Original Article

Journal of Microbiology and Related Research
Volume 5 Number 2, July - December 2019
DOI: http://dx.doi.org/10.21088/jmrr.2395.6623.5219.6

Evaluating the Pattern of Bloodstream Infections Among Pediatric and Adult Patients and Role of Drug-resistant Acinetobacter Species in a Tertiary Care Hospital, Kashmir

Sumaira Qayoom Beigh[1], Roomi Yousuf[2], Amrish Kohli[3], Muzafar Amin[4], Afreen Rashid[5], Talat Masoodi[6], Syed Khurshid[7]

Author Affiliation: [1,3,4,5]Senior Residents, [6]Lecturer, [7]Professor and Head, Department of Microbiology, SKIMS Medical College Hospital, Bemina, Srinagar, Jammu and Kashmir 190018, India. [2]Medical officer, Division of Epidemiology, Public Health Lab, Barzulla, Srinagar, Jammu and Kashmir, India.

Corresponding Author: **Amrish Kohli,** Senior Resident, Department of Microbiology, SKIMS Medical College Hospital, Bemina, Srinagar, Jammu and Kashmir 190018, India.

E-mail: amrishkohli.ganu@gmail.com

Received on 09.04.2019, **Accepted on** 04.05.2019

Abstract

Background: Bloodstream infections (BSIs) are one of the most important infections responsible for morbidity and mortality among hospitalized patients worldwide. The emergence of resistant bacteria makes it a requisite to know the prevailing antibiotic susceptibility pattern of the pathogens causing bloodstream infections.

Objectives: The present study was undertaken to analyze the various microorganisms causing BSIs and study the antimicrobial resistance patterns of *Acinetobacter* spp. in a tertiary care hospital.

Material and methods: A total of 2700 blood specimens from clinically suspected cases of BSIs were studied for a period of 2 years from January 2017 to December 2018. Blood specimens were processed following aseptic guidelines and cultured for 7 days. Growth was identified using biochemical tests. All isolates of *Acinetobacter* spp. were subject to antibiotic sensitivity testing using Clinical and Laboratory Standards Institute (CLSI) guidelines.

Result: Out of 2700 specimens, 404 (15%) yielded growth. Out of these, 48% were Gram positive isolates and 52% were Gram negative isolates. Among Gram positive isolates, Coagulase negative Staphylococcus (CONS) was the most predominant organism (31%) followed *Staphylococcus aureus* (11%). Among Gram negative isolates, *Acinetobacter* spp. (16%) were the predominant isolates, followed by *Escherichia coli* (10.6%), *Citrobacter* spp. (8%), *Pseudomonas* spp. (6.5%) and *Klebsiella* spp. (6%). Out of 64 (16%) isolates of *Acinetobacter* spp. 5 (8%) were multi-drug resistant (MDR), 5 (8%) were extensive drug-resistant (XDR) and 2 (3%) were Pandrug-resistant (PDR).

Conclusion: Successful treatment of sepsis depends on early diagnosis and appropriate antimicrobial therapy. The knowledge of etiology and the antibiogram of isolated pathogens help in framing the antibiotic policies for any healthcare institute and improve infection control practices by formulating those policies for empirical antibiotic therapy.

Keywords: *Bloodstream infections* (BSIs); *Sepsis*; *Blood culture, Antibiotic susceptibility testing*; *Multi-drug resistant* (MDR); *Extensive Drug-resistant* (XDR); *Pandrug-resistant* (PDR); *Intensive care unit* (ICU).

How to cite this article:

Sumaira Qayoom Beigh, Roomi Yousuf, Amrish Kohli, *et al*. Evaluating the Pattern of Bloodstream Infections Among Pediatric and Adult Patients and Role of Drug-resistant Acinetobacter Species in a Tertiary Care Hospital, Kashmir. J Microbiol Relat Res. 2019;5(2):91-97.

