



St. Paul's Hospital Millennium Medical College

Post-Graduate Study Program

Determinants of Neonatal Mortality among Newborns Admitted to Neonatal Intensive Care Unit at SPHMMC and TBGH, Addis Ababa, Ethiopia: Unmatched Case Control Study

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Abstract

Background: Neonatal mortality, the death of infants within the first 28 days of life, is a crucial indicator of a population's health. Despite a global decline in infant mortality, neonatal deaths remain a major concern, particularly in sub-Saharan Africa. Ethiopia experiences a high neonatal mortality burden. The leading causes include preterm birth complications, birth asphyxia, and infections. However, limited research exists on the factors influencing neonatal mortality in Ethiopia.

Objective: To assess the determinants of neonatal mortality among newborns admitted to the Neonatal Intensive Care Unit (NICU) at St. Paul's Hospital Millennium Medical College (SPHMMC) and Tirunesh Beijing general hospital (TBGH) in Ethiopia

Methods: Institutional based case control study was conducted among neonates, cases (80) and controls (160), at SPHMMC and TBGH from December, 2023 up to November, 2024. Data was collected using a structured and pre-tested checklist from medical records. Study units are selected using simple random sampling methods. Data was checked for completeness and consistency, entered using Kobo toolbox, and transported to SPSS version 26 for analysis. The binary logistic regression model was used, variables with p-value < 0.25 were entered to final multivariable analysis. In multivariable analysis variables with p-value < 0.05 at 95% confidence interval was set as a statistically significant association between the independent and outcome variables.

Result: Neonatal age at admission (AOR = 0.49, 95%CI = 0.25–0.95), length of stay in NICU (AOR = 14.4, 95%CI = 5.6–36.8) and number of gestations (AOR = 4.54, 95% CI = 1.82–11.34), were found to be determinants of neonatal mortality.

Conclusion: The study found that the length of hospital stays, age at admission, and gestational age were the main risk factors for neonatal mortality. To reduce neonatal mortality, prioritize early admission of neonates to NICU, and optimize length of stay based on individual needs, and implement targeted interventions for multiple gestations.

Keywords: Neonatal mortality, newborn, NICU, Addis Ababa, Ethiopia

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Abbreviations

AOR:	Adjusted Odds Ratio
ECMO:	Extracorporeal Membrane Oxygenation
HDP:	Hypertensive Disorders of Pregnancy
HIE:	Hypoxic-Ischemic Encephalopathy
IVH:	Intraventricular Hemorrhage
KMC:	Kangaroo Mother Care
LBW:	Low Birth Weight
LMICs:	Low- and Middle-Income Countries
NICU:	Neonatal Intensive Care Unit
NMR:	Neonatal Mortality Rate
PNA:	Perinatal Asphyxia
PROM:	Premature Rupture of Membranes
RDS:	Respiratory Distress Syndrome
SPHMMC:	Saint Paul's Hospital Millennium Medical College
TBGH:	Tirunesh Beijing General Hospital
VLBW:	Very Low Birth Weight
WHO:	World Health Organization

1. Introduction

1.1 Background

The World Health Organization (WHO) defines neonatal mortality as any newborn death that occurs during the first 28 days of life. The neonatal mortality rate (NMR), which measures the number of infant deaths in the first 28 days of life per 1,000 live births in a given year, is a key indicator of the general health of the population. The deaths that happen in the first week of life are called early neonatal mortality. Deaths between the eighth and the twenty-seventh day of life are referred to as late neonatal mortality [1, 2].

Half of all under-five deaths worldwide happen during the neonatal period. Globally in 2019 on average 6,700 newborns died during the first month of life every day [3]. Though worldwide infant mortality rates dramatically declined since 1990 this progress hasn't been consistent, particularly sub-Saharan Africa and South Asia alone were responsible for roughly four-fifths of all newborn deaths worldwide [4, 5].

Ethiopia faces a significant neonatal mortality burden, with approximately 87,000 infants dying within the first month of life annually. A significant proportion of child deaths in Ethiopia occur during the neonatal period, with newborns deaths accounting for 56% of all under-five mortality. This rate is among the world's highest. Moreover, the trend is alarming, as neonatal mortality rates increased from 29 to 30 deaths per 1,000 live births between the Ethiopian Demographic and Health Surveys of 2016 and 2019, respectively [6, 7].

Globally, including in Ethiopia, the leading causes of neonatal deaths are complications from preterm births, issues that arise during childbirth, and infections. Recent studies indicate that there are between 27.2 and 32 newborn deaths for every 1,000 neonates in NICUs across Ethiopia. The primary contributors to infant mortality in these NICUs are infections, birth asphyxia, and complications related to premature birth [8, 9].

An extensive review of existing literature highlighted a significant lack of research focused on the determinants of neonatal mortality in Ethiopia. To fill this critical gap, we undertook a case-control study in Addis Ababa aimed at identifying the key factors contributing to neonatal deaths.

The insights gained from this study will be instrumental in crafting targeted interventions designed to effectively reduce neonatal mortality rates in Addis Ababa.

1.2 Statement of problem

Neonatal death remains a significant public health concern worldwide, with an estimated 2.4 million neonates dying in 2020, predominantly in low- and middle-income countries [10]. The neonatal period is important for survival because it is when the danger of death is greatest. Complications from preterm, infections, birth asphyxia, and congenital defects are the primary causes of neonatal death. Despite international efforts to reduce these rates, such as the Sustainable Development Goals (SDGs), progress has been uneven, with many regions falling behind. Newborn mortality rates are particularly high in Africa, accounting for almost 40% of global newborn deaths [8]. Sub-Saharan Africa faces challenges as a result of inadequate healthcare infrastructure, restricted access to experienced birth attendants, and socioeconomic inequities that worsen health outcomes [11, 12].

