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ORIGINAL ARTICLE

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

**Raad Saad Luty[1*], Adil Ghalib Fadil[2], Jasim Mohammed Najm[3], Hala Haitham Abduljabbar[4], Sarmad Abdul Abbas Kashmar[5]**

*[1]Department of Oral and Maxillofacial Surgery, University of Basrah, College of Dentistry, Basrah, Iraq*
*[2]Department of Pediatric and Preventive Dentistry, University of Basrah, College of Dentistry, Basrah, Iraq*
*[3]Department of Laboratories, Laboratory of Microbiology, Al-Basrah Teaching Hospital, Basrah, Iraq*
*[4]Department of Pharmacy, Al-Basrah Teaching Hospital, Basrah, Iraq*
*[5]Department of Pharmacy, Al-Fayhaa Teaching Hospital, Basrah, Iraq*

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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

*Corresponding author: Raad Saad Luty, Ph.D, Department of Oral and Maxillofacial Surgery, University of Basrah, College of Dentistry, Basrah, Iraq.
Tel: +964-07710856122
Email: rslph80@gmail.com

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 ≥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, 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 isolates (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).

**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) |
| | 15-2 4 | 38 (11.8) |
| | 25-44 | 80 (24.80) |
| | 45-64 | 92 (28.6) |
| | 65 + | 54 (16.8) |
| | Total | 322 |

**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 (≥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% ≥) 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 (%) |
|---|---|---|---|
| *Escherichia coli* | 161 (50.0) | *Staphylococcus haemolyticus* | 37 (11.5) |
| *Klebsiella pneumoniae* | 32 (9.9) | *Staphylococcus aureus* | 6 (1.9) |
| *Klebsiella oxytoca* | 1 (0.3) | *Staphylococcus epidermidis* | 3 (0.90) |
| *Pseudomonas aeroginosa* | 11 (3.4) | *Staphylococcus saprophyticus* | 2 (0.6) |
| *Pseudomonas luteola* | 4 (1.2) | *Staphylococcus hominis* | 2 (0.6) |
| *Proteus mirabilis* | 10 (3.1) | *Staphylococcus lugdunensis* | 1 (0.3) |
| *Proteus vulgaris* | 2 (0.6) | *Staphylococcus agalactia* | 8 (2.5) |
| *Enterobacter cloacae* | 7 (2.2) | *Staphylococcus pnemoniae* | 2 (0.6) |
| *Citrobacter freundi* | 3 (0.9) | *Enterococcus faecalis* | 19 (5.9) |
| *Citrobacter koseri* | 2 (0.6) | *Enterococcus casseliflavus* | 1 (0.3) |
| *Serratia rubidaea* | 1 (0.3) | | |
| *Serratia marcescens* | 3 (0.9) | | |
| *Acinetobacter baumanni* | 2 (0.6) | | |
| *Aeromonas hydrophila* | 1 (0.3) | | |
| *Yersinia kristensenii* | 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%) | | | | |
|---|---|---|---|---|---|
| | ***Staphylococcus haemolyticus* (37)** | ***Staphylococcus aureus* (6)** | ***Staphylococcus epidermidis* (3)** | ***Staphylococcus saprophyticus* (2)** | ***Staphylococcus hominis* (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, trimethoprim/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%) | | | | |
|---|---|---|---|---|---|
| | ***Staphylococcus lugdunensis* (1)** | ***Streptococcus agalactiae* (8)** | ***Streptococcus pneumoniae* (2)** | ***Enterococcus faecalis* (19)** | ***Enterococcus casseliflavus* (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%) | | | | | |
|---|---|---|---|---|---|---|
| | ***Escherichia coli* (161)** | ***Klebsiella Pneumonia* (32)** | ***Klebsiella Oxytoca* (1)** | ***Pseudomonas aeruginosa* (11)** | ***Pseudomonas Luteola* (4)** | ***Proteus mirabilis* (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
[b]determined for only 44 *E. coli* isolates

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

| Antibiotics | Resistance percentage R (R%) | | | | | |
|---|---|---|---|---|---|---|
| | ***Proteus vulgaris* (2)** | ***Enterobacter cloacae* (7)** | ***Citrobacter freundi* (3)** | ***Citrobacter koseri* (2)** | ***Serratia marcescens* (3)** | ***Acinetobacter baumanni* (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% | Fusidicacid[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% | | |

[a]Nitrofurantoin, and Fosfomycin determined for only 44 *E. coli* isolates.

