Premature Rupture of Membrane and Birth Asphyxia Increased Risk of Neonatal Sepsis among Neonates Admitted in the Neonatal Intensive Care Unit at the University of Gondar Specialized Referral Hospital, Northwest Ethiopia, 2019

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Abstract

Background: Neonatal Sepsis (NS) is the infection of neonates in the first 28 days of life. It is a severe infection of neonates that leads to death and life hindrance. NS is a major cause of infant mortality more overtly in developed and developing countries. In developing countries like Ethiopia, it causes 30-50% of the neonatal deaths per year.

Objective: This study aimed to assess the prevalence and associated factors of neonatal sepsis among neonates in a Neonatal Intensive Care Unit (NICU) at the University of Gondar specialized referral hospital, Gondar, northwest Ethiopia, 2019.

Methods: An institution-based retrospective, cross-sectional study was conducted from 1st February 2018 to 30 January 2019, and a total of 292 neonates included in the study. The systematic random sampling technique was used to select medical charts. The data was collected using the data extraction tool. Descriptive statistics like frequencies, and percentages, charts, and graphs, were computed. Logistic regeneration of Bi-variable, and multivariable analyses, were conducted. The interpretation, made with the adjusted odds ratio of p-values less than 0.05, with a 95% CI.

Results: The prevalence of neonatal sepsis among neonates was 59% with a 95% CI (53.4-64.7). Age of neonates (AOR=2.48; 95%CI: (1.20-5.10)), PORM (AOR=2.97; 95%CI: (1.22-7.26)), Catheterization (AOR=1.95; 95%CI: (1.02-3.14)), Birth asphyxia (AOR=2.81; 95% CI: (1.14-6.93)) and Oxygen via mask (AOR=4.0; 95% CI: (1.2-13.9)) were statistically significant to neonatal sepsis.

Conclusion and Recommendations: The prevalence of neonatal sepsis in the last one year in NICU at the University of Gondar specialized referral hospital was 59%. The most risk factors of neonatal sepsis were, identified as Age of neonates, PROM, catheterization, birth asphyxia, and oxygen via masks strongly associated with the prevalence of NS. Based on these results, we recommend the concerned body to focus on the prevention of risk factors rather than treating the disease after it occurs.

Keywords: Neonatal sepsis; Neonates; Associated factors; NICU; Gondar; Ethiopia

Abbreviaons: APGAR: Activity Pulse Grimace Appearnance Respiration; BW: Birth weight; EONS: Early On Set of Neonatal Sepsis; LBW: Low Birth Weight; MSAF: Meconium Stained Amniotic Fluid; NICU: Neonatal Intensive Care Unit; NS: Neonatal Sepsis; PROM: Prolonged Rupture of Membrane; UTI: Urinary Track Infection; WHO: World Health Organisation

Introduction

Neonatal Sepsis (NS) is a systemic inflammatory response syndrome of suspected or proven infections, characterized by systemic manifestations after the bacterial invasion, and multiplication in the bloodstream. It is a serious infection of neonates from birth to 28 days of life [1-5].

The clinical presentation of neonatal sepsis is non-specific except that it includes lethargy, poor feeding/feeding intolerance, irritability, temperature instability, Brady/

tachycardia, glucose instability, poor perfusion, apnea, bleeding tendency, jaundice, absence of Moro reflex, convulsions and bulging fontanel. Conventionally, with durations of infections, NS is classified as Early Onset Of Neonatal Sepsis (EONS) infection<7 days, and Late-Onset Of Neonatal Sepsis (LONS) infection in 8-28 days of life [4,6,7].

The World Health Organization (WHO) states that nearly 4 million newborns die each year, of which 75% occurs in the first week of life, and 30%-50% of the deaths take place in developing countries [8,9]. Worldwide, nearly 2,202 cases of neonatal sepsis per 100, 000 live births occur per year, of these 3 million as severe neonatal sepsis. Neonates admitted for sepsis into the Neonatal Intensive Care Unit (NICU) need a prolonged hospital stay, increasing medical costs, and possibly resulting in poor neurodevelopment outcomes of cognitive, physical, and mental health impairments after discharge [10-13].

