TREATMENT OUTCOME AND ASSOCIATED FACTORS OF NEONATAL SEPSIS AT MIZAN TEPI UNIVERSITY TEACHING HOSPITAL, SOUTH WEST ETHIOPIA: A PROSPECTIVE OBSERVATIONAL STUDY.

By: Yohannes Wobie (B.pharm)

A Thesis Submitted To the Department of Clinical Pharmacy, School Of Pharmacy, College Of Health Sciences, Jimma University In Partial Fulfilment Of The Requirements For The Master of Science In Clinical Pharmacy

June 2020

Jimma Ethiopia

JIMMA UNIVERSITY

INSTITUTE OF HEALTH

SCHOOL OF PHARMACY

TREATMENT OUTCOME AND ASSOCIATED FACTORS WITH NEONATAL SEPSIS AT MIZAN TEPI UNIVERSITY TEACHING HOSPITAL, SOUTH WEST ETHIOPIA: A PROSPECTIVE OBSERVATIONAL STUDY

BY: YOHANNES WOBIE (B.PHARM)

ADVISOR: LEGESE CHELKEBA (PHD, ASSOCIATE PROFESSOR)

June 2020

Jimma Ethiopia

Abstract

Background: Neonatal sepsis is the most serious problem in neonates, resulting in significant morbidity and mortality. Globally 6.9 million neonates were diagnosed with possible serious bacterial infection needing treatment and 2.6 million of these occurred in sub Saharan Africa (SSA). Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries.

Objectives: The aim of this study is to evaluate, treatment outcome and associated factors of neonatal sepsis at Mizan Tepi university teaching hospital, south west Ethiopia.

Method: Hospital based prospective observational study was conducted at Mizan Tepi University Teaching Hospital from May to October. Data was collected by using semi-structured questionnaires for interviewing mothers of the patients, and checklists for which abstraction of information from patients chart, these adapted from review of related literatures. Data was collected by four data collectors. Bivariate and multivariate Cox regression used to analyze the association between dependent and independent variables and P-value <0.05 at 95% CI was declared statistically significant association. Finally statement, tables, charts and graphs were used for data presentation.

Result: Of 211 neonatal sepsis patients, 110 (52.1%) were females, 161(76.3%) were admitted with late onset of sepsis, 16 (7.6%) were very low birth weight, and 156(73.9%) were term (37–42 weeks). Most, 165 (78.2%) neonates were treated with ampicillin plus gentamycin. About 143 (67.8%) were discharged with good outcome after completing the treatment, 68(32.2%) were discharged with poor outcome, of these, 31 (14.7%) were died, 12(5.7%) complicated, 12(5.7%) deteriorated, 8(3.3%) self-discharged and 6(2.8%) were referred. Very low birth weight [P=0.006, AHR=1.692, 95% CI: (1.245, 4.36)], age of neonate less than 4 days at admission [P= 0.001, AHR=9.67, 95%CI: (2.24, 41.70)], maternal infection [P=0.032, AHR=3.186, 95%CI: (1.32,30.68)], prolonged length of hospital stay [(P= 0.017, AHR=12.29, 95%CI: (1.55, 96.31), were significantly associated to mortality.

Conclusion: This study indicated that neonatal sepsis was the frequently occurring neonatal disease. Mortality rate of neonatal sepsis was found to be high. Age of neonate <4 days, birth weight of the neonate < 1500gm, prolonged length of hospital stay, maternal infection during pregnancy were found to be independently associated with mortality.

Key words: neonatal sepsis, treatment outcome, associated factors

Acknowledgement

Firstly I need to acknowledge Jimma University, Collage of Health Sciences, School of pharmacy, for providing me the chance to conduct this study and assign advisor. Then I would like to express my deepest gratitude to my advisor Dr.Legese Chelkeba (PhD, Associate Professor) for all his guidance and support in doing my thesis. Then, I need to thank Mizan Tepi University Teaching Hospital administrators and staffs who support in collecting the data and providing background information about the hospital in doing this study. Lastly I would like to thank my colleagues who contributed directly or indirectly to the successful completion of this thesis work.

Table of Contents

List of Tables

List of Figures

List of Abbreviations and Acronyms

AGE.....Acute gastro enteritis

AHR.....Adjusted hazard ratio

ANC.....Ante natal care

CHD.....Congenital heart disease

EDHS.....Ethiopian demographic health survey

ELBW.....Extreme low birth weight

EONS…… Early onset neonatal sepsis

GBS.....Group B streptococcus

IDMs.....Infants of diabetic mothers

CHR.....Crude hazard ratio

LBW.....Low birth weight

LONS……..Late onset neonatal sepsis

MTUTH……. Mizan Tepi university teaching hospital

NGO.....Nongovernmental organization

NICU.....Neonatal intensive care unit

NS……Neonatal sepsis

PROM.....Premature rapture of membrane

SAM.....Sever acute malnutrition

SDGs.....Sustainable development goals

SNNPR.....South nation nationality and peoples region

SPSS..... Statistical Package for Social Sciences

SSA.....Sub Saharan Africa

USA.....United States of America

VLBW.....Very Low Birth Weight

WHO.....World Health Organization

1. Introduction

1.1 Background

According to the international paediatrics consensus conference, neonatal sepsis (NS) is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate. Neonatal sepsis is the most serious problem in neonates, resulting in significant morbidity and mortality(1). Neonatal sepsis is divided into early-onset and late-onset sepsis, based on timing of infection and presumed mode of transmission. Early-onset sepsis (EONS) is defined by onset in the first 72 hours that are caused by maternal intrapartum transmission of invasive organisms. Late-onset sepsis (LONS) is usually defined as infection occurring after 72 hours of birth and is attributed to pathogens acquired postnatally(2).

The pathophysiology of neonatal sepsis and mechanisms of multiple organ system dysfunction are due to the host response to an infection is initiated when innate immune cells, particularly macrophages, recognize and bind to microbial components, the host response to infection is a complex process that localizes and controls bacterial invasion, while initiating the repair of injured tissue. It involves the activation of circulating and fixed phagocytic cells, as well as the generation of proinflammatory and anti-inflammatory mediators that leads to Sepsis when the response to infection becomes generalized and involves normal tissues remote from the site of injury or infection (3)

130 million infants born each year worldwide, 1 4 million die in the first 28 days of life (4). Three quarters of neonatal deaths occur in the first week, and more than one-quarter occur in the first 24 hours. Neonatal deaths account for 40% of deaths under the age of 5 years worldwide. Two-thirds of the world's neonatal deaths occur in just mostly in Asia and Africa (5). The incidence of NS varies from 6 to 9 cases per 1,000 live births, but is higher among low-birth-weight neonates. Bacterial sepsis is considered to be an important cause of neonatal mortality(6).

Early onset sepsis (EONS) (sepsis that presents during the first 5-7 days of life) usually is caused by organisms acquired from the maternal genital tract. The most common pathogens found in EONS are Group B Streptococcus (50%) and Escherichia coli (20%). Other primary pathogens include Listeria monocytogenes, Enterococcus, and other Gram-negative bacilli (e.g., Haemophilus influenzae, Klebsiella pneumoniae whereas, the majority of pathogens for

LONS around 70% in the developed world is due to Gram-positive infections, with CoNS, Staphylococcus aureus, Enterococcus (7).

The most common clinical manifestations of neonatal sepsis are altered behaviour or responsiveness, altered muscle tone, Feeding difficulties (for example, feed refusal, Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension, temperature instability, hypotension, poor perfusion with pallor and mottled skin, metabolic acidosis, tachycardia or bradycardia, apnea, respiratory distress, grunting, cyanosis, irritability, lethargy, seizures, petechiae, purpura, and bleeding. Therefore neonatal sepsis can be diagnosed if at least two the above clinical feature and at least two of the following laboratory values is positive such as, Complete blood count (CBC) with differential, Blood culture, urine culture Chest radiograph (if respiratory signs present),Gram stain, Lumbar puncture (CSF) examination especially for late onset sepsis and late late sepsis(8).

The spectrum of organisms that causes neonatal sepsis changes over time; this is due to the changing pattern of antibiotic use and changes in lifestyle. The local epidemiology of neonatal sepsis should be constantly updated to detect changes in the pattern of causative organisms and their susceptibility to various antibiotics(9). Early diagnosis and proper management of neonatal sepsis by rational antimicrobial therapy and supportive care can reduce mortality. Blood culture is the gold standard for diagnosis of sepsis but blood culture reports are usually available after 48 to 72 hours. There is need to Identify the common bacteria causing such infections in every hospital and their susceptibility patterns in order to provide necessary information for timely intervention(10).

Neonatal sepsis is usually treated by a combination of antimicrobial therapy especially for EONS; a widely accepted empirical regimen is a combination of ampicillin plus an aminoglycoside. In combination, ~94% of EONS isolates (GBS, CoNS, non-pyogenic streptococci, and E. coli) are sensitive to a combination of penicillin plus gentamycin, and 100% of these organisms are sensitive to the combination of amoxicillin plus cefotaxime for 10 to 14 days. Empirical antimicrobial therapy for suspected LONS should, ideally, cover both Gram-positive and Gram-negative organisms. 95% of organisms causing LONS are sensitive to a combination of gentamycin with either amoxicillin or flucloxacillin, or amoxicillin plus cefotaxime. Only 79% of organisms are sensitive to cefotaxime alone. In countries where invasive CoNS is increasing, vancomycin may be recommended as part of empirical therapy(8)

1.2 Statement of the problem

Globally, neonatal sepsis is one of the major causes of morbidity and mortality among neonates(11). World Health Organization estimated that there were approximately five million neonatal deaths per year of which 98% occur in developing countries, The number of children dying from sepsis in the world has almost doubled in the past 20 years(1). In Africa sepsis accounts 28% neonatal deaths and infectious causes accounts 68 deaths per 1000 live births(12).

Neonatal sepsis is estimated to cause 26% of all neonatal deaths worldwide(13). In sub Saharan Africa, 17% of neonatal deaths are attributed to neonatal sepsis. In Tanzania it is estimated that neonatal sepsis account 31% of the neonatal deaths(14). Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries(15). There are only a few data on the precise prevalence and treatment outcome of neonatal bacterial sepsis in sub-Saharan Africa (16).

In 2012, burden of sepsis has estimated that around 6.9 million possible serious bacterial infections occurred in neonates in South Asia, sub-Saharan Africa, and Latin America(13). In 2015, among the 5.9 million of all deaths in children under the age of 5 years, 45% died in the neonatal period(17). Neonatal sepsis is the third most common cause of death in this age group with an estimated 0.4 million of deaths in 2015, the vast majority of which are in developing countries(18)

In Ethiopia studies indicates that neonatal sepsis is the major newborn killer accounting for more than one third of neonatal deaths(19). High mortality, high fertility, and low life expectancy characterize the country's demography like most sub-Saharan African countries. In the past decade, however, the country witnessed an unprecedented decline in under-5 mortality from 166 per 1000 to 88 per 1000 live births in 2011; an average decline of 47%. However still today, among neonatal death in Ethiopia, approximately 42% of mortality is contributed by neonatal sepsis, which needs further studies and actions (20).

According to Ethiopian demographic health survey (EDHS, 2016), Ethiopia is among the countries with the highest neonatal mortality with the rate of 29 deaths per 1000 live births and there are a number of important gaps in identifying factors for poor outcome of neonatal sepsis(21)

There is a need for studies looking at identifying predictors for increasing risk of mortality. Even though there are some other studies that focus on neonatal sepsis in Ethiopia, most of them were cross sectional in their study design. As far as literature searching showed, there is no study conducted at mizan tepi university teaching hospital, on treatment outcome and associated factors of neonatal sepsis. Therefore, this study was aimed to give information on hospital prevalence and treatment outcome of neonatal sepsis. Furthermore it was designed to identify factors that determine treatment outcome of neonatal sepsis at mizan tepi university teaching hospital, south west Ethiopia.

1. 3 Significance of the study

The finding of this study will provides more evidence on prevalence, treatment outcome and associated factors of neonatal sepsis at Mizan Tepi university teaching hospital for health care providers.

This study will give an insight to guide government and other stake holders to resource allocation for the hospital necessary for management of neonatal sepsis.

It will provide early recognition of risk factors for a poor treatment outcome among neonatal sepsis patients could help health professionals prioritize the management of those patients.

It will also give information for the health institutions, NGOs and as a whole the society to understand about the prevalence of neonatal sepsis, and different risk factors that determine the treatment outcome to prevent mortality.

Further, it will serve as an input data or information for further researchers.

2. Literature Review

2.1 Prevalence of Neonatal Sepsis

According to world health organization (WHO), 2018 reports that, over three million neonatal sepsis cases and more than half million neonatal deaths due to sepsis in Europe alone, in United States data based on electronic medical records indicate that 5.9% of all admissions of neonates had sepsis, which means 1.67 million sepsis cases per year with 260 000 deaths only in the USA, In Germany mortality due to sepsis is more than 40%(22). In most high-income countries, the incidence of culture confirmed neonatal sepsis has decreased or remained relatively stable around 0.4–0.8 cases per 1000 live-born term infants over the last decade(23). Another study done in United States of America(USA),the incidence of culture-proven early-onset neonatal sepsis is estimated to be 0.77 to 1 per 1,000 live births, thus the incidence and mortality are higher when very-low birth-weight (VLBW) infants are considered exclusively; for infants with a body weight of 1,000 g, the incidences are estimated to be 26 per 1,000 and 8 per 1,000 live births in premature infants with a birth weight of between 1,000 and 1,500 g(24).

