

Uropathogens antibiotic susceptibility as an indicator for the empirical therapy used for urinary tract infections: a retrospective observational study

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ABSTRACT

Background and Objectives: Urinary tract infection (UTI) is a common infection affects people of different ages. It is important to explore the antibiotics susceptibility of the bacterial agents to improve the empirical antibacterial prescription because of emerging of multi-drug resistant (MDR) bacteria.

Materials and Methods: This is a retrospective observational study including 322 patients with UTI at the largest hospital at the center of Al-Basrah Governorate in the far south of Iraq from August 2018 to November 2019. Bacterial isolates from urine samples with significant bacteria were investigated by automated VITEK® 2 compact system to determine the causative bacteria and their antibiotics susceptibility.

Results: *Escherichia coli* and *Klebsiella pneumoniae* were the first and second most frequent Gram-negative isolates, whereas *Staphylococcus haemolyticus* and *Enterococcus faecalis* were the first and second most frequent Gram-positive isolates. Fosfomycin, tigecycline, colistin, meropenem, imipenem, amikacin and nitrofurantoin had high susceptibility rates against Gram-negative isolates. Nitrofurantoin, tigecycline, daptomycin, teicoplanin, vancomycin and linezolid had a high effect against Gram-positive isolates.

Conclusion: The leading causative isolates especially the most predominant Gram-negative isolates *E. coli* and *K. pneumoniae* show high resistance rates against important antibiotics including penicillin/β-lactamase inhibitors piperacillin/tazobactam, ceftazidime cefepime, ciprofloxacin, levofloxacin and trimethoprim/sulfamethoxazole which call for reconsidering them for treatment of UTI.

Keywords: Urinary tract infections; Antibiotics resistance; *Escherichia coli*; *Klebsiella pneumoniae*

INTRODUCTION

Bacterial urinary tract infection is one of the most common infections that affects about 150 million

people each year. It affects both sexes at different ages, in both outpatients and inpatients settings but it's incidence is higher in females. About 50% of women are affected by UTI at some time of their life (1). UTI is caused by a variety of bacteria including most commonly *Escherichia coli*, in addition to others such as *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* (2, 3). Urinary tract infection due to multidrug resistance (MDR) bacteria treated with inappropriate empirical antibiotics

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therapy is associated with serious complications such as sepsis and increased mortality rate in addition to the increased treatment cost and hospital length of stay, and loss of working days (4, 5). The resistance to the prescribed antibiotics is highly affected by the geographical location (6), as so, local susceptibility studies are required to determine the most effective drugs which highly improve the empirical prescribing and decrease the treatment cost and duration (7). Irrational antibiotics use with increased consumption and inappropriate prescribing and lack of regulations to the availability of antibiotics over the counter which promotes overuse are important causes for increased bacterial antibiotic resistance (8, 9). In Al-Basrah governorate, there is widespread dissemination of the over the counter of nearly all antibiotics without medical prescription and overuse.

The effective antibiotics against *E. coli* which is the most common causative pathogen may include one of these drugs depending on the local resistance pattern: nitrofurantoin, fosfomycin, fluoroquinolones, cefoxitin, piperacillin/tazobactam, carbapenems, ceftazidime/avibactam, ceftolozane-tazobactam and aminoglycosides (10). The increase in the resistance of UTI causative bacteria has been reported in various studies (11-13). Treatment options for UTIs caused by multidrug-resistant (MDR)-*Pseudomonas* spp. include fluoroquinolones, ceftazidime, cefepime, piperacillin-tazobactam, carbapenems, aminoglycosides, colistin, ceftazidime/avibactam, and ceftolozane/tazobactam (10, 14). The increasing resistance of *E. coli*, the most common causative agent has been found and reported in many studies and surveys (3).

