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Urinary tract infections and antimicrobial resistance: Across sectional study

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Abstract
Background: Urinary infections are important microbial diseases common worldwide. Besides, the growth of antibiotic resistance is an ongoing concern for community health, especially in low-income countries. Therefore, this study aimed to identify common urinary pathogens and antibiotic sensitivity pattern in some cases of urinary tract infection (UTI) in Baghdad, the capital of Iraq.
Methods: A total of 289 participants with urinary symptoms (dysuria, frequency, and urgency) underwent general urine examination procedures in the laboratories of the government general hospitals and urine samples were cultured followed by sensitivity tests of the isolates against different types of antibiotics, from the beginning of January 2020 until the end of the month July 2021.
Results: The highest proportion of patients was females (78%), and *E. coli* was the most isolate organisms (45.7%), followed by mirabilis protein (16.3%). Different bacterial pathogens showed a high sensitivity especially to imipenem (99%), PTZ (97%), and amikacin (91%). The resistance of *E. coli* isolates was higher to imipenem and PTZ versus lower to amoxicillin. *Pseudomonas aeruginosa* isolates were not resistant to some antibiotics such as nitrofurantoin, ceftriaxone, cephalexin, and amoxicillin.
Conclusion: The widespread use of antibiotics has led to the emergence of resistance development among the most commonly used drugs in acquired UTI. Therefore, clinical diagnosis should be followed by sensitivity testing, to avoid the failure of direct empirical treatment. Therefore, it is recommended that specialists closely monitor the resistance of the urinary tract infection drugs used on the local level.

Keywords: Urinary symptoms, infection, bacterial pathogens

Introduction

Infection of any part of the urinary tract, whether in the kidneys, ureters, bladder or urethra, is called a urinary tract infection (UTI). The kidneys and ureters are located in the upper parts while the bladder and urethra occupy the lower parts of the urinary tract [1]. Approximately (50%) of women will begin acute cystitis at least once during their lifetime [2], and about a quarter will have a recurrence [3]. The lifetime prevalence of UTI in men is about (12%) [4]. It has been confirmed that the majority of urinary infections are caused by the retrograde ascension of microbes from the fecal flora through urethra passage to the bladder and ending with the kidneys. This has been particularly noted in females because they have a shorter and wider urethra and thus facilitate the passage of microorganisms [5]. Escherichia coli (*E. coli*) can be considered as one of the most common micro-organisms in urinary tract infection and is not associated with complications of other Enterobacteria like *P. mirabilis* and K. pneumoniae or even other bacteria such as S. saprophyticus. As for other pathogenic bacteria species, very few are isolated in urinary tract infections [6]. Escherichia coli isolates arise from the normal intestinal flora of humans. On the other hand, these bacteria may colonize fecal matter around the urethra, causing urinary tract infection, and they are known as uropathogenic *E. coli* [7]. In general, there are two satisfies of urinary tract infection, the first is health care-associated UTI and the second is community-acquired UTI [8]. As for treatment, historically it varies from three days to six weeks, recovery rates are perfect especially with the application of the therapy in a mini dose that extends only for (3) days. *E. coli* resistance to common antimicrobials is variant in regions of the country, and if the resistance proportion is major than 50%, an alternative drug should be selected [9]. To this day, antimicrobial resistance continues to grow, especially in gram (-) bacteria that cause bladder infections as well as pyelonephritis.

This hinders the experimental treatment of infection. It is worth noting that the geographical location is one of the most important determinants of resistance proportions. Besides, other factors that affect the pathogen extent also influence resistance rates [10]. One of the most prominent public health problems facing the world is the emergence of antibiotic resistance in the remediation of urinary infections, especially in the developing countries. The residents of those areas suffer from a large spread of counterfeit medicines of questionable quality and many bad health practices, as a result of poverty and ignorance [5]. Knowledge of local data on different etiology and susceptibility information on urinary tract infections may help clinicians to select appropriate empirical therapy [11]. Therefore, we conducted this study to determine uropathogens and their antimicrobial resistance in some government hospitals in Baghdad, Iraq.

Methods

A total of 289 individuals enrolled in the current cross-sectional study admitted to some general governmental hospitals in Baghdad, the capital of Iraq, which extended from January 2020 to July 2021 (about18 months). Fundamentalist approvals were obtained from the local health directorates to carry out this scientific research.

