

BMJ Open Determinants of neonatal sepsis among neonates admitted to the neonatal intensive care unit of public hospitals in Hawassa City Administration, Sidama Region, Ethiopia, 2020: an unmatched, case-control study

Kalkidan Bejital,¹ Rekiku Fikre,² Tebeje Ashegu,² Andualem Zenebe ³

To cite: Bejital K, Fikre R, Ashegu T, *et al.* Determinants of neonatal sepsis among neonates admitted to the neonatal intensive care unit of public hospitals in Hawassa City Administration, Sidama Region, Ethiopia, 2020: an unmatched, case-control study. *BMJ Open* 2022;**12**:e056669. doi:10.1136/bmjopen-2021-056669

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-056669>).

Received 25 August 2021
Accepted 08 April 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Midwifery, Bule Hora University, Bule Hora, Ethiopia

²Department of Midwifery, Hawassa University College of Medicine and Health Sciences, Hawassa, Ethiopia

³Department of Public Health, Hawassa College of Health Science, Hawassa, Ethiopia

Correspondence to

Andualem Zenebe;
anduz143@gmail.com

ABSTRACT

Objective This study was conducted to assess the determinants of neonatal sepsis in the neonatal intensive care units of public hospitals in Hawassa City Administration, Sidama Region, Ethiopia, in 2020.

Design Institutional-based, unmatched, case-control study.

Setting The study was conducted in three public hospitals (Hawassa University Teaching Hospital, Adare General Hospital and Hawela Tula Primary Hospital) of Hawassa City, Ethiopia.

Participants A total of 331 (110 cases and 221 controls) neonates with their index mothers were included in the study from 1 August to 30 September 2020.

Outcome measures A pretested, interviewer-administered questionnaire and data extraction checklist were used to collect data. Data were coded and entered into EpiData V.3.1 before being exported to SPSS V.20 for analysis. The factors associated with neonatal sepsis were assessed using bivariable and multivariable logistic regression analyses. P value of less than 0.05 was used to establish statistically significant association of variables.

Results Caesarean section delivery (adjusted OR (AOR)=2.56, 95% CI 1.3 to 5.00), maternal anaemia (AOR=2.58, 95% CI 1.45 to 4.6) and lack of vaccination with tetanus toxoid (AOR=3.5, 95% CI 2.07 to 6.19) were all identified as factors significantly associated with neonatal sepsis.

Conclusions Caesarean section delivery, maternal history of anaemia and lack of vaccination with tetanus toxoid were found to be risk factors for neonatal sepsis. Establishing preconception care practice, strengthening the quality of antenatal care and standardising infection prevention practice are needed to improve neonatal health.

INTRODUCTION

Neonatal sepsis is a systemic infection occurring in infants ≤ 28 days of life.¹ Neonatal sepsis is a common and fatal condition affecting neonates globally² and is the major cause of mortality and morbidity particularly

Strengths and limitations of this study

- ⇒ The study was a prospective study and addressed all of the public hospitals found in Hawassa City.
- ⇒ The study used both primary and secondary data sources.
- ⇒ The study relied on clinical and haematological criteria to diagnose neonatal sepsis.
- ⇒ As the associations between exposure and outcome variables were measured using OR, the true relationship might have been overestimated as OR tends to overestimate relative risk.
- ⇒ No matching was applied, which would have strengthened the findings of this study.

in developing countries.³ Neonatal sepsis is characterised as early-onset neonatal sepsis or late-onset neonatal sepsis based on the onset of symptoms.⁴

Reducing neonatal sepsis by improving the quality of care is both a global and a local priority. Worldwide, neonatal mortality rate is showing a decreasing trend from 36 deaths per 1000 live births in 1990 to 19 per 1000 live births in 2015.⁵ Neonatal deaths have decreased as well, from 5.1 million in 1990 to 2.4 million in 2020.⁶ When comparing neonatal and postneonatal mortality rates (1–59 months), neonatal mortality decreased at a slower rate than postneonatal mortality, at 47% and 58%, respectively.^{5 6} Neonatal mortality remains an urgent concern and is an indicator of child health, development and well-being.⁷

