Research Article

Admission Outcome and Antimicrobial Resistance Pattern of Bacterial Isolates among Neonates with Suspected Sepsis in Neonatal Intensive Care Unit at Dessie Comprehensive Specialized Hospital, Dessie, Northeastern Ethiopia

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Background. Neonatal sepsis is a major cause of morbidity and mortality globally. The aim of this study was to assess admission outcome and antimicrobial susceptibility pattern of bacterial isolates among neonates with suspected sepsis at the Dessie Comprehensive specialized Hospital (DCSH), Northeastern Ethiopia. Method. Cross-sectional study was conducted from August 2017 to March 2018. Two hundred forty-six neonates were recruited, and each patient’s blood specimen was collected aseptically using bottle containing Brain Heart Infusion for blood culture. Both clinical and laboratory data such as bacterial culture growth and antimicrobial susceptibility pattern were collected from the neonate; clinical data from the mothers were also included. Antimicrobial susceptibility testing was performed using Kirby-Bauer disk diffusion method. The data were analyzed using SPSS version 20. Results. Bacteria were identified from 67 (27.2%) blood cultures. The predominant pathogen was Escherichia coli (35.8%) followed by Staphylococcus aureus (26.8%), and Coagulase Negative Staphylococcus (CoNS) (19.4%). The isolated bacteria showed resistance to Ampicillin 55 (82%), third-generation Cephalosporins 21 (58.3%) and other tested antimicrobials. Overall, 68.6% bacterial isolates demonstrated Multidrug resistance (MDR) and total registered mortality rate was 12/246 (4.8%). Both neonatal factors such as neonatal temperature, septic umbilicus and utilization of indwelling medical device during delivery; and maternal factors such as age, antenatal urinary tract infection (UTI), mode of delivery and prolonged rupture of membrane (PROM) had shown statistically significant association with bacterial sepsis. Conclusion. The rate of bacterial growth was found to be high; E. coli and S. aureus were the predominant organisms. Both maternal and neonatal related data were strong predictors for bacterial infection of the neonate. Therefore, improving infrastructures for screening of bacteremia as well as active surveillance in clinical setting needed to ensure proper empirical therapy.

1. Introduction

Neonatal sepsis is a major cause of morbidity and mortality; the third leading cause of mortality globally [1], and more than half sepsis-related deaths occurred within 28-days of life in developing countries [2]. According to Ethiopian Federal Ministry of Health report (2016), in Ethiopia one neonate died in every 35 children within the first months of life [3]. Moreover, neonatal sepsis is the most common clinical diagnosis and second cause of admission in neonatal intensive-care unit (NICU), in Ethiopia [4].

Neonatal sepsis is characterized by a systemic condition of bacterial, viral, or fungal origin that is related to hemodynamic changes and other clinical manifestations during
2.1. Study Setting and Study Design. An institution based cross-sectional study was carried out from August 2017 to March 2018 at DCSH, Dessie, South Wollo Zone, Amhara region. Dessie is located at the latitude of 11°8′N and longitude of 39°38′E with an elevation between 2,400 and 3,200 meters above sea level. The town is found 401 km distant from the capital city of Ethiopia (Addis Ababa). The hospital catchment population is about 7 million, and in 2016 the entire outpatient attendants were 205,454. The NICU is part of the pediatric department wards and the average total number of neonates’ admissions per year is almost 1600. In addition to the populations in Dessie town, the hospital also serves as a referral site for neighboring North Wollo, Oromiya zone of Amhara regional state, and Afar regional state.

2.2. Study Population. In this study, the clinical diagnosis of sepsis was made by considering the Integrated Management of Neonatal and Childhood Illness (IMNCI) guideline [21].

All neonates presented with one or more clinical features found in IMNCI guideline and who were admitted to DCSH-NICU during the study period were the study populations. Neonates admitted to NICU and whose mothers and/or caregivers provided written consent were included in this study. Neonates who showed gross congenital anomalies, severe anemia and those who received antibiotics prior to blood specimen collection were not included. During the study period, a total of 932 neonates were admitted with various types of clinical diagnosis. Of these, a total of 246 neonates who fulfilled the above inclusion criteria were enrolled consecutively (Figure 1).

2.3. Study Variables. In this study, the dependent variable was the presence of bacterial growth (infection), whereas independent variables were maternal and neonatal characteristics.

2.4. Data Collection. This study uses data that were collected from both structured questionnaire and from bacteriological laboratory work results of blood culture. Socio-demographic characteristics and other associated variables of each delivered mother and clinical data of their neonate were collected and extracted from their medical history.

2.5. Specimen Collection and Processing. From each study subject, 2.5 ml of venous blood was collected aseptically and transferred into double 20 ml of Brain heart infusion blood culture bottle. After collection, all blood specimens were incubated at 35–37°C in the DCSH laboratory until transported to the bacteriology laboratory of the Amhara Public Health Institute (APHI), Dessie branch.

