



St. Paul's Hospital Millennium Medical College

DEPARTMENT OF PUBLIC HEALTH

**ASSESSMENT OF RISK FACTORS OF NEONATAL SEPSIS
AMONG NEONATES ADMITTED TO NEONATAL
INTENSIVE CARE UNIT OF ST. PAUL'S HOSPITAL
MILLENNIUM MEDICAL COLLEGE**

**A STUDENT RESEARCH PROJECT TO BE SUBMITTED TO THE
DEPARTMENT OF PUBLIC HEALTH, SPHMMC, IN PARTIAL
FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF MEDICINE**

July, 2018

Addis Ababa, Ethiopia



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LIST OF ABBREVIATIONS AND ACRONYMS

AA- Addis Ababa

ABD- Assisted Breech Delivery

APGAR -Activity, Pulse, Grimace, Appearance, Respiration

CI- Confidence Interval

CONS - Coagulase-Negative Staphylococcus Group

DIC- Disseminated intravascular coagulation

EDHS - Ethiopia Demographic and Health Survey

EONS - Early onset neonatal sepsis

GBS - Group B Streptococcal

LMIC- low and middle income countries

LONS - Late onset neonatal sepsis

LBW- low birth weight

MDG - Millennium development goal

MSAF - Meconium stained amniotic fluid

NHB- Neonatal hyper bilirubinemia

NMR - Neonatal mortality rate

NICU - Neonatal intensive care unit

NBW- Normal birth weight

NS - Neonatal sepsis

PNA- Perinatal Asphyxia

PROM - Prolonged rupture of membrane

PSBI - Possible severe bacterial infection

RDS- Respiratory distress syndrome

SDG - Sustainable Development Goals

SPHMMC - St. Paul's Hospital Millennium Medical College

SPSS - Statistical Package for Social science

UN - United Nation

UTI - Urinary tract infection

WHO - World health organization

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ABSTRACT

Background: Neonatal sepsis is one of the major causes of neonatal morbidity and mortality especially in developing countries. Socio-demographic, maternal, neonatal and medical factors were associated with risk of infection. The clinical signs and symptoms of neonatal sepsis are nonspecific and the confirmation of diagnosis is challenging and time consuming. Therefore, the diagnostic approach should depend up on consideration of risk factors.

Objective: - To assess risk factors of neonatal sepsis among neonates admitted to NICU of SPHMMC.

Methodology: An institution based retrospective documentary review study design was used to assess associated risk factors of neonatal sepsis among neonates admitted to neonatal intensive care unit of SPHMMC from September 11, 2016 to February 7, 2018. Sample size was calculated by using single population proportion formula. Study subject were selected using systematic random sampling method, and adopted data collection tool were used. Data was checked for completeness and clarity and analysis was made using statistical package for social sciences (SPSS) version 21.3. Descriptive statistics, binary logistic regression were used. The degree of association was calculated using odds ratio with 95% CI. P-value less than 0.05 were considered as significance level for associations between dependent and independent variables.

Result: the overall prevalence of neonatal sepsis was 18.9% with mortality rate of 14.9% from total admission (4843) of neonates in the past one year and six months. Prematurity (<37weeks) [AOR =7.727; (2.150-27.767)] were identified as the possible risk factors for the occurrence of early onset neonatal sepsis. It also pointed out that pre term neonates have 86% less chance to develop late onset neonatal sepsis than preterm neonates (AOR=0.136; 95%CI 0.038-0.487; p-value= 0.002)

Conclusion: The present study had identified prematurity as a major risk factor for early onset neonatal sepsis. So measures that reduce preventable causes of preterm delivery need to be taken as to reduce the occurrence of early onset neonatal sepsis.

Keyword: Neonatal sepsis, neonates, associated factors,

1. INTRODUCTION

1.1. Background

According to the international pediatric consensus conference of 2005, 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. Infection could be of bacterial, viral, fungal, or rickettsial origin(1). Bacterial sepsis is considered to be an important cause of neonatal mortality. (1). Neonatal sepsis encompasses various systemic infections of the newborn, such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis etc.(2).The normal fetus is sterile until shortly before birth as the placenta and amniotic sac are highly effective barriers to infections. At birth, the newborn loses the protection afforded to it in the uterus and gets exposed to the microbial world (3). Depending on the age of onset, neonatal sepsis is divided into early neonatal sepsis or late onset sepsis. Early neonatal sepsis (sepsis that presents during the first 3 to 5 days of life) is mainly due to organisms acquired before and during delivery (or maternal fetal infection).The most common pathogens 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 late onset sepsis (sepsis presenting after 4–7 days postnatal age) is due to organisms acquired after delivery from the environment (nosocomial or community sources) such as coagulase negative staphylococci (CONS), particularly *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas species*, anaerobes, and *Candida species*(4).It is more helpful to differentiate between early and late-onset infections according to per partum pathogenesis, because both have different source of infection, onset of disease occurrence, mode of transmission, management and risk factors (5).

The clinical presentation of neonatal sepsis is non-specific and includes: fever, respiratory distress, lethargy, impaired or refusal of feeding, jaundice, absent Moro reflex, hypothermia, convulsion, bleeding disorder and bulging fontanel (6).

