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Original Article

Antimicrobial susceptibility pattern of *Escherichia coli* and *Klebsiella pneumoniae* isolated from patients with urinary tract infections in a tertiary care hospital

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Abstract

Aim: To determine etiological microorganisms from urine samples in patients diagnosed with UTI and to detect the antimicrobial susceptibility pattern of *Escherichia coli* and *Klebsiella pneumoniae* in a Tertiary Care Hospital.

Materials and Methods: A cross-sectional study was conducted using urine culture samples and sensitivity reports collected retrospectively from our laboratory records over a period from Jan 2013 to Dec 2017.

Results: A total of 729 urine culture isolates from 660 patients were included. Two-hundred eighty-four (41.8%) of the patients were male and 384 (58.2%) were female. The most common microorganisms were 46.4% *E. coli,* 18.2% *K. pneumoniae* and 12.1% *Enterococcus spp*., respectively. A total of 284 urine culture isolates produced extended spectrum beta-lactamases (ESBL), of which 186 (65.5%) were *E. coli* and 98 (34.5%) were *K. pneumoniae*. The most susceptible antimicrobials are meropenem, imipenem, amikacin, and fosfomycin, respectively. We determined that the antimicrobial drugs with the lowest susceptibility rates for both *E. coli* and *K. pneumoniae* were amoxicillin-clavulanate (24.5%), trimethoprim-sulfamethoxazole (30.7%) and ceftriaxone (43.2%). Additionally, their susceptibilities have gradually decreased. Ertapenem susceptibility has decreased more in *K. pneumoniae* isolates than *E. coli*.

Conclusion: Antimicrobial resistance and ESBL-producing for both *E. coli* and *K. pneumoniae* have been increasing over the years. Our findings may contribute to choosing the proper antibiotic for the empirical treatment of UTI and preventing treatment failure.

Keywords: Adult patients; antimicrobial susceptibility; urinary tract infections; tertiary care

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common infections in general population and a major cause of morbidity. It is estimated that around 150 million people per year have UTIs worldwide (1). UTIs also occur as the most common healthcare-associated infections in many hospitals, accounting for about 35% of all hospital-acquired infections (2). The incidence of UTIs is higher in women than in males, but in population older than 50 years, the incidence is similar (3). Advanced age, female gender, pregnancy, urinary tract abnormalities and dysfunctions, continuous catheterized patients with spinal cord injury, the presence of structural kidney disease, diabetes mellitus and immunosuppression are predisposing factors that increase the risk of UTIs (4). The predominant uropathogens for UTIs are gram negative bacteria and *E. coli* accounting for the highest prevalence in most cases. Other commonly seen pathogens are *Klebsiella spp., Staphylococcus saprophyticus, Enterococcus spp., Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter spp., Enterobacter spp., Citrobacter spp., Proteus spp. and Candida albicans* (5).

The distribution and antimicrobial sensitivities of uropathogens may vary locally (6). Irrational and excessive use of antimicrobial drugs contributes significantly to antimicrobial resistance, and approximately 15% of all prescribed antibiotics are for UTI treatment (7). Healthcare-associated UTIs are usually treated with broad-spectrum antibiotics, which are initiated empirically at the beginning, and then de-escalated to antibiotics to which it is sensitive to the agent grown in the urine culture. One of the most important factors to consider when selecting the

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proper antimicrobial therapy depends on the knowledge of susceptibility of the organism causing the UTI and local antimicrobial susceptibility data (8). Increasing resistance to many antimicrobial drugs, especially in ESBL-producing gram-negative microorganisms, has become a significant threat. Therefore, local antimicrobial therapy guidelines need to be constantly updated for the rational treatment. These guidelines are highly beneficial for patients diagnosed with UTIs to begin empirical antimicrobial therapy, so that initiating appropriate antimicrobial therapy can contribute to a decrease in antimicrobial resistance rates and to prevent treatment failure (9).

In current literature, there are many studies reporting the results of growing microorganisms and local antimicrobial sensitivity in the urine cultures of patients diagnosed with UTI in tertiary care hospitals. In our study, it was aimed to evaluate the microorganisms isolated in urine cultures and their sensitivity in patients admitted with a diagnosis of UTIs.

