 calls for ending all preventable deaths of newborns and children under the age of five by 2030, and addressing the problem of preterm birth is crucial to reaching this goal (38). Well-designed, context-specific, representative cohort studies from low- and middle-income countries on preterm birth are therefore required to address data gaps on preterm birth, learn from

successes, and adopt best fit models in low- and middle-income settings, as the majority of the evidence on care for preterm babies comes from high-income settings (6, 39).

In Ethiopia, a large number of preterm birth-related deaths are avoidable, particularly deaths of moderateto late-preterm births (32–37 weeks) (40). Ethiopia has adopted the target to lower preterm birth-related deaths by 2030 (41). The country is implementing a number of policies and initiatives, such as an expanded Neonatal Intensive Care Unit (NICU), integrated management of neonatal and pediatric disorders, and a quality improvement program, to address newborn fatalities and accomplish the goal. Preterm infant mortality remains stubbornly high despite these measures (36, 42). Every year, 320,000 premature births occur, and direct preterm problems result in the deaths of 23,100 children under the age of five (43). Although some studies were done in Ethiopia on the incidence and predictors of preterm death, the risk factors were different across the studies. The majority of these studies used secondary data, which is prone to missing data and variables. There is no information about the incidence and predictors of preterm death in the study area.

Understanding the consequences of preterm births and the factors that increase their risk of death and morbidity affects how healthcare providers treat expectant mothers and their babies and facilitates the efficient use of available resources. It contributes to improving newborn care and lowering unfavorable outcomes in these kinds of difficult births. Estimating the incidence of mortality and its predictors among preterm neonates admitted to the NICU of NEMMCSH is the aim of this study.

2. Methods and Materials

Study Area and Period

This study was carried out at NEMMCSH, which is located in Hossana town, Haddiya zone, from January to December 2022. Hossana Town, the capital of Central Ethiopia, is situated 230 kilometers from Addis Ababa, the capital of Ethiopia. In addition to providing general and specialty medical care, NEMMCSH is a public hospital that serves as a teaching hospital for medical and other health science students. The neonatal Intensive Care Unit (NICU) offers newborn care services to both inborn and out born term and preterm neonates. A hospital-based prospective follow-up study was carried out.

Treatment protocols in NICU.

The treatment protocol in a Neonatal Intensive Care Unit (NICU) varies depending on the specific medical conditions and needs of the newborn. NICUs are specialized units that provide intensive medical care for premature or ill newborns. Many premature infants have underdeveloped lungs and may require assistance with breathing. This can include mechanical ventilation and continuous positive airway pressure (CPAP). Premature babies often struggle to maintain their body temperature. Incubators or radiant warmers are used to keep the baby's temperature stable. Continuous monitoring of vital signs such as heart rate, respiratory rate, and oxygen saturation is crucial in the NICU. This helps healthcare providers promptly address any changes in the baby's condition. Neonates in the NICU are susceptible to

infections, so strict infection control measures are implemented. This includes proper hand hygiene, aseptic techniques, and the judicious use of antibiotics. Many newborns experience jaundice, a yellowing of the skin and eyes due to elevated bilirubin levels. Phototherapy may be used to treat jaundice. NICUs often emphasize family-centered care, involving parents in the care of their newborns. This includes education on baby care, involvement in decision-making, and support for emotional well-being. Medications may be administered to address specific medical conditions or to support the baby's physiological functions (44).

Population

All preterm neonates admitted to the NICU of NEMMCSH were the source population whereas all preterm neonates admitted to the NICU at NEMMCSH from January to November 2022 comprised the study population.

Inclusion and exclusion criteria

Preterm neonates admitted to the NICU during the time of data collection were included in the study. Preterm neonates of mothers who are unable to speak and those with no immediate caregiver were excluded from the study.

Sample size determination and sampling technique

Using Stata version 14, the sample size was calculated with respect to a hazard ratio of 2.186 for gestational age, a standard deviation of 0.186, a 95% confidence interval, a 5% probability of type I error, 80% power, and a 29.31% probability of success (death). Taking into account the aforementioned criteria, a total of 197 preterm neonates were included in the study (45).

Data collection tool and technique

Until the required sample size was attained, the study participants were consecutively recruited into the study. The data collection tool and the follow-up data collection tool were adapted from different studies. Upon admission, the data collectors recruited study subjects and continued to follow them throughout their stay in the facility, documenting all clinical events until the neonates die or censored. Data collection was done by trained nurses and supervision was done by two public health experts. Interviews and a review of medical charts were used to collect data from mothers. Up until the neonatal death or censorship, newborn data were prospectively gathered from medical records. The neonates were followed for a maximum of 28 days from birth. To assure the quality of the data, the data collection tool was evaluated by pediatricians, and 1 day of training was given to the data collectors and supervisors about general research protocols. The Principal investigator reviewed the data before entering it to ensure it was consistent and complete.

Study Variables

Dependent Variable

Mortality of preterm neonates.

