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Determination of Antimicrobial Resistance Patterns in Bloodstream Infections-Isolated Bacteria From a University Tertiary Hospital Patients

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Abstract

Background: Bloodstream infections are considered a significant medical concern associated with high morbidity and mortality rates. Therefore, physicians should be guided to use antimicrobial susceptibility patterns in order to select appropriate empiric antimicrobial agents to treat the patients who suffer from bacteremia.

Objective: The present study aimed to determine antimicrobial resistance and susceptibility patterns in isolates collected from bloodstream infections.

Materials and Methods: To achieve this, a total of 710 bacterial blood culture isolates were collected from Sina hospital, and then susceptibility patterns to a number of antibiotics were analyzed according to Clinical and Laboratory Standards Institute guidelines.

Results: The identified isolates included *Staphylococcus aureus* 14 (20.6%), *Escherichia coli* 14 (20.6%), *Acinetobacter baumannii* 12 (17.6%), *Pseudomonas aeruginosa* 11 (16.2%), Coagulase-negative *Staphylococcus* 8 (11.8%), *Klebsiella pneumoniae* 6 (8.8%), and *Enterobacter* spp. 3 (4.4%). The total resistance rate to co-trimoxazole, ceftriaxone, ceftazidime, cefotaxime, ofloxacin, gentamicin, ciprofloxacin, levofloxacin, amikacin, and imipenem was 44 (64.7%), 42 (61.8%), 39 (57.4%), 38 (55.9%), 35 (51.51%), 32 (47.1%), 31 (45.6%), 25 (36.8%), and 27 (39.7%), respectively. Finally, the susceptibility rate to amikacin and imipenem was 43 (63.2%) and 41 (60.3%), respectively.

Conclusion: In general, *A. baumannii* strains isolated from blood cultures were resistant to most antibiotics and the greatest sensitivity was observed to gentamicin (58.3%) compared to other antibiotics. Therefore, gentamicin was found as the most effective antibiotic for treating bloodstream infections caused by *A. baumannii*.

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Background

The entrance of the bacteria into the bloodstream is called bacteremia, which is a serious and important infection that causes irreparable consequences including significant mortality rates. Accordingly, appropriate and immediate treatment is required for reducing remarkable morbidity and mortality rates.[1] Bacteremia in hematological disorders leads to remarkable fatality rates.[2] In the United States, approximately 200 000 cases of bacteremia and sepsis are reported annually, with 50% fatalities.[3] Because of the severity and life-threatening features, doing multiple cultures from patients and prescription of broad-spectrum antibiotics are of great importance.[4] The obtained results from the disk diffusion method and blood cultures determine the type of the prescribed antibiotics.[3] In addition, in South Africa and Ethiopia, the mortality rate due to sepsis is nearly 53%, which is considered an important health concern in developing countries.[5] Blood infections caused by opportunistic bacteria are considered as one of the major problems related to hospitalized and immunosuppressive patients.[6] Further, a blood infection caused by nosocomial organisms is regarded as one of the major problems of hospitalized patients. According to several studies, such infections comprise the major group of infections in some hospitals.[7,8] Different bacteria are involved in bloodstream infections such as coagulase-negative *Staphylococcus*, *S. aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter* spp., and *Escherichia coli*.[9] Each of these strains displays different susceptibility to various antibiotics. For example, the obtained results from an American study revealed that 22% of the fatal bloodstream infections cases were due to *E. coli*.[10] The most common method for laboratory diagnosis of blood infections is the culture and isolation of bacteria, followed by antimicrobial susceptibility testing.[11] Therefore, according to the interpretations of the common antibiotic resistance patterns, broad-spectrum antibiotics are prescribed as the first choice for treatment in most suspected septicemia cases.[12] Studying the involved bacteria in blood infections and antibiotic resistance patterns has an important role in empiric treatment. Furthermore, blood culture is still the best method used for detecting incriminated bacteria in bloodstream infections.[12,13] Accordingly, the current study sought to investigate the prevalence of different bacteria isolated from blood cultures in bloodstream infections and their antibiotic susceptibility patterns in patients residing in Sina hospital in Tabriz during (June) 2015-(July) 2016.

