Does Preterm Birth Significantly Associated With Neonatal Sepsis?

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ABSTRACT

Background: Neonatal sepsis is a systemic infection that occurs in neonates within the first 28 days of life. Neonatal sepsis has an estimated global burden of 2,202 per 100,000 live births, and it is a major cause of neonatal morbidity and mortality in developing countries. According to the findings, bacteria cause the vast majority of neonatal sepsis. In fact, the Ethiopian ministry of health has made countless efforts to reduce neonatal mortality, among them the community-based newborn care program and the integrated management of neonatal and child illness program. However, there was a scarcity of data on the severity of neonatal sepsis and its predictors in the study area. Therefore, the purpose of this study was to evaluate neonatal sepsis and its associated factors.

Methods: Institutional-based cross-sectional study design was conducted, among neonates admitted to neonatal intensive care unit at public hospitals in Southern Ethiopia, from May 1 to June 30, 2021. A total of 292 subjects (mother-neonate pairs) were selected using a systematic random sampling technique and pre-tested and structured questionnaires were used to collect data. Epi-data version 3.1 was used for data entry and data was exported to SPSS version 25 for further analysis. Multi-variable logistic regression analysis was fitted to identify factors associated with neonatal sepsis. Adjusted Odds Ratio (AOR) with the corresponding 95% Confidence Interval (CI) was used to show the strength of associations and variables with p-values of <0.05 were considered as statistically significant.

Results: Overall prevalence of neonatal sepsis was 83.9% (95% CI: (79.2-87). Gestational age <37 weeks (AOR=3.2; 95% CI (1.45, 6.94), being male (AOR=2.2; 95% CI (1.04, 4.44) and birth asphyxia (AOR=3.9; 95% CI (1.02, 14.7) were significantly associated with neonatal sepsis.

Conclusion: The prevalence of neonatal sepsis was high. Gestational age <37 weeks, being male, and neonate diagnosed with birth asphyxia were identified factors for neonatal sepsis. Special attention should be given to preterm neonates, use of partograph to hasten the second stage of labor to prevent birth asphyxia, early detection and prevention of infection should be applied to save neonates.

Keywords: Neonatal; Sepsis; NICU; Southern Ethiopia

Abbreviations: AOR: Adjusted Odd Ratio; ANC: Ante Natal Care; APGAR: Appearance, Pulse, Grimace, Activity and Respiration; COR: Crude Odd Ratio; CS: Cesarean Section, DC: Data Collector; EDHS: Ethiopian Demographic Health Survey; NICU: Neonatal Intensive Care Unit, NS: Neonatal Sepsis; PROM: Premature Rupture of Membrane; RH: Reproductive Health; UTI: Urinary Tract Infection; WHO: World Health Organization

INTRODUCTION

Neonatal sepsis is a systemic infection that occurs in infants within the first 28 days of life and is a leading cause of morbidity and mortality in newborns [1]. Neonatal sepsis is classified as either early neonatal sepsis or late-onset sepsis based on the onset of symptoms. The former occurs primarily within the first 72 hours of life, whereas the latter usually appears after 72 hours of age [2]. Neonatal sepsis is one of the most important causes of morbidity and mortality [3]. Neonatal mortality accounted for 45.1% of all child deaths worldwide [4]. The global incidence of neonatal sepsis was estimated to be 2,202 per 100,000 live births [5]. In Sub-Saharan Africa, 17% of neonatal deaths are attributed to neonatal sepsis [6].

Neonatal infection is the most significant public health problem, particularly in developing countries, where it contributes significantly to neonatal morbidity and mortality and imposes numerous complications such as cognitive disability and developmental delays [7]. Neonatal sepsis has an economic impact, especially in developing countries that lack adequate sanitation and clean working environments. According to studies, the financial burden of neonatal sepsis in Sub-Saharan Africa could be lowered through appropriate treatment and prevention [8].

Ethiopia ranks among the top ten countries in terms of neonatal morbidity and mortality, with over 100,000 newborn deaths per year. According to the 2016 Ethiopian Demographic Health Survey, the Newborn Mortality Rate (NMR) in Ethiopia was 29 per 1000 live births (EDHS). This is a significant decrease from the previous EDHS report of 37/1000 live births in 2011. Nonetheless, according to the mini EDHS 2019, the newborn mortality rate has risen to 30 deaths per 1000 live births. Furthermore, the prevalence of newborn sepsis in Ethiopian neonates admitted to hospitals across the country ranged from 11.7% to 77.9% [9].

