TREATMENT OUTCOME OF NEONATAL SEPSIS AND ITS PREDICTORS AMONG NEONATES ADMITTED TO PEDIATRIC UNIT OF JIMMA UNIVERSITY MEDICAL CENTER, SOUTH-WEST ETHIOPIA

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ABSTRACT

Background: Neonatal sepsis is a major cause of morbidity and mortality in newborns. It accounts more than one third of neonatal deaths in Ethiopia. Identifying, preventing, and prompt management of factors predicting this burden will reduce impacts associated with neonatal sepsis.

Objective: To assess treatment outcome of neonatal sepsis and its predictors among neonates admitted to pediatric ward of Jimma University Medical Center, South-West Ethiopia.

Methods: A Hospital based prospective cohort study was conducted at Jimma University Medical Center. Semi-structured questionnaire was used to collect data. The data was collected between May1 and July 31, 2018 G.C. Data was coded and entered intoEpi data4.2 then exported to the Statistical Package for Social Science 20 for analysis. Descriptive analysis was done to present baseline characteristics with Chi-squared test ($\chi 2$). Bivariate Cox regression was done to see associations between the dependent and independent variables. Multivariate Cox-regression analysis was conducted to evaluate the predictors of mortality. Variables having P-values < 0.05 was considered as statistically significant.

Results: The study included 201 neonates (62.2% were males) with clinically diagnosed sepsis patients admitted to pediatrics ward of Jimma University medical center. From this 45(22.4%) incidence of in hospital death were recorded. The mean length of hospital stay was 10.50 ± 7.237days. About 37.3% of neonatal sepsis patients developed in hospital complication. Male gender [AHR= 0.32, 95%CI, [0.16-.66], P=0.002], neonatal age at admission ≤7days (EONS) [AHR= 4.82, 95%CI, [1.82-12.78], P=0.002], urban residency of the family [AHR= 2.38, 95%CI, [1.13-5.02], P=0.023], maternal age >35years [AHR= 3.86, 95%CI, [1.50-9.87], P=0.005], convulsion [AHR= 2.87, 95%CI, [1.34-6.14], P=0.006], hypothermia [AHR= 4.16, 95%CI, [1.58-10.91], P=0.004], low red blood cell count [AHR= 3.65, 95%CI, [1.80-7.39], P<0.001], and thrombocytosis [AHR= 5.10, 95%CI, [1.94-13.40],P=0.001] were independent predictors of in hospital mortality.

Conclusion and Recommendation: Neonatal sepsis contributes high mortality**.** It is important to pay attention to septicemic babies with any of the identified predictors of mortality such as neonatal age at admission ≤7days (EONS), family urban residency, maternal age >35years, patients presented with convulsion and hypothermia at admission, low red blood cell count, and thrombocytosis.

Key Words: Neonatal sepsis, treatment outcome, Jimma university medical center, Ethiopia

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ACRONYMS AND ABBREVIATIONS

APGAR	Activity, Pulse, Grimace, Respiration
BE	Base Excess
BSI	Bacterial Severe Infection
C/S	Cesarean section
CoNS	Coagulase Negative Staphylococcus
DRP	Drug Related Problems
EONS	Early Onset Neonatal Sepsis
ESGA	Estimated Gestational Age
HIC	High Income Country
HR	Heart Rate
IMCI	Integrated Management of Childhood Illness
INR	Indian National Rupee
JUMC	Jimma University Medical Center
Kg	Kilogram
LBW	Low Birth Weight
LONS	Late Onset Neonatal Sepsis
LMIC	Low and Middle Income Country
MDG	Millennium Development Goal
ML	Milliliter
NICU	Neonatal Intensive Care Unit
NVD	Non-Vaginal Delivery
PNA	Post Natal Age
PROM	Prolonged Rupture of Membrane
PPROM	Prolonged Preterm Rupture of Membrane
QALY	Quality Adjusted Life Years

RM	Malaysian Ringgit
RR	Respiratory Rate
SDG	Sustainable Development Goal
STI	Sexually Transmitted Disease
SD	Standered Deviation
UTI	Urinary Tract Infection
USD	United States Dollar
USA	United States of America
WHO	World Health Organization
₦	Nigerian Naira

1. INTRODUCTION

1.1 Background

The neonatal period is the age starting from birth to 28 days of life (1). Due to the immaturity of their immune system, neonates tend to acquire infections easily. So, there is a likelihood of developing severe infection such as neonatal sepsis with a higher probability of unfavorable outcome (2). Neonatal sepsis is a clinical syndrome of bacteremia with systemic signs and symptoms of infection in the first 4 weeks of life and is a major cause of morbidity and mortality (3). It can be classified into two based on the postnatal ages at onset: early onset neonatal sepsis (EONS), which occurs in the first seven days of age, and late-onset neonatal sepsis (LONS), which occurs after the seventh day of age. EONS is caused by microorganisms from the maternal genital tract before or at the time of birth, while LONS is due to organisms acquired after delivery and considered nosocomial community acquired infections (4).

Neonatal sepsis can be defined by the presence of at least two clinical symptoms and at least two laboratory signs in the presence of or as a result of suspected or proven infection (i.e. positive culture, microscopy or polymerase chain reaction). Clinical signs and symptoms include: temperature greater than 38.5 °C or less than 36 °C, bradycardia, or tachycardia, reduced urinary output (less than 1 mL/kg/h), hypotension, mottled skin, impaired peripheral perfusion, skin and subcutaneous lesions, respiratory instability(apnea episodes or tachypnea episodes), gastrointestinal (feeding intolerance, poor sucking, abdominal distention), non-specific symptoms including irritability, lethargy and hypotonia. Laboratory findings include white blood cells (WBC) count: <4000 $x10^9$ cells/L or>20,000 $x10^9$ cells/L, immature to total neutrophil ratio (I/T) greater than 0.2, platelet count <100,000 $x10^9$ cells/L,C- reactive protein > 15 mg/L or procalcitonin ≥ 2 ng/ml, glucose intolerance confirmed at least 2 times, hyperglycemia (blood glucose >180 mg/dL) or hypoglycemia (glycaemia < 45 mg/dL)and metabolic acidosis (base excess (BE)<-10mEq) (5).

But, in resource-limited settings with limited and/or intermittent access to laboratory evaluations this definition is not workable. It is recommended that initiation of antibiotics should be prompted by clinical signs of possible serious bacterial infection (PSBI), a highly sensitive definition aiming to reduce the number of false negatives (i.e. missed cases of sepsis).World health organizations (WHO's) integrated management of childhood illness

(IMCI) guideline defines neonatal sepsis as presence of danger signs (not feeding well, convulsions, drowsiness or unconsciousness, movement only when stimulated or no movement at all, fast breathing ≥60 breaths/min, grunting, severe chest in-drawing, raised temperature >38°C, hypothermia <36.5°C or central cyanosis) and priority signs (severe jaundice, severe abdominal distension or localizing signs of infection) (6).

The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region even within the same hospital. This is due to the changing pattern of antibiotic use and changes in lifestyle (7). In high income countries (HIC), the most common causes of EONS are group B streptococcus (GBS) and Escherichia coli (E.coli). The remaining cases of EONS are caused by Staphylococcus aureus (S. aureus), coagulase-negative staphylococci (CoNS), listeria monocytogenes and other gram-negative bacteria (7).

In LONS (mainly in very-low-birth-weight infants), the main pathogens are CoNS, responsible for half of the episodes. Other important etiologic agents are E. coli, Klebsiella spp. and Candida spp. less common causes of LONS include S. aureus, Enterococcus spp. and Pseudomonas aeruginosa (6, 7). In Low and middle income country (LMIC), the commonest causes of neonatal bacteremia are: S. aureus, E. coli and Klebsiellaspp (8). GBS is responsible for only 2–8% of cases in LMIC. It is possible that infants with GBS infection are underreported, since this pathogen usually presents very early in life and infected newborns might die or be adequately treated before blood cultures or other relevant microbiological samples are obtained (9).

Worldwide, it is estimated that more than 1.4 million neonatal deaths annually are the consequence of invasive infections (10). Rates of infection vary by geographic region, resource endowment, maternal and infant risk factors. Neonatal sepsis results in death or major disability for 39% of those affected even with timely antimicrobial treatment (11). It remains one of the leading causes of morbidity and mortality both among term and preterm infants (12).

WHO recommends that serious bacterial infection or sepsis should be managed by administration of oxygen by nasal catheter in cyanosed infants, extensive fluid management and antimicrobials in combinations of penicillin or ampicillin and gentamicin. This regimen covers most likely causative bacteria. WHO also recommends hospitalization for suspected

cases of sepsis and ten or more days of parenteral therapy with penicillin/ampicillin and gentamycin for neonates with serious bacterial infections or sepsis. A change of antibiotics is recommended if the condition is not improving in 2-3 days after initiation of therapy (6, 13).

1.2 Statement of the problem

Globally, 5.9 million of under-five children die yearly: from these 2.7 million accounts neonatal mortality, 98.7%of these occur in developing region. In Africa, neonatal mortality rate ranges from 11 to 49 per 1000 live births in South Africa and Angola, respectively. Sub-Saharan countries shares 38.6% of neonatal mortality and 49.6% of under-five mortality globally. One of twelve children in sub-Saharan Africa die before his or her fifth birthday, far higher than the average ratio of 1 in 147 in high-income countries (1).

The decline in neonatal mortality from 1990 to 2015 has been slower than that of post-neonatal under-five mortality, which was 47.0% compared with 58.0%, globally (1).

Worldwide, from all under-five children death,7% is due to neonatal sepsis and it is estimated to cause 26.0% of all neonatal deaths (1, 14). Neonatal sepsis is highly prevalent in sub-Saharan Africa and contributes up to 69.0% of neonatal mortality in developing countries (15).

Ethiopia has achieved the millennium development goal (MDG) by reducing child death by more than two thirds over the past 20 years, but neonatal mortality rate remains high (16). In Ethiopia, neonatal mortality rate is 29 per 1000 live births, of these neonatal sepsis accounts more than one third of the case (17). In Jimma Zone, neonatal mortality rate is as high as 35.5 per 1000 live births, of these neonatal infections accounts 34.3% (18).

There are numerous complications associated with neonatal sepsis such as necrotizing enter colitis, vision impairment, impaired head growth, functional disability in terms of difficulties in standing, and locomotion eye-hand co-ordination or limb movement disorders that have long-term consequences for the neonates. It predisposes an infant to increased risk of future neurological impairment (19, 20).

In sub-Saharan Africa the estimated 5.29–8.73 million DALYs are lost annually due to neonatal sepsis, and the corresponding value of a statistical life method predicts an annual economic burden ranging from $10 billion to $469 billion (21).

The outcome in newborn sepsis has not changed particularly in the resource-poor parts of the developing world where the mortality rates remain high (22). Despite this huge burden, high-quality data from community-based epidemiological studies on etiology, risk factors, and

appropriate management are lacking from areas in which newborns experience the greatest mortality (23).

Focusing on neonatal mortality associated with infections such as neonatal sepsis is becoming increasingly important to achieve the Sustainable Development Goal (SDG) target on child survival because of the share of under-five deaths occurring during the neonatal period has been increasing particularly in high mortality countries such as sub-Saharan Africa (1).

So, this study aims to assess treatment outcome of neonatal sepsis and its predictors among neonates admitted to pediatrics unit of Jimma university medical center, South west Ethiopia.

1.3 Significance of the study

By 2030 sustainable development goal (SDG) targets to end preventable deaths (like deaths due to infections) of newborns and to reduce neonatal mortality to at least as low as 12 deaths per 1,000 live births worldwide (1).

So, the finding of this study will be used as inputs for clinicians, policy makers and program implementers at national, regional as well as local levels to design strategies to achieve sustainable development goal (SDG) targets of newborns. The study will also give some inputs on economic burden of neonatal sepsis from patient's perspective, which may encourage funding resources in this area. Furthermore, the study finding will be used as an input for future study.

2. LITERATURE REVIEW

2.1 Mortality and its associated factors

It possible to save most cases of neonatal sepsis related deaths if diagnosed early and treated aggressively with antibiotics and good supportive care. However, if early signs or risk factors are missed mortality increases. Residual neurological damage occurs in 15 to 30 % of neonates with septic meningitis. Mortality from neonatal sepsis may be as high as 50% for infants who are not treated (24).

A single Centre, prospective, observational study in Bosnia and Herzegovina reported that risk of death was significantly higher in the VLBW infected infants compared to the others (48% versus 12.2%). Mortality associated with sepsis (EOS and LOS) was 12.5%(25). Prospectively conducted study from Turkey revealed that low birth weight, mechanical ventilation and parenteral nutrition were significant risk factors for mortality and the mortality rate reported was 6.8% (26).