Materials and Methods

Bacterial Isolation

This experimental study was conducted by using 68 isolates which were positive to the blood cultures of all 710 collected samples from patients in Sina hospital during 2015-2016. Totally, 5 to 10 mL of blood sample was collected from each patient in order to identify the infectious agents. Then, the samples were cultured on the blood culture containing Kastanda medium in sterile conditions and incubated on the eosin methylene blue culture media and sheep blood agar for 24 hours. Negative cultures were cultivated on two mediums after 48 and 72 hours of incubation. Next, laboratory diagnostics were performed by using methods of diagnostic microbiology and tests such as Gram staining, biochemical tests, oxidase, motility, urea hydrolysis, indole production, production of SH2, and gelatin hydrolysis in order to detect Gram-negative bacterial isolates. Additionally, the catalase test, coagulase, optochin and hippurate and sample identification were implemented to detect Gram-positive bacteria.[14-16] Materials were purchased from Mast Group Ltd Company.

Disk Diffusion Agar Method

Disk diffusion method was conducted to determine resistance rates according to Clinical and Laboratory Standards Institute guidelines.[17,18] After thorough incubation, the diameter of the inhibition zone was measured and the bacteria were classified as resistant or sensitive. The used antibiotic disks included ciprofloxacin (5 μg), gentamicin (10 μg), co-trimoxazole (25 μg), imipenem (10 μg), ceftazidime (30 μg), cefotaxime (30 μg), levofloxacin (2 μg), amikacin (10 μg), and ceftriaxone (30 μg) purchased from Mast Diagnostics Ltd, the UK.

Analysis

The results were analyzed employing SPSS software, version 19.

Results

In the present study, a total of 710 blood samples were collected from patients residing in Sina hospital out of which 68 (9.6%) cases were positive to bacteria and susceptible to bloodstream infections. Forty-one (60.3%) and 27 (39.7%) of the collected samples belonged to male and female patients, respectively. In addition, the highest value of positive cultures was gathered from the intensive care unit ward, followed by emergency, burn, and internal wards (Figure 1). The identified isolates from the blood cultures were 14 *S. aureus* (20.6%), 14 *E. coli* (20.6%), 12 *A. baumannii* (17.6%), 11 *P. aeruginosa* (16.2%), 8 coagulase-negative *Staphylococcus* (11.8%), 6 *K. pneumoniae* (8.8%), and 3 *Enterobacter* spp. (4.4%), The details of which are provided in Table 1. Further, the total resistance rate to co-trimoxazole, ceftriaxone, ceftazidime, cefotaxime, ofloxacin, gentamicin, ciprofloxacin, levofloxacin, amikacin, and imipenem, was 44 (64.7%), 42 (61.8%), 39 (57.4%), 38 (55.9%), 35 (51.51%), 32 (47.1%), 31 (45.6%), 25 (36.8%), and 27 (39.7%), respectively.

Sensitivity and resistance rates to antibiotics in a different type of bacteria had various statistics. The greatest sensitivity to antibiotics belonged to *S. aureus* bacteria and *Enterococcus*, *A. baumannii*, and *P. aeruginosa* were the most resistant bacteria (Table 2).

Most antibiotic sensitivity among all the isolated

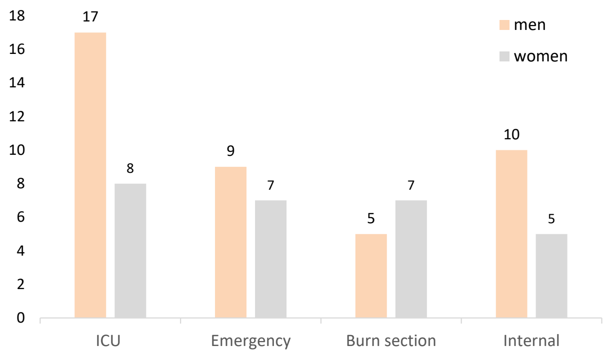

Figure 1. Distribution of Bacteria Isolated From Various Sectors in Terms of Gender.