Microbial species that are normally susceptible to a particular antibiotic may develop more resistant strains through spontaneous mutation or by the acquisition of new resistance genes followed by selection. The genetic alterations induce various mechanisms that stand behind resistance such as modification of antibiotic target site, decreased accumulation of the drug due to decreased permeability or increased efflux and enzymatic inactivation. Antibiotics eradicate drug-sensitive competitors, leaving resistant bacteria to reproduce and predominate as a result of natural selection. This represents the basis that irrational use, over prescription, and extensive agricultural use of antibiotics increase the bacterial resistance (8, 15). Unfortunately, data and studies about the distribution and antibiotics susceptibility profile

of the causative bacterial agents of UTI are lacking in Al-Basrah Governorate, the southernmost of Iraq. This study aimed to determine the distribution and antibiotics susceptibility profile of causative bacterial agents in patients with UTI in the largest hospital at the center of Al-Basrah Governorate by using an automated VITEK® 2 compact system which is an accurate technique recently applied in the microbiological laboratory. The VITEK® 2 compact system is a new automated system designed to provide accurate identification and antibiotics susceptibility testing for most clinical isolates of both Gram-positive and negative bacteria. Other advantages of the system include shortened turnaround times, improved specimen handling, enhanced quality control, reproducibility, and the ability to track results (16).

MATERIALS AND METHODS

Study design. This is a retrospective observational study on clinical urine samples cultured for species identification and antibiotics susceptibility testing. The study was performed from August 2018 to November 2019 in Al-Basrah Teaching Hospital which is the largest general hospital in Al-Basrah Governorate. Approval was obtained from the Scientific Committee of the Center of the Training and Human Development/ Research Unit in the Health Directorate of Al-Basrah Governorate (Date 10-July-2019/ NO. 375) after the agreement of Al-Basrah Teaching Hospital. Urine samples were collected from 322 patients with suspected UTI, including outpatients attending the urology consultant clinic, and inpatient from all hospital clinical departments, irrespective of their age or sex. Urine samples were collected in a wide-mouth sterile container and transported to the microbiology laboratory.

Samples culture. The specimens were inoculated on blood agar and MacConkey agar by streaking a loop-full of each sample by a sterile calibrated loop (0.001 mL). The inoculum was distributed evenly throughout the plate. The plate is incubated for 24 hr at 37°C. The growth of the aerobically incubated bacteria was identified by colony characteristics and Gram staining (15). The number of bacteria per mL of urine sample was determined by counting the number of colonies. Colony counts yielding bacterial growth of $\geq 100,000$ colony forming units (CFU)/mL

of urine were diagnosed as significant bacteriuria. The urine samples that didn't show positive bacteria were not processed further for species identification and antibiotics susceptibility testing and were not included in this study.

Species identification and antibiotics susceptibility. Species identification of Gram-positive bacteria (GPB), and Gram-negative bacteria (GNB) and antibiotics susceptibility testing were determined with VITEK® 2 compact system (bioMérieux, France) using GN, GP, AST-P641, AST-N326, and AST-N327 cards. The investigated antibiotics by VITEK® 2 cards were the following: piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, aztreonam, imipenem, meropenem, amikacin, gentamicin, netilmicin, tobramycin, ciprofloxacin, levofloxacin, tetracycline, tigecycline, trimethoprim/sulfamethoxazole, fosfomycin, nitrofurantoin, benzylpenicillin, erythromycin, clindamycin, linezolid, daptomycin, teicoplanin, vancomycin, and fusidic acid. Isolates with resistance or intermediate susceptibility were considered non-susceptible to the antibiotic agent. The results were interpreted according to the 2015 Clinical and Laboratory Standards Institute (CLSI) criteria.

RESULTS

Patients characteristics. In the present study, three hundred twenty-two urine samples yielded significant bacteriuria of which 202 were obtained from females and 120 from males. The sex and age distribution of the UTI patients are presented in Table 1. The young and middle-aged patients (25-64 years) constitute 53.4% of the UTI cases. Pediatric patients (0-14 years) represent 18% and elderly patients (≥ 65 years) represent 16.8% of the total number. Patients of 45-64 years of age group represent the highest number (28.6%) of the total UTI cases, followed by the patients in the age group of 25-44 years (24.8%).

The distribution and frequency of the isolates. The distribution and frequency of the Gram-negative and Gram-positive bacterial isolates are presented in Table 2. Of the total 322 bacterial isolates, they include 25 species, 81 were Gram-positive (3 genera, 10 species), whereas 241 were Gram-negative iso-

Table 1. Sex and age distribution of UTI patients.