Introduction

Bloodstream infections (BSIs) are the leading cause of morbidity and mortality among the hospitalized patients worldwide, representing about 15% of all nosocomial infections and affecting approximately 1% of all hospitalized patients, with an incidence rate of 5 per 1,000 central-line days.[1] The recovery of

a microbial pathogen in blood culture by virtue of infection (not specimen contamination) is referred to as Bloodstream Infection.[2] A hospital-related BSI is defined to have occurred after a patient has completed ≥48 hours of stay in the hospital or has a central line for 48 hours or more. A BSI is primary when the central line is the only probable source of infection and secondary when there is an underlying cause (genitourinary/respiratory infection or any other obvious source of infection in the body).[3]

Among the bacterial causes of BSIs *Staphylococcus aureus*, Coagulase negative *Staphylococci*, and *Enterococcus faecalis* are the commonest among gram positive organisms; *Escherichia coli*, *Klebsiella pneumonia*, and *Serratia* spp. are the commonest among Enterobacteriaceae; and *Pseudomonas* spp. and *Acinetobacter baumannii* are the commonest amongst the non-fermenter gram negative organisms. Among fungi, it is non-albicans *Candida* spp. followed by *Candida albicans* that are common.[3]

As bacteriological profile and drug resistance pattern tend to be peculiar to an institute that is dealing with a special category of patients, this study was conducted in our tertiary care center to report the profile and the trend of resistance prevalent among these isolates in our institute that would in turn help to guide the policy on implementation of antibiotic stewardship programme and standardized infection control guidelines.

Material and Methods

Study Setting

This study was carried out in the Department of Microbiology, Sher-i-Kashmir institute of medical sciences (SKIMS) medical college hospital, Bemina from January 2017 to December 2018. A total of 2700 patients with suspected blood stream infection from all out-patient departments (OPDs), in-patient departments (IPDs) and intensive care units (ICUs) in the hospital were included regardless of age, sex and occupation of the patient for the present study.

Study type

The present study is a retrospective observational study.

Patient Data

The blood samples from the patients suspected of septicemias were routinely processed in the department of Microbiology following routine microbiological techniques. Data collection included the results of the blood culture and antimicrobial susceptibility testing (AST).

Blood culture

Blood samples were collected under all aseptic precautions. About 5–10 ml of blood from adults and 2 ml from pediatric age group was collected, which was then inoculated in 50 ml and 10 ml brain heart infusion broth respectively. Blood culture bottles were incubated at 37°C aerobically for 24 hours followed by subcultures on blood agar and MacConkey agar. No sign of growth in blood culture bottles (lack of turbidity) was followed by subculture and reincubation on 2nd, 3rd, and 7th day to be reported negative on 7th day after final subculture. Isolates were identified by standard microbiological procedures including Gram's stain, colony morphology, and biochemical reactions.

Isolates of *Acinetobacter* spp. were subject to antimicrobial susceptibility testing and the results were interpreted as per CLSI guidelines.[4] The following discs of antimicrobial agents were used: ceftriaxone (30 μg), ceftazidime(30 μg), cefoperazone (30 μg), piperacillin-tazobactam (100/10 μg), imipenem (10 μg), meropenem (10 μg), ciprofloxacin (5 μg), amikacin (30 μg), gentamicin (10 μg), polymyxin B. Multidrug-resistance (MDR) was defined as resistance to 3 or more of the following antibiotics: anti-pseudomonal pencillins, anti-pseudomonal cephalosporins, anti-pseudomonal fluoroquinolones and aminoglycosides. Extensive drug resistance (XDR) was defined as isolates that are MDR and carbapenem resistant. Pandrug-resistance (PDR) was defined when XDR isolates also showed resistance to Polymyxin B.[5]

Statistical analysis

This was done using appropriate formula and the results were calculated.

Results

During a period of 2 years, a total of 2700 blood culture samples were received in the microbiology laboratory of the hospital. Out of these, 1660 (61%) samples were from male patients and 1058 (39%) were from female patients. Male: female ratio was approximately 1.5:1. Median age of the patients was 35 years with range of 1 day to 80 years.

Among all the samples, 405 (15%) samples showed significant growth on aerobic culture (Fig. 1).

