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Prevalence and antibiotic resistance pattern of extended spectrum beta lactamase producing *Escherichia coli* isolated from urinary tract infection

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ABSTRACT

Introduction: Urinary tract infection (UTI) due to extended spectrum beta-lactamase (ESBL)-producing bacteria including Escherichia coli has become widespread. Studies have shown a trend toward higher mortality, longer hospitalization, greater hospital expenses and reduced rates of clinical and microbiologic response in ESBL UTI.

Objectives: The aim of this study is to determinate the prevalence and antibiotic resistance pattern of ESBL producing *E. coli* isolated from UTI.

Patients and Methods: This cross-sectional study was conducted on 3126 samples. Urine specimens were cultured on Eosin Methylene Blue (EBM) and blood agar. The disk diffusion standard method (Kirby Bauer) was used to test the susceptibility of the drug on Muller-Hinton agar plates and results were reviewed based on Clinical and Laboratory Standards Institute (CLSI) criteria. The reviewing of ESBL-producing uropathogens was carried out using Combined Disk Test (CDT) by using cefotaxime (CTX; 30 µg) and cefotaxime-clavulanic acid (CTX; 30 µg /CA:10 µg) disks and CLSI protocol.

Results: Out of 291 *E. coli* isolates, 108 (37.11%) are ESBL-producer and 183 (62.89%) are non–ESBL-producer. Among ESBL-producing *E. coli*, the highest antibiotic resistance was observed with cefotaxime (100%), amoxicillin (97.22%) and piperacillin (96.3%) and the highest antibiotic sensitivity was observed with meropenem (93.5%), nitrofurantoin (81.48%) and gentamicin (55.56%).

Conclusion: We recommended that cephalosporins, penicillins and cotrimoxazole are not suggested in the treatment of ESBL-producing *E. coli*. On the other hand, carbapenems as a first line and aminoglycosides as the next step in the treatment of ESBL-producing *E. coli* are recommended.

Implication for health policy/practice/research/medical education:
Knowing the prevalence and antibiotic resistance pattern of extended spectrum beta lactamase producing *Escherichia coli* as the most common urinary tract infection pathogen, in addition to alert to health system policymakers about increasing antibiotics resistance, helps therapists to prescribe appropriate antibiotics to treat them.

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Introduction

Urinary tract infection (UTI) is one of the most common infectious disease that affects about more than 150 million people every year (1). *Escherichia coli* is the most common urinary tract pathogen, accounting for 50% to 90% of UTI isolates (2). *E. coli* as an enterobacteriaceae

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member is gram negative and facultative anaerobic bacterium (3). β-lactam antibiotics (beta-lactam antibiotics) are the commonly prescribed antibiotics for UTI. Beta-lactam antibiotics are a class of broad-spectrum antibiotics, consisting of all antibiotic agents that contain a beta-lactam ring in their molecular structure (4). Beta-lactamases are enzymes that hydrolyze beta-lactam ring, inactivating the antibiotic (5). Extended-spectrum beta-lactamase (ESBL) are enzymes that confer resistance to most common beta-lactam antibiotics such as penicillins, cephalosporins and monobactam (6). ESBL-producing bacteria were first reported in 1983, and now infection due to ESBL-producing bacteria including *E. coli* has become widespread (7). Studies have shown a trend toward higher mortality, longer hospitalization, greater hospital expenses and reduced rates of clinical and microbiologic response in ESBL UTI (8,9).

Objectives

The aim of this study is to determinate the prevalence and antibiotic resistance pattern of ESBL-producing *E. coli* isolated from UTI.

Patients and Methods

Patients

This cross-sectional study was conducted on all urine samples (3126 samples) sent to the cultivating to the central laboratory of Tohid hospital in Sanandaj from October 2016 to September 2017.

