

Bacterial and Fungal Profile, Drug Resistance Pattern and Associated Factors of Isolates Recovered From Blood Samples of Patients Referred to Ethiopian Public Health Institute: Cross-Sectional Study

Etsehiwot Adamu Tsegaye (✉ etseadamu@gmail.com)

Ethiopian Public Health Institute

Dejenie Shiferaw Teklu

Ethiopian Public Health Institute

Zelalem Tazu Bongor

Ethiopian Public Health Institute

Abebe Assefa Negeri

Ethiopian Public Health Institute

Tesfaye Legesse Bedada

Ethiopian Public Health Institute

Adane Bitew

Addis Ababa University

Research Article

Keywords: Blood stream infections, Bacterial and fungal profile, Antimicrobial resistance pattern, Risk factor, Ethiopia.

Posted Date: July 19th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-628943/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published at BMC Infectious Diseases on November 29th, 2021. See the published version at <https://doi.org/10.1186/s12879-021-06896-w>.

Abstract

Background

Blood stream infections are serious infections that usually induce prolongation of hospital stay, morbidity and mortality in several countries including Ethiopia. The aim of this study was to determine bacterial and fungal profile, their drug resistance patterns, and risk factors associated with blood stream infections.

Methods

A cross sectional study design was conducted from February 23 to June 23, 2020 at Ethiopian public health. A structured questionnaire was used to collect data on socio-demographic factors and clinical conditions. Blood specimens were analyzed using standard microbiological techniques. Antimicrobial susceptibility tests were performed using Kirby-Bauer disc diffusion technique and Vitek compact 2. Simple and multiple logistic regressions were used to assess the potential risk factors.

Results

A total of 175 pathogens isolated from 346 blood specimens. Of these, 60% Gram-negative bacteria, 30.86% Gram-positive bacteria and 9.14% fungal isolates were identified. *Burkholderia cepacia* and *Coagulase negative staphylococcus* were the predominant pathogen among Gram-negative and Gram-positive bacteria respectively. Among fungus, *Candidia krusei* (56.25%) was the most predominant isolate. The highest proportions of antibacterial resistance were observed among 3rd generation cephalosporin and penicillin. Most fungal isolates expressed resistance to fluconazole. Sex ($p = 0.007$), age ($p < 0.001$) and use of invasive medical devices ($p = 0.003$) were identified as risk factors for bacterial blood stream infections.

Conclusion

The study showed high prevalence of blood stream infection was due to *Burkholderia cepacia* and non-*Candidia albicans* spp. This finding alarming ongoing investigation of blood stream infection is important for recognizing future potential preventive strategies including environmental hygiene and management of comorbid medical diseases to reduce the problem.

Background

Blood stream infections (BSIs) are the major public health problems that are responsible for the cause of self-limited infection to death worldwide (1). These infections can be intravascular or extravascular. Most bacterial species and many fungal species have been associated with extravascular bloodstream infections (2).

According to the global report of the World Health Organization, sepsis affected 49 million individuals and related to approximately 11 million potentially unavoidable deaths worldwide (3). In the United States, there are about 200,000 cases of bacteria and fungi occurred annually, with mortality rates ranging from 20–50% (4).

Several recent studies have shown that the conditions that predispose an individual to BSIs vary with age, gender, and underlying diseases. More than half of all cases of global sepsis occurred among adolescents and children (5). There is around 53% mortality rate among children in sub-Saharan Africa, including Ethiopia (6). The elderly population is exposed to BSIs associated with the use of a variety of medical procedures (7).

Diabetes mellitus, renal failure requiring dialysis, widespread use of broad-spectrum antibiotics, hepatic cirrhosis, gender, age, and malignancy are the main risk factors that lead to BSIs (1, 8). Other factors that enhance BSIs among hospitalized patients include decreased immunity, increased variety of medical procedures and the transmission of drug-resistant bacteria among crowded hospital populations (9).

As many studies highlighted, bacteria are the primary causative agents of BSIs (10–12). However, fungal pathogens began to be recognized as important causes of disease related to increasing numbers of immunocompromised patients and nosocomial infections. Among them, 65% of the BSI cases are induced by *Candida* which is responsible for raising the number of mortality rate by 38% and extending hospital stays of 30 days (13).

A large variety of organisms can cause bloodstream infections, which vary by institution and geographic distribution (14). Coagulase-negative staphylococcus, *Staphylococcus aureus* and *Enterococcus* spp are the most common BSIs causing Gram-positive bacterial pathogens. *Klebsiella pneumoniae*, *Escheria coli*, *Pseudomonas* spp and *Acinetobacter baumannii* are also the commonest among Gram-negative organisms. *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida krusei* also become frequent from fungal species (15).

In Ethiopia, systemic review done in bloodstream infections showed that the proportion of blood stream infections ranged from (12.84–18.15) %. The common pathogens isolated from bacterial infected patients were *Staphylococcus aureus* and *Escheria coli* (16). However, it is difficult to generalize these findings to all levels of health care facilities in Ethiopia.

Blood culture remains the gold standard for bacterial and fungal detection from BSIs. Irrational use of drugs has led to an increase of multidrug-resistant organisms and thus worsened the condition. Therefore, preliminary results of Gram staining, final identification and AST results are essential for providing safe, effective, and efficient care of patients (15, 17).

The burden of bloodstream infections due to antifungal resistance and associated risk factors in Ethiopia remains poorly reported. Although previous studies have been performed in the same laboratory, they have been limited to bacterial causative agents and showed the past trends of the pathogen (18). Therefore, this study was designed to determine the current status of organisms causing bloodstream infections, their antimicrobial-resistant patterns, and associated factors related to the infections among patients referred to Ethiopian Public Health, National clinical bacteriology, and mycology reference laboratory.

Methods

Study design, period and setting

An institutional based cross-sectional study was conducted on blood specimens from February 23 to June 23, 2020. The specimens were referred from all health care facilities in the chain of referral systems of the Department of Clinical Bacteriology and Mycology laboratory. The laboratory is the national referral laboratory in the country responsible for providing high-level diagnostic laboratory testing services for patients and specimens referred from all regional and federal health facilities. It was accredited by the Ethiopian National Accreditation office. In addition, the laboratory conducts research, capacity of a regional and federal laboratory and participates in AMR surveillance. The health care facilities involved during the study period were Ras Desta Hospital, Abet Hospital, St Peter Hospital, Federal Police Hospital, Yekatit Hospital, Minilik Hospital, Ring Road Hospital, Girum Hospital and Armed Force Hospital.