Independent variables

maternal age, place of residence, marital status, level of education, occupation, monthly income and sex of neonates, multiple pregnancy, parity, history of abortion and/or preterm birth, Birth interval, prolonged labour, ANC visits, human immunodeficiency virus (HIV) status, DM and place of delivery, mode of delivery, type of birth attendant, antenatal corticosteroid use, neonatal postnatal age at admission, anomalies, KMC, BMI, birth weight, 1 and 5-minute APGAR score and resuscitation history, gestational age, obstetric haemorrhage, eclampsia and preeclampsia, mal-presentation, feeding problem, asphyxia, neonatal sepsis, hypothermia, jaundice, HR, RR, SPO2, and hypoglycaemia.

Data analysis

Data were entered into Epi-data for Windows and analyzed using Stata version 14. Percentages and frequencies were used to summarize categorical variables. The results were presented in tables, texts, and graphs based on the nature of the variables. The distribution of the continuous variables was checked by a box plot. Mean with standard deviation and median with interquartile range were used to summarize normally and non-normally distributed continuous variables, respectively. The Kaplan-Meier Survival and failure curve was used to describe the proportion of deaths over time and to compare groups.

Multivariable Cox proportional hazards regression

The independent effects of covariates on the hazard of death were analyzed using the multivariable Cox proportional hazards model. Adjusted hazard ratios with their 95% confidence interval (CI) were estimated, and a p-value less than 0.05 was used to declare the presence of a significant association between predictors and preterm neonatal death.

Assessing model assumptions: the proportional hazard assumption states that the effect of the covariate is the same over time. It was tested using the global test running the estat phtest command in stata. The assumption was satisfied (p-value: 0.2042).

Operational Definitions:

Gestational age: from the LNMP to the date of delivery.

Event: Death

Discharged (Recovered): Those who left the hospital with clinical improvement confirmed by a physician.

Time to death: the time from admission to when the neonate died.

Time zero: the time when a neonate is being admitted to the NICU.

Censored: A neonate lost to follow-up, discharged, or alive until after 28 days.

The median time of death is the time when 50% of the neonates have died.

3. Results

Socio-demographic characteristics of the study participants

More than half (51.27) of the neonates were males, and 82.23% were aged less than 24 hours at admission. The median gestational age was 35 weeks (IQR: 34 weeks, 35.8 weeks), and 90.82% were born at or after 32 weeks of conception. 86.29% of the neonates were born at a health facility. The mean age of the mothers was 28.74 years (SD: 5.72 years), and more than half (55.33%) of them were from rural areas (Table 1).

Table 1 Frequency and percentage distribution of sociodemographic characteristics of the neonates and their mothers in NEMMHS, 2022.

Variable	Category	Survival status		Total (%)
		Died (%)	Censored (%)	
Age at admission	< 24 hors	41(20.81)	121(61.42)	162(82.23)
	<=24 hours	7(3.55)	28(14.21)	35(17.77)
Sex of neonates	Male	24(12.18)	77(39.09)	101(51.27)
	Female	24(12.18)	72(36.55)	96(48.73)
Gestational age	< 32 weeks	6(3.05)	13(6.60)	19(9.64)
	>= 32 weeks	42(21.32)	136(69.04)	178(90.36)
Mother age	< 20 years	1(0.51)	8(4.10)	9(4.62)
	20-34	33(16.92)	113(57.95)	146(74.87)
	above 34	13(6.67)	27(13.85)	40(20.51)
Occupation	house wife	23(11.68)	76(38.58)	99(50.25)
	student	9(4.57)	26(13.20)	35(17.77)
	employer	11(5.58)	38(19.29)	49(24.87)
	merchant	5(2.54)	9(4.57)	14(7.11)
Education	unable to read and write	11(5.58)	30(15.23)	41(20.81)
	primary	13(6.60)	49(24.87)	62(31.47)
	secondary	12(6.09)	33(16.75)	45(22.84)
	Tertiary and above	12(6.09)	37(18.78)	49(24.87)
Place of residence	Urban	25(12.69)	84(42.64)	109(55.33)
	Rural	23(11.68)	65(32.99)	88(44.67)
Marital status	married	42(21.32)	138(70.05)	180(91.37)
	Widowed or divorced	2(1.02)	4(2.03)	6(3.05)
	Single	4(2.03)	7(3.55)	11(5.58)
Place of delivery	Home	8(4.06)	19(9.64)	27(13.71)
	Health institutions	40(20.30)	130(60.99)	170(86.29)

Maternal medical and obstetrics related characteristics

All mothers had ANC follow up and 66.33% of the neonates were born to mothers who had > = 3 ANC follow up. 31.98% of the women had multiple pregnancies, and 43.65% of the neonates were born to multipara mothers. More than three-fourths (77.66%) of the neonates were born to mothers who had not taken corticosteroids during pregnancy. More than half (21.32%) of the mothers had prolonged labor, and 3.55% of the mothers had obstetric hemorrhage. 22.34% of the neonates were born to mothers who had a history of abortion or preterm birth, and 13.71% and 9.64% of the women had preeclampsia and eclampsia, respectively (Table 2).

Table 2 Frequency and percentage distribution of Maternal medical and obstetrics related characteristics in NEMMCSH, 2022.

