Institutional Delivery Predisposes to Neonatal Sepsis and Its Associated Factors Among Neonates Admitted to Neonatal Intensive Care Units in Central Gondar Zone Primary Hospitals, Northwest Ethiopia, 2019.

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Research

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Abstract

**Background:** Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge particularly in developing countries. Studies conducted on proportion and risk factors of neonatal sepsis in Ethiopia are from referral hospital which may not be generalized to primary health care units where a significant proportion of mothers give birth in these health facilities. This study sought to determine the proportion of clinical neonatal sepsis and associated factors in the study areas.

**Methods:** Institutional based cross-sectional study was conducted from March to April 2019, in Amhara regional state, central Gondar zone public primary hospitals in Ethiopia. A total of 352 subjects (mother-neonate pairs) were selected using systematic random sampling technique and pre-tested and structured questionnaires were used to collect data. Multivariable 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:** The overall proportion of neonatal sepsis was 64.8% (95% CI (59.2, 69.2)). Being male neonate (AOR=3.7; 95% CI(1.76,7.89)), history of urinary tract infections during the index pregnancy (AOR =6.26; 95% CI (1.16,33.62)), frequency of per-vaginal examination greater than three during labor and delivery (AOR=6.06; 95% CI((2.45,14.99)), neonatal resuscitation at birth (AOR=6.1; 95% CI (1.71,21.84)), place of delivery at the health center (AOR=3.05; 95% CI(1.19,7.79)), lack of training of health workers on neonatal resuscitation and infection prevention practices (AOR=2.14; 95% CI (1.04,4.44)), late age of neonate at onset of illness (AOR=0.05; 95% CI(0.01, 0.21)) and maternal age of 30-34 years (AOR=0.19; 95% CI(.047, 0.81)) were significantly associated with neonatal sepsis.

**Conclusion:** The proportion of neonatal sepsis is high. Maternal, neonatal and health service related factors were identified for neonatal sepsis. Therefore, training of health workers, provision of health care services as per standards and monitoring and evaluation of obstetrical/neonatal cares during labor and delivery are mandatory.

**Background**

Neonatal sepsis (NS) is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate(1). Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is an ongoing major global public health challenge (10). According to the World Health Organization (WHO), globally each year over 4 million neonates died within 28 days of birth (11). Infections are considered to be the leading cause of neonatal deaths (35%) followed by deaths resulted from preterm births (28%), intra-partum related complication (24%), and asphyxia (23%) (12) .
Globally 7% of mortality in children under 5 years and 15% in neonates was related to sepsis and meningitis in 2016(13). Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30-50% of the total neonatal deaths each year in developing countries (12). It is estimated that in 2012 about 6.9 million neonates were diagnosed with possible serious bacterial infection needing treatment and 2.6 million of these occurred in Sub Saharan Africa (2, 14).

In Ethiopia; prematurity (37%), infection (28%), and asphyxia (24%) are the most common causes of death in neonates. Neonatal conditions which used to account for a quarter of under-five deaths in 2004 have recently increased to 43%. According to the current united nation estimate in Ethiopia, the neonatal deaths were reduced slowly by 48% in 2013 from the 1990 as compare to significant reduction rate of under-five mortality by 67%(15).

Ethiopia demographic and health survey (EDHS, 2016) reported that neonatal mortality rate was 29/1000 live birth, which was reduced slowly from 39/1000 in 2005 and 37/1000 live births in 2011. Particularly Amhara region of the country was at the top in infant and neonatal mortality rates (NMRs). It was 67 and 47 per 1,000 live births, respectively (16).

Neonatal sepsis also has an economic impact resulted from increased medical costs, prolonged hospital stay and potentially poor long-term neurodevelopmental outcomes. Despite of this fact, the world is witnessing a steady decline in the number of neonatal deaths due to sepsis (17, 18).

Multiple factors including maternal, fetal and environmental factors have been associated with increased risk of infections in neonatal life(6).

Early identification of the risk factors for neonatal sepsis would enable early clinical diagnosis and treatment aiming to reduce neonatal morbidity and mortality(2).Implementation of certain clinical strategies are also effective in reducing the incidence of neonatal sepsis(7) .

The burden of neonatal sepsis and its complications can be averted and the target of Sustainable Development Goals for child survival can be achieved through expansion of clinical care for babies and mothers (13). Hence, there have been many advances in prevention, assessment and treatment of neonatal sepsis in the past few decades. However, the morbidity and mortality associated with sepsis remains high for susceptible neonates(8).

World Health Assembly resolution(WHA) makes a number of recommendations including prevention, diagnosis and treatment of sepsis in national health systems, training all health professionals on infection prevention and patient safety, promoting research, and others. Therefore, sepsis is considered as a good example of a cross-cutting approach for measurable reductions in neonatal mortality (13).

