

# Empiric Guideline Therapy for Simple Urinary Tract Infection at Outpatient Clinics: A Prospective Observational Study

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## ABSTRACT

**Background:** Community-acquired urinary tract infection is a widespread problem encountered in the outpatient clinics of most hospitals. UTI has various clinical presentations; some are simple UTIs that can be managed with outpatient antibiotics. The current treatment of UTI is empirical, based on the limited and predictable spectrum of etiological microorganisms.

**Objectives:** To collect information on the susceptibility tests of microorganisms in simple urinary tract infections (UTIs) and outline the best empiric antimicrobial prescribed for them.

**Methods:** A total of 117 patients from 14 to 70 years of age (mean age = 43.61 years, standard deviation =  $\pm$  24.5) received the care of our surgical and urological outpatient clinics in Alnuman Teaching Hospital, Baghdad, Iraq, between March 1, 2019, and September 1, 2020. The patients who were showing symptoms of simple uncomplicated UTI and were prescribed empiric antibacterial treatment and requested for a sample of midstream urine for culture and sensitivity tests were enrolled in this prospective study. The susceptibility test for (ciprofloxacin, trimethoprim, gentamycin, and ceftriaxone) was performed using the Kirby–Bauer disc diffusion method. The data were input into SPSS 22.0 for statistical analysis. Pearson's chi-squared test was used to compare parameters. The data have been presented as the number of variables (n) and percentages (%). Statistical significance was set at  $P < 0.05$ .

**Results:** The frequencies of isolated uropathogens were as follows: *E. coli*, n = 65 (77.4%); *Klebsiella* spp., n = 9 (10.7%), *Proteus* spp., n = 3 (3.57%), *Enterobacter* spp., n = 3 (3.57%), *Staphylococcus* spp., n = 2 (2.38%), *Pseudomonas* spp., n = 1 (1.19%), and *Candida* spp., n = 1 (1.19%). The resistance rates of the most prevalent microorganisms were *E. coli* isolates to trimethoprim, ciprofloxacin, gentamycin, and ceftriaxone. The lower resistance rates to ceftriaxone in *E. coli* isolates (29.7%) was not clinically significant, with  $p < 0.05$ . Gentamycin showed significant sensitivity and resistance rates of 58.3% and 33.3% respectively, among the antimicrobials used ( $p < 0.05$ ).

The clinical effectiveness of empirical antimicrobial use in the treatment of simple UTIs showed no statistically significant correlation with  $P < 0.05$ .

**Conclusions:** Trimethoprim and ciprofloxacin should not be used in empirical therapy for UTIs because of their increased resistance rates. A review of the local guidelines should be considered.

**Keywords:** simple urinary tract infection, empirical antimicrobials in UTI, urine culture and susceptibility test, common uropathogens, antibiotics resistant bacteria in UTI.

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## INTRODUCTION

Community-acquired urinary tract infections (UTIs) are a widespread problem encountered in the outpatient clinics of most hospitals. UTI has various clinical presentations; some are simple UTIs that can be managed with outpatient antibiotics.<sup>1</sup> Most cases present acute uncomplicated UTIs that occur in otherwise healthy patients with a normal genitourinary tract.<sup>2</sup> The current treatment of UTI is empirical, based on the limited and predictable spectrum of etiological microorganisms.<sup>3</sup> However, as with many community-acquired infections, resistance rates to antimicrobials that are commonly used in UTI are increasing and the susceptibility of microorganisms is showing significant geographical variations, so the knowledge of antibiotic resistance trends is important for improving evidence-based recommendations for the empirical treatment of UTIs.<sup>4,5</sup> Urinary tract infections are a common problem worldwide. Knowing the clinical characteristics and susceptibility rates of bacteria is significant in determining the treatment of the infection and its span or duration. The most important driving factor for resistance is the overuse of antimicrobials.<sup>4,5</sup> Increased antimicrobial resistance complicates UTI treatment by increasing patient morbidity, costs of reassessment and re-treatment, and the use of broad-spectrum antibiotics. Appropriate knowledge about local and national antimicrobial resistance trends is thus of utmost importance in developing evidence-based recommendations for the empirical antibiotic treatment of UTI.<sup>3-6</sup> Many bacteria are resistant to

common antibiotics, meaning these drugs cannot kill the bacteria. Sensitivity analysis is a useful tool for quickly determining whether bacteria are resistant to certain drugs. The results from the test can help physicians identify the drugs that are most effective in the treatment of the infection. Bacterial responses to antibiotic drug treatments that contribute to cell death are not as well understood and have proven to be complex as they involve many genetic and biochemical pathways.<sup>7,8</sup>