Retrospectively done case-control study in Thailand revealed that laboratory results including hyperglycemia and thrombocytopenia were significant contributors to fatality in neonatal sepsis. Among all clinical features, lethargy, apnea, poor feeding, hypothermia and jaundice were significantly associated with fatality. The reported mortality rate was 25.5% (27). A 6-Year retrospectively chart reviewed analysis in a neonatal care unit in Taiwan revealed mortality is higher in EONS (10% vs. 7% in LONS) with a mortality rate of 20% (28). Another prospective study in Northern Taiwan revealed that independent risk factors of sepsis-attributable mortality were infectious complications, history of one or more than one previous episode(s) of bacterial severe infection (BSI), and underlying secondary pulmonary hypertension in neonates; the reported mortality was 6.8% (29).

Retrospectively conducted cohort study in Mexico showed prematurity(gestational age ≤37 wks), low birth weight (≤2500 g), perinatal asphyxia, low Apgar score at birth (≤5), and the requirement of assisted ventilation or invasive medical or surgical procedures during the hospital stay emerged as independent factors for increment of mortality; the overall mortality rate of sepsis was 9.5 % (30).

Retrospectively conducted study in Malaysia revealed that patients having respiratory distress associated with apnea, grunting and cyanosis was the most common clinical presentation

identified (18.2%), followed by jaundice (10.7%) and these were associated with increment in death. The overall clinical outcomes of the treatment of neonatal sepsis showed that 88.4% of the patients were clinically stable on discharge and the mortality rate was 3.3 % (31).

A prospectively carried out study in Iraq revealed that age< 7 days, birth weight(Mean ± SD, 1.97 ± 0.67), gestational age(<37weeks), thrombocytopenia, neutropenia, positive blood culture for Klebsiella spp, prolonged capillary refilling time, sclerma and signs of dehydration were predictive factors of the outcome of death in neonatal sepsis. Overall in hospital mortality rate was 44.2% (32). A prospectively carried out study in Baghdad revealed death of neonate with early onset sepsis was more than in neonate with late onset sepsis (52.4% versus 47.6%), also the delivery at home, fever or infection during pregnancy and early rupture of membrane > 18 h were significantly associated with increment in death rate. Among the clinical features lethargy, convulsion, jaundice, bleeding tendency, temperature instability and diarrhea were significantly associated with increment in death rate. With an overall mortality of 26.3% (33).

Prospectively conducted descriptive study in India reported low birth weight babies (64.2%) and prematurity (64.2%) constitute major group and associated with increase in neonatal sepsis related mortality. An overall mortality rate was 28.0% (34). Other prospective studies in India raveled that patients needing chest compression, birth weight <1000 grams, total leukocyte count <5000cell/mm$^{\wedge 3}$, and platelet count <50000 (75%) were predictors of mortality. An overall mortality rate reported was 16.0% (35) premature rupture of membranes (PROM)>24 h, Apgar score <6 at 5 min, birth weight ≤1.5 kg, shock, and lethargy were proved to be independent predictors of mortality; with an overall mortality rate of 30% (36). Other retrospectively conducted studies in India showed low birth weight, prematurity, total high leukocyte count, and low platelet count were found to be significant independent risk factors for mortality in babies with sepsis; with overall mortality of 8.3% (37) prematurity, very low birth weight and male gender were factors associated with poor outcome; with overall mortality of 7.0 % (38) low birth weight and prematurity were significantly associated with mortality; reported mortality incidence of 28.3% (39).

Prospective study in Nigeria reported that deaths occurred in 36.0% of neonates with neonatal septicemia. Birth after prolonged labour, place of delivery, respiratory distress, poor cry, and convulsion were among the predictors of mortality (40). Other retrospectively conducted

studies in Nigeria, delivery outside health facility, babies with estimated gestational age (EGA) less than 32 weeks, weight less than 1.5 kg, temperature less than 38ºC, respiratory distress, abdominal distension, poor skin color, hypoglycemia, and infection with gram-negative pathogens were significantly associated with neonatal death. Multivariate analysis of these risk factors confirmed that EGA less than 32 weeks, respiratory distress, abdominal distension, poor skin color, and hypoglycemia had significant independent contributions to the occurrence of death among babies with culture-proven septicemia, over all out of 174 babies with septicemia, 32.2% were died (41) birth weight < 2500g, prolonged rupture of membranes (PROM), prolonged preterm rupture of membranes (PPROM), multiple gestation, an infectious clinical diagnosis, and frequent changes in antibiotics were identified as risk factors for mortality. Sepsis accounts a mortality rate of 15.7% (42).

A prospective cross sectional study conducted in Tanzania reported the overall mortality rate was 19%. Among the factors that predicted deaths were positive blood culture, gram negative sepsis and infection with ESBL or MRSA isolates (43). A prospective observationally carried out study in Sudan showed tachypnea (69.4%), abdominal distention (19.4%), cyanosis (12.9%), and temperature instability (11.3%), vomiting (9.7 %), lethargy (4.8%), fever (4.8%), poor cry (3.2%) were most common presentations reported and were associated with mortality. An overall reported mortality was 14.5% (44).

In Ethiopia studies on predictors of mortality in neonatal sepsis were limited. A prospectively study at Gondar University Hospital neonatal unit revealed that 24.1% of neonates with positive blood culture died compared to only 7.3% of those with negative blood culture (culture proven sepsis have high significant mortality). The overall mortality rate reported was 8.84 % (45). An institution based quantitative retrospective chart review study conducted in Bahirdar revealed the independent predictor of poor outcome of neonatal sepsis were; respiratory distress syndrome and history of meconium aspiration syndrome. Those neonates with respiratory distress syndrome were 74.2% more likely to develop poor outcome than neonates without respiratory distress syndrome. Meconium aspiration syndrome was significantly associated with poor outcome of sepsis. Neonates with meconium aspiration syndrome were 80.2% more likely to develop poor neonatal outcome than neonates without history of meconium aspiration syndrome.Overall4.0% of neonates with sepsis were expired in the hospital (46).

2.2 Factors associated with length of hospital stay and cost

Retrospective population-based cohort study in USA showed, from 158,907 newborns, mean duration of treatment was5.3days. The cost of admissions for infants born at ≥35 weeks started on antibiotics and discharged home after no more than 3 days of antibiotics was $76,692,713 or $646.5 per patient (47).Another study in USA reported neonates without risk factors treated with antibiotics with mean duration of antibiotics treatment and length of hospital stay 3.22±1.8, and 4.32±1.8 days respectively, whereas neonates with any risk factor treated with antibiotics with mean duration of antibiotics treatment and length of hospital stay 3.60±2.0,and 4.31±1.9 days respectively (48).

A prospective observational study in India reported patients recovered completely with the mean duration of definitive therapy being 8.57±2.38 days and the mean antibiotic acquisition cost 529.80±384.47 rupees. Over all 74% of neonatal septic patient were recovered completely while 26% of cases resulted in either death/ had a minimal improvement in their clinical condition (49).

Prospectively conducted study in southeast Nigeria showed neonatal sepsis accounts 61.3% of neonatal illness with duration of hospital admission (days) Mean ± SD (15.3±9.6) and causes (₦) 10,239±3,830drug related expenditure, (₦) 10,110±3,169 laboratory tests costs, (₦) 23,499±14,987hospital and utility expenditure and (₦) 42,611±19,011total cost of illness (50).

2.3 Neonatal sepsis related in hospital Complications

Descriptive study conducted in Pakistan revealed that disseminated intravascular coagulation (DIC) (73%), respiratory failure (48%), septic shock (1.7%), meningitis (1.7%), and symptomatic hypoglycemia (1.7%) were complications observed among EONS patients. most common cause of death was DIC, followed by respiratory failure. The reported case fatality rate was 40% (51).

2.4 Conceptual framework

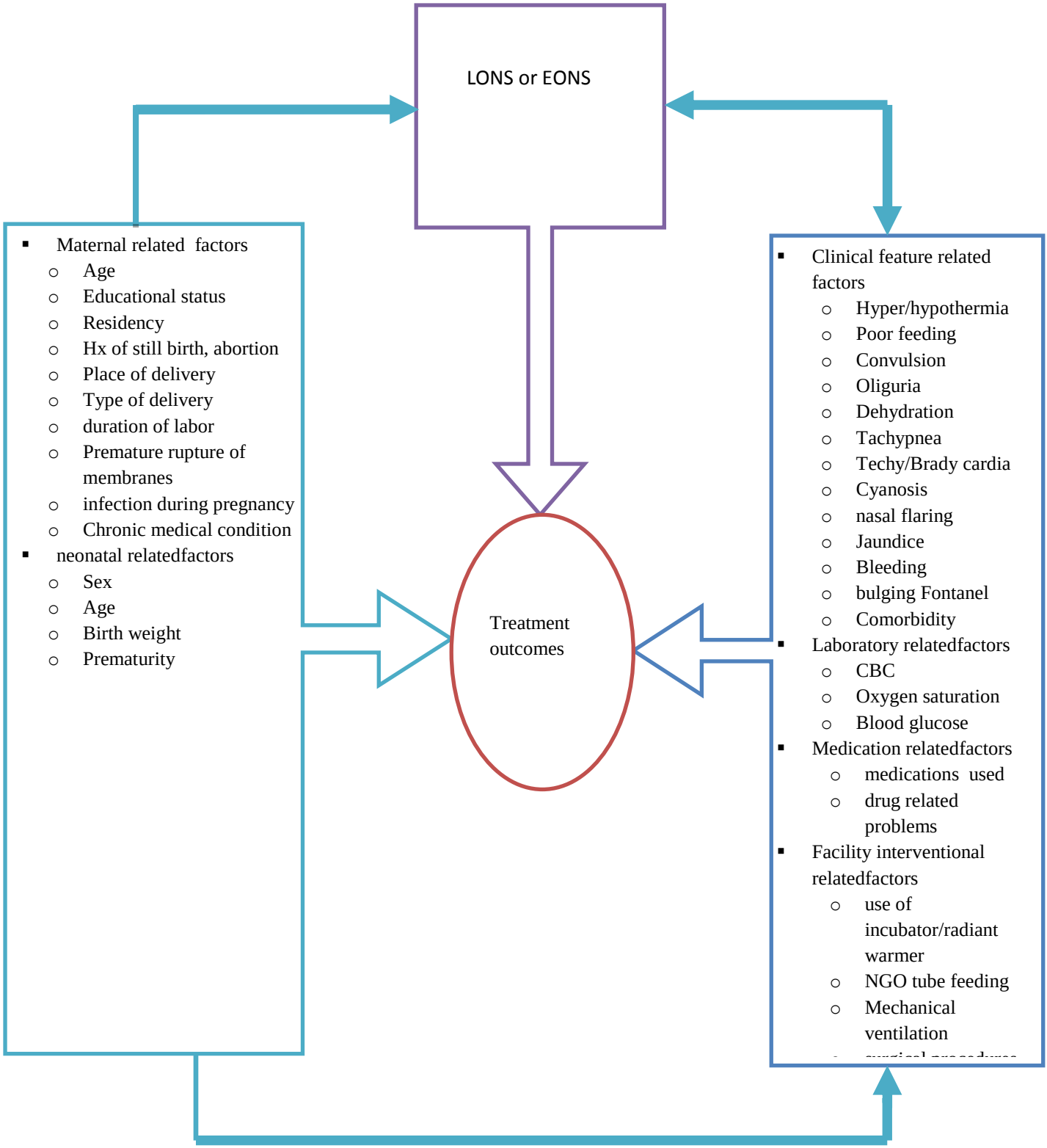

Figure 1: Conceptual framework

3. OBJECTIVES

3.1 General Objective

- To assess treatment outcome of neonatal sepsis and its predictors among neonates admitted to pediatrics unit of Jimma University Medical Center, Ethiopia, May- July, 2018.

3.2 Specific Objectives

- To determine the death associated with neonatal sepsis among neonates admitted to pediatrics unit of Jimma University Medical Center.
- To determine length of hospital stay of septicemic neonates among neonates admitted to pediatrics unit of Jimma University Medical Center, South-West Ethiopia.
- To determine complications associated with neonatal sepsis among neonates admitted to pediatrics unit of Jimma University Medical Center, South-West Ethiopia.
- To determine out of pocket cost for neonatal sepsis among neonates admitted to pediatrics unit of Jimma University Medical Center, South-West Ethiopia.
- To identify contributing factors of mortality associated with neonatal sepsis among neonates admitted to pediatrics unit of Jimma University Medical Center.