Sample collection and processing

Aseptic precautions were followed to collect a total of 346 blood samples from suspected patients. Blood obtained from each participant was transferred into two blood culture bottles containing tryptic soy broth, 50 ml for adults and 25 ml for children respectively. A blind subculture was done after overnight incubation to appropriate solid culture media. Bottles that showed turbidity were subjected to Gram staining followed by sub-cultured onto blood agar plates (Oxoid Ltd, UK), chocolate agar plates (Oxoid Ltd, UK) and MacConkey agar plates (Oxoid Ltd, UK). Blood agar and chocolate agar plates were incubated in 5% CO₂ for 24-72 hours. MacConkey agar plates were placed aerobically for 24 hours. Two plates of Sabouraud dextrose agar plates were inoculated and incubated at 37°C and 25°C. Identification of bacterial isolates was carried out according to the standard bacteriological technique. A terminal sub-culturing was done on chocolate agar for bottles that did not show visible growth within 7 days before being reported as negative. Species identification of some bacteria and yeasts were determined by the automated Vitek 2 compact machine (bioMérieux, France) using GN and YS 07 cards respectively.

Antibiotic Susceptibility Testing

Antibiotic susceptibility testing was conducted on Muller-Hinton agar by Kirby-Bauer Disk diffusion method according to Clinical Laboratory Standard Institute (CLSI) guidelines. Antimicrobial agents used for testing bacterial isolates were Penicillin (MIC), oxacillin (30µg), gentamycin (10µg), vancomycin (MIC), vancomycin (30µg), chloramphenicol (30µg), cefotaxime (30µg), cefazidime (30µg), meropenem (10µg), trimethoprim-Sulphamethoxazole (1.25/23.75µg), amoxicillin-clavulanic acid (20/10 µg), piperacillin-tazobactam (100/10µg), ceftriaxone (30µg), cefepime (30µg), amikacin (30µg) and ciprofloxacin (5µg). These antimicrobial agents were selected based on current availability and frequently prescribed for the management of bacterial infections in Ethiopia (19).

Antifungal susceptibility tests for Amphotericin B (10µg), caspofungin (5µg), flucytosine, fluconazole (25 µg), Micafungin and Voriconazole (1 µg) were done for all yeasts isolates by automated VITEK 2 compact system (bioMérieux, France) using AST-YS01 cards. The quality controls of the drugs were checked for its performance by using *E. coli* (ATCC-25922), *S. aureus* (ATCC-25923), *P. aeruginosa* (ATCC-27853) and *C. albicans* (ATCC-10231).

Data collection

Socio-demographic data and clinical status of patients were collected through a standard questionnaire.

Statistical analysis

Data were collected and analyzed using WHONET and R software programs. Simple and multiple logistic regression analyses were used to assess the possible risk factors of bloodstream infections. Multiple logistic regression models were done only for variables with p-value less than 0.25. P-value <0.05 was considered statistically significant for all cases.

Ethical issues

The study was conducted after obtaining ethical clearance and approval from the department of medical laboratory sciences, Addis Ababa University. An official permission letter was obtained from Addis Ababa Public Health Research and Emergency Directorate for all referral hospitals for sample collection. Data collection was started after written informed consent/assent was obtained from the study participants.

Results

Socio-demographic characteristics of patients

The study involved a total of 346 patients with suspected BSIs. Out of them, 126 (36.42%) were female. The majority of the study participants were infants 186 (53.76%) and few participants 16 (4.62%) were elderly age groups (Table 1). More than half participants in the study were from NICU (51.16%) (Figure 1).

Clinical condition of study participants

Invasive medical devices such as catheter usage were observed in 178 (54.60 %) study participants during their hospital stay. Patients' histories revealed that they had different underlying clinical conditions. Most study participants 169 (48.84 %) developed sepsis. One hundred twenty-five (36.13 %) of the patients had a previous history of hospital admission related to similar symptoms with the current infections or with other health problems. Other comorbidities were also observed in study participants. These included: history of surgery 70 (20.23 %), prolonged rupture of membrane 15 (4.34 %), malignancy 20 (5.78 %), diabetic mellitus 28 (8.09 %), hepatic problem 29 (8.38 %), hemodialysis 12 (3.47 %) and 32 (9.25 %) had other complications. One patient was with a history of bone marrow transplantation.

The majority of patients 286 (82.66 %) were treated with empiric antibiotics prior to blood culture results. Of these, most of the patients (67.84 %) were treated with a combination of aminoglycoside, Beta-lactam inhibitor and third generation cephalosporins. The rest of the participants (25.87 %) had taken a combination of carbapenem and glycopeptide. A few patients (6.29 %) were treated with metronidazole as well.

Fungal and bacterial isolates

Positive growth was observed in 175 (50.58%) isolates under aerobic cultural environments. All positive blood samples were detected for a single type of organism. From the recovered isolates 54 (30.86 %) were Gram-positive bacteria, 105 (60 %) were Gram-negative bacteria and 16 (9.14 %) were fungal isolates. Among Gram-positive isolates, Coagulase-negative staphylococcus (74.07 %) was the predominant bacteria followed by *Enterococcus* spp (14.81 %). On the other hand, *Burkholderia cepacia* was the predominant bacteria among Gram-negative bacterial isolates which accounted for (61.90 %). All fungal isolates identified were non-*Candida albicans* spp. The most frequently isolated fungi was *C. krusei* (56.25 %) (Figure 2).

Antimicrobial Resistance patterns

The microbial isolates showed varying degrees of resistance to different antibiotics tested. Overall, Gram-positive bacteria exhibited a high degree of resistance to Penicillin. Methicillin resistance was detected in 89.7% of Coagulase-negative staphylococcus (Table 2).

