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Time to Death and its Predictors Among Neonates Admitted with Neonatal Sepsis at Public Referal Hospitals of Bahir Dar City, Northwest Ethiopia, 2021

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ABBREVIATIONS AND ACRONYMS

AHR	Adjusted Hazard Ratio
ANC	Antenatal Care
APGAR	Appearance, Pulse, Grimace, Activity and Respiration
APH	Anti Partum Hemorrhage
CHR	Crude Hazard Ratio
CI	Confidence Interval
EBF	Exclusive Breast Feeding
EONS	Early Onset Neonatal Sepsis
ERB	Ethical Review Board
FHCSH	Felege-Hiwot Comprehensive Specialized Hospital
ICU	Intensive Care Unit
IDR	Incidence Density Rate
LONS	Late Onset Neonatal Sepsis
NEC	Necrotizing Entrocolities
NICU	Neonatal Intensive Care Unit
PIH	Post Infectious Hydrocephalus
PROM	Premature Rupture of Membrane
PPROM	Prolonged Premature Rupture of Membrane
RDS	Respiratory Distress Syndrome
SSA	Sub Saharan Africa
TGSH	Tibebe-Ghion Specialized Hospital
UNESCO	United Nations Educational, Scientific and Cultural Organization
UTI	Urinary Tract Infection
WHO	World Health Organization

ABSTRACT

INTRODUCTION: In spite of recent advances in health care, neonatal sepsis is still one of the major causes of morbidity and mortality in neonates and is an ongoing major global public health challenge. Its incidence of mortality varies from health institution to health institution and within the same health institution at varied times and depends on predisposing factors.

OBJECTIVE: The objective of this study was to determine the time to death and its predictors among neonates admitted with neonatal sepsis at public referral hospitals of Bahir Dar city, northwest Ethiopia, 2021.

METHODS: An institutional based retrospective cohort study was conducted among 500 randomly selected neonates admitted with neonatal sepsis at neonatal intensive care unit from January 1, 2019 to December 31, 2020. The data was entered using Epi data version 3.1, exported to and analyzed at STATA version 14. Bivariable and multivariable cox regression analysis were conducted to identify predictors of mortality. Association was summarized using adjusted hazard ratio (AHR) and statistical significances were declared at 95% CI and P-value <0.05. Proportionality assumption was tested by a global test based on Schoenfeld residuals analysis.

RESULTS: During the follow up time, 58 (11.6%) neonates were died with neonatal sepsis while the rest were censored. In this study the overall death incidence rate was 20.5 per 1000 neonate days. Comorbidity(AHR: 1.81, 95%, CI: 1.04, 3.17), late initiation of exclusive breast feeding over one hour(AHR: 2.29, 95%CI: 1.13,4.63), history of intra-partum fever(AHR: 7.37 95%CI: 2.28,23.79), admission weight <2500 grams(AHR: 3.37, 95%CI: 1.54, 7.34) and place of delivery(AHR: 3.83, 95%, CI: 1.24, 11.83) were found potential independent predictors of mortality among neonates with neonatal sepsis.

CONCLUSION: In this study, high death incidence rate was observed. The mean time to death among neonates died was 4.41 days. With regard to predictors: admission weight <2500 grams, comorbidity, late initiation of exclusive breast feeding over one hour,

history of intra partum fever and place of delivery were found statistically significant predictors of mortality among neonates admitted with neonatal sepsis.

KEY WORDS: Neonatal sepsis, mortality, time to death, predictors

1. INTRODUCTION

1.1. Background

Neonatal sepsis is a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the bloodstream (1, 2). According to the international pediatric sepsis consensus conference of 2005, neonatal sepsis can also be defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate which presents with clinical features of temperature instability, respiratory problems, feeding intolerance, and isolation of bacteria or other pathogens from the bloodstream(3). Neonatal sepsis occurs when pathogenic bacteria gain access into the blood stream causing overwhelming general infection. The most common isolated bacteria were gram-negative(4).

Neonatal sepsis is classified into two major categories based on the time of onset: Early-onset neonatal sepsis (EONS) and Late-onset neonatal sepsis (LONS). Early onset neonatal sepsis appears within the first seven days of life and is mainly due to bacteria acquired before and during delivery and most cases appear with in the first 24 hours(5). Generally the neonate inhales infected amniotic fluid or vaginal fluid during labor and delivery. Hence, respiratory distress is the commonest mode of presentation. While late onset neonatal sepsis occurs after 8 days of infants life and is due to bacteria acquired after delivery. Late onset neonatal sepsis presents with either features of pneumonia or other features of sepsis (6-8).

Sepsis is diagnosed by: a complete white blood cell count with differential, blood culture, urine cultures, and lumbar puncture for cell count and culture. To clear the diagnosis of early onset neonatal sepsis factors that predispose the neonate for sepsis such as maternal infection and prolonged rupture of membranes, and prematurity are also considered (12).

Since most of the neonatal sepsis related deaths are preventable if suspected early and treated with appropriate antibiotics, appropriate antibiotic therapy and supportive care are essential in management of neonates with sepsis and the choice of antibiotic therapy is best guided by the knowledge of etiologic agent. However, it is usually not immediately

possible. So, treatment is most often started before a definitive causative agent is identified (13). In nosocomial sepsis, the flora of the neonatal intensive care unit (NICU) must be considered. Antimicrobials used to treat sepsis in neonates mostly are combinations of penicillin and aminoglycoside (14).

1.2. Statement of the problem

According to the World Health Organization (WHO) report in 2006, out of the 130 million live births every year, 4 million die within the first four weeks of life. Of these deaths, 99% occur in developing countries (19). Globally, almost 3 in 4 neonatal deaths were caused by preterm birth complications, complications during labour and delivery (intra partum-related complications), and sepsis which accounts(35%, 24% and 15%) respectively (20). In 2010 worldwide, 7.6 million children less than 5 years old died, predominantly due to infectious causes including sepsis; neonatal deaths accounted for 40% of the total lives lost (21).

Neonatal sepsis is accountable for 15% of global neonatal deaths and 30-50% of neonatal deaths in developing countries (22). In sub Saharan Africa, 17% of neonatal deaths are due to neonatal sepsis (23). Around 37% of Ethiopian neonates also died due to neonatal sepsis, which accounts for more than one third of neonatal deaths (24).

Risk factors for early onset of neonatal sepsis include premature rupture of membrane (PROM), maternal fever, repeated vaginal examination, chorioamnionitis, place of birth, meconium stained amniotic fluid, prematurity, low birth weight, low appearance pulse grimace activity respiration (APGAR) scores, and complicated or instrument-assisted delivery. Whereas risk factors for late-onset of sepsis include acquiring nosocomial infections and having invasive procedures during hospital admission (9, 10). The most identified associated factors of neonatal sepsis are home delivery, preterm, prolonged labor, PROM and maternal history of urinary tract infection (UTI) (11).

Sepsis is still one of the major causes of morbidity and mortality in neonates. In spite of recent advances in health care units it is an ongoing major global public health challenge. Its incidence varies from health institution to health institution and within the same health institution at varied times and depends on factors predisposing to infection. On the other hand, the survivors of neonatal sepsis are vulnerable to short and long-term neurodevelopmental morbidity (25). Despite advances in neonatal care, overall case-fatality rates from sepsis ranges from 2% to as high as 50% (26).

Neonates suffering from neonatal sepsis face an increased risk of mortality and severe complications (15). Septicemia is one of the major causes of morbidity and mortality in the neonatal period and it often has a rapid and fulminant course (16).

The incidence of sepsis is highest in neonates and children, yet the global burden of sepsis in these age groups has not been sufficiently assessed. According to WHO report in 2012, sepsis caused approximately 12% of the 2.9 million neonatal deaths (27). The prevalence of neonatal sepsis in developing countries is 29.92%(28). The prevalence of neonatal sepsis in East Africa in particular is 29.76%(11). In Ethiopia, neonatal sepsis accounts for 30-35% of neonatal deaths next to prematurity (1).

Sepsis-related morbidity and mortality are increasing concerns in all NICU with reported incidences that were dramatically high regardless of the improvements in the quality of neonatal assistance (29). Mortality ranged from 9% to 20% for severe sepsis (30). Among those who survive, impaired quality of life, increased dependence, and re-hospitalization increase healthcare consumption and, along with increased mortality, all contribute to the humanistic and economic burden of sepsis (31).

The burden of neonatal sepsis in sub-Sahara Africa (SSA) including Ethiopia is paramount. In the first place, neonates could face death from sepsis unless they are treated promptly. On the other hand they could face long-term survival with post infectious hydrocephalus (PIH), which could result in childhood mortality or survival with PIH with resulting neurological impairment and this long-term survival from sepsis with neurodevelopmental impairment could result in cerebral palsy or lifetime neurodevelopmental impairment without cerebral palsy; or uncomplicated recovery following an acute 2-week period of neonatal sepsis (32).