4. METHODS AND PARTICIPANTS

4.1 Study area and period

The study was conducted at Jimma University Medical Center (JUMC), a tertiary teaching hospital in Jimma town, Jimma zone, Oromia, South-West of Ethiopia. It is located 352 kilometers from Addis Ababa, the capital. The medical center has a total of more than 1448 staffs, of which 587 are supportive and 861 professionals. It is providing services for approximately 15,000 inpatient, 160,000 outpatient attendants, 11,000 emergency cases and 4500 deliveries in a year for clients coming to the hospital from the catchment population of about 15 million people. The pediatrics unit has six units that include neonatal intensive care unit (NICU), surgical unit, level I and II unit, nutritional rehabilitation unit and oncology unit. It has a total of 32 rooms (including 2 ICU room) with 110 beds. Investigational modalities including electrocardiography (ECG), echocardiography, CT-scan, basic hematologic and chemistry tests are readily available. The study was conducted from May1 to July 31, 2018 G.C.

4.2 Study Design

A hospital based prospective cohort study was conducted.

4.3 Population

4.3.1 Source population

- All neonates admitted to pediatric unit of JUMC during the study period.

4.3.2 Study population

- All neonates admitted with the diagnosis of sepsis at pediatrics unit of JUMC during the study period and fulfills inclusion criteria.

4.4 Eligibility Criteria

4.4.1 Inclusion criteria

- All neonates with features of suspected sepsis (diagnosed as either LONS or EONS) admitted at pediatric unit of JUMC, during the study period.
- Age <90 days.
- Their parents/families willing to give assent

4.4.2 Exclusion criteria

- Neonates died or discharged before initiation of treatment
- Cerebrospinal fluid analysis done within 24 hours of admission and suggestive for meningitis(i.e. total leucocyte count >20cells)

4.5 Sample size determination

Sample size was calculated by using the single population proportion formula

$n = [\frac{Za}{2}]^2$*p(1-P)$/d^2$

Where:

n=sample size

Z= Standard normal deviate at 95% confidence interval.

P= prevalence (P=0.5)

q= 1-p

d= expected margin of error

Z=1.96, p=0.5, 1-P=1-0.5=0.5, d=0.05

Thus;

n=[1.96]²*0.5(0.5)/0.0025 =384

Since the source population is less than 10,000, use the correction formula

nc=n/(1+n/N)

The estimated source population during the study period (3 month) is 380.

nc=384/(1+384/380) =191

Adding 5% contingency

The final target sample size planned was a minimum of 200 neonates with clinically suspected sepsis, 201 neonates were enrolled in this study.

4.6 Study variable

4.6.1 Dependent variable

- Treatment outcome

4.6.2 Independent variable

- Sociodemographic characteristics of mothers and neonates
- Obstetric data,
- Neonatal data
- In hospital interventional related factors
- Clinical features at admission, Co-morbidity
- Laboratory investigations
- Medication regimen, Drug therapy problems
- LONS or EONS

4.7 Data collection instrument

Semi-structured questionnaire was used for this study. This was prepared by reviewing patient chart and different literatures for important variables that used to assess treatment outcome and its predicting factors (26, 28, 30, 31, 33, 34, 52). Data was taken from both patients' medical chart and parents/caregivers of the patient.

4.8 Data collection process and management

Two data collectors (one B.Pharm and one BSc nurses) and one supervisor (pediatric resident) were trained on the detail of data collection tools/checklists for one day prior to data collection started. Then, data collection was started following written assent obtained from parents/caregivers. Then, sociodemographic data of the neonate and mother, and obstetric data was recorded for each study participant via face to face interview and reviewing medical charts. Medical charts were reviewed to gather data on medical assessment, laboratory and medications taken.

4.9 Data quality assurance

The questionnaires were translated from English to Afaan Oromo and Amharic, and back translated into English by independent person to assure its consistency. Data collection tool was tested on 10 (5%) of randomly selected patients prior to the main data collection started and then the necessary adjustment was done. Data was compiled, cleared, coded and checked for consistency. All steps in data collection and recording were closely monitored by the principal investigator and any gaps identified were immediately communicated to the data collectors

4.10 Data processing and analysis

The data was coded and entered into Epi data 4.2 then exported to Statistical Package for Social Science (SPSS) 20 for analysis. Descriptive analysis was done to present baseline charactestics of EONS and LONS patients with Chi-squared test ($\chi 2$). Continuous outcome variables were described with mean ± standard deviation. Kaplan Maier survival curve was done to see in hospital survival difference between sepsis types. Bivariate analysis was done to see associations between mortality and independent variables. Then, variables having P-value, <0.25 were a candidate for stepwise multivariate Cox regression analysis to evaluate independent predictors of mortality due to neonatal sepsis. Those variables having P-value, <0.05 was considered as statistically significant.

4.11 Outcome Measure and Validating Methods

Mortality (in hospital) after hospital admission of the patient was the clinical outcome of the study. Cohorts of septic neonates were followed starting from patient hospital admission until patient died in hospital / till hospital discharge. Death ascertainment for those who died during hospitalization was based on physician on duty note along with immediate causes of death.

4.11.1 Primary outcome

In hospital mortality: Cohorts of admitted neonates were followed during hospital stay till discharge. Mortality was considered as a primary outcome, which was recorded either from

patient chart or neonatal discharge registration data base. The time at which the patient admitted till outcome occurrence during the hospital stay was recorded.

4.11.2 Secondary outcome

Complication: In hospital complication were assessed via following patient starting from admission to discharge; if the patient develops new event after admission associated with sepsis and that is either confirmed by clinical assessment made by clinicians or laboratory parameters.

Length of hospital stay: length of hospital stay was recorded either from patient chart or neonatal discharge registration database.

Cost of illness: all out of pocket cost expending by the patient's family/care givers to seek their neonate's medical care. That includes transport cost, laboratory investigation cost, medications cost, and hospital bed costs cost.

4.12 Ethical considerations

Ethical clearance & approval was obtained from institution review board (IRB) of Jimma University. The data that were collected from JUMC pediatrics unit was preceded by a formal request letter from Jimma University. The raw data were not made available to any one and not used as the determinant of the participant. Strict confidentiality was assured through anonymous recording and coding of questionnaires and placed in safe place. Written assent was obtained from mothers/parents of neonates after explaining the purpose and objective of the study prior to data collection and no personal identity was disclosed.

4.13 Dissemination plan

The result of the study will be presented and disseminated to School of Pharmacy, Institute of Health of Jimma University, JUMC, different levels of health facilities, governmental and nongovernmental organizations and other concerned bodies. Attempts will also be made to publish the finding on peer reviewed journal.

4.14 Definition of terms

Neonatal sepsis: clinically suspected systemic infection characterized by the presence of danger signs such as poor feeding, convulsions, drowsiness or unconsciousness, movement only when stimulated or no movement at all, fast breathing ≥60 breaths/min, grunting, severe chest in-drawing, raised temperature >38°C, hypothermia <36.5°C or central cyanosis(6)during the 1st3months of age (53).

Early onset sepsis: clinically suspected systemic infection within 7 days of age (53).

Late onset sepsis: clinically suspected systemic infection between 7 & 90 days of age (53).

Treatment outcome: all events that is occurred during hospital stay that includes death, improved and discharged, length of hospital stay, complications developed, and costs.

Cost: all family/caregiver out of pocket costs to get care for their neonates with sepsis.

Complications: newly occurring medical events during hospital stay that are associated with severity of sepsis.

Leucopenia: white blood cell count less than 5000cell/mm^3 (24).

Leukocytosis: white blood cell count greater than 12x 10^3 cell/mm^3 (24).

Normal white blood cell count: white blood cell count between 5-12x 10^3 cell/mm^3 (24).

Low red blood cell count: red blood cell count<3500x 10^3 cell/mm^3 (25).

Normal red blood cell count: red blood cell count>3500x 10^3 cell/mm^3 (25).

Thrombocytopenia: platelet count less than 150x 10^3 cell/mm^3 (25).

Thrombocytosis: platelet count greater than 450x 10^3 cell/mm^3 (25).

Normal platelet count: platelet count between 150-450 x 10^3 cell/mm^3(25).

Hypoglycemia: blood glucose less than 44mg/dl (5).

Hyperglycemia: blood glucose greater than 180mg/dl (5).

Normal blood glucose: blood glucose between 44mg/dl and 180mg/dl (5).

Hypothermia:axiliary body temperature <36.5°C (6).

Hyperthermia:axiliary body temperature >38.0°C (6).

Normal body temperature:axiliary body temperature between 36.5°C and 38.0°C (6).

Low birth weight: birth weight less than 2.5kg (30).

Prolonged duration of labour: labor lasts for approximately 24 hours or more (54).

Preterm: neonates delivered at a gestational age less than 37 weeks (55).

Microcephaly: head circumference for age <3rd percentile (56).

Bradypnea: respiratory rate <40 beat/minute (6).

Tachypnea: respiratory rate >60 beat/minute (6).

Normal respiratory rate: respiratory rate between 40-60 beat/minute.

Tachycardia: heart rate >160 beat/minute (5).

Normal heart rate: heart rate between 100 and 160 beat/minute.

Drug related problem: an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (57).

5. RESULTS

5.1 Study participant's enrollment information

A total of 380 neonates were admitted to pediatrics unit of Jimma university medical center during the study period. Of these, 201 neonates with clinically diagnosed sepsis and who fulfilled inclusion criteria were included in this study. One hundred twenty two (60.6%) were early onset neonatal sepsis and 79(39.4%) were late onset neonatal sepsis patients.

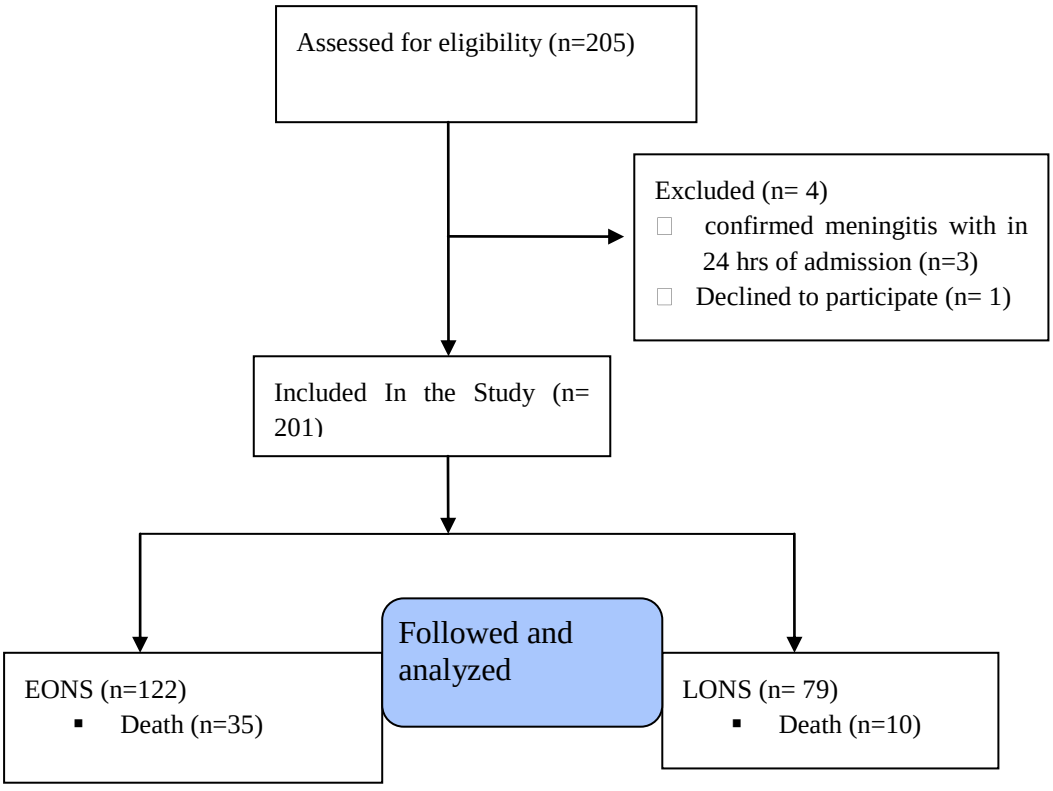

Figure 2: Patient flow chart

5.2 Baseline characteristics

5.2.1 Socio-demographic characteristics of neonates and mothers

From a total of neonatal sepsis case admission, 122(60.6%) were early onset neonatal sepsis. Majority of neonates in this study were males 125(62.2%). Most (55.7%) of the babies had birth weight ≥2.5kg. One hundred forty nine (74.1%) neonates were term neonates and 52(25.9%) neonates were preterm babies. One hundred seventy seven (88.1%) neonates mothers 'age were between 20-35 years (177, 88.1%). More than half of families were residing at urban area. About 39.3% of neonates' mother cannot read and write. (**Table1**).