Although the causes of neonatal deaths are preventable, the burden is higher in the poorest countries that hard to control. UNICEF estimates, neonatal mortality declined from 48% since in 1990 to 28 per 1000 live births in 2013, while the reduction rate of under-five mortality is 67%. UNICEF 2018 reported 17% of neonatal deaths in Sub-Saharan Africa (SSA). Of these, 6% of deaths occurred in high-income countries. According to the Ethiopian Demographic Health Survey (EDHS), 2005, and 2011, neonatal mortality was 37 and 29 per 1000 live births, respectively. The major causes of the mortalities were birth asphyxia, (31.6%), prematurity, (21.8%), and sepsis (18.5%) [14-17].

Although neonatal mortality dropped to 41% in the past 16 years, it remains the killer of 33% of the newborns [16-18]. Studies at different institutions used a variety of designs, and participants have not been able to identify the burden of NS. Our study aimed to investigate the progress in reducing neonatal mortality ever since the launching of the third Sustainable Development Goal (SDG). Therefore this study aimed to assess the prevalence and associated factors of neonatal sepsis among neonates who were admitted to the NICU at the University of Gondar specialized referral hospital. This provides awareness into valuable information to child health indicators and could assist in better evidence-based interventions in Ethiopia aimed at further reducing neonatal mortality.

Methods

An institution-based cross-sectional retrospective study was conducted at the University of Gondar specialized referral hospital Neonatal Intensive Care Unit (NICU), from 1st February 2018 to 30 January 2019. University of Gondar specialized referral hospital is found in Gondar town central Gondar zone northwest Ethiopia. It is 727 km from Addis Ababa, the capital city of Ethiopia. The town has one referral hospital and eight health centers. The University of Gondar established since 1954 as a public health college provides out and in-patient services to over seven million people in the catchment area as per the three-tier health care policy of the country. The

Neonates who had to admit in the NICU have separately in pre-term, term, and critically ill rooms.

Source and study population

All neonates' birth up to 28 days aged, admitted and treated at the University of Gondar specialized referral hospital in NICU from 1st February 2018 to 30 January 2019 were source population, and those neonates' who had the diagnosis and treated to sepsis was study populations.

Inclusion and exclusion criteria

Medical records with full information were included in the study, but a piece of incomplete patient information was excluded from the study.

Sample size determination

The sample size was determined by using the single population proportion formula, of 77.9%sepsis was taken from the previous study done in Ethiopia [19], with a 95% Confidence Interval (CI), and 5% marginal error. Where n=required sample size, 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 77.9%, d=margin of error that can be tolerated, 5% (0.05) q=proportion of population that do not possess the character of interest.

$$n = \left([(1.96)]^2 \ 0.779(1-0.779) \right) / \left([0.05]^{()}2 \right) = 265$$

By adding a 10% nonresponse rate, the final sample size was=292

Sampling technique and procedure

The study subjects were selected using a systematic random sampling technique. The Kth interval was calculated, after extracting of the first medical chart, and then every three intervals were preferred until the required sample size.

Data collection technique and quality control

A pre-tested data collection tool was used to compile the required information by adapting from previous literature done on NS [19]. The data were collected by using a checklist of reviewing the neonatal chart in the NICU. The questionnaire contained four parts of Part one socio-demographic characteristic, part two maternal risk factors, part three neonatal risk factors, and part four contain medical risk factors for neonatal sepsis.

Data were collected by trained four professional nurses and one supervisor. The data collectors and supervisors were given training on data collection procedures by the principal investigator. The assigned supervisor has assured the quality of the data at the time of data collection. The principal investigator has checked the data its completeness, consistency, and clarity at the time of data collection periods.

