Determinants of Neonatal Sepsis among Neonates Admitted in a Neonatal Intensive Care Unit at Injibara General Hospital, Awi Zone, and Amhara Regional State, Ethiopia

Ephrem Yeshambel, MSc[1], Addisu Alehegn Alemu, MSc[2,3],
Bewket Yeserah Aynalem, MSc[2] (iD), and Yewbmirt Sharew Bayile, MSc[2]

Abstract

Introduction. Neonatal sepsis is the primary cause of increased newborn morbidity and mortality worldwide, particularly in developing countries. In Ethiopia, the factors of neonatal sepsis are not well understood. Therefore, the purpose of this study was to determine the factors associated with neonatal sepsis in the study area. *Methods.* A case-control study design was conducted among 60 cases and 120 controls. Variables with $P \leq .25$ in the bivariate analysis were entered into multivariable logistic regression, and statistical significance was declared at $P < .05$. *Result.* Birth weight <2500-g (AOR = 4.05 [1.44, 11.36], number of ANC visits <3 (AOR = 4.49 [1.70, 11.86], duration of rupture of membrane ≥ 18 hours (AOR = 4.42; [2.02, 9.66], first minute APGAR score <7 (AOR = 3.09 [1.10, 8.70], birth at a health-center (AOR = 0.22 [0.08, 0.60]) and instrumental delivery (AOR = 0.30 [0.10, 0.88]) were factors associated with neonatal sepsis. *Conclusion.* Neonatal sepsis was associated with different factors like prolonged membrane rupture, birth weight, and antenatal care visits.

Keywords

case-control, Injibara, neonate, sepsis

Introduction

Neonatal sepsis is a systemic inflammatory response to the presence of or as a result of suspected or proven infection in a neonate, and it may be bacterial, viral, fungal, or rickettsia in origin.[1,2] In neonatal intensive care units (NICUs), maternal infections in medical settings continue to be a leading source of overestimated mortality and morbidity worldwide.[2]

Neonatal sepsis (NS) accounts for 15% of neonate deaths worldwide, with 30% to 50% of cases occurring in low and middle-income countries (LMIC).[3-6] About 6.9 million neonates are reported to have a possible serious sepsis every year in sub-Saharan Africa, south Asia, and Latin America.[3,7] Around 5.94 million children under the age of 5 experienced sepsis in 2015; of these, 45% died,[8] from neonatal sepsis, the third leading cause of newborn death.[7,9] Again, 2.6 million infants lost their lives in 2016 to mostly avoidable causes; over 2 million of these deaths happened in the first week of life, and 1 million happened on the day of birth in Africa.[10]

Neonatal sepsis is a major newborn killer in Ethiopia and accounts for more than one-third of neonatal deaths. It causes 37% of neonatal deaths, with an incidence rate as high as 10 per 1000 live births.[11,12] A recent population-based studies in a rural part of Ethiopia showed that sepsis is the first consequence of neonatal death.[13] According to the 2019 Mini Ethiopian Demographic

[1]Mizan Aman Health Science College, Bonga, Mizan Aman, Ethiopia
[2]Debre Markos University, Debre Markos, Ethiopia
[3]University of New South Wales Sydney, Sydney, Australia

Corresponding Author:
Bewket Yeserah Aynalem, Debre Markos University, Health Science College, Debre Markos Po.Box 269, Ethiopia.
Email: by123bewket@gmail.com

Health Survey (EDHS) report, the neonatal mortality rate (NMR) in Ethiopia is 30/1000 live births, and this significant number of deaths is greatly attributed to neonatal sepsis.[14]

Various factors contribute to this elevated mortality, including under-recognition of illness, delay in healthcare seeking at the household level, delay in initiation of treatment, and lack of access to both properly trained health workers and high-quality services to manage sepsis.[15,16] Thus, identifying determinant factors prevailing in the different geographical contexts has become a crucial issue for optimizing neonatal care.[1] The World Health Organization (WHO) has set global objectives to reduce neonatal and under-five mortality to as low as 12/1000 and 25/1000, respectively, by 2030 in African nations to achieve the Sustainable Development Goals (SDGs).[17] In several developing countries, the identification of determinants for neonatal sepsis and the management of neonates with sepsis are unsatisfactory.[11]

Although a large amount of research has been done in Africa and other developing countries on the factors associated with newborn sepsis,[5,18,19] very few studies have been done in the Amhara region, particularly in the study area. Therefore, identifying determinant factors of neonatal sepsis will be crucial for reducing neonatal mortality and proposing appropriate interventions. Thus, this study aimed to identify determinants of neonatal sepsis among neonates admitted to the NICU ward in Injibara General Hospital in Awi Zone, Amhara Region, Amhara Regional State, Ethiopia.

