Bacterial profile and their antibiotic resistance patterns from blood culture in Intensive Care Unit patients at the University Of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia.

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Abstract

Abstract Background: The burden of bloodstream infection and antibiotic resistance in intensive care unit (ICU) is high when compared with other settings. The data on the changing antibiotic resistance trends are important for infection control activities. There is no sufficient data in the intensive care units of this hospital. **Objective:** The aims of this study were to assess the magnitude and risk factors of bacterial pathogens and their antibiotic resistance patterns of blood culture isolates from ICU patients at the University of Gondar Comprehensive Specialized Hospital, Gondar, Ethiopia. **Materials and Methods:** A cross-sectional study was conducted from February to May 2018. Blood specimen were collected from 384 patients and inoculated on appropriate culture media. Identification of bacterial pathogens and antibiotic susceptibility tests were performed using bacteriological standard methods. Presence of Extended Spectrum Beta Lactamase (ESBL) enzymes was confirmed by combined disk diffusion method. Data were analyzed using SPSS version 20. **Result:** Of the total 384 study participants, 96(25%) were culture positive. Majority of bacteria isolates 67(69.8%) were Gram negative. The commonly isolated bacterial species were *K.pneumoniae* 18(18.8%), Coagulase negative *Staphylococcus* 13(13.5%), *K.ozanae* 10(10.4%), *K.rhino*se 8(8.3%) and *E.coli*, *E.cloacae*, *Citrobacter* species, *S.aureus* each accounts 7(7.3%). Gram negative isolates were found to be resistant to ampicillin 66(98%), amoxicillin/clavulanate 64(95%) and ceftriaxone 52(77.6%). However, amikacin 64(95.5%), meropenem 58(87%) and Ciprofloxacin 56(83.6%) were relatively effective drugs. Gram positive isolates were found to be resistant to Penicillin 28(96.5%), amoxicillin/clavulanate 27 (93.1%) and erythromycin 26(90%). They were sensitive to ciprofloxacin 22(79%) and clindamycin 24(83%). Methicillin resistant *S.aureus* accounted 4(57.1%) and ESBL enzyme producing Gram negative isolates accounted 41(78.8%). **Conclusion:** *Klebsiella* species were the predominant bacterial isolates in ICU settings. Antibiotic resistance due to ESBL enzyme production is alarmingly high. This result might be a reflection of inappropriate use of antibiotics and poor infection prevention control practice in these settings. **Key words:** Antibiotic resistance, ICU, ESBL, Gondar Ethiopia.

Introduction

Intensive care units (ICUs) are the most lifesaving units in a hospital in looking after critically ill patients by highly specialized clinicians and care giving nurses (1). Most condition which are treated at ICU are life threatening, severe injuries and illnesses, which require constant follow up and support from specialized equipment's and medications in order to ensure normal body functions (2).

The rate of infections in the ICUs is rising, mainly because of increasing use of invasive procedures and specialized devices used (3). Some contribute to the wide spread of drug resistance among the hospital acquired organisms includes; antibiotic overuse and misuse partly due to incorrect diagnosis, irrational antibiotic market combinations; and irregular consumption due to either wrong prescription or poor compliance are among the reasons (4, 5).

Other risk factors, such as prolonged length of hospital stay, also seem to predispose patients to infection with antibiotic-resistant bacteria (6). Occurrence of antibiotic-resistant bacterial infection due to inadequate infection control practices, failure to identify the presence of antibiotic resistance are also important factors promoting the spread of antibiotic resistance (7, 8).

Antibiotic resistance can be reduced by using antibiotics carefully based on guidelines of antimicrobial stewardship programs (9). The most frequently reported pathogens in ICU settings are *Staphylococcus aureus*, *enterobacteriaceae*, *Pseudomonas species*, *Enterococci species*, *Candida species*, *coagulase-negative staphylococci (CoNS)* and *Acinetobacter species* (10, 11).

ICU-acquired infections have been associated with significant morbidity, mortality and rising healthcare costs in developing countries with limited resources (12, 13). Globally, patients in the ICU have encountered an increasing emergence and spread of antibiotic-resistant pathogens. The overall incidence rate is 23.7 infections per 1000 ICU admission days. Nosocomial infections in ICU account for about 20% to 25% of all nosocomial infection (13-15).