Variable	Category	Survival status		Total (%)
		Died (%)	Censored (%)	
Number of ANC visits	1	5(2.54)	8(4.06)	13(6.60)
	2	11(5.58)	43(21.83)	54(27.41)
	>=3	32(16.24)	98(49.75)	130(65.99)
Multiple pregnancy	yes	18(9.14)	45(22.84)	63(31.98)
	no	30(15.23)	104(52.79)	134(68.02)
Parity	primipara	19(9.64)	65(32.99)	84(42.64)
	multipara	19(9.64)	67(34.01)	86(43.65)
	grand multipara	10(5.08)	17(8.63)	27(13.71)
Prolonged labor	Yes	13(6.60)	29(14.72)	42(21.32)
	No	35(17.77)	120(60.91)	155(78.68)
Mal-presentation	Yes	9(4.57)	11(5.58)	20(10.15)
	No	39(19.80)	138(70.05)	177(89.85)
Corticosteroid intake	yes	13(6.60)	31(15.74)	44(22.34)
	No	35(17.77)	118(59.90)	153(77.66)
Antepartum hemorrhage	Yes	3(1.57)	4(2.03)	7(3.55)
	No	45(22.84)	145(73.60)	190(96.45)
Preeclampsia	Yes	4(2.03)	23(11.68)	27(13.71)
	No	44(22.34)	126(63.96)	170(86.29)
Eclampsia	Yes	7(3.55)	12(6.09)	19(9.64)
	No	41(20.81)	137(69.54)	178(90.36)
History of abortion or preterm birth	Yes	15(7.61)	29(14.72)	44(22.34)
	No	33(16.75)	120(60.91)	153(77.66)
Maternal sero status	positive	4(2.03)	12(6.09)	16(8.12)
	negative	44(22.34)	137(69.54)	181(91.88)
Maternal Diabetes mellitus	yes	10(5.08)	16(8.12)	26
				(13.20)

	No	38(19.29)	133(67.51)	171(86.8)
Type of birth attendant	skilled	38(19.29)	128(64.97)	166(84.26)
	unskilled	10(5.08)	21(10.66)	31(15.74)

Neonatal admission diagnosis and treatment related characteristics

Nearly three-fourth (75.63%) of the neonates were hypothermic at admission and 74.62% of them had neonatal sepsis. More than one-third (38.58%) of the neonates had jaundice and hypoglycemia, and nearly one-fourth of them had asphyxia (24.87%). More than one-third (34.04%) of the neonates had received CPAP, and 83.25% were given early antibiotics. More than half (58.88%) of them had received KMC, and 29.44% were resuscitated (Table 3).

 Table 3

 Frequency and percentage distribution of Neonatal admission diagnosis and treatment related characteristics in NEMMCSH, 2022.

Variable	Category	Survival status		Total (%)
		Died (%)	Censored (%)	
Neonatal sepsis	Yes	36(2018.27)	111(56.35)	147(74.62)
	No	12(6.09)	38(19.29)	50(25.38)
Jaundice	Yes	15(7.61)	61(30.96)	76(38.58)
	No	33(16.75)	88(44.67)	121(61.42)
Hypoglycemia	Yes	24(12.18)	52(26.40)	76(38.58)
	No	24(12.18)	97(49.24)	121(61.42)
Anomaly	Yes	5(2.54)	10(5.08)	15(7.61)
	No	43(21.83)	139(70.56)	182(92.39)
1 minute APGAR score	3-6	28(14.21)	73(37.06)	101(51.27)
	>=7	20(10.15)	76(38.58)	96(48.73)
5 minute APGAR score	< 3	3(1.52)	0	3(1.52)
	3-6	8(4.06)	16(8.12)	24(12.18)
	>=7	37(18.78)	133(67.51)	170(86.29)
KMC	Yes	11(5.58)	105(53.30)	116(58.88)
	No	37(18.78)	44(22.34)	81(41.12)
exclusively	Yes	12(6.09)	122(61.93)	134(68.02)
breast feed	No	32(16.24)	21(10.66)	53(26.90)
CPAP	Yes	18(9.57)	46(24.47)	64(34.04)
	No	27(14.36)	97(51.6)	124(65.96)
Early antibiotic provision	Yes	38(19.29)	126(63.96)	164(83.25)
	No	10(5.08)	23(11.68)	33(16.75)
Birth weight	< 100	2 (1.02)	2(1.02)	4(2.04)
	1000-1499	14(7.11)	27(13.71)	41(20.81)
	1501-2499	32(16.24)	111(56.35)	143(72.59)
	>=2500	0	9(4.57)	9 (4.570

Hypothermia	Yes	36(18.27)	113(57.36)	149 (75.63)
	No	12(6.09)	36(18.27)	48(24.37)
Asphyxia	yes	24(12.18)	25(12.69)	49(24.87)
	No	24(12.18)	124(62.94)	148(75.13)

Incidence of mortality

The mean duration of admission was 9.42 days (SD = 6.64) and the mean time to death was 5.68 days (SD = 5.54). The total person-day observation was 1840 days. Out of 197 neonates, 48 of them died. The incidence of mortality was 26.08 (95% CI: 19.65, 34.61) per 1000 person days. The incidence of mortality was the highest (46.13 per 100 person days) within the first 24 hours. Between 2nd to 7th, 8th to 14th, 15th to 21st, and 22nd to 28th, the incidence of mortality was 29.65, 24.39, 11.42, and 18.86 per 1000 person days, respectively. The cumulative probability of mortality within the first 7, 14, 21, and 28 days was 0.1715, 0.3077, 0.3569, and 0.4664, respectively. The Kaplan-Meir graph increases rapidly during the first 5 days and between the 8th and 14th days, showing most neonates died during these periods (Figs. 1 and 2).

