



**Hawassa University College of Medicine and  
Health Sciences School of Public Health**

**PREDICTORS OF PRETERM NEONATES MORTALITY  
AT HAWASSA COMPREHENSIVE SPECIALIZED  
HOSPITAL, SIDAMA REGION, ETHIOPIA: A  
RETROSPECTIVE COHORT STUDY.**

**BY: TIHUN FELEKE (BSC)**

**April, 2021**

**Hawassa, Ethiopia**

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HAWASSA COMPREHENSIVE SPECIALIZED HOSPITAL,  
SIDAMA, ETHIOPIA: A RETROSPECTIVE COHORT STUDY.**

**By: Tihun Feleke (Bsc)**

**A proposal submitted to Hawassa University  
College of Medicine and Health Sciences  
School of Public Health**

**In partial fulfillment of the Requirements for  
Master Degree of Public Health in Epidemiology**

**Advisors: Dr. Taye Gari (MPH, PHD)**

**Co-advisor: Mr. Deresse Legesse (MPH)**

**April, 2021**

**Hawassa, Ethiopia**

## Approval Sheet

### Assurance of investigator

The undersigned to accept responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per term and conditions of research and publication office of the Hawassa University College of Medicine and Health Science School of Public Health.

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## **List of abbreviation and acronyms**

<b>ANC</b>	Ante Natal Care
<b>AHR</b>	Adjusted Hazard Rate
<b>CPD</b>	Cephalo Pelvic Disproportion
<b>DC</b>	Data Collectors
<b>EDHS</b>	Ethiopian Demographic and Health Survey
<b>FMOH</b>	Federal Ministry Of Health
<b>IUGR</b>	Intrauterine Growth Retardation
<b>KMC</b>	Kangaroo Mother Care
<b>HIV</b>	Human Immune deficiency Virus
<b>HMD</b>	Hyaline Membrane Disease
<b>HUCSH</b>	Hawassa University Comprehensive Specialized Hospital
<b>MCH</b>	Maternal and Child Health
<b>MOH</b>	Ministry of Health
<b>NICU</b>	Neonatal Intensive Care Unit
<b>NMR</b>	Neonatal Mortality Rate
<b>PNA</b>	Prenatal Asphyxia
<b>PROM</b>	Premature Rupture of Membrane
<b>RDS</b>	Respiratory distress Syndrome
<b>SPSS</b>	Statistical Package for Social Science
<b>WHO</b>	World Health Organization

## **Abstract**

**Background:** Globally more than 1 million preterm neonates died out of 15 million babies born preterm every year. The burden of preterm neonatal mortality is profound particularly during the first 28 days of life, accounting for 35% of all neonatal deaths and for 18% of all deaths of children aged under 5 years worldwide. The issue of preterm neonate has paramount significance for achieving aims to end all preventable deaths of newborns and children aged under 5 years by 2030.

**Objectives:** The aim of this study will be to assess survival status and predictors of preterm neonate mortality admitted in neonatal intensive care units of Hawassa University Comprehensive Specialized Hospital, Sidama, Ethiopia.

**Methods:** Retrospective cohort study will be conducted from May1, 2021 to May 30, 2021. The study population will be all preterm neonates admitted to neonatal intensive care units (NICU) at Hawassa University Comprehensive Specialized Hospital (HUCSH) from April 1, 2019 to March 30, 2021. Data will be collected by trained data collectors using pretested data extraction format from chart and registry book of each neonate and mother. Data will be entered into Epi-data version 3.1, and analyzed using STATA version-14 statical software. Furthermore, Kaplan Meir will be used to estimate mean survival time and cumulative probability of survival. Log-rank tests will be used to compare group's survival curves after admission to NICU. Cox proportional hazards regression analyses will be used to identify predictors. The crude and adjusted hazard ratios together with their corresponding 95% confidence intervals will be computed and interpreted accordingly. P-value <0.05 will be considered as statistically significant.

**Work plan and Estimated Budget:** - The study will be conducted from February to June 17, 2021, and the estimated budget will be 26,224 ETB.

# **1.Introduction**

## **1.1 Background**

The World Health Organization (WHO) defines preterm births as live births before 37 completed weeks of gestation or fewer than 259 days since the first day of a women's last menstrual period(1). Preterm birth can be classified based on gestational age as late preterm (babies born between 33 to <37 completed weeks of gestation), very preterm (babies born between 28 to 32 completed weeks of gestation) and extreme preterm (babies born before 28 completed weeks of gestation) (2-4). Twenty eight completed weeks of gestational age is considered as GA of viability in developing country including Ethiopia. The neonatal period begins at birth and includes the first 28 days of life and subdivided in to very early neonatal period (birth < 24 hours), early (birth<7days), and late (7 to< 28 days)(4). Preterm neonatal mortality is death of preterm neonates within the first month (28 days) of life. Antepartum hemorrhage, preeclampsia, eclampsia, multiple pregnancies, premature rupture of membrane, smoking or substance use during pregnancy are the most common factors associated with preterm mortality(5).

During pregnancy a fetus passes marked physiologic growth and developmental transitions till final weeks of pregnancy, which help the developing baby learn to respond to many forms of external stimuli (6, 7). However, preterm neonate born before reaching maturity are fragile, small, weighing less than full term infants and face a variety of physiologic handicaps which predispose them to many short term and long term complications like respiratory problems, sepsis, seizures, feeding difficulty, altered body temperature and hypoglycemia(2, 8). Furthermore, those preterm neonates who survive often face a lifetime of ill-health including disability, learning difficulties, visual and hearing problems, psychological crises, financial hardships and economic burden for the families and broader society due long term complex health care needs(9, 10).

Owing to this, preterm birth complications is a significant public health problem across the world because of associated morbidity and mortality(8, 9). Mortality due to preterm birth complications are supreme which is more than 1 million out of 15 million babies born preterm every year worldwide(10). As a result, complications related to preterm births are now single, direct leading cause of death, accounting for 18% of all deaths in under five children and the first leading cause of neonatal mortality worldwide (10, 11).

