

Uropathogens Causing Urinary Tract Infections in Females and Their Susceptibility to Antibiotics

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ABSTRACT

INTRODUCTION: Understanding the uropathogens causing urinary tract infection (UTI) and their susceptibility to antibiotics is important to physicians who are choosing antibiotic therapy. The purpose of the study was to evaluate the uropathogens causing UTI and their antibiotic susceptibility in females residing in Saudi Arabia.

METHODS: The participants were 150 females with UTI that was proven by culture and sensitivity tests. Their mean age was 32 years (SD, 2.4; range, 6-55). There were 8 children and 142 adults. Of the adults, 92 patients were not pregnant and 50 were pregnant. All patients were treated with antimicrobials; the most common was fluoroquinolone for patients who were not pregnant and third-generation cephalosporin for patients who were pregnant. The distribution of uropathogens was compiled. Antimicrobial sensitivity testing was completed for each antibiotic administered.

RESULTS: The majority of UTIs occurred in the lower urinary tract for all patients. *Escherichia coli* was the most common pathogen, occurring in 52% of the patients who were pregnant and 53% of the patients who were not pregnant. *Klebsiella* was the second most commonly occurring pathogen, occurring in 15% and 16% of the patients who were not pregnant and pregnant, respectively. In females who were not pregnant, *Pseudomonas* and *Staphylococcus aureus* were also relatively common; in females who were pregnant, *Staphylococcus epidermidis* and nonhemolytic *Streptococcus* were more frequently found. The antibiotic susceptibility for *E. coli* ranged from 97% for fluoroquinolone to 48% for cefaclor; nitrofurantion was also high at 96%. *Klebsiella* had the highest response to gentamicin (80%).

CONCLUSION: *E. coli* was the most frequently isolated uropathogen in females with UTI, followed by other Gram-negative bacteria. There were some differences in the types of pathogens when compared with previous literature. These may be due to variations in geographic location, patient characteristics, or treatment methodology. Susceptibility rates are essential for determining the most sensitive antimicrobial for the causative organism.

KEYWORDS: Urinary Tract infection; Uropathogen; Antimicrobial

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Abbreviations and Acronyms

AMC, amoxicillin-clavulanic acid

E. coli, *Escherichia coli*

IV, intravenous

TMX, trimethoprim-sulfamethoxazole

UTI, urinary tract infection

INTRODUCTION

A urinary tract infection (UTI) is defined as significant bacteriuria in the presence or absence of symptoms. It is the most common bacterial infection in women, affecting an estimated 20% of women at some point during their lifetimes and resulting in significant morbidity and healthcare costs. UTIs are more common in women than men, primarily because women have a short urethra that is located close to the vagina and rectum. A UTI may affect the lower urinary tract (ie, bladder and urethra) or upper urinary tract (ie, kidney and ureter). The manifestations may reflect the location; patients with upper UTIs are usually febrile whereas patients with lower UTIs are usually afebrile [1,2]. The diagnosis of UTI is made on the basis of symptoms and the presence of bacteriuria (more than 10^3 bacteria per mL of urine by examination of a midstream sterile urine sample) [3].

UTI is also one of the most common bacterial infections during pregnancy. The prevalence rate of bacteriuria in women who are pregnant is essentially the same as in women who are not pregnant [4]. However, when pregnant women have a UTI, it occurs more frequently in the upper than lower urinary tract. UTIs are associated with risks to both the fetus and the mother, including pyelonephritis, preterm birth, low infant birth weight, and increased perinatal mortality.

A limited and predictable spectrum of organisms cause UTIs in females. Among both outpatients and inpatients, *Escherichia coli* (*E. coli*) is the primary urinary tract pathogen, accounting for 75% to 90% of uncomplicated urinary tract infection isolates. *Staphylococcus saprophyticus* (*S. saprophyticus*), *Klebsiella spp.*, *proteus spp.*, *Enterococcus spp.*, and *Enterobacter spp.* are pathogens less commonly isolated from outpatients [1,5].

