# Empiric Therapy for Simple Urinary Tract Infection at Outpatient Clinics

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### ABSTRACT

**Background:** Urinary tract infection is a widespread problem in outpatient clinics in most hospitals. Urinary tract infection has several different clinical presentations; some of which are simple that can be managed with outpatient antibiotics. The current treatment of urinary tract infection is empirical, based on a predictable spectrum of etiological microorganisms. **Objectives**: To collect information on empiric therapy in simple urinary tract infections.

**Methods:** A total of 117 patients, aged from 14 to 70 years, attended the care of outpatient clinics in Alnuman Teaching Hospital, Baghdad, Iraq during the period between March 1, 2019 and September 1, 2020, with symptoms of simple urinary tract infection. Empiric antibiotics had been prescribed and susceptibility tests were requested to them. The data were inserted into SPSS 22.0 for statistical analysis and 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, 65 (77.4%), *Klebsiella* spp., 9 (10.7%), *Proteus* spp., 3 (3.57%), *Enterobacter* spp., 3 (3.57%), *Staphylococcus* spp., 2 (2.38%), *Pseudomonas* spp., 1 (1.19%) and *Candida* spp., 1 (1.19%). The resistance rates of the most prevalent microorganisms were *E. coli* isolates to trimethoprim, ciprofloxacin, gentamycin, and ceftriaxone. Gentamycin showed significant sensitivity and resistance rates of 58.3% and 33.3%, respectively, among the antimicrobials used. The clinical effectiveness of antimicrobial used as empirical in the treatment of simple urinary tract infections showed no statistically significant correlation at *P* < 0.05.

**Conclusions:** Trimethoprim and ciprofloxacin should not be used as empirical therapy in urinary tract infections. A review of the local guidelines should be considered.

Keywords: Simple urinary tract infection, Empirical antimicrobials, Urine culture and susceptibility test, Common uropathogens, Antibiotics resistance. Iraqi Medical Journal Vol. 68, No. 1, Jan-June 2022; p. 36-45.

Community-acquired urinarv tract infections (UTIs) are a widespread problem in outpatient clinics in most hospitals. UTI has several different clinical presentations; some are simple UTIs that can be managed with outpatient antibiotics<sup>(1)</sup>. Most cases present with 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 and predictable limited spectrum of etiological microorganisms<sup>(3)</sup>.

However, as with many communityacquired infections, resistance rates to antimicrobials that are commonly used in UTI are increasing and susceptibility of microorganisms shows significant geographical variations, and knowledge of antibiotic resistance trends is important for improving evidence based recommendations for empirical treatment of UTIs<sup>(4,5)</sup>. Urinary tract infections are a common problem worldwide. The clinical characteristics and susceptibility rates of bacteria are significant in determining the treatment of the infection and its span or duration. The most important driving factor resistance for is the overuse of antimicrobials<sup>(4,5)</sup>. Increasing antimicrobial resistance complicates UTI treatment by increasing patient morbidity, costs of reassessment and re-treatment, and use of broad-spectrum antibiotics. Appropriate

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knowledge about local and national antimicrobial resistance trends is of utmost importance in establishing evidence-based recommendations for empirical antibiotic treatment of UTI(3-6). Many bacteria are resistant to several antibiotics. This means that the drug 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 determine which drugs are most effective in the treatment of the infection. The 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, the objectives of this observational study were to gather information on the sensitivity and resistance rates of common microorganisms in patients with simple uncomplicated urinary tract infections and to identify the best empiric antimicrobial prescribed to them in relevant settings at outpatient clinics in Alnuman teaching hospital, Baghdad, Iraq.

-Methods

A total of 117 patients aged from 14 -70 years (mean 43.61years,  $\pm$ 24.5) who attended the care of surgical and urological outpatient clinics in Alnuman teaching hospital, Baghdad, Iraq during the period between 1 March 2019 and 1 September 2020, with symptoms of community acquired acute UTI and to whom empiric antibacterial treatment had been prescribed and requests for midstream urine for culture and sensitivity test (MSU C/S) were enrolled in this study.

The diagnosis of symptomatic uncomplicated UTI was defined by a group of symptoms including dysuria, frequency, suprapubic uraencv. and 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 the treatment of UTI in outpatient clinic were recorded.