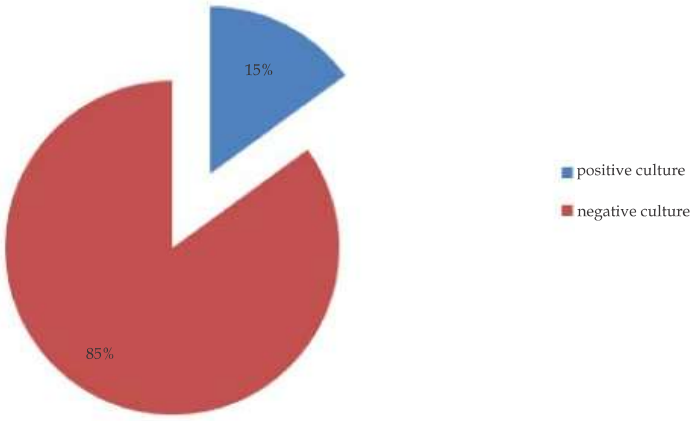

Fig. 1: Total Blood cultures (*n*=2700)

Out of 405 positive cultures, 243 (60%) belonged to infants and the rest (40%) belonged to adults (Fig. 2). About 193 isolates (48%) were gram-positive, 211 (52%) were gram-negative and one isolate was found non albicans *Candida* spp. after germ tube test. Coagulase negative *Staphylococcus* (31%) were the most common isolates, followed by *Acinetobacter* spp. (16%), *Staphylococcus aureus* (11%), *Escherichia coli* (10.6%), *Citrobacter* spp. (8%), *Pseudomonas* spp.(6.5%), *Klebsiella* spp. (6%), *Enterococcus* spp. (4%), *Salmonella Typhi* (2%), and *Enterobacter* spp. (1.7%). The least common isolates were *Streptococcus* spp., and *Proteus* spp. (1% each) (Fig. 3).

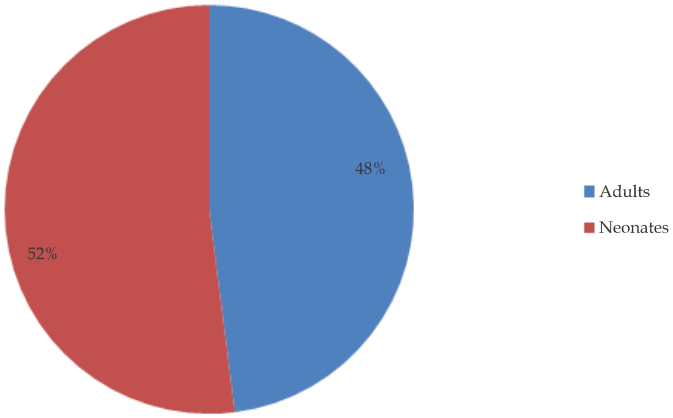

Fig 2: Distribution of positive blood cultures

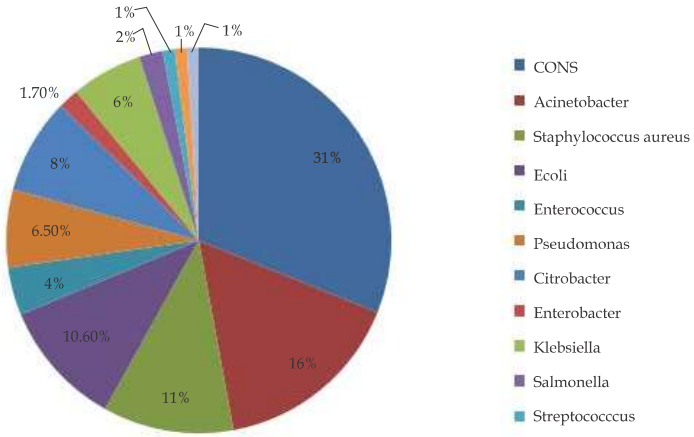

Fig 3: Bacterial Isolates (*n*=2700)

On comparing the data, it was found that the isolation of *Acinetobacter* spp. was increased in year 2018 (16.5%) in comparison to 15% in the year 2017. Likewise, *Escherichia coli* and *Klebsiella* spp. increased respectively from 9% and 5% in 2017 to 12% and 7.3% in 2018. The increase in the percentage of isolates was however not statistically significant ($p>0.05$). CONS isolation from blood culture was reduced to less than half (19%) in 2018 in comparison to year 2017 (43.5%) (Fig. 4). This difference was statistically significant ($p<0.05$) indicating improvement in the use of aseptic precautions by the Health care workers while collecting the blood samples.

