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Research Article

Factors Associated with Sepsis among Neonates Admitted to Neonatal Intensive Care Unit of Bale Zone Public Hospitals, South-East Ethiopia, 2017/2018: Unmatched Case-Control Study

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ABSTRACT

Background: Neonatal sepsis is a major cause of newborn deaths worldwide and one of the main factors contributing to high neonatal mortality. The incidence of neonatal sepsis varies from country to country and mostly diagnosed in developing countries. This study was aimed to determine the factors associated with neonatal sepsis among neonates admitted to neonatal intensive care unit in Bale zone public hospitals, Oromia region, south-east Ethiopia, 2017/2018.

Method: An institution based unmatched case-control study was conducted in neonatal intensive care units of public hospitals in Bale zone, Oromia region, southeast Ethiopia. Pretested structured questionnaire was used to collect the data. Ninety-seven (97) cases and 194 controls were calculated by using a 1:2 ratio with Openepi version 2.3.1. Cases were selected using systematic random sampling with their index mother whereas controls were selected conveniently for each case. Data was entered using epidata 3.1 and analyzed using SPSS version 21. The result was reported using crude and adjusted odds ratios with their 95% confidence interval.

Results: Ninety-seven cases and 194 controls were included with a response rate of 100%. The identified risk factors were maternal age (AOR=8.018; 95% CI (1.2, 52.1)), APGAR score less than 7 at the 1st minute (AOR=2.2; 95% CI (1.0, 4.6)) and 5th minute (AOR=4.5; 95% CI (1.5, 13.0)) minute and neonatal birth weight of ≥ 2500 gm (AOR=6.1; 95% CI (2.1, 17.5)).

Conclusion: Both maternal and neonatal factors had contributed to the risk of neonatal sepsis. Maternal age, low APGAR score at 1st and 5th minutes and low birth weight were identified as independent risk factors of neonatal sepsis. Strengthening of antenatal screening of mothers, perinatal care of newborns and interventions of babies born with complications should be sought for all newborns.

Keywords: Neonatal sepsis; Bale zone; Unmatched case-control

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INTRODUCTION

Neonatal sepsis is a major cause of newborn deaths worldwide and one of the main factors contributing to high neonatal mortality. The international pediatric consensus conference of 2001 defines neonatal sepsis as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate. The incidence of neonatal sepsis varies from country to country and mostly diagnosed in developing countries [1].

Neonatal sepsis is clinically diagnosed by a combination of clinical signs, laboratory tests and microbiologically confirmed by detection of bacteria in blood by culture. The signs and symptoms are nonspecific, may be unapparent for some time and mistaken for conditions typical of this period of life, such as respiratory disorders caused by prematurity.

Early diagnosis and proper management of neonatal sepsis by rational antimicrobial therapy and supportive care can reduce death from neonatal sepsis. The management of neonatal sepsis is with empirical antimicrobial therapy and supportive care. Once the clinical diagnosis is known, treatment should be started immediately after obtaining samples for culture rather than waiting for the culture results.

Diseases and conditions readily preventable or treatable in the first month of life result in many deaths. In 2015, out of 5.9 million child deaths, 2.7 million deaths or roughly 45% of all under-five deaths, occur during the neonatal period. The main causes of neonatal deaths were preterm birth complications (35%), intrapartum-related complications (24%) and sepsis (15%).

The risk of neonatal death become 6 times higher in developing countries compared to that of developed countries. According to 2011 united nations international's children emergency fund report, neonatal deaths accounted for 52% of all under-five child mortality in south Asia, 53% in Latin America and the Caribbean and 34% in sub-Saharan Africa. In Africa and other developing countries, a small number of data were available on risk factors associated with neonatal sepsis.

In spite of Ethiopia's remarkable success in achieving Millennium Development Goal (MDG 4) three years before, the reduction in neonatal mortality was comparatively low and at the end of MDG era the international community was in agreement on new framework, the Sustainable Development Goals (SDGs), to reduce under-five mortality to at least as low as 25 per 1000 live birth by 2030.

The 2016 Ethiopian demographic and health survey results show that the neonatal, infant and under-5 mortality rates for 5 years before the survey are 29, 48, and 67 deaths per 1,000 live births, respectively. In other words, in Ethiopia 1 in every 35 children dies within the first month, 1 in every 21 children dies before celebrating the first birthday and 1 of every 15 children dies before reaching the fifth birthday. Out of the neonatal conditions which cause under-five mortality, neonatal sepsis accounts 9%.