Urine samples were collected after the patient was taught using the midstream urine technique. Clean-catch urine samples were obtained from these patients and then inoculated onto 5% blood agar with 0.01 ml calibrated loops by a semi-quantitative technique. Culture plates were incubated for 18-24 h at 37°C. A threshold of > 10<sup>5</sup> organisms per ml of urine was defined as a positive culture. The isolated bacteria were identified by 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 to identify the most effective antibiotic to kill an infecting microorganism. These colonies be susceptible, can resistant. or intermediate in response to antibiotics<sup>(11)</sup>.

Susceptibility means that they 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 was indicative of ineffective antibiotics.

Intermediate means a higher dose of the antibiotic is needed to prevent growth.

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

Ethical approval was granted for this study by Alnuman teaching hospital administration.

-Results

A total of 117 patients were included in the study, who were diagnosed with simple uncomplicated UTI, requested urine culture and sensitivity tests, and were prescribed empirical antimicrobials. There were 33 males and 84 females, mean age of the study population was 43.61 (±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), (Table1).

A total of 30 physicians in Al-Numan hospital were surveyed and requested to choose the first empirical antibiotics for UTI treatment in the outpatient clinics; they were ciprofloxacin prescribed 11 (36.7%), trimethoprim 9 (30%), ceftriaxone four (13.3%),gentamycin three (10%). levofloxacin two (6.6%) and nitrofurantoin one (3.3%). The last two antimicrobials were not included in the present study as they were least frequently prescribed and unfortunately, their discs for susceptibility

testing were not available in our laboratory during the study period, (Table 2).

The frequency of isolated uropathogens in 84 positive urine cultures for both sexes was *E.* coli 65 (77.4%), *Klebsiella* spp. 9 (10.7%), *Proteus* spp. three (3.57%), *Enterobacter* spp. three (3.57%), *Staphylococcus* spp. two (2.38%), *Pseudomonas* spp. one (1.19%) and *Candida* spp. one (1.19%), (Table 3).

The antibiotic resistance and sensitivity rates of the isolates are shown in table 4. The resistance rates of the most prevalent microorganisms were E. coli isolates to trimethoprim, ciprofloxacin, gentamycin, and ceftriaxone and which were 57.1%, 56%, 33.3% and 29.7%, respectively. 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, weak intermediate whereas the or 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 (weak sensitive culture result). Nevertheless, only gentamycin showed significant sensitivity and resistance rates of 58.3% and 33.3%, respectively, among other antimicrobials at p < 0.05.

Bacterium	Male No. (%)	Female No. (%)	Total No. (%)
No growth culture	10 (8.54)	23 (19.65)	33 (28.2)
All growth culture	23 (19.65)	61 (52.13)	84 (71.8)

#### Table 2: Choice of empirical antimicrobials.

	Antimicrobials No. (%)							
	Ciprofloxacin	Ciprofloxacin Trimethoprim Ceftriaxone Gentamycin Levofloxacin Nitrofuranto						
Physicians' choice n=30 (100%)	11 (36.7)	9 (30)	4 (13.3)	3 (10)	2 (6.6)	1 (3.3)		

Bacterium	Male	Female	Total
n=84 (71.8%)	No. (%)	No. (%)	No. (%)
E. coli	16 (19.05)	49 (80.3)	65 (77.4)
Klebsiella spp.	3 (13.04)	6 (9.8)	9 (10.7)
Proteus spp.	1 (4.3)	2 (3.2)	3 (3.57)
Enterobacter spp.	3 (13.04)	0	3 (3.57)
Candida spp.	0	1 (1.6)	1 (1.2)
Staphylococcus spp.	0	2 (3.2)	2 (2.38)
Pseudomonas spp.	0	1(1.6)	1 (1.2)