Neonatal sepsis caused an estimated 750 000 yearly neonatal deaths worldwide, with mortality rates highest in Sub-Saharan Africa.⁸ Despite the fact that newborn deaths are preventable, the problem is concentrated

in the world's poorest countries, with low-income and middle-income countries accounting for 85% of all neonatal deaths.⁹ Studies have indicated that neonatal sepsis presents a financial burden of \$10–\$469 billion, which could be reduced through successful treatment and prevention, in Sub-Saharan Africa.⁸

Neonatal death rate has also decreased in Ethiopia, from 39 per 1000 live births in 2005 to 30 in 2019, according to the Ethiopian Demographic and Health Survey (EDHS). However, compared with the 29 neonatal deaths per 1000 live births reported in the 2016 EDHS, there was a modest increase in neonatal mortality in 2019.¹⁰

In terms of the prevalence of neonatal sepsis in Ethiopia, studies have found it as high as 77.9% in Shashemene and as low as 33.8% in Wolaita Sodo, although the studies asserted neonatal sepsis using physicians' medical diagnosis stating 'neonatal sepsis' on the neonate's medical record chart.^{11 12} Among the factors, maternal intrapartum fever, season of birth, season of admission, vaginal mode of delivery and preterm gestational age at birth increased the risk of neonatal sepsis.¹³

Recognising the determinants of neonatal sepsis is important for public health advocacy aiming to reduce the risk of exposure. In Ethiopia, few investigations are available on neonatal sepsis and have primarily been prevalence studies based on secondary data. Studies on determinants of neonatal sepsis would provide data to identify high-risk neonates. Thus, this study aimed to identify the determinants of neonatal sepsis among neonates admitted to the neonatal intensive care unit (NICU) of public hospitals in Hawassa City Administration.

METHODS

Study area

Hawassa City Administration is located in Ethiopia's Sidama Region. It is located 275 km south of Ethiopia's capital city, Addis Ababa, which has a population of 385 257 people. Males and females account for 191 858 and 193 399 people, respectively. Of the entire population, 89 765 were women of reproductive age and 13 330 were pregnant women.¹⁴ The city is divided into 8 subcities and 32 kebeles, with 21 urban and 11 rural kebeles. There are 8 hospitals (3 public and 5 private) in Hawassa City, as well as 12 public health centres and 18 health posts. The three public hospitals are Hawassa University Comprehensive Specialized Hospital (HUCSH), Adare General Hospital (AGH) and Hawela Tula Primary Hospital (HTPH), all of which have NICU. The NICU of the three hospitals provides services free of charge. In terms of types of respiratory assistance available, all three institutions provide oxygen, assisted breathing (non-invasive assisted ventilation) and surfactant. Diagnosis of neonatal sepsis depends on clinical decision in all three hospitals. The hospitals follow Ethiopia's National Standard Treatment Guideline for Hospitals, which advises broad-spectrum antibiotics such as penicillin and aminoglycosides for treatment of neonatal sepsis.¹⁵

Study design and period

An institutional-based, unmatched, case-control study was conducted from 1 August to 30 September 2020.

Source population

The source population included all neonates admitted to the NICU of public hospitals in Hawassa City Administration.

Study population

Cases were neonates with sepsis while controls were neonates without sepsis who were admitted to the NICU of public hospitals in Hawassa City Administration during the study period.

Sample size determination

The sample size required for the study was calculated using double population proportion formula (using Epi Info V.7.2), taking the proportion of neonates with Premature Rupture of Membrane (PROM) among the controls as 8.5% and an adjusted OR (AOR) of 2.812, which was estimated from a study conducted in Debre Markos Referral Hospital,¹⁶ along with 95% CI, 80% power and a case to control ratio of 1:2, resulting in a total sample size of 315 (105 cases and 210 controls). By adding 5% as the non-response rate, the final sample size became 331 (110 cases and 221 controls).

Sampling technique

All three public hospitals in Hawassa City Administration were considered in this study. The calculated final sample size was proportionally allocated for each hospital based on newborn sepsis records from the previous 6 months. The 2-month case flow was calculated using each hospital's previous 6-month case flow.

Data collection tools and procedures

Data were collected using a pretested, interviewer-administered questionnaire and a data extraction checklist. The questionnaire was adapted from other similar studies, with some contextual modification based on the main objective of the study.^{9 13 17} Data were gathered by interviewing the mothers and reviewing the medical records of the neonates.