Thus, this prospective observational study aimed to gather information on the sensitivity and resistance rates of common microorganisms in our patients with simple uncomplicated urinary tract infections and to identify the best empiric antimicrobial prescribed to them in relevant settings at the outpatient clinics in our hospital.

## PATIENTS AND METHODS

### Data collection:

A total of 117 patients aged 14–70 years age (mean = 43.61 years, standard deviation =  $\pm$  24.5) who received the care of our surgical and urological outpatient clinics in Alnuman Teaching Hospital, Baghdad, Iraq, between March 1, 2019 and September 1, 2020. The patients who were showing symptoms of community-acquired acute UTI and were prescribed empiric antibacterial treatment and requested for a sample of midstream urine (MSU) for culture and sensitivity (C & S) test were enrolled in this prospective study.

The diagnosis of symptomatic uncomplicated UTI is defined by a group of symptoms including dysuria, frequency, urgency, and suprapubic pain or tenderness

that had been made and treated with the most frequently used empiric antimicrobials by our physicians. Patients with complicated UTI (signs of pyelonephritis, recurrent attacks of UTI, long-term episodes of UTI, structural and congenital abnormalities, hospitalized patients with or without Foley's catheter, any urological surgery, current pregnancy, diabetic patients, immunocompromised patients, and any patients on any antimicrobials) were excluded from the study.

Demographic data, urine culture results, pathogen microorganism sensitivity, and resistance rates to the most frequently used antimicrobials in UTI treatment in our hospital were recorded.

#### Laboratory methods:

Urine samples were collected after the patients were taught to perform the midstream urine technique. Clean-catch urine samples were obtained from the patients and then inoculated onto 5% blood agar with 0.01 mL calibrated loops using a semi-quantitative technique. Culture plates were incubated for 18–24 h at 37°C. A threshold of  $> 10^5$  organisms per mL of urine was defined as a positive culture. The isolated bacteria were identified using conventional methods, and BBL Crystal Enteric/NF 4.0 identification kits (Becton Dickinson NY, USA) were used when needed.<sup>9</sup> The susceptibility test of each isolated pathogen to antibiotics (ciprofloxacin, trimethoprim, gentamycin, and ceftriaxone) was performed using the Kirby–Bauer disc diffusion method and an automatic system (Vitek2 compact).<sup>10</sup>

Sensitivity analysis, also called susceptibility testing, helps identify the most effective antibiotic to kill an infecting microorganism. Bacterial colonies can be susceptible, resistant, or intermediate in response to antibiotics.<sup>11</sup>

- **Susceptible** means that the bacteria cannot grow if a drug is present. This indicates that antibiotics are effective against bacteria.
- **Resistant** means that the bacteria can grow even if the drug is present. This indicates the ineffectiveness of antibiotics.
- **Intermediate** means a higher dose of antibiotics is needed to prevent growth.

#### Statistical analysis:

The data of the study were input into MS Excel, coded, and transferred into SPSS 22.0 for statistical analysis. Pearson's chi-squared test was used to compare parameters. Data have been presented as the number of variables (n) and percentages (%). Statistical significance was set at  $P < 0.05$ .

#### Ethics

Ethical approval for this study was granted by the Alnuman Teaching Hospital administration.

## RESULTS

### Patients' demographics:

The study included a total of 117 patients (33 men and 84 women) who were diagnosed with simple uncomplicated UTI and prescribed empirical antimicrobials as well as urine culture and sensitivity tests.

The subjects' age fell in the range 14–70 years, and the mean age of the study population was 43.61 with a standard deviation of  $\pm 24.5$ . A total of 84 patients (71.8 %) had positive culture results (23 men and 61 women), while 33 patients (28.2%) had no growth culture results (10 men and 23 women) (Table 1).

