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ORIGINAL RESEARCH

Neonatal Sepsis and Associated Factors Among Newborns in Woldia and Dessie Comprehensive Specialized Hospitals, North-East Ethiopia, 2021

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Introduction: Neonatal sepsis is a clinical illness characterized by infection-related signs and symptoms in the first month of life, with or without bacteremia. Septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections are all examples of systemic illnesses that can affect newborns. Hence, the main aim of this study was to assess the prevalence and factors associated with neonatal sepsis among newborns in Woldia and Dessie Comprehensive Specialized Hospitals, northeast Ethiopia, from January 1 to July 30, 2021.

Methods: This institution-based cross-sectional study was conducted from January 1 to July 30, 2021, on 344 randomly selected neonates who visited the hospital. A systematic random sampling technique was used to select samples, and data were collected using a pre-tested standardized questionnaire. For data entry and analysis, Epi Data version 4.1 and SPSS version 24 applications were used, respectively. The goodness-of-fit was tested by the Hosmer–Lemeshow statistic test. Bivariable and multivariable binary logistic regressions were used to identify associated factors at a 95% confidence interval. Significance was considered at p-value <0.05.

Results: In this study, the prevalence of neonatal sepsis was 79.4% (95% CI: 75.2–83.6%). Maternal UTI/STI history [AOR: 3.1; 95% CI (1.5–7.1)], gestational age <37 weeks [AOR: 4.4; 95% CI (1.0–8.9)], PROM [AOR: 4.9; 95% CI (2.5–6.8)], and new-born resuscitation history [AOR: 2.3; 95% CI (1.5–4.3)] were all significantly associated with neonatal sepsis.

Conclusion: This study indicates that the proportion of neonatal sepsis is high. A history of maternal PROM, being a preterm neonate, a history of maternal UTI/STIs, and having received resuscitation at birth were identified as risk factors for neonatal sepsis.

Keywords: neonatal sepsis, neonatal infection, neonatal intensive care unit, hospitals, north east, Ethiopia

Introduction

Neonatal sepsis is a systemic illness that affects neonates under the age of 28 days. Early-onset neonatal sepsis is defined as sepsis that occurs within 72 hours of delivery and <7 days in term infants,[1,2] and late-onset sepsis is defined as sepsis that occurs beyond 72 hours in NICU infants and after 7 days in full-term infants.[3,4]

Neonatal sepsis is a clinical illness characterized by infection-related signs and symptoms in the first month of life, with or without bacteremia. Septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections are all examples of systemic illnesses that can affect newborns.[5]

In 2019, approximately 2.4 million neonates died in the first month of their lives around the world. Over 6700 babies die every day, with nearly a third of all neonatal deaths occurring during the first day of life and more than three-quarters by the end of the first week. In low- and middle-income nations, the majority of newborn deaths occur. In under-developed nations, neonatal sepsis is a leading cause of infant mortality and morbidity.[6]

The number of newborns who die during their neonatal period is rising. The Millennium Development Goal for child survival will not be realized unless newborn mortality is significantly reduced. Every year, over 4 million newborns die in

their first four weeks of life (the neonatal period). A similar number of neonates are stillborn and 0.5 million mothers pass away as a result of pregnancy problems. The vast majority of neonatal deaths (99%) occur in low- and middle-income countries, with nearly half occurring at home. Many newborns who die in disadvantaged communities go unidentified and unreported, indicating that their deaths are seen as inevitable.[7]

According to Ethiopia's demographic and health census, the neonatal death rate was 29 per 1000 live births (EDHS, 2016). The infant and newborn death rates were highest in the Amhara region of the country. It was 67 per 1000 live births and 47 per 1000 live births, respectively.[8]

Prematurity, asphyxia, tetanus and sepsis are reported as the main causes of neonatal death in Ethiopia. Many women do not generally seek formal health care during pregnancy, childbirth, or puerperium. Less than a third of women receive antenatal care and 90% are assisted by unskilled attendants: TBAs (26%), relatives (58%), or alone (6%). Almost no one (3.5%) receives postnatal care.[8]

Therefore, assessing the prevalence and identifying the associated factors is critical to preventing neonatal problems and achieving sustainable development goals by reducing newborn mortality. This is helpful in designing strategies to prevent and/or treat neonatal sepsis.