Prematurity, asphyxia, tetanus, and sepsis are the leading causes of neonatal death in Ethiopia. Many women do not seek professional medical attention during their pregnancy, childbirth, or puerperium. Less than a third of mothers receive prenatal care from TBAs (26%), families (58%), or women alone (6%). Postnatal care is received by almost no one (3.5%). As a result, determining the prevalence and identifying the associated factors is key to preventing neonatal illnesses and achieving long-term development goals by reducing newborn mortality. This contributes to the development of methods of preventing neonatal sepsis. In fact, the Ethiopian Ministry of Health has made numerous efforts to reduce neonatal mortality, such as the Community-Based Newborn Care (CBNC) and Integrated Management of Neonatal and Child Illness (IMNCI) programs the burden of neonatal sepsis remained high. Therefore, this study was aimed to assess neonatal sepsis and associated factors among neonates admitted to NICU at Public Hospitals of southern Ethiopia.

MATERIALS AND METHODS

Study design and settings

Facility-based cross-sectional study was conducted among neonates admitted to NICU at public hospitals of Southern Ethiopia from May 1 to June 30, 2021. The area is bordered by Kenya in South, on the West and North by the Southern Nations, Nationalities, and Peoples Region, and East by the Somali Region. It contains three administrative zones of the Oromia Region (Borena, West Guji, and Guji Zone). There are four general hospitals, five primary hospitals and one hundred seventy (170) health centers in the study area. The general hospitals (Adola Wayu, Bule Hora, Yabello, and Nagele) have been providing services like an obstetric, gynecologic, emergency, medical, surgical, laboratory, and radiology.

Study population

All neonates who were admitted to NICU at public hospitals in Southern Ethiopia were source population while all randomly selected neonates who were admitted to the NICU at public hospitals during data collection period were study population.

Sample size and sampling procedure

The sample size was determined using single population proportion by assuming 5% margin of error and 95% confidence interval (σ=0.05) and proportion of neonatal sepsis 77.9% [10] from previous study.

$$n=(Z\alpha/2)^2 P (1-p)/d^2$$

Where,

n: required sample size, p: proportion of neonatal sepsis (77.9%), Z: the value of the standard normal curve score corresponding to the given confidence interval 1.96 and d is the margin of error (the required precision)=5% and double population proportion formula was used to calculate factors associated with neonatal sepsis. Therefore; by adding 10% of non-response rate, the final sample size was 292. Four public hospitals in southern Ethiopia namely (Adola Wayu, Bule Hora, Yabello, and Nagele) were selected. Then sample size was proportionally allocated for each hospital by considering the previous 2 months case flow to estimate the expected number of neonates that visited the hospitals in two months. Then, a systematic random sampling technique was used to get study units from neonates admitted to the neonatal intensive care unit. The sampling interval (K) was calculated by taking the two months neonates' admission report from NICU which was 452. Then K=N/n, 452/292=2. Every two women with her neonate were interviewed; the first woman was selected randomly.

Data collection procedures

The data on socio-demographic factors, obstetric factors, maternal medical condition and neonatal factors were collected from study participants using data extraction checklist. The data were collected by health professionals after they had been given adequate orientation.

Measurement of study variables

Dependent variable for this study was neonatal sepsis: Neonatal sepsis was when the neonate shows one or more neonatal dangerous signs such as hypothermia (<36°C), hyperthermia (<38°C), tachycardia (HR>180), bradychardia (HR<80), tachypnea (RR>60), bradypnea (RR<30), poor feeding, abdominal distention, recurrent vomiting, diarrhea, unexplained hypoglycemia or hyperglycemia, history of convulsions, sever jaundice, bulging fontanel, seizures, lethargy, premature or low birth weight <2 kg plus diagnosed by the physician was coded as "1" and for those didn't have any of these signs and symptoms and not diagnosed by physician would be given"0" [11].

Independent variables: Socio-demographic factors, obstetric factors, maternal medical condition and neonatal factors.