Table 1: Neonatal and maternal socio-demographic characteristics of septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Variables		Types of Neonatal sepsis		Total:201	P-value
		EONS: 122(60.7%)	LONS: 79(39.3%)		
Gender of neonate	Male	75(37.3)	50(24.9)	125(62.2)	0.795
	Female	47(23.4)	29(14.4)	76(37.8)	
Birth weight	<2.5kg	42(24.4)	20(11.5)	62(35.5)	0.646
	≥2.5kg	72(64.3)	40(35.7)	112(64.5)	
Gestational age(wks)	Preterm	31(15.4)	21(10.4)	52(25.9)	0.853
	Term	91(45.3)	58(28.9)	149(74.1)	
Maternal age (years)	<20	1(0.5)	2(1.0)	3(1.5)	0.16
	20-34	109(54.2)	68(33.8)	177(88.1)	
	>34	12(57.1)	9(42.9)	21(10.4)	
Family residency	Urban	65(32.3)	41(20.4)	106(52.7)	0.848
	Rural	57(28.4)	38(18.9)	95(47.3)	
Maternal educational status	Cannot read & write	44(21.9)	35(17.4)	79(39.3)	
	Primary school	20(10.0)	23(11.4)	43(21.4)	0.16
	Secondary school	33(16.4)	14(7.0)	47(23.4)	
	College and above	25(12.4)	7(3.5)	32(15.9)	
Family occupation	Farmer	58(28.9)	40(19.9)	98(48.8)	
	Merchant	24(11.6)	13(6.5)	37(18.4)	
	Gov't employee	14(7.0)	8(4.0)	22(10.9)	0.279
	Non-gov't employee	22(10.9)	10(5.0)	32(15.9)	
	House wife	4(2.0)	8(4.0)	12(6.0)	

EONS, Early onset neonatal sepsis, LONS, Late onset neonatal sepsis

5.2.2 Obstetrics characteristics

About 194 (96.5%) of the mother had antenatal care follow up. Nineteen (9.5%) mothers had history of still birth and 11 (5.5%) mothers had history of abortion. Seventy nine (39.3%) of mothers had history of infection or fever during pregnancy. Thirteen (6.5%) mothers had chronic medical condition. About 121(60.2%) of neonates included in this study were delivered at hospital. More than three fourth of the neonate were delivered via spontaneous vaginal delivery. Seventy four (36.8%) neonates had prolonged rupture of membrane, there is

significant difference between EONS and LONS in terms of prolonged rupture of membrane (P<0.001). More than seventy five percent of mothers gave birth with normal duration of labor. (**Table 2)**

Table 2: Obstetrics characteristics of septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Variables		Types of Neonatal sepsis		Total	P-value
		EONS	**LONS**		
ANC follow up	Yes	118(58.7)	76(37.8)	194(96.5)	0.845
	No	4(2.0)	3(1.5)	7(3.5)	
History of still birth	Yes	13(6.5)	6(3.0)	19(9.5)	0.469
	No	109(54.2)	73(36.3)	182(90.5)	
History of abortion	Yes	7(3.5)	4(2.0)	11(5.5)	0.837
	No	115(57.2)	75(37.3)	190(94.5)	
Duration of labor(hrs)	Prolonged	34(16.9)	14(7.0)	48(23.9)	0.099
	Normal	88(43.8)	65(32.3)	153(76.1)	
Place of delivery	Hospital	86(42.8)	35(17.4)	121(60.2)	0.001
	Health Center	25(12.4)	23(11.4)	48(23.9)	
	Home	11(5.5)	19(9.5)	30(14.9)	
	Private Clinic	0	2(1.0)	2(1.0)	
Mode of delivery	Spontaneous Vaginal Delivery	86(42.8)	67(33.3)	153(76.1)	0.052
	Instrumental Vaginal Delivery	5(2.5)	1(0.5)	6(3.0)	
	Caesarean Section	31(15.4)	11(5.5)	42(20.9)	
Prolonged membrane rupture(>18 hrs)	Yes	57(28.4)	17(8.5)	74(36.8)	p<0.001
	No	65(32.3)	62(30.8)	127(63.2)	
History of infection during pregnancy	Yes	46(22.9)	33(16.4)	79(39.3)	0.564
	No	76(37.8)	46(22.9)	122(60.7)	
Maternal chronic medical condition	Yes	9(4.5)	4(2.0)	13(6.5)	0.515
	No	113(56.2)	75(37.3)	189(93.5)	

ANC- antenatal care

5.2.3 Clinical features

Among clinical features, most neonates had poor feeding, 182 (90.5%) at presentation. More than half of the neonates were presented with tachypneic appearance of respiratory rate. Other clinical features recorded during admission were subcostal/intercostal retraction (55.7.0%), grunting (55.2.0%), respiratory distress (35.8%), vomiting(22.9%),convulsion(20.4%), Irritability(12.4.0%), petechial bleeding (11.9%), jaundice(9.5%), septic rash (15,7.5%), and cyanosis (9,4.5%). Thirty nine (19.4%) neonates were microcephaly. Diarrhea, vomiting, subcostal/intercostal retraction, jaundice; petechial bleeding, cough, dehydration and heart rate were significantly differ between EONS and LONS patients. (**Table 3**)

Table 3: Clinical features of septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Clinical features		Types of Neonatal Sepsis		Total	P-value
		EONS	**LONS**		
Poor feeding	Yes	114(56.7)	68(33.8)	182(90.5)	0.081
	No	8(4.0)	11(5.5)	19(9.5)	
Diarrhea	Yes	4(2.0)	9(4.5)	13(6.5)	0.022
	No	118(58.7)	70(34.8)	188(93.5)	
Convulsion	Yes	28(13.9)	13(6.5)	41(20.4)	0.264
	No	94(46.8)	66(32.8)	160(79.6)	
Vomiting	Yes	15(7.5)	31(15.4)	46(22.9)	P<0.001
	No	107(53.2)	48(23.9)	155(77.1)	
Respiratory distress	Yes	45(22.4)	27(13.4)	72(35.8)	0.696
	No	77(38.3)	52(25.9)	129(64.2)	
SC/IC retraction	Yes	61(30.3)	51(25.4)	112(55.7)	0.042
	No	61(30.3)	28(13.9)	89(44.3)	
Grunting	Yes	62(30.8)	49(24.4)	111(55.2)	0.119
	No	60(29.9)	30(14.9)	90(44.8)	
Cyanosis	Yes	5(2.5)	4(2.0)	9(4.5)	0.740
	No	117(58.2)	75(37.3)	192(95.5)	
Jaundice	Yes	19(9.5)	0	19(9.5)	P<0.001
	No	103(51.2)	79(39.3)	182(90.5)	
Septic rash	Yes	9(4.5)	6(3.0)	15(7.5)	0.954
	No	113(56.2)	73(36.3)	186(92.5)	
Abdominal distension	Yes	15(7.5)	6(3.0)	21(10.4)	0.283
	No	107(53.2)	73(36.3)	180(89.6)	
Petechial bleeding	Yes	21(10.4)	3(1.5)	24(11.9)	0.004
	No	101(50.2)	76(37.8)	177(88.1)	
Difficulty of feces	Yes	10(5.0)	8(4.0)	18(9.0)	0.640
	No	112(55.7)	71(35.7)	183(91.0)	
Cough	Yes	4(2.0)	18(9.0)	22(10.9)	p<0.001
	No	118(58.7)	61(30.3)	179(89.1)	
Dehydration	Yes	15(7.5)	2(1.0)	17(8.5)	0.015
	No	107(53.2)	77(38.3)	184(91.5)	
Body temperature(°c)	Hypothermia	24(11.9)	6(3.0)	30(14.5)	0.063
	Hyperthermia	49(24.4)	37(18.4)	86(42.3)	
	Normothermia	49(24.4)	36(17.9)	85(42.2)	
Respiratory rate(beat/minute)	Bradypnea	8(4.0)	8(4.0)	16(8.0)	0.114
	Tachypnea	68(33.8)	52(25.9)	120(59.7)	
	Normal	46(22.9)	19(9.5)	65(32.3)	
Heart rate (beat/minute)	Tachycardia	10(5.0)	22(10.9)	32(15.9)	P<0.001
	Normal	112(55.7)	57(28.4)	169(84.1)	
Head circumference for age	Microcephaly	25(12.4)	14(7.0)	39(19.4)	0.628
	Normal	97(48.3)	65(32.3)	162(79.6)	
Co morbidity	Yes	61(30.3)	35(17.4)	96(47.8)	0.430
	No	61(30.3)	44(21.9)	105(52.2)	

5.2.4 Laboratory parameters

Out of 201 neonates enrolled, 59.5% of the neonates had leukocytosis; there was statistically significant difference between sepsis types (p=0.001). Seventy nine (39.5%) of neonates had low red blood cell count; from these more than half of them were diagnosed with EONS (P<0.001). More than half of the neonate (56.6%) had normal platelet count, of these 60(29.9%) and 53(26.4%) were EONS and LONS patients, respectively (p=0.004). Eighteen (9.0%) and 14 (7.0) patients had hyperglycemia and hypoglycemia respectively. Around three fourth (74.6%) of the neonate had arterial oxygen <90mmHg at admission.(**Table 4**).

Table 4: Laboratory parameter results of septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Laboratory Parameters		Types of Neonatal Sepsis		Total	P-Value
		EONS	**LONS**		
White blood cells	Leucopenia	15(7.5)	8(4.0)	23(11.4)	0.001
	Leukocytosis	83(41.3)	36(17.9)	119(59.2)	
	Normal	24(11.9)	35(17.4)	59(29.4)	
Red blood cells	Low Red Blood Cell	36(17.9)	43(21.4)	79(39.3)	P<0.001
	Normal	86(42.8)	36(17.9)	122(60.7)	
Hemoglobin	Low	16(8.0)	29(14.4)	45(22.4)	P<0.001
	Normal	106(52.7)	50(24.9)	156(77.6)	
Platelet count	Thrombocytopenia	49(24.4)	14(7.0)	63(31.3)	0.004
	Thrombocytosis	13(6.5)	12(6.0)	25(12.4)	
	Normal	60(29.9)	53(26.4)	113(56.3)	
Blood glucose	Hypoglycemia	11(5.5)	3(1.5)	14(7.0)	0.144
	Hyperglycemia	8(4.0)	10(5.0)	18(9.0)	
	Normoglycemia	103(51.2)	66(32.8)	169(84.0)	
Oxygen saturation	<90mmHg	86(42.8)	64(31.8)	150(74.6)	0.094
	≥90mmHg	36(17.9)	15(7.5)	51(25.4)	

5.2.5 Management

Ampicillin with gentamicin (188, 93.5%) was the most initial antibiotics used as initial antibiotics. Among the common non-antibiotic medications used, Paracetamol (17, 18.3%), Phenobarbital (11, 11.8%), and maintenance fluid (10, 10.8%) accounts higher. One hundred twenty eight (63.8%) patients were stayed in radiant warmer/incubator; there was statistically

significant difference between the sepsis types (p<0.001). More than half (52.2%) of EONS patients were feed via nasogastric tube, and 15.4% of LONS patients were feed via nasogastric tube (p<0.001). Eleven (4.5%) patients were under gone surgical procedure. Thirty four (16.9%) neonates were used mechanical ventilation; there was statistically significant difference between the sepsis types (p<0.001). (**Table 5**)

Table 5: Medications and other interventions used during management of septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Medications& interventions		Types of Neonatal Sepsis		total n=201	p-value
		EONS 122(60.6) n (%)	LONS 79(39.4) n (%)		
Ampicillin + Gentamicin		119(59.2)	69(34.3)	188(93.5)	0.01
Ceftriaxone + Gentamicin		1(0.5)	8(4.0)	9(4.5)	
Ampicillin + Ceftriaxone		2(1.0)	1(0.5)	3(1.5)	
Ceftazidime+Vancomycin		0(0.0)	1(0.5)	1(0.5)	
Other Medications(n=93)					
Paracetamol		3(3.2)	14(15.1)	17(18.3)	0.002
Dextrose		11(11.8)	3(3.2)	14(15.0)	
Phenobarbital		8(8.6)	3(3.2)	11(11.8)	
Maintenance Fluid		10(10.8)	0	10(10.8)	
Vitamin K		5(5.4)	0	5(5.4)	
Iron + Folic Acid		2(2.2)	3(3.2)	5(5.4)	
Cimetidine		2(2.2)	3(3.2)	5(5.4)	
Paracetamol + Vitamin K		4(4.3)	1(1.1)	5(5.4)	
Paracetamol + Phenobarbital		2(2.2)	2(2.2)	4(4.8)	
Phenytoin +Phenobarbital		2(2.2)	2(2.2)	4(4.4)	
Calcium Gluconate+phenobarbital		3(3.2)	1(1.0)	4(4.2)	
Phenobarbital + Vitamin K		3(3.2)	0	3(3.2)	
Insulin		1(1.1)	2(2.1)	3(3.2)	
Others		0	3(3.2)	3(3.2)	
Other interventional related factors (n=201)					
Stayed in radiant	yes	111(55.2)	17(8.5)	128(63.8)	p<0.001
warmer/incubator	no	11(5.5)	62(30.8)	73(36.2)	
Feed by	yes	105(52.2)	31(15.4)	136(67.7)	p<0.001
nasogastric tube	no	17(8.5)	48(23.9)	65(32.3)	
Surgical	yes	7(3.5)	2(1.0)	9(4.5)	0.283
procedure done	no	115(57.2)	77(38.3)	192(95.5)	
Mechanical	yes	30(14.9)	4(2.0)	34(16.9)	p<0.001
ventilation	no	92(45.8)	75(37.3)	167(83.1)	