Infection is a leading cause of death in the ICU as high as 60% and twice as much in those patients with a nosocomial infection (3). Intensive care units are one of the potential sources of nosocomial infections even in developed countries where extensive infection control measures are implemented (15). But the prevalence of ICU-acquired infections is significantly higher in developing countries than in industrialized countries and the pooled cumulative incidence density is 17.0 episodes per 1000 patient-days in adult high-risk patients in developed countries. On the other hand, the incidence of ICU-acquired infection among adult patients in developing countries ranged from 4.4% up to 88.9% and pooled cumulative incidence density was 42.7 episodes per 1000 ICU days. Patients in ICU are a significant subgroup of all hospitalized patients accounting for about 20-25 % of all hospital infections (16, 17).

The mortality and morbidity rates of bloodstream infections (BSIs) in ICU are higher due to limited resources available associated with the quality of health care system in ICU. However, available data are lacking in developing countries like Ethiopia. Therefore, the overall aim of this study was to assess the magnitude of bacterial isolates, predominant associated risk factors and their resistance patterns from blood specimens in the ICU at the University of Gondar Comprehensive Specialized Hospital.

Methods

Study design, area and period

An institution based cross-sectional study was conducted at the University of Gondar Comprehensive Specialized Hospital from February to May 2018. The hospital is a teaching hospital which is located in Gondar town, 750 km far from Addis Ababa in the Northwest Ethiopia. In this town there are 8 health centers, 21 private clinics and one hospital in the town. The hospital provides surgical, medical, pediatric, gynecologic, obstetric, oncologic and ophthalmologic services to the community for over 5 million inhabitants. The hospital has only 4 beds for adult ICU (AICU), 6 beds for pediatric ICU (PICU) and 36 beds for neonatal ICU (NICU) (18).

Sample size and sampling technique

A total of 384 septicemia suspected ICU patients were enrolled by using convenient sampling technique. All patients who were admitted to AICU, PICU and NICU due to BSIs during the study period were included in the study.

Socio demographic data and sample collection

Socio demographic data such as age, sex, educational background, occupation, residence, patient setting, reason for ICU admission, antibiotic taken, and devices used during admission were collected using structured questioner. Two bottles of blood samples were collected by trained nurse working in the ICU under the supervision of the investigator by taking all aseptic techniques. Ten ml, 5ml and 1ml of blood sample was collected from adults, pediatrics and neonates respectively which were then inoculated in to tryptic soya broth. Blood samples were collected twice from different sites (19).

Laboratory processing

After inoculation the blood samples were incubated immediately at 35-37⁰C aerobically. After 18 hour of incubation, Gram stain was done and subcultured on to 5% sheep blood agar, MacConkey agar and Chocolate agar. MacConkey agar was incubated at 35-37⁰C for 18 to 24 hours. Blood agar and Chocolate agar plates were incubated at 35-37⁰C in 5% CO₂ for 18 to 24 hours. If there is no growth on the Blood agar and chocolate agar, they were further incubated for 24 hours. Still if no growth Chocolate agar only was incubated for further 24 hours. The bottles were incubated for up to seven days under observation. If there is sign of growth sub cultured it: if not, sub cultured again at 3rd and 6th days of incubation.

Preliminary identification: Presumptive identification of bacteria was based on sign of growth on blood culture bottle, Gram reaction, and colony characteristics of the organisms like hemolysis on blood agar and changes in physical appearance in differential media..

Biochemical tests: were performed on isolated colonies for identification of bacterial pathogens based on their biochemical reactions. Catalase, coagulase, bacitracin and optochin tests were performed for Gram positive bacterial pathogens. For Gram negative bacteria isolates triple sugar iron agar, indole, citrate utilization, urease production, lysine decarboxylase and motility test were performed and interpreted.

Antibiotic susceptibility testing: Susceptibility testing was performed using the modified Kirby- Bauer disk diffusion method by using Muller Hinton Agar (Oxoid), chocolate agar (Oxoid), Muller Hinton agar with 5% sheep blood (Oxoid) agar based on the type of bacteria isolated. The suspension of the test organism was prepared by picking parts of similar test organisms with a sterile wire loop and suspend in test tube containing sterile physiological saline. The density of suspension was determined using 0.5 McFarland standards. Then they were inoculated to agar by using sterile swab. The inoculums were allowed to dry for 5–15 minutes. Antibacterial discs were distributed 15mm away from the edge and ≥ 24 mm apart from each other and incubated at 37⁰C for 24 hours. The results were expressed as susceptible, intermediate or resistant based on the 2017 CLSI guideline (20).