## 1.2 Statement of the problem

The first month of life is the most crucial period for child survival. One million children die each year out of an estimated 15 million preterm births globally(3, 10).The distribution of mortality in age include 909,000 death occur in the neonatal period and more than 100,000 after the neonatal period, often after long hospital stays(9, 10). The burden of preterm neonatal mortality were supreme accounts for 35% of all neonatal deaths worldwide(9). In addition preterm related complications are the first leading cause for neonatal mortality and the second leading cause of under-five mortality globally (12).India and Iran indicate lower mortality rates among preterm infants of 18.7% and 12%,respectively compared to America and European Counteris (5, 13). Studies conducted in Ethiopia indicated that high burden of preterm neonatal death was 37% in Felege Hiwot specialized hospital(14).

One third of all preterm neonatal deaths occur within the first day after birth, and close to three quarters preterm neonatal death occur within the first week of life worldwide(2, 3, 9, 10). Seventy-three percent of deaths occurred within the first week of life in Nigeria(15). In another study in Ethiopia among preterm neonates admitted to a NICU, 11.4% died in the first 24 hours and 85.27% died in the first 7 days(16). Thus, these findings indicate that the first few days are the most important period for the survival of preterm neonates. The survival rates of preterm babies mainly depends on the economic status of the country they born and the capacity of the health system to respond to their needs (9).

Preterm neonate born in sub-Saharan Africa is 10 times more likely to die than preterm neonate born in any developed countries (10, 17). Furthermore, specifically preterm neonate born in sub-Saharan Africa is 12 times more likely to die than a preterm babies born in Australia and New Zealand (10, 18). Additionally, over 90% of extremely preterm babies born in low income countries die within the first few days of life however less than 10% of extremely preterm babies die in high income countries (3, 17). Moreover, in high-income countries, almost all of these babies born at or above 32 week were survive. Whereas, in low income setting half of the preterm babies born at or above 32 weeks were die due to a lack of feasible, cost-effective care, such as warmth, breastfeeding support, and basic care for infections and breathing difficulties (15, 18). Although in middle income setting suboptimal use of technology causing an increased burden of disability among preterm babies who survive the neonatal period (17).

In east Africa 94.6% of preterm neonates born at or after 34 weeks of gestation survive while only 52.6% of those preterm neonates born before 34 weeks survive (19). Fifty five percent (55.2%) of preterm neonate survival was achieved at or after 31 weeks of gestation(20).The most common factors associated with increased risk of preterm neonatal mortality were hypothermia, respiratory distress, Sepsis, low gestational age, low birth weight, being female, feeding problem of the neonate, not received ANC, very low birth weight and length of time on ventilator(8, 16).Moreover, male sex, congenital anomalies, perinatal asphyxia(PNA), hyaline membrane disease(HMD), jaundice, hypoglycemia, timely initiation of breastfeeding upon birth and kangaroo mother care (KMC) were reported as factors of preterm neonatal death(16, 20).

World Health Organization sets a target of 50% reduction in preterm deaths by 2025 in countries with a neonatal mortality rate above 5 per 1,000 live births(3). Similarly reducing the burden of preterm mortality has dominant significance for achieving United Nations Sustainable Development Goal 3 target #3.2 (21). More than three-quarter of these preterm neonatal deaths can be averted by feasible and cost-effective interventions like stabilization, prevention and early treatment of infection, preventing hypothermia as well as early introduction of breast milk and further intensive neonatal care(22).On the other hand , seven countries reduced mortalities of preterm neonates by half (50%)through application of quality and cost effective interventions of newborn.(18, 23). The government of Ethiopia showed its effort to improve the survival of preterm neonate through application quality, feasible and cost-effective interventions mainly through the inclusion of high impact life-saving neonatal interventions in its Health Sector Transformation Plan and Newborn and Child Survival Strategy.

Despite this effort, mortality due to complication of preterm births is still not reduced as expected, prematurity is first cause of neonatal mortality and the fourth cause of under-five mortality in the country(24, 25). Thus, this study will have vital contribution in filling the gap on knowledge of preterm neonatal mortality, will lay fertile ground for further studies and other interventional measures specially for Sidama region since there is a scarcity of evidence even if, few studies conducted in other parts of a country. This study will be conducted to assess the time to death of preterm neonate and predictors of preterm neonates mortality in Hawassa Comprehensive Specialized Hospital, Sidama Region, Ethiopia, 2021.

### **1.3 Significance of the Study**

Approximately one million babies die every year due to complications of preterm birth globally. The Time to death issue of preterm neonate has paramount significance as indicator for quality of care provided for babies and for achieving global aims of sustainable development goal to end all preventable deaths of newborns and children aged under 5 years by 2030. Nationally, there is a paucity of evidence regarding the survival status and predictors of preterm neonatal mortality with the exception of few studies as my knowledge on the central and northern part of the country. There is also inconsistency of report among those published articles Moreover; in Sidama region could not find published research article on a similar topic.

Therefore, the evidence from this study will be helpful for patients, health professionals, and managers on better cost effective services that improve time to death of preterm neonates. Also to identify and design interventions that is essential at institutional level of Sidama region for expansions and strengthening of quality health service that has significant importance on reduction preterm neonatal mortality and to avert the long term impact of problem on survivors. Also will serve as the base for further researches in the region.

## **2. Literature Review**

### **2.1 Overview of Preterm Neonate Mortality**

Each year, more than one in ten of world's babies are born preterm; resulting in 15 million newborns are born too soon (which accounts 11% of all deliveries) with the highest proportion (60–80%) occurred in African and South Asian countries (26, 27). Global data revealed that approximately 1 million children die due to complications related to preterm birth before the age of five years; accounting for 18% of all deaths among children and 35% of all deaths among newborns (3, 8, 10, 26, 27). The survival status of newborn babies varies from region to region. India alone share 33% of total global deaths related to preterm birth(3, 10) whereas North America and Western Europe accounts 28% of preterm deaths compared to 13% in Sub-Saharan Africa and 25.5% in South Asian countries(10).