Blood culture is a definitive diagnostic tool for neonatal sepsis. However, this ‘gold standard’ testing method is time-consuming and may result false positive results as well as false negative results, which can be attributed to the difficulties in discriminating a true CONS infection from sample contamination(7) . In addition to this neonatal sepsis is diagnosed based on a

combination of clinical appearance and the use of positive septic screening parameters such as :Total Leukocyte Count(TLC) < 5000/mm, band to total polymorph nuclear cells ratio of >0.2, C-reactive protein (CRP) >1mg/dl and micro Erythrocyte Sedimentation rate(ESR) > 10 mm-first hour (8).

The management of neonatal sepsis is with empirical antimicrobial therapy and supportive care. Once the clinical diagnosis is known, the neonate become critically ill .Due to this reason treatment should be started immediately after obtaining samples for culture rather than waiting for the culture results (9).

1.2. Statement of the problem

Globally neonatal sepsis is one of the most significant causes of morbidity and mortality among neonates during the neonatal period (0-28 day). Out of 5.9 million child deaths in 2015, almost 1 million occur in the first day of life and close to 2 million occurs in the first week of life. The main causes of neonatal deaths were preterm birth complications (35 %), intrapartum related complications (24 %), and sepsis (15%) globally (10).

The incidence of neonatal bacterial sepsis varies from 6 to 9 cases per 1,000 live births in developed countries, with great difference over time and geographic location(5)

In the last two decades, a remarkable progress has been shown on maternal and child deaths, but the neonatal health is a part of the 'unfinished agenda'. The world is experiencing an increase in the proportion of less than five deaths occurring in the neonatal period. Yet despite the neonatal deaths are preventable, they are concentrated in the world's poorest countries. And 85% of all the neonatal deaths were occurred in low and middle income countries (LMICs) even though they are home to only 62% of the world's newborns. Furthermore, it is also associated with increased medical costs, prolonged hospital stay and potentially poor long-term neurodevelopment outcomes. Surviving infants, approximately one-fourth of neonates, have significant neurological sequelae as a consequence of CNS involvement, septic shock or hypoxemia secondary to severe parenchymal lung disease (11, 12).

On the continent of Africa, Seventeen percent of neonatal deaths in sub Saharan Africa are attributed to neonatal sepsis as compared to only 6% of neonatal deaths are due to sepsis in high income countries (12).

In spite of Ethiopia's remarkable success in achieving millennium development goal (MDG 4) three years before, the reduction in neonatal mortality was comparatively low and at the end of MDG era the international community was in agreement on new framework the sustainable development goals (SDGs) to reduce under-five mortality to at least as low as 25 per 1000 live birth by 2030 (13). According to 2016 EDHS report the neonatal mortality rate (NMR) was 29/1000 live births, which has not revealed significant reduction from the 2011 EDHS report of 337/1000 live births. Neonatal conditions which were causing under-five mortality in 2004 have recently increased to 43%. Out of these conditions which cause under five mortality, neonatal sepsis accounts 9% (14).

Despite of improvements in diagnosis and management of neonatal sepsis in recent years, NS become a leading cause of admission and death in neonatal units especially in developing countries due to different conditions that are responsible for neonatal mortality (15).

Many factors contribute to the high mortality due to delays in the identification and treatment of newborns with infection, specifically; including under-recognition of illness, delay in care seeking at the household level, delay in initiation of treatment, and lack of access to both appropriately trained health workers and to high quality services to manage sepsis. It is particularly poignant that many neonatal deaths occur in the community, without the newborn ever having contact with the appropriate health services (16, 17). Indeed, strategies that can prevent and treat neonates with sepsis are essential to accelerate the progress of newborn survival. In many developing country settings, however, the identification and treatment of newborns with infection is unsatisfactory and epidemiological data from developing countries showed differences in the incidence, risk factors, pattern and antimicrobial sensitivities of pathogens and mortality from that of developed countries(12, 18). Identification of risk factors and early institution of therapy, thereby can improve neonatal mortality and morbidity. So the purpose of the present study was to examine the risk factors neonatal sepsis at NICU of SPHMMC.

1.3. Significance of the study

The result of this study help the policy makers and other responsible body to plan necessary training program based on the result for health professionals which helps them to improve their knowledge regarding the problem.

It will also help to create awareness to the community because based on the result finding, health professionals give health education to mothers about different risk factors at the time of ANC follow up which help them to get screened and treated early.

It will be a baseline for other researcher to do prospective study for the future because it assess the past event , this study result will also provide insight to health care provider in identification mechanism of common risk factors of neonatal sepsis to overcome the challenge of early diagnosis and management of sepsis..

2 .LITERATURE REVIEW

2.1 Epidemiology of Neonatal Sepsis

According to global health observatory data report of 2015, around 4.5 million (75%) of all under five mortality occurred within the first year of life which was highest in Africa and accounts 55/ 1000 live birth. but this was greater than five times higher than that of European (10 per 1000live birth)(19). In developing countries, neonatal mortality per 1000 live births from all causes was about 34; most of these deaths occur in the first week of life, mostly on the first day of life (20).

The prevalence of neonatal sepsis was more common in developing countries than that of developed countries. A study conducted in Japan indicated that the incidence of neonatal sepsis was 0 .74% and out of this 0.13% was EONS (21).