[b]Fosfomycin, Fusidic acid, Clindamycin, and Nitrofurantoin applied for only 44, 51, 53, 43 gram positive isolates respectively

Iraq in 2018 (17).

Fosfomycin and nitrofurntion 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.

## REFERENCES


1. McLellan LK, Hunstad DA. Urinary tract infection: pathogenesis and outlook. *Trends Mol Med* 2016; 22:946-957.
2. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection, and treatment options. *Nat Rev Microbiol* 2015; 13:269-284.
3. Jean S-S, Coombs G, Ling T, Balaji V, Rodrigues C, Mikamo H, et al. Epidemiology and antimicrobial susceptibility profiles of pathogens causing urinary tract infections in the Asia-Pacific region: Results from the Study for Monitoring Antimicrobial Resistance Trends (SMART), 2010–2013. *Int J Antimicrob Agents* 2016; 47:328-334.
4. Lee YC, Hsiao CY, Hung MC, Hung SC, Wang HP, Huang YJ, et al. Bacteremic urinary tract infection caused by multidrug-resistant Enterobacteriaceae are associated with severe sepsis at admission. *Medicine (Baltimore)* 2016; 95(20):e3694.
5. Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. Carbapenem resistance, inappropriate empiric treatment and outcomes among patients hospitalized with Enterobacteriaceae urinary tract infection, pneumonia and sepsis. *BMC Infect Dis* 2017; 17:279.
6. Tandogdu Z, Wagenlehner FME. Global epidemiology of urinary tract infections. *Curr Opin Infect Dis* 2016;29:73-79.
7. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the infectious diseases society of America and the European society for microbiology and infectious diseases. *Clin Infect Dis* 2011;52(5):e103-20.
8. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *P T* 2015; 40:277-283.
9. Zaman S Bin, Hussain MA, Nye R, Mehta V, Mamun KT, Hossain N. A review on antibiotic resistance: alarm bells are ringing. *Cureus* 2017; 9(6):e1403.
10. Bader MS, Loeb M, Brooks AA. An update on the management of urinary tract infections in the era of antimicrobial resistance. *Postgrad Med* 2017; 129:242-258.
11. Bartoletti R, Cai T, Wagenlehner FM, Naber K, Bjerklund Johansen TE. Treatment of urinary tract infections and antibiotic stewardship. *Eur Urol Suppl* 2016; 15:81-87.
12. Asadi Karam MR, Habibi M, Bouzari S. Urinary tract infection: Pathogenicity, antibiotic resistance and development of effective vaccines against Uropathogenic *Escherichia coli*. *Mol Immunol* 2019; 108:56-67.
13. Waller TA, Pantin SAL, Yenior AL, Pujalte GGA. Urinary tract infection antibiotic resistance in the United States. *Prim Care* 2018;45:455-466.
14. Shakhatreh MAK, Sweden SF, Al-Odat MA, Khabour OF. Uropathogenic *Escherichia coli* (UPEC) in Jordan: Prevalence of urovirulence genes and antibiotic resistance. *J King Saud Univ Sci* 2019; 31: 648-652.
15. Cynthia Nau Cornelissen, Bruce D. Fisher RAH (2013). *Lippincott's Illustrated Reviews: Microbiology*, 3rd ed.Lippincott Williams & Wilkins. Philadelphia.
16. Donay JL, Mathieu D, Fernandes P, Prégermain C, Bruel P, Wargnier A, et al. Evaluation of the automated phoenix system for potential routine use in the clinical microbiology laboratory. *J Clin Microbiol* 2004; 42:1542-1546.
17. Al-Naqshbandi AA, Chawsheen MA, Abdulqader HH. Prevalence and antimicrobial susceptibility of bacterial pathogens isolated from urine specimens received in rizgary hospital-Erbil. *J Infect Public Health* 2019;12:

330-336.
18. Al Wutayd O, Al Nafeesah A, Adam I, Babikir IH. The antibiotic susceptibility patterns of uropathogens isolated in qassim, Saudi arabia. *J Infect Dev Ctries* 2018;12:946-952.
19. Bitew A, Molalign T, Chanie M. Species distribution and antibiotic susceptibility profile of bacterial uropathogens among patients complaining urinary tract infections. *BMC Infect Dis* 2017;17:654.
20. Stefaniuk E, Suchocka U, Bosacka K, Hryniewicz W. Etiology and antibiotic susceptibility of bacterial pathogens responsible for community-acquired urinary tract infections in Poland. *Eur J Clin Microbiol Infect Dis* 2016; 35:1363-1369.
21. Zanichelli V, Huttner A, Harbarth S, Kronenberg A, Huttner B, Swiss Centre For Antibiotic Resistance Anresis. Antimicrobial resistance trends in *Escherichia coli, Klebsiella pneumoniae* and *Proteus mirabilis* urinary isolates from Switzerland: a retrospective analysis of data from a national surveillance network over 8 years (2009-2016). *Swiss Med Wkly* 2019;149:w20110.
22. Kresken M, Körber-Irrgang B, Biedenbach DJ, Batista N, Besard V, Cantón R, et al. Comparative *in vitro* activity of oral antimicrobial agents against Enterobacteriaceae from patients with community-acquired urinary tract infections in three European countries. *Clin Microbiol Infect* 2016; 22(1):63.e1-63.e5.
23. Curto C, Rosendo I, Santiago L. Antimicrobial susceptibility patterns in outpatient urinary tract infection in the district of Coimbra, Portugal: A cross-sectional study. *Acta Med Port* 2019; 32:568-575.
24. Lee JH, Subhadra B, Son YJ, Kim DH, Park HS, Kim JM, et al. Phylogenetic group distributions, virulence factors and antimicrobial resistance properties of uropathogenic *Escherichia coli* strains isolated from patients with urinary tract infections in South Korea. *Lett Appl Microbiol* 2016; 62:84-90.
25. Losada I, Barbeito G, García-Garrote F, Fernández-Pérez B, Malvar A, Hervada X, et al. Antimicrobial susceptibility of *Escherichia coli* producers of community urinary tract infections in Galicia (Spain). *Aten Primaria* 2020; 52:462-468.
26. Ny S, Edquist P, Dumpis U, Gröndahl-Yli-Hannuksela K, Hermes J, Kling AM, et al. Antimicrobial resistance of *Escherichia coli* isolates from outpatient urinary tract infections in women in six European countries including Russia. *J Glob Antimicrob Resist* 2019; 17:25-34.
27. Sanchez GV, Baird AMG, Karlowsky JA, Master RN, Bordon JM. Nitrofurantoin retains antimicrobial activity against multidrug-resistant urinary *Escherichia coli* from US outpatients. *J Antimicrob Chemother* 2014; 69:3259-3262.
28. Walker E, Lyman A, Gupta K, Mahoney MV, Snyder GM, Hirsch EB. Clinical management of an increasing threat: outpatient urinary tract infections due to multidrug-resistant uropathogens. *Clin Infect Dis* 2016; 63:960-965.
29. Cohen-Nahum K, Saidel-Odes L, Riesenberg K, Schlaeffer F, Borer A. Urinary tract infections caused by multi-drug resistant proteus mirabilis: Risk factors and clinical outcomes. *Infection* 2010; 38:41-46.
30. Khawcharoenporn T, Vasoo S, Singh K. Urinary tract infections due to multidrug-resistant Enterobacteriaceae: prevalence and risk factors in a Chicago emergency department. *Emerg Med Int* 2013; 2013:258517.