The cumulative probability of deaths was higher among neonates who were born to mothers who had mal-presentation, eclampsia, neonates who were not exclusively breast-fed, were not resuscitated, and neonates with a 1 minute APGAR score of 4–7 (Fig. 3–7).

Predictors of mortality

In a bivariable cox regression ANC, preeclampsia, eclampsia, malpresentation, KMC, hypoglycemia, and exclusive breast feeding were considered for multivariable cox regression. In multivariable Cox regression, eclampsia, exclusive breast feeding, and KMC were found to be significant predictors of death among preterm neonates.

Preterm neonates of mothers with eclamsia had 3.03 times higher hazards of death as compared to neonates of mothers without eclamsia (AHR = 3.03).

The hazards of death were 2.26 times higher for preterm neonates who have not received KMC as compared to those who have received the care (AHR = 2.26). Preterm neonates who have not exclusively breastfed had 4.4 times higher hazards of death as compared to neonates who have exclusively breastfed (AHR = 4.4) (Table 4).

Table 4Predictors of mortality among preterm neonates in NEMMCSH, 2022.

Variable	Category	CHR (95% CI)	AHR (95% CI)
Age at admission	< 24 hors	1.87(0.35, 1.98)	
	>=24 hours	1	
Sex of neonates	Male		
	Female	1.48(0.87, 2.87)	
Gestational age	< 32 weeks	2.58 (0.33, 3.78)	
	>= 32 weeks	1	
Mother age	< 20 years	1	
	20-34 years	0.91(0.26, 2.22)	
	Above 34 years	0.16(0.042, 1.83)	
Place of residence	Urban	0.34(0.12, 4.13)	
	Rural	1	
Marital status	Married	0.79(0.42, 1.98)	
	Widowed or divorced	0.29(0.13, 1.56)	
	Single	1	
Place of delivery	Home	1.48(0.51, 2.79)	
	Health institutions	1	
Hypothermia	Yes	2.58(0.50, 3.78)	
	No	1	
Asphyxia	yes	3.56(0.51, 4.98)	
	No	1	
Number of ANC visits	1	1.82(0.45, 1.98)	
	2	1.87(0.25, 2.88)	
	>=3	1	
Multiple pregnancy	yes	1.32(0.79, 2.77)	
	no	1	
Parity	primipara	1	
	multipara	0.69 (0.23, 1.79)	

	grand multipara	0.89 (0.39, 1.55)	
Prolonged labor	Yes	1.72(0.40, 2.38)	
	No	1	
Mal-presentation	Yes	1.16(0.042, 1.63)	
	No	1	
Corticosteroid intake	yes	2.37 (0.73, 3.53)	
	No	1	
Antepartum hemorrhage	Yes	2.37 (0.73, 3.53)	
	No	1	1
Preclamsia	Yes	2.32(1.5, 3.65)	2.69(0.74, 9.77)
	No	1	1
Eclampsia	Yes	4.76(2.13, 5.78)	3.03(1.52, 9.09)*
	No	1	1
History of abortion or preterm birth	No	1	
	Yes	1.25(0.64, 2.67)	
Maternal sero-status	Negative	1	
	Positive	2.15(0.81, 3.90)	
Maternal Diabetes mellitus	No	1	
	yes	1.36(0.51, 3.98)	
Type of birth attendant	skilled	1	
	unskilled	2.78(0.50, 3.95)	
Neonatal sepsis	Yes	1.87(0.45, 1.68)1	
	No	1	
Jaundice	Yes	1.42(0.77, 2.67)	
	No	1	
Hypoglycemia	Yes	2.59 (1.33, 4.78)	1.76(0.40, 1.92)
	No		
Anomaly	Yes	1.91(0.36, 2.32)	
	No	1	

1 minute APGAR score	3-6	1	
	>=7	0.72(0.40, 1.28)	
КМС	Yes	1	1
	No	5.37 (2.73, 10.53)	2.26(1.04, 4.90)*
Exclusively	Yes	1	1
breast feed	No	7.34 (3.81, 14.13)	4.40(2.09, 9.24)*
CPAP	Yes	1	
	No	0.79(0.43, 1.96)	

4. Discussion

Preterm neonates were followed for 1840 person-days. The mean time to death was 5.68 days (SD = 5.54). The incidence of mortality was 26.08 (95% CI: 19.65, 34.61) per 1000 person days. This is nearly similar to the incidence of death reported from studies in Addis Ababa and Northern Ethiopia (46), and Northern Ethiopia (47).