Study variables

Dependent variables:

Neonatal sepsis

Independent variables:

Socio-demographic characteristics

- Address of the neonate
- Sex of the neonate
- Age of the neonates
- Maternal age

Maternal risk factors

- Gestational age
- Maternal urinary tract infection
- Place of delivery
- Mode of delivery
- Prolonged Rupture of Membrane (PROM)
- Foul smell liquor
- Meconium Stained Amniotic Fluid (MSAF)
- Duration of labor
- Antenatal Care (ANC)

Neonatal risk factors

- Low Birth Weight
- Term baby
- Preterm baby
- Birth asphyxia
- APGAR score<7 first five minute

Medical risk factors (invasive and non-invasive procedures)

- Mechanical ventilation
- Oxygen via nasal catheter
- Oxygen via mask
- IV Secure
- Urinary catheterization
- Nasogastric tube insertion

Operational definitions

- **Neonate:** Baby from birth until 28 days of life
- **Neonatal sepsis:** neonate develop systemic infections within 0-28 days of life

- **Diagnosis of neonatal sepsis:** Diagnosis of neonatal sepsis in developing countries based on the presence of clinical signs, WHO Integrated Management of Childhood Illness (IMCI) clinical algorithms the time from 0-28 days of life [20]
- **Early-onset neonatal sepsis:** neonate with sepsis within 0-7 days
- **Late-onset neonatal sepsis:** neonate with sepsis within 8-28 days
- **Low birth weight:** the weight of the newborn <2.5 Kg
- **Preterm birth:** live birth before 37 weeks of gestation
- **Post-dated:** live birth after 42 weeks of gestation
- **Prolonged rupture of the membrane:** Rupture of amniotic membrane >=18 hour
- **Catheterization:** Introduction of a catheter via the urethra into the urinary bladder
- **Birth asphyxia:** Infants have not breathed or gasping or breathing less than 30/minute

Data processing and analysis

Data completeness was checked, entered into Epi-data version 3.1 statistical software, and exported to SPSS version 20 for further analysis. Descriptive statistics of percentage through tables, pie-chart, and bar graphs were used to summarize the results.

Logistic regression of Bi-variable and multivariable analysis was done. In the bi-variable analysis, variables of p-values less than 0.2 were entered into the multivariable analysis to control confounders. A multivariable analysis degree of association between dependent and independent variables was examined by odds ratio with 95% confidence intervals (CI), and p-value less than 0.05 considering statistically significant.

Results

Socio-demographic characteristics

A total of 292 neonates participated in the study with a response rate of 100%. The mean age of the neonate's mothers was 27 (SD+0.4) years; 162 (55.4%) of the neonates were male, and their mean age was 6.9 (SD+2) days; 164 (56.2%) were born to urban families **Table 1**.

Table 1: Distribution of Socio-demographic characteristics of mothers and neonates admitted in NICU at the University of Gondar specialized hospital, northwest Gondar, Ethiopia 2019 (n=292).

Variables	Categories	Frequency	Percent
Address	Urban	164	56.20%
	Rural	128	43.80%
Sex of neonates	Male	162	55.40%
	Female	130	44.60%
Age of neonates	0-7 days	223	76.40%
	8-28 days	69	23.60%
Maternal Age	<18	10	3.40%
	18-36	248	84.90%
	>36	33	11.30%

Maternal factors for neonatal sepsis

Of the 292 mothers of neonates, 250 (85.6%) had a history of fever; the majority 263 (90.1%) attended ANC follow-ups, and 203(69.5%) delivered at hospitals.

More than two-thirds of the neonates, 194 (66.4%), were born by spontaneous vaginal delivery **Table 2**.

Table 2: Maternal related factors of those neonates admitted in NICU at the University of Gondar specialized referral hospital Gondar, northwest, Ethiopia 2019, (n=292).

Variables	Categories	Frequency	Percent
History of PROM	No	231	20.90%
	Yes	61	79.10%
History of antenatal care	No	29	9.90%
	Yes	263	90.10%
History of maternal UTI	No	256	87.70%
	Yes	36	12.30%
Party	Primi parous	112	38.40%
	Multi parous	180	61.60%
Place of delivery	Hospital	203	69.50%
	Health center	83	28.4
	Home	6	2.10%
History of maternal fever	No	250	85.60%
	Yes	42	14.40%
History of foul-smelling vaginal discharge	No	258	88.40%
	Yes	34	11.60%
Miconium stained amino tic fluid	No	261	89.40%
	Yes	31	10.60%
Duration of labor	<6 hrs	31	10.60%
	6-12 hrs	166	56.80%
	Dec-24	66	22.90%
	>24	29	9.90%
Chorine amenities	No	265	90.8
	Yes	27	9.2

Neonatal related factors

Most of the neonates, 221 (75.7%), were born at normal gestational age; nearly 71%, 207 (70.9%), was born with normal birth weight, and 276 (94.5%), were cured **Table 3**.