Data quality control

The preliminary assessment of the adequacy of the checklist was carried out and the variables on which the data were not available were excluded from the checklist. Trained health professionals have been assigned as data collectors. In addition, to ensure that the data quality of the completed checklist was checked for consistency and completeness. Strict supervision has been made by supervisors during data collection.

Data processing and analysis

Data was entry using Epi Info-7 and exported to SPSS statistical software 25 for further analysis. Descriptive statistics such as mean, median, Standard Deviations (SDs) and tables have been used to summarize the characteristics of the study participants.

To control for potential confounders, bivariable analysis was performed, and all variables with a P-value of 0.25 in the bivariable analysis were included in the final model of multivariable analysis. Adjusted Odds Ratios (AOR) and 95%CI were estimated in the final model of multivariable logistic regression analysis to identify the true effects of independent variables on outcome variables. The statistical significance level was set at P-value .05.

The Multivariable logistic regression was used to identify predictors of neonatal sepsis. Hosmer and Lemeshow statistic test were examined to determine the fitness of the model.

The factors significantly associated with neonatal sepsis in the bi-variable analysis at p-values below 0.25 were included in the multivariable logistic regression model. AOR of the final model and their 95% confidence intervals were used as a measure of association between the predictors and the outcome variable. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

Socio-demographic characteristics

The median age of the mothers was 25 years with ± 9 IQR. More than a half 166 (56.8%) of neonates were in the early neonatal period and 173 (59.2%) of them were male. Majority 165 (56.5%) of mother were from rural and 125 (42.8%) of them were not educated (Table 1).

Table 1: Socio demographic characteristics of mothers and neonates at public hospitals of Southern Ethiopia 2021 (n=292).

Variable	Category	Frequency	Percent (%)
Maternal age	15-19	35	12
	20-24	98	33.6
	25-29	79	27.1
	30-35	44	15.1
	>=35	36	12.3
Sex of neonates	Male	173	59.9
	Female	119	40.8
Place of residence	Urban	127	43.4
	Rural	165	56.5
Age of the neonate in days	0-7	166	56.8
	8-28	126	43.2
Marital status	Single	56	19.2

	Married	225	77.1
	Divorced	11	3.7
Educational status of the mother	Not educated	125	42.8
	Primary education	85	29.1
	Secondary education	54	18.5
	Collage and above	28	9.6
Occupation of the mother	Housewife	190	65.1
	Governmental employee	23	7.9
	Merchant	35	12
	Private organization	14	4.8

Obstetric characteristics of the mothers

From the total mothers of neonate, 196 (67.1%) of them were multipara and about 202 (69.2%) of them had antenatal follow-up. About 267 (91.4%) of neonates were born through spontaneous vaginal delivery and 70 (24%) of mothers were delivered at home (Table 2).

Table 2: Obstetric characteristics of the mothers of neonates at public hospitals of Southern Ethiopia 2021 (n=292).

Variable	Category	Frequency	Percent
Parity	1	96	32.9
	≥ 2	196	67.1
ANC follow up	Yes	202	69.2
	No	90	30.8
Current mode of delivery	SVD	225	77.1
	ID	31	10.6
	C/S	36	12.3
Onset of labor	Spontaneous	267	91.4
	Induced	25	8.6
Duration of labor	<12 hr	220	75.3
	>=12 hr	70	24
Place of delivery	Home	70	24
	Health institution	222	76
History of pregnancy related hypertension	Yes	13	4.5
	No	278	95.6
Premature rupture of membrane	Yes	110	37.7

	No	182	62.3
Duration of rupture of membrane in hours	<18	96	32.9
	>18	15	5.1
Fever during pregnancy	Yes	96	32.9
	No	196	67.1

Maternal medical condition

279 (95.5%) of mothers did not have Diabetes mellitus. About 96 (32.9%) of mothers had a history of UTI during their current pregnancy and 4 (1.4%) of them were HIV positive. 18 (6.2%) of mothers were positive for syphilis (Table 3).

Table 3: Medical condition of the mothers at public hospitals of Southern Ethiopia, 2021 (n=292).