Countries in this sub-Saharan region frequently face high rates of poverty, malnutrition, and communicable diseases, all of which lead to poor newborn health outcomes. Moreover, the COVID-19 pandemic has strained healthcare systems, diverting essential resources from maternal and child health services. This shift may have reversed some of the progress made in reducing infant mortality, highlighting the urgent need to refocus efforts on these critical areas in the post-COVID[13, 14]. Despite tremendous improvements in mother and child health over the last decade, Ethiopia still has high neonatal mortality rates. The Ethiopian Demographic and Health Survey (EDHS) 2019 reports a newborn mortality rate of 29 deaths per 1,000 live births [15]. This result emphasizes the critical need for focused interventions that address the underlying causes of newborn mortality. The magnitude of the gap in addressing neonatal mortality in Ethiopia is evident in the disparity between the current neonatal mortality rate (NMR) and the Sustainable Development Goal (SDG) target of reducing NMR to 12 deaths per 1,000 live births by 2030. This gap is further exacerbated by the limited capacity of NICUs, which are often under-resourced, understaffed, and unequipped to handle the high volume of critically ill neonates. Additionally, socioeconomic factors such as poverty, low maternal education, and inadequate access to healthcare services contribute to the high burden of neonatal mortality. The lack of comprehensive data on the determinants of mortality among neonates

admitted to NICUs in Ethiopia further hinders the development of evidence-based interventions. [2,3,6].

While existing literature provides valuable insights into the causes of newborn mortality in Ethiopia, a notable gap remains in understanding the specific factors affecting neonates admitted to Neonatal Intensive Care Units (NICUs). The unique environment of NICUs, characterized by advanced medical procedures and specialized care, may present distinct risk factors compared to broader community settings. Factors such as staffing levels, availability of medical resources, infection control practices, and overall quality of care can significantly influence newborn outcomes, yet these aspects have not been thoroughly explored. Additionally, prior research often relied on cross-sectional or descriptive methodologies, which limited their ability to establish causal relationships between various factors and newborn mortality. This study aims to fill this critical gap by employing a more robust analytical framework to investigate the specific influences on neonatal outcomes within NICUs, thereby providing clearer insights into the causal links that could inform targeted interventions[16]. A case-control study design is required to identify and analyze these drivers in a systematic manner.

1.3 Significance of study

While neonatal mortality has been researched throughout Ethiopia, this study focusses on two metropolitan hospitals, SPHMMC and Tirunesh Beijing General Hospital to allow for a more in-depth evaluation of infant outcomes in the NICU. This urban approach may uncover different determinants than rural investigations. Many existing studies use cross-sectional or cohort designs, which can limit the capacity to demonstrate causal correlations. Using a case-control methodology, this study intends to identify specific risk variables related to newborn mortality, offering further evidence for focused interventions. This study will look at a variety of determinants, including clinical, socioeconomic, and environmental factors, as well as healthcare delivery characteristics including staffing and resource availability. This comprehensive approach is uncommon in previous studies and can provide a more nuanced understanding of the diverse nature of newborn death.

Given Ethiopia's quickly shifting healthcare scene, this study will give up-to-date information on current practices and difficulties. This relevance is critical for policymakers and healthcare practitioners looking to implement effective policies in light of current trends. The findings could

have a direct impact on national health policies and programs targeted at lowering infant mortality rates, making the study both academically and practically valuable. Given Ethiopia's commitment to reaching the Sustainable Development Goals (SDGs), this study is pertinent and important. The study's identification of actionable newborn death variables will help national efforts to enhance mother and child health outcomes. Overall, while newborn death is a well-studied topic, this study's unique focus on individual hospitals, methodological rigor, and thorough assessment of numerous variables distinguishes it as a valuable contribution to Ethiopia's existing body of knowledge.

2. Literature review

Neonatal mortality is a major worldwide health issue, especially in low- and middle-income countries (LMICs). The World Health Organization (WHO) defines neonatal mortality as the death of a live-born baby during the first 28 days of life. Understanding the causes of newborn death is critical to creating effective therapies [8]. Globally, infant mortality rates have decreased, yet they remain unacceptably high. According to WHO statistics, nearly 2.4 million newborn fatalities occurred in 2020, accounting for 56% of all under-five mortality [17]. Birth weight, gestational age, mother health, socioeconomic level, and access to healthcare are all important factors to consider.

Birth weight and gestational age

Low birth weight (LBW) and preterm birth are both major risk factors for infant mortality. A meta-analysis found that LBW significantly raises the risk of newborn death. Preterm infants are especially vulnerable, with a higher fatality rate than term infants [18, 19].

Maternal health.

Maternal health influences newborn outcomes significantly. Hypertension, diabetes, and pregnancy-related infections all play a substantial role in neonatal death. A South Asian study discovered that maternal infections tripled infant mortality [20]. Furthermore, maternal education and socioeconomic level are substantially associated with newborn survival, with educated women having a lower risk of neonatal mortality.