KMC, exclusive breastfeeding, and eclamsia were significant predictors of death among preterm neonates. The hazards of death were higher for preterm neonates who have not received KMC as compared to those who have received KMC. This finding is in line with the findings in studies done at Aksum Hospital (48), the University of Gondar (49), Addis Ababa Public Hospital (46), and Southern Ethiopia (50). The higher hazards of death among preterm neonates who have not received Kangaroo Mother Care (KMC) might be due to poor temperature and respiratory regulation. KMC involves skin-toskin contact between the mother and the preterm baby, which helps regulate the baby's body temperature. Preterm infants often struggle with temperature regulation, and without KMC, they may be more susceptible to hypothermia or hyperthermia, both of which can result in death (51, 52).

KMC has been shown to improve respiratory function in preterm infants. The close contact with the mother's chest can enhance the baby's breathing patterns, reducing the risk of respiratory distress or complications. Preterm neonates who have not received KMC are prone to respiratory distress, which increases the risk of death (53, 54). Poor nutritional status, increased risk of infection, and stress level could also explain the higher hazards of death among preterm neonates devoid of KMC. KMC supports breastfeeding, and breast milk is crucial for the nutrition and growth of preterm infants. Babies who have not received KMC are more likely to be undernourished, which makes them prone to infection and other complications (55, 56). The physical closeness in KMC provides a protective environment that can help prevent infections. Preterm infants are more vulnerable to infections, and KMC has been associated with a lower incidence of infections. The calming effect of KMC can help reduce stress levels in preterm infants. Neonates who are devoid of KMC can have elevated stress levels, which can negatively affect the various physiological processes and overall health of neonates (57, 58). It's important to note that KMC is

recognized as an evidence-based practice for the care of preterm infants and has been associated with positive outcomes. KMC encourages the natural development of the infant's neurological and motor functions by providing sensory stimulation. Preterm infants who do not receive such care can have poor neurodevelopmental outcomes, which might lead them to death (59).

Preterm neonates who have not initiated exclusive breastfeeding have greater hazards of death as compared with those who have initiated exclusive breastfeeding. Similar findings were observed in studies done in Tanzania (60), Ghana (61), India (62), and two systematic reviews (63, 64). The increased risk for infection due to low immunity may explain the higher hazards of death among preterm neonates who have not practiced exclusive breastfeeding. Breast milk provides essential nutrients and antibodies that support the developing immune system of preterm infants (65). Breast milk contains antibodies and other immune-boosting factors that help protect preterm infants from infections. Exclusive breastfeeding reduces the risk of infections, which can be particularly crucial for the vulnerable immune systems of preterm neonates.

Breast milk also contains growth factors and hormones that support the development of preterm infants and help reduce the risk of complications. Preterm neonates who have not been exclusively breastfed lack these advantages and are prone to different infections that can result in death (66). Breast milk is easily digestible, and exclusive breastfeeding can contribute to better digestive health in preterm infants. This is important for the absorption of nutrients and the prevention of gastrointestinal issues. Those neonates who have initiated other foods than breast milk might develop gastrointestinal disorders (67, 68).

The hazards of death were higher among preterm neonates of mothers who have eclampsia compared to neonates of mothers without eclampsia. A similar finding was observed in a study done in Addis Ababa (69). The inadequate blood flow to the placenta and complications during labor and delivery could explain the greater hazards of death among preterm neonates. Eclampsia can lead to inadequate blood flow to the placenta, which can result in poor oxygen and nutrient supply to the fetus. As a result, preterm neonates of mothers with Eclampsia may be born with complications such as low birth weight, respiratory distress, and organ immaturity, which increase their risk of mortality. Also, inadequate blood flow to the placenta can result in intrauterine growth restriction. IUGR is associated with low birth weight and an increased risk of neonatal mortality. Eclampsia can cause complications during labor and delivery, including placental abruption or fetal distress, which can contribute to adverse outcomes for the neonate (70).

Conclusion and recommendation

Preterm neonates were followed for 1840 person-days. The mean time to death was 5.68 days (SD = 5.54). The incidence of mortality was 26.08 (95% CI: 19.65, 34.61) per 1000 person days. Eclamsia, KMC, and exclusive breastfeeding were significant predictors of death among preterm neonates. Awareness should be created for parents and caregivers about the benefits and importance of KMC for preterm

neonates. The role of KMC in reducing mortality rates and improving outcomes has to be emphasized for mothers and families. Caregivers have to ensure that mothers and families receive adequate support and resources to facilitate KMC, including access to lactation support, counseling, and assistance with practical aspects of caregiving. Early and thorough nutritional assessments for preterm neonates are essential to identify those who may face challenges with exclusive breastfeeding. Counseling and practical support to enhance breastfeeding initiation and continuation have to be strengthened. Special attention has to be given to the preterm neonates of mothers with eclampsia.