Methods

Study Area and Period

The study was conducted in the Injibara General Hospital, Awi Zone, Amhara Region, Ethiopia, from March 16, 2020, to April 16, 2020, and a case-control study design was employed. The Injibara General Hospital is located in Injibara, in the town of Awi Administrative Zone. Injibara town is also located in both the Northwestern area of Ethiopia and the Southwest part of the Amhara region. The town is about 447 km away from Addis Ababa, the capital city of Ethiopia, and 118 km from Bahir Dar, the capital city of the Amhara Regional State. It is located at 10°57′N, 36°56′E, at an elevation of 2560 m above sea level. Injibara is situated in a predominantly mountainous location.[20] The hospital was established in February 2015 by the government and provides services in emergency, outpatient, inpatient, and operation room theater departments. The Injibara General Hospital serves more than 1.32 million people in the Awi Zone community. On average, 6 neonates were admitted to the NICU per day, and there were 4 physicians, 12 nurses, and 15 beds in the NICU.

Population

Source population. All neonates who were admitted to Injibara General Hospital were the source population.

Study population. The study population was all neonates admitted to the NICU wards of Injibara General Hospital during the study period.

The cases were all neonates admitted to Injibara General Hospital with their mothers, and peripheral vein blood culture was obtained from them within the first 28 days of life and validated the clinical suspicion of sepsis.[21]

The controls in this study were neonates admitted to the NICU of Injibara General Hospital in the Awi zone of Amhara, Ethiopia, during the study period, but without sepsis. Neonates without mothers, with incomplete charts, and who weren't given a sepsis diagnosis weren't included in the case. Similarly, newborns admitted without their mothers and those with inadequate charts were not included in the study's control group.

Sample size determination. The sample size for the study was determined using a double population proportion exposure difference formula by using major determinant variables.[22]

$$n = \frac{(r+1)}{r} \frac{(\bar{p})(1-\bar{p})(Z_{\beta+} Z_{\alpha/2})^2}{(p_{1-}p_{2)}^2}$$

Based on the above calculation, the place of delivery had the largest size, 163, which determined the final sample size (Table 1).

Sampling Procedure

Using the log books as the sample frame and a physician's diagnosis as the basis for selection, a simple random sampling was employed to choose research participants. Through record review, cases and controls were identified following diagnosis by NICU physicians. Cases were chosen from among newborns hospitalized in Injibara General Hospital's NICUs sequentially. Similarly, the next 2 corresponding controls were selected among newborns hospitalized at Injibara General Hospital's NICUs on the same day.

Data Collection and Data Quality Control

Neonatal sepsis was a dependent variable, and sociodemographic variables, maternal/obstetric variables,

Table 1. Sample Size Calculation to Identify Determinants of Neonatal Sepsis Among Neonates Admitted in a Neonatal Intensive Care Unit IGH, Awi Zone Amhara Regional State, Ethiopia, 2020.

		Sample size		
Variables	Proportions	Case	Control	Total
Urinary tract infection	P1 = 51.3% P2 = 13.5%	20	40	60
Premature rupture of membrane	P1 = 30.5% P2 = 3.8%	26	52	78
Intrapartum fever	P1 = 28.2% P2 = 4.5%	32	63	95
APGAR score 5th min <7	P1 = 21.8% P2 = 1.9%	34	68	114
Place of delivery	P1 = 26.9% P2 = 8.3%	54	109	163

By considering 10% non-response the final sample size was 180. Then the estimated sample size for cases and controls was 60 and 120 respectively, using 1:2 ratios.

and neonatal variables were independent variables. Neonatal sepsis diagnosed as septic was considered a case,[21] and neonates diagnosed with other problems except sepsis were controlled. A prolonged rupture of the membrane is characterized as a labor that lasts more than 18 hours after the membrane ruptures.[23] Neonates were babies with 28 days of life, and babies weighing less than 2.5 kg were deemed to have low birth weights.[24] Those mothers who could not read and write the Amharic language were considered unable to read and write. Those who live in areas accessed by infrastructure and connectivity health facilities were considered urban residents. In contrast, those who live in rural areas usually don't have access to infrastructure and connectivity.