#### Table 3: isolated uropathogens in 117 urine samples.

Bacterium	Trime	ethoprin	n n =	Cip	rofloxa	cin	Ge	entamy	cin	Ce	eftriaxo	ne
n (%)		9(30)			11(36.7			n=3(10)			=4(13.3	
n=84(71.8)	1	No. (%)			۸o. (%)	,		No. (%)			No. (%)	
	S.	R.	Ι.	S.	R.	I.	S.	R.	I.	S.	R.	Ι.
E. coli	22	38	5	19,	38	8	36	25	4	22	22	21
n=65(77.4%)	(33.8)	(58.4)	(7.7)	(29.2)	(58.5)	(12.3)	55.3	38.5	6.15	(33.8)	(33.8)	(32.3)
Klebsiella spp.	5	4	0	3	4	2	7	2	0	5	2	2
n=9(10.7%)	(55.5)	(44.4)	(0.0)	(33.33)	(44.4)	(22.2)	(77.8)	(22.2)	(0.0)	(55.5)	(22.2)	(22.2)
Proteus spp.	1	2	0	1	0	2	2	0	1	1	0	2
n=3(3.6%)	(33.3)	(66.6)	(0.0)	(33.3)	(0.0)	(66.6)	(66.7)	(0.0)	(33.3)	(33.3)	(0.0)	(66.6)
Enterobacter	1	2	0	1	2	0	2	0	1	1	0	2
spp.	(33.3)	(66.6)	(0.0)	(33.3)	(66.6)	(0.0)	(66.7)	(0.0)	(33.3)	(33.3)	(0.0)	(66.6)
n=3(3.6%)												
Candida spp.	0	1	0	0	1	0	0	1	0	0	1	0
n=1(1.2%)	(0.0)	(100)	(0.0)	(0.0)	(100)	(0.0)	(0.0)	(100)	(0.0)	(0.0)	(100)	(0.0)
Staphylococcu	1	1	0	0	1	1	2	0	0	0	0	2
s spp.	(50)	(50)	(0.0)	(0.0)	(50)	(50)	(100)	(0.0)	(0.0)	(0.0)	(0.0)	(100)
n=2(2.4%)												
Pseudomonas	0	0	1	0	1	0	0	0	1	0	0	1
spp.	(0.0)	(0.0)	(100)	(0.0)	(100)	(0.0)	(0.0)	(0.0)	(100)	(0.0)	(0.0)	(100)
n=1(1.2%)												

S.=sensitive, R.=resistant, I.=intermediate sensitivity.

Although we excluded levofloxacin and nitrofurantoin from the study because of the causes mentioned above, the frequent antimicrobials prescribed as first-line defenders against simple UTI in the outpatient clinics showed sensitivity and resistance in the order of frequency to gentamycin, trimethoprim, ceftriaxone, and ciprofloxacin were (58.3%, 33.3%), (35.7%, 57.1%), (34.5%, 29.7%), and (28.6%, 56%), respectively. Only gentamycin yielded a statistically significant correlation with 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 ceftriaxone antimicrobial 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 with a good and significant result (P < 0.05), (Table 6).

Despite this result, if we compare the clinical effectiveness of all antimicrobials used as empirical in the treatment of simple UTI against not using any one of them in the treatment of the same samples, that is if we want to find the clinical effectiveness of this empiric therapy in the treatment of simple UTI, we have to study and analyze two theories, (Table 7).

1- The null hypothesis theory states that there is no clinical effectiveness of the empiric therapy.

2- Alternative hypothesis which is states that there is clinical effectiveness of the empiric therapy.

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

was the true-negative result, the n= 33 from the total of 117 urine samples was a falsepositive result for antimicrobial use, as there was actually no growth of bacteria in the colonies; the last n=84 from the total represented 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 this empiric treatment that was used against simple UTI (P> 0.05). Therefore, a review of such prescriptions should be considered, (Table 7).

Antimicrobial n=30, (%)	Sensitive No. (%)	Resistance No. (%)	Intermediate No. (%)	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

#### Table 5: Antimicrobials used and its clinical correlations.

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

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

Antimicrobial	Susceptibil	Chi-square = (p value)	
No. (%)	Positive (Antimicrobial effective) No. (%)	Negative (Antimicrobial not effective) No. (%)	
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 empiric therapy in the treatment of UTI.

Cultures	Antimicrobial's susce	Marginal Row Totals	
Positive cultures	True positive(S) 56	False negative(R) 84	140
Negative cultures	False positive(S) 33	True negative (R) 28	61
Marginal Column Totals	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 most frequent antimicrobial agents used as an empirical choice in the treatment of simple uncomplicated UTIs at Alnuman Teaching Hospital in Baghdad City, Iraq.