5.2.6 In hospital survival curve for mortality among sepsis types

The Kaplan Meier survival curve showed that there is a significance difference of in hospital survival curve of mortality for LONS and EONS patients. LONS patients had an estimated median survival time of 30 days, while EONS patients had 24 days (p=0.009). (**Figure 3)**

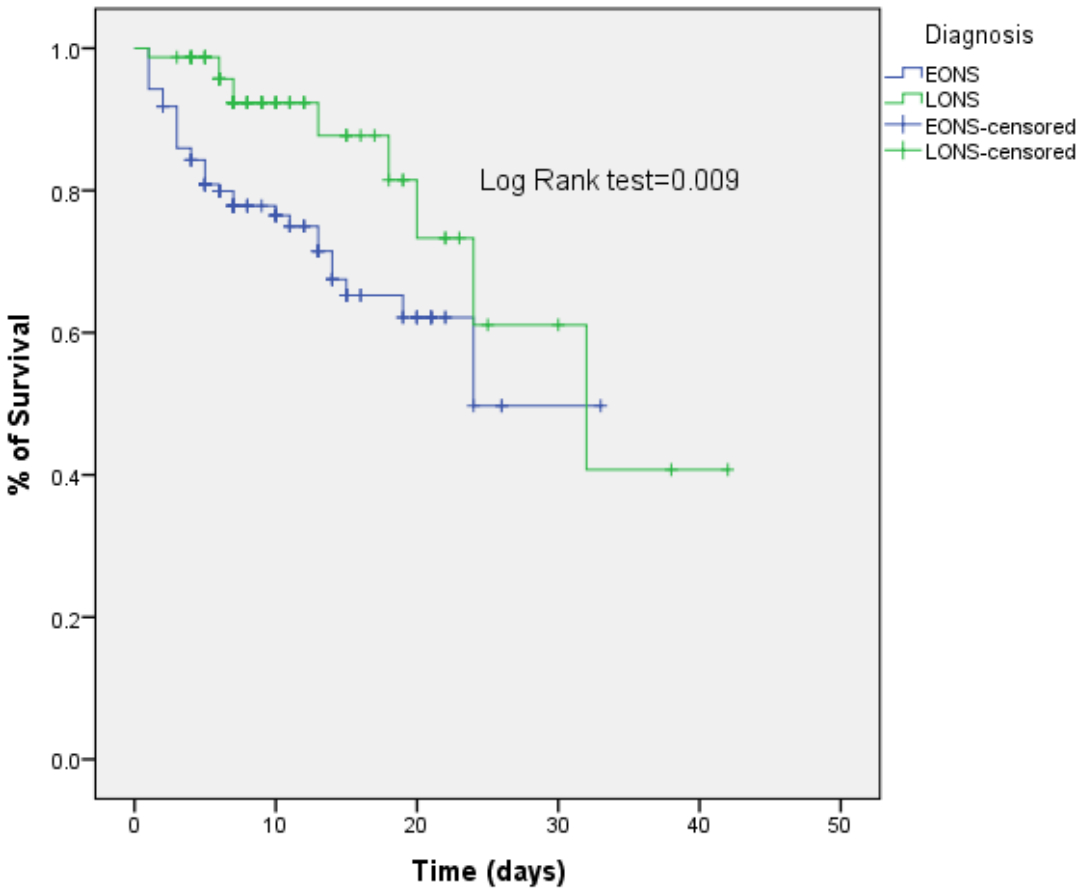

Figure 3: Kaplan Maier survival curve showing in hospital survival for EONS and LONS patients admitted to pediatrics unit of Jimma University Medical Center, May- July, 2018.

5.4 Treatment outcome

5.4.1 In hospital mortality

During the study period 14.4% (55/380) all cause neonatal mortality were recorded. From the total neonates admitted, 201 neonates with clinically diagnosed sepsis patients were enrolled; from these 45(22.4%) were died in the hospital. (**Figure 4**)

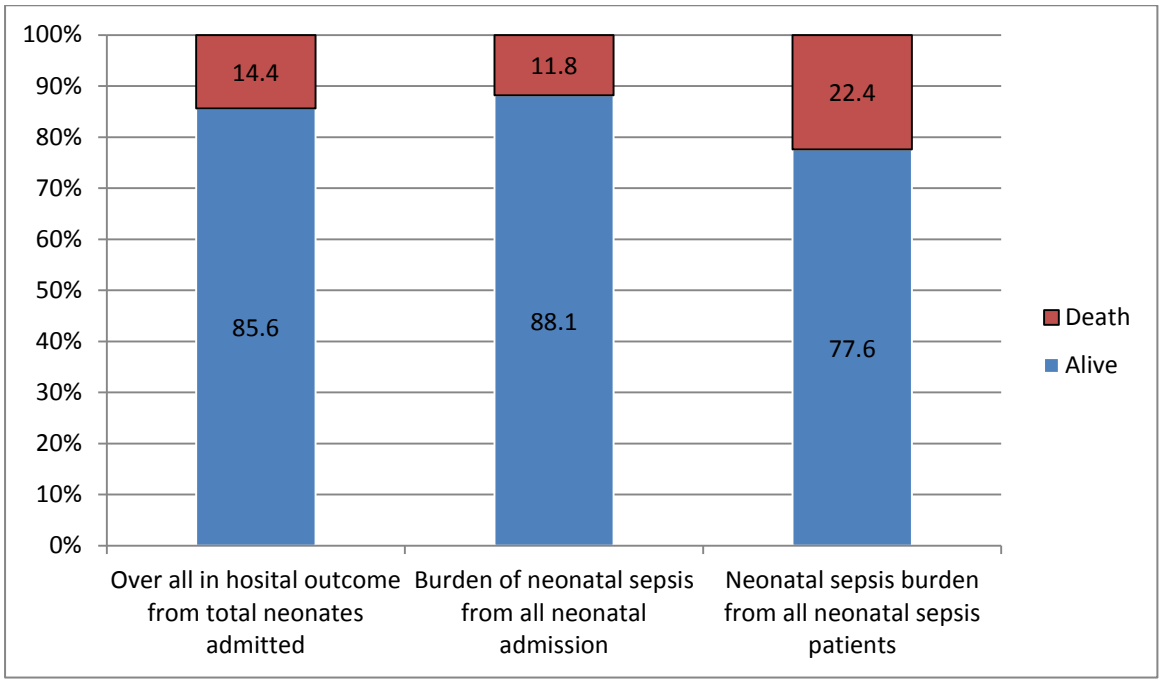

Figure 4: Burden of neonatal sepsis, among all neonates and septicemic neonates admitted to pediatrics unit of Jimma University Medical Center, May- July, 2018.

5.4.2 Length of hospital stay and cost

The mean± SD length of hospital stay was 10.50 ± 7.237days. With regard to total out of pocket cost for illness, it was estimated to be mean(±SD) of 513.98(±414.997) Birr; from this, laboratory investigation cost, medication/drug related cost, hospital bed cost, and transport cost was estimated to be mean(±SD) of 151.24(±187.429) birr, 205.19(±230.734)birr,135.71(±87.405)birr, and 124.45(±197.752) birr, respectively.

5.4.3 Incidence of in hospital complications

From a total of 201 neonates enrolled, 75 (37.3%) neonates were developed in hospital complication. From these seizure (30, 40.0%) accounts highest followed by disseminated intravascular coagulation (DIC) (17, 22.7%), and septic shock (13, 17.3%).

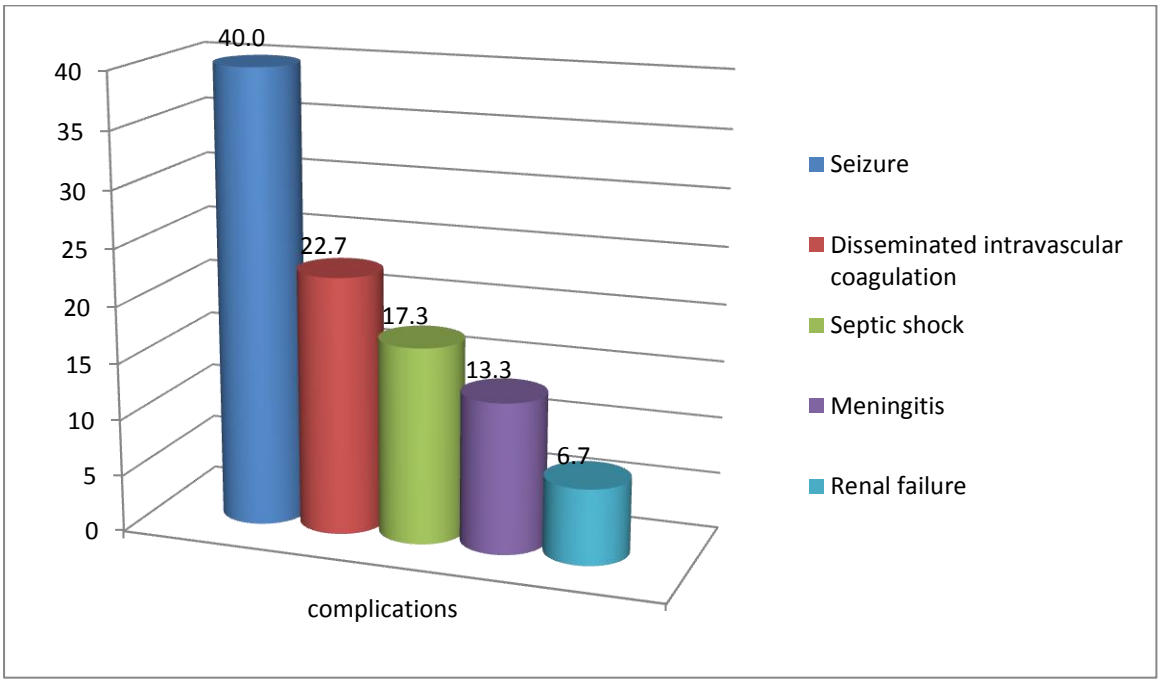

Figure 5: Distribution of in hospital complications among 75(37.3%) septicemic patients admitted to pediatrics unit of Jimma University Medical Center, May- July, 2018.