Antibiotic discs such as amoxycillin/ clavulanate(30 μ g), ciprofloxacin (5 μ g), gentamicin (10 μ g), trimethoprim/sulphamethaxazole(25 μ g), chloramphenicol (30 μ g) and ceftriaxone (30 μ g) were used for both Gram positive and Gram negative isolates. Penicillin (10 μ g), tetracycline (30 μ g), clindamycin(10 μ g) and erythromycin (15 μ g) were used only for Gram positive isolates. Cefoxitin (30 μ g) were tested as a surrogate marker for oxacillin (methicillin). Ampicillin (10 μ g), cefotaxime (30 μ g), ceftazidime(30 μ g), amikacin(30 μ g) and meropenem(10 μ g) were used only for Gram negative bacterial isolates.

Presence of ESBL for *Enterobacteriaceae* was suggested by screening resistance to a third generation cephalosporins such as cefotaxime (30 μ g), ceftriaxone (30 μ g) or ceftazidime (30 μ g) according to the CLSI screening criteria. The breakpoints indicative of suspicion for ESBL production was ≤ 22 mm for ceftazidime, ≤ 25 mm for ceftriaxone or ≤ 27 mm for cefotaxime. A combined disk method was used as a confirmatory phenotypic method for ESBL detection. ceftazidime (30 μ g) and cefotaxime (30 μ g) disks alone and their combinations with clavulanate (30 μ g/10 μ g) were used for phenotypic confirmations of ESBL presence. A ≥ 5 mm increase in zone diameters for either of the cephalosporin disks or their respective cephalosporin/clavulanate disks was interpreted as ESBL producer (20).

Data analysis and interpretation

Data were entered, coded and cleaned using Epi-info version 7.0 statistical software and then transferred to SPSS software version 20 for further data processing and analysis. Text descriptions, tables, and figures were used to describe the relevant findings of the study. The crude odds ratios with a 95% confidence interval were estimated in the binary logistic regression analysis to assess the association between each independent variable and the outcome variable, and to select candidate variables for the multivariate logistic regression analysis. Thus, only those independent variables with a p - values of 0.20 or less in the bivariate logistic regression were included in the multivariate logistic regression to get the adjusted effect of each covariate. Adjusted Odds Ratio with a 95% confidence interval was estimated to assess the strength of the association. P-value ≤ 0.05 were considered as statistically significant.

Results

Socio-demographic characteristics of study participants

From the total of 384 septicemia suspected ICU patients 205 (53.4%) of the study participants were males and 179 (46.6%) were females. The age of the study participants ranged from 1 day-80 years with a median age of 21 days. Majority of the study participants were Neonates 207(53.9%) and rural dwellers, 267(69.5) (Table 1).

Clinical information of study participants

Most common reasons for hospital admission included early onset neonatal sepsis 157 (40.9%) followed by pyogenic meningitis 55(14.3%) and late onset neonatal sepsis 38(9.9%). Of the total admitted patients, 210(54.7%) were admitted in NICU, 110(28.6%) admitted in PICU and the rest 64(16.7%) admitted in AICU. Of those patients 231(60.3%) were referred from other wards. In relation to antibiotic usage, 167(43.5%) had taken antibiotic before sample collection and 217(56.5%) didn't take any antibiotics. Most commonly prescribed drugs for those patients were ampicillin plus gentamicin 88(22.9%) and metronidazole plus ceftriaxone 27 (7%). Different mechanical devices were used for 172(44.8%) of the study participants (Table 2).

Etiologic Agents

Bacterial profile in ICU

Among 384 blood samples, 96 (25%) organisms were isolated. Majority of bacterial isolates were Gram-negative, 67 (69.8%) while the remaining 29(30.2%) were Gram positive. The predominant isolates were *K.pneumoniae* 18(18.8%) followed by *CoNS* 13 (13.5%), *K.ozanae* 10(10.4%), *K.rhinose* 8(8.3%), *E.coli* 7(7.3%), *E.cloacae* 7(7.3%), *Citrobacter species* 7(7.3) and *S.aureus* 7(7.3%) (Figure 1).

Figure 1: Percentage of bacterial isolates from blood culture of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Majority of the bacterial isolates were found from neonates 65(67.7%). The distribution bacterial isolates in NICU were *K.pneumoniae* 10(15.4%), *CoNS* 8(12.3%), *K.ozanae* 8(12.3%), *K.rhinose* 7(10.7%) and *Citrobacter species* 6(9.3%). The rest of bacterial isolates were summarized in table 3 (Table3).

