

CONTEMPORARY REVIEW ARTICLE

Recurrent Urinary Tract Infection (UTI) in Women

¹Randhir Puri, ²Jaideep Malhotra

¹Classified Specialist, Obstetrics and Gynecology, Military Hospital, Camp, Belgaum - 590009, Karnataka, India

²Vice President, FOGSI 2010, Malhotra Nursing and Maternity Home (P) Ltd. 84, MG Road, Agara 282010, Uttar Pradesh, India
e-mail: mmhagraivf@gmail.com

Correspondence: Randhir Puri, Classified Specialist, Obstetrics and Gynecology
Military Hospital, Camp, Belgaum - 590009, Karnataka, India, Ph: 9740339978, e-mail:randhir0256@gmail.com

Abstract: Recurrent lower urinary tract infections (UTIs) are usually defined as two or more episodes of such infection occurring in the preceding 12 months. In most cases, such infections are the result of sexual habits and hygiene (e.g., women who are sexually active, especially those using diaphragms and/or spermicides).

A clean-catch or catheterized specimen for culture typically reveals greater than 100,000 organisms per milliliter of urine. The typical infecting organism is *Escherichia coli*. The route of infection is ascending from the perianal area and vagina via the urethra and into the bladder.

However, in uncomplicated lower UTIs, there is complete clearing of bacteriuria and hematuria with appropriate antimicrobial therapy. In some cases, single-dose antimicrobial therapy after intercourse or at the onset of irritative voiding symptoms is adequate to control frequent recurrences of cystitis.

Uncomplicated recurrent lower UTIs in women must be differentiated from "reinfection," which may indicate causes such as a vesicovaginal or vesicoenteric fistula or a paravesical abscess with fistula to the bladder. Furthermore, "bacterial persistence" is defined as an infection with the same organism, typically from a site within the urinary tract, after the bacteriuria has resolved for at least several days and antimicrobial therapy has ceased. Causes of bacterial persistence include calculi, foreign bodies, urethral or bladder diverticula, infected urachal cyst, and postoperative changes such as a remaining ureteral stump that retains urine and results in stasis. In such patients with frequent recurrences and reinfections with the same bacteria, imaging is indicated to detect a treatable condition and monitor its progress. Compromised immunity needs attention to avoid longstanding morbidity. Vaccine developed will lead more prevention in future.

Keywords: UTI, recurrence, women

INTRODUCTION

The term Urinary Tract Infection (UTI) encompasses a variety of clinical entities, ranging from asymptomatic bacteriuria to cystitis, and pyelonephritis. The main symptoms seen in an attack of UTI are suprapubic pain, increased frequency and urgency of urination, dysuria, and nocturia, hematuria, cloudy urine, and foul or strong urine odor. The other constitutional

symptoms are fever, chills, malaise, nausea, vomiting, weight loss, flank or back pain. In general demographic spectrum, between 1 and about 50 years of age, UTI is predominantly a disease of females. The women numbered 50 to 80% of in the general population acquire at least one UTI during their lifetime.

Recurrent UTI, (RUTI) in healthy nonpregnant women is defined as three or more episodes of UTI during a twelve month period. About 20 to 30% of women who have had one episode of UTI will have recurrent episodes.

INCIDENCE

Recurrent UTI is responsible for eight to ten million hospital visits, resulting in one million hospital admissions in US annually. The women have propensity to acquire recurrent UTI due to various inherent, genetic factors making it a common infection, 30 times more than males. At least 40% of women have UTI at some point in their lives. The school girls aged 5 to 14 years are affected up to 3-5%. Adolescents and young adults make numbers to 4% and additional 1-2% increase per decade of age.

DEFINITIONS

The urinary tract infection is designated along with few of prevalent definitions, which needs to be understood well. They are as given below:

- Bacteriuria* denotes presence of bacteria in urine in a patient, who may be asymptomatic. Bacteriuria without pyuria indicates bacterial colonization rather infection.
- Pyuria* is defined as presence of WBC in urine. Pyuria without bacteria needs evaluation for tuberculosis, stone or malignancy.
- Significant bacteriuria* the diagnosis of UTI was based on quantitative urine culture yielding >100000 CFUs of bacteria per ml of urine.

The value was chosen because of its high specificity even in asymptomatic patients. Recent studies have established that >100 CFU is significant in symptomatic women.

PATHOGENESIS

The main reason attributed to increased frequency of recurrent UTI in women and that too in almost all age groups are many. The female anatomy by itself is a starting point in consideration. The urethra in males is four times longer than the female, thus taking a long-time for organisms to reach a favorable environment, i.e. the urinary bladder. Besides this the close proximity of the rectum to the urethral opening increases the chances of infection especially *E. coli*. Besides this, the increase in UTI in reproductive age group is also attributed to frequent sex.

Recently, there is increasing evidence that genetically determined factors may influence susceptibility to recurrent UTI. Women with recurrent UTI demonstrate a propensity for persistent vaginal colonization with *E. coli*, even during asymptomatic periods. Vaginal and periurethral mucosal cells from women with recurrent UTI bind threefold more uropathogenic bacteria than do mucosal cells from women without recurrent infection.