Data quality assurance and data quality control

The questionnaire was prepared in English and then translated to Amharic language for data collection. Pretest was conducted in 5% (6 cases and 11 controls) of patients at Leku Primary Hospital to determine the amount of time needed for the interview and the consistency of the questionnaire. Appropriate modifications were made based on the results of the pretest. Three BSc midwives collected the data while one BSc midwife supervised the data collection process. One-day training was given to the data collectors and the supervisor on the aim of the study, questionnaire and how to approach cases and controls in similar ways. Completeness of collected questionnaires

was checked by the supervisor and corrective discussion was made with data collectors.

Data processing and analysis

The collected data were coded and entered into EpiData V.3.1 and then exported to SPSS V.20 for analysis. Descriptive statistics were carried out and presented using texts and tables. χ^2 tests were conducted to observe the comparability of variables among cases and controls. Bivariable logistic regression analyses were performed to select candidate variables for multivariable logistic regression analyses. Variables with a *p* value of <0.25 in the bivariable analysis were considered as candidates for multivariate logistic regression analyses. Multicollinearity was checked to determine the correlation between the independent variables, and the Hosmer-Lemeshow goodness-of-fit statistics was used to assess the fitness of the model. Variables with a *p* value of <0.05 in the multivariable analyses were considered statistically significant. Finally, the findings of the analysis were summarised using crude OR and AOR with 95% CI.

Operational definition

Case definition (neonatal sepsis)

The study included newborns aged 0–28 days who were admitted to the NICU of public hospitals in Hawassa City Administration during the study period. One or more established integrated management of neonatal and childhood illness (IMNCI) clinical features of neonatal sepsis were used in the diagnosis of neonatal sepsis. The clinical features include; either not feeding well, or convulsion, or drowsiness, or unconscious, or movement only when stimulated or no movement at all, or fast breathing >60 breaths per minute, or grunting or severe chest indrawing, or raised temperature (>38°C) or hypothermia (<35.5°C), or central cyanosis or severe jaundice, or severe abdominal distention, or many or severe skin pustules, or bulging fontanelles, along with one or more haematological criteria (total white cell count <5000 or >20000; or C reactive protein <0.9 or >15.8; or platelet count <150 cells/mm³ or >440 cells/mm³; or absolute neutrophil count <1500 cells/mm³ or >7500 cells/mm³; or erythrocyte sedimentation rate >15/1 hour).¹⁸ Those who fulfil the operational definition of neonatal sepsis (≥1 IMNCI criteria along with ≥1 haematological criteria) with their index mother were considered as cases.

Control definition

Controls

Controls for the study were neonates 0–28 days old with their index mothers who were admitted to the NICU of public hospitals in Hawassa City Administration during the study period and did not meet the case definition (such as neonates admitted to the NICU due to prematurity needing supportive care, neonatal hyperbilirubinaemia needing phototherapy, etc).

After describing the goal of the study and study participants' rights, each study subject/guardian gave written

and verbal consent. Confidentiality of the records was ensured by keeping them locked.

Patient and public involvement

Patients and/or the public were not involved in the design, development, analysis and publication of this study.

RESULTS

Sociodemographic characteristics of the mothers

A total of 331 study participants (110 cases and 221 controls) participated, with a response rate of 100% (50 cases and 101 controls from HUCSH, 42 cases and 84 controls from AGH, and 18 cases and 36 controls from HTPH). More than half of the mothers of cases (70, 63.6%) and more than two-thirds of the controls (152, 68.8%) were between the ages of 25 and 34 years. A higher proportion (60.4%) of mothers of cases and three-fourths (72.4%) of controls were urban dwellers (*p*=0.024). No significant differences were found between the other basic characteristics of the two groups (table 1).

Obstetric-related factors

The mothers of 85 (77.7%) cases and 161 (72.9%) controls were multiparous. The mode of delivery was vaginal in 85 (77.3%) cases and 195 (88.2%) controls, according to the statistics (table 2).

Maternal medical illness

During their recent pregnancy, 15 (13.6%) mothers of cases and 20 (9%) of controls had experienced urinary tract infections. Thirty-five (31.8%) cases and 39 (17.6%) controls had a history of anaemia during their recent pregnancy. Syphilis was found in 10 (9.1%) cases and 15 (6.8%) controls (table 3).