In Ethiopia various efforts have been made to reduce neonatal morbidity and mortality. However, some studies conducted in referral hospitals of the country showed that neonatal morbidity and mortality related to neonatal sepsis is still high.(9).
Despite a considerable burden of neonatal sepsis in our setting, there were no studies conducted to assess proportion and associated factors of neonatal sepsis among neonates admitted in NICUs of recently established primary hospitals in Ethiopia. Therefore, this study was carried out to determine the proportion of neonatal sepsis and factors contributing to it among neonates in central Gondar Zone public primary hospitals of Amhara region in Ethiopia.

**Methods**

**Study design, setting and period**

Institutional based cross-sectional study was conducted in Amhara region at central Gondar zone public primary hospitals in Ethiopia from March to April, 2019. These hospitals were established recently in the last few years. They are providing preventive, promotive and curative health care services to the population in central Gondar zone of the region and serve as a referral centers for the local health centers in the area. These primary hospitals are found in five districts (Dembali, Chilga, Wogera, Delgi, and East Belesa) in central Gondar zone of the region. They are 781, 780, 787, 832 and 867 km away from Addis Ababa, the capital city of Ethiopia towards the Northwest, respectively. All hospitals have a total number of 341 health workers. The neonatal intensive care units of each hospital have five neonatal beds for neonatal admission and have three clinical staff (one physician and two clinical nurses) and one cleaner. More than three thousand neonates were admitted in these hospitals annually to get medical services.

**Study population and sampling procedure**

All neonates admitted to neonatal intensive care units in central Gondar Zone primary hospitals were included in the study. The sample size was determined by using single population proportion formula and the proportion was taken from the previous literature in Ethiopia. According to study conducted at Gondar University teaching hospital, the prevalence of neonatal sepsis was 69.7% (23). By considering 95% confidence interval (CI), 5% marginal error, and 5% non-response rate. Therefore the final minimum adequate sample size was 352.

The study participants included 352 mother-neonate pairs who were admitted to NICUs during the study period and consented to participate in the study. The study enrolled neonates from birth to 28 days of age. Neonates with sepsis admitted for two or more time during the study period were considered to be excluded to avoid double count. However, there were no such cases in this study. The study populations were neonates admitted and treated in NICUs of central Gondar zone public primary hospitals in Ethiopia. According to the data obtained from these hospitals in 2018, the annual number of neonates admitted in neonatal intensive care units (NICUs) of these hospitals was estimated to be 3000 i.e. on the average 375 neonates were estimated to be admitted during the study period. Systematic random sampling technique was used to select study subjects during the study period. In this study neonatal sepsis is asserted when a medical diagnose of the neonate is stated as ‘neonatal sepsis’ by the physician in the neonate's medical record chart.
Data collection tool, measurements, and quality management

The tool was developed from different literatures to gather the desired information from the sample population. The questionnaire was initially prepared in English language and translated in to Amharic (local language) and again it was retranslated back to English language to check for any inconsistencies or distortions in the meaning of words and concepts. Two days training was given to five data collectors (clinical nurses, diploma) and two supervisors (BSc nurses) prior to the beginning of data collection. Data collectors collected the data from the mother or care giver of the neonates by using interviewer administered structured Amharic version questioner that contains detail questions comprising all the variables of the study. Admission diagnosis of neonates was taken from the diagnosis of physician in the unit.

The WHO IMNCI criteria were applied to assess babies for clinical sepsis. The IMNCI criteria uses the following clinical features to make a diagnosis of clinical neonatal sepsis: not feeding well, convulsions, drowsy or unconscious, movement only when stimulated or no movement at all, fast breathing (60 breaths per min), grunting severe chest in-drawing, raised temperature > 38 °C, hypothermia < 35.5 °C, central cyanosis or could be severe jaundice, severe abdominal distension or localizing signs of infection were diagnosed as having neonatal sepsis(35).

A retrospective review of the history was taken to find out if the neonate had the symptoms suggestive of neonatal sepsis since birth. A conclusion of clinical neonatal sepsis was ascertained if the baby had any one of the symptoms of sepsis listed in the IMNCI criteria and admitted in NICUs. Medical documents from the health units attended were also used to get information on presentation of the patient to the health units and the treatment received.

Data were checked for its completeness & accuracy during data collection. Close supervision of trained data collectors (five diploma nurses) was undertaken by the trained supervisors (two BSc nurses). The supervisor strictly supervised the data collection process and provided on-site advice and feedbacks to the data collectors on daily basis. Daily exchange of information between the principal investigator and supervisors was undertaken by telephone. The principal investigator had had regular onsite supervision of supervisors and data collectors on weekly basis.

Operational definitions

Neonatal sepsis: Neonates presented with any one of the systemic manifestation of danger signs:- not feeding well, convulsions, drowsy or unconscious, movement only when stimulated or no movement at all, fast breathing (60 breaths per min), grunting severe chest in-drawing, raised temperature > 38 °C, hypothermia < 35.5 °C, central cyanosis or could be severe jaundice, severe abdominal distension or localizing signs of infection were diagnosed as having neonatal sepsis(35).

