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Prevalence and Antimicrobial Resistance Pattern of Uropathogenic *Escherichia coli* at a Tertiary Care Hospital: A Retrospective Study

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ABSTRACT

Background: Uropathogenic *Escherichia coli* (UPEC) is the most common cause of urinary tract infection in humans including cystitis and pyelonephritis. Antimicrobial resistance (AMR) in UPEC is one of the global public challenges that is due to prevalent use of antibiotics in healthcare setting. Therefore, the purpose of this study is to investigate the frequency and antibiotic resistance pattern of UPEC isolated from patients admitted to Modares Hospital in Saveh, Iran.

Methods: In this study, in total 633 isolates were evaluated. UPEC isolates were obtained from patients with urinary tract infection and identified using conventional microbiological protocols. Antibiotic resistance pattern of UPEC against different antibiotic were determined using disk diffusion method. SPSSTM software was used for statistical analysis.

Results: In this study, the most sample was related to outpatients and the lowest sample was related to the CCU wards. The highest antibiotic resistance showed against cephalothin (63.8%) and nalidixic acid (62.2%) antibiotics. The highest effective antibiotics for the tested UPEC was nitrofurantoin (90.7%) and gentamicin (77.3%). Cephalothin and nalidixic acid in hospitalized patients in ICU and emergency wards, respectively, showed the highest antibiotic resistance. Out of 633 UPEC, the rate of Multi Drug Resistant (MDR) isolates were 343 (54.2%).

Conclusion: The result of this study highlighted the role of UPEC as one of the important cause of UTI in individuals. Also, nitrofurantoin then gentamicin are the most effective antibiotics against UPEC infections. Logical prescription of antibiotics and infection control strategies are needed for prevention and control of nosocomial infections especially urinary tract infection.

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Introduction

Escherichia coli (*E. coli*) includes a wide range of different strains in ecosystems with high diversity in their genomes and some types of strains cause serious diseases such as urinary tract infections (UTIs) (1). Uropathogenic *Escherichia coli* (UPEC) is the most common cause of urinary tract infection in humans including cystitis and pyelonephritis (2). The epidemiology studies showed that UPEC frequency is 75% in uncomplicated UTIs and 65% in complicated UTIs (3). UPEC led to UTIs through expression of a broad spectrum of virulence factors that adhesive molecules play important role in pathogenicity (4). UPEC infection led to symptoms include discomfort, polyuria, and fever with consequence of urosepsis, kidney damage, and death (5). The gold treatment in uncomplicated UTIs therapy are fosfomycin trometamol, nitrofurantoin, and pivmecillinam and cephalosporins can be used as an alternative treatment (6). Antimicrobial resistance (AMR) in UPEC is one of the global public challenges that is due to prevalent use of antibiotics in healthcare setting. In AMR, antibiotic resistant genes (ARGs) shows the main function in the transfer and acquisition of AMR (7). One of the AMR is extended spectrum beta-lactamase (ESBL). ESBL plasmid genes in UPEC transfer resistance to third generation cephalosporins and other antibiotics (8). Among the different genotypes, SHV, TEM and CTX-M are dominant among Enterobacterales family (9). The presence of TEM causes resistance to penicillin, ampicillin and first generation cephalosporins such as cephalothin (9). The presence of this enzyme is responsible for 90% of ampicillin resistance in UPEC (10). Recently, there has been an increase in ESBL-carrying strains in UPEC that cause urinary tract infection, and this has made the treatment of these strains a serious challenge (11). The pattern of antibiotic sensitivity of the isolates can be different in the type of medical center and their facilities, the geographical area, the study environment and the evaluation period of sensitivity in the pathogen. So this should be done in different geographical areas and even different medical centers that can be useful in controlling antibiotic resistance (12). The investigation of the antibiotic resistance pattern should be evaluated continuously every year because of antibiotic resistance increase in bacterial isolates and also change resistance pattern (13). Therefore, the purpose of this study is to investigate the frequency and antibiotic resistance pattern of *Escherichia coli* causing urinary tract infections isolated from patients admitted to Modares Hospital, Saveh, Iran.

Materials and Methods

Study Design and Bacterial Identification

This retrospective cross sectional study, was done during one year (2022-2023) with 633 UPEC isolates from Modares Hospital in Saveh, Iran. Sampling was done from various wards of hospital including CCU (cardiac care unit), ICU (intensive care unit), Internal, ER (emergency), pediatric, surgery and outpatients wards. UPEC isolates were obtained from patients with urinary tract infection and identified using conventional microbiological protocols consist of reaction with Triple Sugar Iron agar, Simmons' citrate agar, Christensen's urea agar, Indole test, Methyl red and Voges-Proskauer tests.