2.6. Bacteriological Culture and Identification. All blood culture bottles were incubated at 35–37°C under aerobic condition for 7 days. According to the standard operating procedures (SOPs) the incubated blood culture bottles were sub-cultured on Blood agar, Chocolate agar and MacConkey agar. The inoculated Blood agar (Oxoid Ltd.) and MacConkey agar (Oxoid Ltd. Basingstoke, Hampshire, UK) plates were incubated aerobically at 35–37°C for 24 hours. Whereas, blood specimen sub-cultured on Chocolate agar (Oxoid Ltd.) plates were incubated at 35–37°C in microaerophilic condition (5–10% CO₂) for 48–72 hours. If CoNS was isolated from a single blood culture bottle, then it was considered as contaminant growth, whereas if it was isolated from two blood culture bottles it was considered as a pathogen [22].

Each bacterial isolate was identified through colony morphology, Gram stain, biochemical test and rapid bench test like catalase and oxidase test. Biochemical tests (Indole production, motility, citrate utilization, urea, triple sugar iron, and decarboxylase/lysine iron agar/test) using conventional methods were performed for Gram-negative isolates. In addition to rapid bench tests, other tests (PYR-test, Optochin, coagulase, Bile solubility, Bile-Escolin,
DNAase) were also used to differentiate Gram-positive isolates [22].

2.7. Antimicrobial Susceptibility Testing. Antimicrobial susceptibility testing was performed for each bacterial isolate using a modified Kirby-Bauer disk diffusion method as per Clinical and Laboratory Standards Institute (CLSI) guideline [23]. Using a sterile wire loop, 3–5 well isolated colonies were picked from the primary inoculated plates. The suspended colony was adjusted for the inoculums’ turbidity equivalent to 0.5 McFarland standard and swabbed on Mueller Hinton Agar (MHA) (Conda Ltd, USA) plate. Standard antibiotic disks were placed aseptically and then the inoculated MHA plate was incubated at 35–37°C for 16–18 hours. In this study the utilized antibiotic concentration per disk (Oxoid UK and BBL-BD USA) were Penicillin-G-10 unit, Ampicillin-10 μg, Gentamicin-10 μg, Clindamycin-2 μg, Erythromycin-15 μg, Trimethoprim-sulfamethoxazole-1.25/23.75 μg, Cefoxitin-30 μg, Amoxicillin-Clavulanic acid-20/10 μg, Piperacillin-Tazobactam 100 μg/10 μg, Ceftazidime-30 μg, Ceftriaxone-30 μg, Cefotaxime-30 μg, Cefepime-30 μg, and Meropenem-10 μg. The zone of inhibition for the above-mentioned antibiotics, with the exception of Cefoxitin, was measured after 16–18 hours of incubation. Based on the CLSI guideline [23], the results obtained from the antimicrobial susceptibility testing were interpreted as susceptible, intermediate and resistance. Multidrug resistance was interpreted as resistance to a minimum of three or more antibiotic classes [24]; intermediate results in this study were categorized as resistance.

2.8. Quality Control. By considering both CLSI guideline and the SOPs of the medical microbiology laboratory unit at Amhara public health institute, all standard procedures in the three important phases were strictly followed. The sterility of culture media was ensured by incubating 5% of each batch of the prepared media at 37°C for 24 hours. In order to assure the performance of all prepared media, we have used standard-strains like Escherichia coli (ATCC)-25922, Pseudomonas aeruginosa (ATCC-27853), Staphylococcus aureus (ATCC-25923), Haemophilus influenzae (ATCC-49247), Streptococcus pneumoniae (ATCC-49029) and Enterococcus fecalis (ATCC-29212).

2.9. Data Processing and Analysis. The data were checked for their completeness and analyzed using SPSS version 20. Frequencies and cross tabulations accustomed to summarize descriptive statistics. Bi-variable and multi-variable logistic regressions were used to assess the association between dependent and independent variables. The odds ratio and
95% confidence interval were computed to assess the presence and degree of association between dependent and independent variables. A P-value < 0.05 was considered statistically significant.

2.10. Ethical Considerations. Ethical clearance was obtained from an institutional ethical review committee of the College of Medicine and Health Science, Wollo University. Additionally, the official permission letter was secured from DCSH using the cooperation letter that was written by Wollo University. After briefly explaining the importance, purpose and procedure of the study, a written assent form was obtained from each study participant’s family.

3. Results

3.1. Characteristics of Study Participants. A total of two hundred forty-six neonates with suspected sepsis participated. Out of the total number of participating neonates, 82.5% (203/246) were suspected of early onset sepsis; 66% (162/246) of them were male; 48.4% (119/246) had low birth weight (<2500 gm) and 45% (111/246) of neonates were preterm. Regarding the clinical characteristics of the neonate; 75 of them showed lethargy, 201 neonates refused to feed, 10 study participants had septic umbilicus and 37 of them had experienced vomiting (Table 1).