Asymptomatic bacteriuria, as the name implies, is a positive urine culture without specific symptoms. Asymptomatic bacteriuria increases the risk for pyelonephritis. Treatment of asymptomatic bacteriuria reduces the risk of asymptomatic infection [6]. The frequency of asymptomatic bacteriuria is 2% to 7% in the general population of women [7]. However, up to 40% of these cases may progress to symptomatic upper-tract infections; hence asymptomatic bacteriuria should be treated as symptomatic bacteriuria.

Host and bacterial virulence factors are important in the pathogenesis of recurrent UTI. General host variables that predispose a woman to recurrent infection are genetic factors, aging, menopause, urogenital dysfunction, sexual behavior, and previous pelvic surgery. Diabetes mellitus and neurogenic

bladder dysfunction are also considered risk factors [8,9].

Understanding the uropathogens causing UTI and their susceptibility to antibiotics is important to the physicians who are choosing antibiotic therapy for these patients. The uropathogens may vary according to geographic location because of cultural, lifestyle, medical, and environmental differences. The purpose of the present study was to evaluate the uropathogens causing UTI and their antibiotic susceptibility in females residing in Saudi Arabia.

METHODS

The prospective study was conducted between January 2009 and December 2009. The participants were obtained from those attending the Urology Outpatient Clinic, Gynecology and Obstetrics Clinic, and the Emergency Department at Al Ansari Specialist Hospital, Yanbu, Saudi Arabia. The protocol was approved by the hospital ethics committee. All participants provided informed consent.

Participants

The participants were 150 females with UTI that was proven by culture and sensitivity tests. Their mean age was 32 years (SD, 2.4; range, 6-55). There were 8 children and 142 adults. Among the adults, 92 patients were not pregnant and 50 were pregnant.

The majority of patients had symptoms of UTI including urinary frequency, urinary urgency, burning on micturition, blood in the urine, strangury, suprapubic pain, or a change of urine color or scent. Ten patients with asymptomatic bacteriuria were referred to the urology clinic from the obstetrics and gynecology clinic during their regular antenatal pregnancy care; all were multigravida.

Preliminary urine analysis of all patients showed pyuria. All patients underwent midstream sterile urine analysis, culture, and sensitivity testing using the disc diffusion method for sensitivity testing and 0.5 McFarland method on blood and MacConkey and Cystine Lactose Electrolyte Deficient (CLED) media.

An ultrasound of the urinary tract was performed for all patients to exclude other pathologies (eg, stones, anatomical abnormalities, obstructive uropathy). Renal function testing included serum creatinine and estimated glomerular filtration rate (GFR). Complete blood picture and blood culture tests were done for patients with a fever to determine if there were infections elsewhere in the body.

Exclusion criteria included: (1) patients who were already on antibiotics, (2) patients with anatomical abnormalities, urinary tract lithiasis, or obstruction in the upper or lower urinary tract, and (3) patients with significant comorbid conditions such as diabetes mellitus.

Procedures

Patients with a delayed menstrual cycle or those with an irregular cycle were asked to take a beta-subunit human chorionic gonadotropin (hCG) pregnancy test before starting the treatment.

All patients with febrile UTIs were admitted to the hospital and treated with intravenous (IV) fluids (dextrose in saline). Usually, we started IV antibiotic infusion with 3rd generation cephalosporin (ceftriaxone), given according to the age and weight of the patient. We also administered an antipyretic and analgesics until the results of the patient's specific culture and sensitivity were obtained.

Patients who were afebrile or patients with asymptomatic bacteriuria were started on oral antibiotics after obtaining the urine sample for the culture and sensitivity test. They were also given analgesics and antispasmodic medications if they had severe irritative lower urinary tract symptoms. The antibiotic of choice depended on several factors, including the age of the patient, known drug sensitivities, and whether or not she was pregnant or lactating. We used empirical antibiotics according to the guidelines of our laboratory department.