Efforts to reduce hospital acquired late onset infections require much closer attention to appropriate hand washing, infection control, and proper techniques for placement and management of central catheters (33). Antenatal corticosteroid treatment for accelerating fetal lung maturation for women at risk of preterm birth has been shown to reduce birth complications including the risk of neonatal sepsis (34).

Even though the impact of neonatal sepsis remains a public health problem in resource limited settings like Ethiopia, limited evidences exist to show the time to death and predictors of this serious public health problem in different parts of Ethiopia particularly in the study setting. Thus, determining the time to death and identifying its predictors among neonates with neonatal sepsis is very important for optimizing neonatal care. Therefore, the aim of this study is to determine time to death and identifying predicting factors for death among neonates admitted with sepsis at public hospitals of Bahir Dar city.

1.3. Significance of the study

Though Ethiopia has made considerable achievement in the reduction of under-five mortality rate, the neonatal mortality burden has not experienced the same reduction, which may be attributed to neonatal sepsis. Neonatal sepsis is a relevant public health issue because it consistently emerges as one of the main causes of neonatal morbidity and mortality. To prevent further this neonatal problem and to achieve sustainable development goal by reducing neonatal mortality, data from different geographical area of Ethiopia is required.

Therefore, evidence on time to death of neonates with sepsis and factors that predicts the death of neonates with sepsis in the area will provide knowledge for health professionals in early identification of high-risk neonates with sepsis and timely intervention for their better survival. It also enhances the current neonatal sepsis management strategies by making sure the various determinants contribute to neonatal sepsis. This study will also be used for future researchers as reference. Also identifying the predictors of neonatal sepsis will be helpful in designing strategies to prevent and/or treat neonatal sepsis. Hopefully, this study will also increase the nursing body of knowledge and helps to promote nursing research, nursing education and even the practical aspect of the profession.

2. LITRATURE REVIEW

2.1. The incidence density rate of mortality among neonates with sepsis

Different studies have been conducted in developed and developing countries to determine incidence density rate of neonatal mortality with sepsis. A study done in Brazil showed that the incidence and the incidence density of sepsis was 22% and 18.6 per 1000 central venous catheter-days, respectively. Considering very low birth weight neonates (VLBW) neonates as the reference group, the hazard ratio (HR) for time to death was 4.06 from day 0 to 60 and for time to the first episode of sepsis was 1.76 from day 0 to 36. Having the heavier neonates group as reference, the HR for time to the first episode of sepsis was 2.94 from day 37 to 90 (35).

A study conducted in Tanzania revealed a mortality rate of 19% in neonates with sepsis and high mortality is seen in early onset neonatal sepsis and showed a survival rate of 47% (36). Another study conducted in Uganda shows that mortality rate due to neonatal sepsis is 18.1% and most of the deaths (84%) occurred in the first 48 hours of admission(37). In Nigeria a study indicate that mortality rate due to sepsis was 15.7%. In this study, low birth weight was 7.2 times more likely to die compared to those who were appropriate for birth weight. Babies that had PROM were 2.5 times more likely to die(18). Another study done in Johannesburg, showed the overall mortality rate for neonatal sepsis was 1.7% (38).

A study done in Sub-Saharan Africa to estimate the incidence density rate of neonatal mortality among neonates the incidence density rate of mortality was significantly high. And the hazard of neonatal mortality in NICUs was increased by comorbidities like sepsis with the hazard of death of neonates with sepsis was 1.94 times than neonates free from sepsis (39).

A study in southern Ethiopia revealed that the incidence rate of mortality among neonates admitted with neonatal sepsis was 14.57 per 1000 neonate days. The cumulative proportion of surviving at the end of the fourth day was 99.5%, and it was 98.2% at the

end of the fifth day. In addition, it was 96.6%, 93.5%, and 91.1% at the end of the sixth, seventh, and eighth day, respectively (1).

2.2. Predictors of mortality among neonates with neonatal sepsis

2.2.1. Socio demographic predictors of mortality

The majority of studies reported that place of delivery, duration of hospital stay, age and sex of the neonate were the most common socio demographic predictors of neonatal mortality secondary to neonatal sepsis.

A study done in India, female neonates had a higher survival chance than male neonates with sepsis and newborn with sepsis who travels a lot to access health care had higher chance of being dead as compared to those who had a health center at the nearby area also neonates admitted at early age were more likely to die and in addition duration of hospital stay contributed to a higher mortality (40). Another study in Iraq shows that among neonates with sepsis, those neonates delivered at hospital were more likely to survive than those delivered at home. Neonates who had not a history of hospitalization had a higher survival chance than those neonates with history of previous hospitalization, in addition in this study those neonates younger than seven days had a higher mortality rate than those with in the age group of 7-28 (41). Another prospective study in Iraq shows that male neonates with sepsis has a higher mortality rate than female neonates with sepsis (42).

A study in Ghana also indicated that cost of treatment and location of patients as the major predictors of death among newborns with sepsis. That is, newborn with sepsis who resides within less than 10 km radius of the hospital had a higher survival rate than those who travels at least 10km to access health care those and also as cost of treatment increases there is likelihood of increases in death of newborns with sepsis. In this study female newborns are more likely to survive of sepsis as compared to their male counterparts (43).

2.2.2. Maternal predictors

According to different studies conducted in developed and developing countries, majority of them reported that premature rupture of membrane, intra partum fever, chorioamniotis, hypertension in pregnancy, and antepartum hemorrhage were the most common maternal predictors of neonatal mortality secondary to neonatal sepsis.

A study in Iraq revealed that the death outcome is higher in neonates with sepsis whose mothers had prolonged rupture of membrane (> 24hrs) and fever than those mothers who had not in both cases(41). Another prospective study conducted in central India showed that neonates born to mothers who had hypertensive diseases during their pregnancy were more likely to die than those born from non-hypertensive mothers. Similarly, this study revealed that neonates born from mothers who had antepartum hemorrhage were more likely to die than those born from mothers who had not antepartum hemorrhage (40). Prolonged rupture of membrane(>48hrs), maternal fever, and chorioamnionitis were found significant predictors of mortality of neonates with sepsis in a retrospective study conducted in Pakistan (44).

In a study conducted in Nigeria indicated that neonates born to mothers who had prolonged rupture of membrane(PROM) had a higher mortality rate than those delivered from mothers who had not PROM (18).

Also a study conducted in Southern Ethiopia shows that newborn with neonatal sepsis has 7 times higher hazard of mortality if labor is initiated by induction as compared with spontaneous initiation of labor and also in newborns delivered from mothers having a history of intra partum fever were 14 times higher risk of death as compared with their counterparts and the risk of mortality among newborns with neonatal sepsis was 5 times higher on those delivered from mothers having a history of diagnosed chorioamnionitis as compared with those with no history of no diagnosed chorioamnionitis. It is also observed in neonates breastfeeding was not initiated within one hour, showed a 3 times higher mortality than those who breast fed within one hour (1).

2.2.3. Neonatal predictors

Different studies were conducted in developed and developing countries to determine neonatal predictors in neonatal sepsis. The majority studies reported that low birth weight, prematurity, and having a history of acute illness were the most common neonatal predictors of neonatal mortality secondary to neonatal sepsis.

A study conducted in Iraq In 2016 revealed that neonates who had medical problem in addition to sepsis had a higher mortality rate than other neonates with no medical problem in addition to sepsis and preterm neonates were more likely to die than term neonates. Also in this study neonates with low birth weight (<2500g) were more likely to die than neonates with normal birth weight (42). When comparing term infants to preterm infants, sepsis in preterm infants is up to 1000-fold more common and is also associated with higher rates of mortality and life-long neurodevelopmental handicaps(21). A prospective study done in Iraq in 2007 neonates with low birth weight(<2500g) were more likely to die than those with normal birth weight premature neonates were more likely to die than term neonates and also a higher number of death is seen among neonates with sepsis who had a history of acute illness during the first few days of life such as respiratory distress due to different causes or birth asphyxia than those who had not (41).

In study undertaken in India on predictors of mortality of neonatal sepsis in 2019 revealed that neonates with admission weight <1500 had a higher mortality rate than others and neonates with a history of acute illness such as hypothermia, respiratory distress, apnea, cyanosis, prolonged capillary refill time and convulsion had a higher mortality rate than (40).