Materials and Methods
Study Setting and Period
Dessie Comprehensive Specialized Hospital is located in Dessie Town. This is the capital city of the South Wollo Zone. It is about 400 kilometers from Addis Ababa, Ethiopia's capital city. Dessie Comprehensive Specialized Hospital, which is one of the frontline hospitals in Ethiopia, serves more than 3.5 million people as a referral hospital. The NICU ward of this hospital has 40 patient beds, 14 incubators, 7 radiant warmers, and 10 phototherapy units for newborn infants. It was the largest NICU in the Amhara regional state with a very high patient admission rate. It also has a very high patient flow of 200 neonates per month on average. The Woldia Comprehensive Specialized Hospital, which is located in Woldia town, is the capital city of the North Wollo Zone. It is located 520 km away from the capital city, Addis Ababa. This hospital serves more than 2.5 million people as a referral hospital. The study was conducted from January 1 to July 30, 2021.

Study Design
An institutional-based cross-sectional study design was conducted at Woldia and Dessie Comprehensive Specialized Hospital, North East Ethiopia, 2021 G.C.

Study Subjects
The study population for this study included all neonates admitted to NICUs in Woldia and Dessie Comprehensive Specialized hospitals during the study period.

Inclusion and Exclusion Criteria
Inclusion Criteria
All neonates who were admitted to the Woldia and Dessie Comprehensive Specialized hospitals for various health issues and whose mothers/caregivers volunteered to participate in the study were included.

Exclusion Criteria
Neonates discharged early prior to data collection, neonates admitted without their mothers, neonates admitted with sepsis two or more times during the study period in order to prevent double counting and neonates with incomplete patient chart information were excluded.

Sample Size Determination
The sample size was determined using a single population proportion formula, and the proportion was taken from previous literature in Ethiopia. According to a study conducted at Wolaitasodo hospital, the prevalence of neonatal sepsis was 33.8%.[9] The sample size was calculated using a 95% confidence interval (CI) and a 5% margin of error:

$$n = \frac{(Z)^2 P(1-P)}{d^2}$$

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 33.8%

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

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

So, the final total sample size was 344.

Sampling Technique and Procedure

The study population consisted of neonates who were admitted and treated in NICUs during the study period. Systematic random sampling was used for the selection of the study subjects and the mothers after calculating the Kth value by dividing the total sample size, which was determined (Figure 1).

Data Collection Methods

The data was collected using a pre-tested interviewer-administered questionnaire and checklists. The tools were created after a thorough examination of the literature. The tools are divided into four sections: socio-demographic parameters, maternal data, neonatal data, and medical factors for neonatal sepsis. The information was collected during the admission of the neonate to the NICU. It was also collected by reviewing the registration book records in the labor ward, NICU, and gynecologic ward in each hospital.