Healthcare Access

Another important factor to consider is access to high-quality healthcare. According to a systematic analysis, insufficient prenatal care doubles the risk of newborn mortality [21]. The presence of neonatal intensive care units (NICUs) can considerably lower mortality rates, particularly among high-risk neonates. Africa has a disproportionately high newborn death rate compared to other regions. In 2020, the continent had an average neonatal mortality rate of 27 per 1,000 live births [22]. Key variables are similar to those seen globally, but they are worsened by systemic issues such as poverty, insufficient healthcare facilities, and high infectious illness rates. Rural areas continue to face barriers to accessing healthcare services. A survey revealed

that neonates born in health facilities had a considerably decreased risk of death compared to those born at home [27].

Socioeconomic factors.

Socioeconomic gaps have a considerable impact on newborn outcomes throughout Africa. A study in Nigeria discovered that couples in the lowest wealth quintile had a newborn mortality rate of 39 fatalities per 1,000 live births, compared to just 15 in the top quintile [23].

Infectious diseases.

Infectious disorders like malaria and HIV/AIDS are serious threats to newborn health. A study found that HIV-positive moms had a twofold higher risk of newborn mortality than HIV-negative mothers [24]. Ethiopia has made substantial progress in lowering infant mortality, but it still confronts significant obstacles. In 2020, the newborn mortality rate was predicted to be 29 deaths per 1,000 live births [25]. Ethiopian-specific determinants include maternal education, access to healthcare, and cultural behaviors.

Maternal education

Maternal education is an excellent predictor of newborn survival in Ethiopia. A study discovered that educated moms had a neonatal mortality rate of only 16 fatalities per 1,000 live births, compared to 39 among illiterate mothers [26].

Conceptual framework

This is the conceptual framework developed specifically for this study by the principal investigator after reviewing related literature in which this study aimed to focus. The framework tries to figure out the determinants of neonatal mortality.

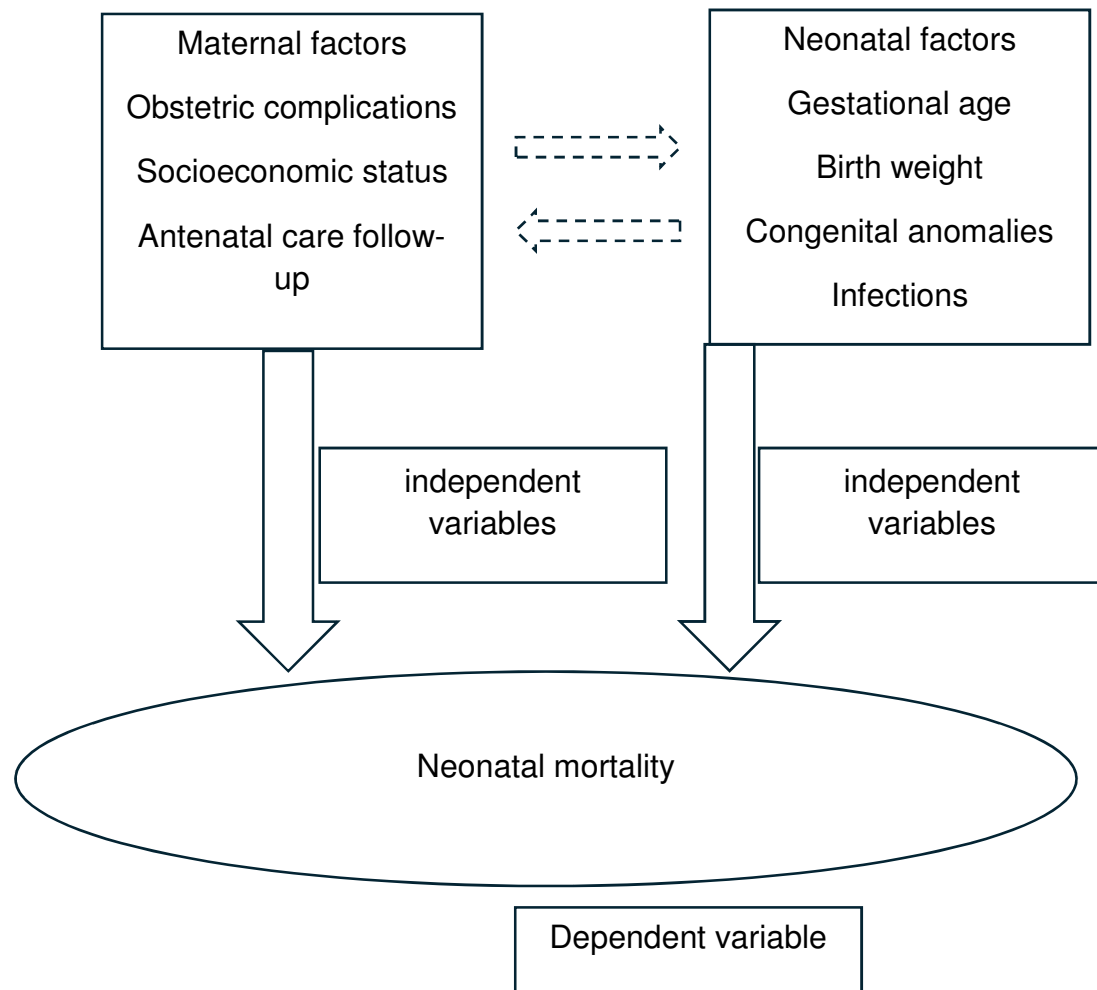


Figure 1: conceptual framework on determinants of neonatal mortality [11, 28-30]