A study in Nigeria showed that low birth weight neonates(<2500g) had a higher risk of mortality than those with birth weight>2500g, and neonates with low APGAR score were more likely to die also in this study neonates who had a history of infectious clinical diagnosis had a higher mortality rate than those neonates with no history of infectious clinical diagnosis (18). A study conducted in Ethiopia also revealed that the hazard of mortality among neonates with neonatal sepsis is three times higher if they did not initiate

exclusive breastfeeding within one hour as compared with those who did initiate within one hour (1)

2.3. Conceptual framework

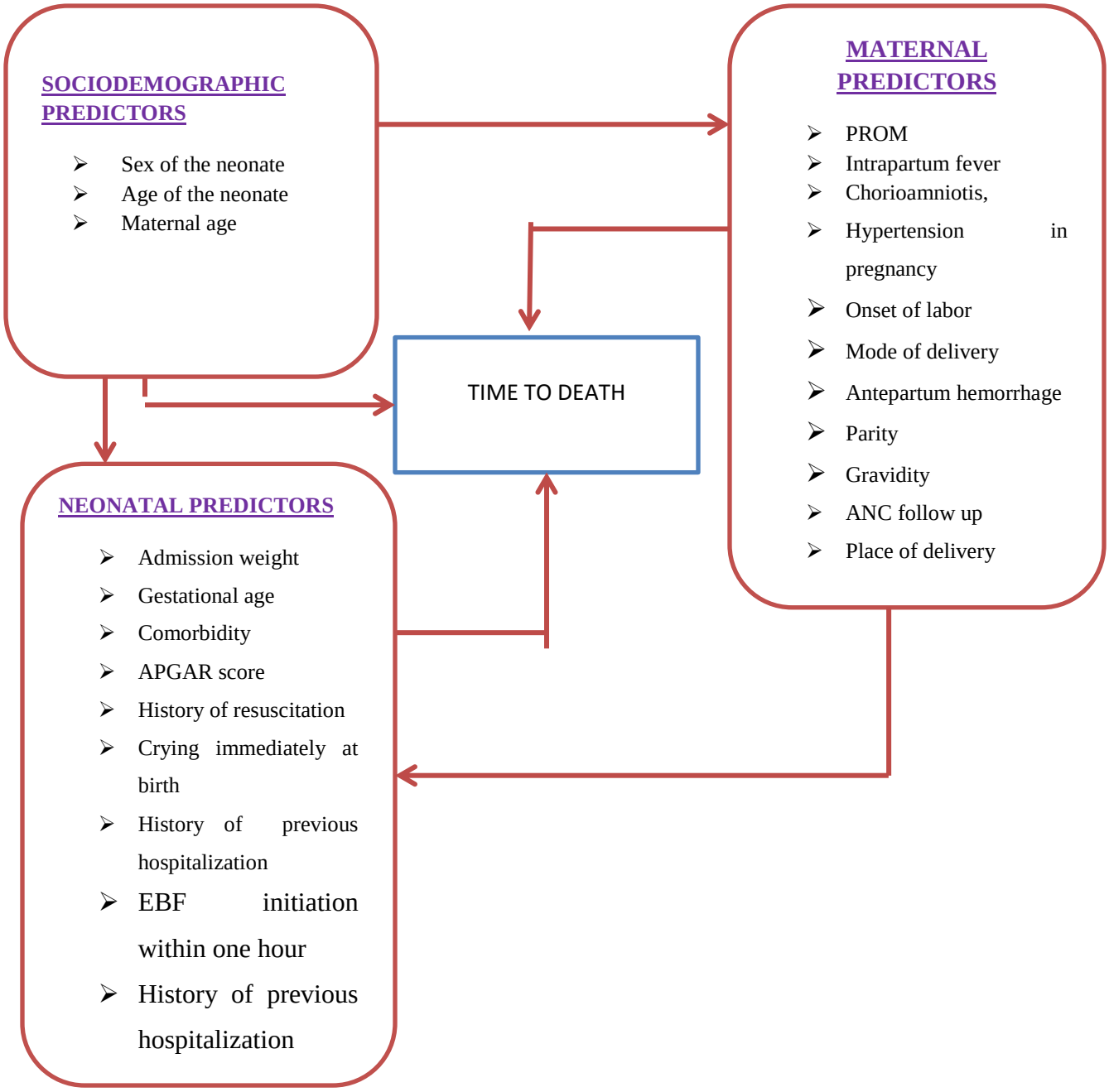

Figure 1: Conceptual framework adapted & slightly modified from related article (1, 14, 27, and 32) to show the relationship between independent variables and outcome variable

3. OBJECTIVES

3.1. General objective

- To determine time to death and its predictors among neonates admitted with neonatal sepsis in public referral hospitals of Bahir Dar city, northwest, Ethiopia, 2021.

3.2. Specific objectives

1. To determine time to death of neonates admitted with neonatal sepsis
2. To identify predictors of death among neonates admitted with neonatal sepsis

4. METHODS

4.1. Study area and period

The study was conducted in Bahir Dar city public referral hospitals from February 1, 2021 to March 1, 2021. Bahir Dar is the capital city of Amhara regional state located in the Northwest of Ethiopia. Bahir Dar city is found 565 km away from Addis Ababa, the capital city of Ethiopia. It is one of the ten most beautiful cities in Africa and it is also one of the twelve UNESCO's Learning Cities Awardee of 2015. According to the National Population and Housing Census projection of 2011, the population of the town was 170,267. Out of this 75,302 (44%) were males and 94,965 (56%) were females with the annual population growth rate within the 2001-2012 was estimated to be 1.8 %.

Currently, the city has two referral hospitals and one primary public hospital. Among these, FHCSH is the first hospital, which was established in 1963 as referral hospital. Now it has 410 beds and serving for more than 5 million people. And TGSTH is the newly opened specialized teaching hospital which is the teaching hospital of Bahir Dar University College of medicine and health sciences to serve with 500+ beds and was established in 2019. These hospitals are organized in different wards; medical ward, surgical ward, gynecology and obstetrics ward orthopedics ward, oncology ward, and pediatrics ward, ICU, NICU, and different outpatient departments.

The NICU in FHCSH has 75 neonatal beds with average annual admission of 3500 neonates whereas the NICU in TGSH has 27 neonatal beds with an average annual admission of 1200 neonates.

4.2. Study design

An institutional- based retrospective cohort study design was employed to conduct a study.

4.3. Population

4.3.1. Source population

All neonates with neonatal sepsis admitted at NICU from January 1, 2019 to December 31, 2020.

4.3.2. Study population

All selected neonates with neonatal sepsis admitted at NICU from January 1, 2019 to December 31, 2020

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All neonates admitted with neonatal sepsis and age less than or equal to 28 days at admission and were admitted during January 1, 2019 to December 31, 2020 were included in the study.

4.4.2. Exclusion criteria

Neonates with incomplete records were excluded from the study.

4.5. Sample size determination and procedure

4.5.1. Sample size determination

The sample size was determined with Epi info version 7 statistical packages using major predictor variables from previous study (1), by assuming CI 95% and power 80%. Accordingly, onset of labor was an independent variable which gives maximum sample size of **454** as mentioned in the table below. Then by adding 10% contingency, the final sample size was **500** (Table 1).

Table 1: Sample size calculation to determine time to death and its predictors among neonates admitted with neonatal sepsis at public referral hospitals in Bahir Dar city, northwest, Ethiopia, 2021

Predictors	Proportions	Sample size	Sample size adding after 10%
Place of delivery	P_1=0.24 P_2=0.04	112	123
Initiate EBF within one hour	P_1=0.196 P_2=0.017	114	125
History of intra partum fever	P_1 =0.44 P_2=0.04	44	48
History of chorioamioniotis	P_1 =0.31 P_2=0.032	70	77
Onset of labor	**P1=0.141** **P2=0.058**	454	500

4.5.2. Sampling procedure

First, medical registration numbers of all neonates with neonatal sepsis admitted for the last two years (January 1, 2019 to December 31, 2020) were obtained from the hospitals' registration logbooks. Then samples were selected by simple random sampling technique using computer generating system, after having lists of the medical registration number of the neonatal charts with neonatal sepsis from both hospitals.

