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Original article

Antibiotic resistance in bacteria isolated from blood cultures in Shiraz, Southwest Iran

Farshad Kakian[1], Arman Jobeiri [2], Zahra Hashemizadeh[1], Babak Shirazi Yeganeh [3], Mohammad Motamedifar [4,5*]

[1] Department of Bacteriology and Virology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
[2] Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.
[3] Department of Pathology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[4] Shiraz HIV/AIDS Research Center, Institute of Health & Department of Bacteriology and Virology, Shiraz University of Medical Sciences, Shiraz, Iran.
[5] Department of Medical Microbiology, School of Medicine, Shiraz University of Medical Sciences, Fars, Iran.

***. Corresponding author:** Mohammad Motamedifar. Shiraz HIV/AIDS Research Center, Institute of Health & Department of Bacteriology and Virology, Shiraz University of Medical Sciences, Shiraz, Iran. Email: motamedm@sums.ac.ir.

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Abstract

Introduction: Bloodstream infections (BSI) are a leading cause of morbidity and mortality around the world. In terms of appropriate therapeutic options, antimicrobial drug resistance among bacterial pathogens is a major source of concern. The purpose of this study was to provide local information on antibiotic resistance patterns in Faghihi Hospital located in Shiraz, Southwest Iran.

Methods: The frequency and antibiogram patterns of blood culture bacterial isolates were studied from January 2018 to December 2019. For antibacterial susceptibility testing, the disk diffusion method was used, which met the standard criteria of the Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing 28th edition.

Result: During the study period, 576 (9.7%) of the 5935 blood cultures tested positive. Gram positive bacteria made up 340 (59.1%) of the positive cultures, while gram negative bacteria made up 236 (40.9%). *S. aureus* was the most common isolate (26.2%), followed by *S. epidermidis* (15.1%) and *E. coli* (14.2%). Vancomycin was the most effective antibiotic against gram positive bacteria, but no antibiotic was available for gram negative bacteria. Amikacin was most effective against *E. coli* isolates, while Imipenem was most effective against *P. aeruginosa* isolates.

Conclusion: Our findings suggest and emphasize the importance of observing resistance patterns that affect empirical therapy and infection control methods on a yearly basis by monitoring blood culture isolates and susceptibility patterns.

Keywords: Bacterial pathogens**,** Blood cultures, Antibacterial susceptibility, Resistance, Iran

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Introduction

Bloodstream infections (BSIs) are infections that occur in the blood and include bacteremia when the infections are bacterial and fungemias when the infections are fungal. Bacteremia can infect and spread throughout the body via the bloodstream (hematogenous spread). Bloodstream infections are among the most common healthcare-associated infections, causing significant morbidity and mortality throughout the world (1). The most common cause of BSI is bacteria. Gram-positive and Gram-negative bacteria are found in BSIs, and their prevalence varies depending on time and location (2). These infections require immediate diagnosis and treatment with appropriate antibiotics. Bacterial resistance frequently leads to treatment failure, which has serious consequences (3). Inadequate empiric antibacterial therapy, defined as using an antibacterial agent for a pathogen that is not sensitive, has been linked to higher mortality rates (3).

Early antimicrobial treatment is critical for reducing morbidity and mortality in patients with bloodstream infections (4). Even though blood cultures have a long turnaround time, resulting in ineffective therapy, they continue to be the gold standard for diagnosing bloodstream infections (5).

As a result, it is critical to determine the prevalence of antimicrobial resistance in specific geographical locations at a single point in time, as well as to provide longitudinal data to track changes over time (6). Antimicrobial chemotherapy is almost always empirical, and it must be based on knowledge of the most isolated etiological agents and their antimicrobial susceptibility patterns (1). The prevalence and antimicrobial susceptibility profiles of blood culture isolates from Shiraz's Shahid Faghihi Hospital in 2018-2019 are reported in this study.

Methods

From January 2018 to December 2019, the results of blood cultures and antibacterial susceptibility tests were obtained from the Faghihi Hospital database (code of ethics: IR.SUMS.MED.REC.1398.616). All blood samples were cultured in BACTEC and stored for 5 days according to hospital standards. The study excluded samples that did not pass an antibacterial susceptibility test. Antibacterial susceptibility testing was performed using the disk diffusion method and the minimum inhibitory concentration (MIC), in accordance with the Clinical and Laboratory Standards Institute (CLSI) Performance Standards for Antimicrobial Susceptibility Testing 28th edition. As the Secretariat of ISO Technical Committee (TC) 212, clinical laboratory testing, and in vitro diagnostic test systems, CLSI contributes to the development of international standards. Antibiotic disks (Padtan-Teb, Tehran, Iran) were used for antibacterial susceptibility test were penicillin, amoxicillin, ampicillin, cefixime, cefotaxime, imipenem, ceftriaxone, gentamycin, co-trimoxazole, ciprofloxacin, cefepime, clindamycin, amikacin, erythromycin, cephazolin, cephalothin, cefoxitin, piperacillin tazobactam, vancomycin (MIC), rifampicin depending of type of the isolated bacteria.