This study included both genders with different age groups of patients who had urinary symptoms (dysuria, frequency, and urgency), and the results of urine culture examination were positive. In contrast, the study excluded patients with a history of antibiotic treatment within the last two weeks, who had suprapubic or urethral catheterization, those with urinary tract infection after cystoscopy or other intravesical procedures, polycystic kidney disease, and neurogenic bladder, and diabetic patients.

Urine samples were collected from individuals suffering from the previously mentioned urinary symptoms by clean catch method and placed in sterilized plastic containers and cultured within (1) hour of collecting. Blood as well as MacConkey were used as laboratory agar media. The presence of significant bacteriuria diagnosed in samples that appeared pure growth of the isolate in urine. Appropriate biochemical assays were performed for accurate identification and antimicrobial susceptibility tests with disc diffusion technology using Muller-Hinton agar as growth medium used according to the instructions of manufacturer.

Antibiotic susceptibility tests were carried out for all bacterial isolates collected for the most common antibiotics used as UTI treatments according to our study, as follows: Trimethoprim, sulfamethaxol (SXT), amikacin, ciprofloxacin, levofloxacin, ceftazidime, cefepime, cefotaxime, ceftriaxone, cefixime, imipenem, amoxycillin-clavulanate (A-C), cephalexin, gentamicin, piperacillin tazobactam (PTZ), and nitrofurantoin.

The data were statistically processed using the SPSS package (IMB, version 26). The results were organized descriptively using frequencies and percentages.

Results

According to the results of this study, the highest percentage (38.8%) of patients was in the age group (40 – 59) years, while the lowest rate (9.3%) noted in the age group (< 20) years old. The results also proved that the rate of females was much higher than males (77.9% versus 22.1%), the majority of the participants (68.5%) were urban residents. The most prevalent micro-organism was *E. coli*, which was isolated from 132 patients (45.7%), followed by *Proteus mirabilis* (16.3%) as shown in Table (1).

The resistance of *E. coli* isolates has increased to imipenem (99%), PTZ (98%), nitrofurantoin (91%), and amikacin (89%). In contrast, it was lowest to amoxicillin (9%). On other hands, *P. mirabilis* isolates were fully resistant to imipenem (100%) followed by PTZ (98%), however the sensitivity pattern was low to different antibiotics such as amoxicillin, cefixime, and cephalexin. Besides, the sensitivity pattern of K. pneumonia isolates was low for several antibiotics including cefixime, amoxicillin, and cephalexin. P. aeruginosa isolates were not sensitive (0.0%) to some antibiotics including nitrofurantoin, A-C, ceftriaxone, cefotaxime, cephalexin, cefixime, and amoxicillin. The resistance of different bacterial isolates to a group of common antibiotics is shown in Table 2.

Table 1: Basic variables of all patients participating (N= 289) in the study

Variable		Frequency (No.)	Percentage (%)
Age (year)	< 20	27	9.3
	20-39	94	32.5
	40-59	112	38.8
	≥ 60	56	19.4
Gender	Male	64	22.1
	Female	225	77.9
Residence	Urban	198	68.5
	Rural	91	31.5
Isolated uropathogen	*E. coli*	132	45.7
	Proteus mirabilis	47	16.3
	Klebsiella pneumoniae	33	11.4
	Staphylococcus aureus	29	10.0
	Pseudomonas aeruginosa	21	7.3
	Staphylococcus saprophyticus	11	3.8
	Enterococcus faecalis	9	3.1
	Citrobacter species	7	2.4

Based on the study data, various pathogenic bacteria were highly sensitive to imipenem (99%), PTZ (97%), amikacin (91%), ceftazidime (70%), and nitrofurantoin (70%) as shown in Figure (1).