Declarations

i. Ethics approval and consent to participate

We obtained ethical approval from the Research Ethics Review Committee of WCU. Permission to conduct the study was granted by the clinical Director of NEMMCSH. In addition, prior to participation in the study, informed consent was obtained from caregivers of preterm neonates.

ii. Consent for publication: Not applicable

iii. Availability of data and materials: All data generated or analysed during this study are included in this published article [and its supplementary information files].

iv. Competing interests: The authors declare that they have no conflicts of interest.

v. Funding: No funding.

vi. Authors' contributions: L.L. conceived the study and prepared the first draft of the manuscript. L.L., A.S., D.E., S.A., A.H., L.M., E.M., and M.G. did data acquisition, statistical analysis, manuscript editing, and manuscript review.

vii. Acknowledgement: We would like to thank Wachemo University for giving us the opportunity to conduct this study.

References

- 1. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The lancet. 2008;371(9606):75-84.
- 2. Walani SR. Global burden of preterm birth. International Journal of Gynecology & Obstetrics. 2020;150(1):31-3.
- 3. Taha Z, Ali Hassan A, Wikkeling-Scott L, Papandreou D. Factors associated with preterm birth and low birth weight in Abu Dhabi, the United Arab Emirates. International journal of environmental research and public health. 2020;17(4):1382.

- 4. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. The Lancet. 2013;381(9862):223-34.
- 5. Wang P, Liou S-R, Cheng C-Y. Prediction of maternal quality of life on preterm birth and low birthweight: a longitudinal study. BMC pregnancy and childbirth. 2013;13(1):1-11.
- Vogel JP, Chawanpaiboon S, Moller A-B, Watananirun K, Bonet M, Lumbiganon P. The global epidemiology of preterm birth. Best Practice & Research Clinical Obstetrics & Gynaecology. 2018;52:3-12.
- 7. Engle WA, Tomashek KM, Wallman C. "Late-preterm" infants: a population at risk. Pediatrics. 2007;120(6):1390-401.
- 8. Barlow S, Finan D, Lee J, Chu S. Synthetic orocutaneous stimulation entrains preterm infants with feeding difficulties to suck. Journal of Perinatology. 2008;28(8):541-8.
- 9. Ward RM, Beachy JC. Neonatal complications following preterm birth. BJOG: An International Journal of Obstetrics & Gynaecology. 2003;110:8-16.
- 10. Baraldi E, Filippone M. Chronic lung disease after premature birth. New England Journal of Medicine. 2007;357(19):1946-55.
- 11. Vincer MJ, Allen AC, Joseph K, Stinson DA, Scott H, Wood E. Increasing prevalence of cerebral palsy among very preterm infants: a population-based study. Pediatrics. 2006;118(6):e1621-e6.
- 12. Ophthalmology AAoPSo. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2013;131(1):189-95.
- 13. Vohr B. Long-term outcomes of moderately preterm, late preterm, and early term infants. Clinics in perinatology. 2013;40(4):739-51.
- 14. De Jong M, Verhoeven M, van Baar AL, editors. School outcome, cognitive functioning, and behaviour problems in moderate and late preterm children and adults: a review. Seminars in Fetal and Neonatal Medicine; 2012: Elsevier.
- 15. Kunle-Olowu OE, Peterside O, Adeyemi OO. Prevalence and outcome of preterm admissions at the neonatal unit of a tertiary health centre in Southern Nigeria. Open Journal of Pediatrics. 2014;2014.
- 16. Tongo O, Orimadegun A, Ajayi S, Akinyinka O. The economic burden of preterm/very low birth weight care in Nigeria. Journal of tropical pediatrics. 2009;55(4):262-4.
- 17. Feldman R, Eidelman AI. Direct and indirect effects of breast milk on the neurobehavioral and cognitive development of premature infants. Developmental Psychobiology: The Journal of the International Society for Developmental Psychobiology. 2003;43(2):109-19.
- 18. Vohr BR, Poindexter BB, Dusick AM, McKinley LT, Higgins RD, Langer JC, et al. Persistent beneficial effects of breast milk ingested in the neonatal intensive care unit on outcomes of extremely low birth weight infants at 30 months of age. Pediatrics. 2007;120(4):e953-e9.
- 19. Hug L, Alexander M, You D, Alkema L, for Child Ul-aG. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic

analysis. The Lancet Global Health. 2019;7(6):e710-e20.