3.2. Maternal Related Information. About 197 (80%) mothers were below 35 years old, 219 (89%) were married and 134 (54.47%) were urban area inhabitants. Most of the mothers delivered in the health facilities, the majority of them gave birth through spontaneous vortex delivery and 8 (3.25%) mothers experienced urinary tract infection (UTI) during their pregnancy period (Table 2).

3.3. Blood Culture Findings. Bacterial growth obtained from 27.2% (67/246) of the total participated neonates and among the overall identified bacterial pathogens near to two-thirds was obtained from neonates with EOS. Bacterial growth was detected among 17% (42/246) of male and 10.2% (25/246) of female study participants. Furthermore, bacterial isolates were identified from 15.8% (39/246) of neonates born preterm and 16.7% (41/246) of neonates with low birth weight (Table 1). The majority (89.55%) of bacterial growth
obtained among neonates who were delivered from currently married mothers and about 74.6% of neonates with bacterial growth result were born from mothers whose age was below 35 years (Table 2).

3.4. Associated Factors for Bacterial Growth. To verify the presence or absence of an association between dependent and independent variables, the logistic regression analysis of data from both neonates and mothers were analyzed. Study participated neonates who had septic umbilicus showed 10 times higher odds of developing bacterial infection in comparison with those neonates who had clear umbilicus (AOR = 10.06, 95% CI = 1.75–57.8, \( P = 0.01 \)). Utilization of an indwelling medical devices has shown 2 times higher likelihood of bacterial infection among the sepsis suspected neonates (AOR = 2.2, 95% CI = 1.12–4.32, \( P = 0.022 \)) (Table 3). Neonates who were born from mothers whose age was less than 35 years had a 57% reduced likelihood of acquiring bacterial infection (AOR = 0.43, 95% CI = 0.2–0.92, \( P = 0.029 \)). Neonate delivered from pregnant mother with UTI had 19 times higher odds (AOR = 19, 95% CI = 2.02–178.7, \( P = 0.01 \)) of bacterial infection to their counterparts (Table 4).

3.5. Isolated Bacteria. From the total positive blood culture, 53.7% (36/67) were found to be Gram-negative and seven different types of bacterial pathogens were identified. The most frequently isolated bacterial species was E. coli, 35.8% (24/67), followed by S. aureus, 26.8% (18/67) and CoNS, 19.4% (13/67). Whereas K. pneumoniae, 8.9% (6/67), K. oxytoca, 19.4% (13/67). Whereas K. pneumoniae, 8.9% (6/67), S. aureus, (24/67), followed by E. coli, 35.8% (24/67), Staphylococcus aureus resistant to Ampicillin and Gentamicin, respectively. More than half of Gram-positive isolates were resistance to Ampicillin, 29 (82.9%); Amoxicillin-Clavulanate, 27 (77%); Trimethoprim-Sulfamethoxazole, 26 (72.2%); Piperacillin-Tazobactam, 23 (63.8%); third-generation Cephalosporins, 21 (58.3%) and Gentamicin, 16 (44.4%). The majority (86%) of Gram-negative isolates were susceptible to Meropenem (Table 5).

Overall 55 (82%) and 24 (35.8%) isolates were resistance to Ampicillin and Gentamicin, respectively. More than half S. aureus isolates, 12 (66.7%) were found to be Methicillin resistant Staphylococcus aureus (MRSA). In addition, 52.4% E. coli isolates and 28.6% Klebsiella species were found to develop resistance to third-generation Cephalosporins.

3.6. Antimicrobial Susceptibility Pattern of Isolated Bacteria. From the total bacterial isolates, 56 (83.5%) were resistance to one or more antibiotics. Out of these resistant isolates, 26 (46.4%) were observed among Gram-positive bacteria while 30 (53.5%) were among Gram-negative bacteria. Higher levels of resistance to Penicillin/Ampicillin, 26/31 (83.87%); Cefoxitin, 22/31(71%) and Trimethoprim-Sulfamethoxazole, 21/31 (67.7%) while lower level of resistance to Clindamycin, 2 (6.45%) and Gentamicin, 8 (25.8%) was observed among Gram-positive isolates. Moreover, most of the Gram-negative bacteria were resistance to Ampicillin, 29 (82.9%); Amoxicillin-Clavulanate, 27 (77%); Trimethoprim-Sulfamethoxazole, 26 (72.2%); Piperacillin-Tazobactam, 23 (63.8%); third-generation Cephalosporins, 21 (58.3%) and Gentamicin, 16 (44.4%). The majority (86%) of Gram-negative isolates were susceptible to Meropenem (Table 5).

Overall 55 (82%) and 24 (35.8%) isolates were resistance to Ampicillin and Gentamicin, respectively. More than half S. aureus isolates, 12 (66.7%) were found to be Methicillin resistant Staphylococcus aureus (MRSA). In addition, 52.4% E. coli isolates and 28.6% Klebsiella species were found to develop resistance to third-generation Cephalosporins.