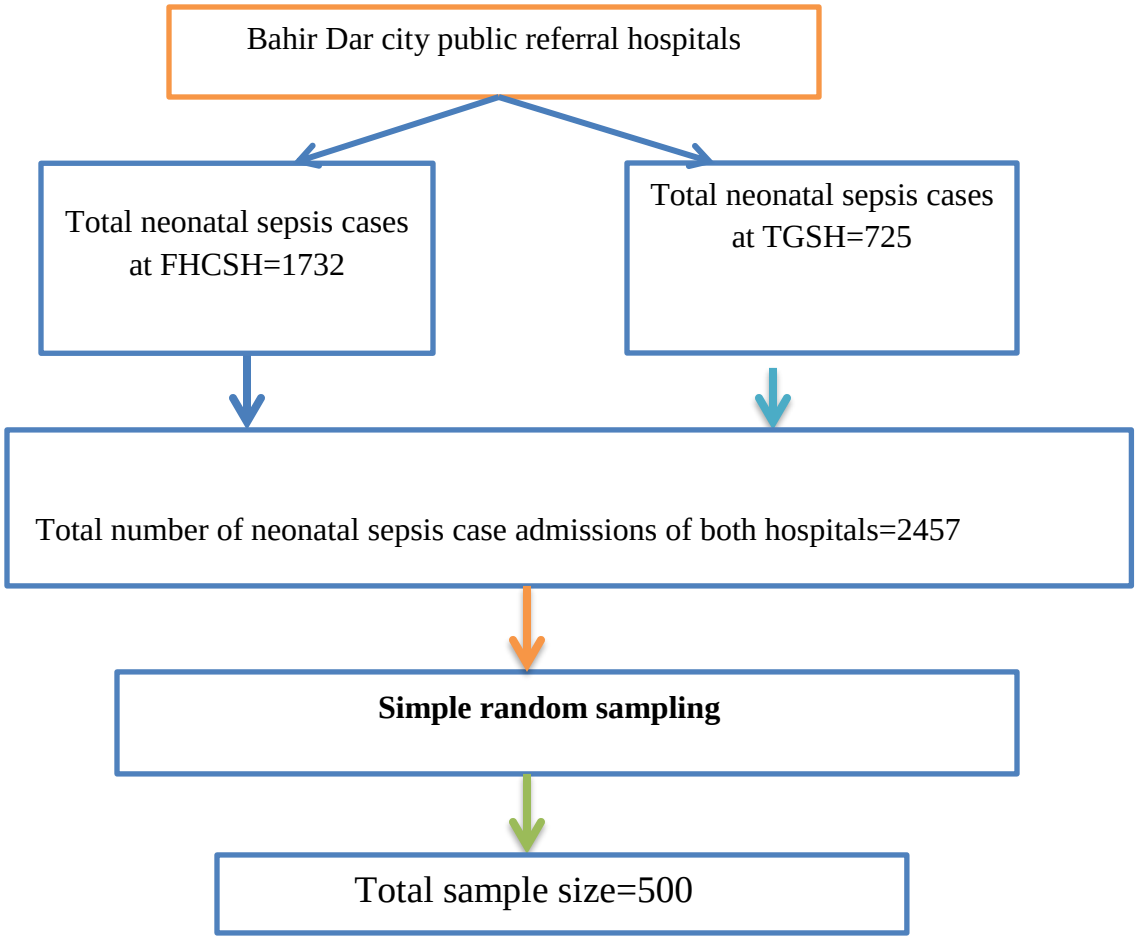

Figure 2: Schematic representation of sampling procedure for determining time to death and its predictors among neonates admitted with neonatal sepsis at public referral hospitals of Bahirdar city, northwest, Ethiopia, 2021

4.6. Variables

4.6.1 Dependent variable

- Time to death

5.6.2. Independent variable

- **Socio demographic factors**
  - ✓ Maternal age in year, neonatal age in days and neonatal sex (male/female) were the socio-demographic factors.
- **Neonatal related factors:**

- ✓ Comorbidity, admission weight, gestational age, APGAR score(1st minute and 5th minute), having history of previous hospitalization, cry immediately at birth, history of resuscitation at birth and EBF initiation within one hour were the neonatal related factors.

- **Maternal factors**
  - ✓ Onset of labor, place of delivery, gravidity, parity , history of Intra partum fever, history of diagnosed chorioamniotis, mode of delivery, premature rapture of membrane(PROM), pregnancy induced hypertension, history of urinary tract infection and ANC follow up were the maternal factors.

4.7. Data collection procedures

4.7.1. Data collection instrument and procedure

A data collection tool was prepared as checklist from standardized national neonatal and delivery registration book to extract required data from selected charts. The checklist include; socio demographic factors of both maternal and neonatal, neonatal medical condition and maternal factors. The data was collected from the 1st date of admission to death or censored (lost to follow up, improved, referred or against medical treatment) or until the end of follow up period (28 days of age).The data was extracted from medical registration card by four BSc. nurses who had work experience in NICU and two MSc. nurses were also recruited for supervision throughout the data collection period.

4.8. Operational definitions

Neonate: A new born from birth until 28 days old

Neonatal sepsis: Sepsis diagnosed and confirmed by physician among neonates.

Early-onset neonatal sepsis: Sepsis diagnosed and confirmed by physician among neonates age less than seven days.

Late-onset neonatal sepsis: Sepsis diagnosed and confirmed by physician among neonates age seven days or more.

Event: Death of neonate admitted with neonatal sepsis.

Censored: Neonates with other than event/death (Improved and discharged, referred to other health facility, against medical treatment)

Time to death: The time in days from admission to death of neonates with neonatal sepsis

Follow up time: Neonatal age period (neonate with neonatal sepsis from admission until either event or censorship occurs).

4.9. Data processing and analysis

Data was cleaned, edited and coded by using Epi data version 3.1. Consistency of data was also checked before analysis to avoid errors during data entry. After that, it was exported to STATA 14 statistical software. Descriptive statistics (mean, standard deviation, frequency and percentages) were computed depending on the nature of variable. Outcome of each participant was dichotomized into censored or death. Incidence density rate (IDR) was calculated for the entire study period. Failure probability table and Kaplan-Meir (KM) failure function was used to estimate mean time to death and cumulative probability of failure. KM plot and log-rank tests were used to compare failure curves. Before performing The Cox-proportional hazard regression, model, goodness-of-fit was checked by Cox Snell residuals and assumptions were also checked by using Schoenfeld residual test. For each independent predictor bivariate coxproportional Hazard regression was performed. Then the variables with p-vale <0.2 were included in multivariable cox proportional hazard regression. AHR with 95% confidence interval and p-values<0.05 was used to measure the strength of association and identify statistical significant predictors.

4.10. Data quality management

Standardized data collection checklist was taken from national neonatal and labor registration book. Training was given for data collectors and supervisors two days before data collection. Pretest was done in 5% of neonatal charts with neonatal sepsis in FHCSH 5 days prior to data collection period and inconsistencies were checked and corrected. A close supervision was carried out by the supervisors during data collection period.

Finally, all the collected data was checked by investigator for its completeness and consistency.

4.11. Ethical clearance

Ethical clearance was obtained from Bahir Dar University College of medicine and health science Ethical Review Board (ERB). Then officials at different levels in the hospitals were communicated through letters. Confidentiality of the information was secured throughout the study process.

4.12. Dissemination of the result

The results will be disseminated to Bahir Dar University, college of Medicine& Health science school of Health Science, department pediatrics and child health nursing in partial fulfillment for Masters of pediatrics and child health nursing. The study result will be also submitted to TGSTH, FHCSH and Amahra regional Health Bureaus. Finally, efforts will be also made to disseminate the findings of the study to scientific world through presentation on scientific conferences and through publication.

5. RESULTS

5.1. Socio-demographic characteristics of the mothers and neonates

In this study, 500 neonatal charts were reviewed. More than half 296(59.2%) were males which accounted for 70.69% of dead neonates as compared with female neonates. The mean (±SD) age of the neonates was 4.41 ±6.75 days. About 82.6% of the neonates had age less than seven days. Among the neonates who died with neonatal sepsis, 37(77.08%) of them died within the first seven days of life. Concerning to mothers' socio demographic characteristics, the mean (±SD) age of mothers was 27.44±5.32 years range from 15 to 44 years (Table 2).

Table 2: Socio-demographic characteristics of neonates admitted with neonatal sepsis at public referral hospitals of Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Variables	Category	Status of the neonate	
		Death	Censored
Maternal age	<20	1(1.72%)	15(3.39%)
	20-34	45(77.59%)	358(81%)
	>34	12(20.69%)	69(15.61%)
Neonatal age	<7	47(81.03%)	366(82.81%)
	7-28	11(18.97%)	76(17.19%)
Neonatal sex	Male	41(70.69%)	255(57.69%)
	Female	17(29.31%)	187(42.31%)

5.2. Obstetrics-related characteristics

In this study nearly three fourth 357 (71.4%) of the mothers were primigravida and majority 38 (65.52%) death was observed in this category. This study result also showed that most of the mothers 483 (96.6%) have received ANC service during their pregnancy

and similarly almost all 55 (94.83%) deaths of neonates were observed among mothers having ANC follow up. With regard to onset of labor, majority 448 (89.6%) had spontaneous onset of labor and again the majority of the mothers 485 (97%) delivered their newborn at health institution and more than half 344 (68.8%) of them delivered by spontaneous vaginal delivery. Regarding rupture of membrane, 122 (24.4%) had history of PROM and out of them 49 (40.16%) were for more than 18 hour duration (Table 3).