Study conducted in Jordan, identified preterm neonatal mortality in rate was 123 per 1000 live births (early neonatal death was 99 per 1000 live births, and late neonatal death was 24 per 1000 live births)(28). Among the 5.9 million under-5 mortalities, 2.7 million mortalities occurred in the neonatal period and the leading under-5 causes of mortalities were preterm birth complications (1.1 million), pneumonia (0.9 million),and intrapartum-related events (0.7 million)(29). In Sub-Saharan countries; approximately 500,000 neonatal deaths were due to preterm birth (10, 13).

In Ethiopia, Preterm is the first cause of neonatal death accounting for 34% and contributes to 12.5% of deaths of under-five children. In 2019, the preterm mortality in Gondar University Comprehensive Specialized hospital Neonatal Intensive care Unit was 28.8%(16). Furthermore, according to institutional based retrospective cohort study conducted in two specialized hospitals of Debre Markos and Felegehiwot in East and West Gojjam; Amhara Regional state in 2020; the magnitude of preterm neonatal Mortality was 37%(14).

Preterm birth is the second leading cause of death for children under-five years of age next to pneumonia and about 24,400 less than 5 years of children die due to the direct effect of Preterm birth in Ethiopia. It remains a public health issue responsible for neonatal morbidity and mortality especially in low-income countries despite the improved antenatal coverage. The survival rates of preterm babies mainly depends on the economic status of the country they born and the capacity of the health system to respond to their needs (9).

Preterm neonate born in sub-Saharan Africa is 10 times more likely to die than preterm neonate born in any developed countries (10, 17). Furthermore, Specifically preterm neonate born in sub-Saharan Africa is 12 times more likely to die than a preterm babies born in Australia and New Zealand(10, 18). Additionally, over 90% of extremely Preterm babies (<28 weeks) born in low income countries die within the first few days of life. However less than 10% of extremely preterm babies die in high income countries (17).

Moreover, in high-income countries, almost all of these babies born at or above 32 week were survive. whereas in low in come setting half of the preterm babies born at or above 32 weeks (2 months early) were die due to a lack of feasible, cost-effective care, such as warmth, breastfeeding support, and basic care for infections and breathing difficulties (15, 18).Although in middle income setting suboptimal use of technology causing an increased burden of disability among preterm babies who survive the neonatal period (17).

In Japan and Sweden survival rate of preterm neonates at GA of 24 weeks were reported 54% and 53 % were reported with aggressive resuscitation respectively(30). In addition in most sites of USA and Norway above 50% survival of preterm neonates is achieved at GA of 24 weeks(31, 32). In east Africa 94.6% of preterm neonates born at or after 34 weeks of gestation survive while only 52.6% of those preterm neonates born before 34 weeks survive (19). Fifty five percent (55.2%) of preterm neonate survival was achieved at or after 31 weeks of gestation at Tikur Anbesa Specialized hospital (TASH)(20).

## **2.2 Predictors of Preterm Neonates Mortality**

### **2.2.1 Socio demographic Predictors of Preterm Neonates Mortality**

According to a study conducted in china Hubei Province mortality from preterm neonates were higher among rural residence than urban residence and low birth weight babies had higher rate of mortality(33).A prospective cohort study conducted in Uganda revealed that preterm neonates whose mothers were aged 35 years and above were 4.5 times more likely to die as compared to those mothers whose age is from 25 to 34 years and male sex were predictors of life to death for preterm neonates(34). Similarly, A study conducted in Ghana revealed that two third of preterm neonatal mortality occurred in less than 72 hours of admission and extremely preterm babies had 12 times more likely to die compared to late preterm births(15).



Subsequently, a retrospective study conducted in Ghana and West India revealed that maternal age and sex of the baby had no association with preterm neonatal mortality(15), which was actually contradicted with the finding of a cross sectional study conducted in five hospitals of Ethiopia identified being female was factors of preterm neonatal death(35). Also another retrospective follow up study in Felegehiwot and Gondar Comprehensive specialized hospital identified home delivery had association with mortality of preterm neonates (14, 16, 35, 36).

### **2.2.2 Maternal Obstetric Predictors of Preterm Neonates Mortality**

According to retrospective cohort studies conducted in Ghana found out that Spontaneous vaginal delivery had lower odds of survival as compared to those preterm newborns through cesarean section(15). as well as prospective follow up studies conducted in Uganda revealed whose mothers did not attend ANC follow up had 4.7 times more likelihood of death and lower gestational age was Predictor for preterm neonatal mortality(34).

In addition, Preeclampsia, number of parity and gravidity, Eclampsia and cesarean section were identified predictors of preterm mortalities in retrospective cohort study conducted in University of Gondar Comprehensive specialized(16). Similarly a cross sectional study conducted in five selected hospitals of Ethiopia revealed preeclampsia and Eclampsia the most common risk factors of preterm mortality(35).

### **2.2.3 Neonatal Related Predictors of Preterm Neonates Mortality**

According to a study conducted in China Province presence of jaundice, hypoglycemia at admission and hyaline membrane disease had significant association with mortality of preterm neonates(33). Also another study conducted in West India in Trinidad and Tobago identified length time on the ventilator, early breast feed initiation and KMC had significant association with survival of preterm neonates(37). Furthermore one study conducted in tertiary hospital of Ghana identified that APGAR scores at 1<sup>st</sup> and fifth minutes and length of stay at neonatal intensive care were significant predictors of preterm death(22).

Respiratory distress syndrome, apnea, hypothermia, kangaroo mother care, early breast feeding, and optimum medical care had significant association with mortality of preterm neonates according to prospective cohort study conducted in Uganda(34).

