

# **CHRONIC URINARY TRACT INFECTION: ETIOLOGICAL AGENTS AND SUSCEPTIBILITY TESTING**

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## **Abstract**

Chronic Urinary Tract Infections (UTIs) are infections of the urinary tract that do not respond to treatment. They may either continue to affect your urinary tract despite getting the right treatment, or may recur after the treatment process. Although UTIs can happen to anyone at any age, they are more prevalent in women. In fact, the National Kidney and Urologic Diseases Information Clearing House estimated that one out of five young adult women suffers from recurring UTI. Therefore, the aim of this study is to strengthen the surveys of the cases of Chronic Urinary Tract Infections (UTIs). In addition, we also aim to evaluate the etiological agents of the chronic urinary tract infections; and finally, the culture characterization and antibiotic susceptibility testing of the isolated pathogenic bacteria. In order to achieve these goals, we carried out a survey of 406 patients that had chronic urinary tract infection. Also, these patients had urine sample in the Department of Microbiology at the Central Laboratory of the Ministry of Health in Amman, which is the capital of Jordan from January to September 2014. Using the urine sample, culture and biochemical test and antisera were performed. A total of 406 urine samples were tested for bacterial infection. Thus, the most commonly isolated organism was *Escherichia coli* (70%).  $\beta$  - Hemolytic *Streptococcus* group B (8%) and *Klebsiella* sp (7.6%) were reported as the next most common organisms. Of all the bacteria isolated from chronic infection, only 21% were sensitive to ampicillin, 23% to ciprofloxacin, and 18% to cotrimoxazole. The highest levels of susceptibility were observed in cephalothin (81%), Gentamicin (40 %), Augmentin (33%), Norfloxacin (28%), Nitrofurantion (23%), Lefloxacin (21%), Nalidixic acid (16%), and Imipenem (14%). Conclusion: Gram-negative agents are the most common cause of UTI. Cephalothin remains the choice among the orally administered antibiotics, which is followed by Gentamicin, Augmentin. For severe disease caused by *Escherichia coli* which is the most common causes of chronic UTI, it requires antibiotics such as nitrofurantion. This is followed by third generation cephalosporins, which were the most

effective.

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**Keywords:** Urinary tract, Infection, Chronic, Bacteria, Antibiotic, Susceptibility

## **Introduction**

Chronic urinary tract infections are mostly common in women. This is due to two different aspects of basic human anatomy. Firstly, the urethra is close to the rectum in women. As a result, it is extremely easy for bacteria from the rectum to reach the urethra, particularly if you wipe back to front instead of front to back. This is why young girls often get UTIs because they have not yet mastered the art of wiping. Secondly, in women, the urethra is shorter than men. So bacteria have a shorter distance to travel to get to the bladder, where they can multiply and cause infection more readily. There are other lifestyle factors that can put you at extra risk of developing a chronic UTI [2]. For example, using a diaphragm during sex can cause problems. Diaphragms push up against the urethra, making it harder to fully empty your bladder. The urine which has not been emptied fully is more likely to grow bacteria. Another example is in constantly changing the bacterial makeup of the vagina. Consequently, if you use antibacterial vaginal douches, spermicides, and certain oral antibiotics regularly, you are basically changing your vaginal bacteria regularly. This can increase your risk of developing a chronic UTI [1]. Menopause can cause similar problems in some women. Menopause causes hormone changes that in turn can cause changes in your vaginal bacteria [5]. Thus, this can increase your risk of chronic UTIs. Diabetes mellitus, neurologic conditions, chronic institutional residence, and chronic indwelling urinary catheterization are important predisposing factors for complicated UTIs. In affected patients, organisms that are typically less virulent may cause marked illness. Nevertheless, *E. coli* infection remains the most common organism in nearly all patient groups. *Klebsiella* and group B streptococcus infections are relatively more common in patients with diabetes. Also, *Pseudomonas* infections are relatively more common in patients with chronic catheterization. *Proteus mirabilis* is a common uropathogen in patients with indwelling catheters, spinal cord injuries, or structural abnormalities of the urinary tract [4]. Symptoms of a UTI that is affecting your bladder include frequent bloody urination or dark urine, burning sensation while urinating, and pain in your kidneys (in your lower back or below the ribs). If the UTI spreads to your kidneys, it might lead to nausea and vomiting, chills, fever, fatigue, and mental disorientation. UTIs are most commonly diagnosed through a lab test performed on a urine sample. A medical professional will examine the sample through a microscope, and will look to see if there are any bacteria in