Antimicrobial resistance levels of Gram-negative organisms for the most commonly causing BSIs were relatively high. *Klebsiella pneumoniae* showed the highest resistance in folate pathway inhibitors (85.7%), fluoroquinolones (83.3%), aminoglycoside (84.2%) and third- generation cephalosporins (81%). From the member of non-enterobacteriaceae *Acinetobacter* Spp showed extreme resistance to ciprofloxacin (100%). On the contrary, *Pseudomonas* spp was susceptible to most of the antibiotics tested. Multidrug drug resistance was observed in 65% of Gram-negative bacterial isolates (Table 3).

The antimicrobial susceptibility patterns of *Candida* species were performed using Vitek compact2 machine according to the M44 guideline (20). *Candida rugosa* and *Candida dubliniensis* were resistance to fluconazole (100%). All *Candida* isolates were susceptible to voriconazole (Table 4).

Multidrug resistance pattern of bacterial isolates

Multidrug drug resistance (MDR) level was 65% that was only seen among Gram-negative bacterial isolates. Highest MDR was observed in *k. pneumoniae* and *Acinetobacter* spp. The *Pseudomonas* spp and *Burkholderia cepacia* found to be non MDR for the antibiotics tested (Table 5).

Risk factors for BSIs

In this study different clinical and socio-demographic factors were observed. The association of prevalence of bacterial infections with independent variables was initially analyzed using a simple regression model. On the basis of cruds odd ratio, the candidate risk factors for the statistical model were Sex, age, place of residence, history of admission, sepsis, surgery, empirical therapy, diabetic mellitus, hepatic problem, and utilization of complicated devices at 0.25 level of significant. The candidate risk factors were filtered using multiple logistic regression models. The model suggested sex (P-value=0.007), age (P-value<0.001) and utilization of medical devices (P-value=0.003) were significant risk factors for bacterial infections (Table 6).

A multiple regressions model was also done for the predominant bacteria with demographic and clinical conditions. *Burkholderia cepacia*, coagulase negative-staphylococcus and *klebsiella pneumoniae* were the predominant bacteria associated with the independent variable. History of admission (P-value=0.006) and utilization of medical devices (P-value<0.001) have significant association with *Burkholderia cepacia*. On the other hand, sex (P-value=0.007) has significant association with infection with coagulase negative staphylococcus. *Klebsiella pneumoniae* has not significant association with all demographic and clinical conditions.

Discussion

Blood stream infections are regarded as the most devastating human diseases that lead to complex treatment procedure (15, 21). The current study mainly illustrated the magnitude of BSIs along with the main risk factors. To our knowledge, this study was the first in addressing *Burkholderia cepacia* as a cause of BSIs in Ethiopia's hospital setting particularly from NICU wards. Furthermore, this study differs from previous research conducted in the same laboratory in BSIs with identification and susceptibility testing for antifungal agents that was not considered a routine testing procedure in many laboratories.

In our study higher prevalence of blood culture confirmed cases [175 (50.58%)] were observed compared to studies conducted in Port Blair India 14.24% (22) and Kanpur 22.3% (23). The differences may be due to blood specimen volume, time of blood culture taken and epidemiological variation of etiologic agents (2, 4). Our finding might be higher due to the emerging of new nosocomial pathogen *Burkholderia cepacia*.

The percentage of bacterial isolation in this study was 159 (45.95%), which was approximately similar to the previous study conducted in Ethiopia [164 (32.8%)] (11). In contrast to the above finding, different studies conducted in European, African countries, and Ethiopia reported a lower isolation rate of bacterial infections (12, 24–30). The possible reason for this variation may be the predominance of *Burkholderia cepacia* detection that may increase the positivity rate in the present study.

The prevalence of bacterial blood stream infections in relation to age groups illustrated that blood culture positivity was higher among infants (77.36%) than other age groups. This finding was in line with the study performed in rural tertiary care hospital in India (21), Gonder university hospital (30) and Nigeria (12). The predominance of bacterial BSIs among infants may be due to immaturity of the immune system which contributes to ease of susceptibility to infections (31).

The predominant pathogens causing BSIs in our study were found to be Gram-Negative bacteria, which is similar to other studies in Rim Hospital (32), Nigeria (12), Jimma (33), Addis Ababa (34) and Tikur Anbesa (27). The higher percentage of Gram-negative bacteria in this study most likely due to a higher number of *Burkholderia cepacia* which is emerging as outbreak NICU wards.

Bacterial isolation varies among country to country. *Burkholderia cepacia*, Coagulase-negative staphylococcus, *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter* spp and *pseudomonas* spp were the most commonly isolated bacteria that caused bloodstream infections in this study, which is more or less similar to previous studies (12, 24, 35–37). Among the Gram-negative bacteria *Burkholderia cepacia* was found as the highest percentage. The predominance of this bacteria may be due to about 77.36% of patients in the current study was infants from NICU and all of these isolates were identified from these patients. *Burkholderia cepacia* is an important nosocomial pathogen that causes outbreak in hospital settings especially in neonatal units. It is also capable of adhering to various medical instruments and colonizing solutions taken as an injection for medication that may be capable of transmitting to neonates (38).

Like many other studies (15, 26, 31, 39–43), Coagulase-negative staphylococcus was the predominant Gram-positive organism in our study as a causative agent of BSIs. The high prevalence of Coagulase-negative staphylococcus could be the higher number of blood samples in our study were from neonatal intensive care unit which was frequently associated with the utilization of intravascular devices that serve as portals of entry to the bloodstream. (44).

Fungemia has been confirmed in 9 (9.14%) cases. The result was consistent with a study conducted in New York City 9.8% (45), Saudi Arabia 9.5% (15) and India 9.2% (46). All fungemia infections in this study were due to *non-candida albicans* species which is in agreement with other studies (23, 40, 47). But our finding was different from studies conducted in Turkey (48) and India (13) which found *Candida albicans* as a cause of BSIs. The major risk factors leading to fungal infection in our study were prolonged hospital stay and previous broadspectrum antimicrobial treatment (13).

Klebsiella spp showed high resistance to folate pathway inhibitors, fluoroquinolones, aminoglycoside, and beta lactamases inhibitors. Third-generation and fourth-generation cephalosporins also exhibited very weak activity against this organism. A similar finding was noted among studies carried out in Nepal (31), Gonder university hospital (30) and India (49).

