

BACTERIAL URINARY TRACT INFECTIONS (UTIS) AND ANTIBIOTIC SUSCEPTIBILITY STUDY IN ALLIED AND DHQ HOSPITAL IN FAISALABAD, PUNJAB

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Abstract

Urinary tract infections (UTIs) remain the common infections diagnosed in outpatients as well as hospitalized patients. Current knowledge on antimicrobial susceptibility pattern is essential for appropriate therapy. Bacterial UTIs can involve the urethra, prostate, bladder, or kidneys. Symptoms may be absent or include urinary frequency, urgency, dysuria, lower abdominal pain, and flank pain. Systemic symptoms and even sepsis may occur with kidney infection. Diagnosis is based on analysis and culture of urine. Treatment is with antibiotics and removal of any urinary tract catheters and obstruction. Among adults aged 20 to 50 yr, UTIs are about 50-fold more common in women. In women in this age group, most UTIs are cystitis or pyelonephritis. In men of the same age, most UTIs are urethritis or prostatitis. The incidence of UTI increases in patients > 50 yr, but the female:male ratio decreases because of the increasing frequency of prostate enlargement and instrumentation in men.

Keywords: Urinary tract infection, antimicrobial resistance, Bacterial UTIs, Cystitis, Urethritis

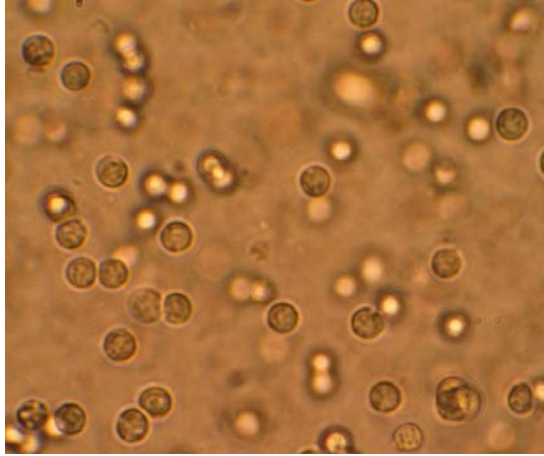
1. INTRODUCTION

A urinary tract infection (UTI) is an infection that affects part of the urinary tract. When it affects the lower urinary tract it is known as a bladder infection (cystitis) and when it affects the upper urinary tract it is known as kidney infection (pyelonephritis).

Symptoms from a lower urinary tract include pain with urination, frequent urination, and feeling the need to urinate despite having an empty bladder.[1] The urinary tract, from the kidneys to the urethral meatus, is normally sterile and resistant to bacterial colonization despite frequent contamination of the distal urethra with colonic bacteria. The major defense against UTI is complete emptying of the bladder during urination. Other mechanisms that maintain the tract's sterility include urine acidity, the vesicoureteral valve, and various immunologic and mucosal barriers. About 95% of UTIs occur when bacteria ascend the urethra to the bladder and, in the case of pyelonephritis, ascend the ureter to the kidney. The remainder of UTIs are hematogenous. Systemic infection can result from UTI, particularly in the elderly. About 6.5% of cases of hospital-acquired bacteremia are attributable to UTI. Symptoms of a kidney infection include fever and flank pain usually in addition to the symptoms of a lower UTI. Rarely the urine may appear bloody. In

the very old and the very young, symptoms may be vague or non-specific. The most common cause of infection is *Escherichia coli*, though other bacteria or fungi may rarely be the cause. Risk factors include female anatomy, sexual intercourse, diabetes, obesity, and family history. Although sexual intercourse is a risk factor, UTIs are not classified as sexually transmitted infections (STIs). Kidney infection, if it occurs, usually follows a bladder infection but may

also result from a blood-borne infection. Diagnosis in young healthy women can be based on symptoms alone. In those with vague symptoms, diagnosis can be difficult because bacteria may be present without there being an infection. In complicated cases or if treatment fails, a urine culture may be useful. In uncomplicated cases, UTIs are treated with a short course of antibiotics such as nitrofurantoin or trimethoprim/sulfamethoxazole. Resistance to many of the antibiotics used to treat this condition is increasing. In complicated cases, a longer course or intravenous antibiotics may be needed. If symptoms do not improve in two or three days, further diagnostic testing may be needed. Phenazopyridine may help with symptoms. In those who have bacteria or white blood cells in their urine but have no symptoms, antibiotics are generally not



needed, although during pregnancy is an exception. In those with frequent infections, a short course of antibiotics may be taken as soon as symptoms begin or long-term antibiotics may be used as a preventative measure. About 150 million people develop a urinary tract infection in a given year.[2] They are more common in women than men. In women, they are the most common form of bacterial infection. Up to 10% of women have a urinary tract infection in a given year, and half of women have at least one infection at some point in their lifetime. They occur most frequently between the ages of 16 and 35 years. Recurrences are common. Urinary tract infections have been described since ancient times with the first documented description in the Ebers Papyrus dated to c. 1550 BC.[3]