Study Variables

The prevalence of neonatal sepsis was the dependent variable, and socio-demographic characteristics of mothers, socio-demographic characteristics of neonates, clinical characteristics of neonates, and obstetric characteristics of mothers were independent variables for this study.
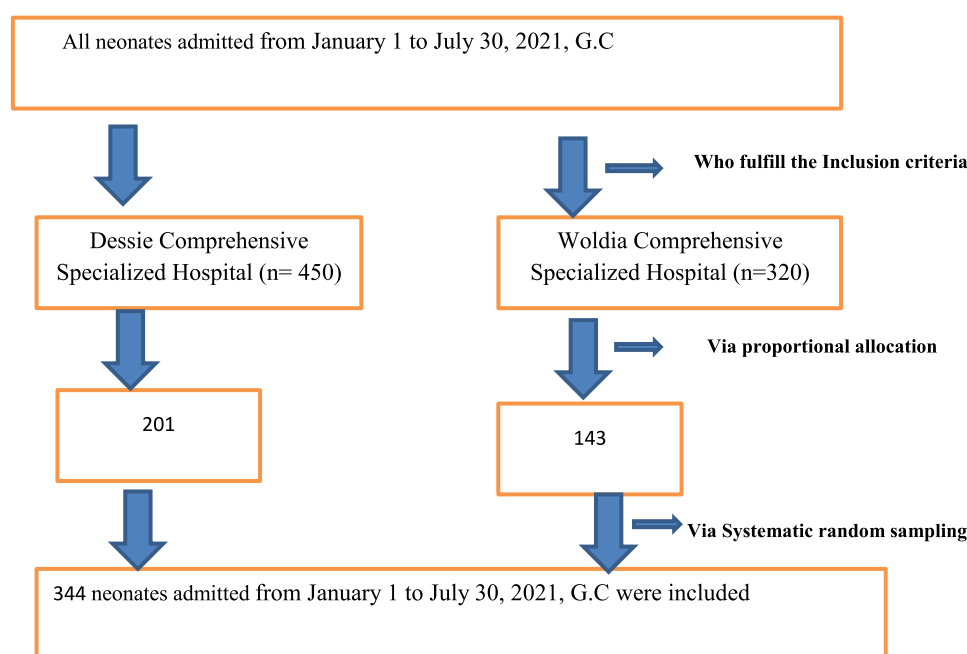

Figure 1 Schematic diagram of sampling procedure among neonates in Woldia and Dessie Comprehensive Specialized Hospitals, north-east Ethiopia, 2021 (n = 344).

Data Quality Assurance

Before the actual data collection process, a pre-test was conducted on 17 neonates (5% of the total sample size) who visited the Hayek primary hospital. The data collection tool had to be prepared in English, then translated into the Amharic language, and then back-translated to English to ensure consistency and sentence appropriateness and to better understand. Three nursing professionals were recruited to extract variables from the patient's medical records and to collect some relevant information from the mothers of neonates after a face-to-face interview. One-day training on the objectives of the study, data extraction, data collection techniques, and ethical issues was given for data collectors. Data completeness and consistency were checked by the primary investigator every day and necessary corrections were made.

Operational Definitions

Neonatal sepsis: According to the Federal Ministry of Health of Ethiopia's Neonatal Intensive Care Unit (NICU) guideline Neonatal sepsis is a clinical illness characterized by infection-related signs and symptoms in the first month of life, with or without bacteremia. The neonate may present with any of the systemic manifestations of danger signs (not feeding well, convulsions, drowsy or unconscious, movement only when stimulated or no movement at all), fast breathing (60 breaths per min), grunting, severe chest in-drawing, raised temperature, > 38°C, hypothermia, < 35.5°C, central cyanosis, or could be severe jaundice, severe abdominal distension, or localizing signs of infection. (Signs of pneumonia, many or severe skin pustules, bulging fontanelle, painful joints, joint swelling, reduced movement …) were diagnosed as having neonatal sepsis.

Early-onset neonatal sepsis is defined as sepsis that occurs within 72 hours of delivery and <7 days in term infants.

Late-onset sepsis is defined as sepsis that occurs beyond 72 hours in NICU infants and after 7 days in full-term infants.

Data Processing and Analysis

The data was initially entered in Epi Data version 4.1 and then exported to IBM Statistical Package for Social Science (SPSS) Statistics 24 for descriptive statistics, cross-tabulation, and analysis of the factors associated with neonatal sepsis. Descriptive statistics were used to express frequency and percentages. Binary logistic regression was performed to test the association between independent variables and neonatal sepsis. Both the Crude Odds Ratio (COR) and the Adjusted Odds Ratio (AOR) with a 95% confidence interval (CI) were computed to test the strength of association. Variables with $p \leq 0.20$ during bivariable analysis were selected for multivariable logistic regression analysis. Factors with $p < 0.05$ in the final model were declared significantly associated with neonatal sepsis. A Hosmer–Lemeshow goodness-of-fit test was used to check model fitness at $p > 0.05$.