Gram-negative isolates demonstrated antibiotic resistances ranging from 13.9% to 82.8% for certain drugs like Carbapenems, Aminoglycosides, Cephalosporins, Trimethoprim-Sulfamethoxazole, Piperacillin-Tazobactam, Amoxicillin-Clavulanate and Ampicillin. Gram-positive isolates

| Table 2: Maternal data in relation to neonates with suspected sepsis admitted in NICU at Dessie Comprehensive Specialized Hospital, Dessie, Northeastern Ethiopia, August 2017 to March 2018. |
|-----------------|-----------------|-----------------|
| Characteristics | Number (%) | NG | BG |
|-----------------|-------------|----|----|
| Age in years    |             |    |    |
| <35             | 147 (59.8)  | 50 (20.3) |  |
| ≥35             | 32 (13)    | 17 (6.9)  |  |
| Marital status  |             |    |    |
| Single          | 18 (7.3)   | 7 (2.8)   |  |
| Separated       | 2 (0.8)    | 0 (0)     |  |
| Married         | 159 (64.6) | 60 (24.4) |  |
| Residence       |             |    |    |
| Rural           | 80 (32.5)  | 32 (13)   |  |
| Urban           | 99 (40.2)  | 35 (14.2) |  |
| Occupation status of mothers |     |    |    |
| Unemployed      | 88 (35.8)  | 29 (11.8) |  |
| Employed        | 91 (37)    | 38 (15.4) |  |
| Educational status |            |    |    |
| Illiterate      | 21 (8.5)   | 11 (4.5)  |  |
| Primary school level | 80 (32.5) | 27 (11)  |  |
| Secondary and above | 78 (31.7) | 29 (11.8) |  |
| No. of parity   |             |    |    |
| 2–4             | 72 (29.3)  | 26 (10.6) |  |
| ≥5              | 14 (5.7)   | 5 (2)     |  |
| Number of ANC visit |         |    |    |
| No              | 1 (0.4)    | 0 (0)     |  |
| <4              | 87 (35.4)  | 25 (10.2) |  |
| ≥4              | 91 (37)    | 42 (17.1) |  |
| Twin pregnancy  |             |    |    |
| No              | 166 (67.5) | 63 (25.6) |  |
| Yes             | 13 (5.3)   | 4 (1.6)   |  |
| Urinary tract infection |   |    |    |
| No              | 178 (72.4) | 60 (24.4) |  |
| Yes             | 1 (0.4)    | 7 (2.8)   |  |
| Vaginal discharge foul smelling |       |    |    |
| No              | 174 (70.7) | 64 (26)   |  |
| Yes             | 5 (2)      | 3 (1.2)   |  |
| Place of delivery |            |    |    |
| Hospital        | 126 (51.2) | 43 (17.5) |  |
| Health center   | 51 (20.7)  | 24 (9.8)  |  |
| Home            | 2 (0.8)    | 0 (0)     |  |
| Mode of delivery |            |    |    |
| Spontaneous vortex delivery | 142 (57.7) | 47 (19.1) |  |
| Assisted vaginal delivery | 7 (2.8) | 9 (3.7) |  |
| Caesarian section | 30 (12.2) | 11 (4.5) |  |
| Duration of labor |         |    |    |
| <18 hrs.        | 170 (69.1) | 62 (25.2) |  |
| ≥18 hrs.        | 9 (3.7)    | 5 (2)     |  |
| Prolonged rupture of membrane |       |    |    |
| <18 hrs.        | 160 (65)   | 39 (15.9) |  |
| ≥18 hrs.        | 19 (7.7)   | 28 (11.4) |  |

(%) *: the percentage in each cell is computed by dividing the cell's value (numerator) with the total study subjects (246) (denominator); NG: No growth; BG: Bacterial growth.
| S.no. | Characteristics | Bi-variable analysis | Multivariable analysis |
|-------|----------------|----------------------|-----------------------|
|       |                | Corollary (95% CI)   | P-value               | AOR (95% CI)   | P-value |
| 1     | Age in days    | 2.56 (1.29–5.06)    | 0.007                 | 2.15 (0.96–4.8) | 0.062 |
|       | Gender         |                      |                       |                       |         |
| 2     |                | 1.21 (0.67–2.17)    | 0.522                 |                       |         |
| 3     | Birth weight in Gram | 1.05 (0.6–1.84) | 0.866 |                       |         |
|       | Neonate gestational age (week) | 1.03 (0.59–1.8) | 0.928 |                       |         |
| 5     | Neonatal temperature, °C | 0.36 (0.07–1.85) | 0.223 | 0.28 (0.04–2.05) | 0.211 |
|       | Respiratory rate | 0.59 (0.34–1.05) | 0.073 | 0.58 (0.29–1.16) | 0.123 |
|       | Pulse rate     | 0.81 (0.41–1.6)    | 0.545                 |                       |         |
|       | Lethargy       | 0.78 (0.43–1.42)   | 0.424                 |                       |         |
|       | Cyanosis       | 0.49 (0.11–2.24)   | 0.356                 |                       |         |
|       | Grunting       | 2.88 (1.23–6.75)   | 0.015                 | 2.14 (0.82–5.56) | 0.119 |
|       | Chest in drawing | 0.998 (0.26–3.88) | 0.998 |                       |         |
|       | Respiratory distress | 0.87 (0.22–3.46) | 0.841 |                       |         |
|       | Feeding        | 0.62 (0.31–1.23)   | 0.168                 | 0.9 (0.39–2.04) | 0.794 |
|       | Umbilicus      | 12.0 (2.48–58.1)   | 0.992                 | 10.06 (1.75–57.8) |       |
|       | Clinical jaundice | 1.66 (0.58–4.77) | 0.344 |                       |         |
| 14    | Indwelling medical devices | 1.83 (1.04–3.24) | 0.037 | 2.2 (1.12–4.32) | 0.022 |
| 15    | Vomiting       | 1.79 (0.86–3.73)   | 0.191                 | 1.51 (0.64–3.59) | 0.350 |
| 16    | Diarrhea       | 3.72 (0.81–17.11)  | 0.091                 | 1.66 (0.29–9.58) | 0.574 |
### Table 3: Continued.