**Table 1:** Urine culture results for 117 samples  
\*number of variable, \*\* frequency of culture result in percent

Bacterium n*(%) ** n = 117	No of male patients (%)	No of female patients (%)
No growth culture n = 33 (28.2)	10 (8.54)	23 (19.65)
All growth culture n = 84 (71.8)	23 (19.65)	61 (52.13)

**Table 2:** Choice of empirical antimicrobials

Antimicrobials	Ciprofloxacin	Trimethoprim	Ceftriaxone	Gentamycin	Levofloxacin	Nitrofurantoin
Physicians' choice n = 30 (100%)	11 (36.7)	9 (30)	4 (13.3)	3 (10)	2 (6.6)	1 (3.3)

**Table 3:** Isolated uropathogens in 117 urine samples

Bacterium n*(%) ** n = 84 (71.8%)	No of male patients (%)	No of Female patients (%)
<i>E. coli</i> : n = 65 (77.4)	16 (19.05)	49 (80.3)
<i>Klebsiella</i> spp.: n = 9 (10.7)	3 (13.04)	6 (9.8)
<i>Proteus</i> spp.: n = 3 (3.57)	1 (4.3)	2 (3.2)
<i>Enterobacter</i> spp.: n = 3 (3.57)	3 (13.04)	0
<i>Candida</i> spp.: n = 1 (1.2)	0	1 (1.6)
<i>Staphylococcus</i> spp.: n = 2 (2.38)	0	2 (3.2)
<i>Pseudomonas</i> spp.: n = 1 (1.19)	0	1 (1.6)

\*number of variable, \*\* frequency of uropathogens in percent

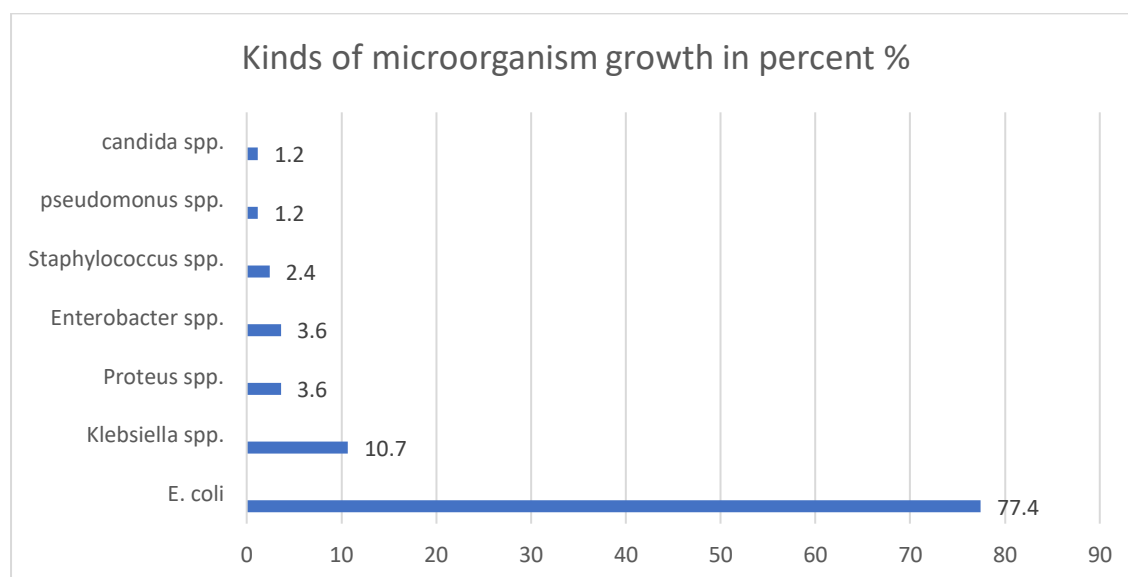
### The choice of empirical antimicrobials:

A total of 30 physicians in our hospital were surveyed and requested to choose the first empirical antibiotics for UTI treatment in our outpatient clinics;

they were prescribed ciprofloxacin (n = 11, 36.7%), trimethoprim (n = 9, 30%), ceftriaxone (n = 4, 13.3%), gentamycin (n = 3, 10%), levofloxacin (n = 2, 6.6%), and nitrofurantoin (n = 1, 3.3%). The latter two antimicrobials were not included in our study as they were least frequently prescribed and as their discs for susceptibility testing were unfortunately not available in our laboratory during the study period (Table 2).