Variable	Category	Frequency	Percent
Diabetes mellitus	Yes	13	4.5
	No	279	95.5
UTI	Yes	96	32.9
	No	196	67.1
HIV/AIDS	Positive	4	1.4
	Negative	233	79
	Unknown	55	18.8
Syphilis test	Positive	18	6.2
	Negative	185	63.4
	Unknown	89	30.5

Neonatal related factors

About 141 (48.3%) of neonates were preterm. About 81 (27.7%) of neonates' birth weight were <2.5 kg. Nearly one third 67 (22.9%) of the neonates had birth asphyxia and the median length of hospital stay was 4 days (Table 4).

Table 4: Neonatal related factors among neonates admitted to NICU at public hospitals of Southern Ethiopia 2021 (n=292).

Variable	Category	Frequency	Percent
Gestational age	<37	141	48.3
	37-42	151	51.7
APGAR score at 1st minute	<7	128	43.8
	>=7	43	14.7
Birth asphyxia	Yes	67	22.9

	No	225	77.1
Birth weight	<2500	81	27.7
	>=2500	193	66.1
Did the neonate was resuscitated	Yes	107	36.6
	No	185	63.4
Neonate cries immediately after birth	Yes	189	64.7
	No	103	35.3
Length of stay	<7 days	261	89.4
	>7 days	31	10.6

Neonatal sepsis

Overall magnitude of neonatal sepsis was 245 (83.9 % (95% CI: 79.2-87) while 47 (16.1%) were admitted due to the causes other than neonatal sepsis.

Factors associated with neonatal sepsis

Age of the mothers, sex of neonates, residence, place of delivery, presence of premature rupture of membrane, presence of fever, presence of UTI, birth asphyxia, gestational age less than 37 weeks, a neonate who is resuscitated at birth and neonate who is not cry immediately were candidate for multivariable logistic regression.

In multivariable logistic regression, birth asphyxia, sex of neonate, and gestational age were found to be independent predictors of neonatal sepsis. The male neonates were about 2 times higher likelihood of developing neonatal sepsis compared to female neonates (AOR=2.2, 95% CI (1.04, 4.44). Neonates less than 37 weeks gestational age were 3 times more likely to develop neonatal sepsis compared to their counterparts (AOR=3.2, 95% CI (1.45, 6.94). Neonates with birth asphyxia were 4 times more likely to develop neonatal sepsis compared to those who didn't diagnosed with birth asphyxia (AOR=3.9, 95% CI (1.02, 14.71) (Table 5).

Table 5: Bivariable and multivariable logistic regression analysis of neonatal sepsis among neonates admitted in NICU of public general hospitals of South Oromia, Ethiopia 2021(n=292).

Variable	Category	Neonatal sepsis		COR 95% CI	AOR 95% CI
		Yes (n, %)	No (n, %)		
Maternal age	15-19	32 (91.4)	3 (8.6)	1	1
	20-24	85 (86.7)	13 (13.3)	0.63 (0.16, 2.29)	2.36 (0.50, 10.99)
	25-29	66 (83.5)	13 (16.5)	0.47 (0.12, 1.79)	0.56 (0.56, 5.02)
	30-35	34 (77.3)	10 (22.7)	0.31 (0.80, 1.26)	1.57 (0.53, 4.66)
	>=35	28 (77.8)	8 (22.2)	0.32 (0.07, 1.35)	0.73 (0.22, 2.42)
Residence	Rural	143 (86.7)	22 (13.3)	1.59 (0.85, 2.98)	1.33 (0.64,2.76)
	Urban	102 (80.3)	25 (19.7)	1	1
Sex of neonate	Male	150 (86.7)	23 (13.3)	1.64 (0.88, 3.98)	2.15 (1.04, 4.44)[*]
	Female	95 (79.8)	24 (20.2)	1	1
Place of birth	Home	62 (88.6)	8 (11.4)	1.65 (0.73,3.72)	2.15 (0.84, 5.51)