Result

Demographic Characteristics of the Study Subjects

A total of 344 neonates were enrolled in the research, with a 100% response rate. In all, 153 (44.4%) were males, 191 (55.5%) were females, 245 (71.2%) were younger than seven days, and 99 (28.7%) were older than seven days (Table 1).

Neonatal Related Risk Factors for Sepsis

Among the 344 neonates, 113 (32.8%) had a low birth weight, 244 (70.9%) were term (37–42 weeks), 113 (32.8%) had a history of birth asphyxia, and the majority (323, or 94.0%) improved after therapy, although 20 (6%) died (Table 2).

Maternal Related Risk Factor for Neonatal Sepsis

The majority of mothers (91.8%) got ANC follow-up, and 45 (13%) had a history of urinary tract infection throughout their pregnancy. About 77 (22.4%) of the mothers were feverish, and 48 (13.9%) of the mothers had a history of foul-smelling. Three hundred and two (87.9%) of mothers had their babies in a health-care facility, while 12.2% had them at home. In terms of rupture of the membrane, 98 (28.5%) had a previous history of PROM, with 43 (13.8%) lasting more than 18 hours. About 14 (21.5%) of the mothers had a history of labor that lasted longer than expected. Sixty-two (18.1%) and 66 (19.1%) of mothers had previously experienced chorioamnionitis and meconium aspiration syndrome, respectively (Table 3).

Table 1 Socio Demographic Characteristics of Neonates and Mothers at Woldia and Dessie Comprehensive Specialized Hospital, North East Ethiopia 2021

Variable		Frequency	Percentage
Sex	Male	153	44.4%
	Female	191	55.5%
Age	<7 day	245	71.2%
	>7 day	99	28.7%
Maternal Age	<18 year	25	7.3%
	18–35 year	266	77.3%
	>35 year	53	15.4%

Table 2 Birth-Related Predisposing Factor for Neonatal Sepsis Among Neonates Admitted in NICU Wards at Woldia and Dessie Comprehensive Specialized Hospital, North East Ethiopia 2021

Variable		Frequency	Percentage
Birth weight	<1500 g	113	32.8.1%
	1500–2499g	214	62.2%
	≥2500g	17	4.9%
Gestational age	Pre-Term <37 weeks	80	23.2%
	Term 37–42 weeks	244	70.9%
	Post Term >42 weeks	20	5.8%
Birth asphyxia of baby	Yes	113	32.8%
	No	231	67.1%
Out come	Died	20	6.0%
	Cured	323	94.0%

Prevalence of Neonatal Sepsis

More than half (55.5%) of the neonates in the study had the early onset of neonatal sepsis, while 23.9% of the neonates had the late onset of neonatal sepsis. In this study, the overall proportion of neonatal sepsis was 79.4% (95% CI: 75.2–83.6%) of newborns (Figure 2). Concerning the composition of the disease and/or the clinical characteristics of neonates with neonatal sepsis, 50 (18.3%) had not fed well, 23 (8.4%) had convulsions, 13 (4.7%) had severe jaundice, 11 (4.0%) had severe abdominal distension or localizing signs of infection, and 8 (2.9%) had severe skin pustules (Table 4).

Factors Associated with Neonatal Sepsis

Bivariable and multivariable logistic regressions were used to fit all variables that met the chi-square assumption. The neonates' age, sex, place of birth, gestational age, birth weight, maternal age, ANC follow-up, history of UTI/STIs, history of PROM, history of foul-smelling liquor, birth asphyxia, place of delivery, birth weight, gestational age of the neonate, and

Table 3 Maternal-Related Risk Factor for Neonatal Sepsis in Woldia and Dessie Comprehensive Specialized Hospital, North East Ethiopia 2021