The quality of the data was assured with 5 trained data collectors and 2 supervisors. The data were collected through face-to-face interviews by BSc nurses after 2-day data collection training was given to them together with 2 MSc holder supervisors. The questionnaire was structured and pre-tested; it was first prepared in English, translated to the local (Amharic) language, and then again translated back to English. A pretest was conducted on 12 respondents of the sample size in Debre Markos Specialized Hospital, and the necessary corrections were made when necessary, but the results of the pretest were not included in the final analysis.

Data Processing and Analysis

Data were entered, cleaned, and coded using Epi Data version 3.1 and exported to STATA software version 14

for analysis.[25,26] Descriptive statistics are presented as frequency and percentages. A Pearson Chi-square test was used to assess the relationship between each independent variable and the outcome variable (neonatal sepsis). Then variables in the bivariate model with a *P*-value ≤ .25 were entered and analyzed by a multivariable logistic regression model to identify the independent effects of different factors on the occurrence of sepsis. Then, the 95% confidence interval of the adjusted odds ratio (AOR) was computed, and a variable having a *P*-value less than .05 in the multivariable logistic regression analysis was considered statistically significant.

Ethical approval and informed consent. Ethical clearance for the study was obtained from the Institutional Research Ethics Review Committee of the Debre Markos University (HSC/R/C/Ser/PG/Co/418/11/12). Written and verbal informed consent was obtained from participants' mothers to confirm their willingness. Participants were interviewed in a separate room, and anonymity and confidentiality of the data providers were strictly maintained.

Results

Socio-Demographic Characteristics of the Respondents

A total of 60 cases and 120 controls admitted to the NICU with their indexed mothers took part in the study. The neonates that were included in the study had ages ranging from 1 up to the 28th day of life, with a mean age of 7.31 (SD ± 5.91) days. Their moms ranged in age from 15 to 45, with a mean age of 28.74 (SD ± 5.48) years. Over half of the participants (60.0%) were male and 56.67% were female, with the majority coming from urban areas (63.33% cases and 64.17% controls). Of the participants, 78.33% of the cases and 75.83% of the control moms identified as Orthodox Christians. Most cases (71.67%) and controls (65.0%) had married couples (Table 2).

Maternal obstetrics and gynecologic characteristics. According to this study, the majority of cases (98.33%) and control women (99.17%) received antenatal care (ANC) services while they were pregnant with the present neonate. The proportion of women who attended ANC service ≤ 3 times was higher in controls (68.07%) than cases (51.67%) respectively. More than half of the women (46 (76.67%) of cases and 56 (46.67%) of controls) had given birth at the hospital (Table 3).

Table 2. Sociodemographic Characteristics of Study Participants for the Study of Determinants of Neonatal Sepsis in Injibara General Hospital, Awi Zone, Amhara, Ethiopia, 2020.

Exposure variables	Responses	Cases N = 60 (%)	Controls N = 120 (%)
Marital status	Single	22 (36.67)	26 (21.67)
	Married	32 (53.33)	74 (61.67)
	Widow	4 (6.67)	10 (8.33)
	Divorced	2 (3.33)	10 (8.33)
Maternal religion	Orthodox	47 (78.33)	90 (75.0)
	Muslim	7 (11.67)	13 (10.83)
	Protestant	5 (8.33)	13 (10.83)
Maternal residence	Urban	38 (63.33)	77 (64.17)
	Rural	22 (36.67)	43 (35.83)
Maternal educational level	Unable to read & write	10 (16.67)	26 (21.67)
	Primary education	22 (36.67)	44 (36.67)
	Secondary education	17 (28.33)	39 (32.50)
	College and higher education	11 (18.33)	11 (9.17)
Maternal age	15-20	3 (5.00)	3 (2.50)
	21-34	46 (76.67)	95 (79.17)
	≥35	11 (18.33)	22 (18.33)
Neonatal age in days	<7	31 (51.67)	79 (65.83)
	7-28	29 (48.33)	41 (34.17)
Neonatal sex	Female	24 (40.0)	52 (43.33)
	Male	36 (60.0)	68 (56.67)