5.5 Factors associated with in hospital mortality

The association of independent variables with the dependent variable was investigated using both Bivariate and multivariate Cox regression techniques. In Bivariate Cox regression; male gender [unadjusted HR=0.53, 95%CI [0.29-0.95], P=0.031], low birth weight [unadjusted HR=2.96, 95%CI [1.57-5.60], P=0.001], and age at onset of diagnosis≤7days [unadjusted HR=2.48, 95%CI [1.22-5.04], P=0.012] were associated with sepsis related neonatal death. Among maternal socio-demographic related factors; urban residency [unadjusted HR=2.36, 95%CI [1.24-4.51], P=.009], and mothers having primary school educational status [unadjusted HR=0.34, 95%CI [0.11-0.99], P=0.05] were associated with sepsis related mortality. Among obstetrics related factors, prolonged rupture of membrane [unadjusted

HR=2.02, 95%CI [1.11-3.69], P=0.021], and maternal chronic medical condition [unadjusted HR=2.83, 95%CI, [1.25-6.37], P=0.012] were associated with mortality. (**Table 6)**

On multivariate analysis male gender [AHR= 0.32, 95%CI, [0.16-.66], P=0.002], and age at admission ≤7days (EONS) [AHR= 4.82, 95%CI, [1.82-12.78], P=0.002] were among independent predictors of in hospital mortality associated with neonatal sepsis. From maternal socio-demographic factors; urban residency [AHR= 2.38, 95%CI, [1.13-5.02], P=0.023], maternal age >35years [AHR= 3.86, 95%CI, [1.50-9.87], P=0.005], and secondary school educational status [AHR= 3.19, 95%CI, [1.14-8.89], P=0.027] were among independent predictors of in hospital mortality associated with neonatal sepsis. (**Table 6)**

Table 6: Bivariate and multivariate Cox regression hazard of risk factor analysis for mortality among septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Neonatal and maternal sociodemographic and obstetrics related factors		In hospital outcome		un adjusted HR[95%CI]	p-value	AHR[95%CI]	p-value
		Alive (156) n (%)	Death (45) n (%)				
Sex	Male	103(51.2)	22(10.9)	0.53[0.29-0.95]	0.031	0.32[0.12-0.66]	0.002
	Female	53(26.4)	23(11.4)	1		1	
Birth weight	<2.5kg	38(21.8)	24(13.8)	2.96[1.57-5.60]	0.001		
	≥2.5kg	96(55.2)	16(9.2)	1		1	
Neonatal age at admission	≤7days (EONS)	87(43.3)	35(17.4)	2.48[1.22-5.04]	0.012	4.82[1.82-12.78]	0.002
	>7days (LONS)	69(34.3)	10(5.0)	1		1	
Gestational age(weeks)	<37 Weeks(Preterm)	34(16.9)	18(9.0)	1.79[0.98-3.28]	0.057		
	≥37weeks(Term)	122(60.7)	27(13.4)	1			
Family residency	Urban	74(36.8)	32(15.9)	2.36[1.24-4.51]	0.009	2.38[1.13-5.02]	0.023
	Rural	82(40.8)	13(6.5)	1		1	
Maternal age	<20years	3(1.5)	0	.000	0.974		
	>35years	13(6.5)	8(4.0)	2.11[0.981-4.546]	0.056	3.86[1.50-9.87]	0.005
	20-35years	140(69.7)	37(18.4)	1		1	
Educational status of the mother	Illiterate	62(30.8)	17(8.5)	0.57[0.259-1.248]	0.159	2.20[0.82-5.93]	0.117
	Primary School	38(18.9)	5(2.5)	0.34[0.11-0.99]	0.05	0.64[0.190-2.196]	0.485
	Secondary School	34(16.9)	13(6.5)	0.83[0.36-1.90]	0.667	3.19[1.11-8.89]	0.027
	Collage And Above	22(10.9)	10(5.0)	1		1	
ANC follow up	No	6(3.0)	1(0.5)	1.513[0.208-11.008]	0.683		
	Yes	150(74.6)	44(21.9)	1			
Mode of	Caesarean	30(14.9)	31(15.4)	0.740[0.37-	.377		

delivery	Section			1.44]	
	Instrumental Assisted Vaginal Delivery	4(2.0)	2(1.0)	2.13[0.47-9.62]	.324
	Spontaneous Vaginal Delivery	122(60.7)	31(15.4)	1	
PROM >18hr	Yes	52(25.9)	22(10.9)	2.02[1.11-3.69]	0.021
	No	104(51.7)	23(11.4)	1	
Duration of labor (hour)	Prolonged	37(18.4)	11(5.5)	1.05[0.53-2.08]	0.888
	Normal	119(59.2)	34(16.9)	1	
Infection or history of fever during pregnancy	Yes	61(30.3)	18(9.0)	1.23[0.67-2.26]	0.487
	No	95(47.3)	27(13.4)	1	
Maternal chronic medical condition	Yes	6(3.0)	7(3.5)	2.83[1.25-6.37]	0.012
	No	150(74.6)	38(18.9)	1	

AHR-adjusted hazard ratio, HR-hazard ratio, CI-confidence interval, PROM-prolonged rupture of membrane

In Bivariate Cox regression; among clinical features presented at admission; convulsion [unadjusted HR=2.05, 95%CI, [1.10-3.81],P=0.022], abdominal distension [unadjusted HR=2.69,95%CI,[1.29 5.61] ,P=0.008], difficulty of feces[unadjusted HR=2.48, 95%CI, [1.10-5.59], P=0.028], and hypothermia[unadjusted HR=3.22, 95%CI, [1.44-7.20], P=0.004] were associated with neonatal sepsis case fatality. Among laboratory parameters low red blood cell count [unadjusted HR=2.88, 95%CI,[1.58 5.25] ,P=.001] ,leucopenia [unadjusted HR =3.83, 95% CI,[1.46-10.03] ,P=0.006] ,thrombocytopenia [unadjusted HR=2.22,95%CI ,[1.11-4.44],P=0.025], and thrombocytosis[unadjusted HR=4.56,95% CI, [2.09-9.92], P<0.001] were associated with mortality **.(Table 7)**

On multivariate analysis; convulsion [AHR= 2.87, 95%CI, [1.34-6.14], P=0.006], and hypothermia [AHR= 4.16, 95%CI, [1.58-10.91], P=0.004] were among clinical features predicting in hospital mortality associated with neonatal sepsis. Among laboratory parameters low red blood cell count [AHR= 3.65, 95%CI, [1.80-7.39], P=<0.001], and thrombocytosis [AHR= 5.10, 95%CI, [1.94-13.40], P=0.001] were among independent predictors of in hospital mortality. **(Table 7)**

Table 7: Bivariate and multivariate Cox regression hazard of risk factor analysis for mortality among septicemic neonates admitted to pediatrics ward of Jimma University Medical Center, May- July, 2018.

Clinical features, laboratory parameters, and interventional related variables		In hospital outcome		un adjusted HR[95%CI]	p-value	AHR[95%CI]	p-value
		Alive (156) n (%)	Death (45) n (%)				
Poor feeding	Yes	143(71.1)	39(19.4)	0.82[0.34-1.96]	0.663		
	No	13(6.5)	6(3.0)	1			
Diarrhea	Yes	10(5.0)	3(1.5)	0.871[0.26-2.84]	0.819		
	No	146(72.6)	42(20.9)	1			
Convulsion	Yes	25(12.4)	16(8.0)	2.05[1.10-3.81]	0.022	2.87[1.34-6.14]	0.006
	No	131(65.2)	29(14.4)	1		1	
Vomiting	Yes	37(18.4)	9(4.5)	0.95[0.45-1.98]	0.892		
	No	119(59.2)	36(17.9)	1			
Irritability	Yes	16(8.0)	9(4.5)	1.75[0.84-3.66]	0.132		
	No	140(69.7)	36(17.9)	1			
Respiratory distress	Yes	56(27.9)	16(8.0)	1.019[0.55-1.87]	0.952		
	No	100(49.8)	29(14.4)	1			
Grunting	Yes	88(43.8)	23(11.4)	0.72[0.39-1.31]	0.285		
	No	68(33.8)	22(10.9)	1			
Cyanosis	Yes	7(3.5)	2(1.0)	1.34[0.32-5.58]	0.685		
	No	149(74.1)	43(21.4)	1			
Jaundice	Yes	12(6.0)	7(3.5)	1.87[0.83-4.20]	0.129		
	No	144(71.6))	38(18.9)	1			
Septic rash	Yes	10(5.0)	5(2.5)	1.876[0.73-4.77]	0.187		
	No	146(72.6)	40(19.9)				
Abdominal distension	Yes	12(6.0)	9(4.5)	2.69[1.29-5.61]	0.008		
	No	144(71.6)	36(17.9)	1			
Petechial bleeding	Yes	19(9.5)	5(2.5)	0.73[0.28-1.88]	0.521		
	No	137(68.2)	40(49.9)	1			
Difficulty of feces	Yes	11(5.5)	7(3.5)	2.48[1.10-5.59]	0.028		
	No	145(72.1)	38(18.9)	1			
Cough	Yes	20(10.0)	2(1.0)	0.36[0.08-1.51]	0.166		
	No	136(67.7)	43(21.4)	1			
Dehydration	Yes	13(6.5)	4(2.0)	1.10[0.39-3.08]	0.855		
	No	143(71.1)	41(20.4)	1			
Respiratory rate category	Bradypnea	11(5.5)	5(2.5)	1.09[0.55-2.17]	0.424		
	Tachypnea	92(45.8)	28(13.9)	1.09[0.55-2.17]	0.796		

	Normal Respiratory	53(26.4)	12(6.0)	1			
Temperature (°c)	Hypothermia	17(8.5)	13(6.5)	3.22[1.44-7.20]	0.004	4.16[1.58-10.91]	0.004
	Hyperthermia	65(32.3)	21(10.4)	1.973[0.95-4.09]	0.068	2.05[0.88-4.75]	0.095
	Normothermia	74(36.8)	11(5.5)	1		1	
Heart rate(beat/minute)	Tachycardia	27(13.4)	5(2.5)	0.62[0.24-1.58]	0.318		
	Normal	129(64.2)	40(19.9)	1			
Co morbidity	Yes	70(34.8)	26(12.9)	1.43[0.79-2.58]	0.242		
	No	86(42.8)	19(9.5)	1			
	Yes	51(25.4)	24(11.9)	1.60[0.88-2.90]	0.117		
Complications							
	No	105(52.2)	21(10.4)	1			
White blood cells	Leucopenia	12(6.0)	11(5.5)	3.83[1.46-10.03]	0.006	2.39[0.76-7.45]	0.132
	Leukocytosis	92(45.8)	27(13.4)	1.67[0.72-3.86]	0.225	0.90[0.33-2.44]	0.837
	Normal	52(25.9)	7(3.5)	1		1	
Red blood cells	Low Red Blood Cell	52(25.9)	27(13.4)	2.88[1.58-5.25]	0.001	3.65[1.80-7.39]	P<0.001
	Normal	104(85.2)	18(14.8)	1		1	
Hemoglobin	Low	31(15.4)	14(7.0)	0.59[0.31-1.12]	0.107		
	Normal	125(62.2)	31(15.4)	1			
Platelet count	Thrombocytopenia	44(21.9)	19(9.5)	2.22[1.11-4.44]	0.025	1.47[0.65-3.31]	0.346
	Thrombocytosis	13(6.5)	12(6.0)	4.56[2.09-9.92]	P<0.001	5.10[1.94-13.40]	0.001
	Normal Platelet Count	99(49.3)	14(7.0)	1		1	
Blood glucose	Hypoglycemia	8(4.0)	6(3.0)	1.89[0.790-4.56]	0.152		
	Hyperglycemia	15(7.5)	3(1.5)	0.67[0.20-2.18]	0.504		
	Normoglycemia	133(66.2)	36(17.9)	1			
Staying in radiant warmer/incubator	Yes	94(46.8)	34(16.9)	1.987[0.999-3.951]	0.050		
	No	62(30.8)	11(5.5)	1			
Feeding via nasogastric tube	Yes	98(48.8)	38(18.9)	2.493[1.111-5.597]	0.027		
	No	58(28.9)	7(3.5)	1			
Surgical procedure done	Yes	7(3.5)	2(1.0)	0.814[0.195-3.406]	0.778		
	No	149(74.1)	43(21.4)	1			
Use of mechanical ventilation	Yes	21(10.4)	13(6.5)	1.725[0.894-3.327]	0.104		
	No	135(67.2)	32(15.9)	1			
DRP	Yes	132(65.7)	41(20.4)	1.90[0.68-5.34]	0.218		
	No	24(11.9)	4(2.0)	1			

DRP-drug related problems

6. DISCUSSION

The findings of this study show that neonatal sepsis is common and contributes to mortality among neonates admitted to pediatrics ward of Jimma University Medical Center. In this study, the overall neonatal mortality was 14.4% (55/380), higher in neonates with sepsis (22.4%) as compared to those without (5.6%). This finding is both higher and lower in compared with other studies from developing and developed countries (25-46, 58). These differences in mortality rate in neonatal sepsis among different countries may be explained by many factors such as socioeconomic, geographical and racial factors, use of ventilators, different strains of microorganisms and use of different antibiotics.

Studies in Ethiopia, from Gonder (45) [8.84%] and Bahirdar (46) [4.0%], reported lower neonatal mortality rate in comparison with our finding. Lower rates of mortality were also reported from other East Africa studies, Tanzania(43), and Sudan (44); and other reports from Bosnia and Herzegovina (25),Turkey (26),Taiwan (28, 29), Mexico (30),Malaysia (31), India (35, 37, 38),and Nigeria (42). It is highly possible that the case fatality rate in septic high-risk babies might improve if intensive care provided in resource-poor settings. Other reason for variation may be due to variation in quality of life and hospital services in different countries. It is tempting to postulate that the difference in mortality rates may be relied on differences in the facilities available for the care of these critically ill babies. Neonatal mortality associated with sepsis in this study is also lower in compared with other previously done studies in Thailand (27), Iraq (32),Baghdad (33), India (34, 36, 39), and Nigeria (40, 41). Collectively, these finding reflect the significant contribution of neonatal sepsis in neonatal mortality worldwide.

In this study the mean length of hospitalization among septicemic babies were 10.50 ± 7.237days. This is differ when compared with studies in USA, a study in India, and a study in Nigeria, mean of length hospital stay were 5.3 days, 4.31±1.9 days, ,8.57±2.38 days, and 15.3±9.6 days, respectively (47-50). This difference may be explained by difference in management approach, based on culture finding and antibiotic susceptibility pattern in these setting, while in our setting management is empirical.