Variables		Frequency	Percentage
History of anti-natal care	Yes	316	91.8%
	No	28	8.2%
History of maternal UTI	Yes	45	13%
	No	299	86.9%
History of maternal fever	Yes	77	22.4%
	No	267	77.6%
History of foul smelling	Yes	48	13.9%
	No	296	86%
Place of delivery	Home	42	12.2%
	Health Facility	302	87.9%
History of chroamoniatus	Yes	62	18.1%
	No	282	81.9%
Meconium stained amniotic fluid	Yes	66	19.1%
	No	278	80.9%
History of rapture membrane	Yes	98	28.5%
	No	246	71.5%
Duration of rapture membrane	<18 hour's	301	87.5%
	≥18 hour's	43	12.5%

history of chorioamnionitis met the variable screening criteria (p-value 0.2) and were entered into multivariable logistic regression analysis. As a result, the history of maternal UTI/STIs, gestational age, PROM, and history of newborn resuscitation were found to be significantly associated with neonatal sepsis at multivariable with p-values less than 0.05 (Table 5).
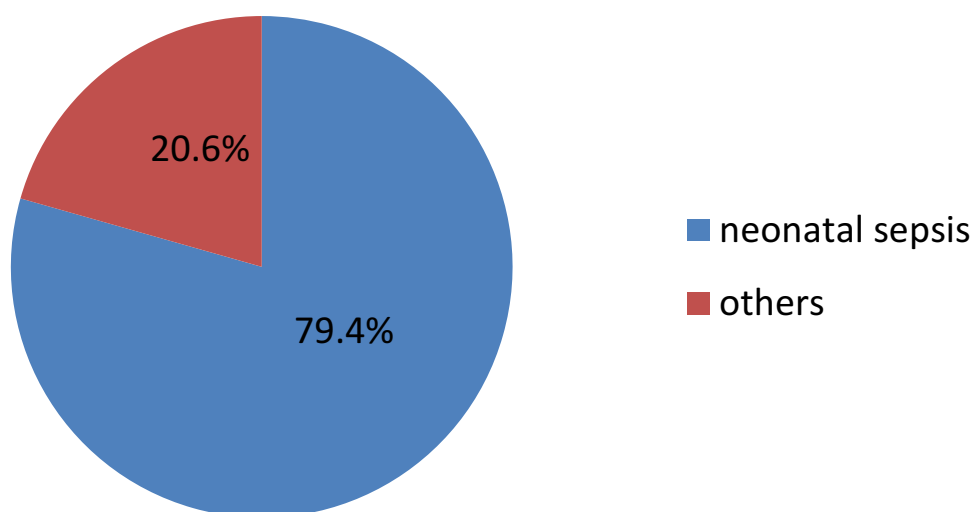

Figure 2 Prevalence of neonatal sepsis among neonates in Woldia and Dessie Comprehensive Specialized Hospitals, from January 1 to July 30, 2021.

Table 4 The Clinical Characteristics of Neonates with Neonatal Sepsis Admitted in NICU Wards at Woldia and Dessie Comprehensive Specialized Hospital, North East Ethiopia 2021

Clinical Characteristics	Frequency (273)	Percentage
Not being able to feeding	50	18.3%
Convulsions	23	8.4%
Drowsy or unconscious	9	3.2%
Movement only when stimulated	17	6.2%
Fast breathing (60 breaths per minute)	70	25.6%
Grunting	27	9.9%
Severe chest in drawing	16	5.8%
Elevated temperature, > 38°C	120	43.9%
Hypothermia, < 35.5°C	32	11.7%
Severe jaundice	13	4.7%
Abdominal distension or localizing signs of infection	11	4.0%
Sever skin pustules	8	2.9%

Table 5 Bivariate and Multivariate Analyses of Factors Associated with Neonatal Sepsis in Woldia and Dessie Comprehensive Specialized Hospitals, North East Ethiopia 2021 (n = 344)