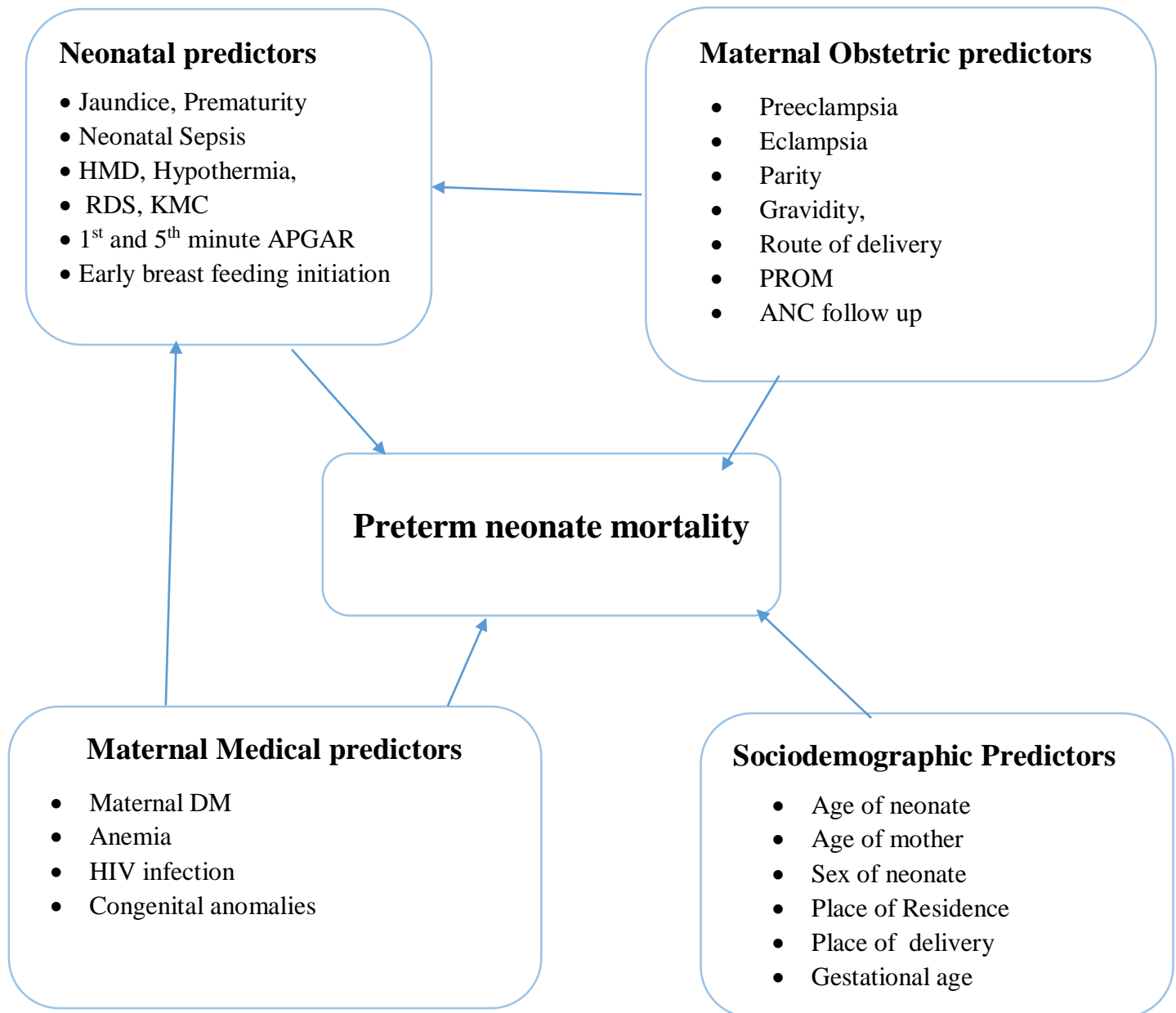
In addition, retrospective cohort study conducted in University of Gondar Comprehensive Specialized hospital in Northern Ethiopia revealed that presence of jaundice, hypoglycemia at admission and hyaline membrane disease were identified as a significant predictors of time to death for preterm neonates(16).Also a retrospective cohort study conducted in Felegehiwot specialized hospital shown RDS, Jaundice, KMC, Sepsis, asphyxia and severe hypothermia as predictors of preterm neonates(14).

#### **2.2.4 Maternal Medical related Predictors of Preterm Neonates Mortality**

According to prospective cohort study conducted in Jordan Congenital anomalies, maternal history of diabetes mellitus, HIV/AIDS infection were the causes of preterm neonatal deaths(28). Moreover Prospective study in Uganda identified maternal HIV infection was a predictor of preterm neonatal mortality(34).Also a retrospective follow up study conducted in University of Gondar Comprehensive specialized identified that Preeclampsia, gestational diabetes mellitus, Eclampsia as the predictors of preterm mortalities(16).

### 2.3. Conceptual Frameworks

The conceptual framework indicates the relationship between outcome variable with Baseline socio-demographic factors, maternal medical, obstetric, neonatal predictors which is adapted in different researches (14-16, 34, 38, 39).



**Figure 1: Conceptual framework for predictors of preterm neonate mortality at Hawassa University Comprehensive Specialized hospital, Sidama, Ethiopia, 2021.**

**Source:** Literatures (14-16, 34,38, 39).

### **3. Objectives**

#### **3.1 General objective**

To assess time to death and predictors for mortality of preterm neonate admitted in neonatal intensive care units of Hawassa University Comprehensive Specialized hospital, Sidama, Ethiopia, 2021.

#### **3.2 Specific objectives**

1. To assess time to death of preterm neonates admitted in neonatal intensive care unit of Hawassa University Comprehensive Specialized hospital, Sidama, Ethiopia, 2021.
2. To identify predictors of mortality among preterm neonates admitted in neonatal intensive care unit of Hawassa University Comprehensive Specialized hospital, Sidama, Ethiopia, 2021.

## **4. Method and Material**

### **4.1 Study setting and period**

The study will be conducted in Hawassa university comprehensive specialized hospital. The hospital is found in Hawassa City which is the capital of Southern Nations, Nationalities and Peoples Regional State (SNNPRS) and Sidama Regional State, the city is located 275 Kilo meter far from of capital of Ethiopia.