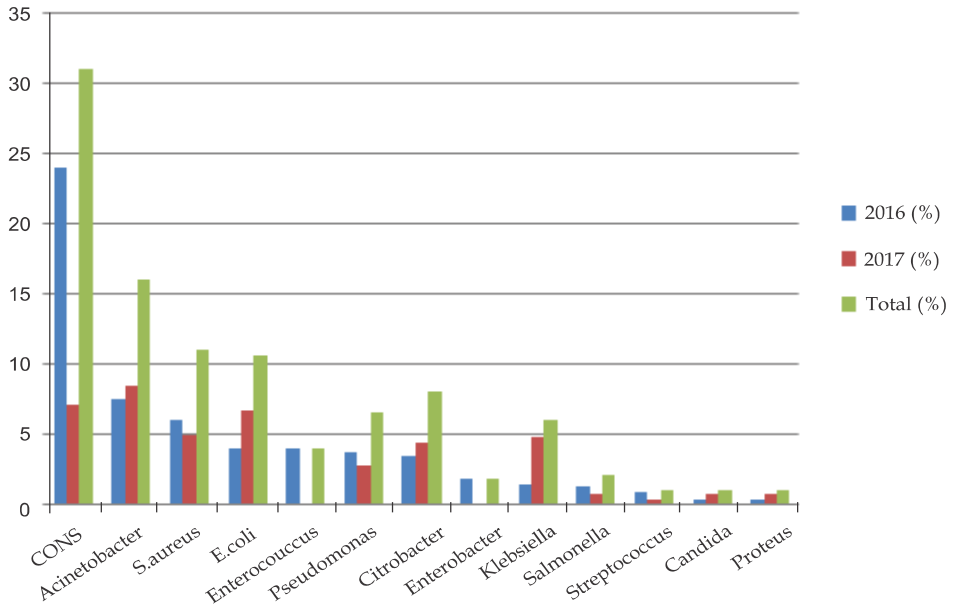

Fig 4: Year-wise distribution of the isolates

Out of 64 isolates of *Acinetobacter* spp., 5 isolates were found to be MDR, 5 were XDR and 2 were PDR. The pattern of drug resistance is depicted in Fig. 5.

The highest resistance was noted among *Acinetobacter* spp. for cefepime (70%), piperacillin/tazobactam (68%), amikacin (65%). gentamicin (62%) and ciprofloxacin (65%). The rates of resistance to Carbapenems was low (11%) and least to Polymyxin B (3%).