| S.no. | Characteristics | Bi-variable analysis | Multivariable analysis |
|-------|----------------|----------------------|------------------------|
|       |                | Corollary (95% CI)   | P-value                | Corollary (95% CI) | AOR (95% CI) | P-value |
| 20    | APGAR score fifth | ≥7 Ref 2.22 (0.99–4.99) | 0.053                  | 1.99 (0.56–6.8) |
|       |                | <7 2.22 (0.99–4.99)   | 1.99 (0.56–6.8)       | 0.053            |            |
| 21    | APGAR score first | ≥7 Ref 2.15 (0.93–4.95) | 0.073                  | 2.04 (0.06–64.01) |
|       |                | <7 2.15 (0.93–4.95)   | 2.04 (0.06–64.01)     | 0.073            |            |

Ref: reference category, * indicates statistically significantly associated factors; °c: Degree Celsius.

### Table 4: Logistic regression analysis of maternal data in relation to neonates with suspected sepsis admitted in NICU at Dessie Comprehensive Specialized Hospital, Dessie, Northeastern Ethiopia, August 2017 to March 2018.

| S.no. | Characteristics | Bi-variable analysis | Multivariable analysis |
|-------|----------------|----------------------|------------------------|
|       |                | Corollary (95% CI)   | P-value                | Corollary (95% CI) | AOR (95% CI) | P-value |
| 1     | Age in years   |                      |                        |                      |              |
|       | 18–34          | 0.64 (0.33–1.25)     | 0.192                  | 0.43 (0.20–0.92)    | 0.029*       |
|       | ≥35            | Ref                  |                        | Ref                 |
| 2     | Marital status |                      |                        |                      |              |
|       | Currently unmarried | Ref                  | 0.871                  |                      |              |
|       | Currently married | 1.08 (0.43–2.68)   | 0.871                  |                      |              |
| 3     | Residence      |                      |                        |                      |              |
|       | Rural          | 1.13 (0.64–1.99)     | 0.667                  |                      |              |
|       | Urban          | Ref                  |                        |                      |              |
| 4     | Occupation status of mothers |            |                        |                      |              |
|       | Unemployed     | Ref                  |                        |                      |              |
|       | Employed       | 1.27 (0.72–2.23)     | 1.27 (0.72–2.23)       |                      |              |
| 5     | Educational status |                      |                        |                      |              |
|       | Illiterate     | 1.41 (0.61–3.28)     | 0.597                  |                      |              |
|       | Primary school level | 0.91 (0.49–1.67) | 0.427                  | 0.427               |              |
|       | Secondary and above | Ref                  | 0.756                  |                      |              |
| 6     | No. Of parity  |                      |                        |                      |              |
|       | Primparity     | 1.08 (0.36–3.23)     | 0.969                  |                      |              |
|       | 2–4            | 1.01 (0.33–3.08)     | 0.885                  |                      |              |
|       | ≥5             | Ref                  | 0.985                  |                      |              |
| 7     | Number of ANC visit |                  |                        |                      |              |
|       | <4             | Ref                  | 0.098                  | 0.005               | 19 (2.02–178.7) | 0.01*   |
|       | ≥4             | 1.62 (0.91–2.89)     | 1.79 (0.92–3.5)        | 0.005               | 19 (2.02–178.7) | 0.01*   |
| 8     | Twin pregnancy |                      |                        |                      |              |
|       | No             | Ref                  | 0.722                  |                      |              |
|       | Yes            | 0.81 (0.26–2.58)     | 0.81 (0.26–2.58)       |                      |              |
| 9     | Urinary tract infection |              |                        |                      |              |
|       | No             | Ref                  | 0.005                  | 19 (2.02–178.7)     | 0.01*       |
|       | Yes            | 20.77 (2.5–172)      | 20.77 (2.5–172)        | 0.005               | 19 (2.02–178.7) | 0.01*   |
| 10    | Vaginal discharge foul smelling |            |                        |                      |              |
|       | No             | Ref                  | 0.511                  |                      |              |
|       | Yes            | 1.63 (0.38–7.02)     | 1.63 (0.38–7.02)       |                      |              |
| 11    | Place of delivery |                    |                        |                      |              |
|       | Hospital       | 0.75 (0.42–1.36)     | 0.350                  |                      |              |
|       | Non-hospital   | Ref                  |                        |                      |              |
| 12    | Mode of delivery |                    |                        |                      |              |
|       | Spontaneous vortex | Ref                  | 0.038                  | 0.038               |
|       | Assisted vaginal delivery | 3.88 (1.37–11) | 0.011                  | 3.61 (1.05–12.41)   | 0.042*      |
|       | Caesarian section | 1.11 (0.52–2.38)    | 0.793                  | 1.45 (0.61–3.42)    | 0.402       |
| 13    | Duration of labour |                  |                        |                      |              |
|       | <18 hrs        | Ref                  | 0.466                  |                      |              |
|       | ≥18 hrs        | 1.52 (0.49–4.72)     | 1.52 (0.49–4.72)       |                      |              |
| 14    | Prolonged rupture of membrane |        |                        |                      |              |
|       | <18 hrs        | Ref                  | 0.000                  | 0.000               |
|       | ≥18 hrs        | 6.05 (3.06–11.93)    | 7.34 (3.44–15.63)      | 0.000               |