		Samples with significant bacteriuria
Sex	Female	202 (62.7)
	Male	120 (37.3)
	Total	322
Age group	< 1	11 (3.4)
	1-14	47 (14.6)
	15-24	38 (11.8)
	25-44	80 (24.8)
	45-64	92 (28.6)
	65 +	54 (16.8)
	Total	322

lates (10 genera, 15 species). The two predominant Gram-negative species were *E. coli*, and *K. pneumoniae*, consisting of 50% and 9.9% of the total isolates respectively (Table 2). *Staphylococcus haemolyticus* and *Enterococcus faecalis* were the first and second most predominant Gram-positive species accounting for 11.5% and 5.9% of the total isolates respectively (Table 2).

Bacterial antibiotics susceptibility. The antibiotics susceptibility profile of Gram-positive bacteria is summarized in Tables 3 and 4. *Staphylococcus haemolyticus*, the most prevalent Gram-positive isolate showed a high susceptibility rate ($>70\%$) to tigecycline, vancomycin, daptomycin, nitrofurantoin, teicoplanin, daptomycin, and levofloxacin but with a high resistance rate to benzylpenicillin, gentamicin, erythromycin, fosfomycin and fusidic acid. The second prevalent Gram-positive isolate *Enterococcus faecalis* showed high susceptibility to linezolid, daptomycin, tetracycline, and tigecycline, whereas it showed a high resistance rate to levofloxacin, erythromycin, and clindamycin.

Regarding the antibiotics susceptibility of Gram-negative isolates, the data obtained by the VITEK® 2 system, showed that the most predominant Gram-negative isolate *E. coli* had a high susceptibility rate ($\geq 70\%$) against fosfomycin, nitrofurantoin, meropenem, colistin, imipenem, tigecycline, and amikacin, while showing high resistance rate ($>70\%$) to piperacillin, ceftazidime, cefepime, and aztreonam.

The second most predominant Gram-negative isolate *K. pneumoniae* showed a high susceptibility rate ($70\% \geq$) to colistin, meropenem, imipenem, amika-

Table 2. Distribution and frequency of Gram-negative and Gram-positive bacterial isolates.

Gram-negative bacteria	N (%)	Gram Positive	N (%)
<i>Escherichia coli</i>	161 (50.0)	<i>Staphylococcus haemolyticus</i>	37 (11.5)
<i>Klebsiella pneumoniae</i>	32 (9.9)	<i>Staphylococcus aureus</i>	6 (1.9)
<i>Klebsiella oxytoca</i>	1 (0.3)	<i>Staphylococcus epidermidis</i>	3 (0.90)
<i>Pseudomonas aeruginosa</i>	11 (3.4)	<i>Staphylococcus saprophyticus</i>	2 (0.6)
<i>Pseudomonas luteola</i>	4 (1.2)	<i>Staphylococcus hominis</i>	2 (0.6)
<i>Proteus mirabilis</i>	10 (3.1)	<i>Staphylococcus lugdunensis</i>	1 (0.3)
<i>Proteus vulgaris</i>	2 (0.6)	<i>Staphylococcus agalactia</i>	8 (2.5)
<i>Enterobacter cloacae</i>	7 (2.2)	<i>Staphylococcus pneumoniae</i>	2 (0.6)
<i>Citrobacter freundii</i>	3 (0.9)	<i>Enterococcus faecalis</i>	19 (5.9)
<i>Citrobacter koseri</i>	2 (0.6)	<i>Enterococcus casseliflavus</i>	1 (0.3)
<i>Serratia rubidaea</i>	1 (0.3)		
<i>Serratia marcescens</i>	3 (0.9)		
<i>Acinetobacter baumannii</i>	2 (0.6)		
<i>Aeromonas hydrophila</i>	1 (0.3)		
<i>Yersinia kristensenii</i>	1 (0.3)		
Total	241 (74.8)		81 (25.2)

Table 3. Antibiotics resistance percentage R (R%) of Gram-positive isolates.