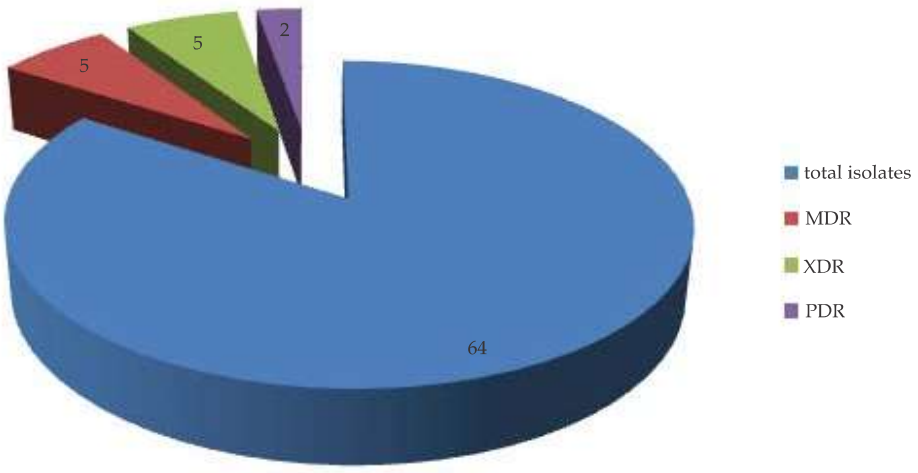

Fig 5: Distribution of resistance pattern in Acinetobacter

Discussion

In this study the isolation rate of blood culture positive cases was 15% which is similar to studies conducted by Mehta M. *et al*.[6], Qureshi M *et al*.[7] and Vijaya Devi A. *et al*.[8] who reported a culture positive rate of 16.4% and 16.6% and 16.8% respectively. The low rate of isolation may be explained by the fact that many of the patients probably received antibiotic therapy before the blood samples were drawn and in some cases the fastidious pathogens could not be grown on the routine culture. However Khanal B *et al*.[9] and Sharma PP *et al*.[10] reported high frequency of positive blood cultures accounting for 44%, 33.9% and 20.2% respectively whereas studies by Anbumani N *et al*.[11] and Arora U *et al*.[12] reported lower frequency of positive blood cultures accounting for 7.89% and 9.94%, respectively.

In the present study, men had high culture positivity (61%) as compared to women (39%). The results were consistent with the study done by Vanitha Rani N *et al*.[13] who reported high culture positivity (65% in males & 35% in female). A similar study was done by Kaur A and Singh V[14] who reported high culture positivity in men (65.22%). The reason for this difference may be due to more male newborns being admitted in NICU as they are more prone to neonatal septicemia as compared to female newborns.[15] However, Zenebe *et al*.[16] reported high culture positivity in women (59.2%) than men (40.8%) in their study.

In this study we found that most of the blood culture positive cases were from infants (60%) than other age groups (40% adults). This is in accordance with study conducted by Ayobola ED *et al*.[17] and Bchitrananda S. *et al*.[18] who reported culture positivity in infants up to 58.3% and 50% respectively. The high rate of isolation from infants may be due to their weak immune system as compared to adults & most infants take medication by means of intravascular devices that may easily introduce bacteria into their blood stream.

The rate of isolation of gram negative bacteria was higher (52%) than gram positive bacteria (48%) which is consistent with the studies conducted by Anbumani N *et al*.[11] where gram negative bacilli (56%) have taken over the gram positive isolates (44%) in terms of frequency of causing BSIs. Other studies conducted by Mehta M *et al*.,[5] Gupta S and Kashyap B[19] and Singh AK *et al*.[20] showed higher incidence of gram negative isolates (80.96%, 58.3% and 51.82%) in comparison to Gram positive isolates (18%, 41% and 46% respectively). In contrast, a study by Gill MK and Sharma S *et al*.[21] showed preponderance of gram positive cocci and Waishun AG *et al*.[22] reported 72% of bacteremias by gram positive cocci and 31% by gram negative bacilli.

The most common organism isolated in our study was Coagulase negative Staphylococcus (31%). It is predominant in all age groups. This observation is in concordance with studies conducted by Katyal A. *et al*.[23] showing CONS as the most predominant isolate (55.5%). However, on the contrary, reported isolation of CONS was 1.12% as studied by Anbumani *et al*[11]. In another study by Vijay Prakash Singha and Abhishek Mehta[3] more strains of *Staphylococcus aureus* (21.9%) were isolated from blood samples compared to CONS (15.6%) that was in contrast to our study. This variation in occurrence of CONS as blood pathogen is due to the fact that they are considered as most common skin commensals and their presence in blood may be the result of contamination due to non compliance of proper aseptic technique of blood collection. However, there are many studies suggesting that there is an increase in the isolation of CONS as true blood pathogen, more so in neonatal septicemia due to increased use of intravascular devices. As only a single blood culture specimen was collected from each patient, it was not possible in the present study to determine if the patients with CONS isolation had true bacteremia or the finding was due to skin contamination. Hence, clinicians are suggested to rule out the possible risk factors and to advice for repeat blood culture in case of CONS isolation.

Acinetobacter baumanii with 64 isolates (16%) was the most common gram negative bacilli followed by 43 isolates of *Escherichia coli* (10.6%), 32 isolates of *Citrobacter* spp. (8%), 26 isolates of *Pseudomonas* spp. (6.5%), 25 isolates of *Klebsiella* spp.(6%), 8 isolates of *Salmonella* Typhi (2%) *and 4 isolates of Proteus* spp. (1%). This finding is in accordance with the study conducted by Katyal A *et al*.[23] wherein *Acinetobacter* spp. were the predominant gram negative isolates (52.3%) followed by *Escherichia coli* (27.7%). However, on the contrary, study by Singh AK *et al*.[20] reported *E. coli* (37%) as the most common isolate followed by *Klebsiella pneumoniae* (26%), *S.* Typhi (25.9%) and *Acinetobacter* spp. (3.7%) respectively.