According to study done in Switzerland shows that, high burden of sepsis in neonates with considerable mortality and morbidity accounts 18%, 12%, and 0% in EONS, hospital-acquired LONS, and community-acquired LONS, and was higher in preterm infants(25). a prospective cohort study done in Uganda, the community based incidence of neonatal sepsis was 11%, lack of financial support from the father and prolonged rupture of membranes more than 18 h prior to delivery were significantly associated with neonatal sepsis mortality. Of the 317 infants who completed the follow up period, one died within the neonatal period giving a neonatal mortality of 0.003%(4).

An institution based cross-sectional study done in NICUs of two governmental hospitals in Shashemene town, (26) Ethiopia, estimated that the incidence of neonatal sepsis was 77.9%, From this 65% and 35% of neonates were early onset neonatal sepsis and late onset neonatal sepsis, respectively. This study found out that age of neonates, birth asphyxia, and use of oxygen via mask was significantly associated with neonatal sepsis death(26). Another prospective cross-sectional study done in Bishoftu General Hospital, Neonatal Intensive Care Unit, Ethiopia, the incidence of neonatal sepsis was 72.22%, Forty (13.1%) of the neonates were expired after admission, 37 (12.09) of the neonates the status of their clinical outcome was unknown because they were referred for further investigation (27).

2.2 Clinical Outcomes of Neonatal sepsis

According to a Prospective Population-Based Cohort Study done at tertiary care neonatal intensive care units in Switzerland with blood culture-proven sepsis between September 2011 and December 2015 showed that 429 new-born infants were identified as blood culture-proven sepsis, among those 87 (20%) episodes were EONS and 357 (80%) were episodes LONS of these, Mortality was 18% for EOS and 12% for LONS (25). Another retrospective study done in NICU of Manipal Teaching Hospital, Nepal showed that mortality outcome of neonatal sepsis was (10%) and sequelae was (7.5%) which was higher in the nosocomial sepsis group. Nosocomial sepsis was an important problem in the study though the outcome was not un-encouraging (28).

According to a retrospective study done at tertiary care center of southern Punjab Sheikh Zayed Hospital, Rahim Yar Khan from 1st January 2009 to 31st December 2013 (5 years) in Pakistan in 2014 shows that, of the total neonatal admissions, 67% were discharged in a satisfactory condition, 3.9% were discharged on request, 3.3% left against medical advice and 25.8% expired (male to female ratio was 2:1) (29). A retrospective health facility based study was conducted by reviewing available data covering the period January 2013 to December 2015 in Tamale teaching hospital indicated that, majority 82.7% of the neonates were successfully treated and discharged, 16.0% of them expired, 1.1% was transferred and 0.3% absconded (30).Another a retrospective study carried out at neonatal care unit of Raparin pediatric teaching hospital (RPTH) in Erbil city of Iraqi Kurdistan Region, showed that the neonate deaths rate was 5.4% and Majority 87.9% of neonates were discharged with unspecified discharge outcome (31).

According to retrospective hospital based study done at NICU of Yenepoya Medical College Hospital, India with blood culture positive neonatal sepsis from January 2016 till June 2016 reviled that, 12.7% of the sepsis cases were died, among the 18 cases of culture positive neonatal sepsis, 8 died while 10 survived (32). Another observational study conducted at Nashik hospital in, India shows that, 48 deaths out of 106 neonatal sepsis cases on treatment were studied making the mortality rate of 45.28% and the survival rate of 54.72% (58/106) cases. Respiratory distress was contributed maximum to mortality (33). Another retrospective study done in rural tertiary care center in Cameroon shown that early neonatal mortality rate was estimated at 12.6% among neonates on treatment of sepsis which was due to prematurity (41.1%), neonatal infection (32.3%) and neonatal asphyxia (26.4%) (34).

According to An institution based quantitative retrospective chart review was conducted from April 30 to May 30, 2016 in Felege Hiwot referral hospital in Bahir Dar, Ethiopia, the clinical outcome of neonatal sepsis was not satisfactory among 225 neonatal sepsis patients, 189 (84%) were improved after treatment, 9 (4%) were died and 13 (5.8%) referred to other organizations for further treatment. Respiratory distress syndrome and meconium aspiration syndrome were the determinant factors for poor outcome of neonatal sepsis (35).

2.3. Factors associated neonatal sepsis treatment outcome

2.3.1. Socio demographic Factors

According to retrospective study done in tertiary care hospital of India Bangalore, males account (54%) and death in males was higher (3.2%) than the females which were (2.7%), though it is statistically insignificant (36). Another retrospective study conducted at a rural hospital in KwaZulu-Natal, South Africa, over half (56.6%) of the deaths took place within the first three days of life and being male sex was significant predictors of neonatal death (37).

According to A retrospective study of medical records for the period 2013–2014 conducted at teaching hospital in India Uttarkhand, indicated that the main causes of mortality were prematurity (25.6%), perinatal asphyxia (19.5%) and respiratory distress syndrome (17.3%) with a statistically higher rate in the out born in comparison with inborn and greater percentage of out born babies (19.95%) were admitted due to lack of practice of simple measures like hygiene at the time of delivery, transport, and handling the babies (38).

2.3.2. Maternal related factors

According to a retrospective study conducted at USA Washington Hospital Center in Washington DC NICU indicates that, admission was higher for African American, male newborns delivered by caesarean section of Primipara with premature rupture of membranes and chorioamnionitis as well as preeclampsia, chronic hypertension and diabetes mellitus were associated with neonatal mortality(39). Another retrospective study conducted in Erie, New York delivery by caesarean section was common among early-term births (38.4%) and increased the risk for NICU admission (12.2%) and morbidity (7.5%) compared with term births. Among vaginal deliveries, early-term neonates (6.8%) had a significantly higher rate of death among NICU admission compared with term neonates (4.4%) (40).

Another study a cross-sectional conducted in Caxias do Sul, southern Brazil public hospitals shown that, preterm were statistically more likely to cause hypothermia/hyperthermia, hypoglycaemia, respiratory pathologies, resuscitation in the delivery room, phototherapy, supplementary feeding, mechanical ventilation, venous infusions, antibiotics and admission to the neonatal intensive care unit, resulting in a nine times greater neonatal mortality rate when compared with full term newborns (41). According to a retrospective study conducted in Bangkola, Thailand, premature rupture of membranes, Antepartum haemorrhage, medical disorders during pregnancy, prenatal estimation of fetal weight, gestational age at delivery, and mode of delivery were significant factors for NICU admission and poor treatment outcome(42).

According to a prospective population based cohort study done in Pakistan tertiary care center shows that, almost 50% of infant deaths occur within first 28 days of life, with infections, birth asphyxia and pre-maturity as the commonest causes of death which was due to factors like poor care during pregnancy like poor nutrition, poor hygiene and unskilled management of complications, deliveries by unskilled personnel, inadequate newborn care and lack of access to emergency care (43). Another study done in Nigeria a special care baby unit of Port Harcourt indicates that, sixty percent of the Infants of diabetic mothers (IDMs) were born to mothers with gestational diabetes, while 40% were born to mothers with presentational DM. The commonest morbidities were hypoglycaemia and hyperbilirubinaemia in 30 (63.8%) and 26 (57.4%) respectively (44).

According to prospective cross-sectional study done at Bishoftu General Hospital, neonatal intensive care unit, Debrezeyt-Ethiopia shows that, A significant number of neonates born from mothers' with urinary tract infections (UTI) developed sepsis and associated to poor treatment outcome and this figure was almost 2.9 times higher compared to neonates born from mothers' with no UTI diagnosis(27).

2.3.3. Neonatal related factors

According to retrospective study conducted at tertiary care hospital in US low birth weight and preterm were significantly associated with neonatal morbidity (45) According to retrospective study conducted at neonatal intensive care unit in Brazil, death in very low birth weight infants was statistically associated with birth weight below 1000g (46). Another retrospective study of medical records for 1 year (January 2014-December 2014) conducted in a tertiary care teaching hospital, Mandya India on comparison of survival among different

birth weight indicated that, there was statistically significant difference between very low birth weight (VLBW) and normal birth weight group and between extreme low birth weight (ELBW) and normal birth weight group, but there was no statistically significant difference among LBW and normal birth weight group (47).

According retrospective study done in Orotta pediatric hospital, Eritrea, a total of 1502 infants were admitted to the NICU with an average preterm gestational age of 35.9 weeks and birth weight <2 kg, birth weight between 2.1 and 2.5 kg and this study shows that, small for gestational age were significantly associated with increased neonatal mortality (48).

According to prospective study conducted in tertiary care hospital in Addis Ababa, Ethiopia shown that, asphyxia and gestational age less than 37 were factors independently associated with neonatal mortality (49). Another A prospective cohort study done among neonates born between April 2014 and July 2014 in seven hospitals, in Tigray region, Ethiopia shows that, of the1152 live births, there were 68 deaths (63 per 1000 live births), Two thirds of deaths were attributable to prematurity 23 (34%) or asphyxia 21 (31%). Slight variance was seen between the mortality patterns in early and late neonatal periods. In the early neonatal period, 37% were due to prematurity, while asphyxia (35%) was more common in the late neonatal period(50).

2.4. Conceptual framework

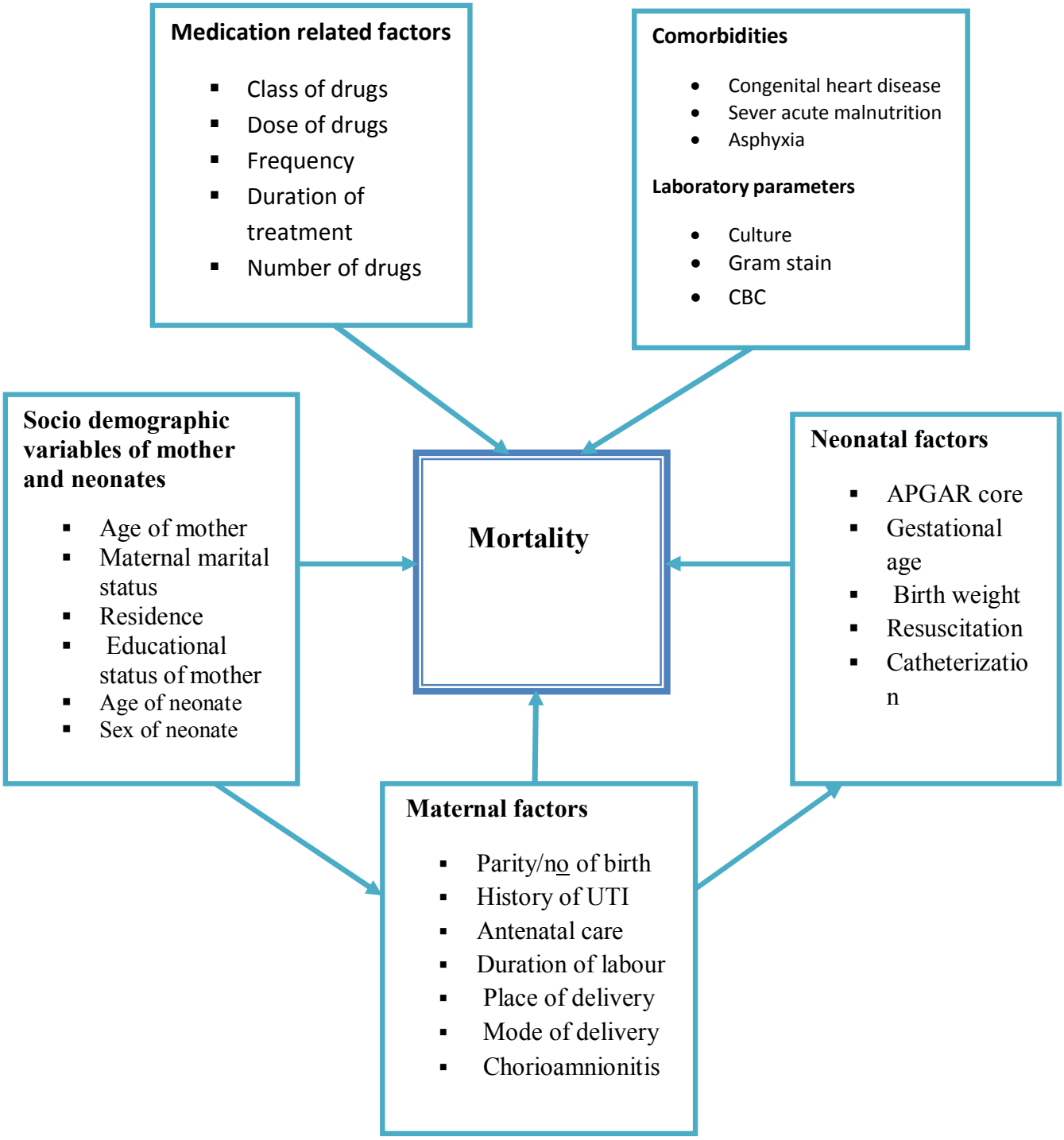


Figure 1 Conceptual frame work of treatment outcome and associated factors of neonatal sepsis among paediatrics ward at Mizan Tepi university teaching hospital, south west Ethiopia, 2018/19

3. Objective

3.1 General Objective

To evaluate treatment outcome and associated factors of Neonatal Sepsis at Mizan Tepi University Teaching Hospital, South West Ethiopia.