Intervention and biochemical measurements

Urine specimens were collected from the midstream urine samples in sterile containers and by using a calibrated loop (0.01 mL), they were cultured in sterile conditions on Eosin Methylene Blue (EBM). The Blood agar and then samples were examined at 37°C after 18-24 hours incubation. The samples that number of colonies grown on their culture medium were more than 10^5 CFU/mL were examined as a positive urine culture to identify genus and bacterial species based on standard methods. After the final diagnosis, the disk diffusion standard method (Kirby Bauer) was used to test the susceptibility of the drug on Muller-Hinton agar plates. Creating or not creating and the size of inhibition zone around the disk were reviewed based on the Clinical and Laboratory Standards Institute (CLSI) criteria. The most commonly used antibiotics in UTIs were reviewed in studied antibiogram. The reviewing of ESBL-producing uropathogens was carried out using Combined Disk Test (CDT) and CLSI protocol. At first, a microbial suspension equivalent to half McFarland was prepared from pure bacterial culture and it was cultured on Muller-Hinton agar medium by sterile swab. Then, the cefotaxime (CTX; 30 µg) and cefotaxime-clavulanic acid (CTX; 30 µg /CA; 10 µg) disks were placed at the distance of at least 2.5 cm from each other in medium. After 24 hours of incubation at 37°C, producing ESBL was studied. If the inhibition zone around the cefotaxime-clavulanic acid was equal 3 mm or it was greater than inhibition zone around cefotaxime, that bacteria was considered as ESBL producing.

Ethical issues

The study was in accordance with the Declaration of Helsinki and all participants gave their informed consent to enter the study. The study was approved by the Research Committee and the Ethical Committee of the Kurdistan University of Medical Sciences. (Ethic code: IR.MUK.REC.1397.5014).

Data analysis

The data were analyzed by SPSS 23 software. To compare qualitative variables, chi-square test was applied. Level of significance was $P<0.05$.

Results

Of 3126 studied urine samples, the results of 708 cultures (22.64%) were positive. Among uropathogens, *E. coli* was the most common bacteria (41.10%). On the other hand, 163 bacteria (23.02%) produced ESBL (Figure 1). Out of 291 *E. coli* isolates, 108 (37.11%) are ESBL-producer and

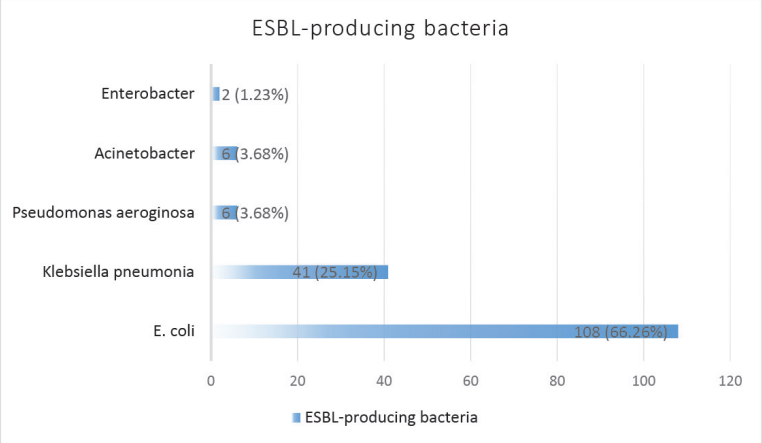

Figure 1. The frequency of ESBL-producing bacteria.