Among non-fermenter, *Acinetobacter* spp showed extremely resistance to fluoroquinolone and carbapenem drugs. They were also moderately resistance to other antibiotics such as aminoglycoside, third and fourth generation cephalosporin, and aminoglycoside and beta lactam inhibitors. This finding was consistent with the study done in Iran which showed that *Acinetobacter* spp was the most resistant bacteria against most antibiotics tested (50). The main reason for this problem may be inappropriate use of antibiotics and lack of standard antibiotic policy in the hospital. Amikacin was the most effective antibiotic against Gram-negative agents that is comparable in studies performed in Asian and Arab countries (47, 50–52).

In our study, a higher degree of resistance was observed in penicillin among Gram-positive organisms which showed conformity with studies done in Jimma (29) and Afghanistan (41). All Gram-positive bacteria were sensitive to vancomycin that is similar to other studies (40, 43, 49, 51, 53). However, different from the study in India, vancomycin resistance and intermediate *Staphylococcus aureus* were observed (46). The difference may be the number of isolates that were identified. MRSA was observed in the predominant organism Coagulase-negative staphylococcus which similar to study in tertiary care hospital in India (49) and Nepal (31).

In our study, the highest resistance rate of azole drugs observed in fluconazole in *Candida krusei* showed similarity in studies conducted in India (35) and Turkey (48). However, Study in Qatar showed most *candida* spp were sensitive to fluconazole, which is different from our study (47). There is no resistance against voriconazole in all candida isolates which was in line with study done in Turkey (48).

Many factors contribute to the prevalence of BSIs. In the current study Sex, Age, and utilization of complicated devices were independent risk factors for BSIs caused by bacterial infection. This finding agrees with a study conducted in Gonder university hospital that has a significant association between age and BSIs (30).

Conclusions

In this study, the frequency of Gram-negative bacteria that causes BSIs was higher compared to Gram-positive bacterial and fungal isolates. Fungemia due to non *Candidia albicans* was common fungal causative agent. Sex, Age, and utilization of complicated devices were found to be the main risk factor that causes BSIs associated with bacterial infections. Both Gram-positive and Gram-negative bacteria showed an increasing level of resistance to most antibiotics that have been used for empirical therapy. This highlights continuing investigation of etiologic agents and assessment of infection control is necessary to reduce the disease impact. In addition, it is important to revise treatment guidelines based on the predominant pathogen and resistance patterns at the health facility level.

Limitation Of The Study

All specimens during the study period were collected from Addis Ababa health care facilities that could not represent the national data of Ethiopia. There was no information whether the cases were community-acquired or healthcare-acquired infections, even though the majority of the isolates were identified from NICU.

Declarations

Ethics approval and consent to participate

Approval was obtained from the department of medical laboratory sciences, Addis Ababa University. Data collection was started after written informed consent/assent was obtained from the study participants.

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 interests

Not applicable

Funding

Not applicable

Author contributions

EA: Study conception and design, Acquisition of data, Drafting of manuscript, Critical revision and approval of the final version. DS, AA, TL and AB: Critical Acquisition of data, revision and approval of the final version. ZT: Acquisition of data and statistical analysis.

Acknowledgement

We would like to thank Ethiopian Public Health Institute, Clinical Bacteriology and Mycology Reference Laboratory for their cooperation to use the laboratory facilities.

References

1. M Tille P. Bailey & Scott's Diagnostic Microbiology Fourteenth Edition. Elsevier; 2017.
2. Weinstein MP. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. *Clinical infectious diseases*. 1996;23(1):40–6.
3. Organization WH. Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions. 2020.
4. Reimer LG, Wilson ML, Weinstein MP. Update on detection of bacteremia and fungemia. *Clinical microbiology reviews*. 1997;10(3):444–65.
5. Pfaller MA, Jones RN, Doern GV, Kugler K, Group SP. Bacterial pathogens isolated from patients with bloodstream infection: frequencies of occurrence and antimicrobial susceptibility patterns from the SENTRY antimicrobial surveillance program (United States and Canada, 1997). *Antimicrobial agents and chemotherapy*. 1998;42(7):1762–70.