### Isolated pathogens:

The frequency of isolated uropathogens in the 84 positive urine cultures for both sexes was as follows: *E. coli*: n = 65 (77.4%), *Klebsiella* spp.: n = 9 (10.7%), *Proteus* spp.: n = 3 (3.57%), *Enterobacter* spp.: n = 3 (3.57%), *Staphylococcus* spp.: n = 2 (2.38%), *Pseudomonas* spp.: n = 1 (1.19%), and *Candida* spp.: n = 1 (1.19%) (Table 3; Fig.



**Figure 1:** Percent of isolated microorganism growth in 117 urine samples

### Frequency of antimicrobials susceptibility test

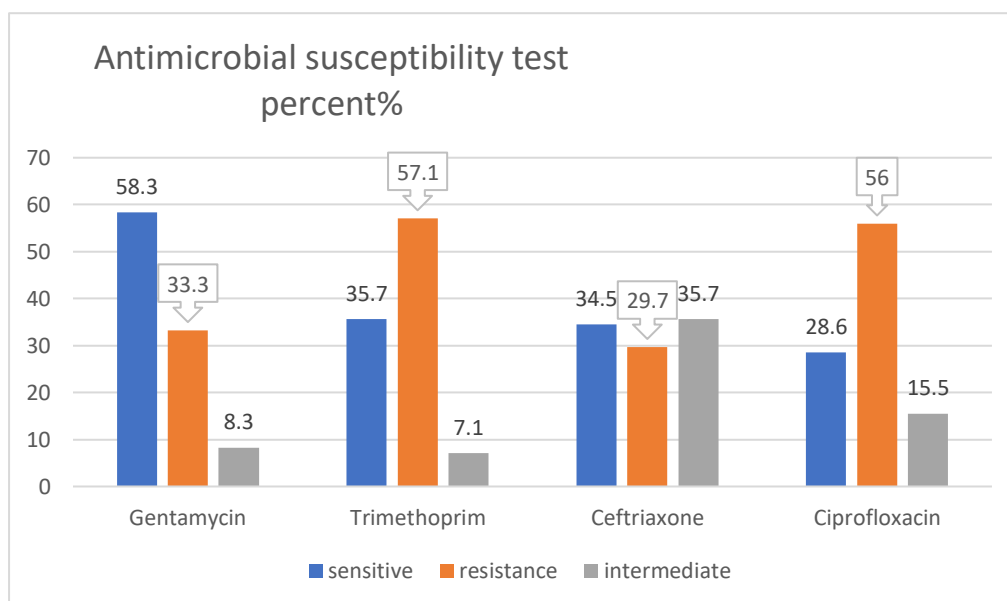
The antibiotic resistance and sensitivity rates of the isolates are shown in Table 4 and Fig. 2. The resistance rates to trimethoprim, ciprofloxacin, gentamycin, and ceftriaxone were the most prevalent in *E. coli* isolates at 57.1%, 56%, 33.3% and 29.7% respectively. The resistance to trimethoprim was higher than that of other antimicrobials used among the *E. coli* isolates. Although there was a

tendency toward lower resistance rates to ceftriaxone in *E. coli* isolates (29.7%), they were not statistically significant at  $p < 0.05$ , whereas the weak or intermediate sensitivity of ceftriaxone (35.7 %) was greater than that of other antimicrobials; thus, ceftriaxone was statistically significant in the treatment of UTI, but only at higher doses ( $p < 0.05$ ). Nevertheless, only gentamycin showed significant sensitivity and resistance rates of 58.3% and 33.3% respectively among other antimicrobials ( $p < 0.05$ ).