3.2. Specific Objectives

- ✓ To determine treatment outcome of patients with neonatal sepsis
- ✓ To identify factors associated with neonatal sepsis mortality

4. Method

4.1 Study area and period

The study was conducted in Mizan Tepi university teaching Hospital (MTUTH) located in Mizan Aman town, Bench magi zone which is one of the zones in south nation nationalities and people region (SNNPR) and situated about 561 Kilometres away from Addis Ababa. Mizan-Aman town is the administrative centre for Bench Maji Zone. It has the total population of 34,080; of which 18,138 are males and 15,942 are females. This town has one teaching hospital, and also the location of two institution of higher education, namely Aman Health science Collage and Mizan-Tepi University. Mizan Tepi University Teaching Hospital was established in 1986. The hospital serves about 1.2 million people from three zones, namely, bench Maji, kefa and sheka zone and a neighbouring region Gambella. It is the only Teaching hospital in the Bench-Maji zone that gives charge free service for pregnant mothers and neonates. The hospital has different department like outpatient, emergency, maternal and child health, paediatrics and NICU, surgery, and genecology. It has total of 136 beds and it runs multidisciplinary health care system with total of 209 staffs, of these 155 are health professionals and the remaining 54 are supportive staffs. NICU has 25 beds with 10 staff members. The study was conducted from May 01/2019 to October 30/2019

4.2 Study design

A hospital based prospective observational study design was used.

4.3 Population

4.3.1.Source population

All neonates admitted to NICU with a diagnosis of neonatal sepsis at MTUTH

4.3.2. Study population

All neonates fulfilling the inclusion criteria who was admitted to NICU of MTUTH with a diagnosis of neonatal sepsis during study period

4.4 Sample Size Determination and Sampling Procedure

4.4.1. Sample Size Determination

The sample size was determined by using single population proportion formula and the proportion was taken from previous study done, in India that proportion of mortality was 12.7%(32). By considering 95% confidence interval (CI) and 5% marginal error the, sample size was calculated as follows:

$$n = \frac{(Z\alpha/2)^2\, p\,(1-p)}{d^2}$$

Where,

n- Required Sample size

z- Standard deviation normal value at 95% CI which is 1.96

p- proportion of mortality among treated neonatal sepsis patients is12.7%(32)

d- Possible margin of error that can be tolerated which is 5% (0.05)

1-p -proportion of population that do not possess the character of interest

$$n = \frac{(1.96)^2\,(0.127)(0.873)}{(0.05)^2} = 170$$

By adding 10% drop out, the final sample size is 187

4.4.2. Sampling Technique

Consecutive sampling technique

4.5 Inclusion and exclusion criteria

Inclusion criteria:

- ✓ All neonates ≤ 28 days who was admitted to MTUTH at NICU
- ✓ Neonates diagnosed with sepsis by the attending physician either clinically or laboratory confirmed.

Exclusion criteria:

- ✓ Incomplete patient chart
- ✓ Neonatal mothers with unable to speak and hear
- ✓ Refused for informed assent

4.6 Study variables

Dependent variable:

- Mortality

Independent variables:

- Socio-demographic variables
  - ✓ Maternal age
  - ✓ Maternal marital status
  - ✓ Residence
  - ✓ Occupation of the mother
  - ✓ Educational status of mother
- Neonatal factors
  - ✓ Age
  - ✓ Sex
  - ✓ APGAR score
  - ✓ Gestational age
  - ✓ Birth weight
  - ✓ Catheterization
- Maternal factors
  - ✓ Parity/number of birth
  - ✓ History of infection
  - ✓ Duration of labor
  - ✓ Place of delivery
  - ✓ Mode of delivery
- Medication related factors
  - ✓ Class of medications
  - ✓ Dose of medications
  - ✓ Frequency of administrations
  - ✓ Duration of treatment
  - ✓ Number of drugs
- Co-morbidity
  - ✓ Severe acute malnutrition
  - ✓ Congenital heart disease

- ✓ Asphyxia

- laboratory parameters
  - ✓ Culture
  - ✓ Gram stain
  - ✓ White blood cell (WBC)
- Clinical parameters and vital signs
  - ✓ Respiratory distress
  - ✓ Body temperature
  - ✓ Heart rate
  - ✓ Feeding intolerance
  - ✓ Irritability

4.7 Data collection

Permission to data collection was obtained from the hospital administrator office. Data was collected by using semi-structured questionnaires for which interviewing mothers of the patients, and checklists for which abstraction of information from patients chart. Data collection tools were adapted from review of related previous literatures. Data were collected by four data collectors with past experience on data collection. The data collection tool included socio-demographic variables (mother's and neonatal age, maternal educations, residence, and occupational status), clinical variables (convulsion, sever chest in drowning, lethargic or unconscious, reduced movement, and not able to fed), Laboratory variables (CBC, culture, gram stain CSF and ESR) and outcome variables (poor and good). In addition vital signs like (PR, RR, and Temperature and oxygen saturation) were collected. Outcome was evaluated based on clinical feature, vital signs, laboratory investigations and patient summery note during discharge from hospital.

4.8 Data analysis

Data was cleaned, coded and entered in to Epi-data version 4.2 software, and then exported to Statistical package for social sciences version 21 for statistical analysis. Continuous variables were reported as mean. Categorical variables were reported as percentages and frequency tables. Cox regression was used to analyze factors that associated with mortality. Bivariate Cox regression was done to see associations between mortality and independent variables. Then, variables having P-value, <0.25 were a candidate for multivariate Cox regression analysis to evaluate time to event and independent associated factors of mortality due to

neonatal sepsis. Those variables having P-value, <0.05 was considered as statistically significant, and results were reported as 95% confidence intervals. For all statistical analysis Statistical Package for Social Sciences (SPSS version 21) was used.

4.9 Ethical clearance

Ethical approval was obtained from Jimma University Ethical Review Committee and permission to conduct the study was obtained from Mizan Tepi university teaching hospital, department of paediatrics. Assent was obtained from patients' parents. Neonatal parents were given information regarding the objectives of the study and they had the right either to decline or participate in this study. Identification numbers was used rather than names to identify patients. Assurance was given to maintain confidentiality of patients information that except principal investigators and data collectors no other person was allowed to access the data abstraction tools.

4.10. Data quality assurance

One day training was given for data collector before entering into data collection process on the method of data collection. Instruction manual was prepared and there were an on-going supervision by principal investigator. Pre-test was done on 5% of the sample to assure clarity, avoidance of ambiguity, comprehensiveness and content uniformity, so that some ambiguity was corrected.

4.11. Outcome measurement and validating methods

Treatment outcomes (good or poor) were measured using parameters such as whether the presence or absence of clinical sign and symptom, vital sign instability and laboratory abnormality and patient summary note while taking and after completion of treatment course. The patients were followed starting from admission to discharge or time to event.

Prevalence was also determined by calculating the number of all neonatal sepsis cases admitted within this study time period (May 01/2019-October 30/2019) including those who did not fulfil inclusion criteria to follow up divided by the size of all neonates admitted to NICU during this period. Thus,

$$Prevalence = \frac{\text{Number of neonatal sepsis disease onsets}}{\text{Sum of all neonates admitted}}$$

4.12. Plan for Dissemination of Results

The result of this study will be presented and submitted to Department of clinical pharmacy, school of pharmacy, College of Health Sciences, Jimma University. The study result will also be submitted to Mizan Tepi university teaching hospital. Effort will be made for publication on reputable Journal and will also be presented in scientific conferences.

4.13. Operational and term definitions

Neonatal Sepsis: sepsis diagnosed either clinically or with laboratory confirmed by professionals or attending physicians during admission of the neonates(2).

Neonate: new-borns from birth to 28 days old(51).

Prevalence: Proportion of neonatal sepsis to the whole admission of neonates during study period.

Early onset: If sepsis is occurred from birth to 3 days of age(51).

Late onset: If sepsis is occurred between 4 and 28 days of age(51)

Treatment outcome: clinical conditions of patients written on patients chart at discharge time.

Poor outcome: the attainment one of the following end results, death and self discharge against medical advice with no improvement, complication, referred, deteriorated.

Good outcome: the attainment of improvement

Primary outcome: mortality

Died: A patient declared as expired in hospital by attending physician

Improved: a patient who free from sign and symptom of neonatal sepsis and also being having stabilised vital signs

Deteriorated: Patient discharged with sever sign and symptom than on diagnosis

Self-discharged: Patients discharged themselves without physicians' decision against medical care

Referred: Patients referred to other health institution for better management of the condition

Co morbidity: coexistence of one or more disease with neonatal sepsis

Length of hospital stay: period from admission to event such as; death, improvement, complication, referred, deteriorated, and self-discharge.

5. Result

5.1. Descriptive statistics results

5.1.1. Socio demographic characteristics

Out of 219 neonates admitted with sepsis, 8 were excluded from the study due to incomplete patient chart at admission. Two hundred eleven (211) were eligible for the study, and included with the overall response rate of 96.4%.

According to this study, the mean age of neonates was 13.4±7.75 (S.D) days and they were in the age group of birth to 28 days. The mean age of mothers was 30.3±5.0 (S.D) with the age group of 19-44 years. More than half neonates (52.1%) were females. From total, 106 (50.2%) mothers were between age 18 and 29 years old, About 117 (55.5%) mothers were rural residents. Majority 181(85.8%) of mothers were married While 13(6.2%), 9(4.3%), and 8(3.8%) of mothers were single, widowed and divorced, respectively. Of the total, 135 (64%) mothers were house wife, and 59(28%) were illiterate or cannot read and write (table 1).

Table 1:- Socio demographic characteristics of neonate with their mothers admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211

Variables	Category	Frequency	Percent
Age of mothers	18-29	106	50.2
	30-34	57	27
	>34	48	22.7
Residence	Urban	94	44.5
	Rural	117	55.5
Maternal status	Married	181	85.8
	Single	13	6.2
	Window	9	4.3
	Divorced	8	3.8
Occupation of mother	house wife	135	64
	Government organization	12	5.7
	Business woman	41	19.4
	Farmer	9	4.3

	Student	14	6.6
Maternal education	Cannot read & write but no formal education	59	28
	Can read & write	75	35.5
	Primary	31	14.7
	Secondary	36	17.1
	College and above	10	4.7
Sex of neonates	M	101	47.9
	F	110	52.1
Age of neonates	birth-3 days	50	23.7
	4-28 days	161	76.3

5.1.2. Prevalence of neonatal sepsis

From May 1/2019 to October 30/2019 there were 838 neonates admitted at Mizan Tepi University Teaching Hospital in NICU. Of the total neonates 453(54.1%) were females. out of the total neonates 219 were diagnosed as neonatal sepsis in which, thus divided by total neonates giving a prevalence of 26.1% neonatal sepsis.

$$\textbf{Prevalence of neonatal sepsis} = \frac{\textbf{Number of neonatal sepsis cases in six month}}{\textbf{Sum of all neonate admited in six month}}$$

$$\textbf{Prevalence of neonatal sepsis} = \frac{\mathbf{219}}{\mathbf{838}}\boldsymbol{x}\mathbf{100} = \mathbf{26.1}\%$$

5.1.3. Neonatal characteristics

Of the total, 161(76.3%) were admitted with late onset sepsis or age greater than 3 days. From total 16 (7.6%) were very low birth weight, 124 (65.9%) were low birth weight, 156(73.9%) were term (37–42 weeks), 72(34.1%) were presented with comorbidities, 114 (54%) of neonates had history of birth resuscitation, and 134 (62.6%) neonates were with APGAR score less than seven. Most, 165 (78.2%) neonates were treated with Ampicillin plus gentamycin (Table 2).