Table 1. Distribution of Bacteria Isolated From Blood Cultures

Bacteria	Number	Percent
Staphylococcus aureus	14	20.6
E. coli	14	20.6
Acinetobacter baumannii	12	17.6
Pseudomonas aeruginosa	11	16.2
Coagulase negative Staphylococcus	8	11.8
Klebsiella pneumonia	6	8.8
Enterobacter	3	4.4
Total	68	100

Table 2. Pattern of Antibiotic Resistance and Antibiotic Susceptibility in the Isolated Bacteria of Blood

Antibiotic	*Staphylococcus aureus*		*Coagulase-Negative Staphylococci*		*E. coli*		*Acinetobacter baumannii*		*Pseudomonas aeruginosa*		*Klebsiella pneumonia*		*Enterococcus*	
	Resistant (R)	Sensitive (S)	R	S	R	S	R	S	R	S	R	S	R	S
Ceftriaxone	4 (28.6)	10 (71.4)	3 (37.5)	5 (62.5)	9 (64.3)	5 (35.7)	12 (100)	0 (0)	11 (100)	0 (0)	3 (50)	3 (50)	0 (0)	3 (100)
Ciprofloxacin	2 (14.3)	12 (85.7)	2 (25)	6 (75)	6 (42.8)	8 (57.1)	12 (100)	0 (0)	9 (81.8)	2 (18.2)	0 (0)	6 (100)	0 (0)	3 (100)
Gentamicin	4 (28.6)	10 (71.4)	0 (0)	8 (100)	6 (42.8)	8 (57.1)	5 (41.7)	7 (58.3)	11 (100)	0 (0)	5 (83.3)	1 (16.7)	1 (33.3)	2 (66.7)
Co-trimoxazole	3 (21.4)	11 (78.6)	2 (25)	6 (75)	10 (71.4)	4 (28.6)	12 (100)	0 (0)	11 (100)	0 (0)	4 (66.7)	2 (33.3)	2 (66.7)	1 (33.3)
Amikacin	3 (21.4)	11 (78.6)	2 (25)	6 (75)	0 (0)	14 (100)	10 (83.3)	2 (16.7)	9 (81.8)	2 (18.2)	1 (16.7)	5 (83.3)	0 (0)	3 (100)
Imipenem	2 (14.3)	12 (85.7)	1 (12.5)	7 (87.5)	2 (14.3)	12 (85.7)	10 (83.3)	2 (16.7)	10 (90.9)	1 (9.1)	2 (33.3)	4 (66.7)	0 (0)	3 (100)
Ceftazidime	1 (7.1)	13 (92.9)	2 (25)	6 (75)	8 (57.1)	6 (42.8)	12 (100)	0 (0)	10 (90.9)	1 (9.1)	4 (66.7)	2 (33.3)	2 (66.7)	1 (33.3)
Cefotaxime	2 (14.3)	12 (85.7)	3 (37.5)	5 (62.5)	7 (50)	7 (50)	12 (100)	0 (0)	10 (90.9)	1 (9.1)	4 (66.7)	2 (33.3)	0 (0)	3 (100)
Levofloxacin	1 (7.1)	13 (92.9)	3 (37.5)	5 (62.5)	4 (28.6)	10 (71.4)	12 (100)	0 (0)	9 (81.8)	2 (18.2)	2 (33.3)	4 (66.7)	0 (0)	3 (100)
Ofloxacin	3 (21.4)	11 (78.6)	4 (50)	4 (50)	6 (42.8)	8 (57.1)	11 (91.7)	1 (8.3)	10 (90.9)	1 (9.1)	1 (16.7)	5 (83.3)	0 (0)	3 (100)

Data are shown as No. (%).

Table 3. Overall Sensitivity and Total Resistance of All Isolates From Blood

Antibiotics	Number of Resistant Isolates(%)	Number of Sensitive Isolates (%)
Co-trimoxazole	44 (64.7)	24 (35.3)
Ceftriaxone	42 (61.8)	26 (38.2)
Ceftazidime	39 (57.4)	29 (42.6)
Cefotaxime	38 (55.9)	30 (44.1)
Ofloxacin	35 (51.5)	33 (48.5)
Gentamicin	32 (47.1)	36 (53.9)
Ciprofloxacin	31 (45.6)	37 (54.4)
Levofloxacin	31 (45.6)	37 (54.4)
Amikacin	25 (36.8)	43 (63.2)
Imipenem	27 (39.7)	41 (60.3)

bacteria was related to amikacin and imipenem at the rate of 43 (63.2%) and 41 (60.3%), respectively. Furthermore, the highest resistance rate was observed to co-trimoxazole and ceftriaxone at the rate of 44 (64.7%) and 42 (61.8%), respectively (Table 3).