Table 3. Obstetrics and Gynecologic Characteristics of Study Participants Admitted to NICU in Injibara General Hospital, Amhara Region, Ethiopia, 2020.

Exposure variables	Responses	Cases N = 60 (%)	Controls N = 120 (%)
Maternal parity	Primiparous	26 (43.33)	44 (36.67)
	Multiparous	34 (56.67)	76 (63.33)
Maternal antenatal care visit follow-up	Yes	59 (98.33)	119 (99.17)
	No	1 (1.67)	1 (0.83)
Number of antenatal care visit services	>3	29 (48.33)	30 (25.10)
	≤3	31 (51.67)	89 (74.79)
Place of birth	Home	1 (1.67)	1 (0.83)
	Health center	13 (21.67)	63 (52.50)
	Hospital	46 (76.67)	56 (46.67)
Mode of delivery	Cesarean section	14 (23.33)	16 (13.33)
	Instrumental	11 (18.33)	37 (30.83)
	Spontaneous vaginal delivery	35 (58.33)	67 (55.83)
Birth attendant	Traditional birth attendant	1 (1.67)	2 (1.67)
	Health professional	59 (98.33)	117 (97.5)
Duration of prolonged rapture of membrane	<18	25 (41.67)	87 (72.5)
	≥18	35 (58.33)	33 (27.5)
Meconium-stained amniotic fluid	Yes	22 (36.67)	24 (20.0)
	No	38 (63.33)	96 (80.0)
Urinary tract infection	Yes	37 (61.67)	52 (43.33)
	No	23 (38.33)	68 (56.67)

Neonatal characteristics. This study showed that, nearly two-fifth (38.33%) of cases and nearly half of controls (60.83%) were delivered at term. Twenty-two (36.67%) cases and 27 (22.50%) controls were delivered before 37 weeks gestational age. Similarly, 50 (83.33%) of cases and 72 (60%) of controls first minute APGAR

Table 4. Neonatal Characteristics of Study Participants Admitted to NICU in Injibara General Hospital, Amhara Region, Ethiopia, 2020.

Exposure variables	Responses	Cases N = 60 (%)	Controls N = 120 (%)
Gestational age	Term	23 (38.33)	73 (60.83)
	Preterm	22 (36.67)	27 (22.5)
	Post-term	15 (25.0)	20 (16.67)
First-minute APGAR score	<7	50 (83.33)	72 (60.0)
	≥7	10 (16.67)	48 (40.0)
Fifth-minute APGAR score	<7	10 (16.67)	8 (6.67)
	≥7	50 (88.33)	112 (93.3)
Birth weight	≥2500 g	31 (51.67)	91 (75.83)
	<2500 g	29 (48.33)	29 (24.17)
Method of oxygen administration	Nasal catheter	6 (10.0)	9 (7.50)
	Ambubag	12 (20.0)	16 (13.33)
Immediate cry at birth	Yes	41 (68.33)	94 (78.33)
	No	19 (31.67)	26 (21.67)
Resuscitation at birth	Yes	19 (31.67)	26 (21.67)
	No	41 (68.33)	94 (78.33)

score was < 7. Moreover, nearly one-third (31.67%) of cases and one-fourth (21.67%) of controls were resuscitated at birth (Table 4).