Ref: reference category, * indicates statistically significantly associated factors.
had exhibited antibiotic resistance rate between 6% and 83.8% against Lincosamides, Aminoglycosides, Macrolides, Trimethoprim-Sulfamethoxazole, Cefoxitin and Penicillins (Table 5).

3.7. Multidrug Resistant Bacterial Isolates. In the current study, 68.6% (46/67) of bacterial isolates exhibited MDR and out of the total MDR isolates Gram-negative bacteria accounted for 52.2% (24/46) while 47.8% (22/46) were Gram-positive bacteria. Moreover, 85.7% (6/7) of K. pneumoniae, 62.5% (15/24) of E. coli and 66.7% (12/18) of S. aureus were found to be MDR (Table 6).

3.8. Admission Outcome in Neonates with Suspected Sepsis. From the total number of participating neonates, 234 (95.2%) were improved to discharge, whereas 12 (4.8%) neonates were died before receiving their complete dosage of antibacterial therapy. Among the total neonates with death outcome 7 were developing EOS and the rest 5 were having LOS. Out of died neonates with EOS condition, 4 were having negative blood culture result and from neonates having death outcome with LOS, 3 were found to be infected by bacterial pathogen. Six (50%) died neonates were having positive blood culture; the bacterial isolated from these study participants were E. coli [3], K. pneumoniae [2] and S. aureus [1]. Most bacteria that were isolated from neonates with death outcome showed higher resistance pattern to virtually all tested antibiotics; only 2 isolates were susceptible to Gentamicin, Meropenem and Piperacillin-Tazobactam (Table 7).

The majority of neonates (231) received Ampicillin plus Gentamicin, thirteen neonates received Ampicillin plus Cefotaxime and the rest 2 received Ceftazidime plus Vancomycin. Among six neonates who had death outcome and had negative blood culture result, four were receiving Ampicillin plus Gentamicin and the remaining two were receiving Ampicillin plus Cefotaxime. Among 6 neonates who had positive blood culture result with death outcome, two had received Ampicillin plus Gentamicin; one had received Ceftazidime plus Vancomycin and three had received Ampicillin plus Cefotaxime.

4. Discussion

In the present study, the overall blood culture positive rate (27.2%) was in agreement with similar studies conducted in Bangladesh (28.4%) [25], Indonesia (24.6%) [26] and Assela, Ethiopia (29.4%) [20]. In contrast, it was lower than studies done in Gondar, Ethiopia (46.6%) [8], Egypt (40.7%) [27] and India (41.7%) [28]. It was also higher than studies done in Botswana (9.8%) [29] and Ghana (17.3%) [30]. Furthermore, a higher proportion of bacterial isolates among EOS were observed in the present study, which was in agreement with studies conducted in Ghana [30] and Gondar, Ethiopia [8]. But a paradoxical result was reported from Tanzania [9]. The difference in proportion of isolated bacterial pathogen across studies might be due to methodological variation and variation in study settings.

According to the results of the present study the proportions of bacterial isolates were higher among low birth weight and preterm neonates; which was similar to other previously conducted studies [8, 19, 27]. Preterm and low birth weight is well-known associated risk factors in the occurrence of bacterial sepsis in the newborn. This is due to limited capacity in cellular innate immune system with inflammatory response factors following infections [5, 7]. However, in the current study there was no statistical significant association between blood culture positive results with the birth weight and gestational age.