Antibiotics	Resistance percentage R (R%)				
	<i>Staphylococcus haemolyticus</i> (37)	<i>Staphylococcus aureus</i> (6)	<i>Staphylococcus epidermidis</i> (3)	<i>Staphylococcus saprophyticus</i> (2)	<i>Staphylococcus hominis</i> (2)
Benzylpenicillin	37 (100%)	6 (100%)	3 (100%)	--	2 (100%)
Gentamicin	27 (73%)	0 (0.0%)	0 (0.0%)	2 (100%)	2 (100%)
Ciprofloxacin	17 (46%)	0 (0.0%)	3 (100%)	2 (100%)	0 (0.0%)
Levofloxacin	8 (22%)	--	--	0 50	--
Erythromycin	33 (89%)	0 (0.0%)	3 (100%)	--	2 (100%)
Clindamycin	16 (43%)	2 (33.3%)	3 (100%)	2 (100%)	2 (100%)
Linezolid	4 (11%)	2 (33.3%)	0 0	2 (100%)	0 (0.0%)
Daptomycin	2 (5%)	0 (0.0%)	0 0	--	--
Teicoplanin	4 (11%)	0 (0.0%)	0 0	--	2 (100%)
Vancomycin	3 (8%)	0 (0.0%)	0 0	--	0 (0.0%)
Tetracycline	20 (54%)	0 (0.0%)	3 (100%)	0 (0.0%)	2 (100%)
Tigecycline	0 (0.0%)	0 (0.0%)	0 0	0 (50.0%)	0 (0.0%)
Fosfomycin	33 (89%)	--	1 33.3	2 (100%)	2 (100%)
Nitrofurantoin	0 (0.0%)	--	0 (0.0%)	0 (0.0%)	--
Fusidic acid	35 (95%)	1 (16.7%)	0 (0.0%)	2 (100%)	2 (100%)
Trimethoprim/Sulfamethoxazole	23 (62%)	0 (0.0%)	3 (100%)	2 (100%)	2 (100%)

cin, and tigecycline, while showing a high resistance rate (>70%) to piperacillin, and ceftazidime. *P. aeruginosa* the third most frequent Gram-negative isolate shows high susceptibility to ceftazidime, cefepime, imipenem, and amikacin, while it shows a high resistance rate to piperacillin/tazobactam, trimetho-

prim/sulfamethoxazole, tigecycline, tobramycin, and netilmicin. The susceptibility profile of Gram-negative bacteria for the 19 antibacterial drugs tested is summarized in Tables 5 and 6.

The collective resistance of Gram-positive isolates was high for fosfomycin, erythromycin, fusidic

Table 4. Antibiotics resistance percentage R (R%) of Gram-positive isolates.

Antibiotics	Resistance percentage R (R%)				
	<i>Staphylococcus lugdunensis</i> (1)	<i>Streptococcus agalactiae</i> (8)	<i>Streptococcus pneumoniae</i> (2)	<i>Enterococcus faecalis</i> (19)	<i>Enterococcus casseliflavus</i> (1)
Benzylpenicillin	0 (0.0%)	0 (0.0%)	2 100	6 (31.6%)	1 (100%)
Gentamicin	0 (0.0%)	--	2 100	--	--
Ciprofloxacin	0 (0.0%)	0 (0.0%)	--	7 (42.1%)	0 (0.0%)
Levofloxacin	0 (0.0%)	4 (50.0%)	2 100	8 (42.1%)	
Erythromycin	--	3 (37.5%)	--	19 (100%)	1 (100%)
Clindamycin	0 (0.0%)	4 (50%)	--	19 (100%)	1 (100%)
Linezolid	0 (0.0%)	0 (0.0%)	--	0 (0.0%)	0 (0.0%)
Daptomycin	0 (0.0%)	0 (0.0%)	--	0 (0.0%)	--
Teicoplanin	--	0 (0.0%)	--	7 (36.8%)	0 (0.0%)
Vancomycin	--	0 (0.0%)	--	8 (42.15%)	1 (100%)
Tetracycline	0 (0.0%)	7 (87.5%)	2 100	4 (21.1%)	1 (100%)
Tigecycline	0 (0.0%)	0 (0.0%)	--	0 (0.0%)	0 (0.0%)
Fosfomycin	0 (0.0%)	--	--	--	--
Nitrofurantoin	0 (0.0%)	--	--	--	--
Fusidic acid	0 (0.0%)	--	--	--	--
Trimethoprim/Sulfamethoxazole	0 (0.0%)	0 (0.0%)	2 (100%)	19 (100%)	0 (0.0%)

acid, and benzylpenicillin with resistance rates of (72.1%-80.2%), and with low resistance rates (0.0%-31.9%) for nitrofurantoin, tigecycline, daptomycin, linezolid, vancomycin, teicoplanin, and levofloxacin, Table 7.