Variables		Neonatal Sepsis		COR(95% CI)	AOR(95% CI)
		Yes	No		
Age	<7 days	190	55	1	1
	>7days	83	16	0.60 (0.31, 1.14)	1.76 (0.88–3.49)
Sex	Male	124	29	1	1
	Female	149	42	1.20 (0.70–2.06)	0.81 (0.46–1.42)
Maternal age	<18	18	7	1.64 (0.50–5.29)	1.83 (0.53–6.38)
	18–35	212	54	1.03 (0.48–2.20)	1.15 (0.52–2.54)
	>35	43	10	1	1
History of maternal UTI /STIs	Yes	36	9	0.79 (0.33–1.88)	3.10 (1.56–7.16)*
	No	237	62	1	1
History of ANC follow up	Yes	252	64	1.14 (0.40–3.21)	0.89 (0.29–2.72)
	No	21	7	1	1
History of maternal fever	Yes	60	17	2.27 (1.32, 3.94)	1.83 (0.13, 3.51)
	No	213	54	1	1
History of birth asphyxia	Yes	90	23	1.73 (1.00, 2.99)	1.52 (0.86–2.70)
	No	183	48	1	1
History of foul smiling	Yes	37	11	0.77 (0.36–1.61)	1.49 (0.69–3.24)
	No	236	60	1	1

(*Continued*)

Table 5 (Continued).

Variables		Neonatal Sepsis		COR(95% CI)	AOR(95% CI)
		Yes	**No**		
History of chorioamnionitis	Yes	43	19	0.54 (0.28–1.02)	1.81 (0.89–3.65)
	No	230	52	1	1
Micounium stained amniotic fluid	Yes	51	15	2.38 (1.37–4.14)	1.95 (0.96–3.46)
	No	222	56	1	1
Gestational age	Pre-term (<37)	72	8	0.53 (0.12–2.26)	4.41 (1.09–8.93)*
	Term (37–42)	184	60	1.48 (0.41–5.35)	1.33 (0.35–5.08)
	Post-term (0.42)	17	3	1	1
PROM	Yes	75	23	1.17 (0.66–2.10)	4.98 (2.52–6.87)**
	No	198	48	1	1
Place of delivery	Home	33	9	1.04 (0.43–2.49)	1.09 (0.43–2.83)
	Health facility	240	62	1	1
Birth weight	1500g	92	21	1.23 (0.17–2.81)	2.14 (0.89–3.78)
	1500–2499g	169	45	2.08 (0.21–3.11)	3.05 (0.15–3.74)
	≥2500g	12	5	1	1
History of neonatal resuscitation	Yes	93	22	2.94 (1.53–4.66)	2.32 (1.51–4.32)**
	No	180	49	1	1
History of NG tube insertion	Yes	74	17	1.11 (0.60–2.05)	1.16 (0.59–2.27)
	No	198	55	1	1

Notes: *Significant at <0.05 α-values, **Significant at <0.01 α-value.
Abbreviations: PROM, premature rupture of membrane; STI, sexually transmitted infection; UTI, urinary tract infection.

Discussion

The total prevalence of newborn sepsis was found to be 79.4% (95 CI: 75.2–83.6%) in this study. This study found that having a history of maternal PROM, being a preterm neonate, having a history of mother UTI/STIs, and receiving resuscitation at birth were all predictors of neonatal sepsis.

This result is consistent with research conducted at government hospitals in Shashemene town, Oromia Regional State, Ethiopia (77.9%),[10] and Arbaminch general hospital, Ethiopia (78.9).[11] Similar results could be the result of similarities in the research population and the time period in which the investigations were conducted. This finding, however, is significantly greater than that of research from Wolaita (33.8),[9] Gondar (64.8),[12] Kenya (28.6),[13] Uganda (11%),[14] Tanzania (31.4%),[15] and Nigeria (34%).[16] This disparity could be due to methodological differences, discrepancies, and variances in diagnostic modalities to confirm newborn sepsis. Furthermore, because these research sites are referral hospitals, they are more likely to receive newborns with difficulties as well as complicated and limited access to health resources. Differences in sample size, the socio-demographic and economic condition of the research population, and access to health services could all be factors.