These observations suggest that epithelial cells from susceptible women may possess specific types or greater numbers of receptors to which *E. coli* can bind, thereby facilitating colonization. This increased susceptibility is determined in part by Lewis blood group type and whether the woman secretes blood group antigens into body fluids. Vaginal epithelial cells from nonsecretors of blood group antigens bind significantly greater numbers of bacteria, and nonsecretors are particularly at risk for recurrent UTI.

Other main medical and surgical conditions commonly associated with UTI are those with any abnormality which impedes flow of urine like renal stone, diabetes or chronic illness impairing the immune system, any condition due to which she was on prolonged cortisone therapy or on chemotherapy and last but not the least a situation where she is inundated with prolonged use of catheters.

BACTERIOLOGY

UTIs may be further characterized as community acquired or nosocomial (generally, catheter associated). Community-acquired infection is caused by *E. coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus*, *Saprophyticus* or

Enterococcus faecalis, while the hospital acquired ones are *E. coli*, *Pseudomonas aeruginosa*, *Proteus sp.*, *Enterobacter sp.*, *Serratia sp.* or *Enterococcus*.

Organism Causing

UTI

- Community-acquired
 - *Escherichia coli*
 - *Klebsiella pneumoniae*
 - *Proteus mirabilis*
 - *Staphylococcus saprophyticus*
 - *Enterococcus faecalis*
- Hospital-acquired
 - *Escherichia coli*
 - *Pseudomonas aeruginosa*
 - *Proteus sp.*
 - *Enterobacter sp.*
 - *Serratia sp.*
 - *Enterococcus*

REINFECTION, RELAPSE

There are two aspects on a recurrent UTI; it can be a reinfection or it can be a relapsing UTI. Relapse, is caused by the reappearance of an organism from a sequestered focus, usually within the kidney, shortly after completion of therapy. Reinfection, on the other hand, the course of therapy has successfully eradicated the infection and there is no sequestered focus, but organisms are reintroduced from the fecal reservoir. The majority of recurrences are thought to be reinfection. The management of the respective type of recurrence is different.

Factors Which Make Women More Susceptible to Recurrent UTI

At Child Birth and at Young Ages

- Vesicoureteral reflux (vur).
- *Primary*: Congenital incompetence of vu valve (shortened submucosal tunnel).
- *Secondary*: Multiple anatomical abnormalities.

At Sexually Active Age

- Irritation of the urethra, allowing germs to move easily travel through urethra into bladder.
- Diaphragms/spermicidal agents.

At Old Age

- Incontinent.
- Functionally impaired.
- Postmenopausal changes.
- Neurological alterations.

DIAGNOSIS AND INVESTIGATION MODALITIES

For initial diagnosis of the UTI, we take a urine sample which is *clean catch* urine sample after initially washing genital area, collecting midstream sample and doing a urinalysis, urine culture and sensitivity test over it.

Specimen collection holds an important place for certain diagnosis of infection.

- *Clean catch mid stream specimens*
 - Most frequently used method.
 - Urethra cleaned prior to collection.
 - First void urine allowed to pass to clear urethra.
 - Midstream collected in sterile container.
- *Collection bags (children)*
 - Used in young children lacking bladder control.
 - Often contaminated.
 - Most meaningful result is a negative culture.

In the scenario of a true relapsing UTI, the detailed urologic and radiologic investigations is suggested which has to be tailored individually to suit the respective patient. Besides this is the class of patients whom we consider for a longer term of treatment.

Ultrasonography, the most popular noninvasive widely used investigation has gradually replaced intravenous urography as screening investigation. But it is unreliable in detecting vesicoureteral reflux, renal scarring or inflammatory changes. *Renal scintigraphy* and *voiding cystourethrography* are recommended, for such changes to be seen. Renal cortical scintigraphy with either technetium-99m-labeled glucoheptonate or dimercaptosuccinic acid (DMSA) are both highly sensitive and specific standard technique for the detection of renal inflammation and scarring.

Dynamic CT scans also can serve as a convenient screen for abdominal aortic aneurysm masquerading as UTI or renal colic. CT scan though sensitive and specific for the detection of acute pyelonephritis, is costlier and there is no study which shows that it has added advantages over scintigraphy. Besides this, the main concern is the high level of radiation she has to get exposed to. Thus, its use is not supported by evidence.

Voiding cystourethrography is a test which is helpful in early identification of vesicoureteral reflux, a risk factor for reflux

nephropathy and renal scars. This test should be delayed until after urinary infection is controlled, because vesicoureteral reflux may be the transient effect of infection but this test is not free of controversy. Its usefulness has been questioned for its low sensitivity and specificity, moreover involves gonadal irradiation and catheterization.

Isotope cystogram is having the advantage over other radiation-based investigations that radiation dosage is only 1% of that used for voiding cystourethrography. Besides this, a continuous monitoring is also more sensitive for identifying reflux than the intermittent fluoroscopic monitoring of voiding cystourethrography.