Determinants of Neonatal Sepsis

After controlling the effect of other variables with binary logistic regression, the number of antenatal care visits, place of birth, mode of delivery, birth weight, duration of the premature rupture of the membrane, urinary tract infection, first-minute apgar score, fifth-minute apgar score, meconium aspiration syndrome, intra-natal fever, immediate cry at birth, resuscitation at birth, oxygen requirement, neonatal age, and gestational age continued to be significantly associated with neonatal sepsis. Finally, after controlling the effect of other variables with multivariable logistic regression analysis, premature rupture of membrane (AOR = 4.42; [2.02, 9.66]), number of maternal ANC visits (OR = 4.49; [1.70-11.86]), AGAR score < 7 (AOR = 3.09 [1.10, 8.70]), place of delivery (AOR = 0.22; [0.08, 0.60]), instrumental delivery [AOR = 0.30; [0.10, 0.88]), and birth weight (AOR = 4.05 [1.44, 11.36]) were the significant factors for neonatal sepsis (Table 5).

Discussion

This study was done to identify determinants of neonatal sepsis in Injibara General Hospital, Awi Zone, Amhara, Ethiopia. Compared to mothers whose fetal membrane rupture was less than 18 hours, those mothers whose ruptured fetal membrane was more than 18 hours were 4.42 times more likely to give birth to neonates who had

sepsis. Studies were carried out in several regions of Ethiopia,[22,27-30] Sudan,[18] Mexico,[31] Pakistan,[32] and Nepal[33] which supported the current study result. The possible reason might be the early fetal membrane rupture, which increases the risk of germs from the birth canal rising into the amniotic sac and causing fetal compromise, hypoxia, and chorioamnionitis or placentitis, which frequently result in infection of the fetus in utero.[34]

Additionally, the number of ANC visits was found to be significantly associated with the incidence of neonatal sepsis; neonates born to mothers who had ANC visits ≤ 3 times were approximately 5 times more likely to develop sepsis than neonates born to mothers who had ANC visits >3 times. These findings were supported by earlier research conducted in Uganda[35] and India.[36] The possible reason might be that women who had completed ANC services may have had better medical attention and knowledge of risk factors than women who received partial ANC services. Individuals with higher ANC follow-up rates may be eligible for an early danger sign diagnosis.

Similarly, neonates with an APGAR score of less than 7 in the first minute had a threefold increased risk of developing neonatal sepsis in comparison to those with a score of 7 or higher. Studies from Ghana,[34] Indonesia,[37] and Nepal[33] that found a first-minute APGAR score of less than 7 to be a risk factor for newborn sepsis supported the above finding. Resuscitation and an immune insult occur when the Apgar score is low. Neonates exposed to resuscitation techniques after birth asphyxia are at risk for microorganisms that cause sepsis. This could be the consequence of using non-sterile assistance

Table 5. Bivariate and Multivariable Logistic Regression Analysis Result for Determinants of Neonatal Sepsis in Injibara General Hospital, Awi Zone, Amhara, Ethiopia, 2020.