As with numerous previous studies had been reported, UTIs caused by E. coli are the most widely recognized diseases in women. The antimicrobial resistance of E. coli is expanding rapidly causing physicians to hesitate when selecting oral antibiotics. We found that most patients with UTI were women under the age of 50 years and the predominant microorganism was E. coli this is consistent with a study by Lee DS et al.<sup>(12)</sup> The microorganisms isolated in Alnuman hospital patients population were similar to those in other comparable studies when they 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 manv auidelines<sup>(14,15,16)</sup>. international The effectiveness and viability of such an exact therapy rely on the intermittent assessment antimicrobial susceptibility of profiles. Although the types of bacteria isolated from patients with UTI worldwide have remained largely unaltered, in 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 UTI<sup>(17)</sup>. in Increasing antimicrobial resistance has been documented worldwide<sup>(11,18,19)</sup>. Recently, one study in Tehran, Iran 2021 reported that E. coli harbored the highest prevalence of resistance to ampicillin (100%), ceftriaxone (100%), 35 cefalexin (98%), piperacillin (96%). ciprofloxacin (76.89%), and gentamicin 37 (68.95%)<sup>(20)</sup>. Resistance rates among strains of E. coli isolated from

ladies 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 reaches 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 urinary tract infections (UTIs) caused by E. coli in recent years. Coresistance to other antimicrobial drugs may increase<sup>(22)</sup> this play role in а 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 countries<sup>(23)</sup>. Ciprofloxacin different resistance in this study was up to 56% and it is utilized as first empirical therapy choice around 36.9% of the physicians of Alnuman hospital again this percent renders the use of ciprofloxacin another bad first starting antimicrobial with no significant sensitivity against most frequent E.coli culture, and this finding is in agree with the study of when Fasudba et al. thev state "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 regulations"<sup>(24)</sup>. Avpak et current al. reported 36% resistance to trimethoprim and 17% resistance to ciprofloxacin among 288 E. coli isolates from patients with UTI in Turkey<sup>(3)</sup>. In addition. Drago et al. concluded "among the tested fluoroquinolones. levofloxacin was the most able to limit occurrence of resistance in vitro. However, in order to limit the occurrence of resistance, appropriate dosages of fluoroquinolones should be respected in the therapy of infections caused by Enterobacteriaceae, as well as use of synergistic combinations in the most complicated infections" (25). Ozvurt et al. found 34% resistance to trimethoprim and 18% resistance to ciprofloxacin among community-acquired E. coli isolates from Istanbul region<sup>(26)</sup>.

Regarding ceftriaxone as an empirical therapy regimen for UTI, we found that ceftriaxone is utilized as the first empirical therapy in managing simple UTI in 13.3% of hospital doctors in the study, with a resistance rate of 35.5% and a sensitivity rate of 34.5%, which renders it unsignificant in outpatient clinic case management: however, at high doses, it was significantly correlated; indeed, this is unwise and not preferred as outpatient therapy and might be considered in hospitalized patients. Our finding was disagreeing with the study done by Wang et al. in a total of 94 patients with UTI in a single tertiary center when they concluded "For patients with UTI requiring hospitalization, ceftriaxone seems to be an effective empiric therapy for most patients" <sup>(27)</sup>. 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 UTIs<sup>(27)</sup>. However, this finding agrees with a study conducted by Sharma et al. when they conclude "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 tetracvcline. On average, over the three years, E. coli showed high resistance to fluoroguinolones (75 %) and aminoglycosides (67 %). Multidrug resistant E. coli ranged between 63 % (2012) to 65 % (2014)"<sup>(28)</sup>.

Finally we found that the gentamicin utilized by 10% of hospital's physicians in the study 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 thing it is good starting antimicrobial at this moments. This finding is in accordance with study of Mostafavi et al. in the study of 1180 patients with UTI, they concluded "gentamicin, cefepime and ceftazidime were acceptable as initial choices in non-UTI" severe infections (29) Although gentamycin is associated with some important side effects, in a study conducted in Australian hospitals regarding

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 to patients not administered gentamicin at all<sup>(31)</sup>. Hence, we agree with this study and recommend the use of gentamycin 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 days)"(32). the short-term (5-7 The different fluctuation among centers confirms the requirement for local resistance prevalence data to be available to professionals who treat 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>.