Health service utilisation

The proportion of mothers who were not vaccinated with tetanus toxoid (TT) during their recent pregnancy was significantly higher in the controls (42, 80.5%) than in the cases (68.2%) (*p*<0.001; table 4).

Neonatal-related factors

Majority of the neonates in this study were under the age of 7 days, 61 (55.5%) cases and 133 (60.2%) controls. Majority (99, 90%) of the cases and 207 (93.7%) controls had normal presentation during delivery. Moreover, a significantly higher (71%) proportion of controls cried immediately after birth as compared with cases (*p*=0.02). Similarly, a higher proportion (54.5%) of cases were not immediately breast fed within 1 hour of delivery as compared with controls (38.5%) (*p*=0.004). The proportion of first minute low Apgar score was higher among cases (26, 23.6%) than controls (23, 10.4%). Seventeen (15.5%) cases and 21 (9.5%) controls had birth asphyxia (table 5).

Table 1 Sociodemographic characteristics of mothers of neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Cases n=110 (%)	Control n=221 (%)	χ^2 (p value)
Maternal age at current birth			
15–24	28 (25.5)	49 (22.2)	0.64
25–34	70 (63.6)	152 (68.8)	
≥35	12 (10.9)	20 (9)	
Marital status			
Single	10 (9.1)	10 (4.5)	0.72
Married	95 (86.4)	194 (87.8)	
Others*	5 (4.5)	17 (7.7)	
Residence			
Urban	67 (60.9)	160 (72.4)	0.024
Rural	43 (39.6)	61 (27.6)	
Mother's educational status			
Cannot read and write	26 (23.6)	40 (18.1)	0.15
Primary first cycle (1–4)	20 (18.2)	31 (14)	
Primary second cycle (5–8)	12 (10.9)	48 (21.7)	
Secondary (9–12)	19 (17.3)	39 (17.6)	
Collage and above	33 (30)	63 (28.5)	
Monthly income (US\$)			
≤39.19	51 (46.4)	95 (43)	0.55
39.2–55.99	13 (11.8)	21 (9.5)	
56–72.79	8 (7.3)	10 (4.5)	
≥72.8	38 (34.5)	95 (43)	
Occupation of the mother			
Government employee	26 (23.6)	42 (19)	0.66
Housewife	57 (51.8)	108 (48.9)	
Merchant	12 (10.9)	33 (14.9)	
Daily labourer	5 (4.5)	19 (8.9)	
Others†	10 (9.1)	19 (8.6)	

*Others: widowed, divorced, separated and cohabiting.

†Others: private organisation and student.
NICU, neonatal intensive care unit.

Results of bivariable and multivariable logistic regression analyses

Residence, mode of delivery, anaemia, cried immediately, immediate breast feeding within 1 hour and TT vaccination were candidates for multivariable logistic regression analyses, with $p < 0.25$ in the bivariable logistic regression analysis. In the multivariable model, maternal TT vaccination, mode of delivery and history of anaemia during pregnancy were found to be significant predictors of neonatal sepsis at $p < 0.05$ with 95% CI.

Accordingly, neonates who were delivered by caesarean section had 2.56 times increased odds of developing neonatal sepsis (AOR=2.56, 95% CI 1.3 to 5.05), while neonates born to mothers with a history of anaemia were 2.58 times at increased odds of developing neonatal sepsis