Invasive and non-invasive medical factors

Of the total 292 participants, 80 (27.4%) were resuscitated through mechanical ventilation. For the majority of the neonates, 265 (90.8%), IV line was opened, and for 161 (55.1%) oxygen was administered via nasal prongs **Table 4**.

Prevalence of neonatal sepsis

Among the total 292 neonates admitted into NICU, the prevalence of NS was 59%, 95% CI: (53.4-64.7); 51%, 95% CI: (26.0-36.6%) were Early Onset Neonatal Sepsis (EONS) and 7.9%, 95%CI: (6.2-13.3) Late-Onset Neonatal Sepsis (LONS) **Figures 1 and 2**.

Table 3: Neonatal related factors of among neonates admitted in NICU at the University of Gondar specialized referral hospitals, Gondar northwest Ethiopia, 2019 (n=292).

Variables	Categories	Frequency	Percent
Gestational age	Pre-term	59	20.20%
	Term	221	75.70%
	Post-term	12	4.10%
Birth weight	<2.5 Kg	74	25.30%
	2.5-3.99 Kg	207	70.90%
	>4 Kg	11	3.80%
APGAR score in first 5 min	<7	150	51.40%
	>7	142	48.60%
Birth asphyxia	No	220	75.30%
	Yes	72	24.70%
Discharge conditions	Cured	276	94.50%
	Dead	15	5.50%

Table 4: Invasive and noninvasive medical factors among neonates admitted in NICU at the University of Gondar specialized referral hospital, northwest Ethiopia, 2019 (n=292).

Variables	Categories	Frequency	Percent
Mechanical ventilation	No	212	72.60%
	Yes	80	27.40%
Oxygen via nasal prong	No	131	44.90%
	Yes	161	55.10%
Oxygen via mask	No	263	
	Yes	29	90.10%
Iv insertion	No	27	9.20%
	Yes	265	90.80%
NG tube insertion	No	170	58.20%
	Yes	122	41.80%
Catheterization	No	190	65.10%
	Yes	102	34.90%

Factors associated with neonatal sepsis

Bi-variable and multivariable logistic regression analyses were done. In the bi-variable analysis duration of labor, mechanical ventilation, Oxygen via nasal catheter, oxygen via mask, history of maternal fever, APGAR score <5 in the first 5 min, ANC visit, history of maternal UTI, birth asphyxia, history of PROM, age of neonate, catheterization, and NG tube insertion were statistically significantly associated with neonatal sepsis at p-values less than 0.05. In the multivariable analysis, birth asphyxia, history of PROM, age of neonate, catheterization, and oxygen via mask remained significantly associated with neonatal sepsis at p-values<0.05, and 95% CI **Table 5**.
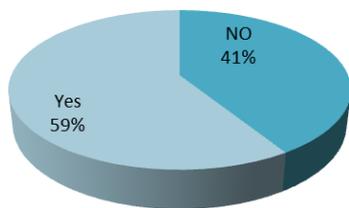
Figure 1: Prevalence of neonatal sepsis in NICU at the University of Gondar specialized referral hospital, Gondar Northwest Ethiopia, 2019 (n=292).
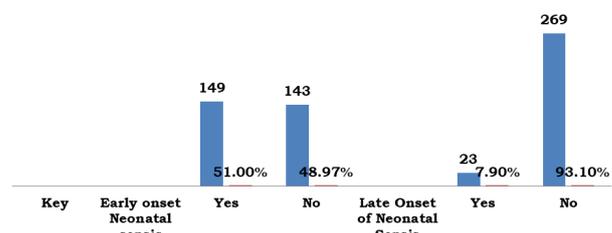

Figure 2: Prevalence of early and late-onset of neonatal sepsis in NICU at the University of Gondar specialized referral hospital, Gondar northwest Ethiopia, 2019 (n=292).