	Institution	183 (82.4)	39(17.6)	1	1
PROM	Yes	100 (90.9)	10 (9.1)	2.55 (1.21,5.36)	1.58 (0.69, 3.60)
	No	145 (79.7)	37 (20.3)	1	1
UTI	Yes	86 (89.6)	10 (10.4)	2.00 (0.94, 4.22)	1.98 (0.87, 4.48)
	No	159 (81.1)	37 (18.9)	1	1
Gestational age	<37	128 (90.8)	13 (9.2)	2.86 (1.44,5.68)	3.18 (1.45,6.94)[**]
	37-42	117 (77.5)	34 (22.5)	1	1
Birth asphyxia	Yes	63 (94.0)	4 (6.0)	3.72 (1.28, 10.78)	3.89 (1.02,14.71)[*]
	No	182 (80.9)	43 (19.1)	1	1
Resuscitation	Yes	95 (88.8)	12 (11.2)	1.84 (0.91, 3.73)	1.44 (0.46, 4.45)
	No	150 (81.1)	35 (18.9)	1	1
Crying immediately after birth	Yes	154 (81.5)	35 (18.5)	1	1
	No	91 (88.3)	12 (11.7)	1.72 (0.85, 3.48)	0.808 (0.27, 2.37)

Note: COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio; CI: Confidence Interval, [*]p-value <0.05, [**]p-value <0.01

DISCUSSION

The overall prevalence of neonatal sepsis in this study was 83.9% (95% CI: 79.2-87). This finding was consistent with Arbaminch's (78.3%) and Shashemene (77.9%) [3,10]. This is because all studies were conducted on populations with similar socioeconomic characteristics and study designs. However, our findings were higher than those of Arsi University (34%), and Wolaita Sodo (33.8%) [5,12]. This disparity could be explained by the accessibility of health facilities, the clinical definition of sepsis in different settings, advancements in laboratory setup compared to current study settings, and proper infection prevention protocol implementation. Male neonates had twice the risk of neonatal sepsis as their female counterparts. This finding is consistent with research conducted in Egypt and Gondar [13,14]. This might occur because male and female neonates have different immune responses. However, the causes of gender differences in disease are still unknown. A gestational age of less than 37 weeks was found to be significantly associated with neonatal sepsis in this study. This finding is consistent with the findings of the Arsi and Gondar studies. Preterm neonates are said to have weakened host defenses, making them more vulnerable to neonatal sepsis. Preterm infants may receive limited enteral feedings and/or be exposed to breast milk, both of which increase the risk of infection. Breast milk contains several bioactive compounds that help the infant's innate immune function. Premature newborns are also more susceptible

to the need for parenteral nutrition via needle insertion into a vein, which can expose them to infections. The odds of neonatal sepsis were 4 times higher among neonates diagnosed with birth asphyxia than their counterpart. This is consistent with the findings of Jinka study (2). This is due to the fact that failure to initiate or sustain breathing results in decreased oxygen to the vital organs, exposing them to an invasive process, and when neonates develop asphyxia, the number of days spent in the hospital increases.

STRENGTHS AND LIMITATIONS OF THE STUDY

The study's strength was that it was carried out in pastoral and agro-pastoral areas of southern Ethiopia where no previous studies had been conducted out, and it included four general hospitals to cover a large geographical area. The true effects of predictors on the outcome variable was not confirmed in this study because it used a cross-sectional design. Additionally, there was no laboratory culture evidence for diagnosing neonatal sepsis, and no list of sepsis-causing bacteria was identified, implying that it was solely relied on clinical sepsis criteria, which could lead to overestimation or erroneous diagnosis.

CONCLUSION

This study found a high prevalence of neonatal sepsis. Male sex, premature delivery, and neonates with birth asphyxia were identified as risk factors for neonatal sepsis. As a result, infection prevention measures and health professional training must be strengthened and implemented. It focuses on specific determinants and gives information about risk factors for neonatal sepsis to assist the population in making behavioral changes.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Bule Hora university's research and publication directorate provided ethical approval. After explaining the objective of the research to participants, informed consent with a written signature was acquired. They were informed that they could withdraw at any time and/or refrain from answering questions. Participants in the study were also notified that all data obtained from them would be kept confidential by using code rather than any personal identifiers. Furthermore, the research procedure was carried out in compliance with the Helsinki declaration of the World Medical Association.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

All necessary information was included in the manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS' CONTRIBUTIONS

EK, AH, YH, AE, AA conceived the idea and designed the study; led data analysis and interpretation; developed the first draft of the manuscript and made all revisions based on coauthors comments and suggestions. AE, AA, AH critically revised the manuscript for important intellectual content; ensured the requirements of submission of the manuscript are met. EK, YH, AH, AE, AA, contributed towards analysis and data interpretation; revision and editing of the manuscript. All authors read and agreed to final version of the manuscript for publication.

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