Table 2 Obstetric-related factors among mothers of neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Case n=110 (%)	Control n=221 (%)	χ^2 (p value)
Gravidity			
≤4	95 (86.4)	192 (86.9)	0.52
≥5	15 (13.6)	29 (13.1)	
Parity			
Primiparous	25 (22.7)	60 (27.1)	0.23
Multiparous	85 (77.3)	161 (72.9)	
Duration of labour			
<6	7 (6.4)	10 (4.5)	0.056
6–12	45 (40.9)	122 (55.2)	
13–23	50 (45.5)	70 (31.7)	
≥24	8 (7.3)	19 (8.6)	
Current pregnancy status			
Single	106 (96.4)	217 (98.2)	
Multiple	4 (3.6)	4 (1.8)	
Place of delivery			
Home	8 (7.3)	10 (4.5)	0.5
Hospital	81 (73.6)	173 (78.3)	
Health centre	21 (19.1)	38 (17.2)	
Mode of delivery			
Vaginal delivery	85 (77.3)	195 (88.2)	0.008
Caesarean section	25 (22.7)	26 (11.8)	
Onset of delivery			
Spontaneous	90 (81.8)	181 (81.9)	0.14
Induced	20 (18.2)	40 (18.1)	
Place of onset of labour			
Home	90 (81.8)	177 (80.1)	0.4
Institution	20 (18.2)	44 (19.9)	
Hypertension			
No	106 (96.4)	215 (97.3)	
Yes	4 (3.6)	6 (2.7)	
Antepartum haemorrhage			
No	105 (95.5)	218 (98.6)	
Yes	5 (4.5)	3 (1.4)	
Premature rupture of membrane			
No	81 (73.6)	167 (75.6)	0.4
Yes	29 (26.4)	54 (24.4)	
Interventions during delivery*			
No	81 (73.6)	182 (82.4)	0.04
Yes	29 (26.4)	39 (17.6)	

*Interventions during delivery include vacuum and forceps deliveries and artificial rupture of membrane.
NICU, neonatal intensive care unit.

(AOR=2.58, 95% CI 1.45 to 4.6), and neonates born to mothers without TT vaccination had 3.5 times increased odds of developing neonatal sepsis (AOR=3.5, 95% CI 2.07 to 6.19) (table 6).

Table 3 Maternal medical illness among mothers of neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Case n=110 (%)	Control n=221 (%)	χ^2 (p value)
Anaemia			
No	75 (68.2)	182 (82.4)	0.03
Yes	35 (31.8)	39 (17.6)	
Diabetes mellitus			
No	106 (96.4)	213 (96.4)	
Yes	4 (3.6)	8 (3.6)	
Urinary tract infection			
No	95 (86.4)	201 (91)	0.13
Yes	15 (13.6)	20 (9)	
Malaria			
No	97 (88.2)	195 (88.2)	0.56
Yes	13 (11.8)	26 (11.8)	
HIV			
No	90 (81.8)	182 (82.4)	
Yes	2 (1.8)	9 (4.1)	
Unknown	18 (16.4)	30 (13.6)	
Syphilis			
No	77 (70)	164 (74.2)	0.66
Yes	10 (9.1)	15 (6.8)	
Unknown	23 (20.9)	42 (19)	

NICU, neonatal intensive care unit.

DISCUSSION

The current study aimed to identify the determinants of neonatal sepsis in order to reduce the burden of neonatal sepsis focusing on the specific factors in the study area. Mode of delivery, history of anaemia and lack of TT vaccination during the recent pregnancy were all found to be predictors of neonatal sepsis in the current study.

The odds of neonatal sepsis among neonates delivered by caesarean section were 2.5 times higher than of neonates delivered vaginally. Furthermore, early-onset neonatal sepsis was higher in proportion among neonates delivered by caesarean section. This link could be related to longer hospital stay, which increases the chance of a hospital-acquired infection during caesarean delivery. There is also less skin-to-skin contact and a later start of breast feeding.¹⁹ Since the initial milk, colostrum, is thought to be the first vaccine, this is crucial in improving newborn immunity.²⁰ This association could also be due to an underlying condition of the mother and lack of asepsis in the operating room. This finding is similar to that of an Egyptian study²¹ which indicated that the incidence of sepsis was greater in neonates born by caesarean section than in those born vaginally. A study conducted in Ghana reported an increased risk of neonatal sepsis among mothers with emergency caesarean section,¹⁷ and

Table 4 Health service utilisation among mothers of neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Case n=110 (%)	Control n=221 (%)	χ^2 (p value)
Antenatal follow-up			
Yes	87 (79.1)	188 (85.1)	0.11
No	23 (20.9)	33 (14.9)	
Number of antenatal follow-up			
<4	36 (41.4)	69 (36.7)	0.13
≥4	51 (58.6)	119 (63.3)	
Tetanus toxoid vaccination			
Yes	75 (68.2)	178 (80.5)	<0.001
No	35 (31.8)	43 (19.5)	
Nutrition counselling			
Yes	61 (55.5)	143 (64.7)	0.06
No	49 (44.5)	78 (35.3)	
Birth preparedness and complication counselling			
Yes	61 (55.5)	138 (62.4)	0.13
No	49 (44.5)	83 (37.6)	
Prevention and treatment of anaemia			
Yes	68 (61.8)	154 (70)	0.08
No	42 (38.2)	66 (30)	

NICU, neonatal intensive care unit.

similarly a study in Gondar, Northern Ethiopia found a fivefold increased odds of neonatal sepsis in neonates born by caesarean section.²² However, there is a finding in Gondar¹³ that contradicts this result. The contradiction to these results may be due to factors that differ between the cohorts, such as asepsis, indications for caesarean section and timing of caesarean section.

