ANTIMICROBIAL RESISTANCE PROFILE OF ESCHERICHIA COLI CAUSING BACTEREMIA IN PATIENTS IN INTENSIVE CARE UNITS

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ABSTRACT

Aims: A crucial mechanism of antibiotic resistance of Escherichia coli (E.coli), a member of gram-negative bacteria that cause infections in intensive care units (ICUs), is beta-lactamase production. This study aims to determine extended-spectrum beta-lactamase (ESBL) production frequency and antibiotic resistance profile of E.coli strains isolated from blood cultures of adult patients in different intensive ICUs at Erciyes University-Kayseri, Turkey.

Materials and methods: This study includes only one E.coli strain per patient. Antibiotic susceptibility test of 81 E.coli strains were performed using Kirby-Bauer disk diffusion method. ESBL-production was determined using double-disc synergy test.

Results: A total of 38 (72%) strains were isolated from patients in internal ICUs while 23 (28%) strains were isolated from patients in surgical ICUs. A total of 44 (54.3%) strains were found to produce ESBL with ESBL-production rate of 55.2% in internal ICUs and 52.2% in surgical ICUs. Difference between the presence of ESBL-producing E.coli in male and female patients in ICUs is not statistically significant. 8 (9.8%), 46 (56.8%), 69 (85.2%), 22 (27.2%), and 44 (54.3%) and zero strains were resistant to amikacin, ciprofloxacin, ampicillin, piperacillin-tazobactam, cefotaxime, and imipenem, respectively, and no strains were resistant to imipenem. Resistance to amikacin, ciprofloxacin, ampicillin and cefotaxime in ESBL producing strains were significantly higher than ESBL non-producing strains (p<0.05). Piperacillin-tazobactam resistance ratio for E.coli strains isolated from surgical ICUs was found to be significantly greater than those isolated from internal ICUs (p<0.05). Despite higher ratios of ESBL-production of E.coli strains, carbapenem resistance was not gratifyingly determined in the ICUs.

Conclusion: Early diagnosis and immediate treatment of nosocomial bacteremia are important for patients’ survival. Therefore, monitoring antibiotic susceptibility profiles of isolated microorganisms will guide clinicians for controlling infections.

Key words: Antimicrobial drug resistance, Bacteremia, Escherichia coli, Intensive care units.

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Introduction

Escherichia coli (E. coli) has an important role amongst gram-negative bacteria in nosocomial and community-acquired bloodstream infections\(^1\)\(^2\)\(^3\). Nosocomial infections are health problems that reduce the quality of life in patients, increase the length of hospitalization, costs, mortality and morbidity rates\(^3\). In patients hospitalized in the intensive care units (ICUs), there has been a tendency to colonization and infection with resistant microorganisms due to the general state of health (presence of chronic diseases in many patients), the heavy use of broad spectrum antibiotics and the more frequent exposure to invasive procedures such as mechanical ventilator, central venous catheter, nasogastric tube and urinary catheter. It is obvious that the ICUs are sources of more than 25% of hospital-acquired infections although ICUs of the hospital create an average of 10% of total bed capacity\(^4\). The pathogens of nosocomial infections in ICUs may vary between hospitals, even between different
ICUs of the same hospital. The most known aspects of these infections are their pathogens’ resistance and the difficulty of their treatments.(5,6)

Extended-spectrum beta-lactamases (ESBLs) consist of a heterogeneous group of enzymes, and are responsible for the development of resistance to broad spectrum beta-lactam group antibiotics in Enterobacteriaceae.(7) Bacteria that contain these enzymes are resistant to penicillin, narrow and broad-spectrum cephalosporins, aztreonam and also aminoglycosides, sulfamethoxazole-trimethoprim and quinolones frequently.(8) ESBL production was seen more in Klebsiella pneumoniae between 1980-1990 but has begun to be seen increasingly in E.coli in the 2000s. In a other study identified some risk factors for ESBL-producing organisms such as prolonged stay in hospital and ICUs, recent exposure to multiple antibiotics and invasive procedures in adults.(9)

In a study conducted in North America, the incidence of ESBL-producing E. coli isolated from patients in the ICUs was reported as 4.5-11.2%.(10). In a study conducted in Turkey, ESBL production rate in E. coli strains isolated from ICUs were 50%.(11) This rate may vary in different studies. ESBL-producing bacteria may be resistant to many drugs, therefore the empiric treatment may fail.(12) It has been reported in a previous study that the mortality rates increased fourfold in ESBL-producing E. coli bacteremia.(13). In various studies, it has been indicated that treatment with carbapenems and other suitable antibiotics as early as possible could reduce mortality in ESBL-producing E. coli bacteremia.(14,15). Due to these factors, monitorization of bacteremia caused by ESBL-producing bacteria regularly, antibiotic resistance patterns of the strains will be important guiding for directing empirical treatment and treatment success.