In this study, the investigation clearly shows that there is a significant increase in trimethoprim and ciprofloxacin resistance among E. coli isolates from patients with UTI in the study area, which makes the empirical treatment of UTI 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 Alnuman hospital outpatients, the studied consisted samples of primarily uncomplicated UTI, and the E. coli isolates were at a higher rate among other causative uropathogens, and it was more likely to be resistant to trimethoprim, ciprofloxacin, and ceftriaxone, and it was only and clearly sensitive to gentamycin. 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 with a higher dose. Nevertheless, gentamycin 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>. Avpak et resistance against al. reported that ciprofloxacin and trimethoprim is strongly a high number of associated with 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, continuous follow up the current and update studies in susceptibility of uropathogens provide important information that allows for the identification of trends in bacterium incidence and antimicrobial resistance. includina identification of emeraina 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, followed closely bv ciprofloxacin (32%), and the average duration of antibiotic therapy was 8.6 days in the United States<sup>(35)</sup>. In this study, we found that although not recommended as a first-line antibiotic, ciprofloxacin was the most frequently prescribed drug in the hospital outpatient clinic for UTI treatment followed by trimethoprim.

As far as anyone is concerned, this is the primary study in Baghdad which directly evaluates the effectiveness of four major utilized antibiotics by the hospital's physicians in management of simple UTI in outpatient clinics in the one of the maior hospitals. Data and information were gathered from a drug surveillance database or from medical records retrospectively with knowledge of the patient's clinical circumstances. The results are based on actual physician habits, and thus provide an accurate description of which antibiotics are prescribed.

Since UTI is relatively common, inappropriate prescriptions widespread increase resistance among uropathogens. this studv. resistance rates In to ciprofloxacin and trimethoprim among the *E. coli* strains were found to be much higher than those reported in other studies. This is in accordance with a study done in Baghdad by Nashtar who concluded "most commonly found organisms in UTI were E. coli and Klebsiella. Penicillins were highly resisted except carbapenem. Trimethprim. generation cephalosporin second (cephalothin) and ciprofloxacin also were highly resisted" <sup>(36)</sup>. 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 in this observational study, although it was local, we reached our goals, which is the obtaining precise scientific data on the susceptibility rates and most common uropathogens in a teaching hospital serving to Alrusafa region in Baghdad. At the same time, we had an opportunity to evaluate the actual prescriptions habits of physicians in a medical condition that is most often improperly treated.

We had a limitation to evaluate the susceptibility patterns to other alternative antimicrobials such as nitrofurantoin and levofloxacin because of the lack of antimicrobial discs in the hospital's laboratory at time of study as well as we deal with the most frequently used empirical antimicrobials in the hospital outpatient clinic.

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

In conclusion; utilization of trimethoprim and ciprofloxacin as empirical therapy in the treatment of uncomplicated UTI should be omitted. Ceftriaxone is not good choice as an empirical therapy because it is effective only at a high dose. Gentamycin is a good empirical therapy for UTI, but physicians should be aware of its side effects. 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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## -References

- Lodise TP, Chopra T, Nathanson BH, Sulham K. Hospital admission patterns of adult patients with complicated urinary tract infections who present to the hospital by disease acuity and comorbid conditions: How many admissions are potentially avoidable?. American journal of infection control. 2021 Dec 1;49(12):1528-34.
- Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nature Reviews Microbiology 2015; 13(5): 269-84.
- Aypak C, Altunsoy A, Düzgün N. Empiric antibiotic therapy in acute uncomplicated urinary tract infections and fluoroquinolone resistance: a prospective observational study. Annals Clinical Microbiology Antimicrobials 2009;8(1):1-7.
- Mouiche MM, Moffo F, Akoachere JF, Okah-Nnane NH, Mapiefou NP, Ndze VN, Wade A, Djuikwo-Teukeng FF, Toghoua DG, Zambou HR, Feussom JM. Antimicrobial resistance from a one health perspective in Cameroon: a systematic review and meta-analysis. BMC Public Health. 2019 Dec;19(1):1-20.
- Kot B. Antibiotic resistance among uropathogenic Escherichia coli. Polish journal of microbiology. 2019 Dec;68(4):403.
- Fair RJ, Tor Y. Antibiotics and bacterial resistance in the 21<sup>st</sup> century. Perspect Medicin Chem 2014;6:25-64.
- Kohanski MA, Dwyer DJ, Collins JJ. How antibiotics kill bacteria: from targets to networks. Nature Reviews Microbiology 2010; 8(6):423-35.
- Logan NZ, Karp BE, Tagg KA, Burns-Lynch C, Chen J, Garcia-Williams A, Marsh ZA, O'Laughlin K, Plumb ID, Schroeder MN, Webb HE. Increase in multidrug resistance (2011–2018) and the emergence of extensive drug resistance (2020) in Shigella sonnei in the United States. In Open Forum Infectious Diseases 2020; 7 Suppl 1): S195.