The most frequently prescribed antimicrobial agent for the 92 adult patients who were not pregnant was fluoroquinolones; these were prescribed for 40 patients (43%). Other drugs used

were trimethoprim-sulfamethoxazole (TMX) for 15 patients (16%), nitrofurantoin for 7 patients (7.5%), and amoxicillin-clavulanic acid (AMC) for 11 patients (12%); 19 patients (20%) received injectable forms of antibiotics (eg, ceftriaxone, ceftazidime). The most frequently prescribed agent for the 50 patients who were pregnant was ceftriaxone, which was prescribed for 18 patients (36%); other drugs used were AMC for 17 patients (34%), cefuroxime (Zinacef; GlaxoSmithKline, Research Triangle Park, NC, USA) for 8 patients (16%), and cefaclor for 7 patients (14%). The 8 children with UTI all received their antibiotics in oral form; 4 patients received AMC and 4 received TMX.

All patients repeated the urine culture and sensitivity testing at least 48 hours after they finished their antimicrobial treatment. Those with negative culture were asked to report again to the urology clinic if they started to experience any urinary symptoms or they noticed a change in the color or scent of their urine.

All pregnant patients were followed monthly throughout their pregnancy. They completed routine urine analysis and culture sensitivity testing to be sure that there was no recurrence of the UTI or any asymptomatic bacteriuria.

Data Analysis

The distribution of uropathogens was compiled for all patients. Antimicrobial sensitivity testing was completed for each antibiotic administered. The microorganism susceptibility was coded as present or absent and analyzed per uropathogen.

RESULTS

Table 1 shows the number of first and recurrent UTIs and their location in children and in adult women (not pregnant and

Table 1. The Number of First and Recurrent Urinary Tract Infections (UTI) and Their Location in Children and in Adult Women (Not Pregnant and Pregnant) (N = 150).

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Variable	Patients - Not Pregnant (n = 100)			Patients - Pregnant (n = 50)	
	Children	Adults		Primigravida	Multigravida
		Not Sexually Active	Sexually Active		
Total n (%n)	8 (8)	6 (6)	86 (86)	15 (30)	35 (70)
First UTI, n (%n)	6 (75)	6 (100)	23 (26.7)	11 (73.3)	14 (40)
Recurrent UTI, n (%n)	2 (25)	0	63 (73.2)	4 (26.6)	21 (60)
Location, n (%n)					
Upper Urinary Tract	0	2 (33.3)	15 (17.4)	6 (40)	12 (34.2)
Lower Urinary Tract	8 (100)	4 (66.6)	71 (82.5)	9 (60)	13 (37.1)

Table 2. Common Pathogens Found in Female Patients With Urinary Tract Infections (Not Pregnant and Pregnant) (N = 150).

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Pathogen	Females - Not Pregnant (n = 100)		Females - Pregnant (n = 50)	
	n	% n	n	% n
<i>Escherichia coli</i>	53	53	26	52
<i>Klebsiella</i>	15	15	8	16
<i>Pseudomonas</i>	12	12	2	4
Combined pathogen	9	9	2	4
<i>Staphylococcus aureus</i>	7	7	4	8
<i>Staphylococcus epidermidis</i>	1	1	5	10
Nonhemolytic <i>Streptococcus</i>	4	4	5	10
MRSA	3	3	2	4
<i>Enterococci</i>	3	3		
<i>Enterobacter</i>	3	3		
<i>Candida</i>	1	1		
<i>Proteus</i>	2	2		
<i>Citrobacter</i>	1	1		

Some patients had more than 1 type of organism in their culture.

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

pregnant). The majority of UTIs occurred in the lower urinary tract for all patients. UTIs occurring in the lower tract were more common in women who were primigravida; UTIs occurred equally in the upper and lower tract for women who were multigravida. Both first and recurrent UTIs were more common in women who were multigravida than primigravida.

Table 2 shows the common pathogens that were found in patients with UTI (not pregnant and pregnant). Some patients had more than 1 organism in their culture. *E. coli* was the most common pathogen for all patients, occurring in 52% of the patients who were pregnant and 53% of the patients who were not pregnant. *Klebsiella* was the second most commonly occurring pathogen, occurring in 15% and 16% of the patients who were not pregnant and pregnant, respectively. In females who were not pregnant, *Pseudomonas* and *Staphylococcus aureus* were also relatively common; in females who were pregnant, *Staphylococcus epidermidis* and nonhemolytic *Streptococcus* were more frequently found.