Seventy five (37.3%) of neonates enrolled this study developed sepsis related in hospital complication. Seizure (40.0%), disseminated intravascular coagulation (DIC) (22.7%), and septic shock (17.3%) were the common complications identified. These patterns of

complication differ in comparison to other study reported by Sheikh AM et.al (51) Disseminated intravascular coagulation (dic) (73%),respiratory failure (48%), and septic shock (1.7%). This difference may be explained by difference in diagnostic approach of complications associated with neonatal sepsis.

A strong statistical association was seen between neonatal age at admission (early onset of neonatal sepsis vs. late onset of neonatal sepsis) and mortality. The risk of death were more than fourfold higher in those early onset neonatal sepsis patients when compared to late onset neonatal sepsis patients during hospital stay. A result is similar to previous studies in India (32) and Bagdad (33); this is expected considering lower birth weights and diminished immune response in the younger age group. The early onset sepsis is mainly related to maternal genito-urinary tract infection while late onset sepsis is mainly related to longer hospital stays with nosocomial infections and the use of invasive devices (4); this allows differ in acquiring etiologies having different virulence for early and late onset sepsis. Another possible reason for our finding is difference in the risk could be due to admission of more patients with early onset sepsis.

In this study, statistically significant association were seen between gender and neonatal mortality from neonatal septicemia, male neonates showed less probability to die compared to female neonates during follow up, resulting in 68% risk reduction in male gender. A result different to other done by Trotman H et.al (38); this might be due to biological difference or might be due to small sample size in this study.

Residency of the parent was statistical associated with survival outcome; patients from families residing at urban had more than twofold increase risk to die than neonates from parents residing in rural area. No previous report found on residency of the family and survival outcome among septicemic neonates, our finding might be explained by due to higher proportion of population in urban seeks more medical attention for their newborn at different health facility which in turn may facilitate acquiring resistant and virulence nosocomial etiologies. Another possible explanation may be more mothers from urban bring their critically ill neonates at this medical center during study period.

More than one third of neonates born from a maternal age of >35 years were died, which is statistically significantly associated with neonatal sepsis related mortality in multivariate Cox regression analysis. Neonatal sepsis patients born from a maternal age >35 years had twofold

higher risk of death than those born from age between 20-35 years. Previously conducted study in Tanzania identified teenager mothers as a predictor of overall neonatal mortality (59). Our finding might be explained by as the age increases complications associated with pregnancy will also increase.

In this study, convulsion was among clinical features that were significantly associated with mortality; patients presented with convulsion were about three times at higher risk of death in compared with those without this feature. Previous study from Baghdad (33) reported similar finding. Neonatal convulsion increases structural brain lesions that include hemorrhage (intracerebral, subarachnoid, intraventricular), infarctions, and congenital anomalies of the brain, this affects overall physiological and hemodynamic stability (60, 61). Another possible reason for increases an acute outcome like mortality is an acute neonatal encephalopathy (includes classic hypoxic-ischemic encephalopathy, both ante- and intrapartum) (61).

In this study, hypothermia was another clinical feature that was significantly associated with neonatal sepsis related case fatality; neonates presented with hypothermia had four fold increase risk of death in compared with normothermic neonates. Our finding is consistent with previous studies in Thailand, Baghdad and Sudan (27, 33, 44). Hypothermia may be caused by environmental factors, disorders that impair thermoregulation like infections (e.g. neonatal sepsis). This reaction increases the metabolic rate and oxygen consumption 2- to 3-fold. Thus, in neonates with respiratory insufficiency (eg, the preterm infant with respiratory distress syndrome), cold stress may also result in tissue hypoxia and neurologic damage; increases the risk of dysfunction of different organs, including acute renal failure and may lead to coagulopathy and finally mortality (62).

In this study, patients having low red blood cell count had more than three times higher risk of death in compared with those having normal red blood cell count. This may be due to erythropoiesis decreases after birth as a result of increased tissue oxygenation due to the onset of breathing and closure of the ducts arteriosus, and a reduced production of erythropoietin (EPO)(63).Red blood cell survival in newborn term infants is approximately 60 to 80 days but infections like sepsis increases susceptibility to oxidant injury, may contribute to shortened red cell survival in the neonate and this may further worsen hypoxemia related cellular death (64, 65).

In this study, patients having higher platelet count (thrombocytosis) were five times at higher risk of death than neonates with normal platelet count during hospital stay. Secondary or reactive thrombocytosis in neonate results from increased thrombopoiesis, as a reactive process due to an underlying infection, and inflammation (66).

Study Strengths

This study has important strengths. Since the study is conducted prospectively; diverse variables were included in the study including neonatal related, maternal related and other facility based interventional factors; some of which was missed in previous literatures. There was no selection bias when babies admitted to facilities with neonatal sepsis were studied.

Study Limitations

We also acknowledge some limitations of this work. This study missed some important variable such as previous antibiotics exposure, Apgar score, and referral source of the patient. This study lacks data on microorganisms including culture findings, drug resistance, and sensitivity pattern. The study misses intangible cost. Lastly, because the study was conducted at a single site in Ethiopia, which consists of many diverse states, the findings may not be representative of the entire community and country.

7. CONCLUSION

Neonatal sepsis contributes high neonatal mortality. Neonatal sepsis patients have also other burdens including longer length of hospital stay, significant in hospital complications and have economic burden on patient's family. Neonatal age at admission ≤7days (EONS), family urban residency, septicemic babies from maternal age of >35years, neonates presented with convulsion and hypothermia, low red blood cell count, and thrombocytosis were significantly found to predict in hospital mortality.

8. RECOMMENDATION

Jimma University Medical Center

Developing appropriate strategies, in preventing /reducing neonatal sepsis, and implementation is very crucial to reduce neonatal sepsis burden at JUMC. Maintaining an appropriate environmental temperature in the neonatal room is critical for preventing hypothermia in NS patients and associated mortality.

Clinicians

Early detection and appropriate management of patients' presentation like convulsion, hypothermia and low red blood cell count is necessary to reduce neonatal sepsis related mortality.

Ethiopian ministry of health

Strengthen neonatal care particularly on neonatal sepsis is vital for achieving SDG targets. Encouraging governmental and nongovernmental organization to exert their effort on neonatal care is very important.

Researchers

Further study is required to reduce community as well as national burdens associated with neonatal sepsis particularly on microorganisms including culture findings, drug resistance, and sensitivity pattern which is not covered yet.

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ANNEX I: PATIENT INFORMED CONSENT SHEET

Jimma University Institute of Health,

School of Pharmacy

Patient Information Sheet

Study Title: treatment outcome of neonatal sepsis and its predictors among neonates admitted to pediatrics unit of Jimma University Medical Center.

Name of the investigator: Mengist awoke yizengaw

Name of study area: Jimma University Medical Center (JUMC)

Research budget covered by: Jimma University

Research objective: To assess treatment outcome of neonatal sepsis and its predictors among neonates admitted to pediatric unit of Jimma University Medical Center, South-West Ethiopia..

Study procedure: Data was collected both from the patient's caregiver and active patient chart using checklist developed by principal investigator. Data collectors extracted data on socio-demography, clinical and laboratory. These data were kept confidential in a way that no other person had access. If patients were willing to participate in this project, they were informed the need to understand and sign the agreement form

Risks: this study didn`t imposed any significant risk on patients.

Participant's right: The patients caregiver had a full right to withdrawal from this study at any time and not to allow review of his/her chart, or to skip any question that he/she does not want to answer.

Benefit: the outcome of this study was expected to identify burden and predictors associated with neonatal sepsis. It is vital for future planning on reducing this burden

Incentives: Patients were not provided any specific incentive for taking part in the research other than acknowledgment.

Confidentialities: The study result didn`t included patient's name, and any personal details that may lead to identification of patient. The information collected during the study period

were kept confidential. Information that will be collected from the study will be stored in a file, which will not have your name on it, but a code number assigned to it.

Contact address to access the principal investigator (PI): contact address was provided to contact the principal investigator if there is any inconvenience or doubt about the study.

Mr. mengist awoke yizengaw:

Phone No: 09143567977, E-mail: mengist93@gmail.com

Patient Written Consent Form

Dear Sir/madam;

My name is Mengist Awoke yizengaw. I am Master's Degree student in clinical pharmacy in Jimma University. As part of my academic requirements, I am expected to conduct a research. This study is aimed to assessing treatment outcome of sepsis and its predictors among septicemic neonates admitted to pediatrics unit of Jimma University Medical Center. The information obtained from this study will facilitate clinicians to improve the provision of care and policy makers in their planning activities. Your participation in this study is voluntary and all data provided will be treated as confidential and anonymous. You have a right not to participate in this study. Therefore; we politely request your cooperation to participate in this study. But your input has great value for the success of the objectives the research.

So, do you agree? 1. Yes 2. No

Thank you for your cooperation!!!

Consent Form

While putting my signature in this sheet, I am giving my consent to participate in this study. I have been informed that the purpose of this study is assessing treatment outcome of neonatal sepsis and its predictors among neonates and I have understood that participation in this study

is entirely voluntarily. I have been told that my answers and other profiles 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 participate in this study will have no effect on me. I understood that participation in this study does not involve risks.

Participant/caregiver`s	***Data collector***	***Supervisor***
Sign……..	Sign……	Sign……
Phone number: …….. ..	Phone number……	Phone number…….

Patient Information Sheet: Amharic Version

የተሳታፊዎች መረጃ ቅጽ

ዋናተመራማሪ፡ መንግስት አወቀ ይዘንጋው

ምርምሩየ ሚካሄድበት ቦታ፡ ጅማ ዩኒቨርስቲ የህክምና ማዐከል

የጥናቱን ወጪ የሚሸፍነው ድርጅት፡ ጅማ ዩኒቨርስቲ

የጥናቱ ዓላማ፤በተጠቀሰው የጤና ማዐከል እና ሆስፒታች ሜዲካል ክፍል ዉስጥተኚተዉ የሚታከሙ ነናታል ስፒሰስ ህ ሙማን የህክምና ዉጤት በተመለከተጥናት ለማድረግ

የአሰራር ቅደም ተከተል፡በዚህ ጥናት እንዲሳተፉ በአክብሮት አየጋበዝን ፍቃደኛ ከሆኑ የመግባቢያ ስምምነትዎን ተረድተው ይፈርማሉ፡፡በመጀመሪያ ስነ-ህዝብ እና ማህበራዊ ጉዳዮችን የተመለከቱ ጥያቄዎችን፣ በመቀጠልም ከህምሞ ጋር የተያያዙ ጥያቄዎችን እንጠይቆታለን፡እንዲዉም የተለያዩ የላብራቶሪ ዉጤቶችን ከካርዶ እንዎስዳለን፡፡

በጥናቱ ምክንያት ሊደርስ የሚችል ጉዳት፡ በጥናቱ በመሳተፍዎ የሚደርስብዎት ጉዳት የለም፡፡

በጥናቱ ያለመሳተፍ ወይም ከገቡ በኋላ የመውጣት መብት ፡ጥናቱ በሙሉ ፍቃደኝነት ላይ የተመሰረተ ነው፡፡በጥናቱም የመሳተፍ ግዴታ የለብዎትም፡፡ለመመለስ ያልፈለጉትን ጥያቄ ማለፍ ይችላሉ ፡፡ በተጨማሪ ባለመሳተፍዎ የሚያገኙት የጤና አገልግሎት ጥቅም ላይ ምንም አይነት ችግር አያስከትልብዎትም፡፡እንዲሁም በማንኛውም ሰዓት ከተሳታፊነት ማቋረጥ ይችላሉ፡፡

በጥናቱ መሳተፍ ያለው ጥቅም፡ በዚህ ጥናት ቢሳተፉ ነናታል ስፒሰስ በሽታ ህክምና ዉጤት ለማሻሻል እና ለመከላከል ይረዳል፡፡

ጥቅማጥቅም፡ በጥናቱ ላይ በመሳተፍዎ ከምስጋና በዘለለ የሚያገኙት የክፍያ ጥቅም አይኖርም፡፡

ሚስጥራዊነት፡በዚህ ምርምር የሚገኝ ማናቸውም መረጃ በሚስጢር ይጠበቃል፡፡ የተሳታፊው ስም ኣይፃፍም፡፡ ከተመራማሪውና የጤና ባለሙያው በስተቀር ሌላ ሰው ኣያየውም፡፡ከጥናቱ የምናገኛቸው መረጃዎች ሚስጢርነታቸው የጠተበቀ ነው፡፡

