

In vitro Resistance to Cephalosporins in Women with Bacterial Urinary Tract Infections

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ABSTRACT:

BACKGROUND:

Urinary tract infections are the most frequent nosocomial and community-acquired infections. Cephalosporins have a role in treating urinary tract infections, but are not recommended for empiric therapy because of the relatively high rates of resistance and low efficacy. Effective management of urinary tract infections has been hampered by the fact that many strains have developed resistance to several antimicrobial agents.

OBJECTIVE:

A. To demonstrate the common local bacterial pathogens and, B. To test the in-vitro the susceptibility to cephalosporins in women with urinary tract infections.

PATIENTS AND METHODS:

One hundred and twenty women from the outpatient department of Albatool Maternity Teaching Hospital from the coauthor's private clinic with signs and symptoms of uncomplicated acute urinary tract infections with no previous history of antibiotic intake were included in the study. Culture and sensitivity tests to cephalosporins and other antibiotics were done to all of them.

RESULTS:

Six types of bacterial species were isolated from the urine samples. E. coli was isolated from 49 cases (40.83%), Klebsiella was found to be the second most common bacteria isolated in 31 cases (25.83%). About one third of E. coli, Klebsiella, Proteus and Citrobacter were resistant to cephalosporins. E. coli and Klebsiella resist most cephalosporins.

CONCLUSION:

Many types of bacteria cause urinary tract infection, most of these bacteria resist cephalosporins. Cephalosporins should not be used as first line therapy and when used have to be preceded by culture and sensitivity testing.

KEY WORDS: urinary tract infection, cephalosporins, bacterial resistance, sensitivity testing.

INTRODUCTION:

Urinary tract infections are the most commonly found bacterial infections, accounting for nearly seven million office visits and one million emergency department visits⁽¹⁾. It is a common clinical syndrome that occurs in women with otherwise normal genitourinary tracts⁽²⁾, and at least 50% of women reported at least one UTI in a lifetime⁽³⁾. Urinary tract infections including cystitis and pyelonephritis are the most frequent nosocomial and community-acquired infections⁽⁴⁾. Women with recurrent urinary tract infection

have an increased susceptibility to vaginal colonization with uropathogens due to a greater propensity for them to adhere to their epithelial cells. Risk factors include frequent sexual intercourse, spermicide use, UTI at an early age and maternal history of UTI⁽⁵⁾.

The microbial etiology of urinary infections has been regarded as well established and reasonably consistent. Escherichia coli remain the predominant uropathogen accounts for 75–90% of all urinary tract infections in both inpatients and outpatients. Others would include Staphylococcus saprophyticus, Klebsiella spp., Proteus spp., Enterobacter spp., Citrobacter spp., and Pseudomonas aeruginosa⁽⁶⁾.

For several decades, trimethoprim-sulfamethoxazole (TMP-SMX), or trimethoprim alone, have been the first-line therapy for urinary tract infection. Nitrofurantoin is a narrow-

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spectrum antimicrobial with no systemic activity. It is indicated only for treatment of urinary tract infection caused by *E coli* and *Staphylococcus saprophyticus*, the two pathogens isolated from 95% of all urinary tract infections. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1531733/-D13> Fluoroquinolones including norfloxacin, ciprofloxacin, ofloxacin, levofloxacin, and gatifloxacin, are effective as 3-day therapy and are well tolerated. Cephalosporins have a role in treating urinary tract infections, particularly in pregnant women, but are not recommended for empiric therapy because of the relatively high rates of resistance and lower efficacy, especially with short-course therapy⁽⁷⁾. The fluoroquinolones and the cephalosporins however may be used in treatment failures, recurrent infections, and allergies to other drugs⁽⁸⁾. In the UK, trimethoprim or nitrofurantoin are usually recommended for empirical treatment of episodes of uncomplicated cystitis in the community, whilst parenteral cephalosporins and aminoglycosides are reserved for complicated infections or pyelonephritis⁽⁹⁾. Effective management of urinary tract infections in the outpatient setting has been hampered by the fact that many strains have developed resistance to several oral antimicrobial agents. Resistance to TMP-SMX now approaches 18% to 22% in some regions of the United States, and nearly 1 in 3 bacterial strains causing cystitis or pyelonephritis demonstrate resistance to amoxicillin. Fortunately, resistance to other agents, such as nitrofurantoin and the fluoroquinolones, has remained low, at approximately 2%⁽¹⁰⁾. The aim of the present study is to demonstrate the common local bacterial pathogens and to test the in-vitro susceptibility of bacterial urinary tract infection to cephalosporins in women. Thereby we may try to change the prescribing practice of the treating physicians.