3. Objectives

3.1 General Objective

1. To assess the determinants of neonatal mortality among newborns admitted to the Neonatal Intensive Care Unit (NICU) at SPHMMC and TBGH in Ethiopia

3.2. Specific objectives

1. To identify maternal and neonatal factors associated with neonatal mortality among newborns admitted to the Neonatal Intensive Care Unit at SPHMMC and TBGH in Ethiopia

4. Methods

4.1 Study Setting

The study was conducted at SPHMMC and TBGH. SPHMMC is one of Ethiopia's top medical schools and a vital referral hospital. The hospital was founded in 1968. More than 2800 clinical, academic, administrative, and support staff members work at the institution. The college teaches medical and nursing students and does basic and applied research and in addition to providing medical specialty services to patients who are referred from all over the country. The College can accommodate more than 700 inpatient beds, and on a daily average, 1200 emergency and outpatient patients are seen. The NICU at SPHMMC is a major hub for clinical practice and research. It consists of more than 120 health professionals and over 60 beds.

TBGH is established as a joint venture between the Chinese and Ethiopian governments. It is situated in the Akaki Kaliti sub-city, Addis Ababa. This institution provides a comprehensive variety of medical treatments for the surrounding Oromia region inhabitants and other neighboring sub-cities inhabitants (Nifas Silk Lafto and Bole) beyond the Akaki Kaliti sub-city inhabitants. It comprises 625 health professionals and 250 administrative experts

TBGH provides a variety of neonatal care services to help neonates stay healthy and thrive. Specialized care for premature and very ill babies, complete with incubators, ventilators, and monitoring systems. Incubators and warming devices are used to manage body temperature in preterm and low birth weight newborns. Services for neonates suffering from respiratory distress, such as oxygen therapy and mechanical ventilation. Infants who are unable to eat normally can receive assistance with breastfeeding, formula feeding, and intravenous nutrition. Protocols for preventing and treating infections in vulnerable neonates. Strategies for supporting infants' physical and neurological development in the NICU. Following discharge, high-risk newborns are monitored to ensure their continuing health and growth.

SPHMMC, a specialized referral hospital, offers a diverse patient population and a wealth of complex neonatal cases. The investigators familiarity with this institution will streamline data collection and analysis. TBGH, a general hospital, provides a more representative sample of neonatal cases, enabling a comparison between specialized and general healthcare settings. By studying these two hospitals, the investigator aims to broaden the applicability of the findings,

pinpoint specific causes of neonatal mortality, and suggest targeted strategies to improve neonatal survival rates.

4.2 Study Design and period

An institution-based unmatched case-control study was conducted. The study period was from December 1, 2023- November 30, 2024

4.3 Source Population

All neonates born in the catchment area of SPHMMC and TBGH during the time period December 1, 2023- November 30, 2024

4.4 Study Population

All neonates who were admitted in the neonatal intensive care unit and registered as died and alive within the first 28 days from December 1, 2023- November 30, 2024

4.5 Eligibility criteria

4.5.1 Inclusion criteria

- Neonates admitted during the study period to the NICU and who died within the first 28 days of life for cases.
- Neonates admitted during the study period to the NICU and who survived during the first 28 days of life for controls.
- Neonates who have been formally admitted to the NICU for medical care, regardless of the reason for admission (e.g., prematurity, birth asphyxia, infections).

4.5.2 Exclusion criteria

Maternal and neonatal records missing key values

Neonatal Charts labeled as death on arrival

4.6. Variables

4.6.1. Dependent variables

Neonatal Mortality

4.6.2. Independent variables

❖ Sociodemographic characteristics of mother and newborn

-Maternal age in years

-Neonatal sex

-Neonatal age in days

❖ Obstetric factors

-ANC follow-up

-Mode of delivery

-place of delivery

-Resuscitation at delivery

-Duration of labor

-Duration of rupture of the membrane

-Maternal fever

-Parity

-Fetal presentation

Newborn conditions

-Gestational age

-APGAR score/immediate crying

-Birth weight in grams

- Sepsis

-Length of stay in NICU

4.7 Sampling procedures

4.7.1 Determination of sample size

Open Epi version 3.01 software was used to calculate the required sample size. Under the assumption of double population proportion formula taking into account infection and HIE as a determinant factor from a previous study conducted in Dessie comprehensive specialized hospital and different sample sizes were produced from the determinants of neonatal mortality [31]. For infection the percentage of controls exposed were 42 and percent of cases exposed were 61.9. After input of case to control ratio 1:2, power 80%, and confidence interval 95%.the optimum sample size obtained was 219. Adding 10 % non-response rate, the total sample size was 240.

Total sample size = 240 160(controls) and 80(cases)

4.7.2 Sampling techniques

The total number of newborns registered in NICU admission book of SPHMMC and TBGH from December 1, 2023, to November 30, 2024, were 4322 and 871 respectively. The total number of newborn deaths registered during this period were 728 and 213 respectively. Study participants were selected by using simple random sampling for both cases and controls. Regarding proportional sample allocation calculation, we took 186 (62 cases, 124 controls) sample from SPHMMC and 54 (18 cases, 36 controls) sample from TBGH, based on their death registered in the last year.

4.8 Data collection procedure

A well-structured, pre-tested modified and adapted checklist written in English enquiring maternal and neonatal condition was used. Kobo collect Version 2021.2.4 software was employed to retrospectively abstract data. The admission history file, neonatal logbook, referral sheet history, and delivery summary was used as the data source. The data was collected by two trained BSC nurses at the health facility.