Early onset of sepsis: If sepsis is occurred from birth to 7 days of age.
**Late onset of sepsis**: If sepsis is occurred between 8 and 28 days of age\(^{(32)}\)

**Data management and analysis**

Questionnaires were checked daily for completeness and accuracy. All data was double entered, cleaned, edited, coded and entered into EPI INFO version 7.0 and exported to SPSS version 20.0 for analysis by binary logistic regression model. Both bivariate and multivariable analysis was used to see the association of different variables. Categorical variables were summarized into percentages and proportions. The continuous variables were summarized into means, medians, standard deviation and ranges and the results were presented with tables and figures. The proportion of clinical neonatal sepsis was obtained by calculating the proportion of neonates with symptoms and signs of clinical neonatal sepsis out of the total number of neonates who were admitted in NICUs during the study period. Bivariate analysis was used to determine association between neonatal sepsis and various independent variables including maternal factors, neonatal factors, and service related factors. Continuous independent variables were categorized and associations established using Chi-squared tests. This was similarly done for categorical variables. Adjusted odds ratio with 95% confidence interval was used to measure the degree of association between variables. P-value of \(< 0.05\) was considered as statistically significant during multivariable logistic regression.

**Ethical consideration**

The proposal was reviewed and approved by the institute review board (IRB) of University of Gondar Institute of Public Health College of Medicine and Health Science before the start of the study. Informed consent was also obtained from mothers. A neonate aged 0 to 28 days of age who met the selection criteria was enrolled in the study. A pretested interviewer administered questionnaire was used to obtain history, physical examination and evaluate factors associated with neonatal sepsis. These included maternal factors, neonatal factors and neonatal health care practices, and service related factors.

**Results**

**Neonatal characteristics**

A total of 338 mother-neonates pairs were included in five primary hospitals of central Gondar Zone making the response rate of 96%. The median age of neonates was 2 days with interquartile range of 4 days. Among all participants, more than half 200 (59.2%) were male neonates with male to female ratio 1.4:1. Nearly two-third of neonates were born at hospitals 212(62.7%). Similarly nearly two-third 218(64.5%) of neonates were term and the remaining one-third 120(35.5%) were preterm. Low birth weight was illustrated among 53.5% of neonates (Table1).

**Mothers socio-demographic and economic characteristics**
The median age of mothers of the neonate was 26 years with an inter quartile range of 8 years and 4 months. Among the participants, one-third of neonates mother 114(33.7%) were in the age range of 25 to 29 years. More than half 195 (57.7%) of them were from rural areas (table 2).

Mothers medical and obstetric conditions

In this study more than half of the mothers 202(59.8%) were multiparous women. Majority of the mothers 314(92.9%) had at least one ANC follow-up at the time of pregnancy and 10 (3%) of them were positive with HIV AIDS. Among the positive mothers, majority 7(70%) were from urban areas. About one-third 101 (29.9%) of them had history of PROM during the index pregnancy and nearly three-fourths 247(73.1%) of neonates were delivered by spontaneous vaginal delivery (table3).

Medical procedures related to neonatal health care services

None of the neonates were on mechanical ventilation. About 2.7% of neonates had history of end tracheal intubation for resuscitation and 61(18%) were on oxygen therapy through intranasal oxygen catheter or face mask (table 4).

Proportion of neonatal sepsis and clinical characteristics of neonates

Two-thirds of the neonates 158 (72.1%) were admitted within one week of age and the overall proportion of Neonatal sepsis was 64.8 %( 95% CI (59.2, 69.2). From these 158(72.1%) were early onset neonatal sepsis. Gross congenital malformation like neural tube defect, cleft palate and hydrocephalus were also found in 7(2.1%) of neonates (table 5 and figure 1).

Factors associated with neonatal sepsis

All the variables which fulfilled the chi-square assumption were fitted into bivariable and multivariable logistic regression. Residency, age of neonate, sex of neonate, place of birth, gestational age, birth weight, maternal age, maternal marital status, parity, ANC follow-up, duration of labor, history of UTI/STIs, history of PROM, history of foul smelling liquor, birth asphyxia, place of delivery and training of health works at NICUs fulfilled the variable screening criteria (p- value < 0.2) and entered into multivariable logistic regression analysis. Consequently, age of neonate, sex of neonates, maternal age, history of UTIs, frequency of PV examination, resuscitation at birth, and getting care from trained health workers were significantly associated with neonatal sepsis at multivariable with less than 0.05 p values.