Exposure variables	Responses	Cases N = 60 (%)	Controls N = 120(%)	COR (95% CI)	AOR (95% CI)
Number of antenatal care visits	>3	29 (48.33)	30 (25.10)	1	
	≤3	31 (51.67)	89 (74.79)	2.77 (1.44, 5.33)*	4.49 (1.70, 11.86)**
Place of birth	Health center	13 (11.67)	63 (53.33)	0.25 (0.12, 0.51)*	0.22 (0.08, 0.60)**
	Hospital	46 (86.67)	56 (45.83)	1	1
Mode of delivery	Cesarean section	14 (23.33)	16 (13.33)	1.67 (0.73, 3.82)*	0.89 (0.25, 3.14)
	Institutional delivery	11 (18.33)	37 (30.83)	0.56 (0.25, 1.25)*	0.30 (0.10, 0.88)**
	Spontaneous vaginal delivery	35 (58.33)	67 (55.83)	1	
Birth weight	< 2500 gm	29 (48.33)	29 (24.17)	2.93 (1.52, 5.66)*	4.05 (1.44, 11.36)**
	≥ 2500 gm	31 (51.67)	91 (74.17)	1	
Duration of the premature rupture of the membrane	≥18	35 (58.33)	33 (27.5)	3.69 (1.92, 7.07)*	4.42 (2.02, 9.66)**
	<18	25 (41.67)	87 (72.5)	1	
Urinary tract infection	Yes	37 (61.67)	52 (43.33)	2.10 (1.11, 3.96)*	2.22 (0.93, 5.27)
	No	23 (38.33)	68 (56.67)	1	
First-minute APGAR score	<7	50 (83.33)	72 (60.0)	3.33 (1.54, 7.20)*	3.09 (1.10, 8.70)**
	≥7	10 (16.67)	48 (40.0)	1	
Fifth-minute APGAR score	<7	10 (16.67)	8 (6.67)	2.8 (1.04, 7.51)*	1.38 (0.33, 5.77)
	≥7	50 (88.33)	112 (93.3)	1	
Meconium aspiration syndrome	Yes	22 (36.67)	24 (20.0)	2.31 (1.16, 4.61)*	2.59 (0.96, 6.97)
	No	38 (63.33)	96 (80.0)	1	
Intra-natal fever	Yes	25 (41.67)	27 (22.50)	2.46 (1.26, 4.80)*	1.37 (0.47, 3.97)
	No	35 (58.33)	93 (77.50)	1	
Immediate cry at birth	Yes	41 (68.33)	94 (78.33)	0.59 (0.29, 1.19)*	1.90 (0.02, 14.15)
	No	19 (31.67)	26 (21.67)	1	
Resuscitation at birth	Yes	19 (31.67)	26 (21.67)	1.67 (0.83, 3.36)*	2.22 (0.08, 6.01)
	No	41 (68.33)	94 (78.33)	1	
Oxygen requirement	Yes	18 (30.0)	25 (20.83)	1.62 (0.80, 3.30)*	1.03 (0.02, 35.96)
	No	42 (70.0)	95 (79.17)	1	
Neonatal age	<7	31 (51.67)	79 (65.83)	0.55 (0.29, 1.04)*	0.69 (0.28, 1.66)
	7-28	29 (48.33)	41 (34.17)	1	
Gestational age	Term	23 (38.33)	73 (60.83)	1	
	Preterm	22 (36.67)	27 (22.5)	1.08 (0.45, 2.60)	1.00 (0.27, 3.64)
	Post-term	15 (25.0)	20 (16.67)	0.42 (0.18, 0.95)*	0.58 (0.18, 1.80)

*P < .25. **P < .05.

tools, which exposes the neonates to sepsis. Furthermore, sepsis may arise from neonates acquiring the pathogen vertically in utero before delivery.

The risk of neonatal sepsis had a significant association with the place of delivery. Compared to women who gave birth in hospitals, there was a 78% lower chance of neonates with neonatal sepsis in health center-born neonates. Studies carried out in Mekele, Ethiopia, supported the finding.[22] This could be because newborns delivered at health centers may receive treatment there or be sent to other medical facilities for diagnosis or treatment.

Neonates delivered via assisted vaginal delivery had a 70% reduced the risk of developing sepsis compared to those delivered spontaneously. This result was consistent with research from Debrezeit, Ethiopia.[38] The primary reason might be that women who used vacuum delivery techniques correctly were able to lessen the duration of labor, which can decrease hypoxia and ascending infection.

Compared to neonates weighing at least 2500 grams, those weighing less than 2500 grams had a 4-fold increased risk of developing sepsis. Research from Arsi, Jinka, Nigeria, Ghana, and India supported the current result.[34,39-42] The possible explanation might be their innate sensitivity to infection and the invasive treatments they undergo. Neonates with low birth weights are more likely to require mechanical ventilation, intravenous

access for medicines, parenteral nourishment via cannula, and longer hospital stays. Compared to neonates of average weight, this may put them at a higher risk of sepsis.[43] This may also be because the newborn's susceptibility to infection is determined by immunological maturity. However, this finding was contrary to the findings of studies conducted in Mekele,[22] Bishoftu,[38] and Bangladesh.[44] The contradiction may be due to socioeconomic and health service-related differences.

Conclusion

This study has found that both maternal and neonatal factors contributed to neonatal sepsis. Prolonged rupture of membrane, birth weight, number of ANC visits, place of birth at a health center, instrumental delivery, and first-minute Apgar score were determinants of neonatal sepsis. The government should augment the political priority given to sepsis by improving awareness of the growing medical and economic burden of neonatal sepsis. Health professionals should provide counseling for mothers who don't have complete ANC services. Primary care organizations should also increase their support for maternal education and include routine neonatal sepsis screening in the care of neonates and mothers.