Study conducted in Egypt indicated, the prevalence was 40.7% with mortality rate of 51% and 42.9% for EONS and LONS, respectively (22). Study from Sudan showed, the prevalence of NS was 17.5 % with mortality rate of 14.5 %(23). Similarly, in Ethiopia a study conducted in Gondar university hospital in intensive care unit indicated that out of 181 neonates 67.4%were EONS and 32.6%LONS based on clinical parameters (18).according to recent studies conducted among three selected governmental hospital in Addis Ababa the prevalence of neonatal sepsis was found to be 14.4% (24).

2.2. Factors associated with Neonatal Sepsis

2.2.1 Socio-demographic Characteristics

Socio-demographic characteristics such as maternal age, sex and age of the neonate were risk factors that contribute to the occurrence of neonatal sepsis. For instance, male neonates were predominantly affected than females. Preterm (<37 weeks) neonates have a 3- to 10-fold higher incidence of infection than full-term (37-42 weeks) neonates (5). There was finding from Iraq revealed that Out of the 50 septic neonates, 32 (64 %) were males versus 18(36%) were females resulting in an overall female to male's ratio of 1: 1.8 (25). Neonatal sepsis definition criteria were not same for term and preterm neonates for whom the developmental stage influence the abnormality associated with host immune response. Thus, a specific agreement in definition was needed for both which is critical for the understanding of observational studies, training for practitioners and implementation of clinical trials in neonates (27). According to study done in

Bishoftu city to assess the incidence and risk factors of NS, Among the total of 306 neonates (age 0-28 days) sampled 249 (81.4%) were age less than or equal to 7 days and 169 (55.23%) of them were male which indicate that, the occurrence of sepsis was high in male neonates and premature or preterm neonate (26).

2.2.2. Maternal risk factors

Neonatal infections became acquired from mother through different routes such as:-prenatally (during pregnancy) with or without occurrence of recognizable sign and symptoms of bacteremia through placental transmission to the fetus and infection which occurs immediately before or during delivery by ascending transmission of micro-organisms to the fetus (28). According to results of several studies conducted in different countries, the main maternal risk factors for the occurrence of neonatal sepsis were: foul smelling liquor, meconium stained amniotic fluid, parity, history of urinary tract infection (UTI/STI), maternal age, Chorioamniotitis, Genital tract colonization with group B Streptococcus (GBS) and prolonged rupture of membrane (PROM) (28, 29, 30).

2.2.3. Neonatal risk factors

A number of neonatal risk factors were identified those play an important role in the occurrence of neonatal sepsis such as: male sex, preterm delivery, gestational age, birth asphyxia, low birth weight <2.5kg, APGAR score less than seven in the first one minute, mechanical ventilation, and prolonged rupture of membranes have significant roles in early and late onset neonatal sepsis, as they do in resource-rich countries (28, 29, 30). According to studies conducted in different areas revealed that the occurrence of early onset neonatal sepsis was frequent than that of late onset neonatal sepsis which was supported by study conducted in Bishoftu hospital showed that among 306 neonates included in the study ,81.0% were EONS and 19% of them were LONS (26). Another study conducted in southeastern Mexico revealed that out of the total (514) neonates sampled 75.3% were EONS and 24.7% were LONS (30).

2.2.4 Medical risk factors

After delivery or in postpartum period neonates could be acquired infection from the surroundings (nosocomial infection), delivery room or in the post natal room through the main pathways, namely the respiratory, gastrointestinal tracts and place of delivery. According to study conducted in Bishoftu hospital identified that significant number of neonates with 95%

were born in health center and developed sepsis. This value was 4.2 times higher when compared to the neonates born at home (26).

Usually, early-onset neonatal sepsis was related with maternal conditions and late-onset was mostly related with the medical and surgical risk factors which includes invasive and non-invasive procedures (vascular catheters, endotracheal tubes, or feeding tubes) needed for neonates who already have the disease (23). There was an evidence revealed that the risk of acquiring sepsis in neonates born using instrumental delivery has almost 6.2 times more common than children born via spontaneous vaginal delivery (26).

3. OBJECTIVE

3.1 General objective

To assess risk factors of neonatal sepsis among neonates admitted to NICU of SPHMMC from September 11, 2016 to February 7, 2018.

3.2 Specific objective

- To identify associated factors of Early onset neonatal sepsis among neonates admitted to neonatal intensive care unit of SPHMMC from September 11, 2016 to February 7, 2018
- To identify associated factors of Late onset neonatal sepsis among neonates admitted to neonatal intensive care unit of SPHMMC from September 11, 2016 to February 7, 2018.

4. METHOD AND MATERIAL

4.1. Study area and period

The study was conducted in St. Paul's Hospital Millennium medical college, Addis Ababa, Ethiopia from March 12 to 7th of May, 2018.

Addis Ababa, Ethiopia's sprawling capital in the highlands bordering the Great Rift Valley is the country's commercial and cultural hub capital city located at heart of the country covering an area of 527 km² with a population of 3,384,569 according to the 2007 population census (40). St. Paul's Hospital was built in 1969 by Emperor Haileselassie in collaboration with German Evangelical church, as a source of medical care for underserved populations. Approximately 75% of the patients receive medical service free of charge. It was transformed to medical school in 2007, in the new millennium era of Ethiopian calendar with the intention to alleviate the severe shortage of medical doctors in the country. It currently has more than 400 beds, with an annual average of 200, 000 populations and a catchment population of more than 5 million. The department of Pediatrics and child Health at SPHMMC has a total of 100 patient beds. Neonatal intensive care unit is among the case team units under the department which encompasses around 50 beds for both term and preterm infants.