the urine. In a urine culture test, a urine sample is placed in a tube to encourage the growth of bacteria [3]. Diagnostic evaluation in the setting of predisposing factors (i.e., complicated UTI) differs in that a urine culture including antibiotic sensitivities is almost always required to guide the therapy. Obtaining a serum chemistry panel and assessing the patient's general medical status (e.g., hydration, toxicity) are important. For older or immunocompromised patients and those who have congenital malformations of the kidney, CT or ultrasonography is usually required [6]. Consequently, the bacteria will be looked at to determine the best treatment measure. If your doctor suspects kidney damage, he or she may order X -rays and kidney scans. However, these are imaging devices that take pictures of parts of your body. If you do have recurring UTIs, your doctor may want to perform a cystoscopy. In this procedure, he or she will use a cystoscope—a long thin tube with a lens at the end—to look inside your urethra and bladder [3]. Your doctor will be looking for any abnormalities or issues that could be causing the UTI to keep coming back. UTIs are treated with antibiotics over the course of one week [1]. Antimicrobial prophylaxis has proved effective in reducing the risk of recurrent UTIs in women with two episodes of infection in the previous year. Continuous prophylaxis for six to 12 months reduces the rate of UTIs during the prophylaxis period, with no difference between the six-month and 12-month treatment groups after cessation of prophylaxis [7]. Prophylactic antibiotic selection should be made on the basis of community resistance patterns, side effects, and local costs. Also, various dosages of prophylactic antibiotics have been suggested.

## **Methods**

A fresh urine sample should be collected in a sterile container. Once it has been collected, the urine should be taken to the laboratory within half an hour after collection or should be transferred to the lab as soon as possible. Selective and differential plating media (EMB Eosin Methylene Blue or MacConky agar and blood agar), were incubated overnight (18-24 hours) at 37C. The plates were then examined for numbers of colonies of significant bacteria. Pure colonies of gram negative bacteria should be screened with the biochemical test media which consists of triple sugar iron agar (TSI), lysine iron agar (LIA), motility-indol-ornithine agar (MIO), Simmons citrate agar, and Biochemical Screening (Use of TSI). Two isolated questionable pure colonies was selected and inoculated in TSI slants and butt. This was together with a sterile platinum inoculating needle. The center of the colony was touched once. Then, the butt was stabbed, and the TSI slant was streaked. Without going back to the colony, it was incubated at approximately 36°C with their caps loose (to prevent excess H<sub>2</sub>S production) for 18-24 hours. Consequently, TSI reactions were examined as a set.

Yellow is an acid reaction, while red or purple is an alkaline reaction in TSI Acid/acid (slant/butt). After 18-24 hours, TSI indicates either lactose, sucrose, or both been fermented. Non-lactose fermenters may utilize the 0.1% glucose causing both the deep and the slant to be yellow. Biochemical identification can be completed using Biolog, bioMerieux API 20E strips, Enterotubes, or equivalent kits. Furthermore, the manufacturer's instructions for each kit should be followed closely. For gram positive bacteria, gram stain and catalase, coagulase, and streptix kit hemolytic characteristics should be done. Finally, the sensitivity to antibiotics of pathogenic bacteria which was isolated should be checked out.

## Results

Based on the biochemical and immuno-reactivity, 406 patients had chronic urinary tract infection  $10^5$  colony-forming units (CFU/mL). Also, they had their urine sampled in the Central Laboratory of the Ministry of Health in Amman, which is the capital of Jordan from January to September 2014. Antimicrobial susceptibility testing was done by the disk diffusion method (Kirby-Bauer) & Antibiotic profile. Statistical analysis was carried out using ANOVA.

Based on the results of the urine cultures of 409 patients that had chronic urinary tract infection, the prevalence of the chronic urinary tract infection in female is almost six times that of male (84% vs. 15%) (Table 1).