Statistical analysis

The data was collected, and frequencies and resistance patterns were extracted using the SPSS program. The significance level was set at P 0.05 for descriptive statistics (frequency, percentage, mean, and standard deviation).

Results

During the study period, 576 (9.7%) of the 5935 blood cultures were positive. 340 (59.1%) of the total positive cultures were gram positive, while 236 (40.9%) were gram negative (Table 1).

Staphylococcus aureus, *Staphylococcus epidermidis*, *methicillin resistant CoNS* (*coagulase negative staphylococcus*), *Methicillin-resistant Staphylococcus aureus* (*MRSA)*, and *Enterococci* sp. were the most common gram-positive organisms, accounting for 56.8% of all isolates. Resistance rates (%) for the most common gram-positive cocci are shown in Table 2.

Acinetobacter spp., *Escherichia coli*, *P. aeruginosa*, *Klebsiella sp*, *Enterobacter spp.*, and *Alcaligenes sp*. were the most common gram-negative bacteria, accounting for 42.3% of all isolates. Resistance rates (%) for the most common gram-negative bacilli are shown in Table 3.

Vancomycin was the most effective antibiotic against gram-positive cocci, while imipenem and piperacillin/tazobactam were the most effective against gram-negative bacilli. Fortunately, MRSA has a high susceptibility to vancomycin (98%). *S. aureus* and *S. epidermidis* were also susceptible at 99.3% and 100%, respectively.

Acinetobacter species and *P. aeruginosa* were the most resistant pathogens among gram negative bacilli. Piperacillin/tazobactam and imipenem were the most effective antibiotics against them.

Table 1. Frequency of isolated bacteria

Bacteria		Frequency	Percent
	Staphylococcus. Aureus	151	26.2
	Staphylococcus. Epidermidis	87	15.1
	E. coli	82	14.2
	Acinetobacter sp.	57	9.9
	MRSA	51	8.9
	Klebsiella sp.	34	5.9
	Alcaligenes sp.	28	4.9
	Enterococci sp.	21	3.6
	Methiciline Resistant CoNS	17	3.0
	Pseudomonas sp.	15	2.6
	Enterobacter sp.	12	2.1
	Non hemolytic *Sterptococcus*	6	1.0
	Alpha Hemolytic *Streptococci*	5	0.9
	Salmonella sp.	3	0.5
	Brucella	2	0.3
	Flavobacter sp.	2	0.3
	Micrococci sp.	1	0.2
	Proteus sp.	1	0.2
	Streptococcus pneumonia	1	0.2
	Total	576	100.0

Table 2. Resistance rates (%) for the most common gram-positive cocci

	S. aureus	*S. epidermidis*	MRSA	MrCoNS	*Enterococci sp.*
Vancomycin	0.7	0	2	0	52.4
Rifampin	4	6.9	35.3	29.4	85.7
Cephalotin	9.9	10.3	72.5	76.5	85.7
Cefazolin	9.9	11.5	76.5	76.5	81
Cefoxitin	7.3	12.6	98	100	95.2
Ciprofloxacin	39.1	43.7	96.1	100	90.5
Amoxicillin	76.2	73.6	100	100	61.9
Clindamycin	55	63.2	96.1	100	100
Ampicillin	77.5	74.7	100	100	66.7
Erythromycin	64.9	67.8	98	100	100
Penicillin	77.5	75.9	100	100	85.7

Table 3. Resistance rates (%) for the most common

	E. coli	*Acinetobacter spp.*	*Klebsiella sp.*	*Alcaligenes sp.*	*P. aeruginosa*	*Enterobacter spp.*
Imipenem	6.1	82.5	44.1	21.4	26.7	25
Ceftriaxone	61	96.5	67.6	92.9	80	33.3
Ampicillin/ sulbactam	51.2	89.5	73.5	100	93.3	66.7
Piperacilin/ tazobactam	8.5	68.4	58.8	10.7	33.3	8.3
Amikacin	4.9	89.5	35.3	92.9	53.3	16.7
Gentamicin	25.6	89.5	58.8	92.9	53.3	16.7
Cotrimoxazole	79.3	80.7	76.5	92.9	80	66.7
Cefepime	42.7	98.2	67.6	85.7	40	25
Ciprofloxacin	54.9	78.9	64.7	78.6	33.3	25

Discussion

Annual reporting of antibiotic resistance rates is critical for developing antimicrobial resistance control programs and making effective empirical therapy recommendations (7, 8). Furthermore, the data will aid in modifying existing techniques for lowering resistance rates and identifying new clinically significant resistances as they emerge (6). Based on this research, the following observations can be made. A comparison with previous Shiraz studies to highlight the changes over time in the same region was also provided. Antibiotic therapy plans and guidelines that are based on evidence-based data may help to improve the current situation of high antibiotic resistance. More than half of the blood samples processed came from emergency departments. This could be described by the local exercise in these wards that emphasizes the importance of blood culture for patients with fever.