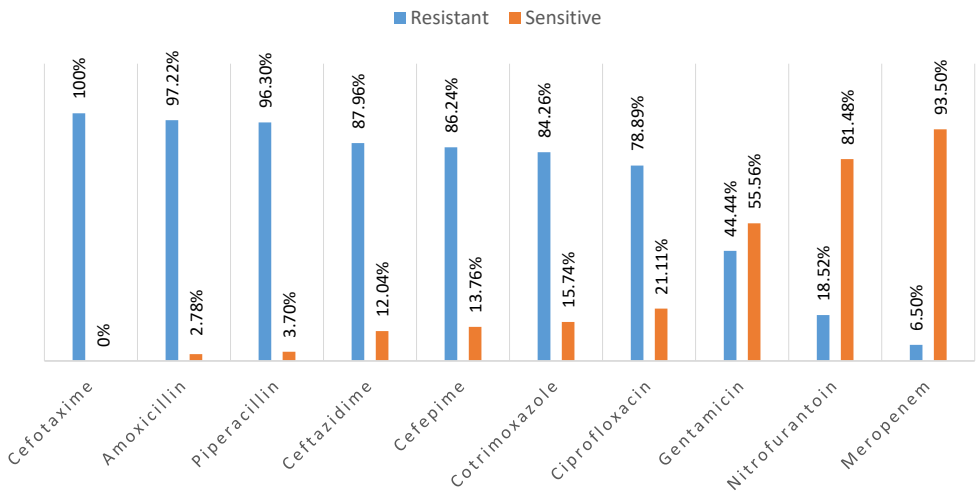

Figure 2. Antimicrobial resistance pattern of ESBL-producing *E. coli*.

183 (62.89%) are non–ESBL-producer.

According to the result of antibiogram, the highest antibiotic resistance among ESBL-producing *E. coli* was observed with cefotaxime (100%), amoxicillin (97.22%) and piperacillin (96.3%). The highest antibiotic sensitivity among ESBL-producing *E. coli* was observed with meropenem (93.5%), nitrofurantoin (81.48%) and gentamicin (55.56%) (Figure 2).

Discussion

This study showed that 163 (23.02%) bacteria isolated from urinary culture were ESBL-producing. Out of 291, *E. coli* isolates, 108 (37.11%) are ESBL-producer and 183 (62.89%) are non–ESBL-producer. Other studies reported a prevalence of ESBL-producer *E. coli* isolates 46.87% (10), 82.6% (11) and 21.4% (12) respectively. This different results may be due to the difference in the risk factors include recent antibiotic therapy, administration of corticosteroids, hospitalization (13).

According to the result of antibiogram, the highest antibiotic resistance among ESBL-producing *E. coli* was observed with cefotaxime (100%), amoxicillin (97.22%) and piperacillin (96.3%). The highest antibiotic sensitivity was observed with meropenem (93.5%), nitrofurantoin (81.48%) and gentamicin (55.56%). This study showed that ESBL-producing *E. coli* were resistant to penicillins and cephalosporins and sensitive to carbapenem, nitrofurantoin and aminoglycoside. Our findings are similar to other studies (14-16) (Table 1).

Conclusion

Given the dramatic increase in the prevalence of ESBL-producing *E. coli* and its consequences, including higher mortality, longer hospitalization, greater hospital expenses and reduced rates of clinical and microbiologic response, evaluation of their prevalence and antibiotic resistance pattern are recommended. According to the results of our study, it is recommended that cephalosporins, penicillins and cotrimoxazole are not administered in the treatment of ESBL-producing *E. coli*. On the other hand, carbapenems as a first line and aminoglycosides as the next step in the treatment of ESBL-producing *E. coli* are recommended.

Limitations of the study

The limitation of this study was that the standard and correct method is the MIC method, while this method has

Table 1. Comparison of results of studies

This study	Yadav et al (14)	Gngane et al (15)	Fernando et al (16)
Antibiotic resistance			
Cefotaxime (100%)	Cephalexin (78.86%)	Ampicillin (100%)	Ceftriaxone (100%)
Amoxicillin (97.22%)	Nalidixic acid (73.98%)	Cotrimoxazole (93.80%)	Ceftazidime (100%)
Piperacillin (96.30%)	Cotrimoxazole (71.54%)	Nalidixic acid (89.70%)	Ciprofloxacin (90.10%)
Antibiotic sensitive			
Meropenem (93.50%)	Imipenem (62.60%)	Imipenem (100%)	Meropenem (96.10%)
Nitrofurantoin (81.48%)	Amikacin (60.97%)	Piperacillin-Tazobactam (88.10%)	Imipenem (73.70%)
Gentamicin (55.56%)	Nitrofurantoin (43.90%)	Nitrofurantoin (71.30%)	Nitrofurantoin (45.90%)

not been used in this study.

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Authors' contribution

All authors passed four criteria for authorship contribution based on recommendations of the International Committee of Medical Journal Editors. MRC and MSF conducted the research. MM and AF wrote the primary draft. MOB And MB prepared the final paper. SH conducted the final check of the paper. All authors read and signed the final paper.

Conflicts of interest

The authors declare that they do not have any conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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