Consent for Publication

All authors have a copy of this manuscript. The authors would like to confirm that this article has not been submitted to any other journal and we fully agree to be published by this journal.

ORCID iD

Bewket Yeserah Aynalem https://orcid.org/0000-0003-2847-4841

References

1. Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med*. 2005;6(1):2-8.
2. Stefanovic IM. Neonatal sepsis. *Biochem Med*. 2011; 21(3):276-281.
3. Seale AC, Blencowe H, Manu AA, et al. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. *Lancet Infect Dis*. 2014;14(8):731-741.
4. WHO. *Every Newborn an Action Plan to End Preventable Deaths. World Health Organization Are Available on the WHO Website (www.hoint) or Can be Purchased from WHO Press*. World Health Organization; 2014:1-58.
5. Shivaprasad BS. Risk factors associated with neonatal sepsis. *Int J Res Med Health Sci*. 2017;5(2):17-19.
6. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, et al. The global burden of paediatric and neonatal sepsis: a systematic review. *Lancet Respir Med*. 2018;6(3): 223-230.
7. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the sustainable development goals. *Lancet*. 2016;388(10063):3027-3035.
8. Lawn JE, Blencowe H, Oza S, et al. Every newborn: progress, priorities, and potential beyond survival. *Lancet*. 2014;384(99-38):189-205.
9. Oza S, Lawn JE, Hogan DR, Mathers C, Cousens SN. Neonatal cause-of-death estimates for the early and late neonatal periods for 194 countries: 2000-2013. *Bull World Health Organ*. 2015;93(1):19-28.
10. UNICEF (ed.). *The World Bank and United Nations. Levels and Trends in Child Mortality: Report 2017*. UNICEF; 2017.
11. UNICEF. *Committing to Child Survival: A Promise Renewed*. Technical Report Series. World Health Organization; 2014:1-100.
12. Csaaa E. *Ethiopia Demographic and Health Survey*, Vol. 1. ICF International Calverton; 2012:1-450.
13. Weldearegawi B, Melaku YA, Abera SF, et al. Infant mortality and causes of infant deaths in rural Ethiopia: a population-based cohort of 3684 births. *BMC Public Health*. 2015;15(1):770.
14. Ethiopian Public Health Institute (EPHI) (Ethiopia) and ICF.21.Ethioipan Mini Demographic Health Survey 2019. Final Report. Rockville, Maryland, USA: EPHI and ICF.
15. Edmond K, Zaidi A. New approaches to preventing, diagnosing, and treating neonatal sepsis. *PLoS Med*. 2010;7(3):e1000213-e1000218.

16. Zaidi AT, Ali S, Khan T. Pathogens associated with sepsis in newborns and young infants in developing countries. *Pediatr Infect Dis J*. 2009;28(1):1-9.

17. WHO. *World Health Statistics: Monitoring Health for the SDGs, Sustainable Development Goals*. WHO Library Cataloguing-in-Publication Data; 2016:1-136.

18. Ahmed MM. Risk factors for neonatal sepsis in paediatric ward at Khartoum North Teaching Hospital, Sudan. *Basic Res J Med Clin Sci*. 2015;4(1):37-43.

19. Schrag SJ, Cutland CL, Zell ER, et al. Risk factors for neonatal sepsis and perinatal death among infants enrolled in the prevention of Perinatal sepsis Trial, Soweto, South Africa. *Pediatr Infect Dis J*. 2012;31(8):821-826.

20. Adera Hailu F. *Physicochemical Properties and Biological Activities of Oil Extracts from Seeds and Leaves of Garden Cress (Lepidium sativum L.)*. Haramaya University; 2021.

21. Dawodu A, Al Umran K, Twum-Danso K. A case control study of neonatal sepsis: experience from Saudi Arabia. *J Trop Pediatr*. 1997;43(2):84-88.