Table 2 Neonatal related characteristics for treatment outcome of Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

Variables	Category	Frequency	Percent
Birth weight	Very low birth weight(1000-1500gm)	16	7.6
	Low birth weight(1501-2500gm)	124	65.9
	Normal birth weight (2501-4000gm)	34	20.9
Age of neonates	birth-3 days	50	23.7
	4-28 days	161	76.3
Gestational age at birth (weeks)	Preterm(<37 weeks)	55	26.1
	Full term(37-42 weeks)	156	73.9
Had resuscitation	Yes	114	54
	No	97	46
APGAR score at 5 minute	<3	1	0.5
	4-6	131	62.1
	>7	63	33.6
Had comorbidities	Yes	72	34.1
	No	139	66.9

Of all admitted neonatal sepsis patients, 161(76.3) were late onset neonatal sepsis (LONS), and 50(23.7%) were early onset neonatal sepsis (EONS) (figure 2)

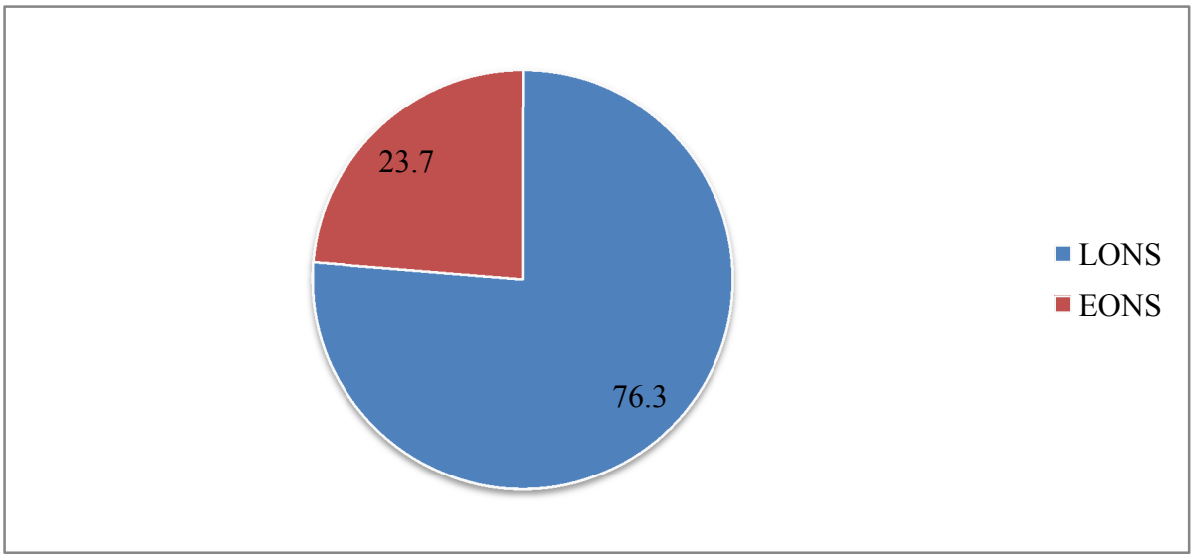


Figure 2 Types of sepsis among Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

5.1.4. Maternal related factors

From the total, more than half of the mothers 124(58.8%) were primigravida. Majority 136(64.5%) of mothers were not received ANC follow up and 60 (28.2%) mothers had history of infection during their pregnancy, of these 35(16.6%) of mothers had history of urinary tract infections. Ten (5.2%) mothers were twin delivered with either of one had neonatal sepsis. One hundred and seventy four (82.5%) mothers delivered their newborn in health institution and 37 (17.5%) mothers delivered by caesarean section. With regard to rupture of membrane, 65 (30.8%) had history of premature rupture of membrane (PROM). (Table 3)

Table 3 Maternal related factors for treatment outcome of Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211).

Variables	Category	Frequency	Percent
Multiple birth	Yes	87	41.2
	No	124	58.8
Place of delivery	Home	37	17.5
	Health institution	174	82.5
Mode of delivery	vaginal delivery	174	82.5
	Caesarean section	37	17.5
Maternal infection	Yes	60	28.4
during pregnancy	No	151	71.6
History of PROM	Yes	65	30.8
	No	146	69.2
ANC follow up	Yes	75	35.5
	No	136	64.5

PROM: premature rapture of membrane; ANC: antenatal care

5.1.5. Clinical parameters

5.1.5.1. Sign and symptom

During admission almost all patients fulfil WHO clinical diagnosing criteria except, that of 60(28.4%) patients who manifested hypotension (table 4).

Table 4: clinical presentation and vital sign of Neonatal Sepsis patients during admission to NICU of Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

Variables	Category	Frequency	Percentage
	Yes	190	90
Convulsion	No	21	10
Unconscious	Yes	192	90.1
	No	19	8.9
RR>60 breath/min	Yes	116	55
	No	95	45
	Yes	155	73.5
Temperature <35.5or>37.5	No	56	26.5
	Yes	133	63
Respiratory distress	No	78	37
	Yes	189	89.5
Lethargic	No	22	10.5
	Yes	191	90.5
Reduced movement	No	20	9.5
	Yes	46	21.8
Unable to breast feed	No	165	78.2
Tachycardia or bradycardia	Yes	109	51.7
	No	102	48.3
Hypotension	Yes	60	28.4
	No	151	71.6

5.1.5.2. Laboratory Findings

Of all neonatal sepsis patients, 203(96.2%) were diagnosed with doing CBC, and in addition 25(11.8%) were diagnosed with culture, 41(19.4%) with gram stain, and 58(27.5%) with CSF test for diagnosing of neonatal sepsis. Among those who have done CBC, 23(11.5%) were reported high (>20000) WBC counts and eight (4%) were low (<5000) WBC counts. Among

25 patients for which culture was done, 14(56%) were culture positive results. Among 41 patients who had done gram stain, 23(56.1%) were positive (Table 5).

Table 5: Laboratory findings for the diagnosis of neonatal sepsis patients admitted to MTUTH, South West Ethiopia from May 1 to October 30, 2019.

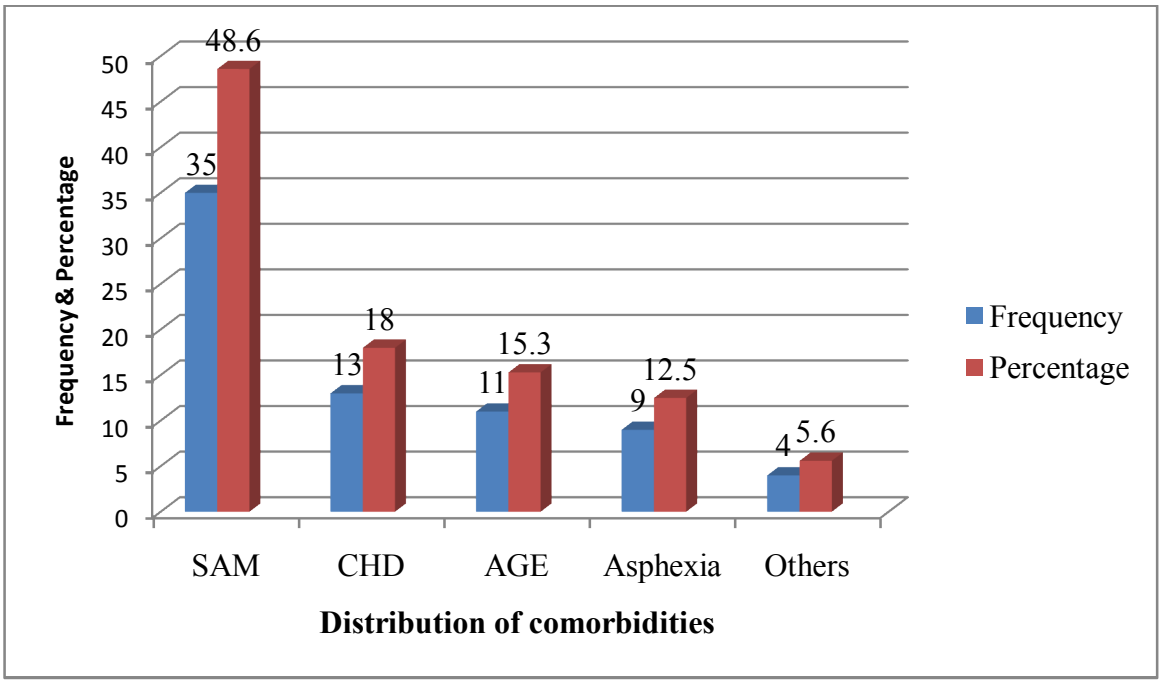
Variables	Category	Frequency	Percent
WBC counts/mm3	5000-20000(normal)	172	84.7
(203)	>20000(high)	23	11.3
	<5000(low)	8	4.0
Platelet counts	<50(extreme low)	2	1
1000 ^{3}/µL(194)	50-150(low)	24	12.4
	150-450(normal)	147	75.7
	>450(high)	21	10.9
Culture done	Culture positive result	14	56
(25)	Culture negative result	11	44
Types of organism	GBS	5	35.7
from culture	E.coli	4	28.5
	CONS	3	21.4
	Listeria monocytogen	2	14.3
Gram stain done	Positive	23	56.1
(41)	Negative	18	43.9
Types of organism	Few gram +ve rod and many	9	39.1
from gram stain	gram +ve cocci		
	Many diplococcic	6	26.1
	Streptococci	5	21.7
	Many gram-ve rods and few	3	13
	gram +ve cocci		

WBC: white blood cell, GBS: group B streptococcus; CoNS: coagulase negative staphylococcus

5.1.5.3. Co morbidities

Of the total neonatal sepsis patients, 72(34.1%) have comorbidities. Of these, 35(48.6%) were comorbid with sever acute malnutrition (SAM), 13(18%) were comorbid with congenital heart disease (CHD), 11 (15.3%) were comorbid with acute gastro enteritis

(AGE), nine (12.5%) were comorbid with Asphyxia, and four (5.6%) were comorbid with others (figure 3).



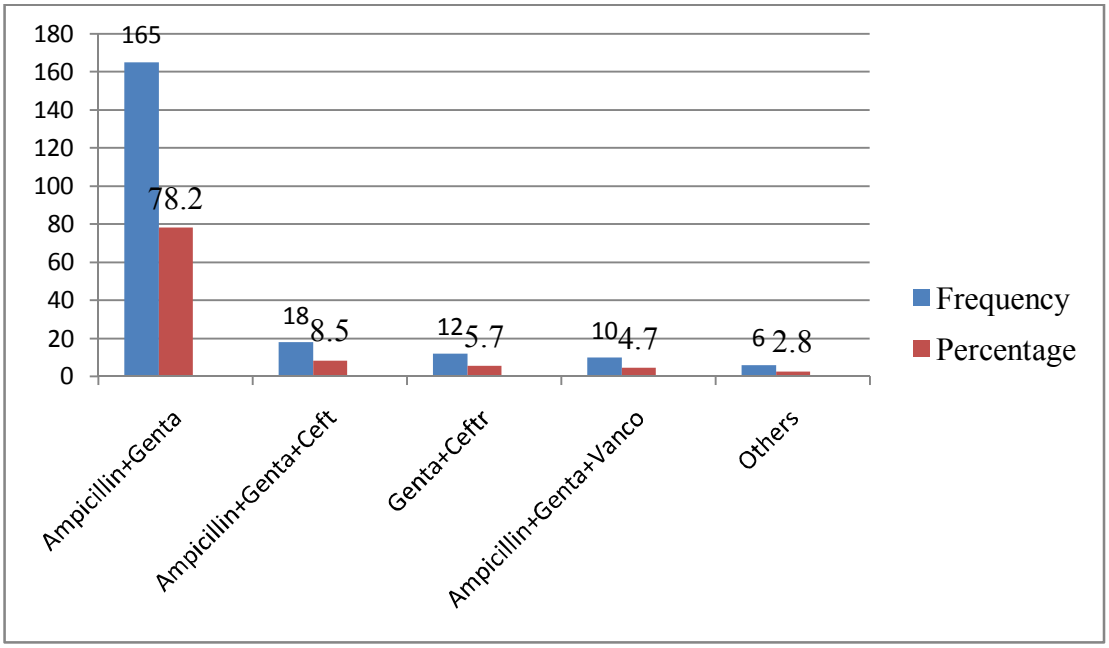
NB: SAM sever acute mal nutrition, CHD congenital heart disease, AGE acute gastro enteritis

Others: Jaundice and whooping cough

Figure 3 Frequency of comorbidities with Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

5.1.5.4. Medication related factors

Of all neonatal sepsis patients, 165(78.2%) were treated with a combination of ampicillin and gentamycin, 18(8.5%) with combination of ampicillin, gentamycin and ceftriaxone; 12(5.7%) with combination of gentamycin and ceftriaxone followed by 10(4.7%) with combination of ampicillin, gentamycin and vancomycin (figure 4).



NB: Others are ampicillin + ceftriaxone +vancomycin, ampicillin + gentamycin +metronidazole, and ampicillin + gentamycin + cloxacillin

Figure 4 Percentage of Medications regimens given for Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

Of all patients, 73(34.6%) were treated with underdose of ampicillin that is <100 mg/kg/day and three (1.4%) were treated with over dose of ampicillin that is >200 mg/kg/day. Among patients treated with gentamycin, 29(13.7%) were treated with underdose (<3.5mg/kg/day) and 55(26.1%) were with over dose (>7.5mg/kg/day) (figure 5).