Table 3: Obstetrics-related characteristics of mothers having neonates admitted with neonatal sepsis at public referral hospitals of Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Variables	Category	Status of the neonate	
		Death	Censored
Gravidity	Primi gravida	38 (65.52 %)	319 (72.17 %)
	Mult gravida	11 (18.97 %)	79 (17.87 %)
	Grandmulti gravida	9 (15.52 %)	44 (9.95 %)
Parity	Primi para	39 (67.24 %)	325 (73.53 %)
	Multi para	11 (18.97 %)	79 (17.87 %)
	Grandmulti para	8 (13.79 %)	38 (8.6 %)
ANC follow up	Yes	55 (94.83 %)	428 (96.83 %)
	No	3 (5.17 %)	14 (3.17 %)
Number of ANC visit	1-3	25 (45.45 %)	97 (22.66 %)
	≥4	30 (54.55 %)	331 (77.34 %)
Onset of labor	Spontaneous	54 (93.1 %)	394 (89.14 %)
	Induced	4 (6.9 %)	48 (10.86 %)
Place of delivery	Health institution	54 (93.1 %)	431 (97.51 %)
	Home	4 (6.9 %)	11 (2.49 %)
Mode of delivery	Spontaneous vaginal Delivery	43 (74.14 %)	301 (68.1 %)

	Assisted instrumental Delivery	7(12.01%)	30(6.79%)
	Cesarean section	8 (13.79 %)	111 (25.11 %)
History of PROM	Yes	18 (31.03 %)	104 (23.53 %)
	No	40 (68.97 %)	338 (76.47 %)
Duration of PROM	<18 hours	10 (55.56 %)	63 (60.58 %)
	≥18 hours	8 (44.44 %)	41 (39.42 %)
History of foul smelling liquor	Yes	5 (8.62 %)	14 (3.17 %)
	No	53 (91.38 %)	428 (96.83 %)
History of fever	Yes	4 (6.9 %)	3 (0.68 %)
	No	54 (93.1 %)	439 (99.32 %)
History of preeclampsia	Yes	3 (5.17 %)	21 (4.75 %)
	No	55 (94.83 %)	421 (95.25 %)
History of APH	Yes	2 (3.45 %)	3 (0.68%)
	No	56 (96.55 %)	439 (99.32 %)
History of chorioamniotis	Yes	3 (5.17 %)	29 (6.56 %)
	No	55 (94.83 %)	413 (93.44 %)

5.3. Neonatal related characteristics of neonates with neonatal sepsis

From 500 neonates admitted with neonatal sepsis, the mean (±SD) weight of neonates at admission was 2715.4 ± 643.8 grams and more than half, 37 (63.79%) of death was observed among neonates with admission age less than 2500 grams. Regarding gestational age, the mean (±SD) gestational age was 38.1±2.7 weeks ranging from 29-45 weeks. Among dead neonates majority, 49 (84.48) of them were neonates who had APGAR score less than seven at the first minute and 37(63.79%) of dead neonates had APGAR score less than seven at fifth minute (Table 4).

Table 4: Neonatal related characteristics of neonates admitted with neonatal sepsis at public referral hospitals of Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Variables	Category	Status of the neonate	
		Death	Censored
Gestational age	Preterm	30 (51.72 %)	97 (21.95 %)
	Term	28 (48.28 %)	345 (78.05 %)
Admission weight	<2500	37 (63.79 %)	86 (19.46 %)
	≥2500	21 (36.21 %)	356 (80.54 %)
Comorbidity	Yes	31 (53.45 %)	133 (30.09 %)
	No	27 (46.55 %)	309 (69.91 %)
First minute APGAR score	<7	49 (84.48 %)	276 (62.44 %)
	≥ 7	9 (15.52%)	166 (37.56 %)
Fifth minute APGAR score	<7	37 (63.79%)	112 (25.34%)
	≥7	21 (36.21)	330 (74.66%)
Cry immediately at birth	Yes	23 (39.66%)	372 (82.96%)
	No	35 (60.34%)	70 (15.84%)
Resuscitated at birth	Yes	20 (34.48%)	41 (9.28%)
	No	38 (65.52%)	401 (90.72%)
EBF initiated within one hour	Yes	18 (31.03%)	297 (67.19%)
	No	40 (68.97%)	145 (32.81%)
History of previous hospitalization	Yes	12 (20.69%)	53 (11.99%)
	No	46 (79.31%)	389 (88.01%)

5.4. Outcome of neonates with neonatal sepsis

During follow up time, 58(11.6%) neonates with neonatal sepsis were died while 442(88.4%) of neonates with neonatal sepsis were censored of which, (77% of the neonates were improved and discharged, 8.2% of the neonates were against medical treatment and 3.2% of the neonates were referred to other hospitals).

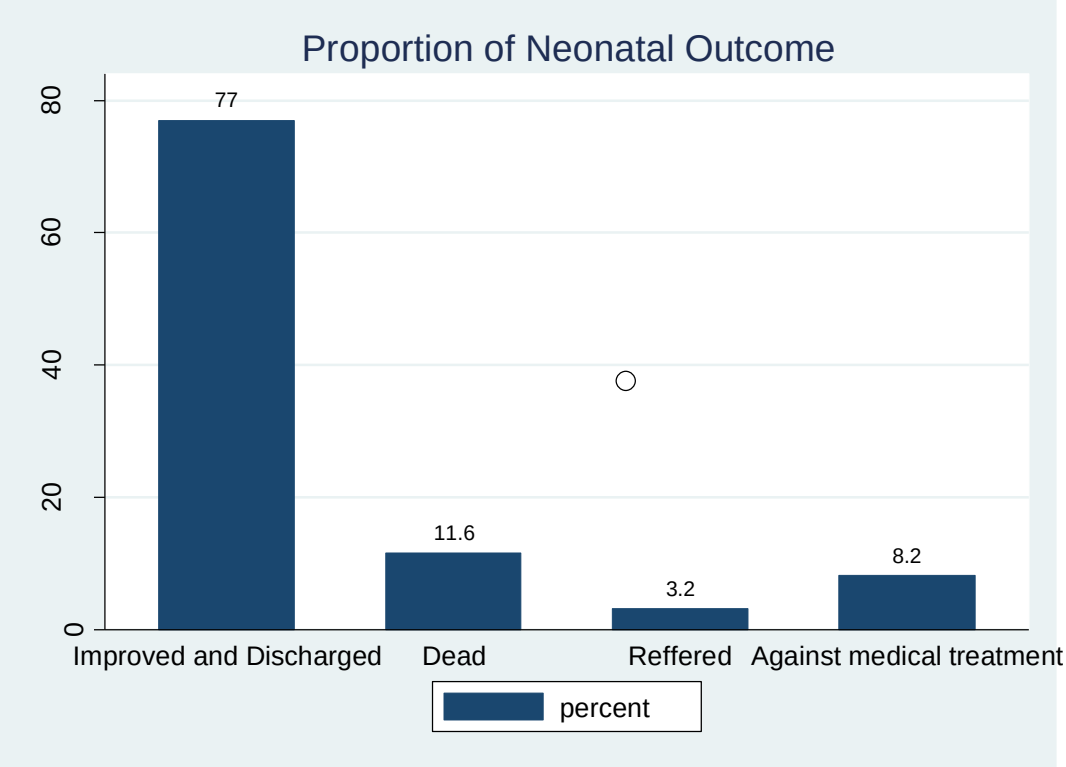

Figure 3: proportion of neonatal outcome among neonates admitted with neonatal sepsis at public referral hospitals, Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

5.5. Failure/Death of Neonates

The neonates were followed for a total of 2848 days. Among them, 58(11.6% [95% CI: 9.07, 14.73]) died during the follow up time and that makes the mortality rate from neonatal sepsis 116 per 1000 live births. The overall death incidence rate in this study was 20.5 per 1000 neonate days (95% CI: 0.01, 0.26).

From all deaths, 13% of the neonates were died in the first 24 hours of life, 20% of the neonates died in the first three days of life and about 81% of death occurred with in the first seven days of life. Death from neonatal sepsis was also further analyzed from the time of admission and consequently, 10.4% of the deaths occurred in the first 24 hours, 46.5% of the deaths occurred with in the first three days and about 90% of the deaths occurred within the first week of admission. At the end of follow up time, the cumulative failure probability was 28.13 % (95% CI: 20.04 38.62).

In this study since the maximum observation time was censored the median time to death was not determined therefore, mean time to death was the appropriate measure of central tendency. Accordingly, the mean time to death among neonates died was 4.41 days (95% CI: 3.62, 5.21).

The probability of death in neonates with neonatal sepsis during the follow-up time was also presented by the failure curve. Accordingly, during the first seven days, the graph went up increasingly showing a higher probability of death. Also, between days 7 and 13, the probability of death continued and the graph moved upward. In the remaining days of the follow-up period, the graph became straight indicating the likelihood of death in neonates with neonatal sepsis remained stable with almost no deaths occurring (figure 4).