Discussion

Bloodstream infections are classified as the most dangerous human diseases.[19] During the past decades, the mortality rate as a result of septicemia has reached up to 78%.[20] Antibiotic resistance is considered as another major concern, which leads to a complicated treatment procedure.[21] The results of blood cultures are clinically and epidemiologically important. The current study attempted to determine the resistance and susceptibility patterns in a number of cephalosporines, co-trimoxazole, carbapenems and, aminoglycosides which are prescribed for treating bloodstream infections.

Based on the results, the highest resistance rate was observed to co-trimoxazole and ceftriaxone and the highest sensitivity was associated with amikacin and imipenem among all the participating bacteria.

A European study reported the excess mortality rates due to the expansion of multidrug-resistant *Staphylococcus aureus* as the main cause of bloodstream infections.[22] According to reported results in Ethiopia, the frequency of contributing gram-positive and gram-negative bacteria was 77.4% and 22.6%, respectively, and the predominant bacterial isolates were *S. aureus* (50.0%), *Klebsiella* (14.02%), *E. coli* (3.6%), and *Acinetobacter* (2.4%), respectively.[23] In another study in India, the most common Gram-positive and negative bacteria in blood culture were *S. aureus* (33.4%), *Enterobacteriaceae* (17%), and *P. aeruginosa* (9.4%). Moreover, antimicrobial resistance pattern in gram-positive and negative bacteria was as Amoxicillin (88.7%), ampicillin (95.6%), and cotrimoxazole (86.7%), respectively.[24] Based on above-mentioned results, *S. aureus* and *E. coli* and other members of Enterobacteriaceae have a main role in the incidence of bloodstream infections in different regions. Additionally, the mentioned findings represent different susceptibility and resistance rates. This finding could be justified based on the prescribed drugs in these areas. The results of the present study regarding the prevalence of involved bacterial species are in line with those of Radha et al[25] including *E. coli* (37.8%), *Klebsiella* (24.2%), *S. aureus* (14.4%), *P. aeruginosa* (13.6%), *and* Enterobacter (1.4%). In addition, based on the results related to the culture in other studies, the percentage and the amount of distribution rate differ from each other.[26] The resistance and susceptibility to antibiotics in studies which were conducted in Iran and abroad are different.[27,28] It probably gives rise to indiscriminate consumption and uncontrolled usage of broad-spectrum antibiotics including the third generation of cephalosporins such as ceftriaxone. Meanwhile, *S. aureus* and *Enterococcus* isolated from blood cultures showed more sensitivity to most antibiotics while *A. baumannii* and *P. aeruginosa* were more resistant to most antibiotics. These 2 species have intrinsic ability to be resistant to more antibiotics by means of acquiring the genes which encode the resistance determinants.[29]

Further, imipenem represented the most activity against all strains. These results are in conformity with the reported data from India, Brazil, and China, as well as the results obtained by Haddad et al about imipenem and its efficacy against the strains in the intensive care unit (30-35). Furthermore, in the present study, the most resistance of *S. aureus* to antibiotics was reported to ceftriaxone and gentamicin and the most resistance of coagulase-negative staphylococci was related to ofloxacin, levofloxacin, and cefotaxime. Moreover, the most resistance of *E. coli* to antibiotics was related to co-trimoxazole and ceftriaxone. Additionally, amikacin and imipenem were the most effective antibiotics against the infections caused by *E. coli*. The high resistance rate to co-trimoxazole in *E. coli* isolates led to a change in therapeutic option to quinolones.[36]

In addition, *A. baumannii* isolates were resistant to most antibiotics (100%) such as ceftriaxone, ciprofloxacin, co-trimoxazole, ceftazidime, cefotaxime, and levofloxacin. Only gentamicin was more sensitive (58.3%) compared to other antibiotics. Recent studies show the importance of resistance to *A. baumannii* to most antibiotics in bloodstream infections.[37-39] In Asia, more antibiotic resistance pattern is relatively similar to the current investigation.[40] The resistance rate of *P. aeruginosa* to imipenem, ceftazidime, and ciprofloxacin in Turkey was reported 26.4%, 47.4%, 29%, respectively.[41] In the present study, the *P. aeruginosa* strains were resistant to most antibiotics, especially imipenem and ceftazidime with a value of 90.9% and the most notable point was the complete resistance (100%) of the isolates to ceftriaxone, gentamicin, and co-trimoxazole. In a study conducted in the United States, resistance to ceftazidime in *Klebsiella* and *Enterobacter* isolates was reported up to 1% and 9%, respectively[42] while in another study conducted in Tehran, the amount of resistance were 94.4% and 42.9%, respectively.[3] Further, the resistance of *Klebsiella* and *Enterobacter* isolates to ceftazidime was 66.7% in the current study. In addition to antibiotic resistance, the other medical concern is the initial antibiotic receiving by the patients, which losses the efficacy of choice antibiotics.[43]