Table 5: Bi-variable and multivariable logistic analysis of neonatal sepsis with different variables neonates admitted to the University of Gondar specialized hospitals NICU, northwest Ethiopia, 2019 (n=292).

Variables	Categories	Neonatal sepsis		COR (95% CI)	AOR (95% CI)
		No	Yes		
Residence	urban	54	110	2.17 (2.17-1.35)	0.64 (0.34-1.20)
	Rural	66	62	1	1
Age of neonate	<7 days	85	138	1.67 (0.97-2.88)	2.48 (1.20-5.10)**
	8-28 days	35	34	1	1
Sex of neonates	Male	74	88	1	1
	Female	46	84	1.54 (0.96-2.47)	1.77 (0.91-3.21)
History of maternal UTI	No	90	166	1	1
	Yes	30	6	9.22 (3.70-22.99)*	0.88 (0.19-4.14)
History ANC	No	23	6	0.15 (0.07-0.39)	0.89 (0.19-4.13)
	Yes	97	166	1	1
History of maternal fever	No	84	166	1	1
	Yes	36	6	11.86 (4.81-29.26)	0.314 (0.08-1.31)
History of PROM	No	75	156	5.85 (3.11-11.02)	2.97 (1.22-7.26)**
	Yes	45	16	1	1
Duration of labor	<6 hrs	13	18	1	1
	6-11 hrs	47	119	3.08 (1.06-8.90)*	0.48 (0.48-0.10)
	12-24 hrs	40	26	5.63 (2.39-13.25)*	1.07 (1.07-0.29)
	>24 hrs	20	9	1.44 (0.57-3.66)	0.64 (0.64-0.17)
Mechanical ventilation	No	149	63	5.86 (3.33-10.33)*	1.02 (0.45-0.33)
	Yes	23	57	1	1
Oxygen via mask	No	161	102	1	1
	Yes	11	18	2.58 (1.17-5.69)	4.0 (1.2-13.9)**
Oxygen via nasal prong	No	36	95	2.88 (1.76-4.71)*	1.664 (0.86-3.21)

	Yes	84	77	1	1
NGT Insertion	No	54	116	2.53 (1.57-4.09)[*]	1.92 (0.96-3.82)
	Yes	66	56	1	1

Neonates who were less than seven days old at birth were 2.48 times (AOR=2.48; 95%CI: (1.20-5.10)) more likely to develop neonatal sepsis compared to those aged greater than seven days. Neonates born to mothers who had prolonged rupture of the membrane more or equal to eighteen hours were 2.97 times (AOR=2.97; 95%CI: (1.22-7.26)) more likely to develop sepsis compared to those who had ruptured of membrane-less than eighteen hours. Neonates who were urinary catheterized were 1.95 times (AOR=1.95; 95%CI: (1.02-3.14)) more likely to develop sepsis than those who were not catheterized. Neonates who had birth asphyxia were 2.81 times (AOR=2.81; 95% CI: (1.14-6.93)) more likely to develop neonatal sepsis compared to those who did not have the problem. The odds of neonatal sepsis were 4.0 times (AOR=4.0; 95% CI:(1.2-13.9)) higher among neonates who were resuscitated via masks compared with neonates who were not treated via a mask.

Discussion

In Ethiopia, the neonatal mortality rate was 28 deaths/1,000 live births, 43 deaths/1,000 live births in rural and 41 deaths in an urban area.The neonatal mortality rates in the poor and rich families of Ethiopia are varied; from 37 to 50/1000 live births, respectively.According to reports of 2015, asphyxia, prematurity, and sepsis were the causes of 31.6%, 21.8%, and 18.5% deaths, respectively [21].