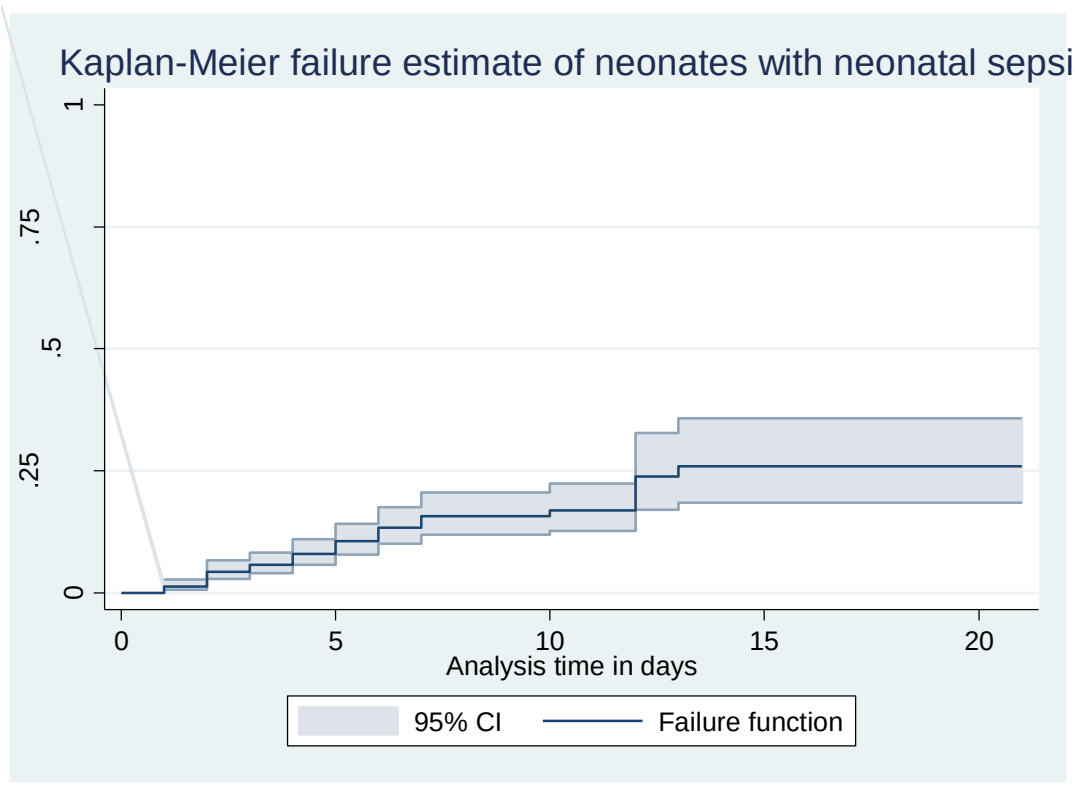

Figure 4: Overall Kaplan-Meir failure estimate of neonates admitted with neonatal sepsis at public referral hospitals, Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

5.6. Log-rank estimate of mortality among neonates with neonatal sepsis across predictors

As shown in the table below the log-rank test estimate between categories of different predictor variables revealed that the survival pattern among neonates with neonatal sepsis was significantly different as there is a highly significant difference among survival curves. The Kaplan-meier together with the log-rank test shows the effect of each predictor on the neonatal mortality with neonatal sepsis (table 5).

Table 5: Log-rank test for equality of different categorical predictors of neonates admitted with neonatal sepsis at public referral hospitals, Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Variables	Category	X^2	P-value
History of liquor	Yes No	4.41	0.03
First minute APGAR score	<7 ≥7	11.17	< 0.001
Fifth minute APGAR score	<7 ≥7	34.87	< 0.001
Admission weight	<2500 ≥2500	42.97	< 0.001
Cry immediately at birth	Yes No	50.29	<0.001
Resuscitated at birth	Yes No	20.44	<0.001
Gestational age	Preterm term	24	<0.001
Place of delivery	Health institution Home	4.12	0.04
History of fever	Yes No	58	< 0.001
Comorbidity	Yes No	12.59	< 0.001
EBF initiated within one hour	Yes No	33.93	<0.001

5.7. Testing overall fitness of the model

Model goodness of fit was checked by using the Cox-Snell residual test. The residuals had a standard censored exponential distribution with hazard ratio. The jagged line with the reference line (Cox Snell residual line) follows the 45˚ line closely. Hence, the overall cox- regression model fits to the data (figure 5).

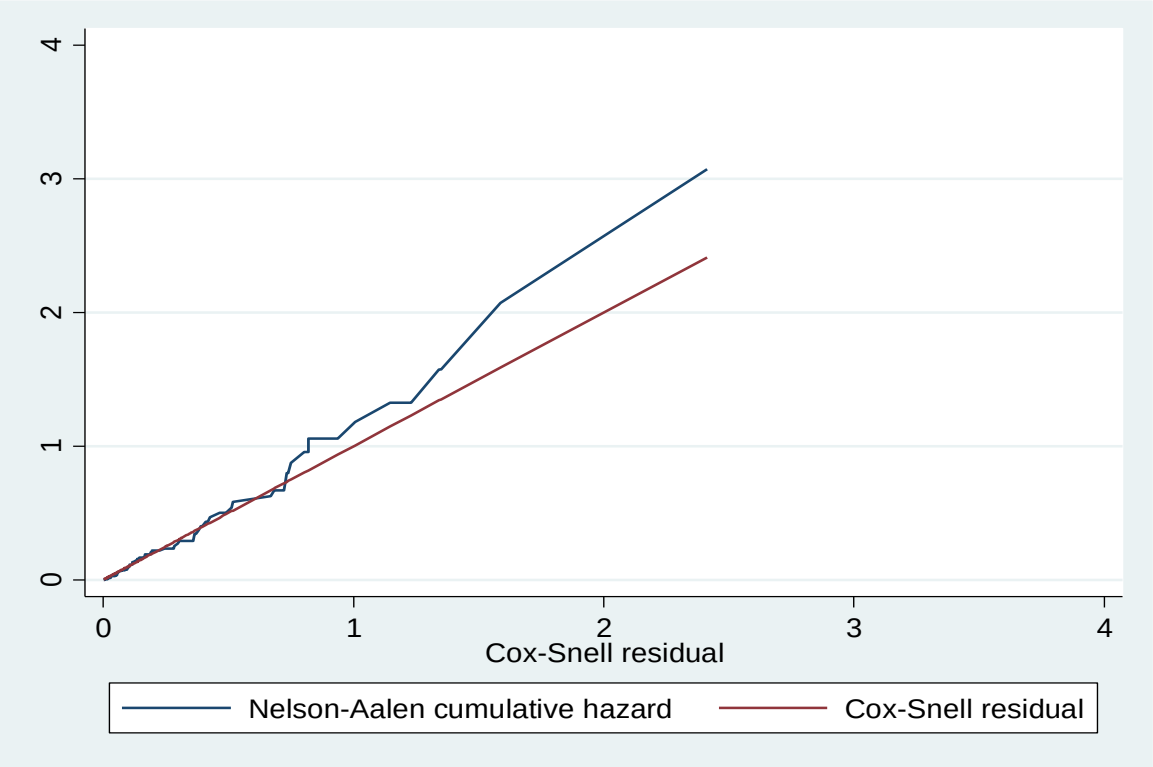

Figure 5:Cox-Snell residual Nelson-Aalen graph showing model goodness of fit for neonates admitted with neonatal sepsis at NICU of public referral hospitals Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

5.8. Cox proportional hazard assumption test

For each covariate, Cox proportional hazard assumption was performed individually & simultaneously (Globally).The test showed that the p-value for each covariate and the whole covariates simultaneously were greater than 0.05 which showed that there were no time-varying covariates in the model (Table 7).

Table 6: Test of cox proportional hazard assumption among neonates admitted with neonatal sepsis at public referral hospitals, Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Variables	Rho	chi-square	df	Prob>chi2

Weight at admission	0.00883	0.01	1	0.9371
Onset of labor	-0.07212	0.32	1	0.5700
Maternal age	-0.14465	1.38	1	0.2407
Gestational age	0.15583	1.68	1	0.1946
History of previous hospitalization	-0.08212	0.34	1	0.5576
EBF initiated within one hour	0.07645	0.41	1	0.5218
Resuscitated at birth	-0.03881	0.13	1	0.7205
Cry immediately at birth	0.13725	1.24	1	0.2655
Fifth minute APGAR score	-0.04866	0.18	1	0.6678
First minue APGAR score	0.19293	2.17	1	0.1403
Medical problem in addition sepsis	0.18874	2.36	1	0.1244
History of chorioamnionitis	0.10922	0.63	1	0.4262
History of APH	0.11192	1.04	1	0.3085
Preeclampsia	-0.14811	1.23	1	0.2677
History of fever	-0.19153	2.25	1	0.1338
History of liquor	-0.17774	1.66	1	0.1981
Mode of delivery	0.18759	2.27	1	0.1316
History of PROM	0.13339	1.03	1	0.3098
ANC follow up	-0.02266	0.02	1	0.8873

Number of Parity	0.15200	1.41	1	0.2346
Gravidity	-0.07892	0.42	1	0.5177
Neonatal sex	-0.07437	0.35	1	0.5533
Neonatal age	-0.04940	0.17	1	0.6798
Global test		23.11	23	0.4545

Notice: Rho is the correlation coefficient between the residuals and time

5.9. Bivariate and multivariable cox proportional hazard regression model for different predictor variables

Cox proportional hazard regression model was fitted and used to identify predictors of mortality in neonates with neonatal sepsis. In bivariate Cox proportional hazard regression: neonatal sex, gestational age, weight at admission, history of PROM, place of delivery, history of liquor, history of fever, comorbidity, cry immediately at birth, resuscitated at birth, EBF initiated within one hour, history of previous hospitalization, first minute APGAR score and fifth minute APGAR score were significant predictors of mortality among neonates with neonatal sepsis with p-value<0.2. In a multivariable proportional hazard model: admission weight, comorbidity, late initiation of EBF over one hour, history of fever and place of delivery remains potential independent predictors of mortality among neonates with neonatal sepsis at (p value<0.05).