PATIENTS AND METHODS:

One hundred and twenty women from the

Table 1: Bacterial species isolated from the urine

Bacterial Species	No. of Cases	%
E. Coli	49	40.83
Klebsiella spp.	31	25.83
Proteus spp.	22	18.31
Enterobacter spp.	8	6.7
Citrobacter spp.	6	5.0
Pseudomonas aeruginosa	4	3.33
Total	120	100

The concentrations of the discs and the inhibition zones are shown in the table 2.

outpatient department of Albatool Maternity Teaching Hospital from the coauthor's private clinic with signs and symptoms of uncomplicated acute urinary tract infections and with no previous history of antibiotic intake were included in the study. The age group was 21-55 years. According to signs and symptoms of the disease, patients were recognized as having cystitis with (dysuria, frequency, urgency and suprapubic pain, and others having pyelonephritis with (fever, rigor, loin pain and tenderness). Patients were asked to submit clean voided midstream urine specimens for culture and sensitivity test. The usual laboratory antibiotic discs were used for culture and sensitivity in addition to the following cephalosporin antibiotic discs as: cefixime, cephalexin, ceftriaxone, cefotaxime, cephalothin, and cefuroxime. Resistance/sensitivity to other antibiotics was ignored as they are outside the scope of this study.

Samples were processed using the following standard microbiological procedures: culture for colonial morphology, biochemical tests for identifying the species of the pathogens, and antimicrobial sensitivity by the Kirby-Bauer Method⁽¹¹⁾. The diagnosis of UTI was made if the urine cultures had $>10^3$ to $>10^5$ colony forming units (CFUs)/mL of a single potential pathogen or two potential pathogens.

RESULTS:

Six types of bacterial species were isolated from the urine samples as *E coli*, *Klebsiella*, *Proteus*, *Staphylococci*, *Streptococci*, and *Pseudomonas* (Table 1). *E coli* was the most common bacteria isolated from the urine of 49 women (40.83%), *Klebsiella* was found to be the second most common bacteria isolated, making up 31 cases (25.83%) of the total isolates. *Proteus* spp. was found in 22 cases (18.31%) and *Enterobacter* spp. was found in 8 cases (6.7%). While *Citrobacter* spp. and *Pseudomonas aeruginosa* were found in 6 (5%) and 4 (3.33%) urine isolates respectively.

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Table 2: Performance for antimicrobial disc sensitivity test

Antibiotic	Disc potency/ µg	Inhibition zone (mm)	Sensitive	intermediate	resistance
Cefixim	30	≥26	25-23	≤22	
Cephalexin	30	≥20	19-17	≤16	
Ceftriaxone	30	≥20	19-17	≤16	
Cefotaxime	30	≥23	22-15	≤14	
Cephalothin	30	≥23	22-20	≤19	
Cefuroxime	60	≥18	17-15	≤14	

The resistance and sensitive isolates to cephalosporins is shown in table 3. In this table we see that about one third (32.7%) of *E. coli* was resistant to cephalosporins, nearly the same as *Klebsiella* (32.3%), *Proteus* (36%) and

Citrobacter (33.3%). While *Enterobacteria* showed the most virulent pattern when (62.5%) was resistant isolates. Only one quarter (25%) of *Pseudomonas* was resistant to this drug.

Table 3: Resistance and sensitive isolates to cephalosporins

Bacterial Species	No. of Resistance isolates (%)	No. of sensitive isolates (%)	Total isolates
<i>E. Coli</i>	16(32.7)	33(67.3%)	49
<i>Klebsiella</i>	10(32.3)	21(67.7%)	31
<i>Proteus</i>	8(36)	14(63.6%)	22
<i>Enterobacter</i>	5(62.5)	3(37.5%)	8
<i>Citrobacter</i>	2(33.3)	4(66.7%)	6
<i>Pseudomonas</i>	1(25.0)	3(75.0%)	4
Total	42(35%)	78(65%)	120

The resistance patterns to cephalosporins are showed in table 4. *E. coli* showed resistance to all tested cephalosporins (multiple drug resistant). *Klebsiella* strains appeared to resist all the tested cephalosporins except cefotaxime and ceftriaxone, while *Proteus* species is resistant to

all the tested cephalosporins except ceftriaxone. *Enterobacteria* are resistant to cephalexine, cefalothin and cefuroxime. *Citrobacteria* showed resistance to cefixime and cephalexine, while *Pseudomonas* resists only cefalothin.