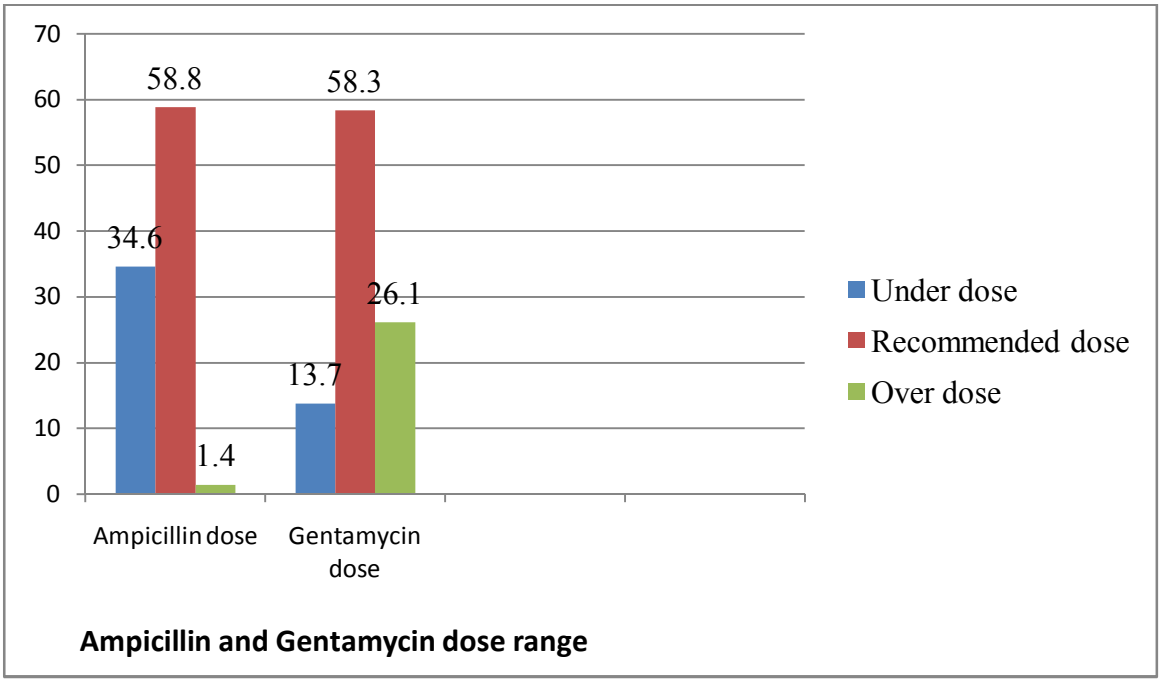


Figure 5 Percentage of Ampicillin and Gentamycin dose range given for Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

5.1.6. Treatment outcome

Treatment outcome of the study were poor outcome and good outcome. Of all neonatal sepsis patients admitted at NICU, 143(67.8%) were discharged with good outcome and 68(32.2%) were poor outcome. Among poor outcomes, 31(14.7%) were died, 12(5.7%) developed complication, 12(5.7%) were deteriorated, 3.3% self-discharged and 2.8% were referred to other health institutions. Among complications, five (41.6%) were meningitis, three (25%) were septic shock, three (25%) were respiratory failures and one (8.4%) was symptomatic hypoglycaemia (figure 6).

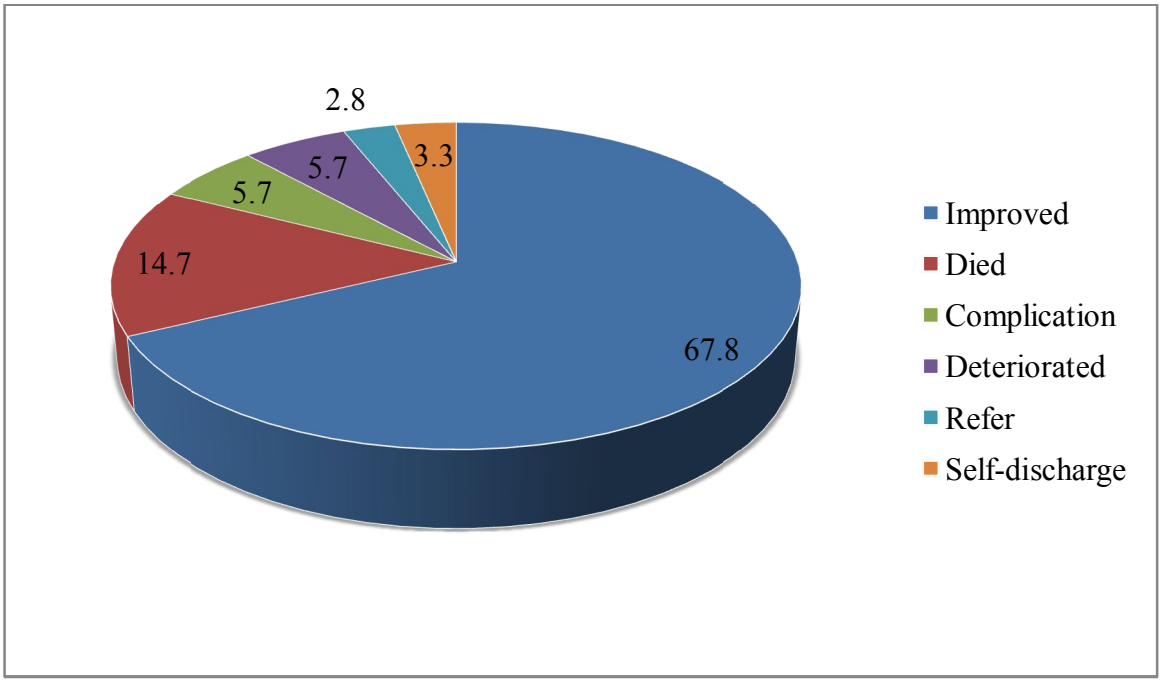


Figure 6 Percentage of Treatment outcome of Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

5.2. Bivariate and multivariable Cox regression analysis results for factors associated with mortality

In binary and multiple Cox regression analysis, maternal history of infection during pregnancy, very low birth weight, age of neonate less than 4 days, length of hospital stay, and maternal educational status, were significantly associated to mortality for neonatal sepsis patients.

Those neonates born from mothers who had history of infection during pregnancy [P=0.032, AHR=3.186, 95%CI: (1.32,30.68)] increase the risk of death by three times compared to those who were born from mothers who had no any maternal infection during pregnancy. Those neonates with early onset sepsis (EONS) [P= 0.001, AHR=9.67, 95%CI: (2.24, 41.70)] were 10 times more likely to cause early death or decrease survival compared to those neonates with late onset sepsis (LONS). Neonates with very low birth weight (1000-1500mg) [P=0.006, AHR=1.692, 95% CI: (1.245, 4.36)] were two times more likely to die compared to those who were born with normal weight.

Neonatal sepsis patients who were stayed for greater than 7 days in hospital [(P= 0.017, AHR=12.29, 95%CI: (1.55, 96.31) were 12 times more likely to be died compared to those who had short hospital stay or <7 days. Those neonates born from mothers who were learned up to secondary school [P=0.008, AHR=0.180, 95% CI: (0.12, 0.282)] were 82% less likely to be died compared to those neonates born from mothers who were learned up to college and above (table 6).

Table 6: Cox regression analysis for factors associated with mortality of Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia, between May 1 to October 30, 2019 (n =211)

Variables	Category	Treatment Outcome		CHR(95%CI)	p-value	AHR(95% C.I)	P-value
		Survived	Death				
Marital status	Married	159	22	1		1	
	Single	6	7	0.098(0.01,0.95) *	0.045	0.619(0.36,10.6)	0.745
	Widowed	8	1	0.116(0.01,0.1.22)	0.073	0.244(0.10,6.128)	0.391
	Divorced	7	1	0.037(0.01,0.77) *	0.033	0.196(0.05,8.03)	0.389
Mothers educations	Illiterate	47	12	0.087(0.09,0.88) *	0.039	0.012(0.01,0.413)	0.014
	Read & write	67	8	0.097(0.09,1.01)	0.052	0.011(.001,0.324)	0.009
	Primary	29	2	0.24(1.18,3.2)	0.28	0.024(0.002,1.103)	0.056
	Secondary	28	8	0.087(0.08,0.92) *	0.40	0.180(0.12,0.282)	0.008*
	College &above	9	1	1		1	
Maternal infectio	Yes	37	23	2.66(1.1,6.5) *	0.030	3.186(1.32,30.68)	0.032*
	No	143	8	1		1	
Mode of delivery	Vaginal delivery	150	24	0.26(0.071,0.95) *	0.043	0.325(0.05,20.56)	0.59
	C/S	30	7	1		1	
Birth weight	1000-1500	14	12	0.25(0.65,0.95) *	0.050	1.692(1.245,4.36) *	0.006*
	1501-2500	120	10	0.38(0.09,0.44)	0.165	0.253(.043,1.481)	0.127
	2501-4000	34	3	1		1	
Gestational age	<37	42	13	2.95(1.03,8.43) *	0.043	0.671(0.61,7.391)	0.745
	37-42	138	18	1		1	
Types of sepsis	EONS	36	14	3.16(1.45,6.88) *	0.004	9.67(2.24,41.70) *	.001*
	LONS	144	17	1		1	
Hospital stay	1-7 days	129	10	1		1	
	8-14 days	51	21	2.13(1.52,2.46) *	0.076	12.29(1.55,96.31)*	0.017*
Comorbidity	Yes	55	17	2.25(1.633,7.98)*	0.210	0.808(0.067,9.73)	0.864
	No	125	14	1		1	

NB:*=p-value<0.05(significant); 1=reference

Survival graph

Survival analysis showed that the probability of survival of neonates with late onset sepsis (LONS) was greater than neonates with early onset sepsis (P= 0.001).The probability survival of late onset sepsis patients during the first 3 days of admission was 1.0 while it was 0.8 in the Early onset neonatal sepsis (EONS), and The probability of late onset sepsis during the first 6 days of admission was 0.8 while 0.6 for early onset sepsis. The mean time taken for the early onset sepsis patients to be died was 5.56± 0.667 days (95%CI, 4.19-6.89) while it was 9.29 ± 0.668 days (95% CI, 7.88-10.578) for late onset neonatal sepsis patients.

Regarding censored data; among 21 EONS patients with poor outcome, 14 were died and 7(33.3%) were censored, of these, 5 patients have the probability of death after discharged from the hospital. On the other hand, among 47 LONS patients with poor outcome, 17 were died and 30(63.8%) were censored, of these, 11 patients have the probability of death (figure 7).

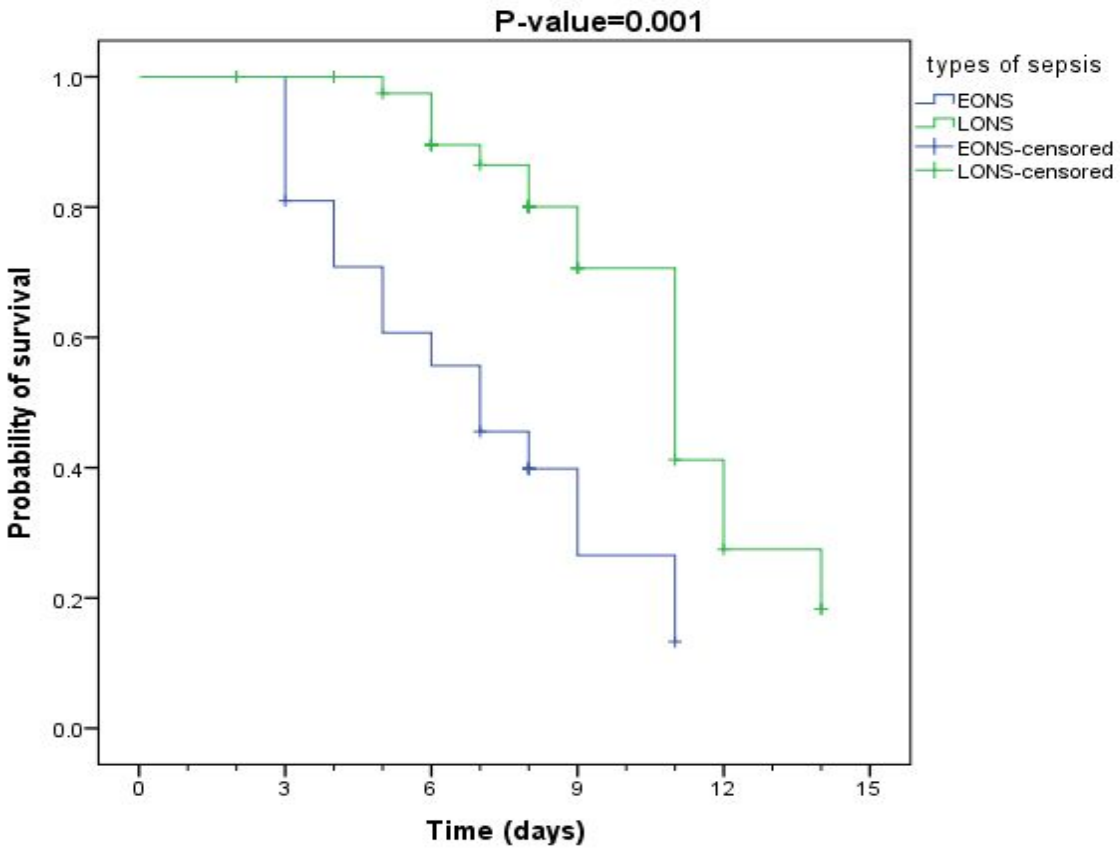


Figure 7 Kaplan–Meier estimation of survival among Neonatal Sepsis patients admitted to Mizan Tepi University Teaching Hospital, South West Ethiopia between May 1 to October 30, 2019 (n =211)

6. Discussion

This study assessed the prevalence, outcome and associated factors among neonatal sepsis patients admitted to Mizan Tepi University Teaching Hospital, south west Ethiopia.