6. Kamga H, Njunda A, Nde P, Assob J, Nsagha D, Weledji P. Prevalence of septicaemia and antibiotic sensitivity pattern of bacterial isolates at the University Teaching Hospital, Yaoundé, Cameroon. *African Journal of Clinical and Experimental Microbiology*. 2011;12(1).
7. Thomas SR, Sajeena Jose C, Damodaran D, Benny E, Jha A, Chandur VK, et al. A Tertiary Care Hospital Based Study on Antimicrobial Sensitivity Pattern Among Septic Patients. *Int J Cur Res Rev* Vol. 2019;11(10):7.
8. Vandepitte J, Verhaegen J, Engbaek K, Rohner P, Piot P, Heuck C, et al. *Basic laboratory procedures in clinical bacteriology*: World Health Organization; 2003.
9. Laupland KB, Church DL. Population-based epidemiology and microbiology of community-onset bloodstream infections. *Clinical microbiology reviews*. 2014;27(4):647–64.
10. Vlieghe E, Phoba M, Tamfun JM, Jacobs J. Antibiotic resistance among bacterial pathogens in Central Africa: a review of the published literature between 1955 and 2008. *International journal of antimicrobial agents*. 2009;34(4):295–303.
11. Kitila K, Taddese B, Hailu T, Sori L, Geleto S. Assessment of Bacterial Profile and Antimicrobial Resistance Pattern of Bacterial Isolates from Blood Culture in Addis Ababa Regional Laboratory, Addis Ababa, Ethiopia. *Clin Microbiol*. 2018;7(312):2.
12. Nwadioha I, Odimayo MS, Omotayo J, Taiwo AO, Olabiyi E. A retrospective cross sectional study of blood culture results in a tertiary hospital, Ekiti, Nigeria. *Open Journal of Medical Microbiology*. 2015;5(04):202.
13. Siddiqui N, Kirmani S, Khan F, Kaushal N, Shukla I, Khan HM, et al. Prevalence and Risk Factors of Candida blood Stream Infections in a Tertiary Care Hospital. *Int J Curr Microbiol App Sci*. 2015;1:157–62.
14. Timsit J-F, Soubirou J-F, Voiriot G, Chemam S, Neuville M, Mourvillier B, et al. Treatment of bloodstream infections in ICUs. *BMC infectious diseases*. 2014;14(1):489.
15. Elbashier AM, Malik AG, Khot AP. Blood stream infections: micro-organisms, risk factors and mortality rate in Qatif Central Hospital. *Annals of Saudi medicine*. 1998;18(2):176–80.
16. Alemnew B, Biazin H, Demis A, Abate Reta M. Bacterial Profile among Patients with Suspected Bloodstream Infections in Ethiopia: A Systematic Review and Meta-Analysis. *International journal of microbiology*. 2020;2020.
17. Organization WH. *Antimicrobial resistance global report on surveillance: 2014 summary*. World Health Organization, 2014.
18. Teshale AM, Abera NA, Ibrahim RA, Dinku SF, Negeri AA, Oda MA, et al. Prevalence and antimicrobial susceptibility of bacterial isolates from blood samples referred to National Reference Laboratory, Ethiopia. *Ethiopian Journal of public health and nutrition*. 2020;2(1).
19. Bauer A, Kirby W, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disk method. *American journal of clinical pathology*. 1966;45(4_ts):493–6.
20. Wayne P. *Method for antifungal disk diffusion susceptibility testing of yeasts*. CLSI m44-a. 2004.
21. Sweta O, Sanjay JM, Kikani MK, Sunil GO. Bacteriological profile and antibiogram of blood culture isolates from patients of rural tertiary care hospital. *Indian J Microbiology & Mycology*. 2016;4(3):1–7.
22. Banik A, Bhat SH, Kumar A, Palit A, Snehaa K. Bloodstream infections and trends of antimicrobial sensitivity patterns at Port Blair. *Journal of laboratory physicians*. 2018;10(3):332.
23. Pal N, Sujatha R. Antimicrobial Resistant Pattern of Blood Culture Isolates, Among Septicaemia Suspected Patients. *National Journal of Laboratory Medicine*. 2016;5(1):17–21.
24. Onken A, Said AK, Jørstad M, Jenum PA, Blomberg B. Prevalence and antimicrobial resistance of microbes causing bloodstream infections in Unguja, Zanzibar. *PloS one*. 2015;10(12):e0145632.
25. Wasihun AG, Wlekidan LN, Gebremariam SA, Dejene TA, Welderufael AL, Haile TD, et al. Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. *SpringerPlus*. 2015;4(1):314.
26. Abebaw A, Tesera H, Belachew T, Mihiretie GD. The bacterial profile and antibiotic susceptibility pattern among patients with suspected bloodstream infections, Gondar, north-west Ethiopia. *Pathology and Laboratory Medicine International*. 2018;10:1.
27. Bitew A. Multi-Drug Resistance Profile of Bacteria Isolated from Blood Stream Infection at Tikur Anbessa Special-ized Hospital, Addis Ababa, Ethiopia. *EC Microbiology*. 2018;14:119–26.
28. Devi AV, Sahoo B, Damrolien S, Praveen S, Lungran P, Devi KM. A study on the bacterial profile of bloodstream infections in Rims Hospital. *J Dent Med Sci*. 2015;14:18–23.
29. Zenebe T, Kannan S, Yilma D, Beyene G. Invasive bacterial pathogens and their antibiotic susceptibility patterns in Jimma University specialized hospital, Jimma, Southwest Ethiopia. *Ethiopian journal of health sciences*. 2011;21(1):1–8.
30. Dagne M, Yismaw G, Gizachew M, Gadisa A, Abebe T, Tadesse T, et al. Bacterial profile and antimicrobial susceptibility pattern in septicemia suspected patients attending Gondar University Hospital, Northwest Ethiopia. *BMC research notes*. 2013;6(1):283.
31. Pokhrel B, Koirala T, Shah G, Joshi S, Baral P. Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary hospital in Nepal. *BMC pediatrics*. 2018;18(1):208.
32. Devi V, Sahoo B, Damrolien S, Praveen S, Lungran P, Devi M. A study on the bacterial profile of bloodstream infections in Rims Hospital. *J Dent Med Sci*. 2015;14:18–23.
33. Kumalo A, Kassa T, Mariam ZS, Daka D, Tadesse AH. Bacterial profile of adult sepsis and their antimicrobial susceptibility pattern at Jimma University specialized hospital, south West Ethiopia. *Health Science Journal*. 2016;10(2):1.

