Asymptomatic and Symptomatic Urinary Tract Infections: Magnitude, Special Settings and Diagnostic Testing

Kehinde Lawal

Definition
From a microbiological view point, urinary tract infection (UTI) is indicated when pathogenic microorganisms are found in the urine, bladder, urethra, kidney, and prostate and a microorganism growth of $\geq 10^5$ per ml is isolated from a mid-stream or clean catch urine specimen. Asymptomatic urinary tract infection is the absence of symptoms in a patient having urinary tract infection. The presence of symptoms in a patient having infection of the urinary tract is referred to as symptomatic urinary tract infection. In both cases, urine culture may be positive or negative. In symptomatic patients, fewer ($10^2 - 10^4$ per ml) may signify infection. Urine specimen from catheterization with colony counts of $10^2 - 10^4$ per ml indicates infection. Occasionally, however, due to mid-stream urine contamination, a colony count of $>10^5$ per ml accompanied by multiple bacteria specie growth may occur. Acute urinary tract infection can either be lower urinary tract infection (urethritis and cystitis) or upper urinary tract infection (acute pyelonephritis).

Clinical Features
Acute cystitis and acute pyelonephritis are two major clinical syndromes mostly encountered. Patients with acute cystitis have infection localized in the bladder. In a typical acute pyelonephritis patient, in which the infection has spread to the kidney, localized kidney pain, fever, nausea, vomiting, chills, malaise are usually observed. Acute urethritis patients often present with symptoms of dysuria, urgency, frequency and non-significant bacteria growth. Catheter-associated UTIs cause minimal symptoms and are often resolved after catheter is removed.

Pathogenesis
Most UTIs result when bacteria gain access to the bladder via the urethra. Ascent of bacteria from the bladder may follow and is probably the pathway for most renal parenchyma infections. Some strains of *E. coli* and *Proteus* are uropathogenic. These strains have violent genes (*e.g.*, genes encoding fimbiae) that mediate attachment to uroepithelial cells. UTIs are caused by a subset of fecal microbial, flora of which *E. coli* is the most common. Some hosts, primarily women, are especially susceptible to infection. In females prone to the development of cystitis, however, enteric Gram-negative organisms residing in the bowel colonize the introitus, the periurethral skin, and distal urethral before and during bacteriuria episodes. Alteration of the normal vaginal flora of normal dominant *H. 02*-producing lactobacilli appears to facilitate colonization of *E. coli*. Antibiotic treatment and other genital infections or contraceptive are contributive factors.

Etiology
Uncomplicated community-acquired UTIs are caused by *E. coli* in 80-85% of cases; other organisms such as *Klebsiella, Proteus* and *Enterobacter* are Gram-negative rods which account for smaller proportions of UTI cases. Gram-positive etiologic agents of UTI include *Staphylococcus saprophyticus* which causes 5-10% acute UTIs among schoolgirls. *E. coli*, *Proteus*, *Klebsiella*, *Enterobacter*, *Serratia*, and *Pseudomonas* are commonly associated with recurrent UTIs and UTI of the calculi. Sexually transmitted organisms such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are urethritis producing agents. Ureaplasma urealyticum is associated with acute dysuria while *Candida* and other fungi species have frequently been isolated from the urine of catheterized patients.

Epidemiology
The magnitude of the epidemiology of UTI can be considered from two perspectives: catheter-associated (nosocomial) and non-catheter associated (community acquired) infections. In both groups, UTIs can either be symptomatic or asymptomatic.

Community-acquired UTIs result in more than 7 million doctor's office visits and 1 million hospital emergency department visits, resulting in 100,000 hospitalizations annually in the United States. These visits involve about 1.2-3.2% of sexually active young girls. Acute symptomatic infection is common among young women, accounting for about 0.9% infections per patient every year among this category.
Asymptomatic bacteriuria is frequently reported among elderly men and women with rates up to 50% in some case studies. UTIs are uncommon in males under the age of 50 years. However, the incidence of UTI in men tends to rise after the age of 50 years. Among older patients residing in nursing homes, UTIs are the most common bacterial infection. UTIs are also the most common reason for antimicrobial drug prescriptions. About 20%-60% of antimicrobial drug treatments are initiated among older patients in nursing homes.