Multivariable analysis resulted that neonates delivered at home had a 3.83 times higher hazard of death than neonates delivered at health institution (AHR: 3.83, 95%, CI: 1.24, 11.83). The hazard of death in neonates with admission weight <2500 grams was 3.37 times higher compared to neonates with admission weight ≥2500 (AHR: 3.37, 95%CI: 1.54, 7.34). Neonates who had comorbidity showed a 1.81 times higher hazard of death

when compared to neonates who had no comorbidity (AHR: 1.81, 95%, CI: 1.04, 3.17). Neonates who were born from mothers who had a history of fever were 7.37 times more likely to die as compared to those neonates born from mothers with no history of fever (AHR: 7.37 95%CI: 2.28,23.79). Neonates who did not get initiated to exclusive breast feeding within one hour showed a 2.44 times higher hazard of death than neonates who did get initiated to exclusive breast feeding within one hour(AHR: 2.29, 95%CI: 1.13,4.63) (table 6).

Table 7: Bivariate and multivariate Cox proportional hazard regression outputs of neonates admitted with neonatal sepsis at public referral hospitals, Bahir Dar city, northwest, Ethiopia, 2021 (n=500)

Covariates	Category	CHR(95%CI)	AHR(95%CI)
Neonatal sex	Male	1.58(0.90, 2.78)	1.82(1.00, 3.31)
	Female	1	1
Gestational age	Preterm	3.22(1.98,5.57)	0.87(0.41,1.81)
	Term	1	1
Weight at admission(gram)	<2500	5.03(2.93, 8.64)	3.37(1.54, 7.34)***
	≥2500	1	
Place of delivery	Health institution	1	1
	Home	2.71(0.98,7.52)	3.83(1.24,11.83)**
History of PROM	Yes	1.46(0.84,2.56)	1.84(0.97,3.48)
	No	1	1
History of Fever	Yes	6.15(2.21,17.16)	7.37(2.28,23.79)***
	No	1	1
History of liquor	Yes	2.55(1.02,6.41)	0.76(0.26,2.29)
	No	1	1
Comorbidity	Yes	2.45(1.46,4.10)	1.81(1.04,3.17)**
	No	1	1
First minute APGAR score	<7	3.13(1.53,6.34)	1.33(0.54,3.29)
	≥7	1	1

Fifth minute APGAR score	<7	4.31(2.52,7.36)	1.14(0.53,2.45)
	≥7	1	1
Cry immediately at birth	Yes	1	1
	No	5.44(3.18,9.16)	1.87(0.86,4.07)
Resuscitated at birth	Yes	3.22(1.87,5.54)	1.44(0.65,3.21)
	No	1	1
EBF initiated within one hour	Yes	1	1
	No	4.46(2.55,7.80)	2.29(1.13,4.63)**
History of previous hospitalization	Yes	1.82(0.96,3.44)	0.52(0.26,1.04)
	No	1	1

Notice: ** significant at (p value<0.05), *** significant at (p value<0.01) and **** significant at (p value<0.001) CHR: Crude Hazard Ratio, AHR: Adjusted Hazard Ratio

6. DISSCUSION

This study showed that the overall incidence rate of mortality was 20.5 per 1000 person days observation which was a little higher than the study conducted at Arba Minch, Southern, Ethiopia which was 14.57 per thousand person-days observation(1). This might be because of the difference in the follow up time that is, in our study we followed the neonates for the entire neonatal period but in the other study the neonates were followed for 14 days.

In this study, neonates with admission weight <2500 grams had 3.37 times higher risk of death compared to neonates with admission weight > 2500 grams among neonates with neonatal sepsis and this was in line with a study done in India which had reported that neonates with admission weight < 2500 grams to have an increased risk of mortality with sepsis (40). A similar study done in Indonesia had also reported that admission weight < 2500 grams was significant predictor of mortality in neonates with neonatal sepsis (45). This might be due to low birth weight neonates over normal birth weight neonates have deficiencies in humeral and cellular immunity as well as high tendencies for prolonged hospitalization, which increases the risk of nosocomial infection.

In the current study, neonates who were delivered from mothers having history of intra partum fever had 7.3 times higher risk of mortality compared to neonates who were delivered from mothers who had no history of intra partum fever. This study is supported by a study done in Arba-minch, Ethiopia which had reported that neonates who were delivered from mothers having history of intra partum fever had 14 times higher risk of mortality compared to neonates who were delivered from mothers who had no history of intra partum. This study was also supported by a study conducted in Iraq which reported that neonates with neonatal sepsis who were born from mothers having history of fever were more likely to die than neonates with neonatal sepsis who were born from mothers who had no history of fever(41). Our study was also in line with a study conducted in India which reported that intra partum fever was significant predictor of mortality related to neonatal sepsis(46). This might be because the fact that the disease-causing agent of maternal infection can ascend to the baby via circulation and during passage through the birth canal.

Another predictor which was found significant in this study was place of delivery. Accordingly, consistent with a study result done at the university of Gondar comprehensive specialized hospital, neonates with neonatal sepsis who were delivered at home had 3.31 times higher risk of death compared to neonates who were delivered at health institution(47). The reason might be due to a lack of basic newborn care and environmental factors when the neonates were delivered at home.

Moreover in this study, the hazard of mortality among neonates with neonatal sepsis having late initiation of exclusive breastfeeding over an hour was 2.4 times higher compared to those neonates with neonatal sepsis who did get initiated to exclusive breast feeding within one hour. This finding is in line with to the studies conducted in India (48) and developing countries(49) . This might be the fact that the many defense factors of the mother's milk include large amounts of secretory Immunoglobulin A antibodies produced by lymphocytes which have migrated from the mother's gut to the mammary glands. Thus breastfeeding modulates the early exposure of the neonate's intestinal mucosa to microbes and limits bacterial translocation through the gut mucosa and neonates who did not get initiated to exclusive breast feeding within one hour could not get this benefit from mother’s milk.

The last predictor variable that predicted the neonatal mortality with sepsis was having comorbidities. In this regard our finding revealed that the hazard of mortality among neonates with neonatal sepsis having comorbidities was 1.8 times higher compared to those neonates without comorbidities. And this result is consistent with a study done in Iraq(41) which revealed that the presence of the likes of hypothermia would increase the likelihood of death among neonates with neonatal sepsis. This might be the fact that the presence of comorbidities would expose the neonate for further overwhelming of the immature immune.

7. STRENGTHS AND LIMITATIONS

7.1. Strengths

Large sample size was used comparing to the other study done in Southern Ethiopia which increases generalization to population and decrease bias.

The study design was retrospective cohort so that it could show the true causal relationship between the predictors and the outcome variable.

7.2. Limitations

Since the study reviewed secondary data, important socio demographic predictors such as maternal educational status, income, maternal occupation and family size were missed from the study. Lack of literature of similar study both nationally and internationally for discussion and Selection bias might be present during chart selection because charts with incomplete data were excluded from the study.

8. CONCLUSION AND RECOMMENDATION

8.1. Conclusion

In this study, high death incidence rate was observed. The mean time to death among neonates was 4.41 days. With regard to predictors: admission weight <2500 grams, comorbidity, late initiation of EBF over one hour, history of intra partum fever and place of delivery were found statistically significant predictors of mortality among neonates admitted with neonatal sepsis.

8.2. Recommendations

Based on the findings of this study we recommend the following points for different concerned bodies and stakeholders:

For federal ministry of health

The federal ministry of health of Ethiopia should give special attention for prevention, early diagnosis and management of sepsis. Health education should be designed at community level towards preventing home delivery.

For FHCSH and TGSH

The two hospitals should encourage health care providers working in NICU to closely follow neonates with neonatal sepsis during their first seven days of life especially for low birth weight neonates and neonates with comorbidity.

For health workers

In our study finding among neonates admitted with neonatal sepsis at NICU of the two hospitals, it was found that from ten neonates with neonatal sepsis one neonate was died. The result also showed that the death rate was also high during the first 7 days of neonatal age. Therefore, we recommend for health care providers working at NICU to give special attention and be focused to these neonatal age groups while providing care to them.

For future researchers

We recommend future researchers to use longitudinal prospective cohort study design to avoid the drawbacks of retrospective cohort design and so as to not to miss important socio demographic predictors.

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ANNEXES

Annex I: Information sheet

Hello! My name is Mekdes Tadesse, Currently I am a graduate student at Bahir Dar University, College of Medicine &Health Sciences, Department of pediatrics & child health nursing. Now I am interesting to conduct a study on the title:-

Title of the research: Survival status and predictors of mortality among neonates admitted with neonatal sepsis at NICU.