Table 4: The resistance patterns of bacteria to cephalosporins.

Cephalosporin	<i>E. coli</i>	<i>Kleb</i>	<i>Proteus</i>	<i>Enterob</i>	<i>Citrobact</i>	<i>Pseud</i>
Cefixime	2	3	1		1	
Ceftriaxone	2					
Cefotaxime	2		1			
Cephalexine	6	3	3	2	1	
Cefalothin	1	2	2	2		1
Cefuroxime	3	2	1	1		
Total	16	10	8	5	2	1

DISCUSSION:

Antimicrobial resistance is now recognized as an increasingly global problem which was observed for the first time in *E. coli* in 1940. The primary

factor responsible for the development and spread of bacterial resistance is the injudicious use of antimicrobial agents⁽¹²⁾. The development of drug

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resistance has been associated with an increased and inappropriate use of antibiotics. There is an inordinate and irrational use of antimicrobial agents in the developing countries⁽¹³⁾.

The most common type of bacteria isolated in the present study was *E. coli* (40.83%), followed by *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp., *Citrobacter* spp., and *Pseudomonas*. Echols et al.⁽¹⁴⁾ reported that the main causative pathogen involved in recurrent UTI in women is *E. coli*, which is responsible for approximately 80% of all episodes of infection. A study conducted at Al-Kindy Teaching hospital found that *E. coli* and *Klebsiella* were also the most common causative bacteria, although their study involved both male and female patients⁽¹⁵⁾. Other significant pathogens include *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, and *Proteus mirabilis*, each cause approximately 4% of all episodes of acute cystitis. *Citrobacter* and *Enterococci* are less likely causes of UTI in women. Brush⁽¹⁶⁾ reported that *E. coli* cause 70-95% of both upper and lower UTIs. Various organisms are responsible for the remainder of infections, including *S. saprophyticus*, *Proteus* species, *Klebsiella* species, *Enterococcus faecalis*, other *Enterobacteriaceae*.

The results of the susceptibility testing of isolates under study to different cephalosporins have shown that the isolates were moderately to highly resistant to many of the tested cephalosporins. This may be due to the heavy use of these antibiotics in medicine and for the long duration of therapy. In case of *E. coli* 16 from 49 isolates of *E. coli* (32.7%) are resistant to all tested cephalosporins (multi resistant). *Klebsiella* and *Proteus* showed nearly similar resistance. The higher percentage of resistance was found by *Enterobacter* (62.5%) against Cephalexin, Cefalothin and Cefuroxime. Okesola et al. has found that the resistance of *K. spp.* to cefotaxime was 69.3%⁽¹⁷⁾.

The emergence of resistance to multiple beta-lactam antibiotics is a major problem in patients infected with organisms that characteristically produce inducible beta-lactamases--e.g., species of *Pseudomonas*, *Enterobacter*, *Serratia*, *Citrobacter*, indole-positive *Proteus*, and *Providencia*. Resistance has emerged in 14%-56% of patients infected with these organisms and treated with one type of cephalosporins. The emergence of resistance has been associated with clinical failure or relapse in 25%-75% of these

patients⁽¹⁸⁾. Antibiotic susceptibilities and beta-lactamase production before and after cefoxitin induction were determined in sequential isolates of individual bacterial strains in a study conducted at 1987, of 49 strains isolated from 44 patients, 25 strains (51%) were eradicated by cephalosporin therapy, 17 strains (35%) persisted with unchanged susceptibility in sequential cultures, and 7 strains (14%) from 7 patients developed multiple beta-lactam resistance during cephalosporin therapy⁽¹⁹⁾.

CONCLUSION:

Many types of bacteria causing urinary tract infections resist cephalosporins. Cephalosporins should not be used as first line therapy and when used have to be preceded by culture and sensitivity testing. Resistance during treatment with cephalosporins is common, and may be caused by the empirical use of these antibiotics.

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