34. Negussie A, Mulugeta G, Bedru A, Ali I, Shimeles D, Lema T, et al. Bacteriological profile and antimicrobial susceptibility pattern of blood culture isolates among septicemia suspected children in selected hospitals Addis Ababa, Ethiopia. *International journal of biological and medical research*. 2015;6(1):4709.
35. Gupta S, Kashyap B. Bacteriological profile and antibiogram of blood culture isolates from a tertiary care hospital of North India. *Tropical Journal of Medical Research*. 2016;19(2):94.
36. Seni J, Mwakyoma A, Mashuda F, Marando R, Ahmed M, DeVinney R, et al. Deciphering risk factors for blood stream infections, bacteria species and antimicrobial resistance profiles among children under five years of age in North-Western Tanzania: a multicentre study in a cascade of referral health care system. *BMC pediatrics*. 2019;19(1):32.
37. Babay HA. Bacterial isolates from fatal cases of bloodstream infections at a university hospital in Central, Saudi Arabia. *Saudi medical journal*. 2007;28(2):231.
38. Schmitt C, Maciel A, Baraldi M, Simonetti M, Cantarelli M, Turcato G, et al. Bloodstream infection outbreak caused by burkholderia cepacia complex: the role of genetic sequencing in the investigation. *Antimicrobial Resistance and Infection Control*. 2015;4(S1):P228.
39. Mpinda-Joseph P, Anand Paramadhas BD, Reyes G, Maruatona MB, Chise M, Monokwane-Thupiso BB, et al. Healthcare-associated infections including neonatal bloodstream infections in a leading tertiary hospital in Botswana. *Hospital Practice*. 2019:1–8.
40. Patel KK, Patel S, Sinha D. Bacteriological profile and antibiotic resistance pattern in blood stream infection in critical care units of a tertiary care hospital in central India. *Blood*. 2016;50:1.
41. Tariq TM. Bacteriologic profile and antibiogram of blood culture isolates from a children's hospital in Kabul. *J Coll Physicians Surg Pak*. 2014;24(6):396–9.
42. Karlowsky JA, Jones ME, Draghi DC, Thornsberry C, Sahm DF, Volturo GA. Prevalence and antimicrobial susceptibilities of bacteria isolated from blood cultures of hospitalized patients in the United States in 2002. *Annals of clinical microbiology and antimicrobials*. 2004;3(1):7.
43. Teshale AM, Abera NA, Ibrahim RA, Dinku SF, Negeri AA, Oda MA, et al. Prevalence and antimicrobial susceptibility of bacterial isolates from blood samples referred to National Reference Laboratory, Ethiopia. *Ethiopian Journal of public health and nutrition*. 2020;1(1).
44. Karunakaran R, Raja NS, Ng KP, Navaratnam P. Etiology of blood culture isolates among patients in a multidisciplinary teaching hospital in Kuala Lumpur. *Journal of microbiology Immunology and Infection*. 2007;40(5):432.
45. Orsini J, Mainardi C, Muzylo E, Karki N, Cohen N, Sakoulas G. Microbiological profile of organisms causing bloodstream infection in critically ill patients. *Journal of clinical medicine research*. 2012;4(6):371.
46. Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile and drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. *BioMed research international*. 2014;2014.
47. Ahmed A, Lutfi S, Al-Hail M, Al-Saadi M. Antibiotic susceptibility patterns of microbial isolates from blood culture in the neonatal intensive care unit of Hamad Medical Corporation (HMC), Doha, Qatar. *Asian J Pharm Clin Res*. 2013;6(Suppl 2):191–5.
48. Aydin F, Bayramoglu G, Guler NC, Kaklikkaya N, Tosun I. Bloodstream yeast infections in a university hospital in Northeast Turkey: a 4-year survey. *Medical mycology*. 2011;49(3):316–9.
49. Rajeevan S, Ahmad SM, Jasmin P. Study of prevalence and antimicrobial susceptibility pattern in blood isolates from a tertiary care hospital in North Kerala, India. *Int J Curr Microbiol Appl Sci*. 2014;3(4):655–62.
50. Nobandegani AS, Motamedifar M. Antibiotic sensitivity profile of the bacterial isolates from the blood samples of the patients in different wards of a major referral hospital, Shiraz, Iran 2015–2016. *Pharmacophore*. 2019;10(2).
51. Fayyaz M, Mirza IA, Ikram A, Hussain A, Ghafoor T, Shujat U. Pathogens causing blood stream infections and their drug susceptibility profile in immunocompromised patients. *J Coll Physicians Surg Pak*. 2013;23(12):848–51.
52. Mehta M, Dutta P, Gupta V. Antimicrobial susceptibility pattern of blood isolates from a teaching hospital in North India. *Japanese journal of infectious diseases*. 2005;58(3):174.
53. Gandhi V, Patel M. Prevalence of Candida Species and Its Antifungal Susceptibility Isolated from Blood Culture at Tertiary Care Hospital, Ahmedabad, India. *Int J Curr Microbiol Appl Sci*. 2017;6:884–92.

Tables

Table 1
Demographic characteristics of study participants referred to Clinical Bacteriology and Mycology laboratory from February 23 to June 23, 2020.

Variables	Category	N (%)
Gender	Female	126 (36.42)
	Male	220 (63.58)
Age	Infant (< 1 year)	186 (53.76)
	Children (1-12yrs)	27 (7.80)
	Adult(13-64yrs)	117 (33.82)
	Elderly (> 65yrs)	16 (4.62)
Place of residence	Outside of Addis Ababa	211 (60.98)
	Addis Ababa	135 (39.02)

Table 2
Antibiotic resistance patterns of Gram-positive bacteria isolated from blood cultures of patients referred to Clinical Bacteriology and Mycology reference laboratory.

Bacterial isolate	Antibiotic							
		PEN	OXA	GEN	AMP	VAN	CHL	CTX
<i>Coagulase negative staphylococcus</i>	%R	40(100)	40(89.7)	39(32.5)	NT	NT	NT	NT
<i>Enterococcus spp</i>	%R	8(75)	NT	NT	NT	8(0)	8(12.5)	NT
<i>Viridans spp</i>	%R	NT	NT	NT	NT	3(0)	NT	3(33.3)
<i>Staphylococcus aureus</i>	%R	2(100%)	2(0)	2(0)	NT	2(0)	NT	NT

Key: PEN: Penicillin OXA: oxacillin GEN: Gentamycin VAN: Vancomycin CHL: chloramphenicol CTX: Cefotaxime FEP: Cefipime NT: Not tested

Table 3
Antibiotic resistance patterns of Gram-negative bacteria isolated from blood cultures among patients referred to Clinical Bacteriology and Mycology laboratory.

Bacterial isolate	CAZ	MEM	SXT	AMC	TZP	CRO	FEP	AMK	GEN	TOB	CIP	CHL
<i>Burkholderia cepacia</i>	65(4.62)	65(0)	65(1.53)	NT	NT	NT	NT	NT	NT	NT	NT	NT
<i>Klebsiella pneumoniae</i>	21(76.2)	21(52.4)	21(85.7)	20(60)	19(31.6)	21(81)	21(66.7)	21(0)	20(65)	21(84.2)	6(83.3)	21(47.7)
<i>Acinetobacter spp</i>	7(57.1)	7(71.4)	NT	NT	7(57.2)	7(42.9)	7(42.9)	7(0)	7(71.4)	7(71.4)	6(100)	NT
<i>Escherichia coli</i>	3(33.3%)	3(0)	3(33.3)	3(33.3)	3(0)	3(66.7)	3(66.7)	3(0)	3(33.3)	2(50)	1(0)	3(0)
<i>Klebsiella ozaenae</i>	3(66.7)	3(0)	3(66.7)	3(0)	3(0)	3(100)	3(33.3)	3(0)	3(33.3)	3(100)	1(0)	3(33.3)
<i>Pseudomonas spp</i>	3(0)	3(0)	NT	NT	3(0)	NT	3(33.3)	3(0)	3(0)	3(0)	2(0)	NT
<i>Enterobacter cloacae</i>	2(50)	2(0)	2(100)	2(100)	2(0)	2(0)	2(0)	2(0)	2(100)	2(100)		2(0)
<i>Enterobacter aerogenes</i>	1(100)	1(0)	1(100)	NT	1(0)	NT	NT	NT	NT	1(0)	1(0)	1(100)