4.2. Study Design

An institution based Retrospective document review study design was conducted in neonatal intensive care unit of SPHMMC from September 11, 2016 to February 7, 2018.

4.3. Population

4.3.1. Source Population

The source population for the study was all neonates who were admitted and treated in the neonatal intensive care unit of SPHMMC from September 11, 2016 to February 7, 2018.

4.3.2. Study population

All neonates admitted with sepsis to the NICU of SPHMMC from September 11, 2016 to February 7, 2018.

4.4. Inclusion and Exclusion Criteria

4.4.1. Inclusion Criteria

All neonates admitted with the diagnosis of sepsis at age equal to or less than 28 days to the NICU of SPHMMC.

4.4.2. Exclusion criteria

- Neonatal card with incomplete information.
- Neonates who were referred to other health facility before completion of treatment.
- Neonates who were admitted with the diagnosis of suspected sepsis but not proven upon discharge.

4.5. Sample Size determination

The sample size was determined by using single population proportion sample size calculation formula and the proportion was taken from the previous literature in Ethiopia. According to study conducted at, three selected governmental hospital in Addis Ababa the prevalence of neonatal sepsis was 14.4 % (24). By considering 95% confidence interval (CI) and 5% marginal error the, sample size was calculated as follows;

$$n = \frac{\frac{Z^2 p(1-p)}{d^2}}{1 + \frac{1}{N} \left(\frac{Z^2 p(1-p)}{d^2} - 1 \right)}$$
$$n = \frac{\frac{(1.96)^2 0.144(1-0.144)}{(0.05)^2}}{1 + \frac{1}{4843} \left(\frac{(1.96)^2 0.144(1-0.144)}{(0.05)^2} - 1 \right)}$$

n= approximately 181

Whereas

n= required sample size

N= Study population

Z= the standard normal deviation at 95% confidence interval; =1.96

P= Expected proportion of neonatal sepsis among neonates admitted in NICU with prevalence of 14.4%

d= margin of error that can be tolerated, 5% (0.05)

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

4.6. Sampling Technique and Procedure

In the study population, there were 914 neonates who were admitted with the diagnosis of sepsis. The sampling technique used was the systematic random sampling. The sampling interval was determined by the formula. $N/n = 914/181 = 5$

And after the calculation it became one in five charts, so one every five neonatal medical record was taken from the HMIS log book with replacement by the next card for those cards which contains incomplete information and then continues every fifth value in similar pattern until the required numbers of samples were collected.

4.7. Data collection procedure and Pretest

The data were collected using checked list questionnaires which were adopted from previous similar studies (41, 42). The questionnaire contains four parts which includes: Socio-demographic characteristics; maternal information, neonatal information and contain medical factors for neonatal sepsis. Records of neonates for the last one year and six month (from September 11, 2016 to February 7, 2018.) were reviewed. This involved going through the HMIS Log book records of neonates with the diagnosis of sepsis from September 11, 2016 to February 7, 2018. Risk factors were identified from medical files of patients with the diagnosis of neonatal sepsis. The medical charts were traced using the patient card numbers on the log book registry. Pre-test was carried out on the 10% of the sample and the questions were then revised based on the data obtained so that questions that induced ambiguity were rephrased.

4.8. Study variables

4.8.1. Dependent variables

- Early onset neonatal sepsis
- Late onset neonatal sepsis

4.8.2. Independent Variables

- Socio-demographic characteristics of mothers with their index neonates (age 0-28 days)
 - Mother's age
 - Mother's place of residency
 - Neonate's age
 - Neonate's sex
- Maternal health related factors
 - Parity
 - ANC follow up
 - Place of delivery
 - Duration of labor
 - Duration of rupture of membrane
 - History of MSAF
 - Antenatal corticosteroid use
 - Chorioaminitis
- Neonatal health related factors
 - Gestational age
 - APGAR score
 - Birth Weight at birth
 - Did the neonate cry immediately after birth?
 - Was the neonate resuscitated at birth?
- Medical Risk Factors(Non-invasive procedures)
 - Oxygen via nasal catheter
 - Oxygen via mask

4.9 Operational definition/standard definition

Neonatal sepsis: neonates with proven or clinical diagnosis of sepsis.

Early onset neonatal sepsis: neonate with sepsis within less than or equal to 3 days

Late onset neonatal sepsis: neonate with sepsis within 4-28 days

Low Birth Weight: weight of the child <2.5kg

Preterm Birth: live birth before 37 weeks of gestation

Neonate: Baby from birth until 28day of life

Neonatal period: The time from 0-28 days of life

Prolonged rupture of membrane: Rupture of amniotic membrane ≥ 18 hour

4.10 Data Quality Assurance

The collected data were manually checked for completeness, accuracy and clarity. Those which were incomplete were left out of the analysis. Then it was transferred to SPSS (Statistical Package for Social science) version 23 for analysis.