Accordingly, sex of neonate showed significant association with the risk of onset of neonatal sepsis. The odds of having neonatal sepsis among male neonates were 3.7 times higher as compared to female
This study showed that, neonates born to mothers who had UTIs during the index pregnancy had 6 times higher odds of developing sepsis as compared to those neonates born from mothers who did not have a UTIs during the index pregnancy [AOR = 6.26; 95% CI [(1.16, 33.62)]. Likewise, increased odds of neonatal sepsis was noted among mothers who have history of more than three PV examination during labor compared to mothers who had PV examination less than or equal to three [AOR = 6.06; 95% CI [(2.45, 14.99).

Similarly, those neonates who were resuscitated at birth had 6 times higher odds of developing sepsis compared to those neonates who were not resuscitated [AOR = 6.110; 95% CI [(1.71, 21.84)]. Nevertheless, the odds of neonatal sepsis decreased by 95% among neonates whose age is less than one week compared to those aged greater than a week [AOR = 0.05; 95% CI [(0.01, 0.21)].

Maternal age was significantly associated with neonatal sepsis. Neonates from older mother whose age is 30 – 34 years were 81% less likely to develop neonatal sepsis when compared to neonates from mothers whose age is 35 years and older [AOR=0.19; 95%CI (0.05, 0.81).

Place of delivery also has significant effect on neonatal sepsis. Neonates delivered in the health center were three times more likely to develop sepsis compared to those delivered at the hospital [AOR=3.05; 95% CI ((1.19, 7.79).

Finally neonates who get care by health workers who had no training on NICU/ IPPs were 2 times more likely to develop sepsis as compared to neonates who get care by trained health professionals. [AOR = 2.14; 95% CI [(1.04, 4.44)] (table 6).

**Discussion**

Neonatal sepsis contributes substantially to neonatal morbidity and mortality and is a major global public health challenge(10). In this study the overall proportion of neonatal sepsis was 64.8 % (95% CI (59.2, 69.2).

This finding is in line with a study conducted in Gondar (67.9 %,) (23). The possible reason for having similar results might be due to similarities of study population studied in the same area and the period in which the studies were conducted. This finding is, however, much higher than findings of studies from Uganda(11%)(14), India(32%)(6), Tanzania(31.4%)(2) and Nigeria(34%)(21). This difference might have been contributed by methodological difference and the difference in diagnostic modality to confirm neonatal sepsis. In contrast to the finding of these studies the prevalence of neonatal sepsis in Bishoftu (72.2%)(3) and Shashemene(77.9%) (9)were much higher than the current finding. This higher prevalence is likely due to the fact that these study sites are referral hospitals, most frequently receiving neonates with complications as well as complicated pregnancies. Furthermore, these differences could be due to
difference in sample size, socio-demographic and economic status of study population and access to health facilities(9).

In this study, neonates born from mothers who had a history of urinary tract infections (UTIs) during the index pregnancy were six times more likely to develop neonatal sepsis. This finding is in agreement with the findings of studies conducted previously in Mekelle(19) and Bishoftu(3) which revealed that maternal urinary tract and sexual infections was a significant factor for the development of neonatal sepsis. This finding may support the reason that maternal health problem is often associated with neonatal sepsis, especially if untreated during the third trimester pregnancy or labor. Hence, neonatal sepsis may result from the colonization of the birth canal by the infectious agent(3,24).

This study also identified significant association between neonatal resuscitation and neonatal sepsis. The odds of developing neonatal sepsis among neonates who has history of neonatal resuscitation at birth were six times higher as compared to neonates who were not resuscitated. This finding was in agreement with studies from Bangladesh(24), Tanzania(2) and Ghana(25) which identified neonatal resuscitation at birth was a significant risk factor for neonatal sepsis. Resuscitation procedures at birth pose greater risk of neonatal sepsis. Many life-supporting procedures such as suctioning and endotracheal intubations can lead to transient and persistent bacteremia(24). Newborn infants are especially vulnerable to nosocomial infections because of their intrinsic susceptibility to infection as well as the performance of invasive procedures for neonatal resuscitation to which they are subjected (25). Studies from china, Korea and Ethiopia revealed that different medical procedures which are undertaken below the optimal level of asepsis (sterility or disinfection) for the management of neonatal health problems predispose the neonate to a great risk of neonatal sepsis(9,28,33) This might resulted from poor practices and non-adherence to guideline by health professionals during resuscitation that may predispose the neonate with a greater risk of developing sepsis(25).

Furthermore, in this study neonatal age was found to be significant factor for neonatal sepsis. Neonates whose age was less than or equal seven days were 95% less likely to develop neonatal sepsis compared with the age of neonates greater than seven days of age. This finding is in line with finding from a study in Ghana(25) and Shashemene (Ethiopia)(9) which revealed that the probability of to develop sepsis increased with increasing neonatal age. In fact nosocomial and community acquired neonatal infections occurs after 3 days of life. Consequently this will have an effect on the prevalence of late onset neonatal sepsis(36). This is also supported by the finding from this study which revealed that majority of neonates were delivered in the health institutions. This may in turn increased the possibility to develop neonatal sepsis after discharged from these institutions at late age.