**Table 4:** Patern of antimicrobial susceptibility test to isolated bacterium

Bacterium n (%) n = 84 (71.8)	Trimethoprim n, % n = 9 (30)			Ciprofloxacin n, % n = 11 (36.7)			Gentamycin n, % n = 3 (10)			Ceftriaxone n, % n = 4 (13.3)		
	S. n (%)	R. n (%)	I. n (%)	S. n (%)	R. n (%)	I. n, (%)	S. n (%)	R. n (%)	I. n (%)	S. n (%)	R. n (%)	I. n (%)
<i>E. coli</i> n = 65 (77.4%)	22 (33.8)	38 (58.4)	5 (7.7)	19, (29.2)	38 (58.5)	8 (12.3)	36 55.3	25 38.5	4 6.15	22 (33.8)	22 (33.8)	21 (32.3)
<i>Klebsiella spp.</i> n = 9 (10.7%)	5 (55.5)	4 (44.4)	0 (0.0)	3 (33.33)	4 (44.4)	2 (22.2)	7 (77.8)	2 (22.2)	0 (0.0)	5 (55.5)	2 (22.2)	2 (22.2)
<i>Proteus spp.</i> n = 3 (3.6%)	1 (33.3)	2 (66.6)	0 (0.0)	1 (33.3)	0 (0.0)	2 (66.6)	2 (66.7)	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	2 (66.6)
<i>Enterobacter spp.</i> n = 3 (3.6%)	1 (33.3)	2 (66.6)	0 (0.0)	1 (33.3)	2 (66.6)	0 (0.0)	2 (66.7)	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	2 (66.6)
<i>Candida spp.</i> n = 1 (1.2%)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)
<i>Staphylococcus spp.</i> n = 2 (2.4%)	1 (50)	1 (50)	0 (0.0)	0 (0.0)	1 (50)	1 (50)	2 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100)
<i>Pseudomonas spp.</i> n = 1 (1.2%)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	0 (0.0)	1 (100)

n = number, % = percent, S. = sensitive, R. = resistant, I. = intermediate sensitivity



**Figure 2:** Bacteria susceptibility test

### Empirical antimicrobial prescriptions in our hospital

We excluded levofloxacin and nitrofurantoin from our study because of the aforementioned causes. The frequently antimicrobials prescribed as first-line defenders against simple UTI in our outpatient clinics showed sensitivity and resistance in descending order of frequency as follows: gentamycin (58.3%, 33.3%), trimethoprim (35.7%, 57.1%), ceftriaxone (34.5%, 29.7%), and ciprofloxacin (28.6%, 56%). Only gentamycin yielded a statistically significant correlation in its use as an empirical antimicrobial against simple UTI ( $P < 0.05$ ) (Table 5). If we considered the weak or intermediate sensitivity acceptable result against simple UTI treatment, the antimicrobial ceftriaxone yielded significant correlations with  $P < 0.05$ ; however, it should be used in high doses in real-time treatment. Nevertheless, gentamycin was still the only antimicrobial that demonstrated a good and significant result ( $P < 0.05$ ) (Table 6).

Despite this result, if we compare the clinical effectiveness of all antimicrobials used in the empirical treatment of simple UTI against not using any of them in the treatment of the

same samples, that is if we want to find the clinical effectiveness of our guideline in the treatment of simple UTI, we have to study and analyze two theories (Table 7).

- 1- The null hypothesis theory states that “our guidelines have no clinical effectiveness”.
- 2- Alternative hypothesis states that “our guidelines have clinical effectiveness”.

The result of the Pearson’s chi-square calculation of the 2 x 2 table was 3.4228, and the P-value was 0.064301, as of the 117 urine samples, only 84 yielded microorganism growth, 56 of them were truly sensitive to the antimicrobials utilized rendering it true-positive results, and the remaining 28 were resistant to antimicrobials which was the true-negative result.

**Table 5:** Antimicrobials used and its clinical

Antimicrobial n = 30, (%)	Sensitive n, (%)	Resistance n, (%)	Intermediate n, (%)	P-Value
Trimethoprim n = 9 (30)	30, (35.7)	48, (57.1)	6, (7.1)	0.059
Ciprofloxacin n = 11 (36.9)	24, (28.6)	47, (56)	13, (15.5)	0.135
Gentamycin * n = 3 (10)	49, (58.3)	28, (33.3)	7, (8.3)	0.042
Ceftriaxone n = 4 (13.3)	29, (34.5)	25, (29.7)	30, (35.7)	0.324

correlations

\*Pearson’s chi-square correlation test was considered significant at  $P < 0.05$ .