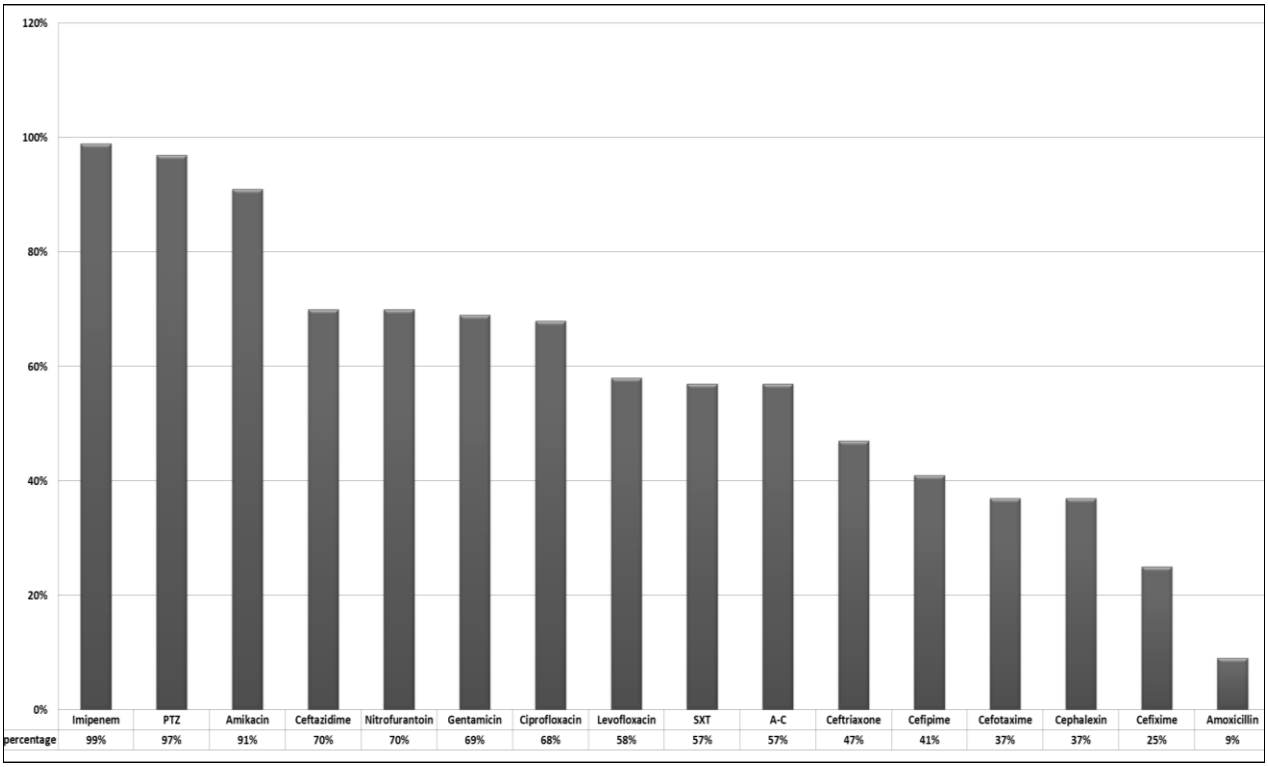

Fig 1: Overall sensitivity pattern of isolates uropathogens to different antibiotics

Table 2: Sensitivity pattern of different uropathogens isolates to different antibiotics

Antibiotic	Sensitivity pattern of certain isolated uropathogens (%)			
	E. coli	**Proteus mirabilis**	**Klebsiella pneumonia**	***Pseudomonas aeruginosa***
Imipenem	99.0	100.0	97.0	95.0
PTZ	98.0	98.0	88.0	90.0
Amikacin	89.0	85.0	91.0	95.0
Ceftazidime	77.0	66.0	61.0	81.0
Nitrofurantoin	91.0	28.0	82.0	0
Gentamicin	67.0	32.0	88.0	76.0
Ciprofloxacin	67.0	77.0	67.0	52.0
Levofloxacin	70.0	28.0	39.0	10.0
SXT	66.0	36.0	79.0	52.0
A-C	42.0	4.0	36.0	0
Ceftriaxone	54.0	36.0	45.0	0
Cefipime	45.0	13.0	42.0	43.0
Cefotaxime	45.0	26.0	36.0	0
Cephalexin	43.0	19.0	33.0	0
Cefixime	36.0	9.0	24.0	0
Amoxicillin	9.0	0	27.0	0