The odds of neonatal sepsis were 3.5 times higher in neonates born to mothers without TT vaccination compared with their counterparts. The rationale could be linked to the principle of antenatal vaccination, in which maternal pathogen-specific antibodies are employed to boost and protect the newborn until appropriate time for infant vaccination or until the period of maximum sensitivity has passed.^{23–25} In neonates, antibodies generated from the placenta and breast milk serve as the primary source of defence against infectious diseases.²⁰

The odds of neonatal sepsis were 2.5 times higher in neonates born to women who had a history of anaemia during a recent pregnancy compared with their counterparts. The findings of a prospective research conducted in India, which found that 9% of neonates born to mothers with anaemia had neonatal sepsis, were in line with this conclusion.²⁶ The possible reason for this could be due to a considerable loss of micronutrients in the breast milk of mothers with anaemia, which can weaken the newborn's

Table 5 Neonatal-related factors among neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Case n=110 (%)	Control n=221 (%)	χ^2 (p value)
Age of neonate during data collection (days)			
0–7	61 (55.5)	133 (60.2)	0.24
8–28	49 (44.5)	88 (39.8)	
Sex of neonate			
Male	57 (51.8)	123 (55.7)	0.29
Female	53 (48.2)	98 (44.3)	
Neonate presentation			
Normal	99 (90)	207 (93.7)	0.166
Malpresentation	11 (10)	14 (6.3)	
Type of malpresentation			
Breach	6 (54.5)	7 (50)	0.66
Others	5 (45.5)	7 (50)	
Gestational age			
Preterm	45 (40.9)	34 (15.4)	<0.001
Term	65 (59.1)	187 (84.6)	
Birth weight			
Low birth weight	43 (39.1)	74 (33.5)	0.331
Normal birth weight	67 (60.9)	147 (66.5)	
First Apgar score			
≥7	39 (35.5)	93 (42.1)	0.03
4–6	15 (13.6)	53(24)	
<4	26 (23.6)	23 (10.4)	
Unknown	30 (30)	52 (23.5)	
Fifth Apgar score			
≥7	53 (48.2)	132 (59.7)	0.15
4–6	18 (16.4)	21 (9.5)	
<4	9 (8.2)	15 (6.8)	
Unknown	30 (27.3)	53 (24)	
Cried immediately after birth			
Yes	65 (59.09)	157(71)	0.02
No	45 (40.9)	64 (29)	
Neonate resuscitated at birth			
No	67 (60.09)	156 (70.6)	0.05
Yes	43 (39.09)	65 (29.4)	
Immediate breast feeding within 1 hour			
Yes	50 (45.5)	136 (61.5)	0.004
No	60 (54.5)	85 (38.5)	
Birth asphyxia			
No	93 (84.5)	200 (90.5)	0.62
Yes	17 (15.5)	21 (9.5)	
NICU, neonatal intensive care unit.			

NICU, neonatal intensive care unit.

immunity and make them more susceptible to sepsis.²⁷ In addition, a study found that mothers with anaemia are more likely to have a caesarean section.^{28 29} There is also a study conducted in Nepal that found maternal anaemia

Table 6 Factors associated with neonatal sepsis among neonates admitted to the NICU of public hospitals in Hawassa City, Sidama Region, Ethiopia, 2020 (N=331)