In this study, neonates born from mothers who had a history of urinary tract infections or sexually transmitted infections (UTI/STIs) during the pregnancy were three times more likely to develop neonatal sepsis. This finding is consistent with previous research in Gondar,[12] Jamma,[17] Mekelle,[18] and Bishoftu,[19] which found that maternal urinary tract and sexual infections were significant risk factors for neonatal sepsis. This finding may support the reason that pregnancy causes numerous changes in the woman's body that increase the likelihood of urinary tract infections (UTIs). Untreated bacteriuria during pregnancy is associated with risks to both the fetus and the mother. In general, pregnant patients are considered immunocompromised because of the physiologic changes associated with pregnancy. These changes increase the risk of serious infectious complications from symptomatic and asymptomatic UTIs, even in healthy pregnant women. This maternal

health problem is often associated with neonatal sepsis, especially if untreated during the third-trimester pregnancy or labor. Therefore, neonatal sepsis may result from colonization of the birth canal by the infectious agent.[20]

This study also identified significant associations between premature rupture of the membrane and neonatal sepsis. The odds of neonatal sepsis among neonates born from mothers who had a history of PROM were 4.9 times more likely as compared to those neonates born before 18 hours of rupture of the membrane. This finding is similar to the findings in Debre Markos, Mekelle, Ethiopia, and Pakistan.[18,21,22] Early membrane rupture increases the risk of bacteria rising from the birth canal into the amniotic sac, resulting in chorioamnionitis and fetal compromise, as well as hypoxia, which usually leads to sepsis.[23]

This research also discovered a link between neonatal sepsis and neonatal resuscitation. The odds of developing neonatal sepsis among neonates who had a history of neonatal resuscitation at birth were 2.3 times higher as compared to neonates who had not been resuscitated. This finding was in agreement with studies from Gondar,[12] Bangladesh,[24] Tanzania[15] and Ghana.[25] Neonatal resuscitation at birth was found to be a substantial risk factor for neonatal sepsis. Many life-saving treatments, like suctioning and endotracheal intubations, can cause transient and persistent bacteremia, and resuscitation may be performed with contaminated equipment, introducing microorganisms into the lungs of the neonate's immune system, which is still developing. Because of the foregoing, resuscitation techniques at birth have a higher risk of complications.

This study revealed that preterm delivery is one of the significant risk factors for neonatal sepsis, which is 4.4 times more likely as compared to post-term delivery. This finding is in agreement with the findings from the study conducted in Debre Markos, Arbaminch general hospital, Ghana, Kenya, and Tanzania.[11,13,15,21,25] It is explained that preterm neonates tend to have poor host defenses and are more likely to suffer neonatal sepsis. Preterm infants may experience limited enteral feedings and/or exposure to breast milk, which collectively increase the risk for infection. Breast milk contains many bioactive molecules that provide an innate immune function to the newborn. Moreover, preterm neonates are also more likely to receive parenteral nutrition through the insertion of a needle into a vein, which might expose neonates to infections.

Conclusion and Recommendation

This study indicates that the proportion of neonatal sepsis is high. A history of maternal PROM, being a preterm neonate, a history of maternal UTI/STIs, and having received resuscitation at birth were identified as risk factors for neonatal sepsis. As a result, health worker training and infection prevention strategies must be strengthened and/or implemented. It focuses on the specific determinants and provides information about neonatal sepsis risk factors to help the community adopt behavioral changes.

Limitation of the Study

The study was done on admitted neonates, so results might lack generalizability to the entire population in the catchment area.

Abbreviations

APGAR, Activity, Pulse, Grimace, Appearance, Respiration; EONS, Early on Set of Neonatal Sepsis; GA, Gestational Age; LONS, Late on Set of Neonatal Sepsis; LBW, Low Birth Weight; NICU, Neonatal Intensive care unit; PROM, Prolonged Rapture of Membrane; UTI, Urinary Tract Infection; WHO, World Health Organization.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

Ethical clearance was obtained from Wollo University, College of Medicine and Health Science, Department of Pediatrics and Child Health Nursing Ethics Review Committee. The reference number of this letter was PCHN-670/

2020. Then, it was submitted to Woldia and Dessie's comprehensive specialized hospital administrators. Verbal informed consent was obtained from newborn mothers or caregivers in the study before data collection. The verbal informed consent was acceptable and approved by the ethical review committee. In order to ensure confidentiality, the names and other identities of study participants were not included. Furthermore, the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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