The occurrence of not so complicated UTIs among females who reside in the communities and who are between the ages of 18-49 years is about 28.2% among every 10,000 women. Approximately 10% of adult women in the United States have at least one UTI each year. Nearly one in three women will experience UTI by the age of 24, which requires antimicrobial therapy. The incidence of UTI among hospitalized patients with indwelling catheters is about 10.2-15.2%. The risk of infection is 3-5% per day of catheterization. Catheterized urinary tract is found to facilitate Gram-negative bacteremia in about 1.2-2.3% cases of hospitalized patients with indwelling catheters.

**Risk Factors**

Under certain special settings, an individual may become predisposed to symptomatic or asymptomatic urinary tract infection. These special settings include:

- **Socio-economic status:** UTI is prevalent among individuals who belong to very low socio-economic class.
- **Pregnancy:** UTIs are detected among 3-9% of pregnant women. Twenty to 30 percent of pregnant women with asymptomatic bacteriuria subsequently develop pyelonephritis structural urinary tract abnormality.
- **Obstruction to the free flow of urine:** Any obstruction to the free flow of urine results in hydronephrosis which greatly increases the frequency of UTI.
- **Sexual behavioral practices:** UTI is prevalent among young schoolgirls and women who are sexually active.
- **Menopause:** Post menopausal women have reduced natural estrogen levels which favors the colonization of uropathogenic Gram-negative bacilli.
- **Vesicoureteral reflux:** An anatomically impaired vesicoureteral junction facilitates the reflux of bacteria, hence, upper urinary tract infection.
- **Genetic factors:** Host genetic factors influence susceptibility to UTIs. Women with maternal history of UTI often experience recurrent UTIs.
- **Bacterial virulence factors:** Certain uropathogenic organisms like *E.coli* and *Proteus* specie have fimbriae that mediate bacterial attachment to specific receptors on epithelial cells. This stimulates UTIs.
- **Diabetes:** The presence of glucose in urine favors the growth of glucose utilizing bacteria; women who have hyperglycemia and poorly managed diabetes are at risk of UTIs.
- **Other special conditions** under which UTIs may be engendered include history of UTI relapse after treatment, prior history of acute pyelonephritis, frequent UTIs with symptoms longer than 7 days and neurogenic bladder dysfunction.

**Diagnostic Testing**

Laboratory evaluation of mid-stream urine specimen or a sample from urethral catheterization is essential. The mid-stream urine should be analyzed for nitrite and leukocyte reactions, pyuria, bacteriuria and hematuria. A positive urine nitrite strongly suggests the diagnosis of UTI. A positive urine leukocyte esterase reaction from pyuria is also a strong indicator. Abnormal pyuria in women is defined as 2 to 5 leukocytes per high power field from a centrifuged urine specimen. The presence of 1 to 2 leukocytes per high power field from the centrifuged urine specimen of a man, accompanied by bacteriuria, is a strong indicator of UTIs. Systemic leukopenia may produce a false negative urine leukocyte
esterase reaction. In women with Chlamydia UTIs, bacteria may be absent. However, more than 15 bacteria per oil immersion field in a centrifuged urine suggests the diagnosis of UTI. In symptomatic patients, Gram-stained uncentrifuged urine specimen should be microscopically evaluated. The detection of bacteria by urine microscopy accompanied by colony count of 10^5 per ml is an evidence of UTI. Asymptomatic bacteriuria is defined as a urine culture with more than 10^5 per ml of a single bacterial specie in an asymptomatic patient. In the urinalysis for hematuria, confirmatory microscopic urine analysis should be performed since a false positive blood urine test strip reaction can occur due to the presence of free hemoglobin, myoglobin, porphyrins or providone-iodine in urine. More than 5 red blood cells per high power field in a centrifuged urine is one of the indicators of UTI.