Per-vaginal examination (PV) during labour and delivery was found to be significant factor for neonatal sepsis. Neonates from mothers who had history of PV examination greater than three were six times more likely to develop neonatal sepsis. This finding was in line with finding from study in Bangladesh in which neonates from mothers who have history of vaginal examination greater than three was found to be 2.5 times more likely to develop neonatal sepsis(24). Vaginal organisms can be introduced into the
cervical canal even during sterile conditions. Hence, babies are at risk from ascending infection thought to be caused by vertical transmission from an infected mother. Therefore vaginal examination can increase the risk of harm for women and their babies(37). However, a study in Mekelle, Ethiopia reported that there was no significant association between PV examination and neonatal sepsis(19) This may also result from difference in study settings where the quality of obstetrical and neonatal health care services provided to mothers and neonates in primary hospitals differs to that of referral hospitals.

Sex of neonate was significantly associated with neonatal sepsis. This study found that being male was 3.7 times more likely to develop neonatal sepsis as compared to their counterparts. This finding is in agreement with finding of a study in Australia. It reported that risk of neonatal sepsis was found increase three times more in male neonates as compared to female neonates(30). Male sex is associated with a higher risk of neurological, pulmonary, cardiovascular and infectious morbidities as well as overall mortality when compared to female infants of similar preterm gestation(29). Important differences in the immune response between male and female preterm neonates have also been noted (31). However, the etiology of sex-specific differences in disease remains relatively undetermined and is likely multifactorial, with genetic, immunological and hormonal influences playing key roles(30).

Place of birth was found to be statistically significant with neonatal sepsis. Neonates delivered at the health center were three times more likely to develop sepsis as compared to neonates delivered at hospitals. This finding is in agreement with findings from studies in Nigeria(21) and Ethiopia(3,19). This might be due to the reason that neonates who were delivered at health center may be less likely to be screened based on a risk approach and treated with intra-partum antibiotic prophylaxis(38). Furthermore, difference in the level of knowledge about the maternal and neonatal health among health workers in hospitals and health centers and level of adherence of health workers to guidelines and protocols on IPPs to prevent infections in newborns might be the possible reason for this finding.

Maternal age was also significantly associated with neonatal sepsis. Neonates from mothers whose age was from 30 - 34 years were 81% less likely to develop neonatal sepsis as compared to those neonates from mothers older than 35 years. However, studies from Bangladesh(24) and Tanzania(2) showed that the attack rates of sepsis increased significantly among neonates born from mothers less than 20yrs of age. This difference may result from the high number of mothers less than 20 years of age in Bangladesh (67%), and Tanzania (17.7%) as compared to the current finding (13.6%) in Ethiopia. Sample size and methodological difference may also have its own impact for this difference.

Training of health workers in NICUs in all matters related to neonatal health and infection prevention in particular was significantly associated with neonatal sepsis. Pathogenic agents can be transmitted by direct contact or indirectly via contaminated equipment, intravenous fluids, medications, blood products, or enteral feedings(36). Poor practices and non-adherence to guidelines by health professionals during resuscitation and other medical procedures may predispose the neonate with a greater risk of developing sepsis(25). This might not be different with the finding of current study.
Residence, ANC, parity, duration of labor, mode of delivery, foul smelling liquor, birth asphyxia, PROM, gestational age, and birth weight were not found to be predictors of neonatal sepsis in this study. This is in against the findings of studies on risk factors of neonatal sepsis in different parts of the world(3,9,19,21,24,25).

**Conclusion**

The proportion of neonatal sepsis is high. Late neonatal age at onset of sepsis, being male sex, 30 -34 years of age of the mother, neonatal resuscitation at birth, history urinary tract infections during pregnancy, frequency of per-vaginal examinations greater than three times during labor and delivery, and place of delivery(health center)were identified risk factors for neonatal sepsis. Therefore; training of health workers, provision of health care services as per standards and monitoring and evaluation of obstetrical/neonatal cares during labor and delivery are mandatory.

**Limitations of the study**

Since the study was done on admitted neonates, these findings may lack generalizability to the entire population in the catchment area. Additionally, Clinical diagnosis of neonatal sepsis may overestimate the proportion of neonatal sepsis.

**Abbreviations**

ANC: Antenatal Care, APGAR: Appearance, Pulse, Grimace, Activity and respiration, CNS: Central Nervous System, EDHS: Ethiopia Demographic and Health Service Survey, EONS: Early Onset Neonatal Sepsis, HEW: Health Extension Workers, HIV: Human Immune Deficiency Virus, LMICs: Low and Middle Income Countries, LONS: Late Onset Neonatal Sepsis, NICU: Neonatal Intensive Care Unit, NMR: Neonatal Mortality Rate, NS: Neonatal Sepsis, PMTCT: Prevention of Mother to Child Transmission, PROM: Premature Rupture of Membrane, PV: Per-vaginal Examination, STIs: Sexually Transmitted Infections, SVD: Spontaneous Vaginal Delivery, UTIs: Urinary Tract Infections, VDRL: Venereal Disease Research Laboratory, VLBW :Very Low Birth Weight, WHO: World Health Organization.