Conclusion

In general, based on the findings of the current study, amikacin and co-trimoxazole were the most susceptible and resistant antibiotics against the pathogen bacteria, respectively. The most significant resistance rate was observed in *A. baumannii* strains and the greatest sensitivity to gentamicin compared to other antibiotics, therefore, gentamicin was found to be the most effective antibiotic in treating the bloodstream infections caused by *A. baumannii*. Considering the importance of bloodstream infections in hospitals and their dramatically high fatalities, selecting an appropriate antibiotic for dealing with these infections is very crucial. Antibiotic resistance poses a serious health concern. Therefore, determining resistance and susceptibility patterns is highly significant. Furthermore, preventing the emergence of more resistance necessitates recognizing the resistance mechanisms.

Authors' Contributions

All the authors had an equal role in designing, working, analyzing, and writing the manuscript. In addition, all the authors read and approved the final manuscript.

Ethical Approval

Informed consent form was not applicable in our study.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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References

1. 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. Ann Clin Microbiol Antimicrob. 2004;3:7. doi:10.1186/1476-0711-3-7
2. Cherif H, Kronvall G, Bjorkholm M, Kalin M. Bacteraemia in hospitalised patients with malignant blood disorders: a retrospective study of causative agents and their resistance profiles during a 14-year period without antibacterial prophylaxis. Hematol J. 2003;4(6):420-426. doi:10.1038/sj.thj.6200334
3. Arbo MD, Snydman DR. Influence of blood culture results on antibiotic choice in the treatment of bacteremia. Arch Intern Med. 1994;154(23):2641-2645.
4. Ebrahimzadeh Leylabadlo H, Pourlak T, Zahedi Bialvaei A, Aghazadeh M, Asgharzadeh M, Samadi Kafil H. Extended-spectrum beta-lactamase producing gram negative bacteria in Iran: a review. Afr J Infect Dis. 2017;11(2):39-53. doi:10.21010/ajid.v11i2.6
5. Aiken AM, Mturi N, Njuguna P, et al. Risk and causes of paediatric hospital-acquired bacteraemia in Kilifi District Hospital, Kenya: a prospective cohort study.