Table 3 contains the results of the antimicrobial sensitivity testing and the susceptible organisms. The percentage of

microorganisms that responded to treatment is presented. The antibiotic susceptibility for *E. coli* ranged from 97% for fluoroquinolone to 48% for cefaclor; nitrofurantion was also high at 96%, but susceptibility to TMX was only 80%. *Klebsiella* had the highest response to gentamicin (80%).

DISCUSSION

Urinary tract infections are common in female patients in general practice [10], and urine is the most frequently received specimen in microbiology laboratories. These common bacterial infections affect half of all women at least once in their lives [11]. Clinical management strategies vary and empiric antibiotics are commonly used. However, many practitioners also use urinary dipstick results and request analysis of midstream urine samples. In over 62% of women presenting with suspected urinary tract infection, the diagnosis is laboratory-confirmed [12]. The current prospective study reports the uropathogens found in female patients with UTI and the susceptibility of the antimicrobial agent that was administered.

UTI is more common in females who are sexually active [13]. This trend was also observed in our study, although the number

Table 3. Percentage of Susceptible Microorganisms that Responded to the Antimicrobial Treatment.

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Pathogen	Genta- micin	Cefaclor	Amoxicillin clavulanic acid	Nitro- furantion	Cefuroxime	Ceftazidime	Cipro- floxacin	Sutrim	Cefixime	Ceftriaxone- triaxone	Nor- floxacin
<i>Escherichia coli</i>	89	48	56	96	51	70	97*	80	50	75	52
<i>Klebsiella</i>	80*	53	53	62	63	67	69	36	51	69	66
<i>Staphylococcus Epidermidis</i>	50	67	84*	67	78	19	64	48	9	69	37
<i>Staphylococcus aureus</i>	73	42	47	83*	44	11	46	75	26	43	59
Nonhemolytic <i>Streptococcus</i>	50	100*	94	51	84	67	29	34	39	94	67
<i>Pseudomonas</i>	72*	33	0	17	46	74	58.5	41	67	55	59
<i>Enterococci</i>	0	0	0	100*	0	0	50	75	0	0	0
<i>Enterobacter</i>	63	50	50	100*	75	75	63	13	63	83	
<i>Proteus</i>	100	100	-	100	-	100	100	0	0	100	100
<i>Citrobacter</i>	100	100	100	100	100	100	100	0	100	100	100

*Indicates the treatment that caused the highest microorganism response.

of women who were not sexually active was very small. UTIs occur most commonly in the lower urinary tract [14]. This result was confirmed in the present study. Most of the patients with UTIs in the present study were in the late-20 and early-30 year age groups; this is also in accordance with published literature regarding UTIs in females [13].

E. coli is the most important uropathogen in the general population [13,15]. It is the most frequently isolated uropathogen in females of all age categories [16,17]. In accordance with the literature, we found that *E. coli* caused most of the UTIs and *Klebsiella* was the second most common cause, whether or not the female was pregnant.

Antibiotic resistance has become a consideration in the treatment of community-acquired UTIs [18,19]. A population study in Spain that included both complicated and uncomplicated UTIs in male and female patients showed that the susceptibility percentage for *E. coli* was low for amoxicillin (41%), TMX (66%), and ciprofloxacin (77%) [13]. According to our study, *E. coli* susceptibility was low for amoxicillin and TMX, whereas ciprofloxacin had the highest rate of response (97%).

A large multicenter international study of 4734 women presenting with symptoms of acute UTI who were 65 years old or younger was published in 2003 [20]. The women were from

252 community health care centers in 17 countries. Urinary tract pathogens were identified and their susceptibility to 12 antimicrobials was determined. Pathogens were present in 3278 (69.2%) patients; *E. coli* accounted for 77.0% of isolates. *E. coli* resistance was highest for ampicillin (29.8%) and sulfamethoxazole (29.1%), followed by trimethoprim (14.8%), trimethoprim/sulfamethoxazole (14.1%) and nalidixic acid (5.4%). However, there were some differences according to the patient's country. The authors concluded that antimicrobial resistance was lowest in the Nordic countries and Austria and highest in Portugal and Spain.