4.9 Data quality assurance

The goals of the study, specifics of the data collecting instruments, and how to protect respondent confidentiality and privacy were covered in a one-day training session for the data

collectors. The lead investigator and the supervisor kept an eye on the entire data collection process.

4.10. Operational definition of variables

Neonatal Mortality refers to the death of a live-born baby within the first 28 days of life [1,22,34]

Gestational age the number of completed weeks of pregnancy, recorded from the first day of the last menstrual cycle, ultrasound or Ballard score. It can be classified as term (37–42 weeks), post-term (>42 weeks), or preterm (<37 weeks) [33].

APGAR score: a scoring system with a rapid assessment of clinical status of the newborn infant at one minute and five minutes establishing immediate management [34].

PROM: is defined as the spontaneous rupture of the amniotic sac and chorion membranes before the onset of labor, occurring before 37 weeks of gestation when preterm, and at or after 37 weeks when term [35], Maternal fever: temperature of >38.5 considered as maternal fever

4.11 Data management.

4.12 Data analysis procedure

The collected data was checked for completeness and consistency and cleaned, exported to SPSS version 26 for analysis. Descriptive statistics, such as frequency or proportion, was used to describe the study participants. Binary logistic regression analysis was carried out, and the candidate variables were selected at a p value of 0.25 for multivariate logistic regression. Multiple logistic regression was performed, and independent determinants of neonatal mortality were identified at a p value of 0.05 along with a 95% CI. In the final multivariate models, the level of multicollinearity was checked and fitted using variance inflation factor (VIF) and found within a tolerable range: all variable values <5. Meanwhile, the model fitness of the study was assessed using the Hosmer and Lemeshow model fitness test with test result of (P-value = 0.67).

4.13. Ethical Consideration

Ethical clearance was obtained from the ethical review committee of SPHMMC. A formal letter of cooperation was written to both SPHMMC and TBGH and permission was obtained from the

hospital administrators. Data was anonymized, and personal identifiers were not included in the checklist to maintain confidentiality.

5. Dissemination of Results

The results of the study will be disseminated to TBGH, SPHMMC School of Medicine and department of Family Medicine, Pediatrics and Child Health and Department of Obstetrics and Gynecology. Results will also be disseminated through publication in peer-reviewed local and international journals and through presenting it in seminars.

5. Result

5.1 Maternal and newborn sociodemographic characteristics

A total of 240 records was reviewed (80 cases and 160 controls) from December 1, 2023- November 30, 2024. The majority of neonates among cases 62 (77.5%) and controls 117 (73.1%) were delivered from mothers in age group between 25- 34 years old. Half of cases, 40 (50.0%) delivered from multipara mothers and 85 (53.1%) controls were born from multipara mothers. A total of 43 (53.75%) of cases and 82 (51.25%) of controls were females. Regarding the age of neonate at admission, 53 (66.25%) of cases were admitted at age ≥ 5 days of age, whereas 90 (56.25%) of controls were admitted at age of 2-4 days of age.

Table 1. Maternal and newborn sociodemographic characteristics of patients admitted to neonatal intensive care unit at SPHMMC and TBGH, Ethiopia, 2024.

Variables	categories	case	control	Total %
Sex	Male	37 (46.25%)	78 (48.75%)	115 (47.9)
	Female	43 (53.75 %)	82 (51.25%)	125 (52.1)
Parity	Primiparous	34 (42.5%)	56 (35.0%)	90 (37.5)
	Multiparous	40 (50.0%)	85 (53.1%)	125 (52.0)
	Grand multiparous	6 (7.5%)	19 (11.9%)	25 (10.4)
Maternal age	18- 24 yrs.	7 (8.7%)	27 (16.9%)	34(14.1)
	25-34 yrs.	62 (77.5)	117 (73.1%)	179(74.5)
	≥ 35 yrs.	11 (13.8%)	16 (10.0%)	27(11.25)
Age of neonate at admission	1 day	17 (21.25 %)	34 (21.25%)	51 (21.25)
	2-4 days	10 (12.5%)	90 (56.25%)	100(41.6)
	≥ 5 days	53 (66.25%)	36 (22.5 %)	89(37.0)

5.2 Obstetric factors

Among the total newborns enrolled in the study, 38 (47.5 %) of the cases and 65 (40.6%) of controls the newborns had delivered through cesarean section delivery respectively. A total of 63.7% of cases and 64.4% of controls were born from mothers with obstetric complication, of them 31 (30.1 %) of controls and 17 (33.3%) born from mothers with APH. Newborns whose mothers had a PROM in the case and control groups accounted for 9(17.6%) and 28(27.2%),

respectively. Additionally, 86.3% of cases and 78.1 % of controls were born from mothers with an ANC follow-up history, of them 88 (62.4%) of controls and 37 (52.1) of cases born from mothers who had ≥ 4 ANC visit. Majority of cases 72 (90.0%) and 131 (81.9%) of controls were singleton respectively. Regarding place of delivery, 47 (59.5%) of the cases and 90 (56.6%) of controls born at hospitals, respectively. Of total cases 55 (68.8%) and 115 (71.9%) were born from mothers who had rupture of membrane <12 hours, respectively.

Table 2. Obstetric factors of neonatal mortality among patients admitted to neonatal intensive care unit at SPHMMC and TBGH, Ethiopia, 2024.