In recent years, despite emerging advanced diagnosis and management of neonatal sepsis, it is a leading cause of admission and death in neonatal units. Non-specific clinical presentation and lack of reliable diagnostic tests result in unsatisfactory identification of etiologic agents and treatment outcome. Prevalence, etiology, risk factors and outcome of the problem identification help in early detection and management.

Delay in commencing treatment increases the mortality rate from neonatal sepsis by 50%. To avoid this problem, knowledge about common risk factors of neonatal sepsis in a given area becomes essential in guiding the local empirical choice of antibiotics and to prevent drug resistance [2].

Maternal factors like maternal age, educational status, economic status, infections and neonatal factors like neonatal asphyxia, premature membrane rupture prematurity; low birth weight birth complications, low APGAR score less than 7 and neonatal resuscitation are some risk factors for neonatal sepsis.

MATERIALS AND METHODS

Study area, design and population

The study was conducted in the NICUs of Bale zone public hospitals on neonates admitted with neonatal sepsis and unmatched case-control study design was employed from December 2017-March 2018.

Inclusion criteria

All neonates admitted to the neonatal intensive care unit during the study period.

Exclusion criteria

Neonates' mother who did not volunteer to participate in the study.

Case and control definition

Case: All neonates admitted to neonatal intensive care unit fulfilling diagnosis criteria for neonatal sepsis.

Neonatal sepsis diagnostic criteria: The hematological criteria along with the established IMNCI (integrated management of neonatal and childhood illness) clinical features of neonatal sepsis was used to diagnose neonatal sepsis [3].

Neonates in the presence of one or more of the established IMNCI clinical features [either of fever (>37.5°C) or hypothermia (35.5°C), fast breathing (>60 breath per minute), severe chest indrawing, not feeding well, movement only when stimulated, convulsion, lethargic or unconscious] along with >2 of the hematological criteria; total leukocyte count (<4000 or >12000 cells/m^3, absolute neutrophil count (<1500 cells/mm^3 or >7500 cells/mm^3), Erythrocyte Sedimentation Rate (ESR) (>15/1 h) and platelet count (<150 or >440 cells/m^3) and who was admitted to neonatal ICU of the public hospitals of Bale zone during the study period were included with their index mothers as cases.

Control: All neonates admitted to NICU not fulfilling diagnostic criteria for neonatal sepsis with their index mother were included as a control [4].

Sample size determination and sampling procedure

The sample size was estimated considering two population proportion formula by using open epi version 3.01. Proportion of mothers with UTI/STI (13% (main exposure variable)) among the controls from study conducted in Ghana, 90% power of the study control to case ratio of 2:1 to detect an odds ratio of 3.007 were used to determine the sample size. The calculated sample size was 88 case and 176 control giving a total sample size of 264. By adding 10% for the non-response rate, 97 cases and 194 controls giving a total sample size of 291 was the estimated sample size in this study [5]. Cases and controls were selected using proportional systematic random sampling.

Four public hospitals in Bale zone providing neonatal intensive care unit services were included in the study. The number of study participants for each hospital was allocated proportionally after identifying the average quarterly admissions of neonatal sepsis [6]. The number of admissions in the last quarter were 45, 48, 39 and 33 for Goba hospital, Robe hospital, Ginnir hospital and Dello Mena hospital, respectively. Then, the proportional allocation of sample size for Goba hospital, Robe hospital, Ginnir hospital and Dello Mena were 27, 28, 23 and 19 cases, respectively.

Cases were selected by using systematic random sampling and for each case, two controls were included in the study conveniently.

Data was collected from neonates diagnosed with sepsis on admission and neonates with no sepsis as case and control, respectively [7]. In addition, information was obtained from respective mothers and chart was reviewed for both case and control.

Data quality control

The structured checklist was adopted from the previous study to collect data. The checklist was pre-tested before the actual administration to the main study. Trained health professionals collected data after receiving training on the objectives, contents, accuracy and consistency of the data for two days.

The checklist contains socio-demographic data, maternal and neonatal risk factors for neonatal sepsis and IMNCI checklist for neonatal sepsis diagnosis. For case subject, data was collected from the mother and neonate diagnosed with sepsis on admission by attending physician depending on the IMNCI criteria and hematologic results while for control subjects, the data was collected from the individual not fulfilling the criteria for sepsis. The questionnaire was prepared in English language and translated to local language (Afaan Oromo) and then it was translated back to English to maintain its consistency. Data were checked for completeness during the data collection by site supervisors and investigators.

Data management and analysis

Data was entered using epidata 3.1 and exported to SPSS version 21 for analysis. Descriptive statistics were used to assess the socio-demographic characteristics of mother and neonate and the result was summarized as frequencies and percentages. Binary and multiple logistic regressions were used, to determine factors associated with neonatal sepsis [8]. Variables with a p-value of <0.05 in bivariate analyses were included in the multiple logistic models. P-values less than 0.05 was considered to declare statistical significance in the model. The result was reported using crude and adjusted Odds Ratios (OR) with their 95% confidence interval.