In Europe, *E. coli* susceptibility for multiple drugs varied from 9% to 40% in uncomplicated UTIs [21,22]; in women, resistance to fluoroquinolones varied from 9% to 16%. However, this susceptibility percentage may be higher than in the community because most cultures are done when treatment fails or in the case of complicated UTIs. Because susceptibility varies with geographic region and population (nosocomial or community), empiric antibiotic prescription should be dependent on the susceptibility percentage of a specific antibiotic over time [13,23-25].

In 2008, Naber et al [26] published a study that included 68 centers (4264 patients) from 9 European countries and Brazil. Their results also showed that *E. coli* was the most frequent

pathogen (76.7%), followed by *Enterococcus faecalis* (4%) and *Proteus* (3.5%). In the present study, *Klebsiella*, *Pseudomonas*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and nonhemolytic *Streptococcus* were more frequently found. This discrepancy may be due to the smaller total number of patients in the present study, the large percentage of patients who were pregnant, or to community differences. Additionally, the age range in the Naber et al study was 18-65 years, whereas the age range in the present study was 6-55 years. Finally, Naber et al focused on cystitis, whereas our study considered all types of UTI.

In the present study, *Klebsiella* had the highest response to gentamicin (80%). The ECO.SENS study [20] found that *Klebsiella* was more resistant to ampicillin (83.5%) and fosfomycin (56.7%).

The high percentage of *Pseudomonas* in the present study is inconsistent with other literature, including Naber et al [26]. This may be explained by the abuse of antibiotics that takes place in our community. Additionally, a large number of patients in the present study had recurrent UTI, which may increase the percentage of opportunistic infections such as *Pseudomonas* and increase the percentage of resistance to different groups of antibiotics.

The policy of our laboratory department is to conduct culture and sensitivity testing every 6 months. The most common pathogen in that specific 6-month period is recorded, and the most susceptible antibiotic is distributed to all departments. Therefore, empirical treatment is chosen according to that report until we obtain the results of the patient's specific sensitivity testing. All of our patients followed the antimicrobial that was specific to their culture soon after the results were obtained unless it was contraindicated for any reason. In such situations, we choose the safest susceptible antimicrobial from the culture. This treatment procedure may lead to development of infections that are different from those in communities that use alternative methods.

Special consideration must be given to patients who are pregnant. In the present study, the most prescribed antimicrobials in adults who were not pregnant were fluoroquinolone, ceftriaxone, TMX, AMC, and nitrofurantoin. In patients who were pregnant, the prescribed antimicrobials were ceftriaxone, AMC, Zinacef, and cefaclor. Fluoroquinolones are contraindicated in pregnancy and patients under the age of 16 years. Additionally, we take into the account the serious effect of the UTI for both the mother and the fetus and always use third-generation cephalosporin in injection form if the

patient is pregnant (especially if the patient has upper UTI and presents with high fever). We prefer hospital admission for pregnant patients with UTI associated with high fever to start IV fluid therapy and the antimicrobial drug. This regimen usually results in rapid improvement to the general condition of the patient and early control of fever.

We treated pregnant patients with asymptomatic bacteriuria in the same manner as a symptomatic patient. We know that about 40% of these patients may progress to symptomatic upper UTI (pyelonephritis), which can have a dangerous effect on the patient and her fetus. All asymptomatic bacteriuria were treated according to the results of culture and sensitivity; we did not give empirical antimicrobial treatment. Patients who are asymptomatic do not have irritative symptoms that would push us to start treatment before the results of culture and sensitivity are obtained.

CONCLUSIONS

All female patients with UTIs should be treated by a specialist who understands the common organisms and most sensitive antimicrobials associated with UTI. Abuse of antibiotics and empirical management of UTIs have caused some antimicrobials to become less sensitive to certain microorganisms than was previously reported. Management of UTI needs a clear plan that considers the patient's age and other factors such as pregnancy, complications, symptoms, and recurrence. We should always depend on antimicrobial susceptibility tests when managing UTI. Laboratory data can be used for updates on recent common organisms and the most sensitive antimicrobial that may be used if empirical treatment is necessary.

Conflict of Interest: none declared.

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