In this research work, the proportion of Gram-positive and Gram-negative bacterial isolates were comparable with other findings reported from African and Asian countries [18, 20, 25–27, 31–34]. The current study revealed that E. coli and S. aureus were the predominant isolates; this was in line with studies done in different parts of Ethiopia like Gondar, [8], Addis Ababa [19], Assella [20] and other developing countries [14, 25, 31]. E. coli is a member of normal microbiota found in the gastrointestinal tract, and associated with severe infections and meningitis in neonates. Following a normal vaginal birth, newborns can be frequently colonized with maternal vaginal and fecal flora, hence, newborns can acquire during or before delivery [5, 35]. Moreover, S. aureus is found as communal bacterium (skin and nose); newborns can easily be contaminated from their mothers during or after delivery and acquire staphylococcal infections [5, 35].

A lower proportion of K. pneumoniae (10.4%) was observed in this study, which was comparable with studies done in different localities of Ethiopia [8, 19, 20] and in some developing countries [26, 28, 30, 31, 36, 37]. This bacterium is an important pathogen causing hospital-acquired bloodstream infections, particularly the ESBL-producing K. pneumoniae species was found to be the most important contributor for the emergency of MDR threat [10, 38]. On the contrary to the present study, Kabwe et al. reported Klebsiella species as the predominant isolates identified among neonatal sepsis suspected populations in Zambia.

![Figure 2: Frequency and types of organisms from neonates admitted in NICU at Dessie comprehensive specialized hospital during the study period.](image-url)
In the present study, most of the isolated bacteria showed resistance to commonly used antibiotics; which was in agreement with studies reported from other developing countries [8, 9, 18–20, 26, 27, 37, 39]. Low level resistance to Meropenem and Clindamyacin were observed among Gram-negative and Gram-positive isolates, respectively. This result was found to be consistent with studies conducted in Gondar, Ethiopia [8], Assella, Ethiopia [20], Asian countries [25, 26, 28] and elsewhere [9, 30, 31, 37]. Meropenem and Clindamyacin are mostly prescribed for culture proven ESBL-Gram-negative bacteria and necrotizing enterocolitis with possible perforation, deep tissue infection caused by anaerobic bacteria, respectively. This low rate of resistance might be due to these antibiotics are not routinely prescribed at the study site and/or are currently used as WHO-recommended empirical therapy in the neonatal age group [40].

Ampicillin and Gentamicin are currently used as WHO-recommended first-line empiric therapy [40]. The present study showed there was a higher level of Ampicillin (82%) and moderate level of Gentamicin (35.8%) resistant isolates. It was in accordance with previous findings reported from Gondar, Ethiopia [8, 18], Addis Ababa, Ethiopia [19], Assella, Ethiopia [20] and elsewhere [26, 28, 30, 36, 37, 39].

Ampicillin has broad-spectrum activity and widely used antibiotic and most bacteria developed resistance to this agent. Mechanisms of resistance could be due to overuse of Ampicillin exerted strong selective pressure on bacterial pathogens by increasing the evolution and transfer of genes; favoring the emergence of resistant strains. Moreover, alteration of Penicillin binding proteins and production of beta-lactamases is a mechanism of development of resistance to Gram-positive and Gram-negative bacteria, respectively [38].

This finding indicated the overall MDR level was 68.6%, which was comparable with studies done in Gondar, Ethiopia [8] and Assella, Ethiopia [20]. However, it was lower than other studies reported from Egypt [14] and Equatorial Guinea [36]. Likewise, this research work showed that MDR level in K. pneumoniae, 6 (85.7%), and E. coli, 15 (62.5%), was comparable with studies done in Gondar, Ethiopia (K. pneumoniae, 74%) [8], and Nigeria (62.5% of K. pneumoniae and E. coli) [39]. However, which was lower than studies conducted in Assella, Ethiopia (E. coli, 91%) [20], Equatorial Guinea (K. pneumoniae, 100%) [36] and Egypt (E. coli, 90%) [14]. Furthermore, 66.7% of S. aureus isolates were found to be MRSA, which was correlated with
other studies reported from Ethiopia and abroad [8, 14, 18, 20, 39]. In the current finding, we observed a significant number of MDR and MRSA bacterial isolates. Bacteria can develop resistance due to the acquisition of plasmids and due to an innate mechanism of bacterial agents to inactivate antibiotics. Globally, the emergence of strains resistant to the common use of antibiotics increased due to several reasons, such as self-prescription and the overuse of broad-spectrum antibiotic agents. Resistance in *K. pneumoniae* and *E. coli* is usually acquired through plasmid mediated ESBL; the enzymes can destroy beta-lactam antibiotics. These ESBL-associated plasmids can carry genes encoding co-resistance to other antibiotics, resulting MDR phenotype [38]. Methicillin resistant *S. aureus* also carries mecA gene that encode a beta-lactam insensitive protein. Thus, the resistance phenotypes can be disseminated between different bacteria within the same host or another host [38, 41]. Therefore, variation of findings in MDR level might be due to difference in patient population, exposure of invasive procedures; selection of antibiotics from different classes/generations, study setting and studying period.