Antimicrobial Sensitivity Testing (AST)

Procedure of Clinical Laboratory Standard Institute (CLSI) guidelines(14) by disk diffusion method was used for antimicrobial susceptibility testing. Briefly, bacterial isolates was cultured on Mueller-Hinton agar (Merck, Germany) and antibiotic disks (HiMedia, India) included cefalothin (CF), cefotaxime (CTX), nalidixic acid (NA), ceftazidim (CAZ), gentamicin (GM), nitrofurantoin (FM), trimethoprim-sulphamethoxazole (SXT), and ciprofloxacin (CP) were used to obtain antimicrobial sensitivity. In this study, for quality control purposes of the antibiogram test, *Escherichia coli* ATCC 25922

strain was used. For results interpretation, the zone of inhibition was measured and compared with the standards (14).

Statistical Analysis

SPSSTM software, version 21.0 (IBM Corp., USA) was used for data analysis. Mean ± standard deviation (continuous variables) or percentages of the group (categorical variables) were used for data analysis. If appreciate, descriptive statistics in terms of relative frequency also was used for data presentation.

Results

In this study, in total 633 sample was enrolled. The mean age of study population was 47.97±25.78. Moreover, study population included 446 female samples (70.5%) and 187(29.5%) male samples.

Moreover, the highest antibiotic resistance is related to cephalothin (63.8%) and nalidixic acid (62.2%) antibiotics. The highest sensitivity is related to the antibiotics nitrofurantoin (90.7%) and gentamicin (77.3%). More details was shown in Table 2.

Antibiotic cephalothin in patients hospitalized in ICU and nalidixic acid in patients hospitalized in emergency department showed the highest antibiotic resistance. More than 90% of patients in the emergency, outpatient and CCU departments were sensitive to nitrofurantoin antibiotic. Outpatients showed less resistance to antibiotics than hospitalized patients. A significant number of bacteria were sensitive to all the investigated antibiotics and fortunately none of the bacteria showed resistance to all antibiotics at the same time. Although a small number of bacteria have been isolated from the CCU and children's departments compared to other departments, most of them have shown relatively high resistance to more than half of the antibiotics used (≥50%). More details was shown in Table 3.

Discussion

In public health, UTI is an important problem with 150 million affected individuals yearly (15). Antimicrobial resistance in UTI ominously is rising and considered as healthcare challenge worldwide. First, this issue was observed highly in diabetes or reflux nephropathy patients, however nowadays, it is common in UTIs (16). Therefore, it is necessary to identify antibiotic resistance in order to adopt appropriate treatment strategies. In our study, the frequency of UTI among females was higher in comparison with males, which can be because of the urethra shortness in females and the urethra to the vagina and anus proximity (17). In according with our results, Seifu et al. (18) reported the higher frequency of UTI in females. Moreover, in the study by Ngwai et al. the results reported that 20% of the urine samples showed significant bacteriuria and the incidence in female (25%) was higher in comparison to male (15%) (19).

Antimicrobial resistance is an important challenge in patient treatment and the correlation of antibiotics resistance and their use was reported. Increasing bacterial resistance to antibiotics led to constantly monitor resistance frequency (20). In our study, the highest antibiotic resistance was related to cephalothin and nalidixic acid. Nitrofurantoin was the most efficient antibiotic in patients. The resistance to antibiotics was lower in outpatients than hospitalized patients. Although a small number of bacteria have been isolated from the CCU and children's departments compared to other departments, most of them have shown relatively high resistance to more than half of the antibiotics used. In the study by Hadadi et.al gentamicin reported as most effective antibiotic against UPEC which belong to aminoglycosides category and mainly used in the treatment of infections caused by Gram-negative aerobic bacilli including UPEC (21). In our study as well, gentamicin was one of the most efficient antibiotics.

Table 1. Frequency of UPEC isolates in different wards of hospital.

Hospital wards	Frequency No. (%)
CCU*	12 (1.9)
ER*	157 (24.8)
ICU*	29 (4.6)
Internal	77 (12.2)
Outpatient	283 (44.7)
Pediatric	34 (5.4)
Surgery	41
Total	633

* CCU: cardiac care unit, ICU: intensive care unit, ER: emergency

Table 2. Antibiotic resistance pattern of UPEC isolates.