This study aimed to assess the prevalence and associated factors of neonatal sepsis among neonates admitted to the NICU at the University of Gondar, College of Medicine and Health Sciences specialized referral hospital. The prevalence of neonatal sepsis in this study was 59% with a 95% CI: (53.4-64.7); Which is in line with the result of a study conducted in Haiti (54.8%) [22]. The possible explanation might be that both of them institution-based cross-sectional retrospective studies and gave similar care at the neonatal intensive care units.

This finding was lower than the previous study done in Ethiopia (77.9%) [19]. The possible explanation for the difference might be the other work was done by using a large sample size in two governmental hospitals, while the currently used one specialized referral hospital.

Our finding was higher compared with those of studies conducted at Sudan tertiary hospitals (17.5%) [16], Egypt (33.4%) [23], Tanzania (31.4%) [24], Uganda (11%) [25] and Mexico (4.3%) [12]. The possible explanation might be that the current study focused on the diagnosis of empirical NS only, whereas the other studies used a combination of blood culture and empirical diagnosis. Besides those studies that were focused on the incident rates of neonatal sepsis, it includes the

community base study of neonatal sepsis and, there was a difference in socioeconomic status across the countries.

Regarding factors associated with neonatal sepsis is the age of neonates; PROM, catheterization, birth asphyxia, and oxygen via masks to newborns were, found to be statistically associated. The neonate's ages less than seven days were 2.48 times more likely to develop neonatal sepsis compared to those ages greater than seven days at birth. This finding is consistent with those of studies conducted in Ethiopia [19] and Ghana [26]. Neonate's ages less than seven days were vulnerable to infections; especially have maternal complications of PROM and fever.

Neonates born to mothers who had prolonged rupture of membranes>18 hrs were 2.97 times more likely to develop sepsis compared to shorter rupture of membranes. This finding is supported by those of studies [27,28]. The possible reason is that in prolonged rupture of membranes>18 hrs ascending infections develop from maternal birth canals to cervix, uterus and infects the fetus with a chance of EONS.

Neonates who had urinary catheters were 1.95 times more likely to develop sepsis than those who were not catheterized. This finding is consistent with that of a study conducted at a London Hospital [28]. Catheterization without aseptic techniques can develop systemic infections most likely LONS.

Neonates who had birth asphyxia were 2.81 times more likely to develop neonatal sepsis compared to those who did not have birth asphyxia. This finding is consistent with that of a study conducted in Ethiopia [19]. Neonates who had birth asphyxia develop neonatal sepsis.

The odds of neonatal sepsis were 4.0 times higher among neonates who were resuscitated via masks compared with neonates who were not resuscitated via a mask. This finding is consistent with that of a study conducted in Ethiopia [19]. Neonates were resituated via mask with non-disinfected in a high-level disinfectant solution, develops infection possibly LONS.

Limitations

Since the study was a retrospective documentary review, it focused only on the registration books and patient charts.

Conclusion and Recommendation

The prevalence of neonatal sepsis in the last one year in NICU at the University of Gondar specialized referral hospital was 59%. The most risk factors of neonatal sepsis were, identified as Age of neonates, PROM, catheterization, birth asphyxia, and oxygen via masks strongly associated with the prevalence of NS. Based on these results, we recommend the

concerned body to focus on the prevention of risk factors rather than treating the disease after it occurs.

Ethical Approval and Consents to the Participants

Ethical clearance was obtained from the ethical review committee of the School of the Nursing University of Gondar in the letter Ref. No. N/D/2119/03/2019 after explained the purpose and benefits of the study to the concerned bodies. The University of Gondar specialized referral hospital clinical director permitted us to collect data. Data was collected in the NICU registration book and patient charts. Confidentiality was kept by data collection as anonyms and not uses medical registration numbers and secured their information.

Consent for Publication

- Not applicable
- Availability of data and materials
- All the necessary data generated, or analyzed during this study are included in this manuscript.

Competing Interests

The authors declare that they have no competing interests for publication.

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Authors' Contributions

DGK-wrote the proposal, participated in data collection, analyzed the data and first draft of the first paper and the manuscript, AWS-wrote the proposal, review the paper and the manuscript, and WAB- review the proposal, analysis, and the paper and the manuscript.

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