6.1. Prevalence of neonatal sepsis

According to this study neonatal sepsis was frequently occurring disease among neonates admitted in NICU that the prevalence was 26.1%. This was many times greater than study done in United States of America(USA),the prevalence of culture-proven neonatal sepsis is estimated to be 0.77 to 1 per 1,000 live births, thus the prevalence and mortality are higher when very-low birth-weight (VLBW) infants, estimated to be 26 per 1,000 (24). The discrepancy might be due to the difference in the diagnosis method that culture confirmed for the previous study whereas clinically for majority of cases in the current study that may causes case selection bias. On the other hand more number of sample size (658) assessed for longer period of time (2005-2008) retrospectively for the previous study compared to this study, which leads to different prevalence of cases with different time period.

This study was lower than a cross-sectional study conducted at Temeke and Mwananyamala Hospitals during augest – september in Dares Salaam Tanzania where 31.4% (14) The variation might be due to the different in design and duration of study, and also because of different in case flow with different time interval. It might be also possible that due to relatively poor caring system during delivery, high prevalence of maternal infection during pregnancy, high patient to few staff ratio reported in the previous study setting.

The finding of this study was lower than a retrospective cross-sectional study done in NICUs of two governmental hospitals in Shashemene town for one month, Ethiopia estimated that the prevalence of neonatal sepsis was 77.9%, From this 65% and 35% of neonates were early onset neonatal sepsis and late onset neonatal sepsis, respectively (26), also lower than from another prospective cross-sectional study done in Bishoftu General Hospital, Neonatal Intensive Care Unit, Ethiopia, that the prevalence of neonatal sepsis was 72.22%(27). The possible reason for this discrepancy might be due to relatively more number of neonates (22.9%) born from mothers having urinary tract infection (UTI) during delivery in previous study.

6.2. Treatment outcome

This study showed that among 211 neonatal sepsis patients admitted at NICU of MTUTH, 67.8% were good outcome and 32.2% were poor outcome of which; 14.7% were died, 5.5% were develop complications, 5.5% were deteriorated, 3.3% were self-discharged and 2.8% were referred. This was lower than a retrospective case control study conducted in Tamale teaching hospital, northern Ghana indicated that, majority 82.7% of the neonates were successfully treated and discharged, 16.0% of them were died(30). The variation might be due to the previous study reviewed large number of sample size (4409) for longer period of time (from 2013-2015), and also the retrospective nature of study design in the previous study.

This study also supported with a study done at tertiary care center of southern Punjab in Pakistan in 2014 showed that, of the total neonatal admissions, 67% were discharged in a satisfactory condition, and 25.8% were died, 3.9% were referred, 3.3% left against medical advice [33, 35], also in line with a retrospective study done in rural tertiary care center in Cameroon showed that early neonatal mortality rate was estimated at 12.6% among neonatal sepsis patients on treatment (34).The outcome of this study was also almost consistent with a prospective cross-sectional study done in Bishoftu General Hospital, Ethiopia showed that mortality rate was 13.1% (27).

In the current study, mortality rate was lower than an observational study conduct ed at Nashik hospital in India showed that, mortality rate of 45.28% and the survival rate of 54.72 (33). Also lower than a prospective cohort study done in Switzerland with blood culture-proven sepsis between September 2011 and december 2015 showed that, mortality was 30% of these, 18% for EOS and 12% for LOS (25). The possible explanation might be due to larger sample size (444) used in the previous study (Switzerland) and may be diagnosis or selection bias in the present study whereas culture confirmed in Switzerland, whereas due to relatively much number of neonates (23.6%) were very low birth weight (VLBW) in case of the study in India, but only (7.6%) were VLBW in the current study.

The current finding was higher than a retrospective study done in NICU of Manipal Teaching Hospital, Nepal where mortality rate of neonatal sepsis was (10%) and complication (7.5%) (28), also above a retrospective study carried out at neonatal care unit of Raparin pediatric teaching hospital, Iraq showed that the neonate deaths rate was 5.4% and Majority 87.9% of neonates were discharged with unspecified discharge outcome (31). The possible explanation

might be due to the agent specific antibiotic therapy in the above study, while empirical therapy is the routine practice in this study setup and also may be due to the prospective nature of the present study.

This finding also higher than the retrospective chart review study conducted from April 30 to May 30 done at Bahir Dar Felege Hiwot referral hospital in Ethiopia, the clinical outcome of neonatal sepsis was not satisfactory that, 84% were improved after treatment, 4% were died and 5.8% referred to other organizations for further treatment (35). The possible reason for the variation might be due to the presence of many risk factors like maternal infections during delivery, very low birth weight and prematurity in the current study, but not in the previous one, in fact those are strong contributing factors for increasing mortality.

6.3. Factors associated with mortality

In this study maternal history of infection like UTI, very low birth weight, age of neonate less than 4 days, maternal education and length of hospital stay were observed significantly associated to increase risk of death for neonatal sepsis patients admitted at NICU of MTUTH.

According to this study, age of neonate less than 4 days was detected as significant predictors of mortality. This finding is almost consistent with studies conducted at a rural hospital in KwaZulu-Natal, South Africa, showed that over half (56.6%) of the deaths took place within the first three days of life and being male sex was significant predictors of neonatal death (37) the possible explanation might be due to environmental sources or horizontal transmission of many types microorganism from direct contacts of mothers because the fact that most early onset sepsis is caused by pathogens (resistant strain) acquired from the mothers.

This study showed that very low birth weight was detected as significant predictors of mortality. This finding is almost similar with study conducted at tertiary care hospital in US low birth weight and preterm were significantly associated with neonatal morbidity (45) an other similar retrospective study conducted at neonatal intensive care unit in Brazil, death in very low birth weight infants was statistically associated with birth weight below 1000g (46). Also in line with another study conducted in a tertiary care teaching hospital, Mandya India on comparison of survival among different birth weight indicated that, there was statistically significant association with that more likely to cause death (47)

This study showed that maternal history of infection during pregnancy detected as significant predictors of mortality. The finding was supported with study done at Bishoftu General

Hospital, neonatal intensive care unit, in Ethiopia shows that, A significant number of neonates born from mothers' with urinary tract infections (UTI) developed sepsis and associated to mortality and this figure was almost 3 times higher compared to neonates born from mothers' with no UTI diagnosis(27).

According to this study, 55(26.1%) of neonates were reported as premature (gestational age <37 weeks) although, were not significantly associated with increasing mortality, this is might be due to the nature of variables in the current study, however a prospective study conducted in tertiary care hospital in Addis Ababa (49), and a prospective cohort study done in seven hospitals, at Tigray region, Ethiopia (50),revealed that, gestational age less than 37 weeks were factors independently associated with neonatal mortality, this is might be due to related to lack of appropriate treatment modalities, such as mechanical ventilation, surfactant administration, and parenteral nutrition for premature neonates as reported in the first study. On the other hand; immature organ of the preterm neonate related to prematurity is most likely lead to death.

This study revealed that, 37(17.5%) of neonates were delivered through caesarean section, but not significantly associated with increasing mortality, this is might be due to small number of neonates were delivered through caesarean section in the current study, but a study conducted at USA Washington Hospital Center in Washington DC NICU indicates that, newborns delivered by caesarean section were associated with increasing risk of mortality(39), this might be due to those new-borns delivered via caesarean section were from mothers having delivery complications such as premature rupture of membrane, chorioamnionitis, fetal distress and birth defect, as well as from mothers developing preeclampsia and diabetes mellitus; therefore this may contribute to increase risk of death in the previous study.

6.4. Strength and Limitation of the Study

Strength

This study employed mixed data collection method (face to face and patient chart). This study identified factors associated with treatment outcome of neonatal sepsis in NICU of Mizan Tepi University Teaching Hospital.

Limitation

In this study most of sepsis cases were not identified based on culture confirmed sepsis. However, it was based on suggestive clinical presentations. This might expose the finding for selection bias because neonates who had sign and symptoms of sepsis could be negative for culture which is the golden standard for diagnosis of sepsis. There was shortage of literature for discussion.

7. Conclusion and Recommendations

7.1. Conclusion

This study indicated that neonatal sepsis was the frequently occurring neonatal disease. Mortality was found to be very high among neonatal sepsis patients admitted at NICU, which showed the need of quality care improvements. Maternal history of infection during pregnancy, age of neonate <4 days, birth weight of the neonate < 1500gm, maternal education, and prolonged length of hospital stay were found to be independent predictors of increasing risk of mortality.

7.2. Recommendations

Based on the finding of this study the following recommendation will be forwarded to concerned bodies.

For Mizan Tepi University Teaching Hospital;

- ✓ It is better to regularly screen out pregnant mothers for infection, and premature rupture of membrane so that they will be alarmed as this can put in risk of neonatal sepsis which may lead to poor treatment outcome even up to end with death.
- ✓ Adoption of an international standard and locally conformable guideline of antibiotic use

For those health professionals who are working in NICU and obstetric unit;

- ✓ Better to giving priority management for patients having those identified factors may significantly decrease proportion of death.
- ✓ Pharmacists have a remarkable role in rational use of drugs by dissemination of drug information to patients and physicians so it is better to involve clinical pharmacists at NICU.

For further researches;

- ✓ Researchers better to do more valuable and large scale studies on this subject matter so as to find more factors associated with neonatal sepsis mortality.

References

1. WHO Global health Observatory Data repository. 2012.
2. Schelonka RL, MacDonald MG, Seshia MMK MM. Bacterial and Fungal infections.Avery's Neonatology, 6th edition Philadelphia: Lippincott Williams & Wilkins. 2005.
3. Cinel I DR. advances in pathogenesis and management of sepsis. Curr opin infec dis. 2007;20(345).
4. Kayom VO, Mugalu J, Kakuru A, Kiguli S, Karamagi C. Burden and factors associated with clinical neonatal sepsis in urban Uganda : a community cohort study. BMC. 2018;18(355):1–8.
5. Jehan I, Harris H, Salat S, Zeb A, Mobeen N, Pasha O, et al. Neonatal mortality , risk factors and causes : a prospective population-based cohort study in urban Pakistan. Bull World Heal Organ. 2009;87(January):130–8.
6. Koda-Kimble MA, Young LY, Alldredge BK, Corelli RL, Guglielemo BJ.et al. the clinical use drugs 9th ed. Lippincott Williams & Wilkins. Applied therapeutic. 2009.
7. Kraus DM, Pham JT. Neonatal therapy. In: KodaKimble MA, Yee YL, Alldredge BK KW, Guglielmo BJ CR. Applied Therapeutics: The Clinical Use of Drugs. 9th Edition. 2009.
8. Coetzee M, Chb MB, Paed M, Sa CN, Mbowane NT, Chb MB. Neonatal sepsis : Highlighting the principles of diagnosis and management. S Afr J Child Heal. 2017;11(2):0–4.
9. Kaistha N, Mehta M, Singla N, Garq R CJ. Neonatal septicaemia isolates and30 resistance patterns in a tertiary care hospital in North India. J infect Dev Ctries. 2009;4(1):5–7.
10. Marchant EA, Guilaine E B, Sadarangani M LP. Neonatal sepsis due to coagulase negative staphylococci. Clin Dev Immunol. 2013;586076.
11. Waters D, Jawad I, Ahmad A, Luksic I, Nair H, Zgaga L TE, Rudan I, Zaidi AKM CH. Aetiology of community-acquired neonatal sepsis in low- and middle-income countries. J Glob Heal. 2011;1(2):154–70.
12. Aggarwal R, Sarkar N, Deorari AK PV. Sepsis in the newborn. New Delhi. 2014;110029.
13. Seale, A.C. et al. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and

meta-analysis. Lancet Infect Dis. 2014;14(8):31–41.