In our study, the most common gram-negative bacteria were *Escherichia coli*, *Acinetobacter spp.*, and *Klebsiella sp.*, and the most common gram-positive bacteria were *S. aureus*, followed by *S. epidermidis*. Our findings are consistent with the findings of a study conducted in 2016 in Iran by Hamishehkar and colleagues, who discovered that the most common gram-positive organisms were *S. aureus* and *S. epidermidis* (9). Furthermore, our findings differ from those of Maham and colleagues in Tehran (2018) hospitals, as well as Pourakbari and colleagues, who found that the most common gram-positive organisms were CoNS (10, 11).

According to some studies in Iran, the most common gram-negative bacteria that cause bloodstream infections are *K. pneumoniae*, *E. coli*, *P. aeruginosa*, and *Enterobacter*. In another study, *Klebsiella* was the most common gram-negative isolated bacteria among 2325 samples in a study conducted by Mahmoudi and colleagues in Iranian hospitals in 2017 (12).

According to some studies, *Acinetobacter species*, *S. typhi*, and *E. coli* are the most common gram-negative bacteria that cause bloodstream infections. *E. coli* and *Klebsiella* were the most common gram-negative isolated bacteria among 3807 samples in a study conducted by Bhullar and colleagues in Brazil's hospitals. The most common gram-positive bacteria in this study in Brazil were *S. aureus* and *Coagulase-negative Strep* (13).

Blair and colleagues found that the most isolated gram-negative bacteria in 2015 were *P. aeruginosa*, *E. coli*, *K. pneumoniae*, and *S. typhi*, rather than *Citrobacter*, *Acinetobacter*, *Proteus*, and *Enterobacter spp* (14). In a study performed by Gales and colleagues, in India, the most frequently isolated gram-positive bacteria was *S. aureus*, followed by *E. feacalis* and the other remaining *Streptococcus* and *Staphylococcus spp* (15).

According to this study, the most important finding was that vancomycin retained potency against *S. aureus*, *Staphylococcus epidermidis*, *methicillin resistant CoNS*, and especially MRSA, which are the most common gram-positive pathogens found in Faghihi Hospital. This is most likely due to logical administration and treatment duration. This study confirmed the findings of a previous study conducted

by Nobandegani and colleagues in Shiraz, Iran (16). The sensitivity to vancomycin among *Enterococci sp.* has decreased from 77.8% in the previous study to 52.8% in this study, indicating that resistance is increasing in this organism (16).

Because *S. aureus* and *S. epidermidis* are more susceptible to rifampin and have a higher prevalence than MRSA, this antibiotic can be used in empirical therapy. It is worth noting that resistance to Rifampin has decreased over time when compared to the previous study, which found 30% of *S. aureus* resistance compared to 4% in this study (16). *MRSA* is almost completely resistant to all cephalosporins, and administration of this class is not advised. There is an alarming rate of resistance (52.4%) to vancomycin, the most effective antibiotic against this organism thus far.

Amikacin is the best choice of antibiotic for the most common gram-negative bacteria, *E. coli*, followed by imipenem. In comparison to the previous study, resistance to Imipenem has increased while resistance to Amikacin has decreased, which may be due to more Imipenem administration overall (16). Notably, *Acinetobacter sp.*, the second most common gram-negative isolate, is resistant to Imipenem and co-trimoxazole, while piperacillin/tazobactam remains the preferred antibiotic with only 3.16% sensitivity. Furthermore, imipenem resistance in *Klebsiella sp.* has increased, and amikacin is now a better option. This suggests that clinicians should reconsider using imipenem as their first line of empirical therapy.

Conclusion

Bacterial bloodstream infections almost always necessitate antibiotic treatment. This is due to the high mortality rates associated with sepsis progression if drug therapy is delayed. Our findings suggest and emphasize the importance of monitoring blood culture isolates and susceptibility patterns in specific geographical locations on a yearly basis in order to observe resistance patterns affecting empirical therapy and infection control methods.

Conflict of Interests: None to declare.

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Ethical Statement

The ethics code IR.sums.med.rec.1398.616 was obtained from Shiraz University of Medical Sciences for the study protocol.

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