Table 1. The prevalence of male vs. female

Months	No of female	No of male
January	30	5
February	26	10
March	25	7
April	26	1
May	30	3
June	33	2
July	34	5
August	21	5
September	35	8
Total	260	46
Percentage	84%	15%

The most commonly isolated organism was *Escherichia coli* (66%).  $\beta$ -Hemolytic *Streptococcus* group B (9.8%) and *Klebsiella* sp (11.4%) were reported as the next most common organisms. Therefore, the other bacteria are summarized in Table 2.

Table 2. Micro-organism isolated in urine

Agents	Number (306)	%
<i>E.coli</i>	202	66
<i>Streptococcus group B</i>	30	9.8
<i>Klebsiella sp</i>	35	11.4
<i>Enterococcus sp</i>	13	4.2
<i>proteus sp</i>	7	2.3
<i>Pseudomonas sp</i>	5	1.6
<i>Staphcoagulase negative</i>	8	2.6
<i>Enterobacter</i>	6	2

The comparison of the susceptibility pattern of organisms to various antimicrobial agents from all the specimens was shown in Table 3. *Escherichia coli* showed high susceptibility to nitrofurantoin (85%). Then, this was followed by gentamicin (73%), cefotaxime fluoroquinolones (70%), Cotrimoxazole (54%), norfloxacin (50%), and ciprofloxacin (35%). Also, there was a low susceptibility pattern of *E. coli* to ampicillin (29%), and amikacin (4%).

Table 3. Antibiotic susceptibility of uropathogens

Antibiotics	<i>E.coli</i> (%)	<i>Streptococcus group B</i> (%)	<i>Klebsiella sp</i> (%)
Ampicillin	27	80	1
Gentamicin	73	12	75
Norfloxacin	50	1	60
Nitrofurantoin	85	19	64
Nalidixic acid	33	3	52
Cefotaxime	70	20	64
Ciprofloxacin	35	0	23
Amikacin	4	0	3
Cotrimoxazole	54	1	55

## Discussion

Recurrent UTIs are common among healthy young women with anatomically and physiologically normal urinary tracts [11]. One study showed that of the college women with a first UTI, 27 percent had at least one culture confirmed recurrence within the following six months; also, 2.7 percent experienced a second recurrence over the same period.[12] In a primary care setting, 53 percent of women older than 55 years and 36 percent of younger women, had a recurrence within one year.[13]. In our study, the prevalence of the chronic urinary tract infection in female is almost six times that of male (84% vs. 15%). Diabetes mellitus, neurologic conditions, chronic institutional residence, and chronic indwelling urinary catheterization are important predisposing factors for complicated UTIs. In affected patients, organisms that are typically less virulent may cause marked illness. Although *E. coli* infection remains the most common organism in

nearly all patient groups, Klebsiella and group B streptococcus infections are relatively more common in patients with diabetes. Also, Pseudomonas infections are relatively more common in patients with chronic catheterization. Proteus mirabilis is a common uropathogen in patients with indwelling catheters, spinal cord injuries, or structural abnormalities of the urinary tract. The most commonly isolated organism was Escherichia coli (66%),  $\beta$ -Hemolytic Streptococcus group B (9.8%), and Klebsiella sp (11.4%). However, this was reported as the next most common organisms. E. coli exhibited resistance to the commonly used antibiotics. Therefore, the most effective in-vitro agents were found to be aminoglycosides: nitrofurantion (85%) and gentamicin (73%) among the injectables, and fluoroquinolonas: norfloxacin (50%) and ciprofloxacin (35%). The organisms showed resistance to commonly used urinary antibiotics like ampicillin (27%) and amikacin (4%). Therefore, this is in disagreement with the data published by others [13,17,18]. In summary, nitrofurantion remains the choice among the orally administered antibiotics, followed by gentamicin. In treating severe illness, one may use the injectable antibiotics. Among them, we should choose aminoglycosides, which are the most effective ones. In addition, the high resistance patterns to ampicillin and amikacin should always be put into consideration.

### **Conclusion**

In conclusion, the most common community acquired UTI is caused by negative-Gram agents. Nitrofurantion remains the choice among the orally administered antibiotics, followed by gentamicin. For severe disease that requires parenteral antibiotics, the choice should be aminoglycosides. Thus, this is regarded to be the most effective method.

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