RESULTS

Socio-demographic characteristics of respondents

Making a 100% response rate, 97 cases and 194 controls were included in the study. Almost half, 149 (51.2%), of the mothers' age was >25. Fifty-four (26.9%) of cases and 120 (61.9%) controls were from urban area. Ninety-three (95.9%) cases and 192 (99%) of controls mothers were married. Majority of mothers, 66 (68%) of cases and 104 (53.6%) of controls, were Muslim followers in religion. Seventy (72.2%) of cases and 102 (52.6%) of controls mothers were housewives and 35 (36.1%) cases and 58 (29.9%) of controls had attended primary education. Sixty-two (63.9%) of the cases and 175 (90.2%) controls out of included neonates were found to be below the age of 7 days. Fifty-eight (59.8%) of cases and 105 (54.1%) of control were male neonates (Table 1).

Table 1: Socio-demographic characteristics of mothers and neonate at four public hospitals of Bale zone, southeast Ethiopia, 2017/2018.

Variables		Case n (97)		Control n (194)	
		Frequency	Percent	Frequency	Percent
Maternal age	<18	5	5.2	6	3.1
	18-25	52	53.6	79	40.7
	>25	40	41.2	109	56.2
Marital status	Married	93	95.9	192	99
	Others	4	4.1	2	1
Religion	Orthodox	22	22.7	62	32

	Muslim	66	68	104	53.6
	Others	9	9.3	28	14.4
Ethnicity	Oromo	85	87.6	172	88.7
	Others	12	12.4	22	11.3
Residence	Urban	54	55.7	120	61.9
	Rural	43	44.3	74	38.1
Maternal education	No education	32	33	52	26.8
	Primary	35	36.1	58	29.9
	Secondary	15	15.5	33	17
	College and higher	15	15.5	51	26.3
Occupation of mother	Housewife	70	72.2	102	52.6
	Government employee	15	15.5	48	24.7
	Others	12	12.3	44	22.7
Neonatal sex	Male	58	59.8	105	54.1
	Female	39	40.2	89	45.9
Neonatal age	<7 days	62	63.9	175	90.2
	≥ 7 days	35	36.1	19	9.8

Maternal related factors of neonatal sepsis

During the pregnancy period of current neonate 190 (97.9%) of the mothers of controls and 92 (94.8%) of the mothers of the case had at least one ANC visit. More than half, 59 (60.8%) of cases and almost all, 175 (90.2) controls were delivered at hospital and 114 (58.8%) of controls and 70 (72.2%) of cases were delivered by spontaneous vaginal delivery [9].

Hundred eighty-six (95.6%) of controls and 84 (86.6%) of cases were attended by skilled birth attendants like doctors, nurses and midwives. This study showed that the proportion of the history of Urinary Tract Infections and Sexually Transmitted Infections (UTI/STI) during the current pregnancy is higher in cases, 10 (10.3%) than controls, 8 (4.1%) (Table 2).

Table 2: Maternal factors of neonatal sepsisat four public hospitals of Bale zone, southeast Ethiopia, 2017/2018.

Variables		Case n (97)		Control n (194)	
		Frequency	Percent	Frequency	Percent
ANC visit	Yes	92	94.8	190	97.9
	No	5	5.2	4	2.1
Place of delivery	Home	13	13.4	5	2.6
	Hospital	59	60.8	175	90.2
	Health center	25	25.8	14	7.2
Mode of delivery	SVD	70	72.2	114	58.8
	Instrumental delivery	11	11.3	39	20.1
	C/S	16	16.5	41	21.1
Birth attendant	TBA	11	11.3	5	2.6
	HEW and relatives	2	2.1	3	1.5
	Health professional	84	86.6	186	95.9
Presence of fever	Yes	10	10.3	20	10.3
	No	87	89.7	174	89.7
Foul smelling amniotic fluid	Yes	19	19.6	28	14.4
	No	78	80.4	166	85.6
Pregnancy-related hypertension	Yes	6	6.2	12	6.2
	No	91	93.8	182	93.8

Antepartum hemorrhage	Yes	8	8.2	3	1.5
	No	89	91.8	191	98.5
STIs/STDs	Yes	10	10.3	8	4.1
	No	87	89.7	186	95.9

DISCUSSION

This study was aimed to assess risk factors for neonatal sepsis and generate information that helps as an input in early detection and management of risk factors for neonatal sepsis [10]. Maternal age, maternal education, occupation of the mother, antepartum hemorrhage, neonatal age, mode of delivery, birth attendant, presence of UTI/STDs, neonatal resuscitation, APGAR score at 1st and 5th minute, birth weight were maternal and neonatal factors for neonatal sepsis included in the study. Of these factors, maternal age, APGAR score at 1st and 5th minute and birth weight were found to have a significant association with neonatal sepsis (Table 3).