Antibiotic susceptibility test for Gram positive isolates

Most of the Gram positive bacterial isolates were found to be resistant to penicillin 28 (96.5%) followed by amoxicillin/clavulanate 27(93%), tetracycline 27(93%), trimethoprim-sulfamethoxazole 26(90%), erythromycin 26(90%), chloramphenicol 21(72%), ceftriaxone 19(65%) and gentamicin 17(59%). On the other hand, majority of the isolates were sensitive to clindamycin 24(83%) and ciprofloxacin 22(76%). *CoNS* were 13 (100%) resistant to penicillin and amoxicillin/clavulanate followed by erythromycin 11(85%), trimethoprim-sulfamethoxazole 11(85%), tetracycline 11(85%), Cefoxitin (61.5%), chloramphenicol 8(61.5%) and ceftriaxone 7(54%). However 12(92.3%) and 8(61.5%) of these isolates were susceptible to clindamycin and ciprofloxacin respectively.

S. aureus, also demonstrated high level of resistance to penicillin 6(86%), erythromycin 6(86%), trimethoprim-sulfamethoxazole 6 (86%), tetracycline 6(86%), amoxicillin/clavulanate 5(71%), chloramphenicol 4(57%), and ceftriaxone 4(57%). Whereas, ciprofloxacin 6(86%), clindamycin 5(72%) were sensitive against this isolate. Among those *S. aureus* strains 4(57.1%) were MRSA. Other Gram positive isolates such as *S.viridans* and *S.pneumoniae* were 9(100%) resistant to penicillin, gentamicin, erythromycin, chloramphenicol, trimethoprim-sulfamethoxazole and ceftriaxone (Table 4).

Antibiotic susceptibility test of Gram negative isolates

Majority of Gram negative isolates were highly resistant to ampicillin 66(98%) followed by amoxicillin/clavulanate 64(95%), trimethoprim-sulfamethoxazole 60(89%), chloramphenicol 52(77.6%) and ceftriaxone 52(77.6%), ceftazidime 45(67%), cefuroxime, and gentamicin 44(66%). However, amikacin 64(95.5%), meropenem 58(87%) and ciprofloxacin 56(83.6%) were relatively effective against Gram-negative bacteria.

K. pneumoniae demonstrated high level of resistance to ampicillin 18(100%), amoxicillin/clavulanate 17(94%), ceftriaxone 17(94%), chloramphenicol (83%), trimethoprim-sulfamethoxazole 16(89%) and gentamicin 9(50%). On the other hand, amikacin 17(94%), meropenem 16 (89%) and ciprofloxacin 13(72%) were effective against this isolate.

E. coli was resistance to ampicillin 6(85.7%), amoxicillin/clavulanate 5(71%) and trimethoprim-sulfamethoxazole 4(57%) but susceptible for ciprofloxacin, amikacin and meropenem (Table 5).

Extended spectrum beta lactamase detection

Among the 67 Gram negative isolates of blood culture, 52 (77.6%) were resistant to third generation cephalosporins (ceftriaxone, ceftazidime and cefotaxime). Based on the CLSI guideline, 43 isolates were checked for the confirmation of ESBL production by combined disk diffusion method. *Providencia species*, *Serratia species*, *Citrobacter species* and *E.cloacae* were excluded from ESBL testing.

The overall prevalence of confirmed ESBL producing Gram negative isolates were 39(90.6%). Among these, *K.ozanae* and *K.rhinose* accounts 18 (100%) followed by *K.pneumoniae* 16(89%). Among the 7 *E. coli* isolate, ESBL was found in 5(71.4%) of the isolate. Among 39 ESBL producing isolates, 25(64%) were found from neonates, 7(18%) from pediatrics and 7(18%) from adults blood culture (Table 6).

Risk factors associated with bacterial bloodstream infections

The association between BSIs and suspected risk factors were assessed using logistic regression. The result of the logistic regression indicated that age (AOR=2.65, 95%CI;1.29-5.42, p=0.008) and Sex(AOR=2.0, 95%CI;1.23-3.27, p=0.005) were significantly associated with bacterial infection. Whereas

residence, place of admission, prior antibiotic therapy and device used were not significantly associated with bacterial infection in ICU settings. Those neonates were 2.65 times more likely to develop bacterial infection than adult age group. Patients who are male were 2 times more likely to develop bacterial infection than females (Table 7).

Discussion

In the current study, the overall prevalence of bacterial isolates was 25% which is similar with other studies conducted in India (23% and 24.7%)(21, 22). However it is higher than another study in India (11.8%), Pakistan (16%), Jimma (15.8%) and Gondar(18.2%)(23-26). This variation may be due to difference in target population, specimen's quality and bacteriological techniques.