MATERIALS and METHODS

Study Design

Between 01 January 2013 and 31 December 2017, total 729 urine isolates from 660 patients who were hospitalized with the diagnosis of UTIs in the Infectious Diseases and Clinical Microbiology Department of Inonu University, a Tertiary Care Hospital, were included in our study. Patients whose urine culture was taken from an external center or who had urine culture before admission to the service were excluded from the study. We picked-up urine culture isolates taken from patients hospitalized with a diagnosis of UTI from the Laboratory in Infectious Diseases and Clinical Microbiology Department records retrospectively for five years. The diagnosis of UTI was made by a combination of symptoms and a positive urine analysis or culture.

Bacteriological Studies

The urine samples taken from midstream or urinary catheter were cultured on blood and Eosin Methylene Blue agar mediums and incubated aerobically at 37°C for 18-24 hours. The strains isolated from plates showing growth suggestive of significant bacteriuria with colony counts ≥105 cfu/ml were identified by conventional methods. The general characteristics, colony morphology, citrate use, presence of urease and oxidase enzymes, motility, indole and catalase effect, growth in bile and saline medium, pyrolidonyl-beta naphilamide (PYR) test positivity of the isolated strains were evaluated. A suspension of a pure colony from each confirmed culture isolate was prepared by using 0.85% sterile normal saline, and the suspension was adjusted at 0.5% McFarland standard. Antimicrobial susceptibility of the strains was determined by Kirby-Bauer disc diffusion method. Antibiotic discs were used to determine the susceptibility (Bioanalyse, Turkey) and susceptibility of strains was interpreted according to the CLSI guideline (10). Extended Spectrum Beta Lactamase (ESBL) production was detected by double disc synergy test (11).

Statistical Analysis

Patients' microbiological data who met our study criteria were retrospectively obtained from our laboratory registration system and were first recorded in the excel program. IBM SPSS Statistics 17.0 software program was used for analysis all of the data.

RESULTS

A total of 729 urine culture isolates from 660 patients diagnosed with UTI were included in the study. In some patients, more than one urine isolate was studied. Two-hundred eighty-four (41.8%) of the patients were male and 384 (58.2%) were female. It was observed that the most common microorganisms isolated from urine samples were 46.4% *E. coli*, 18.2% *K. pneumoniae* and 12.1% *Enterococcus spp*., respectively. The frequency of the isolated microorganisms is summarized in Table 1.

Table 1. The frequency of the isolated microorganisms

Mikroorganisms	Number (n)	Ratio (%)
Escherichia coli	338	46.4
Klebsiella pneumonia	133	18.2
Enterococcus spp	88	12.1
Pseudomonas aeruginosa	70	9.6
Acinetobacter spp	53	7.3
Enterobakter spp	26	3.6
Others	21	2.8
Total	**729**	**100**

A total of 284 urine culture isolates produced ESBL, of which 186 (65.5%) were *E. coli* and 98 (34.5%) were *K. pneumoniae*. The most susceptible antimicrobials for *E. coli* are meropenem, imipenem, amikacin and fosfomycin, respectively. Antibiotics with the highest sensitivity were also the same for *K. pneumoniae* isolates, but their order was different (fosfomycin, imipenem, meropenem and amikacin). We determined that the antimicrobial drugs with the lowest susceptibility rates for both *E. coli* and *K. pneumoniae* were amoxicillin/clavulanate (24.5%), trimethoprim/sulfametoxazole (30.7%) and ceftriaxone (43.2%). Additionally, their susceptibilities have gradually decreased. Ertapenem susceptibility has decreased more in *K. pneumoniae* isolates than *E. coli*. While the susceptibility of *E. coli* isolates to aminoglycoside (amikacin) showed a horizontal course, the sensitivity in *K. pneumoniae* isolates gradually decreased. The susceptibility of piperacillin/tazobactam has gradually increased for both microorganisms. The antimicrobial susceptibilities of *E. coli* and *K. pneumoniae* isolates by years and the distribution of ESBL-producing isolates are summarized in Table 2.