Table 3: Neonatal factors for neonatal sepsis at four public hospitals of Bale zone, southeast Ethiopia, 2017/2018.

Variables		Case n (97)		Control n (194)	
		Frequency	Percent	Frequency	Percent
Gestational age	<37	32	33	51	26.3
	37-42	65	67	143	73.7
Birth weight	<2500	35	36.1	7	3.6
	>2500	62	63.9	187	96.4
APGAR score 1st minute	<7	77	79.4	116	59.8
	>7	20	20.6	78	40.2
APGAR score 5th minute	<7	27	27.8	12	6.2
	>7	70	72.2	182	93.8
Neonate cry after birth	Yes	86	88.7	182	93.8
	No	11	11.3	12	6.2
Neonate resuscitated	Yes	12	12.4	8	4.1
	No	85	87.6	186	95.9

The present study indicated that maternal age had a significant association with neonatal sepsis. Neonates who had born from mothers aged 18-25 had higher odds of developing sepsis 8 times compared to those who were >25 years of age. Unlike the current study, another study showed that maternal age of less than 20 was found to be a significant factor for the occurrence of neonatal sepsis. The difference may be, in the current study the number of participants aged less than 20 was small (5 (5.5%)) when compared to the other study conducted in Bangladesh (30 (66.7%)).

About two-thirds (63.9%) of cases were with early onset neonatal sepsis (<7 days) which is almost comparable with the studies conducted in Mekele and Bishoftu which were 76.9% and 81.4%, respectively [11].

APGAR scores less than seven at first (p<0.045) and fifth minute (p=0.006) showed association with neonatal sepsis. A similar study done in Ghana showed that significant association with apgar score at 1st (p<0.000) and 5th minutes (p<0.000) and neonatal sepsis. The respiratory response in the first minute is crucial for the survival and wellbeing of the newborn. Birth asphyxia, predisposing the newborn for resuscitation, is a risk for sepsis. Thus low apgar score is mostly associated with neonatal sepsis. Neonatal birth weight showed a significant association with neonatal sepsis. In this study neonate with a birth weight of less than 2500 mg (LBW) (p=0.001) showed a higher risk of acquiring neonatal sepsis than neonates having a birth weight greater than 2500 gm.

This is comparable with other study done in Nepal in which low birth weight was found to be a risk factor for neonatal sepsis (<0.05). The ability to defend infections in low birth weight neonates is poor and they are more prone to develop an infection. Mostly parenteral nutrition happens in low birth weight neonates and there is the risk of infection from contamination of IV cannulas [12].

CONCLUSION

In this study, some of the maternal and neonatal factors found to be risk factors for the onset of neonatal sepsis. Of these factors, maternal age, low apgar score at 1st and 5th minutes and low birth weight were identified as risk factors of neonatal sepsis. In contrast, residence, parity, ANC service utilization, mode of delivery, foul-smelling liquor, prematurity and not crying immediately after birth had no effect on the occurrence of neonatal sepsis. Even if there is no association between neonatal age and neonatal sepsis, this study observed that there is a higher incidence of sepsis among neonates after the first week of birth. Early antenatal screening, detection and management of problems, proper intrapartum care and prevention of infection and timely management of complications should be sought for all newborns.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Ethical clearance and approval were obtained from Madda Walabu university research and technology transfer office. The health institution directors and each study subjects were adequately communicated the necessary information about the study and the right to withdraw at any time during the interview. Informed consent was obtained from parents prior to the beginning of the interviews and they were told that the services they receive at the facility will not be affected if they declined to participate in the study. The identity of the participants was kept anonymous.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIAL

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

COMPETING INTEREST

The authors affirm that they have no competing interests.

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The budget for proposal development and result write-up was covered by Madda Walabu university research and technology transfer office.

AUTHORS CONTRIBUTION

GG contributed to the conception of the research idea, study design, data collection, analysis, interpretation and the drafting of the manuscript. BL contributed to conception of research idea, study design data collection, analysis and interpretation. FL, AM, FK and BWM data collection, analysis and interpretation and supervision. All authors read and approved the final manuscript.

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DECLARATION

We, the authors, declare that this paper is our original work and all sources of materials used for this paper have been fully acknowledged.

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