Thirty-three samples from the total 117 urine samples gave a false-positive result for antimicrobial use as there was actually no growth of bacteria in the colonies; the remaining 84 samples yielded the false-negative results in the case of no antimicrobials used. Therefore,

we cannot reject the null hypothesis or the false positive (type 1 error), which yielded no statistically significant correlation with our guideline treatment used against simple UTI ( $P > 0.05$ ).

Therefore, a review of such prescriptions should be considered (Table 7).

**Table 6:** The antimicrobial response and its clinical correlation.

Antimicrobial n, % 30	Susceptibility test result		Chi-square = (p-value)
	Positive (Antimicrobial effective)	Negative (Antimicrobial not effective)	
Trimethoprim 9 (30)	36, 30.9%	48, 69.04%	0.050365
Ciprofloxacin 11 (36.9)	37, 44%	47, 56%	0.120078
Ceftriaxone * 4 (13.3)	59, 41.6%	25, 58.3%	0.043772
Gentamycin * 3 (10)	56, 61.9%	28, 38.1%	0.023881
No antimicrobial	33, 28.2%	84, 71.8%	0.064301

\*Pearson's chi-square correlation test was considered significant at  $P < 0.05$ .

**Table 7:** Clinical effectiveness of our guideline in the treatment of UTI

Cultures	Antimicrobial's susceptibility test n = number		Marginal Row Totals
	True positive(S)	False negative(R)	
Positive cultures	56	84	140
Negative cultures	33	28	61
Marginal Column Total	89	112	201 (Grand Total)

The chi-square statistic was 3.4228, and the p-value was 0.064301, not significant at  $p < 0.05$ .



## DISCUSSION

This study shows the distribution of microbial species isolated from patients with UTI and their sensitivity and resistance rates to the antimicrobial agents most frequently used as an empirical choice in the treatment of simple uncomplicated UTIs at Alnuman Teaching Hospital in Baghdad City, Iraq.

As numerous previous studies have reported, urinary tract infections (UTIs) caused by *Escherichia coli* (*E. coli*) among the most widely recognized diseases in women. The antimicrobial resistance of *E. coli* is increasing rapidly, causing physicians to hesitate when prescribing oral antibiotics. We discovered that most of our patients with UTI were women under the age of 50 years, they were infected with *E. coli*.<sup>12</sup> The microorganisms isolated in our patient population were similar to those in other comparable studies, which reported that “*E. coli* is more common in women owing to the loss of estrogen and consequent changes in vaginal flora especially after menopause”.<sup>13</sup>

Empirical therapy for UTI treatment is recommended in many international guidelines.<sup>14-16</sup> The effectiveness and viability of such an exact therapy rely on the intermittent assessment of antimicrobial susceptibility profiles. Although the types of bacteria isolated from patients with UTI worldwide have remained largely unaltered, among which *E. coli* is the most common microorganism, there have been significant changes in the susceptibility

patterns of microorganisms over the past few decades, and antibiotic resistance has become a significant issue from UTI.<sup>17</sup> The increase of antimicrobial resistance has been documented worldwide.<sup>11,18,19</sup> A 2021 study in Tehran, Iran, reported that *E. coli* harbored the highest prevalence of resistance to ampicillin (100%), ceftriaxone (100%), 35 cefalexin (98%) , piperacillin (96%), ciprofloxacin (76.89%), and 37 gentamicin (68.95%).<sup>20</sup> Resistance rates among strains of *E. coli* isolated from women with UTI average 30% for both sulfonamides and ampicillin, shifting from 17% to 54% in different countries.<sup>21</sup> Trimethoprim resistance in our patients reached up to 57.1%, making it unsuitable for use as first-line empirical therapy for simple uncomplicated UTI. Mulder *et al.* reported high frequencies of trimethoprim resistance in UTIs caused by *E. coli* in recent years. Co-resistance to other antimicrobial drugs may play a role in this increase.<sup>22</sup> Trimethoprim is prescribed as a first-line agent empirically for uncomplicated cases of UTI in many guidelines; however, the resistance of *E. coli* to its action is high in different countries.<sup>23</sup> Ciprofloxacin resistance observed in our study was up to 56%, and the drug is utilized as the first empirical therapy choice by around 36.9% of our physicians; again, this percent shows the use of ciprofloxacin, another bad starting antimicrobial with no significant sensitivity against most frequent *E. coli* cultures. This finding is in agreement with the study of