Table 1. The frequency of the isolated microorganisms

	Escherichia coli (%)						*Klebsiella pneumonia (%)*					
Years	**2013 n=77**	**2014 n=60**	**2015 n=81**	**2016 n=72**	**2017 n=48**	**Mean n=338**	**2013 n=19**	**2014 n=22**	**2015 n=23**	**2016 n=43**	**2017 n=26**	**Mean n=133**
Ceftriaxone	52	40.7	43.9	39.4	51.0	**43.2**	47.4	19	19	16.7	34.6	**27.3**
Ceftazidime	50.7	42.4	43.9	36.6	47.9	**44.3**	38.9	36.4	14.3	19.5	24.6	**26.7**
Pip/tazo	71.4	60	71.4	70	78.9	**70.3**	50	50	60	50.8	54.5	**53.1**
Fosfomycin	100	95.6	92.5	90	93.3	**94.3**	90	88.6	92.3	91.1	87.7	**89.9**
Ciprofloxacin	39.5	40.7	41.9	50	52.1	**44.8**	52.9	45	40	47.4	38.5	**44.8**
TMP/SMX	33.8	21.4	33.3	33.3	31.6	**30.7**	26.2	40	30	28.3	23.1	**29.5**
İmipenem	98.7	98.3	97.6	98.6	90.5	**96.7**	89.5	95.5	80	85.7	93.3	**88.8**
Meropenem	98.7	100	97.6	98.6	95.8	**98.1**	89.5	95.5	80	85.7	73.1	**84.8**
Ertapenem	81.8	90	82.9	76.2	81.6	**82.5**	73.7	72.7	61.9	60.5	57.7	**65.3**
KAM	36.8	13.3	24.4	16.9	31.2	**24.5**	26.3	14.3	19.5	14.3	16.9	**18.3**
Amikacin	98.7	87.9	98.6	100	95.8	**96.2**	94.7	81	84.2	71.4	93.3	**84.9**
Cefoxitin	85.5	79.7	83.5	87.1	91.6	**85.5**	84.2	75	61.9	73.2	65.4	**71.9**
ESBL-producing	45.5	60	56.8	60.6	54.1	**55.4**	52.6	81.8	81	85.7	65.3	**73.3**

Pip/tazo: Piperacillin/tazobactam, TMP/SMX: Trimethoprim/sulfamethoxazole, KAM: Amoxicillin-clavulanate, ESBL: Extended Spectrum Beta Lactamase

DISCUSSION

Monitoring the resistance profiles is necessary to cope with antimicrobial resistance in UTIs and to determine empirical treatment guidelines. Therefore, statistical analysis of surveillance data on a hospital and/or provincial basis or at regular intervals at the national level will significantly help clinicians to start empirical treatment for both outpatient and hospitalized patients (12). It was thought that our study, which includes the antimicrobial susceptibility of urinary isolates of patients followed up in our clinic, may also contribute positively to this process.

In a study including 209 urine isolates, conducted by Pandey et al. (13), they reported that the most common etiological organisms of UTIs isolated were *E. coli* (52.5%) followed by *Klebsiella species* (24.4%), P. aeruginosae (5.7%) and others. In another study were reported by Balkhi et al (14) the most common agents were similar (52.2%, 24.4% and 4.8%, respectively). In current literature, when compared with similar studies on this subject, we found that our uropathogens incidence rates were compatible. Yousef et al. (15) they analyzed that 680 positive urine samples (288 men and 392 women) and reporting 520 (76.5%) *E. coli* and 160 (23.5%) *K. pneumoniae*. Additionally, it had been reported that among these isolates were a total of 296 (218 *E. coli* and 78 *K. pneumoniae*) ESBL-producing. In our study, the prevalence of UTIs in females (58.2%) is more than in males (41.8%). It correlates to the findings of Pandey et al, Balkhi et al and Yousef et al who have also reported high prevalence rate of UTI among females as compared to males (13-15).