4.11 Data Processing and Analysis

After the data entry was made into IBM SPSS version 21.3. The entered data was subjected to cleaning using simple frequency and tabulation to ensure the validity of the data. Then, the analysis was made with IBM SPSS version 21.3. Descriptive statistics such as frequency distribution cross tabulation and some major of central tendency and variability (Mean and Standard deviation) were computed to describe the major variables of the study. Odds ratio and p-value were computed to see whether any relationship exists between the exposure and outcome variables. P-value less than 0.05 considered statistically significant. Multinomial Binary logistic regression was done to see the effect of each of the independent variables on the outcome variable by simultaneously suppressing the effect of extraneous variables.

4.12. Ethical Consideration

Ethical clearance was sought from St. Paul's Hospital Millennium Medical College, Department of Public Health ethical review Committee. After explaining about the purpose and the possible benefit of the stud, permission to gather data was obtained from the department of pediatrics and child health, and head nurse of the neonatal intensive care unit. The data was collected anonymously and Confidentiality of the information was maintained.

4.13. Dissemination of the result plan

The results of the study will be presented to the Department of Public Health in SPHMMC and following which the final edition will be submitted to the department. Dissemination of the result

will also be made to Department of Pediatrics and Child Health, neonatal intensive care unit case team and to the department of Obstetrics and Gynecology.

5. Result

5.1 Diagnosis of Neonatal Sepsis

Among the total admission (4843) of neonates in NICU of SPHMMC from September 11 2016 to February 7 2018, prevalence of neonatal sepsis was 18.9% , more than three fourth 152 (84%) of the neonates were diagnosed as early onset neonatal sepsis and around one fourth 29 (16%) of them were diagnosed as late onset neonatal sepsis. CRP was positive in almost all neonates (98%) who were diagnosed to have Sepsis at the time of admission. Blood culture was sent for 80% of those neonates who were diagnosed to have sepsis and nearly one third (32%) of them had culture growth within the first seventy two hours while the vast majority of them had negative culture result 88 (32%).

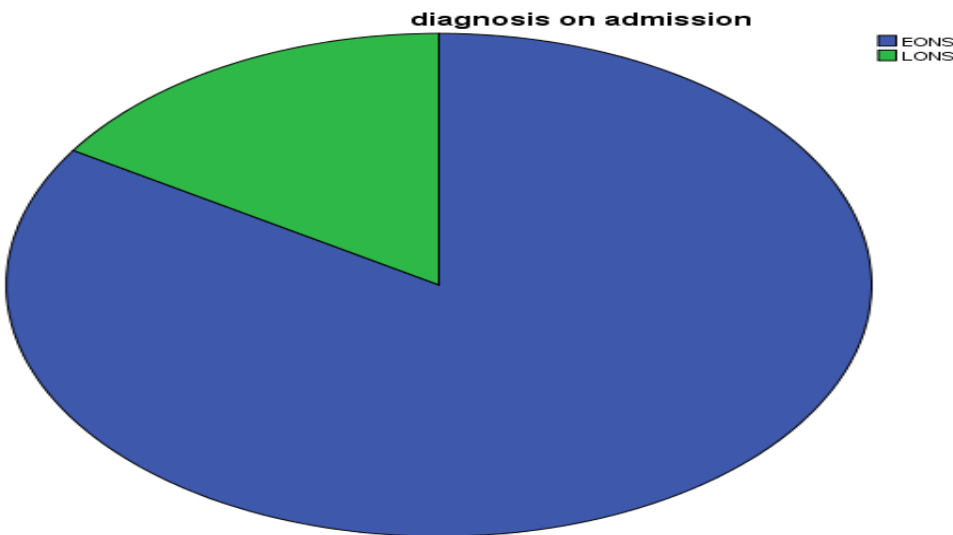


Figure 1: Distribution of diagnosis of Early and Late onset neonatal sepsis among neonates admitted with the diagnosis of sepsis in NICU of SPHMMC, Addis Ababa, Ethiopia, 2018

5.2 Socio demographic Characteristics

One hundred eighty one (181) mothers and children's pair was included in the study with replacement for incomplete neonatal records from September 11, 2016 to February 7, 2018 in SPHMMC. 110(60.8%) of mothers were from outside Addis Ababa. Among neonates who were enrolled in this study, more than half of them 94 (51.9%) were male .

The highest proportion of children in the survey 152 (84 %) were admitted at the age of less than 96 hours and the other (16%) were admitted at the age four days, with the mean age of admission being 28.3 hours and the minimum and the maximum being 20 minutes and 6 days respectively.

Table 1: Socio demographic characteristics of neonates and mothers admitted with the diagnosis of neonatal sepsis in NICU of SPHMMC, Addis Ababa, Ethiopia, 2018.(n=181)

Variable		Frequency	Percentage
Maternal age	Maximum	41	
	Minimum	16	
	Mean	26	
Place of residence of the mother	Addis Ababa	71	39.2
	Out of Addis Ababa	110	60.8
Neonatal age at admission	Maximum	6 day	
	Minimum	20 minutes	
	Mean	28.3 hours	
Sex of the child	Male	94	51.9
	Female	87	48.1

5.3 Maternal Risk Factors for Neonatal Sepsis

All of the mothers of neonates who developed neonatal sepsis had at least one ANC visit up at their referral health facility or at this hospital. More than half of the mothers were multiparous (94 ,51.9%). more than two third of the neonates 131 (72.4%) were delivered at hospital and around one fourth of the neonates were delivered at health center and six neonates(3.3%) were home deliveries. the majority of neonates were delivered By SVD(63%) and cesarean section were the second most common mode of delivery accounting for 28.7% while 7.2% and 2 % of neonates were delivered by instrumental vaginal delivery and ABD respectively. around 38.1%(69) of neonates had maternal history of premature rupture of membrane and the vast majority of neonates also had maternal history of prolonged rupture of membrane(78,43.1%). more than one third of neonates had maternal history of chorioamnionitis(35.4%) and fifty percent of them had meconium stained amniotic fluid and received steroid antenatally.