This study aimed to investigate ESBL frequency and in vitro antibiotic resistance patterns of E. coli strains isolated from blood cultures of adult patients in the ICUs and compare whether there was a difference in resistance patterns between the ICUs.

Materials and methods

A total of 81 strains isolated from blood culture samples of adult patients suspected of sepsis in ICUs of Erciyes University, Gevher Nesibe Hospital between January 2007 - January 2010 were included in this study. All strains were isolated consecutively and only one strain from each patient included in the study. The blood cultures were incubated in BacT/Alert3D (bioMerieux, France) automatized blood culture system for five days. During this period, blood cultures that where bacterial growth was detected were inoculated into blood agar, eosin-methylene blue agar (EMB) and chocolate agar plates. Identification of bacteria was performed using routine microbiological methods and Phoenix 100 (Becton Dickinson, USA) automatized blood culture system. The susceptibility to various antibiotics of strains identified as E.coli was performed using Kirby-Bauer disk diffusion method and method of ESBL was investigated by double-disk synergy test. In double-disk synergy test, amoxicillin/clavulanic acid (AMC, 20/10 mg), cefotaxime (30 mg), ceftazidime (30 mg), and aztreonam (30 mg) disks were used according to the Clinical Laboratory Standards Institute (CLSI) recommendations. Antibiotic susceptibility and double-disk synergy test results were interpreted according to the CLSI recommendations (16). E. coli ATCC 25922 was used as a quality control strain. Statistical evaluations were performed with Chi-square ($\chi^2$) test and $P \leq 0.05$ was considered as statistically significant.

Results

There were a total of 52 bed capacity in ICUs; 30 were in internal ICU and 22 in surgical ICU. In a 3-year period, a total of 81 patients were diagnosed with E. coli bacteremia. Amongst these patients, 44 patients were male and 37 were female, and the mean age was 61.2 ± 14.7. A total of 58 (72%) strains were isolated from internal ICUs inpatients and 23 (28%) strains were isolated from surgical ICUs inpatients. A total of 44 (54.3%) strains were ESBL-positive and ESBL production rate was found as 55.2% in internal ICUs, and 52.2 in surgical ICUs. The rate of ESBL production was found as 54% and 54.5% in female and male patients, respectively. There were no statistically significant difference between ICUs, and genders in terms of ESBL production (p>0.05 for each). The rate of ESBL production was found as 54% and 54.5% in female and male patients, respectively. Resistance to amikacine was found in eight (9.8 %), to ciprofloxacin was found in 46 (56.8%), to ampicillin was found in 69 (85.2%), to piperacillin-tazobactam was found in 22 (27.2%) and to cefotaxime was found in 44 (54.3%) strains. Resistance to imipenem was not detected in all strains.
Antimicrobial susceptibility patterns of ESBL-positive and -negative strains are shown in Table 1. The rate of ESBL production and antibiotic resistance patterns of strains isolated from internal and surgical ICUs are shown in Table 2.

Table 1: Antibiotic susceptibility patterns of ESBL positive and negative strains for all antibiotics.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>ESBL Positive</th>
<th>ESBL Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n:44</td>
<td>n:37</td>
<td>n:81</td>
</tr>
<tr>
<td>Amikacin</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>36</td>
<td>10</td>
<td>46</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>44</td>
<td>25</td>
<td>69</td>
</tr>
<tr>
<td>Imipenem</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PTZ</td>
<td>14</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>44</td>
<td>0</td>
<td>44</td>
</tr>
</tbody>
</table>

* p ≤ 0.05 statistically significant, ** PTZ: Piperacillin/Tazobactam, ESBL: extended-spectrum beta-lactamases

Table 2: Antibiotic resistance patterns between strains isolated from internal and surgical ICUs.

<table>
<thead>
<tr>
<th>ICU Type</th>
<th>Internal ICU</th>
<th>Surgical ICU</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n:58</td>
<td>n:23</td>
<td>n:81</td>
</tr>
<tr>
<td>ESBL Producer</td>
<td>32</td>
<td>12</td>
<td>44</td>
</tr>
<tr>
<td>Amikacin</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>33</td>
<td>13</td>
<td>46</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>49</td>
<td>20</td>
<td>69</td>
</tr>
<tr>
<td>Imipenem</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>11</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>32</td>
<td>12</td>
<td>44</td>
</tr>
</tbody>
</table>

* ps 0.05 statistically significant

ESBL: extended-spectrum beta-lactamases

Discussion

In patients hospitalized in the ICUs, the risk of colonization and infection with resistant bacteria is higher than in patients hospitalized in other departments of hospitals due to the general condition of the patients and medical procedures applied. Beta-lactamase production is the most important resistance mechanism of E. coli strains, which has an important role in infections occurring in ICUs. Ineffectiveness of many antibiotics in infections with ESBL-producing E. coli limits antibiotics that can be used, increases mortality-morbidity rates, and causes serious economic losses. Determining the rate of ESBL-producing strains, monitoring the rate of resistance to other antibiotics in ESBL producing and non-producing strains, detection of antibiotics in empiric treatment in light of these data for each institution will be very important in decreasing mortality, morbidity rates and economic losses.