Fasugba *et al.* that stated as follows, “Ciprofloxacin resistance in *E. coli* UTI is increasing and the use of this antimicrobial agent as empirical therapy for UTI should be reconsidered. Policy restrictions on ciprofloxacin use should be enhanced especially in developing countries without current regulations”.<sup>24</sup> Aypak *et al.* reported 36% resistance to trimethoprim and 17% resistance to ciprofloxacin among 288 *E. coli* isolates from patients with UTI in Turkey.<sup>25</sup> In addition, Ozyurt *et al.* found 34% resistance to trimethoprim and 18% resistance to ciprofloxacin among community-acquired *E. coli* isolates from the Istanbul region.<sup>26</sup>

Regarding ceftriaxone as an empirical therapy regimen for UTI, we found that it is used as the first empirical therapy in managing simple UTI by 13.3% of our doctors, with a resistance rate of 35.5% and a sensitivity rate of 34.5%, which renders it insignificant in the management of outpatient clinic cases; however, at high doses, it was significantly correlated; indeed, this is unwise and not preferred as outpatient therapy, although it might be considered in hospitalized patients. However, our finding disagrees with the study done by Wang *et al.* in a total of 94 patients with UTI in a single tertiary center. Their study concluded, “For patients with UTI requiring hospitalization, ceftriaxone seems to be an effective empiric therapy for most patients.” The choice of empiric antibiotic therapy should be based on local antibiogram data. More data are required to examine the effectiveness of local and source-specific antibiograms on clinical outcomes when guiding the treatment of patients with UTI.<sup>27</sup> Nonetheless, our

findings are in agreement with the study conducted by Sharma *et al.*, which concludes, “Over the successive years, resistance to ceftriaxone tends to increase from 53.39 % (2012) to 73.33 % (2014). *E. coli* showed absolute resistance (100 %) to cotrimoxazole and tetracycline. On average, over the three years, *E. coli* showed high resistance to fluoroquinolones (75 %) and aminoglycosides (67 %). Multi-drug resistant *E. coli* ranged between 63 % (2012) to 65 % (2014)”.<sup>28</sup>

Finally, we find that the gentamicin was utilized by 10% of our physicians, and it was with significant susceptibility test as empirical therapy in simple uncomplicated UTI with 61.9% sensitivity and 38.1% resistance rates. Thus, we think it is a good starting antimicrobial at this moment. This finding is in accordance with study of Mostafavi *et al.* involving 1180 patients with UTI; they concluded that “gentamicin, cefepime and ceftazidime were acceptable as initial choices in non-severe infections UTI”.<sup>29</sup> Although gentamycin is associated with some important side effects, a study conducted in Australian hospitals regarding gentamycin empiric antimicrobials in patients aged > 65 years with some renal impairment showed that empiric gentamicin use in patients with advancing age is associated with low rates of predominantly transient renal impairment.<sup>30</sup> In another study, empirical intravenous (IV) antibiotic treatment prescribed for 152 patients with severe UTI showed that the overall duration of IV antibiotic treatment was significantly shorter for patients administered gentamicin empirically as

initial treatment compared with patients who were not administered gentamicin at all.<sup>31</sup> Hence, we agree with this study and recommend the use of gentamicin as an empirical therapy for a short time, which is also in accordance with the study of Ekmen *et al.*, who concluded that “gentamicin does not affect the hearing test when it is used in the short-term (5-7 days)”.<sup>32</sup> The fluctuation among different centers confirms the requirement for local resistance prevalence data to be made available to professionals treating UTIs, particularly where empirical treatment is being utilized for urinary infections. Previous antibiotic treatment, hospital admission, and UTI, especially <1 month before the current episode, were all associated with high rates of resistance. These findings are important and may assist physicians in choosing an appropriate empiric treatment for UTI.<sup>33</sup>

Our investigation clearly shows that there is a significant increase in trimethoprim and ciprofloxacin resistance among *E. coli* isolates taken from patients with UTI in our study area, which makes its empirical treatment challenging. The reported rates of resistance among the most frequent microorganisms in numerous research articles may vary depending on whether the study sample consists primarily of outpatients with uncomplicated UTI or patients with complicated infections.