A total of 64 isolates of *Acinetobacter* spp. were recovered from blood cultures and their antibiotic sensitivity testing was included in our study. Most of these isolates were reported from patients in critical care units (ICU, PICU, NICU). Out of 64, 5

(8%) isolates were Multidrug resistant (MDR) and 5 (8%) were extensively drug resistant (XDR). 2 (3%) isolates were found to be Pan-drug resistant (PDR). Among patients with bacteremia caused by *Acinetobacter spp* an overall mortality exceeds 50%.[24,25] In comparison with susceptible strains of *Acinetobacter,* MDR infections are associated with additional increase in morbidity, mortality, length of hospital stay, and health care costs.[26] Providing effective treatment for infections caused by MDR *Acinetobacter spp* is a challenge. MDR strains typically require therapy with colistin, an older and relatively toxic polymyxin antimicrobial, and which attains poor serum and urine levels and has a limited track record in treating serious infections, including those caused by *Acinetobacter spp*. The rise in the incidence of MDR *Acinetobacter* is compounded by the lack of new antimicrobials in the pharmaceutical industry research and developmental pipeline. Overall, the proportion of global XDR strains of *Acinetobacter* has increased from <4% in 2000 to >60%, while the proportion of XDR strains of *Acinetobacter* in some regional nosocomial settings has more recently approached 90%.[27] In a recent study, authors reported that the increase in consumption of Carbapenems was significantly related to the development of resistance in *Acinetobacter* to Imipenem and Meropenem.

Organis Drawbacks

This study has certain limitations. First, it was a single-center study. Therefore the findings may not be generalized to other settings. Second, it was not possible to assess the infection control strategy, which could be an important risk factor.

Conclusion

Blood stream infections caused by *Acinetobacter* spp. is a tremendous challenge for physicians. When this pathogen is susceptible, *β*-lactam antibiotics are the preferred treatment. For XDR strains, combination Carbapenem-Polymyxin therapy is a rational approach. Given our limited therapeutic options, we must combine a multidisciplinary approach, including vigilant infection control practices, antimicrobial stewardship, and the combined efforts of multiple health care providers while addressing the infections caused by *Acinetobacter* species. In the meantime, we must learn how to optimize the efficacy of our current antimicrobials, to combat the crisis of infections caused by multi drug resistant *Acinetobacter* species.

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, or publication of this article.

References

1. Hugonnet S, Sax H, Eggimann P, *et al.* Nosocomial Bloodstream Infection and Clinical Sepsis**.** Emerging Infectious Diseases. Emerg Infect Dis. 2004 Jan;10(1):76–81.
2. Shah H, Bosch W, Kristine M. *et al.* Intravascular Catheter-Related Bloodstream Infection. Neurohospitalist. 2013 Jul;3(3):144–151.
3. Singh VP, Mehtab A. Bacteriological profile of bloodstream infections at a Rural tertiary care teaching hospital of Western Uttar Pradesh. Indian Journal of Basic and Applied Medical Research; 2017 June:6(3):393–401.
4. CLSI-Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twenty-second informational supplement. Wayne, PA, USA. CLSI, 2015.
5. Falagas ME, Koletsi PK, Bliziotis IA. The diversity of definitions of MDR and PDR *Acinetobacter baumanii* and *Pseudomonas aeruginosa.* Journal of Medical Microbiology. 2006;55:1619–29.
6. Mehta M, Pyria D, Varsha G. Antimicrobial susceptibility pattern of blood isolates from a teaching Hospital in north India. Japan J Infec Dis. 2005;58:174–76.
7. Qureshi M, Aziz F. Prevalence of microbial isolates in blood culture and their antimicrobial susceptibility profile. Biomedica. 2011;27:136–39.
8. Vijaya Devi A, Sahoo B, Damrolien S, Praveen SH, Lungran P, Ksh Mamta Devi. A Study on the Bacterial Profile of Bloodstream Infections in Rims Hospital. *(IOSR-JDMS).* 2015;14(1):18–23.
9. Khanal B, Harish BN, Sethuraman KR, Srinivasan S. Infective endocarditis: Report of prospective study in an Indian Hospital. Trop Doct. 2002;32:83–85.
10. Sharma PP, Halder D, Dutta AK. Bacteriological profile of neonatal septicemia. Ind. Pediatr. 1987;24:1011–17.
11. Anbumani N, Kalyani J, Mallika M. Original research distribution and antimicrobial susceptibility of bacteria isolated from blood cultures of hospitalized patients in a tertiary care hospital. Indian Journal for the practicing doctor. 2008;5(2). Available at: http;//www. indmedica. com/journals.php?journalid+3&is