Variable	Cases n=110 (%)	Control n=221 (%)	COR (95% CI)	AOR (95% CI)
Residence				
Urban	67 (60.9)	160 (72.4)	1	1
Rural	43 (39.1)	61 (27.6)	1.683 (1.04 to 2.7)	1.3 (0.7 to 2.2)
Mode of delivery				
Vaginal delivery	85 (77.3)	195 (88.2)	1	1
Caesarean section	25 (22.7)	26 (11.8)	2.206 (1.204 to 4.04)	2.56 (1.3 to 5.00)*
History of anaemia				
No	75 (68.2)	182 (82.4)	1	1
Yes	35 (31.8)	39 (17.6)	2.2 (1.28 to 3.69)	2.58 (1.45 to 4.6)*
Cried immediately				
Yes	65 (59.1)	157 (71)	1	1
No	45 (40.9)	64 (29)	1.698 (1.1 to 2.7)	0.98 (0.5 to 1.9)
Immediate breast feeding				
Yes	50 (45.5)	136 (61.5)	1	1
No	60 (54.5)	85 (38.5)	1.92 (1.2 to 3.05)	1.3 (0.7 to 2.5)
Tetanus toxoid vaccination				
Yes	75 (68.2)	178 (80.5)	1	1
No	35 (31.8)	43 (19.5)	3.33 (2.02 to 5.4)	3.5 (2.07 to 6.19)*

*P<0.05.

AOR, adjusted OR; COR, crude OR; NICU, neonatal intensive care unit.

reduces resistance to infections in both the mother and the newborn.³⁰

As a strength, this study was a prospective study and included all public hospitals in the study area. The study used both primary and secondary data sources. The following limitations should be taken into account when interpreting the results of this study. First, as the study was limited to hospitals, external validity might have been compromised. Second, some of the variables in the findings are prone to subjective bias. Third, the study relied on clinical and haematological criteria for diagnosis of neonatal sepsis, which may have led to overestimation of the prevalence of neonatal sepsis. Fourth, unmatched design was applied. Finally, as the association between the outcome and exposure variables was measured using OR, the true relationship might have been overestimated as OR tends to overestimate relative risk.

CONCLUSION

According to the findings of this study, obstetric-related factors, health service utilisation and maternal medical illness were the factors that contribute to neonatal sepsis. More specifically, caesarean mode of delivery, maternal history of anaemia and not being vaccinated against tetanus were identified as risk factors for neonatal sepsis. Improving infant health requires standard antenatal care, intrapartum care and improving maternal nutritional

status during pregnancy by proper counselling and micronutrient supplementation as well as timely TT vaccination. Due to the lack of culture for identification of neonatal sepsis, neonates may be treated with antibiotics that are unnecessary. Thus, the government and other stakeholders should work towards incorporating bacterial cultures in hospitals in order to reduce utilisation of antibiotics. Finally, studying the determinants of early-onset and late-onset neonatal sepsis separately and more investigation into the rate of neonatal sepsis among mothers with a history of anaemia and those who did not receive TT immunisation are recommended.

Acknowledgements We thank the data collectors and supervisors for helping realise the study.

Contributors KB conceptualised the study and analysed and interpreted the data. RF, TA and AZ participated in designing the study and supervised the fieldwork and analysis of data. All authors drafted, reviewed and approved the final manuscript. KB is the guarantor for the overall work of the study.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study involves human participants. On behalf of Hawassa University's institutional review board (ref no: IRB/09/12), ethical approval was acquired from the Hawassa University College of Medicine and Health Science ethical review committee. A letter of collaboration was written for each hospital and permission was acquired from the medical directorate of each hospital (ref no: MID/395/12). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data for this study are available upon reasonable request to the principal authors.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Andualem Zenebe <http://orcid.org/0000-0002-7799-5320>