- 20. WHO. WHO Fact sheet Preterm Birth N°363, . November 2015.
- 21. Chawanpaiboon S, Vogel JP, Moller A-B, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. The Lancet Global Health. 2019;7(1):e37-e46.
- 22. Soon BT. The global action report on preterm birth. Geneva: World Health Organization. 2012.
- 23. Sheet WRF. Preterm births. Geneva, swizterland. 2016.
- 24. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bulletin of the World Health Organization. 2010;88:31-8.
- 25. Adane AA, Ayele TA, Ararsa LG, Bitew BD, Zeleke BM. Adverse birth outcomes among deliveries at Gondar University hospital, Northwest Ethiopia. BMC pregnancy and childbirth. 2014;14(1):1-8.
- 26. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller A, et al. Chapter 2: 15 million preterm births: Priorities for action based on national, regional and global estimates. Born too soon: the global action report on preterm birth. 2012.
- 27. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. The Lancet. 2016;388(10063):3027-35.
- 28. Onalbaeva B, Baigazieva G, Zhubanyshova K, Ernazarqyzy A, Bakir A, Sarbas A, et al. MODERN STATE OF THE PROBLEM OF PREMATURELY BORN CHILDREN WITH EXTREMELY LOW BODY MASS (LITERATURE REVIEW). Bulletin of the Kazakh National Medical University. 2020(4):214-20.
- 29. Lawn JE, Davidge R, Paul VK, von Xylander S, de Graft Johnson J, Costello A, et al. Born too soon: care for the preterm baby. Reproductive health. 2013;10(1):1-19.
- 30. Mini E, Demographic E. health survey 2019: key indicators report. The DHS Program ICF. 2019.
- 31. Kinney MV, Rhoda NR. Understanding the causes of preterm birth: solutions depend on context. The Lancet Global Health. 2019;7(8):e1000-e1.
- 32. Agbeno EK, Osarfo J, Ashong J, Anane-Fenin B, Okai E, Ofori AA, et al. Determinants of preterm survival in a tertiary hospital in Ghana: A ten-year review. PloS one. 2021;16(1):e0246005.
- 33. Aynalem YA, Mekonen H, Akalu TY, Gebremichael B, Shiferaw WS. Preterm Neonatal Mortality and its predictors in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: a retrospective cohort study. Ethiopian journal of health sciences. 2021;31(1).
- 34. Haghighi L, Nojomi M, Mohabbatian B, Najmi Z. Survival predictors of preterm neonates: Hospital based study in Iran (2010-2011). Iranian journal of reproductive medicine. 2013;11(12):957.
- 35. Mekasha A, Tazu Z, Muhe L, Abayneh M, Gebreyesus G, Girma A, et al. Factors Associated with the Death of Preterm Babies Admitted to Neonatal Intensive Care Units in Ethiopia: A Prospective, Cross-sectional, and Observational Study. Global pediatric health. 2020;7:2333794X20970005.

- 36. Mengesha HG, Wuneh AD, Lerebo WT, Tekle TH. Survival of neonates and predictors of their mortality in Tigray region, Northern Ethiopia: prospective cohort study. BMC pregnancy and childbirth. 2016;16(1):1-13.
- 37. Opio C, Malumba R, Kagaayi J, Ajumobi O, Kamya C, Mukose A, et al. Survival time and its predictors among preterms in the neonatal period post-discharge in Busoga region-Uganda June–July 2017. Journal of Interventional Epidemiology and Public Health. 2019;2(9).
- 38. Nations. U. Sustainable Development Goal 3. Ensure healthy lives and promote well-being for all at all ages. https://www.un.org/ susta unable edevelopment/health/.
- 39. Organization WH. Survive and thrive: transforming care for every small and sick newborn: key findings. World Health Organization, 2018.
- 40. Ahmad A, Madanijah S, Dwiriani CM, Kolopaking R. Complementary feeding practices and nutritional status of children 6–23 months old: formative study in Aceh, Indonesia. Nutrition research and practice. 2018;12(6):512-20.
- 41. Organization WH. Born too soon: the global action report on preterm birth. 2012.
- Bekele A, Mussema Y, Tadesse Y, Taylor ME. Reaching Every Newborn: Delivering an Integrated Maternal and Newborn Health Care Package: Reaching Every Newborn. Ethiopian Medical Journal. 2019(3).
- 43. USAID P, GAPPS A. Profile of Preterm and Low Birth Weight Prevention and Care-Ethiopia.; 2017. 2019.
- 44. Sharma Y, Bansal S, Kaur R. Decision making in NICU–Role of neonatal scores in predicting/maintaining neonate's health. Published on 24 Mar 2017.
- 45. Mekasha A, Tazu Z, Muhe L. Factors Associated with the Death of Preterm Babies Admitted to Neonatal Intensive Care Units in Ethiopia: A Prospective, Cross-sectional, and Observational Study. 2020;7:2333794x20970005.
- 46. Birhanu D, Gebremichael B, Tesfaye T, Tadesse M, Belege F, Godie Y, et al. Survival status and predictors of mortality among preterm neonates admitted to neonatal intensive care unit of Addis Ababa public hospitals, Ethiopia, 2021. A prospective cohort study. BMC pediatrics. 2022;22(1):1-12.
- Girma B, Berhe H, Mekonnen F, Nigussie J. Survival and predictors of mortality among preterm neonates in Northern Ethiopia: A retrospective follow-up study. Frontiers in Pediatrics. 2023;10:1083749.
- 48. Gebremeskel TG, MAMO S. Proportion And Factors Of Death Among Preterm Neonates Admitted In Aksum University Compressive Specialized Hospital Neonatal Intensive Care Unit Northern Ethiopia 2019. 2020.
- 49. Yismaw AE, Gelagay AA, Sisay MM. Survival and predictors among preterm neonates admitted at University of Gondar comprehensive specialized hospital neonatal intensive care unit, Northwest Ethiopia. Italian journal of pediatrics. 2019;45:1-11.
- 50. Huka AE, Oljira L, Weldesenbet AB, Bushra AA, Ahmed IA, Tura AK, et al. Predictors of time to death among preterm neonates admitted to neonatal intensive care units at public hospitals in southern

Ethiopia: A cohort study. Plos one. 2023;18(10):e0283143.