The current study indicated that the overall proportion of neonatal death was similar with study done in Bahir Dar, Ethiopia (4%) [42], and comparably another higher death outcome was reported by Gebrehiwot et al. (8%) [43]. On the contrary to the present study, a much higher mortality rate was reported from Asian and African countries which ranges from 14% to 51% [9, 27, 44, 45]. In the present study, there was no statistical significant difference between death outcome and blood culture result. However, a given study in Ethiopia indicated an association between death outcome and significant bacterial growth [43]. In other way, Gram-negative MDR isolates were found to be higher among neonate with death outcome, which was similar with studies reported from other countries [9, 14, 42–45]. Various studies also indicated that the fatality rate is higher in neonates exposed to bloodstream infections with MDR pathogens compared to non-MDR pathogens [1, 2, 9, 11].

Similar to published article in Ghana [46], the result in the current study had shown both maternal and neonatal factors are responsible for the development of neonatal sepsis. In the present study neonatal data such as presence of septic umbilicus and utilization of indwelling medical devices during delivery had strong statistical association with blood culture positive results. Similar to the current study neonatal sepsis had shown strong association with umbilical pus discharge in a study conducted in Tanzania [47].

In addition to the above-mentioned variables, maternal age below 35 years old, having history of UTI, assisted vaginal delivery and prolonged rupture of membrane greater than or equals to 18 hours are determinants for the bacterial infection among the neonates. Comparably, another study which was conducted in public hospitals in central Ethiopia showed younger maternal age had reduced likelihood of neonatal sepsis [48]. In the current study neonates born to mothers who had antenatal UTI showed 19 times higher odds of acquiring bacterial sepsis in comparison with their counterparts. In agreement with this result, systematic review and meta-analysis in Ethiopia reported that maternal UTI during antenatal care demonstrated remarkable association with the development of neonatal sepsis [49]. Other similar studies in Ethiopia and Bangladesh also exhibited the UTI during pregnancy, prolonged rupture of membrane, place where delivery has done as potential predictor for the occurrence of neonatal sepsicaemia [48, 50, 51].

Similar studies in Ethiopia and Bangladesh indicated that 5th minute APGAR score had shown association with culture confirmed bacteria [20, 50], whereas in the present study both 1st and 5th minute APGAR score did not indicate significant association with bacterial infection.

### 4.1. Limitation of Study

This study was done on hospitalized neonates (NICU) from a single institution, but the results may not be applied to the catchment area or the entire country. Due to unavailability of facilities, Genotypic and specific phenotypic characterization of MDR (ESBL and MRSA) for the isolated bacteria were not performed.

### 5. Conclusion

The prevalence of bacterial growth among neonatal sepsis was found to be high; almost two-third of bacterial growth...
was detected from neonates with EOS. *E. coli* and *S. aureus* were the predominant organisms. Moreover, almost half of the bacterial isolates showed resistance to multiple antibiotics. Both maternal and neonatal variables were showing statistically significant association with bacterial culture positive result. Therefore, it might be necessary to improve the infrastructures for screening of bacteremia, as well as active surveillance during a clinical setting, to ensure adequate empirical therapy. Further studies should be conducted by using highly sensitive and specific techniques like PCR; phenotypic and genotypic characterization of ESBL, MRSA; active surveillance with large cohort study on neonatal sepsis should be addressed.

**Abbreviations**

AMR: Anti-microbial resistant  
ATCC: American type culture collection  
CoNS: Coagulase negative *Staphylococcus*  
DCSH: Dessie comprehensive specialized hospital  
EOS: Early onset neonatal sepsis  
ESBL: Extended spectrum beta lactamase  
LOS: Late onset neonatal sepsis  
MDR: Multidrug Resistant  
MRSA: Methicillin resistant *Staphylococcus aureus*  
NICU: Neonatal intensive care unit  
SPSS: Statistical package for social science  
WHO: World health organization  
PROM: Prolonged rupture of membrane  
MHA: Mueller hinton agar.

**Data Availability**

The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the manuscript.

**Ethical Approval**

This research work had reviewed ethically and approval was obtained from Wollo University ethical review committee. Permission was obtained and communicating with the stakeholders of DCSH official. Written consent was obtained from the parents/guardians of the neonate. Those neonates who were positive for blood culture were linked to the hospital to be treated. Data were maintained confidentially and used just for the aim of this study.

**Conflicts of Interest**

The authors declare there are no any conflicts of interest.

**Authors’ Contributions**

GM*, DG, YM, AS, HK were involved in proposal writing, designed the study and participated in all implementation stages of the project. GM and DG were involved in laboratory; GM*, DG, YM, and AS participated in analyzing the data and finalizing the write up of the manuscript. AS, YM, HK and DG were responsible for critical revision of the manuscript. All authors reviewed and approved the final manuscript.

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