Fig 1: Multiple white cells seen in the urine of a person with a urinary tract infection using a microscopy

1.1. SIGNS AND SYMPTOMS

Urine may contain pus (a condition known as pyuria) as seen from a person with sepsis due to a urinary tract infection. Lower urinary tract infection is also referred to as a bladder infection. The most common symptoms are burning with urination and having to urinate frequently (or an urge to urinate) in the absence of vaginal discharge and significant pain.[4] These symptoms may vary from mild to severe and in healthy women last an average of six days. Some pain above the pubic bone or in the lower back may be present. People experiencing an upper urinary tract infection, or pyelonephritis, may experience flank pain, fever, or nausea and vomiting in addition to the classic symptoms of a lower urinary tract

infection. Rarely, the urine may appear bloody or contain visible pus in the urine.



Fig 2: Urine may contain pus (a condition known as pyuria) as seen from a person with sepsis due to a urinary tract infection.

1.3. CHILDREN

In young children, the only symptom of a urinary tract infection (UTI) may be a fever. Because of the lack of more obvious symptoms, when females under the age of two or uncircumcised males less than a year exhibit a fever, a culture of the urine is recommended by many medical associations. Infants may feed poorly, vomit, sleep more, or show signs of jaundice. In older children, new onset urinary incontinence (loss of bladder control) may occur.[5]

4. ELDERLY

Urinary tract symptoms are frequently lacking in the elderly. The presentations may be vague with incontinence, a change in mental status, or fatigue as the only symptoms, while some present to a health care provider with sepsis, an infection of the blood, as the first symptoms.[6] Diagnosis can be complicated by the fact that many elderly people have preexisting incontinence or dementia.

It is reasonable to obtain a urine culture in those with signs of systemic infection that may be unable to report urinary symptoms, such as when advanced dementia is present. Systemic signs of infection include a fever or increase in temperature of more than 1.1 °C (2.0 °F) from usual, chills, and an increased white blood cell count.

5. CAUSE

Uropathogenic *E. coli* from the gut is the cause of 80–85% of community-acquired urinary tract infections, with *Staphylococcus saprophyticus* being the cause in 5–10%. [4] Rarely they may be due to viral or fungal infections. [23] Healthcare-associated urinary tract infections (mostly related to urinary catheterization) involve a much broader range of pathogens including: *E. coli* (27%), *Klebsiella* (11%), *Pseudomonas* (11%), the fungal pathogen *Candida albicans* (9%), and *Enterococcus* (7%) among others. [6] Urinary tract infections due to *Staphylococcus aureus* typically occur secondary to blood-borne infections. *Chlamydia trachomatis* and *Mycoplasma genitalium* can infect the urethra but not the bladder. [7] These infections are usually classified as a urethritis rather than urinary tract infection.

6. SEX

In young sexually active women, sexual activity is the cause of 75–90% of bladder infections, with the risk of infection related to the frequency of sex. The term "honeymoon cystitis" has been applied to this phenomenon of frequent UTIs during early marriage. In post-menopausal women, sexual activity does not affect the risk of developing a UTI. Spermicide use, independent of sexual frequency, increases the risk of UTIs. Diaphragm use is also associated. [8] Condom use without spermicide or use of birth control pills does not increase the risk of uncomplicated urinary tract infection. Women are more prone to UTIs than men because, in females, the urethra is much shorter and closer to the anus. [As a woman's estrogen levels decrease with menopause, her risk of urinary tract infections increases due to the loss of protective vaginal flora. Additionally, vaginal atrophy that can sometimes occur after menopause is associated with recurrent urinary tract infections. Chronic prostatitis in the forms of chronic prostatitis/chronic pelvic pain syndrome and chronic bacterial prostatitis (not acute bacterial prostatitis or asymptomatic inflammatory prostatitis) may cause recurrent urinary tract infections in males. Risk of infections increases as males age. While bacteria is commonly present in the urine of older males this does not appear to affect the risk of urinary tract infections. [9]

7. URINARY CATHETERS

Urinary catheterization increases the risk for urinary tract infections. The risk of bacteriuria (bacteria in the urine) is between three and six percent per day and prophylactic antibiotics are not effective in decreasing symptomatic infections. The risk of an associated infection can be decreased by catheterizing only when necessary, using aseptic technique for insertion, and maintaining unobstructed closed drainage of the catheter. Male scuba divers using condom catheters and female divers using external catching devices for their dry suits are also susceptible to urinary tract infections.