Table: 2 Distribution of Maternal risk factors for EONS and LONS among neonates admitted with the diagnosis of neonatal sepsis in NICU of SPHMMC, Addis Ababa, Ethiopia, 2018(n=181).

Variable		Frequency	Percentage
Parity	Primiparous	87	48.1
	Multiparous	94	51.9
Place of delivery	Hospital	131	72.4
	Health center	44	24.3
	Home	6	3.3
Mode of delivery	SVD	114	63
	Instrumental delivery	13	7.2
	Cesarean section	52	28.7
	ABD	2	1.1
Duration of labour	Maximum	38 hours	
	Minimum	1 hours	
	Mean	7.6 hours	
History of maternal PROM	Yes	69	38.1
	No	112	61.9
Duration of ROM	≥ 18 hours	78	43.1
	< 18 hours	73	40.3
	Intrapartum	30	16.6
Maternal History of MSAF	Yes	27	14.9
	No	154	85.1
History of maternal chorioamniotitis	Yes	64	35.4
	No	117	64.6
History of antenatal corticosteroid administration	Yes	29	16
	No	152	84

5.4 Distribution of Neonatal factors for neonatal sepsis

62.4 % (113) of neonates were preterm with late preterm's accounting for 61% (69) and early preterm accounting for 39 % (44) and the rest 37.6 % (68) were delivered at term. Regarding Birth weight nearly two third of neonates (119, 65.7%) had birth weight less than 2500 gram and the remaining 62(34.3%) of neonates had normal birth weight. forty-one percents of neonates APGAR score was less than seven at the first minute and only six percent of them had persistent low APGAR score. Hypothermia was the most common co morbid disorder at the time of admission occurring in nearly 86% (155) of neonates followed by Hypoglycemia (70%) and RDS (26%). Perinatal asphyxia occurred in six percent of children. Around 76.8% (139) of neonates had respiratory distress requiring CPAP and around 22% of them were supported via Nasal catheter and the remaining two did not require any respiratory support.

Table 3: Distribution of neonatal risk factors for EONS and LONS among neonates admitted with the diagnosis of neonatal sepsis in NICU of SPHMMC, Addis Ababa, Ethiopia, 2018(n=181).

Variable		Frequency	Percent
Gestational age	Preterm	113	62.4%
	Term	68	37.6
Birth weight	LBW	119	65.7
	NBW	62	34.3
APGAR score at 1 st minute	<7	92	50.8
	>= 7	75	41.4
APGAR score at 5 th minute	<7	10	5.5
	>= 7	157	86.7
Comorbid diagnosis at admission	Hypothermia	155	85.6
	Hypoglycemia	126	69.6
	RDS	47	26
	PNA	11	6.1
	NHB	6	3.4
	MAS	8	4.4

	Others	30	16 %
Respiratory support	CPAP	139	76.8
	Nasal Catheter	40	22
	None	2	1.2

5.5 Treatment out come

Among the one 181 neonate who were recruited for the study 151 (83.4%) were successfully treated and discharged home and fifteen of them died (14.9%) and three of them survived with complication. the most common cause of death being Multi organ failure (37%), and DIC accounted for 26% .NHB occurred as a complication in 42% (23.2) of them being followed by DIC (14, 7.7%) and Meningitis (12, 6.6%).The most common antibiotics used for treatment is Ampicillin and Gentamycin for around 80% of patient followed by Ampicillin and cefotaxime 31(17.1%).

5.6 Factors Associated with Early Onset Neonatal Sepsis

In this study the association of different factors with early onset neonatal sepsis was investigated at both bivariate and multivariate analysis levels. Those variables which have an association on bivariate analysis such as place of delivery, history of maternal prom, duration of rupture of memberane,history of maternal antibiotics use, birth weight and gestational age, was taken to multivariate analysis to control the confounders and to observe the significant association between more than two variables . Variables that showed significant association in binary logistic regression model were only gestational age of the neonate. According to this study those neonates who were born before 37 weeks of gestation are eight times [AOR =7.727; (2.150-27.767); 95%CI p-value= 0.002) more likely to develop EONS than those who were delivered at term.