Hawassa university Comprehensive specialized hospital (HUCSH) is the only specialized and teaching hospital in the city which offers both diagnostic and treatment services including delivery and Neonatal Intensive care Unit (NICU) service for more than 3 million populations per year. The hospital has about 450 beds for medical, gynecological and obstetrics, surgical, pediatrics, emergency, orthopedic and outpatient department (OPD) services.

The Neonatal Intensive Care Unit of the hospital had about 1000-1500 annual admissions of neonates, and on average 359 premature neonate was admitted to NICU per year for the past two years. From a total of 717 admission of preterm neonates per two years, mortality of preterm neonate were 158 (22.03%). The study will be conducted from May1, 2021 to May 30, 2021 at HUCSH.

### **4.2 Study design**

Retrospective cohort study design will be conducted among preterm neonates admitted in neonatal intensive care units of Hawassa University Comprehensive Specialized Hospital.

### **4.3 Populations**

#### **4.3.1 Source population**

All preterm neonates admitted to neonatal intensive care unit of Hawassa University Comprehensive Specialized Hospital.

#### **4.3.2 Study population**

Preterm neonates admitted in neonatal intensive care unit of Hawassa Comprehensive Specialized Hospital from April 1, 2019 to March 30, 2021

## 4.4 Inclusion and exclusion criteria

### 4.4.1 Inclusion criteria

All live preterm babies within 28 days of their birth born with in the hospital or referred from other health institution admitted to NICU of HUCSH from April 1, 2019 to March 30, 2021

### 4.4.2 Exclusion criteria

Preterm neonates with incomplete records or missing important variables (baseline characteristics, outcome preterm neonate and duration of stay) or whose card is not available in the card room at the time of data collection.

## 4.5 Sample size determination and sampling procedure

### 4.5.1 Sample size determination

The sample size is determined by using a formula for two population proportion formula. The sample size calculation formula is:

$$n = \frac{\left\{ Z_{1-\alpha/2} \sqrt{2\bar{P}(1-\bar{P})} + Z_{1-\beta} \sqrt{P_1(1-P_1) + P_2(1-P_2)} \right\}^2}{(P_1 - P_2)^2} \quad \text{Where} \quad \bar{P} = \frac{(P_1 + P_2)}{2}$$

The assumptions specified will be P1: is proportion of exposed with the outcome, P2: is proportion of non-exposed with the outcome;  $Z_{\alpha/2}$ : 95 % level of confidence,  $Z_{\beta}$ : power of 80% and r: ratio of exposed to unexposed 1:1. Even though this is the formula for calculation of cohort study, openepi.com software used to calculate the sample size. The final sample size calculated will be 640. A total preterm neonate admitted to neonatal intensive care unit of Hawassa Comprehensive Specialized Hospital from April 1, 2019 to March 30, 2021 were 717. As shown in Table 1 below.

**Table 1: Summary of Sample size calculation for main predictors of mortality among preterm neonates by using open epi.com by taking adjusted HR of previous studies as follows**

S. N	Suspected exposure variables. (Exposed: Yes ; Unexposed: No)	% of outcome in unexposed	% of outcome in exposed	AH R	Sample size	Reference
1	Hyaline membrane disease	13.1	21.6	1.9	576	(39)
2	Respiratory distress syndrome	21.6	54.1	2.31	222	(14)
3	Hypothermia	14.8	39.8	2.3	284	(34)
4	Neonatal Sepsis	25.9	81.8	1.78	<b>640</b>	(40)
5	Maternal DM	80	20	2.29	388	(40)

#### **4.5.2 Sampling technique and procedure**

List of medical record number of premature neonates admitted at NICU will be obtained from the medical record unit. The total preterm neonates admitted to neonatal intensive care unit from April 1, 2019 to March 30, 2021 were 717. A total of 640 subjects will be selected randomly from the obtained list by using a SPSS Version-23 software.

#### **4.6. Variables of the study**

##### **4.6.1 Dependent variable**

Time to death of preterm neonates

##### **4.6.2 Independent variables**

- **Sociodemographic characteristics:** Age of preterm neonate, gestational age of preterm neonate, sex of neonate and weight of preterm neonate. Age, residency, place of delivery, length of stay.
- **Maternal obstetric related factors:** PROM, preeclampsia, breast feeding initiation, ANC follow up, gravidity, Parity, mode of delivery and multiple pregnancies.
- **Maternal medical related factors:** DM, HIV/AIDS, anemia, infection, Hypertension.
- **Neonatal related factors:** RDS, sepsis, jaundice, hypothermia, APGAR score, PNA, and congenital anomalies.

#### **4.7. Data Collection tools and procedure**

Data extraction format is adapted and modified from different related studies which is prepared in English (14, 36). The comprises baseline socio-demographic characteristics of both for premature neonate and the mother, maternal medical disorders, obstetric factors, common medical disorders in the neonate, date of admission, discharge and outcome of the premature birth.

The starting point for follow-up time will be the first date of admission and the endpoint will be date of death, censored (date of discharge, or alive at the end of the study) until the last neonatal period. Premature neonatal chart number will be taken from the card room (health management information system (HMIS) – database).

Before collecting the data, the chart will be reviewed (both for baseline and follow up records). The record of all study participants will be selected according to the eligibility criteria and reviewed by four BSc nurses from neonatal registries. The available information on the chart of neonate will be extracted by using data abstraction format. The survival status of study participants will be obtained from the medical record. Death will be confirmed by reviewing medical death certificate in the hospital.

#### **4.8 Data quality and management**

Data quality will be assured by using standard data abstraction format that was adapted from a studies done in Felegehiwot and Gonder Specialized Hospital(14, 16). Pretest will be done on 5% (32 premature neonate's card) one weeks prior to the actual study to check consistency of recorded variables on the patient's medical record and modification will be made after pretest accordingly, The data will be collected by four experienced BSc nurses after one day training will be given concerning the data abstraction tool and data collection process for both data collectors and supervisor.