Majority 67 (69.8%) of bacteria isolates were Gram-negative while the remaining 29(30.2%) were Gram positive isolates. The result is in line with a study done Kanpur, India reported that 60% Gram negative and 30%Gram positive organisms (21). However, our study is different from study reported from North India in which Gram negative to Gram positive rate was 39.3% and 53% respectively (22). This discrepancy may be due to the study participants were in the ICU admitted patients and quality of the specimen collection and processing methods.

According to the present study, the predominant and the commonest bacterial isolates was *K. pneumoniae* (18.8%). This finding is similar with those studies conducted in India(19.7% and 22%) (21, 22) and higher than reported in Jimma (6.7%) (26). This may be the study population in Jimma was adults but in the current study most participants were neonates. In this finding the percentage of *E.coli* was 7.3% which is similar with study done in Bangladesh (10.3%) and Gondar (7%) (23, 27). However, our result is lower than research conducted in India which is 22% (21).

The result of the present study showed that among Gram positives isolates, *CoNS* (13.5%) was the first in rank of isolation which is comparable with those reported in Kanpur, India (15%), Jimma (13.3%) and Indonesia (14.9%)(15, 21, 26). These similarities may be due to *CoNS* are common saprophyte which causes disease among immunocompromised patients. *S.aureus* was second isolate which accounts 7.3%. This result almost comparable with the study conducted in Bangladesh (5.3%)(27). However, it is lower than study conducted in Canada (21.1%), India (33.5%)(28, 29).

Majority (67.7%) of the bacterial isolates were identified from NICU which is in line with the finding in India (66.3%) but higher than the study conducted in Gondar(46.6%). The most prevalent isolate in this ICU was *K.pneumoniae* (15.4%) similar to a previous study conducted in Gondar (28, 30). This may be due to the same study area after five years.

Among common isolates of Gram positive bacteria, *S.aureus* was found to be 7.3%. Of these 57.1% was MRSA which was higher than other research conducted in Saudi Arabia(43%) (31). Cefoxitin resistance *CoNS* has become the predominant pathogen. Cefoxitin resistance *CoNS* was also isolated in our findings (61.5%).

In this investigation ciprofloxacin were relatively sensitive (78%) to both Gram positive and Gram negative bacteria. In the current finding amikacin (95.5%) was a drug of choice for gram negative bacteria similar to in North India(90.8%)(32).

In the current findings, the overall prevalence of confirmed ESBL producing bacteria was 39(90.6%). This result is higher than the finding in Mali (61.8%), Addis Ababa (78.57%) and Jimma (38.4%) (33-35). The prevalence of ESBL production in *E.coli* and *K.pneumonia* was 71.4% and 89% respectively. The prevalence of ESBL producing *K.pneumonia* was higher from a report in Mali (71.4%) and *E. coli* lower than a report in Ethiopia (100%). Our study also was inconsistent with a report in Dhaka which was 81.8% of *E.coli* and 11.7% of *Klebsiella* species had ESBL activity(32-34).

Furthermore, the logistic regression result indicated that independent risk factor for bacterial isolation in this finding was age (AOR=2.65, 95%CI; 1.29-5.42, p=0.008), which is consistent with result from United States and Sex (AOR=2.0, 95%CI; 1.23-3.27, p=0.005), similarly results shown in Italy (6.0% vs. 8.9%, P = 0.001). Sex is significantly associated with severe sepsis in men than women(36, 37). This may be due to a combination of differences in chronic disease burden, environmental and social factors, and genetic disposition causing differences in the host immune response to infection likely contribute to the observed differences(38).

Limitations of the study

This study did not include other important pathogens responsible for sepsis such as anaerobic bacteria, fungus and viruses due to lack of laboratory facility. The study was also limited to conduct carbapenemase production among Gram negative isolates due to shortage of materials.

Conclusion

Gram-negative pathogens were the predominate isolates in bloodstream infections. *Klebsiella* species were the predominant bacterial isolates followed by *CoNS* identified in this study. The distribution of bacterial isolates was high in NICU followed by PICU and AICU. Ciprofloxacin and clindamycin were effective for Gram positive isolates. For Gram negative isolates, ciprofloxacin, amikacin and meropenem were effective. Extended spectrum beta lactamase production in gram negative isolates as well as methicillin resistant *Staphylococcus* species is alarmingly high. This leads to an increased patient hospital stay, cost and mortality. The current finding may be useful to formulate treatment guideline to avoid unnecessary use of broad spectrum antibiotics for the ICU patients and to promote researchers to conduct advanced studies on current challenges of antibiotic resistance. The data on the changing antibiotic resistance trends is also important for disease control activities in ICU settings.