The collective resistance of Gram-negative isolates was high for piperacillin, ceftazidime, cefepime, trimethoprim/sulfamethoxazole, tetracycline, and piperacillin/tazobactam with resistance rates of (60.1%-90%) and with low resistance rates (2.3%-17.6%) for fosfomycin, tigecycline, colistin, imipenem, meropenem, and nitrofurantoin (Table 7).

DISCUSSION

The determination of the bacterial pathogens distribution and their antibiotics susceptibility to one of the most common infections such as UTI at the level of the local area is a pressing execution to explore the effective antibiotics and to improve the empirical treatment. We are in the era of increasing antibiotics resistance, so continuous surveillance of antibacterial susceptibility of the clinical isolates is recommended to keep an eye on the changes in the efficacy of the antibiotics against uropathogenic bacteria especially the antibiotics resistance in our region is expected to

be higher than elsewhere, a situation sensed by the health workers in the clinical practice.

Regarding the etiological bacterial agents, the findings in this study were in agreement with others where the Gram-negative isolates were higher in incidence and constitute 74.7%, with *E. coli* taking the lead which constitutes 50.0% of the total isolates, a finding that is consistent with studies on urinary tract infection (3). *S. haemolyticus* and *K. pneumoniae* were the second and third most frequently isolated bacteria with percents of 11.5 and 9.9% respectively in addition to a wide range of other isolates that constituted low percent.

The antibacterial susceptibility was performed with an automated VITEK® 2 compact system using a panel of 16, and 19 antibiotics for both Gram-positive and negative bacteria respectively. The testing for a high number of antibiotics broadens the options available for clinicians to choose the effective drugs in the treatment of UTI. The antibacterial susceptibility of Gram-positive bacteria showed that the collective resistance was low (< 20%) for nitrofurantoin, tigecycline, daptomycin, linezolid, vancomycin, and teicoplanin, while the resistance was high (> 70%) for benzylpenicillin, fusidic acid, erythromycin, and fosfomycin as explained in Table 5. Similar findings were reported in a study conducted in Erbil north of

Table 5. Antibiotics resistance percentage R (R%) of Gram-negative isolates^a

Antibiotics	Resistance percentage R (R%)					
	<i>Escherichia coli</i> (161)	<i>Klebsiella Pneumonia</i> (32)	<i>Klebsiella Oxytoca</i> (1)	<i>Pseudomonas aeruginosa</i> (11)	<i>Pseudomonas Luteola</i> (4)	<i>Proteus mirabilis</i> (10)
Piperacillin	151 (93.8%)	30 (93.8%)	1 (100%)	6 (54.5%)	2 (50.0%)	8 (80.0%)
Piperacillin / Tazobactam	105 (65.2%)	16 (50.0%)	0 (0.0%)	9 (81.8%)	0 (0.0%)	6 (60.0%)
Ceftazidime	128 (79.5%)	23 (71.9%)	0 (0.0%)	4 (36.4%)	2 (50%)	9 (90.05)
Cefepime	119 (73.9%)	20 (62.5%)	0 (0.0%)	3 (36.4%)	0 (0.0%)	6 (60.0%)
Aztreonam	83 (82.0%)	13 (68.8%)	0 (0.0%)	5 (63.6%)	2 (100%)	7 (70.0%)
Meropenem	6 (3.7%)	8 (25.0%)	0 (0.0%)	5 (45.5%)	0 (0.0%)	8 (80.0%)
Imipenem	8 (5.0%)	4 (12.5%)	0 (0.0%)	4 (36.4%)	0 (0.0%)	7 (70.0%)
Ciprofloxacin	105 (65.2%)	16 (50.0%)	0 (0.0%)	6 (54.5%)	0 (0.0%)	5 (50.0%)
Levofloxacin	94 (58.4%)	14 (43.8%)	0 (0.0%)	6 (54.5%)	0 (0.0%)	4 (40.0%)
Trimethoprim/Sulfamethoxazole	108 (67.1%)	14 (43.8%)	0 (0.0%)	11 (100%)	1 (25.5%)	10 (100%)
Tetracycline	104 (64.6%)	20 (62.5%)	0 (0.0%)	7 (63.6)	0 (0.0%)	8 (80.0%)
Tigecycline	0 (0.0%)	6 (18.8%)	0 (0.0%)	11 (100%)	0 (0.0%)	10 (100%)
Gentamicin	60 (37.3%)	14 (43.8%)	0 (0.0%)	7 (63.6%)	0 (0.0%)	7 (70.0%)
Amikacin	23 (14.3%)	6 (18.8%)	0 (0.0%)	4 (36.4%)	0 (0.0%)	0 (0.0%)
Tobramycin	88 (54.7%)	18 (56.3%)	0 (0.0%)	8 (72.7%)	--	8 (80.0%)
Netilmicin	80 (49.7%)	14 (43.8%)	0 (0.0%)	7 (72.7%)	--	8 (80.0%)
Colistin	4 (2.5%)	0 (0.0%)	0 (0.0%)	5 (54.5%)	4 (100%)	10 (100%)
Fosfomycin ^b	1 (2.3%)	--	1 (100%)	6 (54.5%)	--	--
Nitrofurantoin ^b	8 (18.2%)	--	0 (0.0%)	9 (81.8%)	--	--