The intravenous urography has advantages in that a precise anatomic image of the kidneys can be seen. Besides that it can readily identify some urinary tract abnormalities (e.g., cysts, hydronephrosis), the main disadvantage is, the decreased sensitivity in comparison to renal scintigraphy in detection of both pyelonephritis and renal scarring. Besides this, the higher dosage of radiation and risk of reaction to contrast medium, is also of concern.

PREVENTIVE STRATEGIES

Recurrence of uncomplicated cystitis is common, and some form of preventive strategy is indicated, if three or more symptomatic episodes occur in one year. For behavioral changes as in avoiding diaphragms and spermicidal products; proper toileting habits (to wipe up downwards), to urinate after an intercourse. A doubtful but increasing tendency of resolving the infection on having cranberry juice, is also seen.

Tips on Preventing Urinary Tract Infections to Patients

- Drink plenty of water to flush out bacteria. Drinking cranberry juice may also help prevent urinary tract infections. However, if you are taking warfarin (brand name: Coumadin), check with your doctor before using cranberry juice to prevent urinary tract infections. Your doctor may need to adjust your warfarin dose or you may need to have more frequent blood tests.
- Do not hold your urine. Urinate when you feel like, you need to.
- Wipe from front to back after bowel movements.
- Urinate after having sex to help wash away bacteria.
- Use enough lubrication during sex. Try using a small amount of lubricant (such as K-Y-Jelly) before sex, if you are a little dry.

Table 1: Antimicrobial regimens for prevention and treatment of recurrent urinary tract infections

<i>Antimicrobial agent</i>	<i>Dosage for treatment</i>	<i>Daily dosage for prevention</i>
Cefalexin	500 mg three times daily for three days	125 mg
Ciprofloxacin	100 mg twice daily for three days	125 mg
Co-amoxiclav	375 mg thrice daily for three days	No data available
Co-trimoxazole	960 mg twice daily for three days	240 mg (or three times a week)
Nitrofurantoin	50 mg four times daily for seven days	50-100 mg
Nitrofurantoin macro crystals and monohydrate	100 mg twice daily for seven days	100 mg
Norfloxacin	200 mg twice daily for three days	200 mg
Trimethoprim	200 mg twice daily for three days	100 mg (or three times a week)

TREATMENT

Principles of Antimicrobial Therapy

- Initial elimination of bacteria.
- Serum vs urinary levels of antibiotics.
- Bacterial resistance.
- Adequate hydration.
- Antimicrobial agent with urinary concentration > MIC, by the widest margin.
- Avoid under dosing.
- Good patient compliance.

In case it seems that recurrence has occurred, despite above preventive strategies, low dose antibiotics are being advised, like single dose of TMP-SMX (one-half of a single-strength tablet, which amounts to 40 mg of trimethoprim and 200 mg of sulfamethoxazole; a fluoroquinolone (one tablet) or nitrofurantoin (50 mg; or 100 mg of nitrofurantoin macro crystals). Typically, a prophylactic regimen is initially prescribed for 6 months and then discontinued.

Another method of treatment currently advocated is “self treatment” for women with less frequent recurrences (fewer than four a year) she is supplied with TMP-SMX or a fluoroquinolone and allows her to self-medicate with short-course therapy (3-5 days) at the first symptoms of infection. She is to contact the physician if more than four episodes occur over a 12 months period or if symptoms persist while being on such therapy.

For a relapsing UTI (where the strain causing the infection is the same causative agent for UTI that has occurred within 2 weeks) the stand taken is somewhat different from that of a recurring UTI. Two factors are to be kept in mind in such a circumstance; firstly that the infection may be due to deep-tissue infection of the kidney that is suppressed but not eradicated by a 14-day course of antibiotics and secondly that there may be structural abnormality of the urinary tract, particularly calculi.

The number of antibiotics available is vast, but urinary tract specific or culture sensitive drugs are more useful, besides the common practice of using broad spectrum antibiotics leads to emergence of bacterial resistance. The common antibiotics are recommended in Table 1.

FUTURE DIRECTIONS

National Institutes of Health, USA, has developed a vaccine for immunocompromised patients with UTI. This research is based on the fact that children and females who lack immunoglobulin are more prone to develop recurrent UTI. Early tests indicates that vaccines helps to develop own natural immunoglobulin. The vaccine may be used as a suppository to place in the vagina or a pill.

The weekly vaginal use of newer probiotics of specific lactobacilli strains (GR-1 and RC-14) was comparable to daily trimethoprim (100 mg), methenamine hippurate (1000 mg) every 12 hr, povidone-iodine perineal cleansing every 12 hr daily cefaclor (250 mg) or daily nitrofurantoin (50 mg). Hence, usage of probiotics usage is becoming common (Reid et al 1995, Brumfitt et al).

CONCLUSION

To summarize, UTI is one infection which is more frequent in women and she has even more chance of having recurrence. But an immediate aggressive treatment is not the norm of management considering the fact that patient may have relapsing infection or getting reinfected frequently. Initially, preventive measures and low dose antibiotics are resorted to, which if fails, we proceed to detailed urologic and radiologic investigations and label them as recurrent and or relapsing UTI for which a long standing infection in kidneys or a structural defect in urinary tract are to be proven and be given long-term treatment. Compromised immunity needs attention to avoid long-standing morbidity.