Key: CAZ: Cefazidime MEM: Meropenem SXT: Trimethoprim-Sulphamethoxazole AMC: Amoxicillin-Clavulanic acid TZP: Piperacillin-Tazobactam CRO: Ceftriaxone FEP: Cefipime AMK: Amikacin GEN: Gentamycin TOB: Tobramycin CIP: Ciprofloxacin CHL: chloramphenicol NT: Not tested

Table 4
Antifungal resistance patterns of fungal isolates from blood culture of patients referred to Clinical Bacteriology and Mycology laboratory.

Fungal isolate		AMB	CAS	FCT	FLU	MIF	VOR
<i>Candida krusei</i>	%R	9(0)	9(0)	9(22.2)	9(77.8)	9(0)	9(0)
	%S	9(100)	9(100)	9(77.8)	9(22.2)	9(100)	9(100)
<i>Candida glabrata</i>	%R	5(40)	5(20)	5(20)	5(80)	5(20)	5(0)
	%S	5(60)	5(80)	5(80)	5(20)	5(80)	5(100)
<i>Candida rugosa</i>	%R	1(0)	1(0)	1(100)	1(100)	1(0)	1(0)
	%S	1(100)	1(100)	1(0)	1(0)	1(100)	1(100)
<i>Candida dubliniensis</i>	%R	1(0)	1(0)	1(0)	1(100)	1(0)	1(0)
	%S	1(100)	1(100)	1(100)	1(0)	1(100)	1(100)

Key: AMB: Amphotericin B CAS: Caspofungin FCT: Flycitosine FLU: Fluconazole MIF: Micafungin VOR: voriconazole

Table 5
Multidrug resistance pattern of bacterial isolates from blood culture of patients referred to Clinical bacteriology and Mycology laboratory.

Bacterial Isolate	Ro	R1	R2	R3	R4	R5	R6	R7	Total MDR
<i>k. pneumoniae</i> (N = 21)	1(4.8)	3(14.3)	2(9.5)	2(9.5)	5(23.8)	3(14.3)	0(0)	5(23.8)	15(71.4)
<i>Acinetobacter spp</i> (N = 7)	0(0)	0(0)	1(14.3)	3(42.9)	3(42.9)	0(0)	0(0)	0(0)	6(85.7)
<i>E.coli</i> (N = 3)	0(0)	1(33.3)	1(33.3)	0(0)	1(33.3)	0(0)	0(0)	0(0)	1(33.3)
<i>K.ozenae</i> (N = 3)	1(33.3)	0(0)	1(33.3)	0(0)	0(0)	1(33.3)	0(0)	0(0)	1(33.3)
<i>Pseudomonas spp</i> (N = 3)	2(66.7)	1(33.3)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)
<i>E.cloacae</i> (N = 2)	0(0)	0(0)	0(0)	0(0)	2(100)	0(0)	0(0)	0(0)	2(100)
<i>E.aeroagens</i> (N = 1)	0(0)	0(0)	0(0)	1(100)	0(0)	0(0)	0(0)	0(0)	1(100)
Total(N = 40)	4(10)	5(12.5)	5(12.5)	6(15)	11(27.5)	4(10)	0(0)	5(12.5)	26(65)

Table 6
Risk factor associated with bacterial cause of blood stream infections among patients referred to Clinical Bacteriology and Mycology reference laboratory.

Characteristics	Categories	Bacterial infection			Pce		Kpn		Scn	
		Number (%)	AOR	P-value	AOR	P-value	AOR	P-value	AOR	P-value
Sex(ref = Male)	Female	74(58.70)	2.05	0.007	0.76	0.424	1.72	0.241	2.68	0.007
	Male	86(39.09)								
Age(ref = Adult)	Infant(< 1 year)	124(66.67)	5.69	0.000		0.984	2.29	0.184	1.98	0.125
	Children(1-17)	5(18.52)	0.66	0.456	1.11	0.999	1.06	0.959	0.67	0.627
	Adult(18-64)	28(23.93)								
	Elderly(> 64)	3(18.75)	0.62	0.484	1.04	0.999	1.61	0.682	0.57	0.617
Place of residence(ref = rural)	Urban	71(52.59)	0.82	0.458	0.80	0.51	0.57	0.594	0.71	0.359
	Rural	89(42.18)								
SURGERY(ref = No)	Yes	25(35.71)	0.86	0.465	1.59	0.371	1.64	0.41	0.71	0.538
Ever admitted(ref = No)	Yes	46(36.8)	0.82	0.652	0.30	0.006	0.75	0.59	2.64	0.012
SEPSIS(ref = No)	Yes	93(55.03)	0.97	0.899	0.70	0.304	1.07	0.888	0.94	0.878
Utilization of complicated devices (ref = No)	Yes	99(52.66)	2.24	0.003	3.52	0.000	1.39	0.508	0.69	0.329

Key: Pce: *Burkholderia cepacia* Scn: Coagulase negative staphylococcus Kpn: *Klebsiella pneumoniae*