- Dibua UM, Onyemerela IS, Nweze EI. Frequency, urinalysis and susceptibility profile of pathogens causing urinary tract infections in Enugu State, southeast Nigeria. Revista do Instituto de Medicina Tropical de São Paulo. 2014; 56:55-9.
- 10. Adegun PT, Odimayo MS, Olaogun JG, Emmanuel EE. Comparison of uropathogens and antibiotic susceptibility patterns in catheterized ambulant middle-aged and elderly Nigerian patients with bladder outlet obstruction. Turkish Journal Urology 2019; 45(1): 48.
- 11. Rodloff A, Bauer T, Éwig S, Kujath P, Müller E. Susceptible, intermediate, and resistant-the intensity of antibiotic action. Deutsches Ärzteblatt International 2008; 105(39):657.
- 12. Hassuna NA, Khairalla AS, Farahat EM, Hammad AM, Abdel-Fattah M. Molecular characterization of Extended-spectrum β lactamase-producing E. coli recovered from community-acquired urinary tract infections in Upper Egypt. Scientific reports. 2020 Feb 17;10(1):1-8.
- Konapa LA, Vesalapu V, Kolakota RK, Mugada V. Pregnancy and hormonal effects on urinary tract infections in women: a scoping review. Int J Res Rev 2018;5(10):407-20.
- Adams LG. Treatment of urinary tract infection (UTI): Guidelines for sporadic and recurrent UTI. Purdue Univ Coll Vet Med. 2019.
- 15. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Moran GJ, Nicolle LE, Raz R, Schaeffer AJ, Soper DE. 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. Clinical Infectious Diseases 2011; 52(5):e103-20.
- Hooton TM. Uncomplicated urinary tract infection. New England Journal of Medicine. 2012 Mar 15;366(11):1028-37.
- 17. Sasirekha B. Prevalence of ESBL, AmpC βlactamases and MRSA among uropathogens and its antibiogram. EXCLI journal 2013;12:81.
- 18. Yekani M, Baghi HB, Sefidan FY, Azargun R, Memar MY, Ghotaslou R. The rates of quinolone, trimethoprim / sulfamethoxazole and aminoglycoside resistance among Enterobacteriaceae isolated from urinary tract infections in Azerbaijan, Iran. GMS Hygiene Infection Control 2018;13.
- 19. Stapleton AE, Wagenlehner FM, Mulgirigama A, Twynholm M. Escherichia coli resistance to fluoroquinolones in community-acquired uncomplicated urinary tract infection in women: A systematic review. Antimicrobial Agents Chemotherapy 2020;64(10):e00862-20.
- 20. Samin KA, Malik S, Sadiq S, Rasheeq T, Sajid NK, Iqbal W. Acute Kidney Injury is A Risk Factor among Type 2 Diabetic Patients after UTI due to Extended-Spectrum Beta-Lactamase Producing Organisms. Pakistan Journal of Medical and Health Sciences. 2021;15(5):1718-20.
- 21. Arredondo-García JL, Amábile-Cuevas CF. High resistance prevalence towards ampicillin, co-

trimoxazole and ciprofloxacin, among uropathogenic Escherichia coli isolates in Mexico City. Journal Infection Developing Countries 2008;2(05):350-3.