Abbreviations

AICU: Adult Intensive Care Unit; BSI: Blood Stream Infection; CLSI: Clinical Laboratory Standards Institute; CoNS: Coagulase negative *Staphylococcus*; EONS: Early Onset Neonatal Sepsis; ESBL: Extended Spectrum Beta Lactamase; HAS: Hospital Acquired Sepsis; ICU: Intensive Care Unit; LONS: Late Onset Neonatal Sepsis; MRSA: Methicillin-resistant *Staphylococcus aureus*; NICU: Neonatal Intensive Care Unit; PICU: Paediatric Intensive Care Unit.

Declarations

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Availability of data and materials

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

Authors' contributions

ST collected the data and wrote the manuscript. AG, FM and ZT gave valuable suggestions of the manuscript and revised the manuscript. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study protocol was approved by the ethical review committee of the School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. The consent forms were taken from all study participants after explaining the objective of the study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1: Socio-demographic characteristics of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Characteristics	Number (%)
Age	Neonate (0-28days)
	207(53.9)
	Pediatrics (29day-18 year)
Sex	Adult (>18 Years)
	64(16.7)
	Male
Residence	Female
	179(46.6)
	Rural
Occupation	Urban
	117(30.5)
	Farmer
Educational status	19(4.9)
	Civil servants
	6(1.6)
	Self-employee
	20(5.2)
	Daily laborer
	4(1)
	House wife
	17(4.4)
	Merchant
	2(0.5)
	Others**
	2(0.5)
	N/A
	314(81.8)
	Illiterate
	17(4.4)
	Primary
	58(15.1)
	Secondary
	28(7.3)
	College and above
	6(1.6)
	N/A*
	275(71.6)

N/A* = Patients who are <6-years-old, others** = Carpenter, Beiger.

Table 2: Clinical information of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Independent Variables		Number (%)
Clinical diagnosis	EONS	157(40.9)
	LONS	38(9.9)
	Pyogenic meningitis	55(14.3)
	HAS	29(7.6)
	Localized infection	26(6.8)
	Pneumonia	37(9.6)
	Complicated UTI	11(2.9)
	Infective endocarditis	21(5.5)
Place of admission	Others*	10(2.6)
	NICU	210(54.7)
	PICU	110(28.6)
	AICU	64(16.7)
Admitted from	Other wards	231(60.2)
	Health center	59(15.4)
	Other hospital	23(6))
	Home	71(18.5)
Prior antibiotic therapy	Yes	167(43.5)
	No	217(56.5)
Mechanical device used	Yes	172(44.8)
	No	212(55.2)

Keys: Others*- multiple trauma, hemorrhagic shock and acute kidney injury. EONS-Early Onset Neonatal Sepsis, LONS-Late Onset Neonatal Sepsis, HAS- Hospital Acquired Sepsis, UTI-Urinary Tract Infection, NICU-Neonatal Intensive Care Unit, PICU- Paediatric Intensive Care Unit, AICU-Adult Intensive Care Unit.

Table 3: Distribution of bacterial isolates of blood culture in different ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Type of organism isolated	NICU N (%)	PICU N (%)	AICU N (%)	Total N(%)
<i>K.pneumoniae</i>	10 (15.4)	6 (30)	2 (18.3)	18 (18.75)
<i>CoNS</i>	8 (12.3)	4 (20)	1 (9.0)	13 (13.54)
<i>K.ozenae</i>	8 (12.3)	0	2(18.3)	10 (10.41)
<i>K.rhinose</i>	7(10.7)	1 (5.0)	0	8 (8.33)
<i>E.coli</i>	3 (4.6)	1 (5.0)	3 (27.4)	7 (7.29)
<i>Citrobacter species</i>	6 (9.3)	0	1 (9.0)	7 (7.29)
<i>E.cloacae</i>	7 (10.7)	0	0	7 (7.29)
<i>S.aureus</i>	4 (6.2)	3 (15)	0	7 (7.29)
<i>S.viridans</i>	4 (6.2)	1 (5.0)	1 (9.0)	6 (6.25)
<i>Providencia species</i>	3 (4.6)	1 (5.0)	1 (9.0)	5 (5.2)
<i>Serratia species</i>	4 (6.2)	0	0	4 (4.17)
<i>S.pneumoniae</i>	1 (1.5)	2 (10)	0	3 (3.12)
<i>Neisseria species</i>	0	1 (5.0)	0	1 (1)
Total	65(67.7)	20(20.8)	11(11.5)	96

Keys: NICU-Neonatal Intensive Care Unit, PICU- Paediatric Intensive Care Unit, AICU-Adult Intensive Care Unit.