Figures

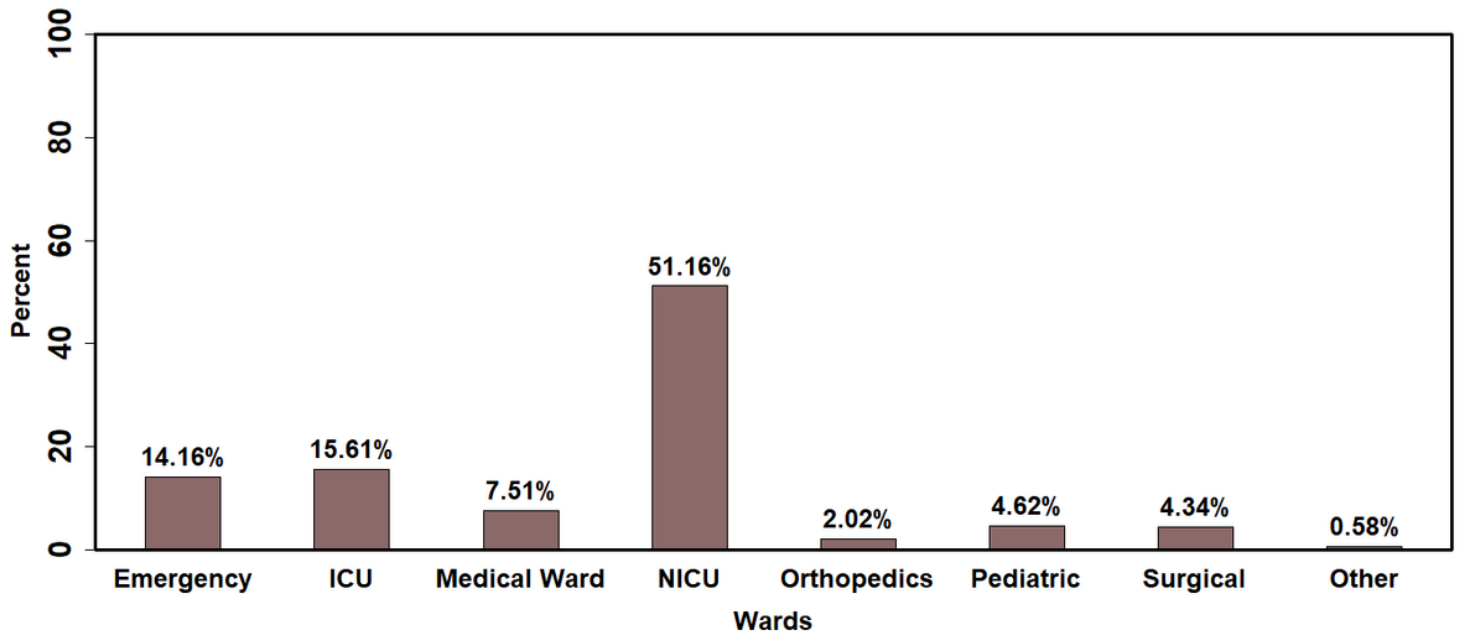


Figure 1

Distribution of patients with suspected BSIs referred to EPHI, Clinical Bacteriology and Mycology reference laboratory from February 23 to June 23, 2020 according to the hospital wards.

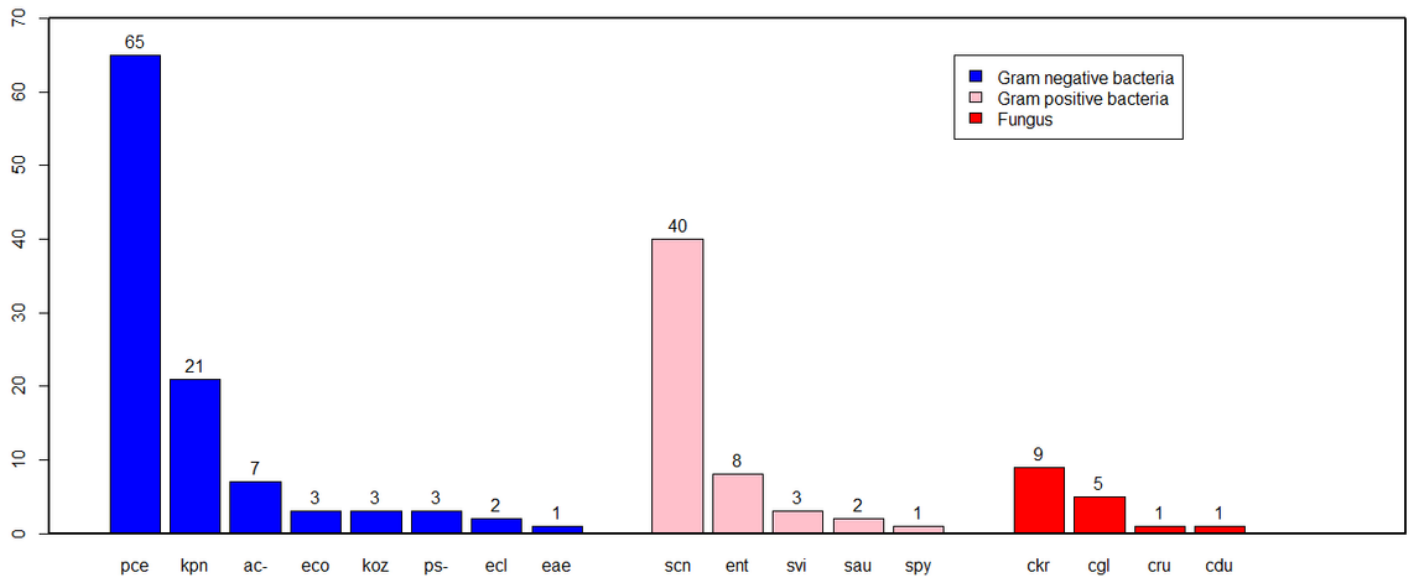


Figure 2

Prevalence of microbial isolates from patients referred to Clinical Bacteriology and Mycology laboratory. Key: Pce: Burkholderia cepacia kpn: Klebsiella pneumonia ac-: Acinetobacter spp eco: Escherichia coli Koz: Klebsiella ozaenae ps: Pseudomonas spp ecl: Enterobacter cloacae eae: Enterobacter aerogenes scn: Coagulase negative staphylococcus ent: Enterococcus spp svi: Viridans spp sau: Staphylococcus aureus spy: Streptococcus pyogenes ckr: Candida krusei cgl: Candida glabrata cru: Candida rugosa cdu: Candida dubliniensis