ስምምነት፡በዚህ ጥናት ላይ የሚሳተፉ ታካሚዎች ሙሉ ፍቃደኛ መሆን አለባቸው፡፡

በጥናቱ ዙሪያ የበለጠ መረጃ ቢያስፈልግዎ፡ የሚመለከተውን ግለሰብ ማነጋገር ይችላሉ፡፡

መንግስት አወቀ ይዘንጋው ስልክ፡+251913567977 ወይም

የኢሜል አድራሻ፡**mengist93@gmail.com**

Patient Informed consent Amharic Version

የስምምነት ሰነድ

ዉድተሳታፊዎች

ስሜ መንግስት አወቀ ይዘንጋው ይባላል፡፡የሁለተኛ ድግሪ የመመረቂያ ጥናቴን ጅማ ዩኒቨርስቲ የህክምና መዐከል ክፍል ዉስጥ ተኺተዉ በሚታከሙ ህሙማን መካከል ነናታል ስፒሰስ የህክምና ዉጤት ያተኮረ ነው፡፡ የዚህ ጥናት አላማ ሊስተካከሉ የሚችሉ ሁኔታዎች መለየት እና የበሽታውንም አጠቃላይ ሁኔታ ማሻሻል ነው፡፡፡

በመሆኑም ከላይ የተጠቀሱትን አላማዎች ለማሳካት የእርሰዎ ትብብር እና ተሳትፎ በጣም አስፈላጊ ነዉ፡፡የሚሰጡት መረጃ ሚስጥራዊነቱ የተጠበቀ ነዉ፡፡ እንዲሁም በጥናቱ ያለመሳተፍ እና በፈለጉት ሰአት ከጥናቱ የመዉጣት መብትዎ የተጠበቀ ነዉ፡፡ከዚህም ባሻገር መመለስ ያልፈለጉትን ጥያቄ መተዉ ይችላሉ፡፡

ይህን የጥናት አላማ ተረድተዉ ተሳታፊ ለመሆን ፍቃደኛ ስለሆኑ በቅድሚያ ምስጋናዬን አቀርባለሁ፡፡

በጥናቱ ላይ ለመሳተፍ መስማማቴን አረጋግጣለሁ፡፡

የተሳታፊው ፊርማ/የጣትአሻራ ----------

ቀን----------ወር----------ዓ.ም.----------

የመረጃ ሰባሳቢው ስም እና ፊርማ----------

ቀን----------ወር----------ዓ.ም.----------

ስለ ትብብርዎ በድጋሜ አመሰግናለሁ፡፡

Patient Information sheet:-Afaan Oromo Version

Odeefannoo hirmaataa

Maqaa Qorataa: Mangist Awwooqa Yizangaaw

Bakka qorannoo: Giddu gala Hospitaala Jimmaa Yunivarsiti,

Baasii qorannoo Kan haguugu: Jimmaa Yuunivarsitii

Kaayyoo qorannoo: Hospitaala Jimmaa Yuunivarsitii keessatti dhukkuba daa'imman kichuu (neonatal sepsis) dhaan qaabanii gara hospital kana kan dhufaan bu'aa yaalii isaani guyyaa qoricha itti eegalan irraa kaasse qorannoo kan irrati goodhamu dha.

Haala deemsa qorannoo: qorannoo kanarratti yoo fedha yoo qabaattan qofa walii galtee qophaa'e hubattanii malatteesitu. Jalqabarratti odeeffanoo hawaasummaa itti aansuun waa'ee dhukkuba daa'imani fi amalloota isa faana hidhata qaban fi firii laaborattoriii singaafachuu fi kardii keessaan irraa nifudhannaa. Odeeffanoo isinirraa argannee, kaayyoo isinnitti himameen ala waan biraaf gonkumaa hin fayyadamnu.

Rakkoo qorannootiin dhukkubsatoota irra ga'u: qooranno kana irraattii hirmaachuu keessaannin rakkoon isinirra ga'u hin jiru.

Mangist Awwooqa Yizangaaw, lakkoofsa mobaayilii +251913567977 yookiin

Imeelii;-mengist93@gmail.com

Hirmaataa/fira	***Data collector***	***Supervisor***
Mallattoo ……..	Mallattoo ……	Mallattoo ……
Laak. Bilbillaa : ……..	Laak. Bilbillaa……	Laak. Bilbillaa…….
Guyyaa ____ ji'a____bara____	Guyyaa ____ ji'a___bara	Guyyaa ____ ji'a___ bara___

Deeggarsaa fi Hirmaannaa keessaniif Galatooma!!

ANNEX II: DATA COLLECTION FORMAT

Jimma University Institute of Health

School of Pharmacy

Name of data collector _____ sign _____ Date_____

Card number_____
Address _____
Admission date_____
Discharge date_____
Diagnosis_____
Phone. No_____

A. NEONATAL RELATED INFORMATION

- Sex_____
- Age_____ days,
- Birth weight (kg)_____current weight_____(kg)
- Anthropometric parameter
  - L_____ Hc_____
  - W/A_____LFA_____
  - W/L_____
- Apgar score
  - at the 1st minute_____
  - at the 5th minute_____
- Foul smelling and/or meconium stained liquor [A] Yes [B] No
- Cried Immediately after Birth [A] Yes [B] No
- Feeding
  - Human milk
  - Fortified human milk
  - Formula preparation
  - Combination
  - None
- Co morbidity [A] Yes [B] No
  If yes which
  - Congenital malformation
  - Blood group incompatibility
  - Intraventricular hemorrhage
  - Other _____
- **V**accination[A] Yes [B] No
  If yes which
  - BCG
  - Pentavalent vaccine

B. ENVIROMENTAL FACTORS

- use of incubator [A] Yes [B] No
- nasogastric tube feeding [A] Yes [B] No
- intravenous nutrition [A] Yes [B] No
- surgical procedures [A] Yes [B] No
- mechanical ventilation [A] Yes [B] No
- The number of siblings_____

C. MATERNALAL RELATED INFORMATION
SOCIO-DEMOGRAPHIC DATA

- Age_____
- Educational background. [A] Illiterate [B] primary school [C] Secondary school [D] College and above
- Residency. [A] Urban [B] Rural
- Occupation
  - [A] farmer
  - [B] Merchant
  - [C] Government employee
  - [D] non-government employee
  - [E] Other, specify_____
- Monthly income_____birr

BEHAVIORAL MEASURES

- Tobacco use [A] Yes [B] No
  If yes
  - Current smoker
    - Average daily cigarette _____
  - X-smoker _____
    - How long ago did you stop_____
- Alcohol intake [A] Yes [B] No
  If Yes
  - Average weekly intake_____ (Bottles, liters etc.)
- Khat chewing [A] Yes [B] No
- Herbal or other traditional medicine use [A] Yes [B] No
  - If Yes (specify)_____ when _____

Other substance use, specify_____

OBSTETRIC DATA

- Gravida_____ para_____
- history of still birth [A] Yes [B] No
- previous abortion [A] Yes [B] No
- Did you visit health facility for ANC during your pregnancy for this neonate? [A] Yes [B] No
  - If yes, how many times did you receive ANC follow up for this patient, _____times?
- Gestational age _____(weeks)
- Multiple gestation [A] Yes [B] No
- Place of delivery
  [A] Hospital
  [B] Health center
  [C] Home
  [D] Other, specify_____
- Type of delivery
  [A] Spontaneous vaginal delivery
  [B] Instrumental vaginal delivery
  [C] Caesarean section
- What was the duration of labor_____(hrs.)
- Premature rupture of membranes [A] Yes [B] No

If yes how long_____(hours)

- Prolonged premature rupture of membrane [A] Yes [B] No
  - If yes how long _____(hours)
- Is there any infection during pregnancy (History of fever)
  [A] Yes [b] No
  - If yes, when_____? Diagnosis (If possible)_____
  - Antibiotic Use [A] Yes [B] No
    - If yes specify the medication (if possible)_____
- Is there hospitalization during pregnancy?
  [A] Yes [B] NO
  - If yes, specify medical condition_____
- Is there chronic medical condition [A] Yes [B] No
  - If yes specify_____
- Other Medication use during Pregnancy [A] Yes [B] No
  - If yes specify what medication_____
- At which trimester used:

[A] First [B] Second [C] Third

D. CLINICAL FEATURES OF THE NEONATE WITH SEPSIS

clinical features during admission

- Poor feeding
- Lethargy
- Diarrhea
- Convulsion
- Vomiting
- Oliguria
- Irritability
- Respiratory distress
- Body temperature(°c) _____
- Dehydrated
- Chest indrawing
- Tachypnea (RR) _____
- Heart rate(HR)_____
- Grunting
- Cyanosis
- Poor Skin Color
- Jaundice
- Septic Rash
- Pallor
- Capillary Refilling time_____sec
- Abd. Distension
- Mottled Skin
- bulging Fontanel
- nasal flaring
- Bleeding tendency
- difficulty of feces

if other specify:----------

E. LABORATORY DATA AND IMAGING INVESTIGATION

Parameter	Value/ Results	Repeated	Ref. range	Imaging	**report**
WBC (cell / mm3)				X-Ray	

neutrophil (cell / mm3)					CT Scan	
lymphocyte (cell / mm3)					Echo	
monocyte (cell / mm3)					ECG	
Rbc (cell / mm3)					US	
Hb (g /dl)						
Hct (%)						
mcv(pg/dl)						
Plt (cell / mm3)						
CRP (mg/dl)						
ESR (mm/hr)						
Blood Group						
Blood Glucose (Mg/dl)						
O2saturation (%)	with out oxygen					
	with oxygen					
Renal function test	Scr					
	BUN					
liver function test	bilirubin direct					
	bilirubin total					
	AST					
	ALT					
CSF analysis	cell					
	protein					
	glucose					
	gram stain					
serum electrolyte	Na+					
	k+					
	cl-					
	ca+2					
	ph					
Urine analysis	Wbc					
	Rbc					
	Epithelial cell					
	glucose					
	protein					
	ketone					
gram stain						
culture						
susceptibility test						
Other ,specify						

F. MEDICATION RELATED DATA

Antibiotic regimen	day 1	day 2	day 3	day 4	day 5	day 6	day 7	day 8	day 9	day 10		
1. Ampicillin (dose, route, frequency, duration) _____ Plus Gentamicin (dose, route,												

frequency, duration) _____												
2. Ampicillin (dose, route, frequency, duration) _____ Plus Ceftriaxone (dose, route, frequency, duration) _____												
3. Ampicillin (dose, route, frequency, duration) _____ Plus Crystalline penicillin (dose, route, frequency, duration) _____												
4. Ampicillin (dose, route, frequency, duration) _____ Plus Cefotaxime (dose, route, frequency, duration) _____												
5.Ceftriaxone (dose, route, frequency, duration) _____ Plus Gentamicin (dose, route, frequency, duration) _____												
6. Ampicillin (dose, route, frequency, duration) _____ Plus Ceftazidime (dose, route, frequency, duration) _____												
7.Ceftazidime (dose, route, frequency, duration) _____ Plus Vancomycin (dose, route, frequency, duration) _____												
8.other antibiotics specify_____												
Other, non-antibiotics medication specify_____												

Is there any shifting of regimen from initial regimen? A) Yes B) No

If yes from which regimen_____to_____ If yes, what is reason for shifting?	
A) Not improved clinically, after _____days on 1st prescribed regimen, Specify which clinical parameter not improved_____	C). Drug resistance etiology Which bacteria _____to which antibiotic is resistance_____ D). Adverse drug events, specify_____
B) Not improved labratorically, after _____days on 1st prescribed regimen,	E. Drug Cost related factors, which drug, specify_____

Specify which laboratory parameter is/are not improved_____	F). not 1st line regimen G). other cause, specify_____
G. DATA ON ECONOMICAL OUTCOME **Costs** - Laboratory investigation costs_____ birr - Medication or drug related costs_____ birr - Hospital bed cost _____ birr - Procedure/imaging cost_____ birr - Transport cost _____ birr	**H. TREATMENT OUTCOME DATA** 1. Length of hospital stay _____days 2. Total cost during hospital stay _____birr 3. Complications developed [A] Yes [B] No If yes, o Septic shock o Necrotizing enterocolitis o Renal failure o Other, specify_____ 4. Time an event occur_____days after admission 5. Patient status during discharge [A] Alive [B] Death

Research paper final endorsement form to be filled before final submission to the school of pharmacy

Here with my signature, I declare that this research paper is done under my advisor ship and I have approved that this draft is the final draft thesis for submission to the school of pharmacy, Student Research Project office of Jimma University.

NAME_____ Signature _____

Here with my signature, I declare that this research paper has been examined by me and I have checked that the student has corrected the comment that I forwarded before final submission.

NAME_____ Signature _____

Here with my signature, I declare that this research paper is done by me as a principal researcher and I assure that this research paper is the final draft for submission to the school of pharmacy, Student Research Project (SRP) office of Jimma University.

NAME_____ Signature _____