Table 4: Antibiotic susceptibility patterns of Gram positive bacterial isolates from blood culture of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Bacterial isolate	Patterns	PG N (%)	Amox/clav N (%)	CIP N (%)	FOX N (%)	GN N (%)	ERY N (%)	CAF N (%)	SXT N (%)	CRO N (%)	DA N (%)	TE N (%)
Gram positive												
<i>CoNS</i>	S	0 (0)	0 (0)	8 (61.5)	5 (38.5)	6 (46.2)	2(15.4)	5 (38.5)	2 (15.4)	5 (38.5)	12(92.3)	2(15.4)
	I	0 (0)	0 (0)	1 (7.7)	0 (0)	1 (7.7)	0 (0)	0 (0)	0 (0)	1 (7.7)	0 (0)	0 (0)
	R	13(100)	13(100)	4 (30.8)	8 (61.5)	6 (46.2)	11(84.6)	8 (61.5)	11(84.6)	7 (53.8)	1 (7.7)	11(84.6)
<i>S.aureus</i>	S	1(14.3)	2(28.6)	6 (85.7)	3(42.9)	4 (57.1)	1 (14.3)	3(42.9)	1 (14.3)	3 (42.9)	5(71.4)	0 (0)
	I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	R	6 (85.7)	5 (71.4)	1 (14.3)	4 (57.1)	3 (42.9)	6 (85.7)	4 (57.1)	6 (85.7)	4 (57.1)	2 (28.6)	7 (100)
<i>S.viridans</i>	S	0 (0)	0 (0)	6(100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (83.3)	0 (0)
	I	0(0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	R	6(100)	6 (100)	0 (0)	6 (100)	6 (100)	6 (100)	6 (100)	6 (100)	6 (100)	1 (16.7)	6(100)
<i>S.pneumoniae</i>	S	0(0)	0 (0)	2 (66.7)	1 (33.3)	1 (33.3)	0 (0)	0 (0)	0 (0)	1 (33.3)	2 (66.7)	0 (0)
	I	0(0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	R	3(100)	3 (100)	1 (33.3)	2 (66.7)	2 (66.7)	3 (100)	3 (0)	3 (100)	2 (66.7)	1(33.3)	3 (100)

Keys: S-Sensitive, I- Intermediate, R- Resistance. PG-Penicillin G, Amox/clav- Amoxicillin/clavulanate, CIP- Ciprofloxacin, FOX-Cefoxitin, GN-Gentamicin, ERY-Erythromycin, CAF-Chloramphenicol, SXT-Trimethoprim-sulfamethoxazole, CRO- Ceftriaxone, DA- Clindamycin, TE- Tetracycline.