### Treatment of UTI

Flouroquinolone therapy is a first-line treatment choice since bacteria resistance is sometimes observed when patients with UTI are treated with routinely used antibiotics. Flouroquinolon, such as ciprofloxacin, levofloxacin or ofloxacin, can be used. Other routinely used antibiotics include co-trimoxazole or trimethoprim, Amoxicillin/Clavulanate, amoxicillin, cephalaxin and nitrofurantoin.

### References


### Table 1. Clinical laboratory evaluation of mid-stream urine

<table>
<thead>
<tr>
<th>Type of test</th>
<th>Laboratory Result</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine leukocyte test strip</td>
<td>Positive</td>
<td>Pyuria</td>
</tr>
<tr>
<td></td>
<td>Male: 1-2 WBCs at (x400) plus CFU of 10^6 per ml. Women: 2-5 WBCs at (x400).</td>
<td>Abnormal pyuria, Acute pyelitis</td>
</tr>
<tr>
<td>Urine nitrite test strip reaction</td>
<td>Positive</td>
<td>Strongly suggestive of UTI.</td>
</tr>
<tr>
<td>Blood urine test strip reaction</td>
<td>Positive plus greater than 5 RBCs at (x400).</td>
<td>Gross Hematuria suggestive of UTI.</td>
</tr>
<tr>
<td>Urine Culture</td>
<td>Significant growth (more than or equal to 10^6 CFU in two consecutive urine samples). No significant growth.</td>
<td>Asymptomatic UTI.</td>
</tr>
<tr>
<td></td>
<td>- with symptoms of urethritis.</td>
<td>Chlamydia trachomatis or N. gonorrhoea.</td>
</tr>
<tr>
<td></td>
<td>- with symptoms of cystitis.</td>
<td>Intercostal cystitis.</td>
</tr>
</tbody>
</table>

### Table 2. UTI recommended empirical treatment

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Course of Therapy</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetloxacin</td>
<td>3 days</td>
<td>250</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>3 days</td>
<td>250-500</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>3 days</td>
<td>200-400</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>7 days</td>
<td>500</td>
</tr>
<tr>
<td>Amoxicilin</td>
<td>7 days</td>
<td>250</td>
</tr>
</tbody>
</table>
Questions for STEP Participants

1. U.T.I may involve just the lower urinary tract.
   A. True
   B. False

2. The two major clinical features mostly encountered in acute U.T.I are:
   A. Urethritis and Cystitis
   B. Cystitis and Pyelonephritis
   C. Prostatitis and Dysuria
   D. Cystitis and Prostatitis

3. U.T.I. is indicated when a microorganism growth of what number is isolated?
   A. < 10^5 per milliliter
   B. > 10^5 per milliliter
   C. ≤ 10^2 per milliliter
   D. ≥ 10^5 per milliliter

4. The most probable pathway for most renal parenchymal infection is
   A. Bladder via Ureter
   B. Bladder via Urethra
   C. Urethra via Urethra
   D. Bladder via Loop of Henley

5. Asymptomatic U.T.I. is indicated when there is
   A. Colony count of less than 10^5 /ML of single bacteria specie.
   B. Colony count of more than 10^5 /ML of single bacteria specie
   C. Colony count of less than 10^4/ML of mixed bacteria specie
   D. Colony count of more than 10^5/ML of mixed bacteria specie

6. Sex is a major risk factor for U.T.I.
   A. True
   B. False

7. The most common fecal microbial flora associated with U. T. I is
   A. Staphylococcus aureus
   B. Klebsiella pneumonia
   C. Entamoeba coli
   D. Escherichia coli

   A. True
   B. False

9. Which of the following special settings is not associated with U.T.I.?
   A. Virulence factor
   B. Pregnancy
   C. Abnormal urinary tract
   D. Race

10. In laboratory diagnostic testing, which of the following suggests the diagnosis of U.T.I.?
    A. 2-5 leukocytes per HPF
    B. A positive nitrite
    C. Less than 5 RBCs in an uncentrifuged urine
    D. Both A and B

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