**Declarations**

**Ethics approval and consent to participate**

Ethical clearance was obtained from the Ethical Review Committee of the Institute of Public Health, the University of Gondar. An official permission letter was obtained central Gondar Zone. Written informed consent was obtained from study participants in their local language after explaining the purpose, potential risks and benefits of the study, along with the right to withdraw from the study at any time. The participants were also assured that the data was confidential.
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

We the authors declare that there is no any competing interest

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The authors have declared that there was no funding.

Authors’ contributions

ZA wrote the proposal, involved in study design, analyzed the data, drafted paper. KAG, and HYY, approved the design, the proposal, involved in data analysis, revised subsequent drafts of the paper and reviewing of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Socio-demographic characteristics of neonates admitted to neonatal intensive care units (NICUs) of central Gondar zone primary hospitals, Northwest Ethiopia, 2019.
| Variables          | Frequency | Percent |
|--------------------|-----------|---------|
| **Age**            |           |         |
| 0-7 days           | 278       | 82.2    |
| 8-28 days          | 60        | 17.8    |
| **Sex**            |           |         |
| Male               | 200       | 59.2    |
| Female             | 138       | 40.8    |
| **Place of delivery** |         |         |
| Home               | 28        | 8.3     |
| Health centre      | 98        | 29      |
| Hospital           | 212       | 62.7    |
| **Gestational age** |           |         |
| < 37 weeks         | 120       | 35.5    |
| 37 – 42 weeks      | 218       | 64.5    |
| **Birth weight**   |           |         |
| <1500 g            | 43        | 12.7    |
| 1500 – 2499 g      | 138       | 40.8    |
| 2500 -3499 g       | 137       | 40.5    |
| ≥ 4000 g           | 20        | 5.9     |

*Table 2. Socio-demographic and economic characteristics of mothers of neonates admitted to NICU in central Gondar zone primary hospitals, Northwest Ethiopia, 2019.*
| Variables                | Frequency | Percent |
|--------------------------|-----------|---------|
| Residence                |           |         |
| Urban                    | 143       | 42.3    |
| Rural                    | 195       | 57.7    |
| Maternal age             |           |         |
| 15 - 19 years            | 46        | 13.6    |
| 20 – 24 years            | 82        | 24.3    |
| 25 – 29 years            | 114       | 33.7    |
| 30 – 34 years            | 46        | 13.6    |
| ≥ 35 years               | 50        | 14.8    |
| Marital status           |           |         |
| Married                  | 322       | 95.3    |
| Unmarried                | 16        | 4.7     |
| Maternal educational level|         |         |
| Unable to read and write | 136       | 40.2    |
| Able to read and write   | 87        | 25.7    |
| Primary education        | 57        | 16.9    |
| Secondary education      | 45        | 13.3    |
| Certificate and above    | 13        | 3.8     |
| Occupation               |           |         |
| Housewife                | 256       | 75.7    |
| Government employee      | 45        | 15.3    |
| NGO(private)             | 14        | 4.1     |
| Others*                  | 23        | 6.8     |
| Monthly income           |           |         |
| < 900 birr               | 97        | 28.7    |
| 900-1200 birr            | 78        | 23.1    |
| 1201- 2050 birr          | 79        | 23.4    |
| > 2050 birr              | 84        | 24.8    |
| Religion                 |           |         |
| Orthodox                 | 330       | 97.7    |
| Muslim                   | 8         | 2.3     |

*Merchant, daily labourer and house servant

**Table 3.** Medical and obstetrical characteristics of mothers of neonates admitted to NICU in central Gondar zone primary hospitals, Northwest, Ethiopia, 2019.
| Variables                        | Frequency | Percent |
|---------------------------------|-----------|---------|
| parity                          | I         | 136     | 40.2   |
|                                 | II        | 58      | 17.2   |
|                                 | III and more | 144    | 42.6   |
| Antenatal care                  | Yes       | 314     | 92.9   |
|                                 | No        | 24      | 7.1    |
| HIV test result                 | Positive  | 10      | 3      |
|                                 | Unknown   | 311     | 92     |
|                                 | Negative  | 17      | 5      |
| VDRL/RPR status                 | Reactive  | 20      | 5.9    |
|                                 | Non-reactive | 272    | 80.5   |
|                                 | Unknown   | 46      | 13.6   |
| Mode of delivery                | Spontaneous vaginal delivery | 247   | 73.1   |
|                                 | Caesarean section | 38    | 11.2   |
|                                 | Instrumental | 53    | 15.7   |
| Duration of labor               | < 6 hours | 118     | 34.9   |
|                                 | 6 - 12 hours | 87    | 25.7   |
|                                 | 12 - 24 hours | 108  | 32     |
|                                 | ≥ 24 hours | 25     | 7.4    |
| Frequency of PV* exam during labor | ≤ 3 times | 143   | 42.3   |
|                                 | >3 times  | 195     | 57.7   |
| History of foul smelling liquor | Yes       | 19      | 5.6    |
|                                 | No        | 319     | 94.4   |
| History of PROM**               | Yes       | 101     | 29.9   |
|                                 | No        | 237     | 70.1   |
| History of high grade fever during pregnancy | Yes | 74 | 21.9 |
|                                 | No        | 264     | 78.1   |