22. Gebremedhin D, Berhe H, Gebrekirstos K. Risk factors for neonatal sepsis in public hospitals of Mekelle City, North Ethiopia, 2015: unmatched case control study. *PLoS One*. 2016;11(5):e0154798. doi:10.1371/journal.pone.0154798

23. Cunningham FG, Leveno KJ, Bloom SL, et al. *Williams Obstetrics*. McGraw-Hill Medical; 2014.

24. Rennie JM. *Rennie & Roberton's Textbook of Neonatology E-book*. Elsevier Health Sciences; 2012.

25. Kafatos G, Verlander N, Gelb D, Arnold E, Charlett A. A comparison of public domain software for outbreak investigations: Epi Info and EpiData. *Wkly Releases*. 2007;12(2):3111.

26. Mehmetoglu M, Jakobsen TG. *Applied Statistics Using Stata: A Guide for the Social Sciences*. Sage; 2022.

27. Woldu M, Lenjisa J, Tegegne G, et al. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia. *Int J Contemp Pediatr*. 2014;1(3):1-41.

28. Gebrehiwot AL, Moges F, Moges B, Anagaw B, Unaka C. Predictors of positive blood culture and death among neonates with suspected neonatal sepsis in Gondar University Hospital, Northwest Ethiopia. *Euro J Exp Bio*. 2012;2(6):212-218.

29. Alemu M, Ayana M, Abiy H, et al. Determinants of neonatal sepsis among neonates in the northwest part of Ethiopia: case-control study. *Ital J Pediatr*. 2019;45:150-158.

30. Yismaw AE, Abebil TY, Biweta MA, Araya BM. Proportion of neonatal sepsis and determinant factors among neonates admitted in University of Gondar comprehensive specialized hospital neonatal intensive care unit Northwest Ethiopia 2017. *BMC Res Notes*. 2019;12:542.

31. Leal YA, Álvarez-Nemegyei J, Velázquez JR, et al. Risk factors and prognosis for neonatal sepsis in southeastern Mexico: analysis of a four-year historic cohort follow-up. *BMC Pregnancy Childbirth*. 2012;12:48.

32. Alam MM, Saleem AF, Shaikh AS, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. *J Infect Dev Ctries*. 2014;8(01):067-073.

33. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. *Kathmandu Univ Med J*. 2006;4(14):187-191.

34. Siakwa MD, Kpikpitse D, Mupepi SC, Semuatu M. Neonatal sepsis in rural Ghana: a case control study of risk factors in A birth cohort. *Int J Res Med Health Sci*. 2014;4(5):77-88.

35. John B, David M, Mathias L, Elizabeth N. Risk factors and practices contributing to newborn sepsis in a rural district of Eastern Uganda, August 2013: a cross sectional study. *BMC Res Notes*. 2015;8(339).

36. Wang ME, Patel AB, Hansen NI, et al. Risk factors for possible serious bacterial infection in a rural cohort of young infants in central India. *BMC Public Health*. 2016;16:1-10.

37. Hayun M, Daud D, Febriani B, Madjid D. The risk factors of early onset neonatal sepsis. *Am J Clin Exp Med*. 2015;3(3):78-82.

38. Alebachew Woldu M, Likisa J, Dinsa H. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia. *Pediatr Ther*. 2014;4(4):1-7.

39. Erkihun K, Mesfin M, Direslegn M, Sultan H, Negussie B. Determinants of neonatal sepsis among neonates admitted in a neonatal intensive care unit at Jinka General Hospital, southern Ethiopia. *Int J Nurs Midwifery*. 2019;11(3):18-24.

40. Sorsa A. Epidemiology of neonatal sepsis and associated factors implicated: observational study at neonatal intensive care unit of Arsi University Teaching and Referral Hospital, South East Ethiopia. *Ethiop J Health Sci*. 2019;29(3):333-342.

41. Ogundare E, Akintayo A, Aladekomo T, et al. Presentation and outcomes of early and late onset neonatal sepsis in a Nigerian Hospital. *Afr Health Sci*. 2019;19(3):2390-2399.

42. Dutta S, Reddy R, Sheikh S, et al. Intrapartum antibiotics and risk factors for early onset sepsis. *Arch Dis Child Fetal Neonatal Ed*. 2010;95:F99-F103.

43. Haque K. Definition of blood stream infection in the newborn. *Pediatr Crit Care Med*. 2010;6:45-49.

44. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE. Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis. *PLoS Med*. 2013;10(8):e1001502.