Lancet. 2011;378(9808):2021-2027. doi:10.1016/s0140-6736(11)61622-x
6. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis. 2004;39(3):309-317. doi:10.1086/421946
7. Pittet D, Li N, Woolson RF, Wenzel RP. Microbiological factors influencing the outcome of nosocomial bloodstream infections: a 6-year validated, population-based model. Clin Infect Dis. 1997;24(6):1068-1078.
8. Ebrahimzadeh Leylabadlo H, Samadi Kafil H, Yousefi M, Aghazadeh M, Asgharzadeh M. Persistent infection with metallo-beta-lactamase and extended spectrum beta-lactamase producer *Morganella morganii* in a patient with urinary tract infection after kidney transplantation. J Nat Sci Biol Med. 2016;7(2):179-181. doi:10.4103/0976-9668.184707
9. Cleven BE, Palka-Santini M, Gielen J, Meembor S, Kronke M, Krut O. Identification and characterization of bacterial pathogens causing bloodstream infections by DNA microarray. J Clin Microbiol. 2006;44(7):2389-2397. doi:10.1128/jcm.02291-05
10. Rodriguez-Bano J, Picon E, Gijon P, et al. Risk factors and prognosis of nosocomial bloodstream infections caused by extended-spectrum-beta-lactamase-producing *Escherichia coli*. J Clin Microbiol. 2010;48(5):1726-1731. doi:10.1128/jcm.02353-09
11. Morrell M, Fraser VJ, Kollef MH. Delaying the empiric treatment of *Candida* bloodstream infection until positive blood culture results are obtained: a potential risk factor for hospital mortality. Antimicrob Agents Chemother. 2005;49(9):3640-3645. doi:10.1128/aac.49.9.3640-3645.2005
12. Zaragoza R, Artero A, Camarena JJ, Sancho S, Gonzalez R, Nogueira JM. The influence of inadequate empirical antimicrobial treatment on patients with bloodstream infections in an intensive care unit. Clin Microbiol Infect. 2003;9(5):412-418.
13. Opota O, Croxatto A, Prod'hom G, Greub G. Blood culture-based diagnosis of bacteraemia: state of the art. Clin Microbiol Infect. 2015;21(4):313-322. doi:10.1016/j.cmi.2015.01.003
14. Burnie JP, Naderi-Nasab M, Loudon KW, Matthews RC. An epidemiological study of blood culture isolates of coagulase-negative staphylococci demonstrating hospital-acquired infection. J Clin Microbiol. 1997;35(7):1746-1750.
15. Jiang JH, Chiu NC, Huang FY, et al. Neonatal sepsis in the neonatal intensive care unit: characteristics of early versus late onset. J Microbiol Immunol Infect. 2004;37(5):301-306.
16. Haley RW, Culver DH, White JW, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol. 1985;121(2):182-205.
17. Forbes BA, Sahm DF, Weissfeld AS. Study Guide for Bailey and Scott's Diagnostic Microbiology. Mosby; 2007.
18. Brown DF, Edwards DI, Hawkey PM, et al. Guidelines for the laboratory diagnosis and susceptibility testing of methicillin-resistant *Staphylococcus aureus* (MRSA). J Antimicrob Chemother. 2005;56(6):1000-1018. doi:10.1093/jac/dki372
19. Dhillon RH, Clark J. ESBLs: A Clear and Present Danger? Crit Care Res Pract. 2012;2012:625170. doi:10.1155/2012/625170
20. Edmond MB, Wallace SE, McClish DK, Pfaller MA, Jones RN, Wenzel RP. Nosocomial bloodstream infections in United States hospitals: a three-year analysis. Clin Infect Dis. 1999;29(2):239-244. doi:10.1086/520192
21. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P t. 2015;40(4):277-283.
22. de Kraker ME, Davey PG, Grundmann H. Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteremia: estimating the burden of antibiotic resistance in Europe. PLoS Med. 2011;8(10):e1001104. doi:10.1371/journal.pmed.1001104
23. Mulu W, Kibru G, Beyene G, Damtie M. Postoperative nosocomial infections and antimicrobial resistance pattern of bacteria isolates among patients admitted at Felege Hiwot Referral Hospital, Bahirdar, Ethiopia. Ethiop J Health Sci. 2012;22(1):7-18.
24. Sangwan J, Mane P, Vohra P, Lathwal S, Malik AK. Bacteriologic Profile and Antimicrobial Resistance of Blood Culture Isolates of Septicemic Patients from Various Intensive Care Units in a Teaching Tertiary Care Institute of Haryana, India. Int J Curr Microbiol Appl Sci. 2016;5(7):599-608. doi:10.20546/ijcmas.2016.507.067
25. Santa A, Rao TS. Retrospective Analysis of Blood Stream Infections and Antibiotic Susceptibility Pattern of Gram Negative Bacteria in a Tertiary Care Cancer Hospital. Health Sciences. 2017;6(12):19-26.
26. Vincent JL, Brealey D, Libert N, et al. Rapid diagnosis of infection in the critically ill, a multicenter study of molecular detection in bloodstream infections, pneumonia, and sterile site infections. Crit Care Med. 2015;43(11):2283-2291. doi:10.1097/ccm.0000000000001249
27. Trecarichi EM, Pagano L, Candoni A, et al. Current epidemiology and antimicrobial resistance data for bacterial bloodstream infections in patients with hematologic malignancies: an Italian multicentre prospective survey. Clin Microbiol Infect. 2015;21(4):337-343. doi:10.1016/j.cmi.2014.11.022
28. Ghadiri H, Vaez H, Khosravi S, Soleymani E. The antibiotic resistance profiles of bacterial strains isolated from patients with hospital-acquired bloodstream and urinary tract infections. Crit Care Res Pract. 2012;2012:890797. doi:10.1155/2012/890797
29. Bonomo RA, Szabo D. Mechanisms of multidrug resistance in *Acinetobacter* species and *Pseudomonas aeruginosa*. Clin Infect Dis. 2006;43 Suppl 2:S49-56. doi:10.1086/504477
30. Mendes C, Oplustil C, Sakagami E, Turner P, Kiffer C. Antimicrobial susceptibility in intensive care units: MYSTIC Program Brazil 2002. Braz J Infect Dis. 2005;9(1):44-51. doi:/S1413-86702005000100008
31. Hadadi A, Rasoulinejad M, Maleki Z, Yonesian M, Shirani A, Kourorian Z. Antimicrobial resistance pattern of Gram-negative bacilli of nosocomial origin at 2 university hospitals in Iran. Diagn Microbiol Infect Dis. 2008;60(3):301-305. doi:10.1016/j.diagmicrobio.2007.10.010
32. Zamani S, Nasiri MJ, Noorazar Khoshgnab B, Ashrafi A, Abdollahi A. Evaluation of antimicrobial resistance pattern of nosocomial and community bacterial pathogens at a teaching hospital in Tehran,Iran. Acta Med Iran. 2014;52(3):182-186.
33. Sahoo D, Mohanty L, Panda SS, Mishra SN. Bacteriological analysis of blood culture isolates in patients with sepsis in a tertiary care hospital of eastern India. Int J Contemp Med Res. 2016;3(12):3448-3450.
34. Opintan JA, Newman MJ. Prevalence of antimicrobial resistant pathogens from blood cultures: results from a laboratory based nationwide surveillance in Ghana. Antimicrob Resist Infect Control. 2017;6:64. doi:10.1186/s13756-017-0221-0
35. Xie Y, Tu B, Xu Z, et al. Bacterial distributions and prognosis of bloodstream infections in patients with liver cirrhosis. Sci Rep. 2017;7(1):11482. doi:10.1038/s41598-017-11587-1
36. Karaca Y, Coplu N, Gozalan A, Oncul O, Citil BE, Esen B. Co-trimoxazole and quinolone resistance in Escherichia coli isolated from urinary tract infections over the last 10 years.