14. Jabiri A, Wella HL, Semiono A, Sariah A, Protas J. Prevalence and factors associated with neonatal sepsis among neonates in Temeke and Mwananyamala Hospitals in Dar es Salaam , Tanzania. Tanzan J Health Res. 2016;18(4):1–7.
15. N. Aijaz, N. Huda and SK. Tertiary Care Hospital, Karachi, Pakistan. Dis Burd NICU. 2012;6.
16. Seale, A.C., Mwaniki, M., Newton, C.R.J.C. & Berkley JA. Maternal and early onset neonatal bacterial sepsis: burden and strategies for prevention in sub-Saharan Africa. Lancet Infect Dis. 2009;9:428–438.
17. Lawn, J.E. et al. Every Newborn: progress, priorities, and potential beyond survival. Lancet. 2014;384(9938):189–205.
18. Liu, L. et al. Global, regional, and national causes of under-5 mortality in 2000: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet. 2016;
19. Gebremedhin, D., Berhe, H. & Gebrekirstos K. Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia. PLoS One. 2015;11(5).
20. Kolola T, Ekubay M, Tesfa E MW. Determinants of Neonatal Mortality in North Shoa Zone, Amhara Regional State, Ethiopia. PLoS. 2016;11(e0164472).
21. (CSA) CSA. Ethiopia Mini Demographic and Health Survey (EMDHS),Addis Ababa, Ethiopia. 2016.
22. Chavannes-de-Bogis, et al Hotel BWC. WHO Sepsis Technical Expert Meeting. HIS. 2018;7(16–17 January).
23. Fjalstad JW, Stensvold HJ, Bergseng H, Simonsen GS, Salvesen B R, AE et al. Early-onset sepsis and antibiotic exposure in term infants: a nationwide population-based study in Norway. Pediatr Infect Dis J. 2016;35(5):1–6.
24. Weston EJ et al. The burden of invasive early-onset neonatal sepsis in the United States, 2005- 2008. Pediatr Infect Dis J. 2011;30:937–41.
25. Ournal THEJ, Ediatrics OFP, Giannoni E, Agyeman PKA, Stocker M, Posfay-barbe KM, et al. Neonatal Sepsis of Early Onset, and Hospital-Acquired and Community-Acquired Late Onset: A Prospective Population-Based Cohort Study. J Pediatr [Internet]. 2018;201:106–114.e4. Available from: https://doi.org/10.1016/j.jpeds.2018.05.048
26. Getabelew A, Aman M, Fantaye E, Yeheyis T. Prevalence of Neonatal Sepsis and Associated Factors among Neonates in Neonatal Intensive Care Unit at Selected

Governmental Hospitals in Shashemene Town , Oromia Regional State , Ethiopia , 2017. Int J Pediatr. 2018;2018(10):7.

27. Woldu MA.etal. Assessment of the incidence of neonatal sepsis , its risk factors , antimicrobials use and clinical outcomes in Bishoftu General Hospital , neonatal intensive care unit , Debrezeit-Ethiopia. Int J Contemp Pediatr. 2014;1(3):135–41.
28. Al C k. et. The clinical spectrum and outcome of neonatal sepsis in a neonatal intensive care unit at a tertiary care hospital in western Nepal: January 2000 to December 2005 - A retrospective study. East J Med. 2012;17:119–25.
29. Muhammad S, Raghib I, Shahzad B, Mubarak Ai KZ. Pattern of neonatal admissions & its outcome in a tertiary care hospital of Southern Punjab. P J M H S. 2014;8(4).
30. Walana W, Acquah Ekuban K, Abdul-Mumin A, Naafu B AE. Pattern, causes and treatment outcomes of neonatal admission in the Tamale teaching hospital. Clin mother child Heal. 2016;13(252):2.
31. Shaker NZ. Disease Patterns and outcomes of Neonatal Admissions at Raparin Pediatric Teaching Hospital in Erbil City. 2015;28(2):39–46.
32. Reshad M, Mundol T, Mithun HK, Prabhu AS. Study of the immediate clinical outcome of neonatal sepsis in the neonatal I . C . U . of a tertiary care hospital. Int J Contemp Pediatr. 2017;4(4):1401–4.
33. Sonawane R, Patil S, Ahire N KN. Outcome of LBW Babies Admitted in the NICUA Hospital based Study. MVP J Med Sci. 2014;1(2):71–4.
34. Koum, Danielle Christiane Kedy Essomba, Noel Emmanuel Odile NBN, Irma Ndanga, Malea Ndombo et al. Factors associated with early neonatal morbidity and mortality in an urban district hospital. 2015;
35. Tewabe T, Mohammed S, Tilahun Y, Melaku B, Fenta M, Dagnaw T. Clinical outcome and risk factors of neonatal sepsis among neonates in Felege Hiwot referral Hospital , Bahir Dar , Amhara Regional State , North West Ethiopia 2016 : a retrospective chart review. BMC Res Notes. 2017;10(265):1–7.
36. SB, Siva Saranappa Madhu, GN Singh R. A study of disease pattern and outcome of newborns admitted to NICU in a tertiary care hospital. Congenit Anom (Kyoto). 2014;29(1):92.
37. Hoque M, Haaq S IR. Causes of neonatal admissions and deaths at a rural hospital in KwaZulu-Natal, South Africa. South African J Epidemiol Infect. 2011;26(1):26–9.
38. Rakholia R, Rawat V, Bano M SG. Neonatal morbidity and mortality of sick newborns admitted in a teaching hospital of Uttarakhand. Res Chrismed J Heal. 2014;1(4):228.

39. Chelliah AM, Vilchez G, Dai J, Bahado-Singh RO SR. Risk factors for neonatal intensive care unit admission after term twin deliveries. Obstet Gynecol. 2014;123(141).
40. Sengupta S, Carrion V, Shelton J, Wynn RJ, Ryan RM, Singhal K et al. Adverse neonatal outcomes associated with early-term birth. JAMA Pediatr. 2013;167(11):1053–9.
41. Fauth de Araújo B, Zatti H, Madi JM, Brussius Coelho M, Bertoletti Olmi F T, C. C. Analysis of neonatal morbidity and mortality in late-preterm. J Paediatr. 2012;88(3).
42. Phaloprakarn C, Manusirivithaya S BP. Risk score comprising maternal and obstetric factors to identify late preterm infants at risk for neonatal intensive care unit admission. J Obstet Gynaecol Res. 2015;41(5):680–8.
43. Rakhia A, Khan M, Memon AA DS. Pattern and outcome of neonatal ailments in a tertiary care hospital. Pakistan J Med Res. 2014;53(1):14.
44. Opara PI, Jaja T OU. Morbidity and mortality amongst infants of diabetic mothers admitted into a special care baby unit in port Harcourt Nigeria. Ital J Pediatr. 2010;36(1):77.
45. Nathan S. Fox MS, Samuel Bender, Chad K. Klauser, Daniel H. Saltzman and A, Rebarber. Active second-stage management in twin pregnancies undergoing planned vaginal delivery in a US population. Obstet Gynecol. 2010;115(2):229–33.
46. Carneiro JA, Vieira MM, Reis TC CA. Risk factors for the mortality of very low birth weight newborns at a neonatal intensive care unit. Rev Paul Pediatr. 2012;30(3):369–76.
47. Sridhar P, Thammanna P SM. Morbidity pattern and hospital outcome of neonates admitted in a tertiary care teaching hospital, Mandya India. Int J Sci Stud. 2015;3(6):126–9.
48. Shah S, Zemichael O MH. Factors associated with mortality and length of stay in hospitalised neonates in Eritrea, Africa: BMJ open. 2012;2(5):e000792.
49. Tekleab AM, Amaru GM TY. Reasons for admission and neonatal outcome in the neonatal care unit of a tertiary care hospital in Addis Ababa: a prospective study. Res reports Neonatol. 2016;6:17–23.
50. Mengesha HG, Sahle BW. Cause of neonatal deaths in Northern Ethiopia : a prospective cohort study. BMC Public Health [Internet]. 2017;17(62):1–8. Available from: http://dx.doi.org/10.1186/s12889-016-3979-8
51. Wynn JL. Defining neonatal sepsis. 2016.

Annex

Data collection tool

Jimma University, College of Health Sciences, School of pharmacy, department of clinical pharmacy

A questionnaire to determine prevalence, treatment outcome and associated factors of neonatal sepsis at Mizan Tepi university teaching hospital, south west Ethiopia.

1. Questionnaire ID number _____
2. Address: Kebele _____

3. Data collection date ___/ ___/ _____

4. Card No _____

5. Date of admission_____

Note: Encircle from the given options and write if any other idea or answer is given

PART I. QUESTIONER FOR INTERVIEW **Socio-demographic characteristics of mothers with their index neonates**			
No.	Question	Response	Remark
1	Mother's age	_____(in years)	
2	Marital status	1.Married 2. Widow 3. Divorced 4. Separated 5. Single	
3	Residence	1. Urban 2. Rural	
4	Maternal education	1. Can't read and write 2. Can read and write 3. Primary 4. Secondary 5. college and higher	

5	Occupation of mother	1. Housewife 2. Governmental organization 3. Business woman 4. Private Organization 5. Daily labourer 6. Farmer 7.Student	
6	Neonate's age	_____in days	
7	Neonate's sex	1. Male 2. Female	
PART II: DATA ABSTRUCTION FORMAT FOR CHART REVIEW AND INTERVIEW **Maternal related factors**			
8	Multiple birth	A. Yes B. No C. If yes, state the number_____	
9	History of UTI/STI/HIV/chorioamnionitis during the pregnancy of this neonate?	Yes_____ No_____ Specify_____	
10	Did you have antenatal care follow up during the pregnancy of this neonate?	Yes_____No_____ Specify_____	
11	History of bleeding during delivery?	Yes_____No_____	
12	Place of delivery	A. home B. Health institution C. Other specify_____	
13	Mode of delivery	A. Vaginal delivery B. C/S	

		C. Instrumental	
14	Duration of Labour	_____in hours	
15	History of rupture of membrane?	Yes_____No_____ If yes duration_____hours	
Neonate related factors			
16	Gestational age	_____ in weeks	
17	APGAR score	At 1st minute_____ At 5th minute_____	
18	Birth Weight at birth	_____ in grams	
	Current weight	_____in kgs	
19	Did the neonate resuscitated at birth?	Yes _____ No ____	
20	Did the neonate had any type of surgery done?	Yes _____ No _____ Specify _____	
21	Was the neonate on oxygen?	Yes _____ No _____	
22	If yes what was the method of oxygen administration?	1. Intranasal catheter 2. Mask 3. Nasal cannula	
23	Did the neonate had endotracheal intubation?	Yes _____ No _____ Specify _____	
24	Did the neonate had NG tube inserted?	Yes_____ No_____	
25	Did the neonate had any catheter inserted?	Yes_____ No_____ Specify_____	
26	Did the neonate had comorbid conditions?	Yes_____No_____ If Yes, specify_____	

Laboratory investigation findings			
27	Complete blood count (CBC)	1. Total WBC_____ /mm3 2. HCT_____gm/dl 3. HG_____gm/dl 4. Platelet count_____cells/mm3 5.WBC with diff Neut._____ Lymph._____ Others_____	
28	ESR	Yes _____no _____ If yes_____/1hr	
29	Blood culture	Yes ____no _____ If yes Identified bacteria_____	
30	Urine culture for LONS	Yes ___no_____ If yes identified bacteria_____	
31	Gram stain	Yes ____no _____ If yes, types of bacteria_____	
32	Lumbar puncture (CSF) for LONS,	Yes __no____ If yes, cell count_____	
33	Chest radiograph (if respiratory signs present	Yes _____no _____ If yes, _____	
34	Blood glucose	Yes ____no____ If yes, 1. RBS _____mg/dl or ____mmol/L 2. FBS_____mg/dl or _____mmol/L	
35	UA if done,	Yes ____no_____ If yes, Blood_____ Protein_____	
CLINICAL FEATURES OF NEONATAL SEPSIS			
36	Convulsions	Yes _____ No ____	

37	Respiratory rate > 60 breaths/min	Yes _____ No ____	
38	Severe chest in drawing	Yes _____ No ____	
39	Tachycardia or bradycardia	Yes _____ No ____	
40	Hypotension	Yes _____ No ____	
41	Redness around umbilicus extending to the skin	Yes _____ No ____	
42	Temperature >37.5oC or <35.5oC	Yes _____ No ____	
43	Lethargic or unconscious	Yes _____ No ____	
44	Reduced movements	Yes _____ No ____	
45	Not able to breast feed	Yes _____ No ____	

PART III:MEDICATION USED FOR NEONATAL SEPSIS

	Medications	Dose, frequency, route, duration	
46			

VITAL SIGNS DURING HOSPITAL STAY

	Date											
47	Vital signs	Temp										
		RR										
		PR										
		BP										
		Oxygen saturatio										
		Breast feeding										

CLINICAL TREATMENT OUTCOME

48	Treatment outcome	A. Improved B. Same C. Deteriorated D. Died E. Self-discharge F. Refer G. Complications_____if complication, specify_____	
49	Time to event	_____days	
50	Length of hospital stay	_____days, discharge date_____	
51	Discharged date	_____d/m/y	

Participant Information Sheet

Good morning/ afternoon?

My name is _____ Currently I am a graduate student at Jimma University, College of Health Sciences, School of pharmacy in clinical pharmacy. And now I am conducting a study to evaluate burden, treatment outcome and associated factors of neonatal sepsis patients admitted at mizan tepi university teaching hospital, south west Ethiopia, 2019.

Title of the research: prevalence, treatment outcome and associated factors of neonatal sepsis patients admitted at mizan tepi university teaching hospital, south west Ethiopia, 2019.
Objective: this study will aimed to evaluate prevalence, treatment outcome and associated factors of neonatal sepsis
Participants: Neonatal sepsis patients admitted to MTUTH at NICU
Potential Risks: There will no risk by being involved in this study.
Benefits: No financial benefits are related with this study. But by participating in this study, most importantly, the result of the study will be beneficial to design effective preventive and control measures for neonatal sepsis. Hence, you are indirectly benefiting other patients and the society in this respect.

