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. Bacteremia in hematological disorders leads to remarkable mortality rates. In the United States, approximately 200,000 cases of bacteremia and sepsis are reported annually, with 50% fatalities. Because of the severity and life-threatening features, doing multiple cultures from patients and prescription of broad-spectrum antibiotics are of great importance. The obtained results from the disk diffusion method and blood cultures determine the type of the prescribed antibiotics. 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. Blood infections caused by opportunistic bacteria are considered as one of the major problems related to hospitalized and immunosuppressive patients. 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. 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 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), cefazidime (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, cefazidime, cefotaxime, ofloxacin, gentamicin, ciprofloxacin, levofloxacin, amikacin, and imipenem, was 44 (64.7%), 42 (61.8%), 39 (57.4%), 38 (55.9%), 35 (51.5%), 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

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>14</td>
<td>20.6</td>
</tr>
<tr>
<td>E. coli</td>
<td>14</td>
<td>20.6</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>12</td>
<td>17.6</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>11</td>
<td>16.2</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>8</td>
<td>11.8</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>6</td>
<td>8.8</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>3</td>
<td>4.4</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>100</td>
</tr>
</tbody>
</table>
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.\(^\text{19}\) During the past decades, the mortality rate as a result of septicemia has reached up to 78%.\(^\text{20}\) Antibiotic resistance is considered as another major concern, which leads to a complicated treatment procedure.\(^\text{21}\) 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.\(^\text{22}\) 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 pneumonia* (17.1%), 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.\(^\text{24}\) 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\(^\text{23}\) 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

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

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Staphylococcus aureus</th>
<th>Coagulase-Negative Staphylococci</th>
<th>E. coli</th>
<th>Acinetobacter baumannii</th>
<th>Pseudomonas aeruginosa</th>
<th>Klebsiella pneumonia</th>
<th>Enterococcus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R (S)</td>
<td>Number of Resistant Isolates (%)</td>
<td>R (S)</td>
<td>R (S)</td>
<td>R (S)</td>
<td>R (S)</td>
<td>R (S)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>4 (28.6)</td>
<td>(71.4)</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td>9 (64.3)</td>
<td>5 (35.7)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>2 (14.3)</td>
<td>(85.7)</td>
<td>2 (25)</td>
<td>6 (75)</td>
<td>6 (42.8)</td>
<td>8 (57.1)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>4 (28.6)</td>
<td>(71.4)</td>
<td>0 (0)</td>
<td>8 (100)</td>
<td>8 (51.4)</td>
<td>5 (38.3)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>3 (21.4)</td>
<td>(78.5)</td>
<td>2 (25)</td>
<td>6 (75)</td>
<td>10 (79.2)</td>
<td>4 (32.8)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>3 (21.4)</td>
<td>(78.5)</td>
<td>1 (12.5)</td>
<td>6 (75)</td>
<td>0 (0)</td>
<td>14 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>2 (14.3)</td>
<td>(85.7)</td>
<td>1 (12.5)</td>
<td>7 (75)</td>
<td>12 (87.5)</td>
<td>12 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>1 (7.1)</td>
<td>(92.9)</td>
<td>2 (25)</td>
<td>6 (75)</td>
<td>8 (57.1)</td>
<td>6 (42.8)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2 (14.3)</td>
<td>(85.7)</td>
<td>3 (12.5)</td>
<td>5 (62.5)</td>
<td>7 (50)</td>
<td>7 (50)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1 (7.1)</td>
<td>(92.9)</td>
<td>3 (12.5)</td>
<td>5 (62.5)</td>
<td>4 (33.3)</td>
<td>10 (100)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>3 (21.4)</td>
<td>(78.5)</td>
<td>4 (50)</td>
<td>6 (50)</td>
<td>11 (100)</td>
<td>1 (100)</td>
<td>3 (100)</td>
</tr>
</tbody>
</table>

Data are shown as No. (%).

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

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Number of Resistant Isolates (%)</th>
<th>Number of Sensitive Isolates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-trimoxazole</td>
<td>44 (64.7)</td>
<td>24 (35.3)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>42 (61.8)</td>
<td>26 (38.2)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>39 (57.4)</td>
<td>29 (42.6)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>38 (55.9)</td>
<td>30 (44.1)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>35 (51.5)</td>
<td>33 (48.5)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>32 (47.1)</td>
<td>36 (52.9)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>31 (45.6)</td>
<td>37 (54.4)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>31 (45.6)</td>
<td>37 (54.4)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>25 (36.8)</td>
<td>43 (63.2)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>27 (39.7)</td>
<td>41 (60.3)</td>
</tr>
</tbody>
</table>
culture in other studies, the percentage and the amount of distribution rate differ from each other. The resistance and susceptibility to antibiotics in studies which were conducted in Iran and abroad are different. 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.

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.

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. In Asia, more antibiotic resistance pattern is relatively similar to the current investigation. The resistance rate of P. aeruginosa to imipenem, ceftazidime, and ciprofloxacin in Turkey was reported 26.4%, 47.4%, 29%, respectively. 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 while in another study conducted in Tehran, the amount of resistance were 94.4% and 42.9%, respectively. Further, the resistance of Klebsiella and Enterobacter isolates to ceftazidime was 66.7% in the present 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.

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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