REFERENCES

- Simonsen KA, Anderson-Berry AL, Delair SF, *et al.* Early-onset neonatal sepsis. *Clin Microbiol Rev* 2014;27:21–47.
- Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, *et al.* The global burden of paediatric and neonatal sepsis: a systematic review. *Lancet Respir Med* 2018;6:223–30.
- Amare D, Mela M, Dessie G. Unfinished agenda of the neonates in developing countries: magnitude of neonatal sepsis: systematic review and meta-analysis. *Heliyon* 2019;5:e02519.
- Singh M, Narang A, Bhakoo ON. Predictive perinatal score in the diagnosis of neonatal sepsis. *J Trop Pediatr* 1994;40:365–8.
- UNICEF. *Levels and trends in child mortality*. New York: UNICEF, 2015.
- UNICEF, World Bank Group. *Levels & trends in child mortality 2020*. New York: United Nations Children's Fund, 2020.
- Tekelab T, Chojenta C, Smith R, *et al.* The impact of antenatal care on neonatal mortality in sub-Saharan Africa: a systematic review and meta-analysis. *PLoS One* 2019;14:e0222566.
- Ranjewa SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa. *BMJ Glob Health* 2018;3:e000347.
- 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:e0154798.
- Ethiopian Public Health Institute (EPHI) [Ethiopia] and ICF. *Ethiopia mini demographic and health survey 2019: key indicators*. Rockville, Maryland, USA: EPHI and ICF, 2019.
- Getabelew A, Aman M, Fantaye E, *et al.* Prevalence of neonatal sepsis and associated factors among neonates in neonatal intensive care unit at selected governmental hospitals in Shashemene town, Oromia regional state, Ethiopia, 2017. *Int J Pediatr* 2018;2018:1–7.
- Mersha A, Worku T, Shibiru S. Neonatal sepsis and associated factors among newborns in hospitals of Wolaita Sodo town, southern Ethiopia. Research and reports in neonatology. *Res Rep Neonatol* 2019;9:1–8.
- Gudayu TW, Zeleke EG, Lakew AM. The role of the season at admission in neonatal sepsis: a retrospective chart review of a 1-year data at University of Gondar comprehensive specialized Hospital. *BMC Res Notes* 2019;12:643.
- Sidama Region Health Bureau. *Sidama region health report*. Hawassa, Ethiopia: SRHB, 2020.
- FMHACA. *Standard treatment guidelines for General Hospital*. Food, Medicine and Healthcare Administration and Control Authority of Ethiopia, 2014.
- 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;45:1–8.
- Adatara P, Afaya A, Salia SM, *et al.* Risk factors for neonatal sepsis: a retrospective case-control study among neonates who were delivered by caesarean section at the trauma and specialist Hospital, Winneba, Ghana. *Biomed Res Int* 2018;2018:1–7.
- World Health Organization. *Pocket book of hospital care for children: guidelines for the management of common childhood illnesses*. Geneva: WHO, 2013.
- Prado DS, Mendes RB, Gurgel RQ, *et al.* The influence of mode of delivery on neonatal and maternal short and long-term outcomes. *Rev Saude Publica* 2018;52:95.
- Maertens K, Orije MRP, Van Damme P, *et al.* Vaccination during pregnancy: current and possible future recommendations. *Eur J Pediatr* 2020;179:235–42.
- Shehab El-Din EMR, El-Sokkary MMA, Bassiouny MR, *et al.* Epidemiology of neonatal sepsis and implicated pathogens: a study from Egypt. *Biomed Res Int* 2015;2015:1–11.
- G/Eyesus T, Moges F, Eshetie S, *et al.* Bacterial etiologic agents causing neonatal sepsis and associated risk factors in Gondar, Northwest Ethiopia. *BMC Pediatr* 2017;17:137.
- Jones C, Heath P. Antenatal immunization. *Hum Vaccin Immunother* 2014;10:2118–22.
- Vojtek I, Dieussaert I, Doherty TM, *et al.* Maternal immunization: where are we now and how to move forward? *Ann Med* 2018;50:193–208.
- Calvert A, Jones CE. Placental transfer of antibody and its relationship to vaccination in pregnancy. *Curr Opin Infect Dis* 2017;30:268–73.
- Shah N, Upadhyay C, Sahota R. Neonatal outcome in anemic mothers: a prospective study. *J Evol Med Dent Sci* 2013;2:8355–9.
- El-Farrash RA, Ismail EAR, Nada AS. Cord blood iron profile and breast milk micronutrients in maternal iron deficiency anemia. *Pediatr Blood Cancer* 2012;58:233–8.
- Drukker L, Hants Y, Farkash R, *et al.* Iron deficiency anemia at admission for labor and delivery is associated with an increased risk for cesarean section and adverse maternal and neonatal outcomes. *Transfusion* 2015;55:2799–806.
- Smith C, Teng F, Branch E, *et al.* Maternal and perinatal morbidity and mortality associated with anemia in pregnancy. *Obstet Gynecol* 2019;134:1234–44.
- Prakash S, Yadav K. Maternal anemia in pregnancy: an overview. *Ijppr Human* 2015;4:164–79.