During the data collection time, Intensive supervision will be done by the investigator and supervisors during the whole period of data collection. Daily evaluation of the data for completeness and encountered difficulties on the time of data collection will be attended accordingly. Finally, all the collected data will be checked by supervisor and investigator for its completeness and consistency during the data management, storage, and analysis. Consistency will be examined through random selection of cards by the principal investigator.



## 4.9 Data entry and analysis

Before analysis, data will be cleaned, edited and coded. Any errors identified at this time will be corrected after the review of the original data using the code numbers. After this data will be entered using Epi-Data version 3.1, then it will be exported and analyzed using STATA statistical software version 14. Descriptive exploratory analysis will be run to assess missing values and presence of outliers. Mean, standard deviation, median, and percentages will be used to describe the baseline demographics and follow up characteristics of preterm neonates.

Descriptive statistics such as Mean with standard deviation or median with Inter Quartile Range for continuous variables depending on the distribution of data and frequency distribution will be used for categorical data. Finally, the outcome of each participant will be dichotomized into censored or death. Incidence rate will be calculated. Survival status of preterm neonates will be calculated as the time between the dates of admission to the date of death, censored or the end of study. Kaplan Meir will be used to estimate mean survival time and cumulative probability of survival and log-rank tests will be used to compare group's survival curves after admission to NICU.

Before running the Cox Proportional Hazard regression model multi-collinearity test will be carried to see the correlation between the independent variables.

Cox Snell residuals will be used to test goodness-of fit of the model. The Cox-proportional hazard regression model assumption will also be checked using Schoenfeld residual test and variables having P-value  $>0.05$  will be considered as fulfilling the assumption. Bivariate Cox-proportional hazards regression model will be fitted for each explanatory variables to identify the predictors. Accordingly, those variables having p-value  $\leq 0.25$  in the bivariate analysis will be fitted to the multivariable cox-proportional hazards regression model with 95% confidence interval and P-value  $< 0.05$  will be considered as statistically significant. The crude and adjusted hazard ratios together with their corresponding 95% confidence intervals will be interpreted accordingly

## 4.10 Operational definition

**Preterm birth:** live birth before 37 completed weeks of gestational age.

**Censored:** Premature neonate still alive at the end of the study or discharged before end of follow up including discharged to home, discharged against medical advice or transfer out to other health institutions without knowing the outcome.

**Follow up time:** From time of admission until either an event or censorship occurs.

**Event:** Death of preterm neonate within 28 days of birth confirmed by observing death certificate.

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

**Medical disorders in the neonate:** Any recorded medical diagnosis for the premature neonates on their medical records.

#### **4.11 Ethical considerations**

Ethical clearance will be obtained from institutional review board of Hawassa University, College of medicine and health science. Then letters of cooperation will be written to concerned bodies of Hawassa University Comprehensive Specialized Hospital. Permission will be obtained from clinical director and subsequent department heads of the hospital. Following these, searching and obtaining of the selected sample medical records will be done with the assigned data collectors. Care will be taken from disclosing confidentiality of patient's records since, the study will be done through reviewing of medical records all collected data will be coded and locked in a separate room before entered into the computer and names will not be included in the data collection format.

#### **4.12 Dissemination of the result**

The result of the study will be submitted and presented to Hawassa University, College of Medicine and Health Science, School of Public Health as a partial fulfillment of masters of public health. The finding the study will also be presented in locally or internationally held seminars, workshops, conferences and meetings and it will be published in internationally recognized journals.

## 5. Work plan

**Table 2: Work plan for study on predictors of preterm neonate at HCSH, Sidama, Ethiopia 2021**

S.N	Activities	March	April	May	June	July	Responsible person
1	Proposal finalization						Principal investigator
2.	Ethical clearance						Institute Research Board
3.	Training and pretesting						Principal investigator
4.	Data collection						Data collectors
5.	Data entry and cleaning						Principal investigator
6.	Data analysis						Principal investigator
7.	Draft thesis						Principal investigator
8.	Final thesis						Principal investigator
9	Defense						Principal investigator

## 6. Estimated budget

**Table 3: Budget breakdown for study on predictors of preterm neonate at HUCSH, Sidama, Ethiopia, 2021**

	Activities/Items	unit	quantity	Unit cost /day	Per diem/other cost			Remarks
					Birr	cents	Total	
<b>1</b>	<b>Personnel</b>							
1.1	Training for data collectors	Days	4	339	339	00	1356	
1.2	Training for Supervisors	Day	1	339	339	00	339	
1.3	Pretest data collectors	Pt card	32	20	20	00	640	
1.4	Data collectors	Pt card	640	20	20	00	12,800	
1.5	Supervisor	Days	15	339	339	00	5,085	
	Sub total		<b>20,220</b>					
<b>2</b>	<b>Stationery</b>							
2.1	Questionnaire duplication	Page	5 *672=3,320	1	3,320	00	3,320	
2.2	Pencil	each	12	5	60	00	60	
2.3	Note book	each	6	30	180	00	180	
2.4	Pen	each	6	10	60	00	60	
	Sub total		<b>3,620</b>					
	Total budget		<b>20,220+3,620= 23,840</b>					
	Contingency budget= 10%		<b>23,840*10%= 2,384</b>					
	Grand Total		<b>23,840+2384=26,224</b>					