In a study conducted by Coskun US including 108 ESBL-producing urine isolates and it had been reported the most effective antibiotics against to *E. coli* and *K. pneumoniae* were carbapanems and susceptibility rates were %100 and %87, followed by fosfomycin 98 % and 83 %, nitrofurantoin 94 % and 30.4% respectively (16). Khan IU et al. (17) found the susceptibility pattern of *E. coli* 96.2% were sensitive to imipenem, 85.1% to amikacin, 80.7% to piperacillin/tazobactam and 72.6% to nitrofurantoin. The antibiogram of *K. pneumoniae* 76.1% were sensitive to imipenem and 52.3% to piperacillin/tazobactam. Nitrofurantoin and imipenem were the most effective antimicrobials for these uropathogens. In a study conducted by Dal et al. (18) emphasized that high levels of resistance to broad-spectrum antibiotics such as cephalosporins, carbapenems, and fluoroquinolones are possible in the near future, and treatment options may become more limited. In the same study, it was suggested that these antibiotics should not be used for the empirical treatment of urinary tract infections due to the high level of resistance to ceftazidim, ciprofloxacin and trimethoprim-sulfamethoxazole. Similarly, we found the most susceptible antimicrobial drugs were imipenem, meropenem and fosfomycin. We think that our results are similar with the findings of many studies and may be effective especially in the initial empirical therapies of ESBL-producing strains. Also piperacillin/tazobactam susceptibility were increased minimally by the years, however overall susceptibility of this antibiotic were 70% for *E. coli* and 53% for *K. pneumoniae*. It means that at least 30% of the isolates were resistant and it makes this antibiotic cannot be chosen empirical treatment for septic patients. Hrbacek et al. (19) stated that resistance to penicillin derivatives for *E. coli* and *Klebsiella spp*. was between 20.4-58.9%, resistance to cephalosporins above 30%, and resistance to fluoroquinolones between 25-35%

in 6897 urine isolates with positive results. In a study, including 3279 patients, conducted by Tekin et al. (20), determined that the sensitivity of amosicillin-clavulanate, co-trimoxazole and ciprofloxacin for ESBL-producing *E. coli* isolates was below 40%, while the sensitivity of nitrofurantoin was 93.1% for outpatient patients and 89.2% for inpatient patients. In this study, they have emphasized that nitrofurantoin especially may be a good treatment option for ESBL-producing *E. coli* isolates. In our study, we found that the lowest sensitivities for both *E. coli* and *K. pneumoniae* were in the form of penicillin derivative amoxicillin-clavulanate, third generation parenteral cephalosporins and trimethoprim-sulfamethoxazole. We can say that these findings, especially in patients hospitalized with a diagnosis of UTI, have to consider our high resistance rates for amoxicillin-clavulanate, third generation parenteral cephalosporins and trimethoprim-sulfamethoxazole when planning to start antimicrobial treatment, can prevent a possible failure of treatment.

Briefly, UTIs was seen in higher incidence in women in our study. The most common etiological microorganisms were identified *E. coli* and *K. pneumoniae*. It can be concluded that the rates of ESBL-producing isolates have increased over the years. It is also noteworthy that ertapenem resistance rates have increased over the years, especially in ESBL-producing isolates.

LIMITATIONS

In our study, patients' demographic data are limited only by gender. Identification of UTIs were not made in laboratory records. Comorbid diseases, facilitating factors and the number of infection attacks of patients were not specified. Some antimicrobial drugs, such as nitrofurantoin, have not been tested in antimicrobial resistance tests.

CONCLUSION

In hospitalized patients diagnosed with UTI, the most effective antimicrobial drugs for the empirical treatment of *E. coli* and *Klebsiella spp*. are carbapenems, amikacin, and fosfomycin. Our findings may contribute to choosing the proper antibiotic for the empirical treatment of UTI and preventing treatment failure. However, it is obvious that more extensive local clinical data is needed.

Competing Interests: The authors declare that they have no competing interest.

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Ethical Approval: This study was obtained from the Inonu University Non-Interventional Ethics Committee (Approval No: 2018/15-27).

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