Name of investigator: Mekdes Tadesse

Name of organization: Bahir Dar University, College of medicine and health sciences, school of health sciences, department of pediatrics and child health nursing.

Purpose of the study: To determine survival status and predictor of mortality among neonates admitted with neonatal sepsis admitted at NICU from 2019-20120.

Data collection time: From 01/02/2021-01/03/2021 (for 1-month duration).

Study unit: neonatal charts with a diagnosis of neonatal sepsis.

Risks: Since all data will be taken from medical chart, no any harm to patient. The name or any identification will not be recorded in the checklist. The confidentiality of all information taken from chart will be maintained.

Benefits: No direct benefits for those subjects whose documents will be reviewed. It is already passed. However, results will be used for policy makers and decision makers for designing appropriate measures to improve their survival. So this study will benefit indirectly other new generations.

Annex II: Consent form

As I mentioned above, I am working a thesis proposal submitted to Bahir Dar University, college of medicine and health sciences, school of health sciences, department of pediatrics and child health nursing, in partial fulfillment of the requirement for degree of

masters science in pediatrics and chilled health nursing. We believe that the findings of this study will be used as an evidence for decision making and reviewing management protocol in the NICU. So that information necessary for the study will be taken from review of neonatal sepsis medical registration card. It will not harm the participant as well as confidentiality will be kept. No name and other identification will be written in the checklist. If you have any questions about this study you may ask principal investigator or advisors

Mekdes Tadesse (MSC student in pediatrics & child health nursing at Bahir Dar university, college of medicine & health science: Principal investigator

Phone number: +251922862838

Mr Minyichil Birhanu (Assistant professor in pediatrics and child health nursing) at Bahir Dar University College of medicine & health sciences: Principal advisor

Phone number: +251911586525

S/r. Azeb Gedif (MSC in pediatrics and child health nursing) at Bahir Dar University, college of medicine and health sciences: Co advisor

Phone number: 0918789456

Annex III: Data collection checklist

Data collection checklist is prepared only for those variables found at neonatal chart. It incorporates socio demographic predictors of both mother & neonate, maternal predictor, neonatal predictors & outcome related information.

Part I: A checklist on both maternal and neonatal socio demographic predictors

No	Questions	Response	Skip
101	Maternal age(years)	_____ years	

102	Neonatal age	_____days	
103	Sex of neonate	M ☐ F ☐	
104	Gestational age	_____weeks	
	Part II. Maternal related predictors		
201	Number of gravidity	_____	
202	Number of parity	_____	
203	Did the mother have ANC follow up?	1. Yes 2. No	If no skip to question number 110
204	If yes, how many times did she have?	1.Once 2.Two times 3.Three times 4.Four times and above	
205	Onset of labor	1.spontaneous 2.induced 3.elective c/s	
206	History of PROM	1.Yes 2.No	
207	Duration of rupture of membrane	1.<18hour 2.≥18 hour	
208	Place of delivery	1.Health institution 2.Home	

209	If delivered at home who was delivery attendant	1.Relatives 2.Trained traditional birth attendant	
210	What was her current mode of delivery?	1.Spontaneous vaginal delivery 2.Assisted instrumental delivery 3.cesarean section	
211	Did the mother has history of foul smelling liquor	1.yes 2.no	
212	Did the mother has history of intra partum fever	1.yes 2.no	
213	Did the mother diagnosed with any health problem during pregnancy?	1.Yes 2.No	If no skip to 301
214	If yes for which of the following was she diagnosed?	1.Preeclampsia 2.Anti partum hemorrhage 3.chorioamnionitis 4.Urinary tract infection 5.Oligohydraminous 6.Polyhydraminous 7.Others_____	
Part III. Neonatal related predictors			
301	Did the neonate diagnosed by any medical problems?	1.yes 2.No	If n o skip to 303
302	APGAR score	1.first minute _____ 2. fifth minute _____	
303	Cry immediately after birth	1.yes 2.no	

304	Resuscitated after birth	1.yes 2.no	
305	Kept in kangaroo mother care within one hour	1.yes 2.no	
306	Weight at admission(gram)	_____	
307	Exclusive breast feeding initiated within one hour	1.yes 2.no	
308	History of meconium stained amniotic fluid	1.yes 2.no	
309	History of previous hospitalization	1.yes 2.no	
Part IV. Outcome related information			
401	Date of admission DD/MM/YY in EC		
402	Date of discharge DD/MM/YY in EC		
403	Length of hospital stay in days		
404	Date of birth DD/MM/YY in EC	_____	
405	Status of neonate	1.improved 2.dead 3.referd 4.against medical treatment	

Annex IV: Life table to estimate cumulative failure probability

Interval		Beg. Total	Deaths	Lost	Cum. Failure	Std. Error	[95% Conf.	Int.]
1	2	500	6	21	0.0123	0.0050	0.0055	0.0271
2	3	473	15	46	0.0452	0.0096	0.0297	0.0685
3	4	412	6	68	0.0603	0.0113	0.0417	0.0869
4	5	338	8	79	0.0855	0.0141	0.0618	0.1178
5	6	251	7	48	0.1137	0.0172	0.0843	0.1525
6	7	196	6	48	0.1446	0.0207	0.1089	0.1908
7	8	142	4	34	0.1720	0.0242	0.1301	0.2255
8	9	104	0	18	0.1720	0.0242	0.1301	0.2255
9	10	86	0	14	0.1720	0.0242	0.1301	0.2255
10	11	72	1	10	0.1844	0.0268	0.1381	0.2438
11	12	61	0	13	0.1844	0.0268	0.1381	0.2438
12	13	48	4	8	0.2585	0.0429	0.1851	0.3541
13	14	36	1	7	0.2813	0.0473	0.2004	0.3862
14	15	28	0	7	0.2813	0.0473	0.2004	0.3862
15	16	21	0	1	0.2813	0.0473	0.2004	0.3862
16	17	20	0	4	0.2813	0.0473	0.2004	0.3862
17	18	16	0	1	0.2813	0.0473	0.2004	0.3862
18	19	15	0	1	0.2813	0.0473	0.2004	0.3862
19	20	14	0	6	0.2813	0.0473	0.2004	0.3862
20	21	8	0	1	0.2813	0.0473	0.2004	0.3862
21	22	7	0	7	0.2813	0.0473	0.2004	0.3862

Annex-v: Test of interaction by multicollinerarity

Variable	VIF	1/VIF
Gravidity	13.03	0.076770
Number of Parity	12.80	0.078102
Cry immediately at birth	2.20	0.454323
Resuscitated at birth	1.96	0.510540
Fifth minute APGAR score	1.75	0.572951
Weight on admission	1.66	0.600740
Mode of delivery	1.51	0.662114
Maternal age	1.50	0.664837
First minute APGAR score	1.48	0.675199
EBF initiated within one hour	1.45	0.689972
History of chorioamnionitis	1.40	0.711838
Gestational age	1.40	0.712846
Onset of labor	1.39	0.718944
History of liquor	1.27	0.788240
History of fever	1.25	0.798769
Preeclampsia	1.19	0.841754
History of PROM	1.18	0.846785
ANC follow up	1.14	0.875410
Place of delivery	1.13	0.882566
History of previous hospitalization	1.10	0.905720
Medical problem	1.10	0.906158
History of APH	1.10	0.908372

Neonatal sex	1.06	0.940027
Mean VIF	2.39	

Annex VI: Declaration

I, Mekdes Tadesse, hereby declare that to the best of my knowledge this thesis is my work; it has not been presented to any institution either partially or in total for any academic award or publication. The works here in are original, where the works of others are cited and appropriate reference has been given.

This research proposal is for partial fulfillment of the degree of Master of Science in Pediatrics and child health nursing of Bahir Dar University.

Investigator: Mekdes Tadesse (BSc)

Signature _____ Date _____

This research will be submitted with the approval of the following advisors and examiners:

Advisors: 1. Minyichil Birhanu (BSc, MSc, Assistant professor)

Signature _____ Date _____

2. SR. Azeb Gedif (BSc, MSc)

Signature _____Date_____

Examiners: 1. Name_____

Signature _____Date_____

2. Name _____

Signature _____Date_____

Annex VII: Approval form

This thesis by Mekdes Tadesse is accepted in its present form by the board of examiners as satisfying thesis requirements for the degree of masters of sciences in pediatrics and child health nursing

Advisor 1

Minyichil Birhanu	(MSc. Assistant professor)	_____
Full name	Rank	Signature and date

Advisor 2

Azeb Gedif	MSc, Lecturer	_____
Full name	Rank	Signature and date

Examiner 1

_____	_____	_____
Full name	Rank	Signature and date

Examiner 2

_____	_____	_____
Full name	Rank	Signature and date

Department head

Azeb Gedif	MSc	_____
Full name	Rank	Signature and date