Variables	Categories	Case (%)	Control (%)	Total (%)
ANC visit	yes	69 (86.3)	125 (78.1%)	194 (80.8)
	NO	11 (13.8)	35 (21.9)	46 (19.2)
Number of ANC visit	1 visit	8 (11.3)	11(7.8)	19(7.9)
	2-3 visit	26 (36.6)	42 (29.8)	68 (28.3)
	≥ 4 visit	37 (52.1)	88 (62.1)	125 (52.1)
maternal obstetric complication	yes	51 (63.7)	103 (64.4)	154(64.1)
	no	29 (36.3)	57 (35.6)	86(35.8)
Type of maternal obstetric complication	Hypertensive disease of pregnancy	15 (29.4)	34 (29.4)	49(31.8)
	APH	17 (33.3)	31 (30.1)	48(31.1)
	PROM	9 (17.6)	28 (27.2)	37(24.0)
	Other *	10 (19.6)	10 (9.7)	20(12.9)
Number of gestations	Singleton	72 (90.0)	131 (81.9)	203 (84.5)
	Multiple	8 (10.0)	29 (18.1)	37 (15.5)
Place of Delivery	Home delivery	1 (1.3)	1 (0.6)	2(0.8)
	Health institute	79 (98.7)	159 (99.4)	238 (99.2)
level of the facility	Health center	20 (25.3)	54 (34.0)	74(31.0)
	Hospital	47 (59.5)	90 (56.6)	137(60.5)
	Private health facility	12 (15.2)	15 (9.4)	27(11.3)
duration of ROM	<12 hours	55 (68.8)	115 (71.9)	170(70.8)

	>=12 hours	25 (31.3)	45 (28.1)	70(29.2)
fetal presentation	Cephalic	54 (67.5)	105 (65.6)	159 (66.2)
	Breech	21 (26.3)	50 (31.3)	71(29.5)
	Other	5 (6.3)	5 (3.1)	10(4.1)
mode of delivery	Vaginal	25 (31.3)	55 (34.4)	80(33.3)
	Instrumental delivery	17 (21.3)	31 (19.4)	48(20.0)
	C/S	38 (47.5)	65 (40.6)	103(42.9)
	Assisted breech delivery	0	9 (5.6)	9(3.7)

* GDM, Prolonged Labor, Malpresentation, ABO incompatibility

5.3 Neonatal related factors

More than half 45 (56.3%) cases and 87(54.4%) controls were born at the gestational age < 37 weeks respectively. Majority of cases 51 (63.7%) and controls 90(56.2%) were weighed >= 2500 gram. Nearly half of the cases, 38 (47.5%) and 83 (51.9%) of controls were resuscitated at delivery, respectively. >= 7 Apgar score at 1st min was reported from more than half 49(61.3%) of cases and majority 97(60.6%) of controls while more than three fourth 62(77.5%) of cases and majority of 138 (86.2%) of controls have >= 7 Apgar score at 5st min. Approximately more than three-fourth 71(88.8%) of cases and nearly half of 77 (48.1%) of controls had 2-7 days of length of stay in NICU, respectively.

Table 3. Neonatal related factors of neonatal mortality among patients admitted to neonatal intensive care unit at SPHMMC and TBGH, Ethiopia, 2024.

Variables	Categories	Case (%)	Control (%)	Total (%)
Newborn resuscitated at delivery	yes	38 (47.5)	83(51.9)	121(50.4)
	NO	42 (52.5)	77(48.1)	119(49.6)
G/A of newborn in completed weeks	<37 weeks	45 (56.3)	87(54.4)	132(55.0)
	>= 37 weeks	35 (43.8)	73 (45.6)	108(45.0)
APGAR SCORE AT 1 ST MIN	<7	31 (38.8)	63 (39.4)	94(39.2)
	>= 7	49 (61.3)	97(60.6)	146(60.8)
APGAR SCORE AT 5 TH	<7	18 (22.5)	22 (13.8)	40(16.7)

MIN	>= 7	62 (77.5)	138 (86.2)	200(83.3)
Birth weight of the newborn	<2500 gram	29 (36.3)	70 (43.8)	99(41.3)
	>= 2500 gram	51 (63.7)	90(56.2)	141(58.7)
Age of neonate at discharge/death	<= 24 hours	11 (13.8)	37 (23.1)	48(20.0)
	2-7 days	64 (80.0)	54(33.8)	118(49.2)
	> 7 days	5 (6.3)	69 (43.1)	74(30.8)
Length of stay in NICU	1 day	3 (3.8)	19(11.9)	22(9.1)
	2-7 days	71(88.8)	77 (48.1)	148(61.7)
	>7 days	6 (7.5)	64 (40.0)	70(29.2)

5.4. Medical diagnoses of neonatal mortality

More than one third 30(37.5%) of cases and 49(30.0%) of controls had neonatal sepsis, while 14 (17.5%) of the cases and 33 (20.6%) of the controls were diagnosed with respiratory distress syndrome (RDS) or Hyaline membrane disease (HMD).

Table 4. Common medical diagnoses of neonatal mortality among patients admitted to neonatal intensive care unit at SPHMMC and TBGH, Ethiopia, 2024.