Table 5: Antibiotic susceptibility patterns of Gram negative bacterial isolates from blood culture of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Bacterial isolate	Pattern	AMP N (%)	Amox/clav N (%)	CIP N(%)	GN N(%)	CAF N(%)	SXT N(%)	CRO N(%)	CAZ N(%)	CAX N(%)	AMK N(%)	MER N(%)
Gram Negative												
<i>K.pneumoniae</i>	S	0(0)	0(0)	13(72.2)	8(44.4)	3(16.7)	2(11)	1(5.5)	1(5.5)	6(33)	17(94)	16(88.9)
	I	0(0)	1(5.6)	2(11.1)	1(5.60)	0(0)	0(0)	0(0)	1(5.5)	0(0)	1(6)	0(0)
	R	18(100)	17(94.4)	3(16.7)	9(50)	15(83.3)	16(89)	17(94.5)	16(89)	12(67)	0(0)	2(11.1)
<i>K.ozanae</i>	S	0(0)	0(0)	10(100)	3(30)	2(20)	0(0)	2(20)	0(0)	3(30)	10(100)	8(80)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	1(10)
	R	10(100)	10(100)	0(0)	7(70)	8(80)	10(100)	8(80)	10(100)	7(70)	0(0)	1(10)
<i>K.rhinose</i>	S	0(0)	0(0)	8(100)	2(25)	1(12.5)	0(0)	0(0)	3(37.5)	2(25)	8(100)	6(75)
	I	0(0)	0(0)	0(0)	0(0)	2(25)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	8(100)	8(100)	0(0)	6(75)	5(62.5)	7(100)	8(100)	5(62.5)	6(75)	0(0)	2(25)
<i>E.coli</i>	S	0(0)	2(28.6)	7(100)	6(85.7)	1(14.3)	0(0)	1(14.3)	0(0)	0(0)	7(100)	7(100)
	I	1(14.3)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	6(85.7)	5(71.4)	0(0)	1(14.3)	6(85.7)	7(100)	6(85.7)	7(100)	7(100)	0(0)	0(0)
<i>E.cloacae</i>	S	0(0)	0(0)	7(100)	2(28.6)	1(14.3)	1(14)	7(00)	7(100)	7(100)	7(100)	7(100)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	7(100)	7(100)	0(0)	5(71.4)	6(85.6)	6(86)	0(0)	0(0)	0(0)	0(0)	0(0)
<i>Citrobacter species</i>	S	0(0)	0(0)	5(71.4)	0(0)	0(0)	0(0)	2(28.6)	2(28.6)	1(14.3)	6(85.7)	6(85.7)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	7(100)	7(100)	2(28.6)	7(100)	7(100)	7(100)	5(71.4)	5(71.4)	1(14.3)	1(14.3)	1(14.3)
<i>Providencia species</i>	S	0(0)	0(0)	3(60)	0(0)	0(0)	0(0)	2(40)	1(20)	1(20)	4(80)	3(60)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	5(100)	5(100)	2(40)	5(100)	5(100)	5(100)	3(60)	4(80)	4(80)	1(20)	2(40)
<i>Serratia</i>	S	0(0)	0(0)	2(50)	0(0)	0(0)	0(0)	1(25)	0(0)	0(0)	4(100)	3(75)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	4(100)	4(100)	2(50)	4(100)	4(100)	4(100)	3(75)	4(100)	4(100)	0(0)	1(25)
<i>Neisseria species</i>	S	0(0)	0(0)	1(100)	1(100)	0(0)	0(0)	0(0)	1(100)	0(0)	1(100)	1(100)
	I	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
	R	1(100)	1(100)	0(0)	0(0)	1(100)	1(100)	1(100)	0(0)	1(100)	0(0)	0(0)

Keys: S-Sensitive, I- Intermediate R- Resistance, AMP-Ampicillin, Amox/clav- Amoxicillin/clavulanate, CIP- Ciprofloxacin GN-Gentamicin CAF-Chloramphenicol, SXT- Trimethoprim-sulfamethoxazole, CRO- Ceftriaxone, CAZ-Ceftazidime, CAX- Cefuroxime, AMK-Amikacin, MER- Meropenem

Table 6: Extended spectrum beta lactamase production confirmed by combined disk diffusion method in Gram negative isolates from blood culture of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Organisms	ESBL* positive	ESBL* negative
<i>K.pneumoniae</i> (18)	16(89%)	2(11%)
<i>K.ozenae</i> (10)	10(100%)	0
<i>K.rhinose</i> (8)	8(100%)	0
<i>E.coli</i> (7)	5(71.4%)	2(28.6%)
Total(43)	39(90.6)	4(9.4)

ESBL*-Extended spectrum beta lactamase.

Table 7. Risk factors associated with bacterial infection from blood culture of ICU admitted patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.

Variables		Organisms isolated		Bivariate analysis		Multivariable analysis	
		Yes	No	COR (95% CI)	p-value	AOR (95% CI)	P-value
Age	Neonates	65	142	2.47(1.22-5.00)	0.012	2.65(1.29-5.42)	0.008
	pediatrics	20	93	1.13(0.5-2.54)	0.775	1.1(0.5-2.5)	0.75
	Adult	11	53	1		1	
Sex	Male	62	143	1.84(1.1-2.9)	0.012	2.0(1.23-3.27)	0.005
	Female	34	145	1		1	
Residence	Rural	73	194	1.54(0.9-2.6)	0.11		0.12
	Urban	23	94	1			
Place of admission	NICU	65	145	2.48(1.2-5.0)	0.011		0.2
	PICU	20	82	1.35(0.6-3.0)	0.46		0.1
	AICU	11	61	1			
Admitted to ICU from	Medical center	85	228	2.03(1.0-4.0)	0.04		0.1
	Home	11	60	1			0.29
Prior antibiotic therapy	Yes	48	119	1.42 (0.8-2.2)	0.13		0.19
	No	48	169	1			
Device used	Yes	46	126	1.18(0.7-1.8)	0.4		0.7
	No	50	162	1			

Keys: COR- Crude odds ratio, AOR-Adjusted odds ratio, NICU-neonatal intensive care unit, PICU- paediatric Intensive Care Unit, AICU- adult intensive care unit.

Figures

Figure 1

Percentage of bacterial isolates from blood culture of ICU patients at the University of Gondar Comprehensive Specialized Hospital from February to May 2018.