*Per-vaginal, **premature rupture of membrane
Table 4. Medical procedures done for neonates who were admitted to NICU in central Gondar zone primary hospitals, Northwest Ethiopia, 2019

| Variables                        | Frequency | Percent |
|----------------------------------|-----------|---------|
| Mechanical ventilation           | No        | 338     | 100     |
| Oxygen administration            | Yes       | 61      | 18      |
|                                  | No        | 277     | 82      |
| Endotracheal tube intubation     | Yes       | 9       | 2.7     |
|                                  | No        | 329     | 97.3    |
| Nasogastric tube insertion       | Yes       | 21      | 6.2     |
|                                  | No        | 317     | 93.8    |
| Central venous catheterization   | Yes       | 50      | 14.8    |
|                                  | No        | 288     | 85.2    |

Table 5. Clinical characteristics of neonates who were admitted to central Gondar zone primary hospitals, Northwest Ethiopia, 2019.

| Variables                        | Frequency | Percent |
|----------------------------------|-----------|---------|
| Birth injury                     | Yes       | 26      | 7.7     |
|                                  | No        | 312     | 92.3    |
| Birth asphyxia                   | Yes       | 56      | 16.6    |
|                                  | No        | 282     | 83.4    |
| Gross congenital malformation    | Yes       | 7       | 2.1     |
|                                  | No        | 331     | 97.9    |
| Cry at birth                     | Yes       | 271     | 80.2    |
|                                  | No        | 67      | 19.8    |