Discussion

This study analyzed antimicrobial resistance patterns among uropathogens that could help determine the empirical therapy of urinary tract infection in the community. In our study, infections of urinary tract were observed more commonly in women of reproductive age which was agreed with other previous studies [12, 13] and this may be due colonization of perineum as well as urine stasis. At the forefront of the most infectious organisms in our study samples were both *E. coli* and *Proteus mirabilis*, and this agreed with the results of similar studies by Fury *et al*. in (2021) [12], Lewis *et al*. in (2013) [14], and Turvet *et al*. in (2018) [15]. There was an increase in resistance toward 3rd generation cephalosporins such as cefotaxime, ceftriaxone and cefixime (susceptibility was only 25-47%) and 4th generation cephalosporins such as cefepime (sensitivity was only 41%). This is an indication that many organisms are extended-spectrum beta-lactamase (ESBL), which makes them capable of destroying ß-lactam antibiotics, thus losing the drug's efficacy [13]. In other words, ESBL has a primary role in disrupting treatment and thus may contribute negatively to preventing infection control [16]. Drugs containing inhibitors, such as PTZ, may be used to treat these organisms, but they should only be used as a last resort. Imipenem resistance is found in a very tiny percentage of organisms (1%), indicating that carbapenemase-producing bacteria are not prevalent in this investigation. Although carbapenems are considered the last line of defense against any disease, it is recommended to use them as a last resort antibiotic to avoid carbapenem resistance. As a result, it is not suitable for empirical therapy. Resistance to amoxicillin and levofloxacin was high, ranging from 42 to 95 percent, although resistance to combination medicines (PTZ), which included amikacin and imipenem, was low. Despite the fact that

fluoroquinolones are among the most effective medications for treating UTIs due to their broad-spectrum activity against most uropathogens, a number of studies have found that fluoroquinolone resistance is rising [17]. Results of our study confirmed the rise level of resistance to levofloxacin (58%). Similar previous studies showed that resistance of *E. coli* to ciprofloxacin, the most effective drug against UTI, was increasing and this is in line with our founding where resistance reached (67%). In 2005, Kurutepe and collagenous found an increase in resistance from 2.9% in 2000 to 11.3% in 2002 (17). Also, a high level of resistance to quinolones was reported (40%) among strains of *E. coli* isolated from urinary tract infected patients in southern Islamic Republic of Iran (18). This study also showed that nitrofurantoin treatment has a tremendous effect (82-91%) against the urinary pathogens (*E. coli* and K. pneumonia) responsible for UTI in the study samples. Due to the low resistance and propensity for side effects to antimicrobials (choice for colonization or infection with multidrug-resistant organisms) another study recommended this antibiotic as the drug of choice for empirical therapy in CAUTI (19). All urinary isolates of Escherichia coli, even multidrug-resistant strains, are highly susceptible to nitrofurantoin. The narrow range of activity, few therapeutic indications, small tissue distribution, and minimal contact with bacteria outside the urinary system may play a role in persistent and high-level resistance of *E. coli* to nitrofurantoin (20). Because of the side-effect profile, doctors are reluctant to give nitrofurantoin, however it is an important first-line treatment for urinary tract infections prior to culture and sensitivity testing. Several studies have shown an association between antimicrobial use and resistance [21-23]. The high rates of resistance among the strains of Escherichia coli in this study could be due, at least in part, to the high consumption of antibiotics in the country, which increased antimicrobial selection pressure. This underlines the importance of continuous monitoring of local resistance to provide optimal treatment to the population of the area. Amikacin has been demonstrated in this study to have strong activity against 91% of pathogens, including Pseudomonas, Klebsiella, and all other species that cause UTI. We can recommend amikacin as an empirical treatment for UTI in complex patients based on this evidence. However, the growing threat of antibiotic resistance must be kept in mind.

Conclusions

We concluded from the results that UTI resistance data must now be shown in order to track UTI resistance in regular practice. Some common antibiotics such as ampicillin and amoxicillin have developed so high levels of resistance that providing them would almost certainly lead to therapeutic failure. The uropathogens are becoming more resistant, hence clinical diagnosis followed by susceptibility testing is required, as direct empiric therapy may result in treatment failure. We recommend a comprehensive examination of medication resistance in our country Iraq to formulate UTI guidelines.

Conflict of Interest

Not available

Financial Support

Not available

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