- 22. Mulder M, Verbon A, Lous J, Goessens W, Stricker BH. Use of other antimicrobial drugs is associated with trimethoprim resistance in patients with urinary tract infections caused by E. coli. European Journal Clinical Microbiology Infectious Diseases 2019; 38(12):2283-90.
- 23. Zhang S, Chen S, Abbas M, Wang M, Jia R, Chen S, Liu M, Zhu D, Zhao X, Wu Y, Yang Q. High incidence of multi-drug resistance and heterogeneity of mobile genetic elements in Escherichia coli isolates from diseased ducks in Sichuan province of China. Ecotoxicology and environmental safety. 2021 Oct 1;222:112475.
- 24. Fasugba O, Gardner A, Mitchell BG, Mnatzaganian G. Ciprofloxacin resistance in community-and hospital-acquired Escherichia coli urinary tract infections: A systematic review and meta-analysis of observational studies. BMC infectious diseases 2015;15(1):1-6.
- Drago L, Nicola L, Mattina R, De Vecchi E. In vitro selection of resistance in Escherichia coli and Klebsiella spp. at in vivo fluoroquinolone concentrations. BMC microbiology 2010;10(1):1-7.
- 26. Ozyurt M, Haznedaroğlu T, Sahiner F, Oncül O, Ceylan S, Ardic N, Erdemoğlu A. Antimicrobial resistance profiles of community-acquired uropathogenic Escherichia coli isolates during 2004-2006 in a training hospital in Istanbul. Mikrobiyoloji Bulteni 2008; 42(2): 231-43.
- Wang SS, Ratliff PD, Judd WR. Retrospective review of ceftriaxone versus levofloxacin for treatment of E. coli urinary tract infections. International journal of clinical pharmacy. 2018; 40(1): 143-9.
- 28. Sharma N, Gupta A, Walia G, Bakhshi R. Pattern of antimicrobial resistance of Escherichia coli isolates from urinary tract infection patients: A three year retrospective study. J Appl Pharm Sci 2016; 6(01):62-5.

- 29. Mostafavi SN, Rostami S, Nejad YR, Ataei B, Mobasherizadeh S, Cheraghi A, Haghighipour S, Nouri S, Pourdad A, Ataabadi P, Almasi N. Antimicrobial resistance in hospitalized patients with community acquired urinary tract infection in Isfahan, Iran. Archives Iranian Medicine 2021;24(3):187-92.
- 30. Sia CS, Ananda-Rajah MR, Adler NR, Yi-Wei B, Liew D, Tong EY, Aung AK. Renal safety of shortterm empiric gentamicin therapy in aged patients. Australasian Journal Ageing 2018; 37(3):227-31.
- 31. Ryanto S, Wong M, Czarniak P, Parsons R, Travers K, Skinner M, Sunderland B. The use of initial dosing of gentamicin in the management of pyelonephritis/urosepsis: A retrospective study. Plos one 2019;14(1):e0211094.
- 32. Ekmen S, Doğan E. Evaluation of Gentamicin Ototoxicity in Newborn Infants: A Retrospective Observational Study. International Journal Pediatrics 2021;9(3):13137-44.
- 33. Hain G, Goldbart A, Sagi O, Ben-Shimol S. High rates of antibiotic non-susceptibility in Gramnegative urinary tract infection in children with risk factors occurring in the preceding month: Considerations for choosing empiric treatment. Pediatric Infectious Disease Journal 2021; 40(7): 639-44.
- 34. Muthanna A, Salim HS, Hamat RA, Shamsuddin NH, Zakariah SZ. Clinical screening tools to diagnose group A streptococcal pharyngotonsillitis in primary care clinics to improve prescribing habits. The Malaysian journal of medical sciences: MJMS. 2018 Nov;25(6):6.
- 35. McEwen LN, Farjo R, Foxman B. Antibiotic prescribing for cystitis: how well does it match published guidelines? Annals Epidemiology 2003; 13(6):479-83.
- Nashtar SB. Assessment of antimicrobial susceptibility patterns in urine culture of patients with urinary tract infection attending Al-Kindy teaching hospital. Iraqi Medical Journal 2018; 64(1): 37-41.

- IMJ 2022; 68(1): 36-45.