- 51. Ludington-Hoe SM, Johnson MW, Morgan K, Lewis T, Gutman J, Wilson PD, et al. Neurophysiologic assessment of neonatal sleep organization: preliminary results of a randomized, controlled trial of skin contact with preterm infants. Pediatrics. 2006;117(5):e909-e23.
- 52. Messmer PR, Rodriguez S, Adams J, Wells-Gentry J, Washburn K, Zabaleta I, et al. Effect of kangaroo care on sleep time for neonates. Pediatric nursing. 1997;23(4):408-15.
- 53. M Ludington-Hoe S. Evidence-based review of physiologic effects of kangaroo care. Current Women's Health Reviews. 2011;7(3):243-53.
- 54. Bera A, Ghosh J, Singh AK, Hazra A, Som T, Munian D. Effect of kangaroo mother care on vital physiological parameters of the low birth weight newborn. Indian journal of community medicine : official publication of Indian Association of Preventive & Social Medicine. 2014;39(4):245-9.
- 55. Heidarzadeh M, Hosseini MB, Ershadmanesh M, Gholamitabar Tabari M, Khazaee S. The Effect of Kangaroo Mother Care (KMC) on Breast Feeding at the Time of NICU Discharge. Iranian Red Crescent medical journal. 2013;15(4):302-6.
- 56. Lamy Filho F, Silva AAMd, Lamy ZC, Gomes MASM, Moreira MEL. Evaluation of the neonatal outcomes of the kangaroo mother method in Brazil. Jornal de Pediatria. 2008;84:428-35.
- 57. Feldman R, Rosenthal Z, Eidelman AI. Maternal-preterm skin-to-skin contact enhances child physiologic organization and cognitive control across the first 10 years of life. Biological psychiatry. 2014;75(1):56-64.
- 58. Cristóbal Cañadas D, Parrón Carreño T. Benefits of Kangaroo Mother Care on the Physiological Stress Parameters of Preterm Infants and Mothers in Neonatal Intensive Care. 2022;19(12).
- 59. Goyal G, Chetan C, Patra S, Gupta G, Prasad H. Early Neonatal Intervention: A Newer Conceptual Paradigm. Journal of Neonatology. 2022;36(4):348-65.
- 60. Natchu UCM, Liu E, Duggan C, Msamanga G, Peterson K, Aboud S, et al. Exclusive breastfeeding reduces risk of mortality in infants up to 6 mo of age born to HIV-positive Tanzanian women. The American journal of clinical nutrition. 2012;96(5):1071-8.
- 61. Edmond KM, Kirkwood BR, Amenga-Etego S, Owusu-Agyei S, Hurt LS. Effect of early infant feeding practices on infection-specific neonatal mortality: an investigation of the causal links with observational data from rural Ghana. The American journal of clinical nutrition. 2007;86(4):1126-31.
- 62. Phukan D, Ranjan M, Dwivedi LK. Impact of timing of breastfeeding initiation on neonatal mortality in India. International Breastfeeding Journal. 2018;13(1):27.
- 63. Sankar MJ, Sinha B, Chowdhury R, Bhandari N, Taneja S, Martines J, et al. Optimal breastfeeding practices and infant and child mortality: a systematic review and meta-analysis. Acta paediatrica. 2015;104:3-13.
- 64. Hossain S, Mihrshahi S. Exclusive breastfeeding and childhood morbidity: A narrative review. International journal of environmental research and public health. 2022;19(22):14804.

- 65. Ip S, Chung M, Raman G, Chew P, Magula N, DeVine D, et al. Breastfeeding and maternal and infant health outcomes in developed countries. Evidence report/technology assessment. 2007(153):1-186.
- 66. Victora CG, Bahl R, Barros AJ, França GV, Horton S, Krasevec J, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. The lancet. 2016;387(10017):475-90.
- 67. Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. Cochrane database of systematic reviews. 2012(8).
- 68. Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatrics. 2001;108(4):e67-e.
- 69. Dilla E, Dessie E. Determinants of Mortality among Preterm Neonates Admitted with Respiratory Distress in Addis Ababa Public Hospitals Neonatal Intensive Care Units, 2021, Multi-Center Prospective Follow-Up Study.
- 70. Backes CH, Markham K, Moorehead P, Cordero L, Nankervis CA, Giannone PJ. Maternal preeclampsia and neonatal outcomes. Journal of pregnancy. 2011;2011.



Cumulative survival probability among preterm neonates in NEMMCSH, 2022.



Figure 2

Cumulative probability of mortality among neonates admitted to NEMMCSH, 2022.



Cumulative probability of mortality by mal-presentation among neonates admitted to NEMMCSH, 2022.



Cumulative probability of mortality by one minute APGAR score among neonates admitted to NEMMCSH, 2022.



Cumulative probability of mortality by eclamsia status of mothers among preterm neonates admitted to NEMMCSH, 2022.



Cumulative probability of mortality by resuscitation among preterm neonates admitted to NEMMCSH, 2022.



Cumulative probability of mortality by exclusive breastfeeding among preterm neonates admitted to NEMMCSH, 2022.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

• Preterm.dta