Antibiotics	Resistant No. (%)	Intermediate No. (%)	Sensitive No. (%)
Nitrofurantoin	48 (7.6)	11 (1.7)	574 (90.7)
Nalidixic acid	394 (62.2)	12 (1.9)	227 (35.9)
Cefalothin	404 (63.8)	15 (2.4)	214 (33.8)
Cefotaxime	319 (50.4)	6 (0.9)	308 (48.7)
Ceftazidime	360 (56.9)	15 (2.4)	258 (40.8)
Ciprofloxacin	320 (50.6)	10 (1.6)	303 (47.9)
SXT	386 (61)	5 (0.8)	242 (38.2)
Gentamicin	135 (21.3)	9 (1.4)	489 (77.3)
Total	633 (100)		

Table 3. Antibiotic resistance patterns of UPEC isolates according to the different wards.

Antibiotics / Wards	Nitrofurantoin No. (%)	NA No. (%)	Cefalothin No. (%)	Cefotaxim No. (%)	Ceftazidim No. (%)	Ciprofloxacin No. (%)	SXT No. (%)	Gentamicin No. (%)
CCU	1 (8.3)	8 (66.6)	9 (75)	4 (33.3)	6 (50)	7 (58.3)	9 (75)	4 (33.3)
ER	10 (6.3)	119 (75.8)	111 (70.7)	97 (61.7)	93 (59.2)	98 (62.4)	97 (61.7)	48 (30.5)
ICU	3 (10.3)	18 (62)	23 (79.3)	21 (72.4)	20 (68.9)	15 (51.7)	20 (68.9)	11 (37.9)
Internal	8 (10.3)	56 (72.7)	59 (76.6)	47 (61)	56 (72.7)	51 (66.2)	44 (57.1)	16 (20.7)
Outpatient	16 (5.65)	145 (51.2)	149 (52.6)	110 (38.8)	145 (51.2)	111 (39.2)	168 (59.3)	45 (15.9)
Pediatric	4 (11.7)	19 (55.8)	25 (73.5)	18 (52.9)	20 (58.8)	16 (47)	25 (73.5)	4 (11.7)
Surgery	6 (14.6)	29 (70.7)	28 (68.2)	22 (53.6)	20 (48.7)	22 (53.6)	23 (56)	7 (17)
Total	48 (7.5)	394 (62.2)	404 (63.8)	319 (50.3)	360 (56.8)	320 (50.5)	386 (60.9)	135 (21.3)

These results showed that aware about the regional antibiotic resistance rates is necessary knowledge for physicians and appropriate antibiotic prescription. Moreover, a line with our survey, in the study by Hadadi et al. nitrofurantoin was one of the effective antibiotic against UPEC(21) that it is still considered as a suitable choice for the treatment of urinary tract infections (22). However, in our and Hadadi studies the rate of ciprofloxacin resistance was remarkable (21). In some reports include Shirvani et al. and Sabir et al. studies similar to our data highest antibiotic resistance rates in UPEC belonged to ampicillin and nalidixic acid (23, 24). In another study, by Malekzadegan and colleagues out of 126 UPEC isolates, the highest and lowest resistance was related to ampicillin and imipenem (25) which was different from our results. Also following studies reported results which contrary to our findings. In this regards, a study was conducted by Nikzad et al. in 2021, 64 isolates of UPEC were isolated. The highest resistance was against cotrimoxazole (40.6%) and ampicillin (31.3%) (26). In another study in Nepal in 2020 by Pandit et al., from 1626 urine samples, *Escherichia coli* bacteria (62.1%) was the most common isolate. Half of the isolates were resistant to cephalosporins and fluoroquinolones. 64.9% of isolates were MDR and 40.3% of isolates were ESBL positive (27). It should be noted that the antibiotic resistance patterns according to both time and geographical area can be vary despite the comparable antibiotic resistance (28, 29). Many studies contrary to our study have showed the high prevalence of MDR in Enterobacterales family (25, 28, 29). But fortunately, it was less compared to the mentioned studies. Therefore, in this medical center, great care should be taken regarding the use of antibiotics to treat urinary tract infections caused by this isolates to prevent the increase in multi-drug resistant strains.

Conclusion

The result of this study highlight the role of UPEC as one of the important cause of UTI in individuals. Meanwhile, we showed that nitrofurantoin then gentimicin are the most effective antibiotic against UPEC infections. On the other hand, high resistance was reported for

some antibiotics, which shows that resistant bacteria are increasing, so the resistance of antibiotics, and the importance of UTIs should be noted by physicians in prescription antibiotics. In this regard, logical prescription of antibiotics and infection control strategies are needed for prevention and control of nosocomial infections especially urinary tract infection.

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Ethics approval and consent to participate

This study was in accordance with the declaration of Helsinki and an ethical permission was sought from the institutional Ethics Committee of Saveh University of Medical Sciences (Approval No. IR.SAVEHUMS.REC. 1402.029). However, because we only used leftovers from clinical specimens, the institutional ethics committee waived the need for informed consent.

Conflict of interest

The authors declare no conflict of interests.

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