Table 4: Bivariate and multivariate analysis showing the association between early onset neonatal sepsis and others different variables in neonates admitted to NICU of SPHMMC, Addis Ababa, Ethiopia, 2018 (n=181)

		EONS		COR(95%CI)	P- Value
		YES	NO		
Place of delivery	Hospital	115(87.8)%	16(12.2%)	5(0.657-38.964.677)	0.12
	Health Center	31(70.54)%	13(29.5%)	1.915 (.248-14.754)	0.533
	Home	4(66.67%)	2(33.33%)	1	
History of maternal PROM	Yes	65(94.2%)	85(75.9%)	.196 (.017-2.3150)	0.196
	No	4(5.8%)	27(24.2%)		
Duration of rupture of membrane	<18 hours	68(93.15%)	5(5.85%)	1.847 (.297-11.485)	0.511
	>=18 hours	59(75.56%)	19(24.36%)	.8444(.272-2.618)	.769
	Intrapartum	23(76.66)	7(30.43%)	1	1
History of maternal antibiotics use	Yes	38(97.4%)	31(91.2%)	12.894(.734-379.314)	.088
	NO	1(2.56%)	3(8.8%)	7.22(.771-67.65)	.083
Gestational Age	Preterm	106(93%)	44(65.67%)	7.727(2.150-27.767)	0.002
	Term	8(7%)	23(34.32%)	1	1
	Post term				
Birth weight	Less than 2.5kg	107(89.2%)	43(70.5%)	1.06(0.325-3.453)	0.923
	Normal Birth weight	13(10.8%)	18(29.5%)	0.905(0.277-2.952)	

	Bog baby				
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5.7 Factors associated with late onset neonatal sepsis

Variables that showed significant association in binary logistic regression model were gestational age of the neonate and place of delivery. These variables were taken to the multiple logistic models to control confounding variables, and only gestational age remained significantly associated with late onset neonatal sepsis. The study showed that neonates who were delivered at term weeks of gestation have 86% high chance to develop late onset neonatal sepsis than preterm neonates (AOR=0.136; 95%CI 0.038-0.487; p-value= 0.002)

Table 5: Bivariate and multivariate analysis showing the association between late onset neonatal sepsis and others different variables in neonates admitted to NICU of SPHMMC, Addis Ababa, Ethiopia, 2018 (n=181)

Variable		LONS		COR(95%CI)	P- Value
		YES	NO		
Place of delivery	Hospital	16(12.2%)	115(87.8)%	.202(.026-1.553)	.124
	Health Center	13(29.5%)	31(70.54)%	.524(.068-4.021)	.534
	Home	2(33.33%)	4(66.67%)		
History of maternal PROM	Yes	85(75.9%)	65(94.2%)	0.29(0.026-	0.207
	No	27(24.2%)	4(5.8%)	3.166)	0.115
Duration of rupture of membrane	<18 hours	5(5.85%)	68(93.15%)	1.2(0.998-1)	0.696
	>=18 hours	19(24.36%)	59(75.56%)		
	Intrapartum	7(30.43%)	23(76.66)		
History of maternal antibiotics use	Yes	31(91.2%)	38(97.4%)	1(1-1.004)	0.102
	NO	3(8.8%)	1(2.56%)		

Gestational Age	Preterm	44(65.67%)	106(93%)	0.127(0.35-0.458)	0.002
	Term	23(34.32%)	8(7%)	1	1
	Post term				
Birth weight	Less than 2.5kg	43(70.5%)	107(89.2%)	0.986(0.305-0.458)	0.986
	Normal Birth weight	18(29.5%)	13(10.8%)		
	Bog baby				
Antibiotics used by the mother for treatment of PROM or chorioamniotitis	Ampicillin plus Erythromycin	0	17(100%)	0.127(0.0035-0.458)	0.13
	Ampicillin plus Gentamycin	1(4.4%)	22(95.6%)		

6. Discussion

In this study, the magnitude and associated risk factors of both early and late onset neonatal sepsis among neonates admitted to the Neonatal ICU of SPHMMC were investigated over the past one year and six months. Accordingly, the overall prevalence of neonatal sepsis was 18.9% with mortality rate of 14.9% from total admission of neonates. Which means out of the total admission (4843) of neonates in the past one year and six months, the total prevalence of neonatal sepsis (early and late onset sepsis) was 18.9% and out of these about 14.9% of them died and the left were cured or discharged improved.

This was smaller compared to study conducted in Blacklion specialized hospital in 2010 which was 44.7 %n (41) and in Gondar university hospital intensive care unit which indicated that out of 181 neonates 67.4%were EONS and 32.6%LONS based on clinical parameters (18).This difference could be due to the attention given to improve quality of health care delivery to mothers and new born. But it is almost comparable with another study conducted in Sudan tertiary hospital that showed the prevalence of neonatal sepsis to be 17.5% (23). The finding of this study showed that there was more early onset neonatal sepsis (EONS) admissions than that of late onset neonatal sepsis admission (LONS). Among the total of neonatal records reviewed, 152 (84%) were diagnosed as EONS and 16% were presented as LONS. That means from a total admission of neonates over the past one year and six months 84% of admissions were early onset sepsis whereas, 16% of them were late onset neonatal sepsis. This study finding was almost consistent with the studies conducted in Bishoftu hospital in 2014 that revealed 81% (26), in southeastern Africa 75.3%(30) and in Mekelle City, in 2015, 76.9% (42) of subjects were diagnosed as early onset neonatal sepsis which was almost comparable with the current study finding . As indicated in other studies, the current study also found that gestational age of newborns were found to be significantly associated with neonatal sepsis that means Preterm neonate (<37 weeks) were eight times more likely at risk to develop early onset sepsis as compared to term neonates (37-42weeks) [AOR =7.846;0.038, 0.487].