Int J Antimicrob Agents. 2005;26(1):75-77. doi:10.1016/j.ijantimicag.2005.03.012

37. Batirel A, Balkan, II, Karabay O, et al. Comparison of colistin-carbapenem, colistin-sulbactam, and colistin plus other antibacterial agents for the treatment of extremely drug-resistant Acinetobacter baumannii bloodstream infections. Eur J Clin Microbiol Infect Dis. 2014;33(8):1311-1322. doi:10.1007/s10096-014-2070-6
38. Munoz-Price LS, Zembower T, Penugonda S, et al. Clinical outcomes of carbapenem-resistant Acinetobacter baumannii bloodstream infections: study of a 2-state monoclonal outbreak. Infect Control Hosp Epidemiol. 2010;31(10):1057-1062. doi:10.1086/656247
39. Hasani A, Ahangarzadeh Rezaee M, Asadi Faezi N, et al. Determination Pattern of Antimicrobial Resistance of Pseudomonas Isolated from Patients in a University Tertiary Hospital. ABCmed. 2017;5(3):8-13. doi:10.7575/aiac.abcmed.17.05.03.03
40. Falagas ME, Karveli EA, Siempos, II, Vardakas KZ. Acinetobacter infections: a growing threat for critically ill patients. Epidemiol Infect. 2008;136(8):1009-1019. doi:10.1017/s0950268807009478
41. Dogru A, Sargin F, Celik M, Sagiroglu AE, Goksel MM, Sayhan H. The rate of device-associated nosocomial infections in a medical surgical intensive care unit of a training and research hospital in Turkey: one-year outcomes. Jpn J Infect Dis. 2010;63(2):95-98.
42. Huang SS, Labus BJ, Samuel MC, Wan DT, Reingold AL. Antibiotic resistance patterns of bacterial isolates from blood in San Francisco County, California, 1996-1999. Emerg Infect Dis. 2002;8(2):195-201. doi:10.3201/eid0802.010102
43. Kang CI, Kim SH, Park WB, et al. Bloodstream infections caused by antibiotic-resistant gram-negative bacilli: risk factors for mortality and impact of inappropriate initial antimicrobial therapy on outcome. Antimicrob Agents Chemother. 2005;49(2):760-766. doi:10.1128/aac.49.2.760-766.2005