sueid=1658&action= article (1 of 9).

12. Arora U, Devi P. Bacterial profile of blood stream infections and antibiotic resistance pattern of isolates. J K Sci. 2007;9:186–90.
13. Vanitha Rani N, Kannan G, Venkata Narendra M, *et al*. A retrospective study on blood stream infections and antibiotic susceptibility patterns in a tertiary care teaching hospital. Int. J Pharm Pharm Sci. 2012;4:543–8.
14. Kaur A, Singh V. Bacterial isolates and their antibiotic sensitivity pattern in clinically suspected cases of fever of unknown origin. JK Science. 2014;16:105–9.
15. Clinical and Laboratory Standards Institute. Performance Standard for Antimicrobial Susceptibility Testing, Twenty fifth informational supplement. M100-S25, 2015.
16. Zenebe T, Kannan S, Yilma D, *et al.* Invasive bacterial pathogens and their antibiotic susceptibility patterns in Jimma University Specialized Hospital, Jimma, Southwest Ethiopia. Ethiop J Health Sci. 2011;21:1–8.
17. Ayobola ED, Egbule OS, Omonigho O. Study of Prevalence and antimicrobial Susceptibility of Blood Culture Bacterial Isolates. Malaysian Journal of Microbiology. 2011;7(2)78–82.
18. Bchitrananda swain, Sarita Otta. Blood stream infection in teaching hospital. Annals of biological research. 2012;3(4):1923–28.
19. Gupta S, Kashyap B. Bacteriological profile and antibiogram of blood culture isolates from a tertiary care hospital of North India. Trop J Med Res. 2016 Jul;19(2):94–99.
20. Singh AK, Venkatesh V, Singh RP, Singh M. Bacterial and antimicrobial resistance profile of bloodstream infections, a hospital based study. CHRISMED J Health Res. 2014 Aug;1(3):140–44.
21. Gill MK, Sharma S. Bacteriological profile and antibiotic resistance pattern in blood stream infection in critical care units of a tertiary care hospital in North India. Indian J Microbiol Res. 2016;3(3):270–74.
22. Waishun AG, Wlekidan LN, Gebremariam SA, *et al.* Bacteriological profile and antimicrobial susceptibility patterns of blood culture isolates among febrile patients in Mekelle Hospital, Northern Ethiopia. Springer plus. 2015 Jul;4:314.
23. Katyal A, Singh D, Sharma M, *et al.* Bacteriological profile and antibiogram of aerobic blood culture isolates from intensive care units in a Teaching Tertiary Care Hospital. J Health Science Res. 2018;9(1):6–10.
24. Paul M, Weinberger M, Siegman-Igra Y, *et al. Acinetobacter baumannii*: emergence and spread in Israeli hospitals 1997–2002. J. Hosp. Infect. 2005;60:256–60.
25. Abbo A, Navon-Venezia S, Hammer-Muntz O, *et al.* Multidrug-resistant *Acinetobacter baumannii*. Emerg. Infect. Dis. 2005;11:22–29.
26. Munoz-Price LS, Weinstein RA**.** *Acinetobacter* infection. N. Engl. J.Med. 2008;358**:**1271–1281.
27. Pankey GA**.** Tigecycline. J. Antimicrob. Chemother. 2005;56:470–80.