Table 6. Bivariable and multivariable analysis of factors associated with neonatal sepsis among neonates admitted at central gonad zone primary hospitals, Northwest Ethiopia, 2019.
| Variables                      | Neonatal sepsis N (%) | COR(95%CI) | AOR(95%CI) |
|-------------------------------|-----------------------|------------|------------|
|                               | Yes                   | No         |            |
| Residence                     |                       |            |            |
| Urban                         | 105(31.1)             | 38(11.2)   | 1          | 1          |
| Rural                         | 114(33.7)             | 81(24)     | 0.51(0.32, 0.81) | 0.75(0.34, 1.66) |
| Parity                        |                       |            |            |
| I                             | 97(28.7)              | 39(11.5)   | 1.49(0.90,2.47) | 1.21(0.41,3.62) |
| II                            | 32(9.7)               | 26(7.7)    | 0.74(0.39,1.370) | 0.58(0.18,1.88) |
| III                           | 90(26.6)              | 54(16)     | 1          | 1          |
| Duration of labor             |                       |            |            |
| < 6 hours                     | 82(24.3)              | 36(10.7)   | 1          | 1          |
| 6 – 12 hours                  | 41(12.1)              | 46(13.6)   | 0.39(0.22, 0.69) | 0.47(0.18,1.19) |
| 12 -24 hours                  | 75(22.2)              | 33(9.8)    | 0.99(0.57, 1.76) | 0.66(0.25,1.77) |
| >24 hours                     | 21(9.6)               | 4(3.4)     | 2.31(0.74, 7.19) | 1.02(0.21,4.93) |
| Frequency of PV examination   |                       |            |            |
| ≤ 3 times                     | 84(24.9)              | 59(17.5)   | 1          | 1          |
| >3 times                      | 135(39.9)             | 60(17.8)   | 1.58((1.01, 2.48) | 6.06(2.45, 14.99)** |
| Sex of neonate                |                       |            |            |
| Male                          | 139(41.1)             | 61(18)     | 1.65(1.05, 2.59) | 3.73(1.76, 7.89)** |
| Female                        | 80(23.7)              | 58(17.2)   | 1          | 1          |
| Gestational age               |                       |            |            |
| < 37 weeks                    | 66(19.5)              | 54(16)     | 0.52(0.32, 0.82) | 0.98(0.35, 2.78) |
| 37 – 42 weeks                 | 153(45.3)             | 65(19.3)   | 1          | 1          |
| History of birth asphyxia     |                       |            |            |
| Yes                           | 31(9.2)               | 25(7.4)    | 0.62(0.35, 1.11) | 0.55(0.18, 1.68) |
| No                            | 188(55.6)             | 94(27.8)   | 1          | 1          |
| History of oxygen administration |                   |            |            |
| Yes                           | 45(13.3)              | 16(4.4)    | 1.67(0.89, 3.09) | 2.06(0.64, 6.59) |
| No                            | 174(51.5)             | 103(30.5)  | 1          | 1          |
| History of NG tube insertion  |                       |            |            |
| Yes                           | 20(5.9)               | 1(0.3)     | 11.86(1.57,89.51) | 10.36(0.81,132.78) |
| No                            | 199(58.9)             | 118(34.9)  | 1          | 1          |
| History IV catheterization    |                       |            |            |
| Yes                           | 42(12.4)              | 8(2.4)     | 3.29(1.49, 7.27) | 2.81(0.89, 8.93) |
| No                            | 177(52.4)             | 111(32.8)  | 1          | 1          |
|                                | Yes          | No           | Odds Ratio (95% CI) | P Value |
|--------------------------------|--------------|--------------|---------------------|---------|
| History of neonatal resuscitation | 37(10.9)     | 12(3.6)      | 1.81(0.91, 3.63)    | 0.0064  |
| Training of Health workers      | 112(33.1)    | 39(11.5)     | 2.17(1.35, 3.42)    | 0.0004  |
| Marital status                  |              |              |                     |         |
| Married                        | 204(60.4)    | 118(34.9)    |                     |         |
| Not married                     | 15(4.4)      | 1(0.3)       | 8.68(1.13, 66.52)   | 0.0140  |
| Maternal age category           |              |              |                     |         |
| 15 -19 yrs.                     | 36(10.7)     | 10(3)        | 1.14(0.44, 2.95)    | 0.2931  |
| 20 -24 yrs.                     | 51(15.1)     | 31(9.2)      | 0.52(0.24, 1.14)    | 0.1435  |
| 25 - 29 yrs.                    | 76(25.5)     | 38(11.2)     | 0.63(0.29, 1.35)    | 0.0024  |
| 30 -34 yrs.                     | 18(5.3)      | 28(8.3)      | 0.20(0.08, 0.49)    | 1       |
| ≥ 35 yrs.                      | 38(11.2)     | 12(3.6)      | 1                    |         |
| VDRL test result                |              |              |                     |         |
| Reactive                       | 17(5)        | 3(0.9)       | 2.62(0.75, 9.18)    | 0.0764  |
| Unknown                        | 16(4.7)      | 30(8.9)      | 0.25(0.13, 0.48)    | 0.0004  |
| Non-reactive                   | 186(55)      | 86(25.4)     | 1                    |         |
| History of UTIs                 |              |              |                     |         |
| Yes                            | 10(3)        | 5(1.5)       | 1.01(0.34, 3.03)    | 0.5462  |
| Unknown                        | 5(1.5)       | 11(3.3)      | 0.23(0.08, 0.68)    | 0.0001  |
| Negative                       | 204(60.4)    | 103(30.5)    | 1                    |         |
| Birth weight                   |              |              |                     |         |
| <1500 g                        | 24(7.1)      | 19(5.6)      | 0.57(0.29, 1.14)    | 0.0001  |
| 1500 - 2499 g                  | 87(25.7)     | 51(15.1)     | 0.77(0.45, 1.26)    | 0.1127  |
| ≥ 2500 g                       | 108(32)      | 49(14.5)     | 1                    |         |
| foul smelling vaginal discharge |              |              |                     |         |
| Yes                            | 9(2.7)       | 10(3)        | 0.47(0.18, 1.18)    | 0.0001  |
| No                             | 210(62.1)    | 109(32.2)    | 1                    |         |
| Neonatal age in days           |              |              |                     |         |
| ≤ 7 days                       | 163(48.2)    | 115(34)      | 0.10(0.04, 0.29)    | 0.0001  |
| >7 days                        | 56(16.60)    | 4(1.2)       | 1                    |         |
| History of PROM                 |              |              |                     |         |
| Yes                            | 73(21.6)     | 28(8.3)      | 1.62(0.98, 2.70)    | 0.0001  |
| Place of delivery | Home   | Health center | 1 | 4.69 | 1 |
|-------------------|--------|---------------|---|------|---|
|                   | 14(4.1)| 70(20.7)      | 1 | 0.57(0.26, 1.26) | 4.06(0.69, 23.86) |
|                   | 14(4.1)| 28(8.3)       |   | 1.43(0.85, 2.39) | 3.05(1.19, 7.79) |
|                   |        |               |   | 1    | * |

Significant at < 0.05 $\alpha$ – values, ** Significant at < 0.01 $\alpha$-value.

**Figures**

![Neonatal sepsis](image)

**Figure 1**

Proportion of neonatal sepsis among neonates admitted in central Gondar zone primary hospitals, Northwest Ethiopia, 2019.
Figure 1

Proportion of neonatal sepsis among neonates admitted in central Gondar zone primary hospitals, Northwest Ethiopia, 2019.