This finding was consistent with study conducted in South Eastern Mexico which revealed that preterm neonates were ten times more likely to develop early onset neonatal sepsis (30). But smaller as compared to study conducted in Indonesia (Makassar) which revealed that, preterm neonates were 13.45 times more likely to have early onset neonatal sepsis [AOR,(13.45 3.91-46.26) (44).

The possible explanation for this result could be due to the difference in geographic location, study design used, and duration of study period. But it was in contrast to study conducted in Bishoftu city which indicated that, preterm neonates did not show significant association with the occurrence of neonatal sepsis (26). This could be due to the difference in study design used, health care delivery systems, and awareness of the community regarding the prevention strategy of sepsis and the numbers of admission of the preterm neonates during the study period. According to this study term neonates who were delivered at term weeks of gestation have 86% high chance to develop neonatal sepsis than preterm neonates (AOR=0.136; 95%CI 0.038-0.487; p-value= 0.002) this is consistent with the study done at three different governmental hospitals in Addis Ababa which showed Neonates with preterm gestation were less likely to develop late onset neonatal sepsis compared to term neonates [COR =0.321(.147, 0 .700] which was indicated as 0.33 times at risk to have late onset neonatal sepsis than term neonates [AOR=0.325(0.116, 0.911](24).

7. Strength and Limitation

7.1 Strength

- As the study design was retrospective documentary review, it will be baseline for prospective study.
- The study may reflect associated factors of early and late onset neonatal sepsis.

7.2 Limitation

- Since the study was retrospective documentary review; this might inevitably be complicated by incomplete data due to lost records
- This study selectively addressed certain factors of neonatal sepsis while various factors are found to cause the disease, such history of maternal colonization with GBS, history of maternal UTI and STI.

7. Conclusion and Recommendation

7.1 Conclusion

The present study had identified prematurity as a major factor for early onset neonatal sepsis. So measures that reduce preventable causes of preterm delivery need to be taken as to reduce the occurrence of early onset neonatal sepsis.

7.2 Recommendation

- The department of pediatrics and child health in collaboration with the department of obstetrics and gynecology should work together to decrease preterm delivery by increasing family planning, improved quality of care especially for adolescent before, between and during pregnancy and strategic investment in innovation and research are required as to decrease the risk of occurrence of early onset neonatal sepsis.
- Further study should be done to see other unexplored associated factors that were not included in this study.

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9. Annexes

9.1 Annex –I: English versions questionnaires

PART I. Socio-demographic characteristics of mothers with their index neonates (age 0-28 days)

No.	Question	Response	Skip
1	Mother's age	_____ (in years)	
2	Residence	1. Addis Ababa 2. others	
3	Neonate's age	_____ in hours	
4	Neonate's sex	Male ☐ Female ☐	
PART II. Maternal health related factors			
5	Parity	_____ in number	
6	Place of delivery	1. Home 2. Hospital 3. Health center 4. Other (specify) _____	If in 'home', skip to 114
7	Mode of delivery	1. Spontaneous Vertex delivery 2. Instrumental vaginal delivery 3. Caesarean section 4. Assisted breech delivery	
8	Duration of labor	_____ in hours	
9	Duration of ROM	_____ in hours	
10	History of maternal PROM	1 Yes 2 No	
11	History of Maternal antibiotics use for treatment of PROM or chorioamnionitis	1 Yes 2 No	If yes
12	What is or are the drugs		
13	Meconium stained amniotic fluid	1. Yes 2. No	
14	History of Chorioamnionitis	1. Yes 2. No	

III: A checklist on neonatal health related factors

15	Diagnosis on admission	1. EONS 2. LONS	
16	Gestational age	_____ in weeks	
17	APGAR score	At 1 st minute _____ At 5 th minute _____	
18	Birth Weight at birth	_____ in grams	
19	Did the neonate cries immediately after birth?	Yes _____ No _____	
20	Did the neonate resuscitated at birth?	Yes _____ No _____	
21	Treatment given		
PART IV :MEDICAL FACTORS			
22	Oxygen via nasal catheter	1. Yes 2. No	
23	Oxygen via mask	1. Yes 2. No	
Laboratory investigations findings			
24	Complete blood count (CBC)	1. Total WBC _____/mm ³ 2. ANC _____/mm ³ 3. CRP _____/1hr 4. Platlet count ___cells/m ³	
	Was Blood culture sent	1 yes 2 no	
25	If yes what is the growth that is identified	_____	

26	What was the Treatment given	1. Ampicillin and Gentamycin 2. Ampicillin and cefotaxime 3. vancomycin and ceftazidime 4. . Others	
27	Duration of hospital stay in days		
28	Out come	1. Died 2. Cured 3. survived with complications	
29	What is/are the complications	1. NHB 2. Hospital acquired infection 3. Hospital acquired infection plus DIC 4. DIC 5. Multi organ failure 6. Mult organ failure plus DIC 7. Meningitis 8. Respiratory Failure 9. others.....	
30	Co morbid diagnosis	1. Hypoglycemia 2. Hypothermia 3. RDS 4. PNA 5. MAS 6. Birth injury 7. NHB 8. Congenital disorder 9. others	