## 7. References

1. WHO. Global action report of Preterm birth. Transforming care for every small and sick newborn. 2018.
2. Save The Children U. Born Too Soon: Every Women Every Child Providing the right care, at the right time, in the right place. Healthy newborn network. 2019.
3. UNICEF. Born Too Soon: The Global Action Report on Preterm Birth. Partnership for Maternal, Newborn & Child Health Knowledge Centre PMNCH publication. 2021.
4. McInerny, KAMAT ACDF. pediatrics textbook 2nd edition. AMERICAN ACADEMY OF PEDIATRICS. 2016.
5. Aramesh Rezaeian MR, Seyede Fatemeh Khatami, Fatemeh Khorashadizadeh & Farshid Pouralizadeh Moghaddam Prediction of mortality of premature neonates using neural network and logistic regression. Journal of Ambient Intelligence and Humanized Computing 2020.
6. WHO. Improving newborns and child survival and well-being. Pediatr Care Med. 2020.
7. United Nation W, World bank. United Nations -Integreted ,child-mortality-report-2020. Journal of pediatrics 2020.
8. WHO. Newborns: improving survival and well-being. Springer. 2020.
9. Save the Children Federation I, a 501(c)(3) organization. Preterm birth complications. Healthy newborn network. 2021.
10. Walani S. Global burden of preterm birth. international journal of obstetrics and gynecology. 2020.
11. William W. Hay J MJL, Judith M. Sondheimer, Robin R. Deterding the new born infant In: current diagnosis and treatment pediatrics new born infant. New York ,Chicago: Elisabeth TiloAdamARosenberg; . 2019;;Volume 9th edition edn.
12. Abhishek Gurung<sup>1</sup> JW, Avinash K. Sunny<sup>1</sup> , Rejina Gurung<sup>1</sup> , Netra Rana<sup>3</sup> Yuba Nidhi Basaula<sup>4</sup>. Incidence, risk factors and consequences of preterm birth – findings from a multicentric observational study for 14 months in Nepal. Archives of Public Health (2020) 78:64. 2020.
13. Orsido TT, Asseffa NA, Berheto TM. Predictors of Neonatal mortality in Neonatal intensive care unit at referral Hospital in Southern Ethiopia: a retrospective cohort study. BMC Pregnancy Childbirth. 2019;19(1):019-2227.

14. Kindie K. Magnitude and predictors of mortality among preterm neonates admitted in NICU at Debre markos and Felegehiwot specialized hospitals. 2020.
15. Evans Kofi Agbeno JO, Joyce Ashong ,Betty Anane-Fenin ,Emmanuel Okai ,Anthony Amanfo Ofori ,Mohammed Aliyu ,Douglas Aninng Opoku ,Sebastian Ken-Amoah ,Joycelyn A. Ashong ,Hora Soltani Determinants of preterm survival in a tertiary hospital in Ghana: A ten-year review. Plos one. 2021.
16. 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):018-0597.
17. Banerjee OLaA. World Prematurity Day: improving survival and quality of life for millions of babies born preterm around the world. WHO. 2020. Epub 2021/02/13.
18. Joy E Lawn\*1, Ruth Davidge3,4,5, Vinod K Paul6, Xylander7 Sv, Johnson8 JdG, Costello9 A. Born Too Soon: Care for the preterm baby. Biomed central. 2018.
19. Willey B KJ, Clarke S, Kariuki S, ter Kuile F, et al. Neonatal mortality risk associated with preterm birth in east Africa, adjusted by weight for gestational age: individual participant level meta-analysis. . PLoS med. 2018.
20. Tilksew Dagnachew\* MY. Survival of Preterm Neonates and its Determinants in Teaching Hospitals of Addis Ababa University. Journal of Women's Health Care. 2019;Vol. 8 (Iss. 2 No: 461).
21. UNICEF. United Nations Interagency Group for Child Mortality Estimation (UN IGME). UNICEF 2020.
22. Adu-Bonsaffoh K, Gyamfi-Bannerman C, Oppong SA, Seffah JD. Determinants and outcomes of preterm births at a tertiary hospital in Ghana. Placenta. 2019;79:62-7.
23. Saifon Chawanpaiboon M, Joshua P Vogel P, Ann-Beth Moller M, Prof Pisake Lumbiganon M, Prof Max Petzold P, Daniel Hogan P, et al. Global, regional, and national estimates of levels of preterm births. Lancet global health. 2018.
24. Ethiopia UI-aGfCMEo. Levels & trends in child mortality UNICEF. 2020. Accessed November 05, 2020. <https://childmortality.org/data/Ethiopia>. J Neonatal Perinatal Med. 2020;10(1):25-31.
25. Health. FMO. National newborn and child survival strategy document brief summary 2015/16-2019/20. FMOH; 2015. MOH. 2021;18(4). Epub 2021/02/14.

26. Harrison MS, Goldenberg RL. Global burden of prematurity. *Semin Fetal Neonatal Med.* 2016;21(2):74-9.
27. Organization WH. New roadmap on human resource strategies to ensure that all newborns survive and thrive. WHO. 2020.
28. Abdel Razeq NM, Khader YS, Batieha AM. The incidence, risk factors, and mortality of preterm neonates: A prospective study from Jordan (2012-2013). *Turkish journal of obstetrics and gynecology.* 2017;14(1):28-36. Epub 2017/03/15.
29. 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. *Lancet.* 2016;388(10063):3027-35.
30. Liu C, Urquia M, Cnattingius S, Hjern A. Migration and preterm birth in war refugees: a Swedish cohort study. *European journal of epidemiology.* 2014;29(2):141-3.
31. Norway NS. Preterm neonate survival, predictors ,magnitude ,distribution Oslo: Statistics Norway. 2018.
32. Gustavo a. United states preterm neonatal survivors. [cgl.ucsf.edu/home/sparky/](http://cgl.ucsf.edu/home/sparky/). 2018.
33. Xu H, Dai Q, Xu Y, Gong Z, Dai G, Ding M, et al. Time trends and risk factor associated with premature birth and infants deaths due to prematurity in Hubei Province, China from 2001 to 2012. *BMC Pregnancy Childbirth.* 2015;15(329):015-0767.
34. Egesa WI, Odong RJ, Kalubi P, Ortiz Yamile EA, Atwine D, Turyasiima M, et al. Preterm Neonatal Mortality and Its Determinants at a Tertiary Hospital in Western Uganda: A Prospective Cohort Study. *Pediatric Health Med Ther.* 2020;11:409-20.
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;7:2333794X20970005-2333794X.
36. Tamene A, Abeje G, Addis Z. Survival and associated factors of mortality of preterm neonates admitted to Felege Hiwot specialized hospital, Bahir Dar, Ethiopia. *SAGE Open Med.* 2020;8:2050312120953646-.
37. Cupen K, Barran A, Singh V, Dialsingh I. Risk factors associated with preterm neonatal mortality: a case study using data from Mt. Hope Women's Hospital in Trinidad and Tobago. *Children.* 2017;4(12):108.