Variables	frequency		
	Case (%)	Control (%)	Total (%)
Sepsis	30 (37.5)	49 (30.6)	79 (32.9)
RDS	14 (17.5)	33 (20.6)	47(19.5)
PNA	3 (3.7)	9 (5.6)	12(5.0)
MAS	19 (23.7)	20 (12.5)	39(16.2)
Congenital Malformation	4 (5.0)	1 (0.6)	5 (2.0)
Hypoglycemia	3 (3.7)	21(13.1)	24(10.0)
Hypothermia	2 (2.5)	5 (3.1)	7(2.9)
Jaundice	5(6.2)	12 (7.5)	17(7.0)
Other*	0	3 (1.8)	3(1.2)

* cephalhematoma, IVH

5.5 Risk factors associated with neonatal deaths

To choose potential variables for multivariate analysis, variables were first examined using bivariate analysis. Age of neonates at admission, length of stay in NICU, parity, birth weight of the neonate, Apgar score at 5th min, Apgar score at 1st min and number of gestation were candidate variables for multivariable analysis with a P-value of less than 0.25. After potential confounders were taken into account in multivariate analysis, age of neonates at admission, length of stay in NICU and number of gestations, were found to be determinants of an increased risk of neonatal mortality.

The odds of neonatal death were 4.5 times more likely observed among cases who had multiple gestation than those with singleton number of gestation (AOR = 4.54, 95% CI = 1.82–11.34); The odds of neonatal death were 14.4 times more likely among neonates who stayed more than seven days in neonatal ICU as compared to those neonates who had stayed only for one day (AOR = 14.4, 95%CI = 5.6–36.8). Among neonatal related determinants, those neonates who had one day of age at admission, were 51.0% (AOR = 0.49, 95%CI = 0.25–0.95) less likely to have neonatal death when compared to those who were age $\geq$ 5 days of age during admission.

Table 5: Determinants of neonatal mortality among patients admitted to neonatal intensive care unit at SPHMMC and TBGH, Ethiopia, 2024.

Variable		Frequency	Case	Control	COR	AOR	Value
Age of neonates at admission	1day	89	53	37	0.34(0.35,1.012)	0.49(0.25,0.95)	0.035
	2-4day	100	10	90	2.8(0.47, 6.32)	0.62(0.73,3.42)	
	$\geq$ 5 days	51	17	53	1	1	1
Length of stay in NICU	1 day	22	19	3	1	1	1
	2- 7 days	148	77	71	5.8((0.38,7.37)	1.8)0.43,8.09)	0.44
	>7 days	70	64	6	0.59(4.01,24.11)	14.4(5.6,36.87)	<0.001
Birth weight of the newborn	<2500gram	99	70	29	0.73(0.42,1.27)	0.68(0.35,1.35)	0.27
	$\geq$ 2500 gram	141	90	51	1	1	1
Apgar score at 5 th min	<7	40	22	18	0.55(0.27,1,1)	0.79(0.322,1.945)	0.611
	$\geq$ 7	200	138	62	1	1	1

apgarscoreat1s tminn	<7	94	63	31	1.03((0.6,1.78)	0.85(0.389,1.87)	0.691
	>= 7	146	97	49		1	1
Number of gestations	Singleton	203	143	60	1	1	1
	multiple	37	17	20	3.0(0.87,4.6)	4.54(1.82,11.34)	0.001

6. Discussion

Our study's results show that the probabilities of infant death were 4.5 times higher in multiple gestation instances than in singleton gestations. This finding is consistent with a growing body of research highlighting the higher dangers of multiple pregnancies. This is consistent with multiple gestational neonatal mortality rates in Ethiopia that have been reported in a number of studies. For example, according to a study at Gonder, preterm delivery and low birth weight are two characteristics that are associated with greater neonatal mortality when multiple gestations are present [28]. Similarly, a study showed that multiple births had significantly higher mortality rates compared to singletons, attributing this to complications arising during delivery and inadequate prenatal care[36].

When examining studies from other African nations, the trend of increased neonatal mortality in multiple gestations is consistent. Research conducted in Nigeria revealed that twins and higher-order multiples faced significantly higher risks of neonatal death due to factors such as prematurity and maternal complications during pregnancy and childbirth [37]. Similarly, studies in South Africa have indicated that while multiple gestations are at greater risk, the degree of risk can vary based on socioeconomic status and access to quality healthcare [38]. Multiple births are associated with increased death rates, according to studies from different locations. These difficulties include pre-term labor, intrauterine growth restriction, and maternal health issues. Numerous studies have been conducted worldwide to examine the connection between multiple gestations and newborn mortality. Due to improved access to healthcare and more sophisticated medical procedures, research from high-income nations frequently shows decreased infant mortality rates for multiple deliveries. Improvements in maternal health services can result in better results, even if multiple gestations normally involve higher risks, according to a meta-analysis [39].

According to our research, newborns who were admitted to the neonatal intensive care unit (NICU) for more than seven days had a 14.4-fold increased risk of dying than those who were released after just one day. This result emphasizes the crucial link between longer NICU stays and a higher risk of death, a pattern noted in other research conducted in Ethiopia and around the world. Numerous research conducted in Ethiopia have demonstrated the link between prolonged NICU stays and unfavorable newborn outcomes. For example, a study conducted in the Amhara

region found that prolonged NICU stays were associated with increased death rates, mostly as a result of problems including respiratory distress and infections [30]. Similarly, studies that neonates requiring prolonged care in the NICU had a significantly higher risk of death, attributing this to the severity of underlying health conditions that necessitated extended treatment [40]. Our result is also in line with Comparative studies across other African nations reveal a similar pattern regarding the risks associated with prolonged NICU stays.