In our outpatients, the studied samples consisted of primarily uncomplicated UTI, and *E. coli* isolates were at a higher rate among other causative uropathogens and was more likely to be resistant to

trimethoprim, ciprofloxacin, and ceftriaxone. In fact, it was only and clearly sensitive to gentamicin. However, the higher rate of intermediate susceptibility to ceftriaxone renders it a significant correlation to use it as an empirical choice in the treatment of UTIs, but in higher doses. Nevertheless, gentamicin sensitivity was the only statistically significant factor. Several studies have shown that physicians' prescription habits are a driving factor for antibiotic resistance.<sup>3,34</sup> Aypak *et al.* reported that resistance against ciprofloxacin and trimethoprim was strongly associated with a high number of prescriptions for this group of antibiotics, and inappropriate antibiotic prescriptions for UTI were documented in 47.3% of patients in a study from Turkey.<sup>3</sup> Thus, surveillance studies provide important information that allows for the identification of trends in pathogen incidence and antimicrobial resistance, including the identification of emerging pathogens at national and global levels. There are generally a couple of studies published on varieties in the treatment of UTI, and McEwen *et al.* found that 37% of physicians actually prescribed trimethoprim, closely followed by ciprofloxacin (32%), and the average duration of antibiotic therapy was 8.6 days in the United States.<sup>35</sup> In our study, we found that although not recommended as a first-line antibiotic, ciprofloxacin was the most frequently prescribed drug in our hospital setting for UTI, followed by trimethoprim.

This is the primary study in Baghdad that directly evaluates the effectiveness of four major antibiotics utilized by physicians in the management of UTI in the outpatient clinics of one of the major hospitals. Data and information were not gathered from a drug surveillance database or from medical records retrospectively without the knowledge of the patient's clinical circumstances. The results are based on actual physician habits and thus provide an accurate description of the prescribed antibiotics. Since UTI is relatively common, widespread inappropriate prescriptions increase resistance among uropathogens. In our study, the resistance rates to ciprofloxacin and trimethoprim among the *E. coli* strains were found to be much higher than those reported in other studies. This might be due to the high utilization of these antimicrobials since they are considered the antimicrobial group of choice in UTI. In addition to increasing the risk of resistance, current prescriptions patterns in our hospital increase medical costs.

We believe that through this observational prospective study, although local, we reached our goals in terms of obtaining precise scientific data on the susceptibility rates of uropathogens in a teaching hospital serving the Alresafa region in Baghdad. At the same time, we had an opportunity to evaluate the actual prescriptions habits of physicians for a medical condition that is most often improperly treated.

We did not have a chance to evaluate the susceptibility patterns to other alternative antimicrobials such as nitrofurantoin and levofloxacin because of the lack of antimicrobial discs in our hospital

laboratory as well as to deal with the most frequently used empirical antimicrobials in our hospital.

Further studies considering a larger number of isolates from different geographical regions in Baghdad are needed to confirm our results. Nevertheless, clinicians should be aware of regional resistance rates, which should be taken into consideration before initiating empirical antimicrobial therapy for UTI.

### CONCLUSIONS

The utilization of trimethoprim and ciprofloxacin as empirical therapy in the treatment of uncomplicated UTI should be discouraged because of the increasing resistance rates to them. Ceftriaxone is a bad choice in an empirical therapy because it is effective only at a high dose. On the other hand, gentamycin is a good empirical therapy for UTI, but physicians should be aware of its side effects. In conclusion, we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of microorganisms and antibiotic sensitivities rather than on universal national guidelines.

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