^a*Aeromonashydrophila* (1), *Yersinia kristensenii* (1), *Serratia Rubidaea* (1) not applied for antibiotics

^bdetermined for only 44 *E. coli* isolates

Table 6. Antibiotics resistance percentage R (R%) of Gram-negative isolates

Antibiotics	Resistance percentage R (R%)					
	<i>Proteus vulgaris</i> (2)	<i>Enterobacter cloacae</i> (7)	<i>Citrobacter freundii</i> (3)	<i>Citrobacter koseri</i> (2)	<i>Serratia marcescens</i> (3)	<i>Acinetobacter baumannii</i> (2)
Piperacillin	2 (100%)	7 (100%)	3 (100%)	2 (100%)	3 (100%)	2 (100%)
Piperacillin/Tazobactam	0 (0.0%)	3 (42.9%)	2 (66.7%)	0 (0.0%)	--	2 (100%)
Ceftazidime	0 (0.0%)	6 (85.7%)	2 (66.7%)	0 (0.0%)	2 (67.7%)	2 (100%)
Cefepime	0 (0.0%)	6 (85.7%)	2 (66.7%)	0 (0.0%)	2 (67.7%)	2 (100%)
Aztreonam	0 (0.0%)	7 (100%)	2 (66.7%)	0 (0.0%)	3 (100%)	2 (100%)
Meropenem	0 (0.0%)	2 (28.6%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	--
Imipenem	0 (0.0%)	2 (28.6%)	2 (66.7%)	0 (0.0%)	--	2 (100%)
Ciprofloxacin	0 (0.0%)	4 (57.1%)	3 (100 %)	0 (0.0%)	1 (33.3%)	2 (100%)
Levofloxacin	0 (0.0%)	5 (71.4%)	3 (100 %)	0 (0.0%)	1 (33.3%)	2 (100%)
Trimethoprim/Sulfamethoxazole	0 (0.0%)	4 (57.1%)	2 (66.7%)	0 (0.0%)	1 (33.3%)	2 (100%)
Tetracycline	0 (0.0%)	5 (71.4%)	1 (33.3%)	0 (0.0%)	0 (0.0%)	2 (100%)
Tigecycline	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gentamicin	2 (100%)	4 (57.1%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	2 (100%)
Amikacin	0 (0.0%)	2 (28.6%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tobramycin	0 (0.0%)	4 (57.1%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Netilmicin	0 (0.0%)	5 (71.4%)	2 (66.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Colistin	2 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (33.3%)	2 (100%)

Table 7. Total antibiotics resistance of Gram-negative and positive isolates.