38. Hassen JA, Handiso MN, Admassu BW. Predictors of Preterm Birth among Mothers Who Gave Birth in Silte Zone Public Hospitals, Southern Ethiopia. J Pregnancy. 2021;2021:1706713-
39. Wesenu M, Kulkarni S, Tilahun T. Modeling determinants of time-to-death in premature infants admitted to neonatal intensive care unit in Jimma University Specialized Hospital. Annals of Data Science. 2017;4(3):361-81.
40. Aynalem1\* YA, HM, TYA, B, Gebremichael2, WSS. Preterm Neonatal Mortality and its predictors in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: a retrospective cohort study. Ethiop J Health Sci January 2021;Vol. 31(No. 1 ).



## 8. Appendix

### Appendix1: Information sheet

**Title of the Research Project:** Predictors of mortality among preterm neonates admitted to neonatal intensive care unit of Hawassa University Comprehensive Specialized hospital from 2019-2021 at, Sidama region, Ethiopia, 2021.

**Name of Investigator:** Tihun Feleke (BSc)

**Name of the Organization:** Hawassa University, College of medicine and health science, school of Public health

**Introduction:** This information sheet is prepared for Hawassa University Comprehensive Specialized hospital administration and NICU coordinating offices. The aim of the form is to make the above-concerned offices clear about the purpose of research, data collection procedures and get permission to conduct the research.

**Purpose of the Research Project:** To determine magnitude and predictors of mortality among preterm neonate admitted to NICU of Hawassa University Comprehensive Specialized hospital, Sidama region, Ethiopia, 2021.

**Procedure:** In order to achieve the above objective, information is necessary for the study will be taken from premature neonatal medical record.

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

**Benefits:** The research have no direct benefit for those whose record is included in this research But it has indirect benefit for the participant and other clients in the program.

**Confidentiality:** To reassure confidentiality of data 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 the institutional review board Hawassa University college of medicine and health science .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.

1. Tihun Feleke, Hawassa University, College of medicine and Health Science School of public health principal investigator Cell phone: +251- 925549649 E-mail: feleketihun@gmail.com
2. Dr. Taye Gari (Mph,PhD.)Hawassa University, College of medicine and Health Science, school of public health main Advisor. Cell phone: +251- 926276598 E-mail: tayegari@gmail.com
3. Mr Derese Legesse (Mph) Hawassa University, College of medicine and Health Science, school of public health Co- Advisor. Cell phone: +251- 912244932 E-mail: delsew@gmail.com

## Appendix2: Data abstraction tool

This data abstraction tool is prepared for the collection of Baseline socio-demographic, maternal medical , maternal obstetrics, premature neonate medical and other major predictors and outcomes related information that are important for the assessment of predictors of preterm neonatal mortality among premature neonates Admitted at Neonatal intensive care units of Hawassa Comprehensive Specialized hospital. All this information will be retrieved from the client's registration book and from an individual patient card without mentioning the name of the clients from 2019-2021. This information will be collected by BSc nurses possibly working in the NICU of the hospital

Question Number	Questions	Possible answers	
<b>I. Checklist for the mothers card</b>			
<b>A. Baseline socio-demographic characteristics</b>			
101	Age in years	_____ years	
102	Place of residence	1. Rural 2. Urban	
103	Family Income per month	_____ birr	
104	Mothers occupation	1. Employed 2. Self employed 3. Housewife 4. Other specify.....	
105	Place of delivery	1. Home delivery 2. Health institutions	
106	Length of hospital stay in days	_____ days	
<b>B. Obstetric related factors</b>			

201	Number of Gravidity	_____	
202	Number of Parity	_____	
203	Does the mother have ANC follow up?	1. Yes 2. No 3. Not specified	
204	Was the current pregnancy multiple (twin?)	1. Yes 2. No 3. Not specified	
205	Which among the following do you have diagnosed? (More than one is possible??)	1. PROM 2. Preclampsia 3. Abruptio placenta 4. Placenta Previa 5. Eclampsia 6. Other_____	
206	What was her Current mode of delivery?	1. Spontaneous vaginal delivery 2. Cesarean section 3. Instrumental	
207	Did the neonate breastfeed?	1. Yes 2. No 3. Not specified	
208	If yes, when was the breast feed initiated	1. <1hour 2. 1hour -2 hours 3. >2hours 4. Not specified	
<b>C. Mothers Medical Problems</b>			
309	Has she been diagnosed with any medical problems	1. Yes 2. No	If no, go

			to #401
310	If yes for question #309, what was the diagnosis(more than option is possible)	1. HIV/AIDS 2. Hypertension 3. Anemia 4. Diabetic mellitus 5. Others_____	
<b>II. Checklist for the premature neonate</b>			
<b>A. Baseline socio demographic / Identifications</b>			
401	ID no		
402	Date of Admission	Day____/Mon____/yr____	
403	Age in day	_____Days	
404	Sex	1. Yes 2. No	
405	Gestational Age in Weeks	_____Weeks	
406	Weight in grams	_____Grams	
407	APGAR score of	1. 1 <sup>st</sup> minute_____ 2. 5 <sup>th</sup> minutes_____ 3. 10 <sup>th</sup> minutes_____	
<b>B. Neonates medical problems</b>			
501	Had the neonate been diagnosed with any medical disorders?	1. Yes 2. No	If no, go to #503

502	If yes to question no #501, what was the diagnosis?	1. Respiratory distress 2. Jaundice 3. Perinatal asphyxia 4. Hypothermia 5. Sepsis 6. Others.....	
503	Length of hospital stay	_____	
504	Date of discharge	Day___/Mon___/year___	
505	Time of neonatal death	_____	
506	Neonatal status at the end	1. Death 2. Alive 3. Referred 4. other	