ESBL production may vary between countries, institutions, and even between different departments of the same institution according to whether community or hospital-acquired infections. The prevalence of ESBL production in E. coli strains isolated from blood culture was reported as 22.5-44% from various studies in Turkey. Additionally, the prevalence of ESBL production in E. coli strains isolated from various clinical specimens in nosocomial infections was reported as 42% in a multicenter study. The prevalence of ESBL producing E. coli in bacteremia was reported as 7.5-27.6% when analyzed data from other countries.

In our study, ESBL prevalence was found as 54.3% and it is remarkable that to be higher than in the researches of the literature. It was thought that the higher rate of ESBL production in our study may be due to the patients selected from ICUs. On the other hand, in another study performed in our country, the prevalence of ESBL production in E.coli strains isolated from blood culture from patients in ICUs was reported as 33% and it has been indicated that ESBL production in E. coli strains is a major problem for our hospital.

The antibiotic resistance rates were found higher in ESBL-producing strains than non-producing strains in various studies. In our study, the same situation was also valid and the difference between resistance rates were statistically significant for the antibiotics except piperacillin-tazobactam.

In our study, when analyzed the antibiotic resistances individually, resistance to amikacine was found as 16% and 2.7% in ESBL-positive and -negative strains, respectively. Uzun et al. reported amikacine resistance rates were 21% and 4% in ESBL-positive and -negative strains, respectively. In another study by Saglam et al. amikacine resistance in ESBL-positive E. coli strains was reported as 11% and no resistance to amikacine was seen in ESBL-negative strains. In a study from Belgium, amikacine resistance in ESBL-positive E.coli strains was reported as 24%. In this context, amikacine resistance rates of our study were consistent with the results of other studies.

According to the literature, resistance to ciprofloxacin is 33-88% and 18.4-33% among
ESBL-positive and negative *E. coli* strains isolated from blood culture, respectively\(^\text{5,6,8,10}\). In our study, ciprofloxacin resistance was 82% and 27% in ESBL-positive and -negative strains, respectively. Although our results were consistent with the literature, it should be noted that our resistance rates were at the upper limit. It is considered that, empirical treatment with ciprofloxacin alone is not appropriate in patients suspected of bacteremia in our hospital.

In the literature, ampicillin resistance rates in ESBL-positive *E. coli* strains isolated from blood culture were 97-100% and in ESBL-negative *E. coli* strains isolated from blood culture were 26-32%\(^\text{18,20}\). Ampicillin resistance rate in ESBL-positive strains was 100% and in ESBL-negative strains was 67% in our study. Ampicillin resistance in ESBL-negative strains was found to be significantly higher than those in the literature.

The resistance rates of piperacillin-tazobactam were found as 32% and 22% in ESBL positive and negative strains, respectively and the difference was not statistically significant. The resistance rates of piperacillin-tazobactam in ESBL positive *E. coli* strains isolated from blood culture were reported as 33-61% and in ESBL negative *E. coli* strains isolated from blood culture were reported as 6-24% by various studies\(^\text{18,22,23}\). In this context, our data were consistent with the literature.

Resistence to imipenem was not detected in our study. In the literature, imipenem resistance rates of both ESBL positive and negative *E. coli* strains isolated from blood culture was reported as 0.5-2% by various studies\(^\text{18,22,23}\). It is gratifying not to see imipenem resistance in our strains and imipenem is one of the first drugs to be preferred in infections with ESBL positive strains, especially in bacteremia.

In our study, 58 (72%) strains were isolated from internal ICUs and 23 (28%) strains were isolated from surgical ICUs. The ESBL production rate was found as 55.2% in internal ICUs and 52.2% in surgical ICUs. The different ESBL production rates between ICUs were not statistically significant. From the perspective of resistance to antibiotics, only resistance to piperacillin-tazobactam was found higher in surgical ICUs than internal ICUs and the difference was statistically significant. It was thought this result may be due to the differences in preferences between departments. There have been few studies comparing ESBL production among intensive care units in the literature. Therefore, it was thought that multi center studies with more patients will give more accurate results.

In conclusion; ESBL production and multidrug resistance in *E. coli* strains isolated from bacteremia patients require quickly and accurately determination in microbiology laboratories. Determination and regular monitorization of antibiotic resistance patterns for empirical treatment during the time required for the final report will be the right approach.

References


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