Gram-negative isolates		Gram-positive isolates	
Antibiotics	% Resistance	Antibiotics	% Resistance
Piperacillin	90.0%	Fosfomycin ^b	86.3%
Ceftazidime	73.9%	Erythromycin	80.2%
Cefepime	66.4%	Fusidic acid ^b	78.4%
Trimethoprim/Sulfamethoxazole	63.5%	Benzylpenicillin	72.1%
Tetracycline	61.0%	Trimethoprim/Sulfamethoxazole	62.9%
Piperacillin/Tazobactam	60.1%	Gentamicin	62.3%
Tobramycin	54.0%	Clindamycin ^b	62.0%
Ciprofloxacin	58.9%	Tetracycline	48.1%
Levofloxacin	53.5%	Ciprofloxacin	36.7%
Aztreonam	51.5%	Levofloxacin	31.9%
Netilmicin	48.9%	Teicoplanin	17.1%
Gentamicin	40.7%	Vancomycin	15.8%
Nitrofurantoin ^a	17.6%	Linezolid	10.1%
Amikacin	15.4%	Daptomycin	2.7%
Meropenem	13.0%	Tigecycline	0.0%
Imipenem	12.2%	Nitrofurantoin ^b	0.0%
Colistin	11.6%		
Tigecycline	11.2%		
Fosfomycin ^a	2.3%		

^aNitrofurantoin, and Fosfomycin determined for only 44 *E. coli* isolates.

^bFosfomycin, Fusidic acid, Clindamycin, and Nitrofurantoin applied for only 44, 51, 53, 43 gram positive isolates respectively

Iraq in 2018 (17).

Fosfomycin and nitrofurantoin showed a comparable susceptibility against *E. coli* to the other countries, the susceptibility profile of both *E. coli*, and *K. pneumoniae* showed higher rates of resistance for several antibiotics including third-generation cephalosporins as ceftazidime, and cefepime, quinolones as ciprofloxacin, and trimethoprim/sulfamethoxazole than other studies conducted recently in Saudi Arabia (18), Ethiopia (19), Poland (20), Swiss (21), Belgium, Germany, and Spain (22), Portugal (23), in addition to Jordan (14), South Korea (24), and Spain (25), and in six European countries including Russia (26) for only *E. coli*. Another interesting finding is that amikacin has a notable higher susceptibility rate than gentamicin against the first and second most frequent Gram-negative isolates *E. coli* and *K. pneumoniae*. This result reveals that the widely prescribed antibiotics on an empirical basis for UTI as quinolones (ciprofloxacin, levofloxacin), cephalosporins (ceftazidime, cefepime), penicillin/ β -lactamase inhibitor combinations piperacillin/tazobactam,

gentamicin, and trimethoprim/sulfamethoxazole has a high resistance rate that is not effective in an acceptable level to be prescribed on an empirical manner. The high incidence of MDR uropathogens may explain this pattern of susceptibility profile which is noted to be high in the previous years in different geographical location and different prevalence rates of the MDR especially among the leading pathogens associated with UTIs, including *E. coli*, *Klebsiella* species and *Proteus* species (20, 27, 28).

One of the risk factors for developing MDR uropathogens is the use of antibiotics before the UTI occurrence as the use of fluoroquinolones and some other β -lactam antibiotics within 4 weeks to 1 year is strongly associated with resistance (29, 30). Other reported risk factors for having UTI due to MDR uropathogens are previous hospitalization during the last 6 months, comorbidities, diabetes, and old age (51-65 years) (26, 30), genitourinary pathologies such as nephritis, hemodialysis, and indwelling catheters (20, 30).

In our region, a high level of bacterial antibiotics

resistance may be attributed to irrational use, inappropriate prescription, and over the counter availability of antibiotics which is a widespread practice in Al-Basrah Governorate, as almost all antibiotics are sold without a medical prescription in the private pharmacies. As so regulations and policies regarding antibiotics handling and prescription by the health authorities at the local and national level is a crucial execution to limit morbidities and mortalities associated with infections, to prevent the serious clinical impacts and consequences, and to maintain the efficacy of different antibiotics categories against the pathogenic bacteria including those implicated in the urinary tract infection.

CONCLUSION

This study explains that an important antibiotics categories which are classically considered options for treatment of urinary tract infection, those as β -lactams including penicillin/ β -lactamase inhibitors as piperacillin/tazobactam, third-generation cephalosporins as ceftazedime, and cefepime, fluoroquinolones as ciprofloxacin, and levofloxacin, and trimethoprim/sulfamethoxazole, and aminoglycosides as gentamicin have high resistance rates which may call for reconsidering their indication in the treatment of urinary tract infection in our community.

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