I would like to ask you few questions. Your honest response to the questions can make the study to achieve its objective. All the information that you give will be kept confidential and private. Only the principal investigator and interviewer will have access to the information. You are kindly requested to respond voluntarily. You can also choose not to participate in this study totally or if you become uncomfortable during the study, you will be allowed to leave the interview at any time. At any time that you have questions, you can contact me by using the following Addresses**:**

Yohannes Wobie
Mobile: 09 35 17 10 96
E-mail: yohannes.w27@gmail.com

Assent form

In signing this document, I am giving my assent to participate in the study entitled "prevalence, treatment outcome and associated factors of neonatal sepsis patients admitted at mizan tepi university teaching hospital, south west Ethiopia".

I have been informed that the purpose of this study is to evaluate burden, treatment outcome and associated factors of neonatal sepsis. I have understood that participation in this study is entirely voluntarily. I have been told that my answers to the questions will not be given to anyone else and no reports of this study ever identify me in any way. I have also been informed that my participation or non-participation or my refusal to answer questions will have no effect on me. I understood that participation in this study does not involve risks. I understood that Yohannes Wobie is the contact person if I have questions about the study or about my rights as a study participant.

Respondent's signature_____

Date of interview: _____ Time started: _____ Time finished: _____

Interviewer Name_____Signature_____Date_____

Supervisor's name _____ signature _____

Results of interview questionnaire

1. Completed
2. Refused
3. Partially completed

የተሳታፊዎች የመረጃ ቅፅ በአሚኖ

እንደምን አደሩ/ዋሉ?

ሥሜ ---------- እባላለሁ፤ በጅማ ዩኒቨርሲቲ፣ ጠፍ ሳይንስ ኮሌጅ፣ ፋርማሲ ትምህርት ክፍል የ2ኛ ዓመት የማስትሬት ደግሪ ተማሪቂ ተማሪ ነኝ፡፡ በአሁኑ ሰዓት በጨቅላ ህፃናት ህክምና አሰጣጥ ሂደትና ውጤት በማናት ላይ ነኝ፡፡

የጥናቱ ርዕስ፡ - በጨቅላ ህፃናት ህክምና አሰጣጥ ሂደትና ውጤት*ማ*ማ*ም* በሚዛን ቴፒ ዩኒቨርሲቲ ቲችንግ ሆስፒታል፣ ደቡብ ክልል ኢትዮጵያ፣2019.

የጥናቱ አላማ - በጨቅላ ህፃናት ህክምና አሰጣጥ ሂደትና ውጤት ለ*ማ*ማ*ም*፡፡

ተሳታፊዎች፡ -ከ28 ቀናት በታች የሆኑ ከእናታቸው ጋር ሆስፒታል ዉስጥ የተኙ ጨቅላ ህፃናት

የጎንየሽ ጉዳት፡ - በዚህ ጥናት መሳተፍ ምንም አይነት ጉዳት የለውም

ጥቅማጥቅም፡ - በጥናቱ ለሚሳተፉ ፍቃደኛ ተሳታፊዎች ምንም አይነት የገንዘብ ክፍያ የለም፡ነገር ግን የጥናቱ ዉጤት የህጻናት ሰዉነት መሟጠጥን ለመቆጣጠርና ለመከላከል ስለሚጠቅም በተዘዋዋሪ መንገድ ለለ ህመምተኛ እንዲሁም ህብረተሰቡን የመጥቀም እደል ያገኛሉ፡፡

ስለዚህ የተዉሰኑ ጥያቄዎችን ልጠይቅዎት እወዳለሁ፡ የእርስዎ በእዉት ላይ የተመሰረተ መልስ ለዚህ ጥናት መሳካት አስተዋፅኦ ያደርጋል፡፡ እርስዎ የሚጠቅ መረጃ ከአጥኚዉና ቃለመጠይቅ አደራጊው በስተቀር በማንኛውም መልኩ ለለለ 3ኛ ወገን ተላልፎ አይሰጥ ም፡ በሙሉ ፈቃደኝት እንዲሳተፉ እየጠየቅሁ ያለመሳተፍ ወይም በማንኛውም ጊዜ ራስዎን ከጥናቱ የማገለል ሙሉ መብት አለዎት፡፡ ማንኛውም ጥያቄ ካለዎት በሚከተለው አደራሻዬ ማገኘት ይችላሉ፡፡

ዮሃንስ ዉቤ
ስ.ቁ. 0935171096
ኢሜይል፡ yohannes.w27@gmail.com

የስምምነት መግለጫፎርም- በአማርኛ

ጅማ ዩኒቨርሲቲ፤ጠቅ ሳይንስ ኮሌጅ፤ ፋርማሲ ትምህርት ክፍል፤ደህረ ምረቃ ፕሮግራም እኔ ለዚህ ጥናት የስምምነት ፊርማዬን ስሰጥ፤የዚህ ጥናት ዓላማ በደንብ የተብራራልኝ ሲሆን የጥናቱንም ዓላማ ተረድቻለሁ፡ በዚሁ ጥናት ላይ መሳተፍ በሙሉ ፈቃደኝነት ላይ የተመሰረተ መሆኑን በሚገባ የተረዳሁ ሲሆን በማንኛውም ጊዜ ከጥናቱ ራሴን የማግለል መብት እንዳለኝ አውቄአለሁ፡ ስለሆነም የምሰጠው መረጃ እስከተጠበቀ ድረስ በዚህ ጥናት ለመሳተፍ ተስማምቻለሁ፡ በጥናቱ ስሳተፍ በህጻኑ/ኗ ወይም በኔ ላይ ምንም አይነት ጉዳት እንደሌለው በግልጽ ተረድቻለሁ፡በዚህ ጥናት ለመሳተፍ ስምምነቴን ስገልፅ ለምጠቀው ጥያቄ በእውነት ላይ የመሰረተ መልስ ለመሰጠት የተስማማሁ መሆኔን አረጋግጣለሁ፡በመጨረሻ ዘሪያም ሆነ ስለ ጥናቱ ማንኛውንም ያልገባኝን ጥያቄ መጠየቅ እንደምችል ተገልጾልኛል፡፡

የመረጃ ሰጪፈርማ_____ቀን _____

የተጀመረበት ሰዓት _____ያለቀበት ሰዓት_____

የጠያቂውስም_____ፊርማ_____ቀን_____

የተቆጣጣሪ፤ስም_____ፊርማ_____ቀን_____

የመጠይቁ ዉጤት

1. መሉበመሉየተሞላ
2. ያልተሰሙ
3. በከፊልየተሞላ

Eoochgahaaga eyrrd gaah ochh

Digme akanne/digame feshkanne

Taa summe_____

Ha satte jimma university hakimam pharmacy temert ketien wursenensush tamary gezaw.Hash taga kaytseskushe ertta,feytse afeea,yeabana dyameskush harew mayskushez zolaga fugamm fursttagesgen neyayantsenda mizan tepi university temarsakush hospitalkan surkakey hakamaseskend tone,deubub meraab ethiopia, 2019

Taga kaytsaga apee: ertta,feytse afeea,yeabana dyameskush harew mayskushez zolaga fugamm fursttagesgen neyayantsenda mizan tepi university temarsakush hospitalkan surkakey hakamaseskend tone,deubub meraab ethiopia, 2019

Ta kaytsaga koyeskushee:tagaa kaytse koyeskushee ertta,feytse afeea,yeabana dyameskush harew mayskushez zolaga fugamm fursttagesgen neyayantsenda dembee.

Taka erte kaytseshesh kursensende:zolaga fugamm fursttagesgen neyayantsenda mizan tepi university temarsakush hospitalkan surkakey hakamaseskend.

Erate atensuye :ere erate neya demb atensarguwee

Ye gatsee:neyayantsa fugee zolam notasensuweshe gatsensuwee,dumars neyayeshen gatsensuwee,dumars aseshe aytasensarguwe achaman eusensuwee,echanemaned neshunagezew,hawush satenagon yefetan tayz ochee koyeshe ta yape bakoyan

Yohannes Wobie

Selk kuteree:0935171096

Tagaa E-mail:w27@gmail,com

መጠይቅ - አሚኛቅጽ

ጅማ ዩኒቨርሲቲ፤ ጠፍ ሳይንስ ኮሌጅ፤ ፋርማሲ ዲፓርትመንት፤ ደህረ ምረቃ ፕሮግራም

ይህ መጠይቅ የተዘጋጀወጠሚዛን ቴፕ ዩኒቨርሲቲ ቲችንግ ሆስፒታል በጨቅላ ህፃናትህክምና አሰጣጥ ሂደትና ዉጤት ለማጠናቀር ነዉ ፡፡

የመጠይቁ መለያ ቁጥር_____አድራሻ፤ ቀበሌ_____ **የገቡበት ቀን**----------

ክፍል አንድ፡ - የጨቅላ ህጻኑ እና የእናቱአጠቃላይሁኔታ

ተ.ቁ	ጥያቄ	መልስ	ይዝለሉ
101	እድሜዎ ስንት ነዉ?	_____(በዓመት)	
102	የጋብቻሁኔታ?	1. ያላገባች 2. ያገባች 3. ባሏየሞተባት 4. ባሏን የፈታች 5. የተለያየች 6. ሳታገባ አብራየምትኖር	
103	የመኖሪያ ቦታዎየት ነዉ?	1. ከተማ 2. ገጠር	
104	የትመህርት ደረጃዎስንት ነዉ?	1. ያልተማሪች 2. የመጀመሪያ ደረጃ 3. ሀለተኛ ደረጃየተማሪች 4. ኮሌጅና ከዛ በላይ	
105	የርስዎየስራሁኔታ ምንይነዉ?	1. የቤት እመቤት 2. የመንግስት ሰራተኛ 3. ነጋዴ 4. በግል ተቋም 5. የቀን ሰራተኛ 6. ተማሪ	
106	የህጻኑ አደማስንት ነዉ?	_____(በቀናት)	
107	የህጻኑ ፆታምንድነዉ?	1. ሴት 2. ወንድ	

ክፍል ሀለት፤ ከእናት ጠፍ ጋር የተያያዙ አጋላጭህኔታዎች

108	ስንት ህጻናት ወሊደዋል (ሞተወየ ተወለዱትንም ጨምሮ)?	_____(በቁጥር)	
109	የ ቅደመወሊድ ክትትል አግኝተዋል?	1. አዎ 2. አላገኘህም	
110	ሜላስዎ አዎ ከሆነ ስንት ጊዜ?	_____ጊዜ	
111	ህጻኑን የ ት ነ ወየ ወለዱት?	1. ቤት 2. ጠፍ ተቃም	
112	ሆስፒታል ወይም ጠጣያከሆነ ቦምን ነ ወየ ወለዱት?	1. በቀዶጥገ ና 2. በመካሪያ በመቃነ ዝ 3. በተፈጥሮ/ምጥ	
113	የ እነ ረሽርት ወሃ ከፈሰሰ በኋላ ምኩ ምንያህል ጊዜ ቆየ ብዎት?	_____በሰዓት	
114	የ እንሽርትወሃ ሰፈስ የ ተለየ / ማከፎ ጠረን ነ በረው?	1. አዎ 2. አልነ በረውም 3. ሌለ የ ጠቀሱ_____	
115	በዚህ ህጻን አርግዝና ጊዜየ ደምመፍሰስ ነ በር?	1. አዎ 2. አልነ በረም 3. ሌለ ይጥቀሱ	
116	በዚህ ህጻን እርግዝና ጊዜያባላዘር በሽታየ ሽንት ቱቦ መሚዝ ታመመላ በር?	1. አዎ 2. አልነ በረም 3. ሌለ የ ጥቀሱ_____	

ክፍል ሦስት፤ ከህጻኑ ጋር የተያያዙ አጋላጭህኔ ታዎች

117	የ እርግዝና እድሜውስንት ነ ው?	_____(በሳምንት)	
118	APDAR score?	1. በ 1 ደቂቃወኋላ___ 2. በ 5 ደቂቃወኋላ___	

119	ሲወለድክብደቱስንት ግራምነ በር?	_____ግራም	
120	ህጻኑ ሲወለድታፍኖ እርዳታተደርጎለት ነ በር?	1. አዎ ተደረገለት 2. አልተደረገለትም	
121	ህጻኑ ቀዶጥገና ተሰርቶለት ነ በር?	1. አዎ 2. አልተሰራለትም 3. ይግለጹ_____	
122	ህፃኑ አክስጅን ላይ ነ በር?	1. አዎ 2. አልነ በረም	
123	ህጻኑ በጉሮሮወየ መቖንፈሻ ቱቦ ገብቶለት ነ በር?	1. አዎ 2. አልገ ባለትም	
124	ህጻኑ ባፍንጫውጓፉ ቱቦ ገብቶለት ነ በር?	1. አዎ 2. አልገ ባለትም	
125	ህጻኑ በእምብርቱ ቱቦ ገብቶለት ነ በር?	1. አዎ 2. አልገ ባለትም	
126	ህጻኑ የሽንት ቱቦ ገብቶለት ነ በር?	1. አዎ 2. አልገ ባለትም	

DECLARATION

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

Name of the student: _____

Date._____ Signature _____

Approval of Advisor

Name of advisor: _____

Date._____ Signature _____

Approval of the examiner

Name of the examiner: _____

Date._____Signature _____