Researches from Africa reported that extended durations in the NICU were associated with higher mortality, although it highlighted improvements in neonatal care over time that have helped mitigate some risks, primarily due to complications such as sepsis and prematurity [41-43]. A systematic review indicated that neonates requiring extended hospitalization due to severe health issues face significantly higher risks of mortality compared to those with shorter stays [8]. Neonates who stay in hospitals for extended periods of time have higher survival rates in high-income nations thanks to advancements in care standards and technology. The same cannot be said for environments with limited resources, when access to and the quality of healthcare may fall short of expectations. Studies from high-income nations, however, show lower odds ratios for newborn death linked to longer NICU stays, which contradicts our findings. This suggests that improvements in neonatal care can successfully manage problems that occur during prolonged hospitalizations.

Neonates admitted to the neonatal intensive care unit (NICU) at one day of age have a 51.0% reduced chance of dying than those admitted at five days or later, according to our research. This result highlights how crucial admission timing is and raises the possibility that early intervention could greatly increase neonatal survival rates. Numerous research has examined the connection between newborn mortality and admission age in Ethiopia. Our results are consistent with Ethiopian studies that showed neonates admitted within the first 24 hours of life had higher survival rates than those admitted later [29, 31, 44, 45]. These studies attributed improved outcomes to timely interventions for conditions such as birth asphyxia and infections, which are more effectively managed when identified early. This suggests that while our findings are consistent with existing literature regarding the benefits of early admission, there are complexities in the cases of late admissions that warrant further investigation. This is also in line with studies done in Africa and high-income countries [46-50]

7. Limitation

Given that it was carried out in two hospitals, the study's limitations are recognized. As a result, the findings are limited to the demographic being studied. Only a few files were accessible at the time the study's data was gathered, which was done retrospectively over a one-year period. Therefore, the current investigation was restricted to the data recorded in the files and was carried out using the files that were available during the data collection period.

8. Conclusion and recommendation

The study found that the three main risk factors for newborn mortality were the length of hospital stay, age at admission, and number of gestation. In order to reduce neonatal deaths and morbidities in healthcare settings, healthcare providers must have a thorough understanding of these risk variables in order to create an efficient risk assessment strategy. Additionally, it will help health care providers take preventive measures to lower these risk factors, which will ultimately help achieve the Sustainable Development Goal of reducing neonatal mortality by ending infant deaths that can be prevented.

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ASSURANCE OF THE PRINCIPAL INVESTIGATOR

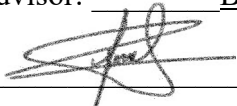
The undersigned agrees to accept responsibility for the scientific ethical clearance and technical conduct of the research project and for the provision of required progress reports as per terms and conditions of the research publications office in effect at the time of grant is forwarded as the result of this application

Name of the student: Dr. Abel Yohannes

Date: _____ Signature: _____

Approval of the Primary Advisor

Name of primary advisor: Berhanu Teshome

Signature:  _____

Date: March 5, 2025

Annex 1: English version Checklist

This is the checklist that was used for the study titled, “Determinants of neonatal mortality among newborns admitted to neonatal intensive care unit at two selected hospitals in Addis Ababa, Ethiopia, 2024: a case control study”

S. No	Questions	Response category	skip
Maternal and newborn sociodemographic information			
1	Maternal age in years		
2	Parity	1. Primiparous 2. Multiparous 3. Grand multiparous 4. Other	
3	Sex of Neonate	1. Male 2. Female 3. Other	
4	Age of neonate at admission	1. < 24 HRS 2. 1-7 DAYS 3. >7 DAYS	
Obstetric factors			
5	ANC visit	1. Yes 2. No	
6	If yes, to question number 5 how many times did the mother visit ANC	1. 1 2. 2-3 3. 4-5	

		4. 6-7 5. ≥ 8	
7	Was there maternal obstetric complication	1. Yes 2. No	
8	If yes to the above question, what was the obstetric complication	1. Hypertensive disease of pregnancy 2. APH 3. PROM 4. Other_____	
9	Number of gestations	1. Singleton 2. Multiple	
10	Place of Delivery	1. Home delivery 2. Health institute	
11	If it is health institute delivery, what is the level of the facility	1. Health center 2. Hospital 3. Private health facility	
12	What is the duration of rupture of membranes	1. <12 hrs. 2. ≥ 12 hrs.	
13	What was the fetal presentation	1. Cephalic 2. Breech 3. Other	
14	What is the mode of delivery	1. Vaginal 2. Instrumental (forceps or vacuum) 3. C/S 4. Assisted breech delivery	

Neonatal factors			
15	Was newborn resuscitated at delivery	1. Yes 2. No	
16	Gestational age of newborn in completed weeks	1. <34wks 2. 34-36+6 wks. 3. > 37 wks.	
17	APGAR SCORE AT 1 ST MIN	1. <7 2. >=7	
18	APGAR SCORE AT 5 TH MIN	1. <7 2. >=7	
19	Birth weight of the newborn	1. <1KG 2. 1-1.5KG 3. 1.6-2.5KG 4. >2.5KG	
20	diagnosis of neonate at admission (Multiple answers can be chosen)	1. sepsis 2. RDS 3. PNA 4. MAS 5. Congenital Malformation 6. Hypoglycemia 7. Hypothermia 8. Anemia 9. Jaundice 10. Other_____	
21	Age of neonate at discharge/death	1. < 24 HRS 2. 1-7 DAYS 3. >7 DAYS	

22	Condition of neonate at discharge	1. Alive 2. Dead	
23	Length of stay in NICU		