8. OTHERS

A predisposition for bladder infections may run in families. This is believed to be related to genetics. [4] Other risk factors include diabetes, being uncircumcised, and having a large prostate. In children UTIs are associated with vesicoureteral reflux (an abnormal movement of urine from the bladder into ureters or kidneys) and constipation. Persons with spinal cord injury are at increased risk for urinary tract infection in part because of chronic use of catheter, and in part because of voiding dysfunction. It is the most common cause of infection in this population, as well as the most common cause of hospitalization. [10] Additionally, use of cranberry juice or cranberry supplement appears to be ineffective in prevention and treatment in this population.

9. PATHOGENESIS

9.1 BLADDER INFECTION

The bacteria that cause urinary tract infections typically enter the bladder via the urethra. However, infection may also occur via the blood or lymph. It is believed that the bacteria are usually transmitted to the urethra from the bowel, with females at greater risk due to their anatomy. After gaining entry to the bladder, *E. coli* are able to attach to the bladder wall and form a biofilm that resists the body's immune response. [6] *Escherichia coli* is the single most common microorganism, followed by *Klebsiella* and *Proteus spp.*, to cause urinary tract infection. *Klebsiella* and *Proteus spp.*, are frequently associated with stone disease. The presence of Gram positive bacteria such as *Enterococcus* and *Staphylococcus*

increased. The increased resistance of urinary pathogens to quinolones has been reported worldwide and might be the consequence of overuse and misuse of quinolones.[11]

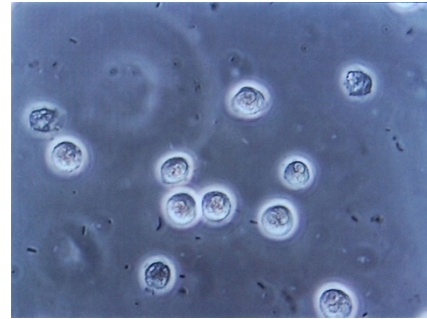


Fig 4: Multiple bacilli (rod-shaped bacteria, here shown as black and bean-shaped) shown between white blood cells in urinary microscopy. These changes are indicative of a urinary tract infection.

Fig 3: Bladder infection

9.2 DIAGNOSIS

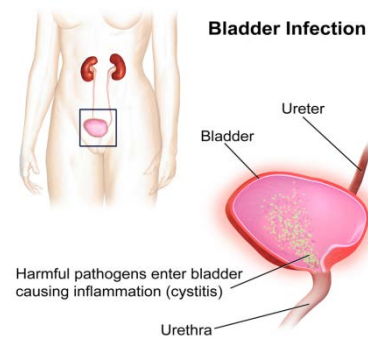
Multiple bacilli (rod-shaped bacteria, here shown as black and bean-shaped) shown between white blood cells in urinary microscopy. These changes are indicative of a urinary tract infection. In straightforward cases, a diagnosis may be made and treatment given based on symptoms alone without further laboratory confirmation.[4] In complicated or questionable cases, it may be useful to confirm the diagnosis via urinalysis, looking for the presence of urinary nitrites, white blood cells (leukocytes), or leukocyte esterase.[12] Another test, urine microscopy, looks for the presence of red blood cells, white blood cells, or bacteria. Urine culture is deemed positive if it shows a bacterial colony count of greater than or equal to 10^3 colony-forming units per mL of a typical urinary tract organism. Antibiotic sensitivity can also be tested with these cultures, making them useful in the selection of antibiotic treatment. However, women with negative cultures may still improve with antibiotic treatment.[4] As symptoms can be vague and without reliable tests for urinary tract infections, diagnosis can be difficult in the elderly.[10]

10. CLASSIFICATION

A urinary tract infection may involve only the lower urinary tract, in which case it is known as a bladder infection. Alternatively, it may involve the upper urinary tract, in which case it is known as pyelonephritis. If the urine contains significant bacteria but there are no symptoms, the condition is known as asymptomatic bacteriuria. If a urinary tract infection involves the upper tract, and the person has diabetes mellitus, is pregnant, is male, or immunocompromised, it is considered complicated. Otherwise if a woman is healthy and premenopausal it is considered uncomplicated. In children when a urinary tract infection is associated with a fever, it is deemed to be an upper urinary tract infection.

11. CHILDREN

To make the diagnosis of a urinary tract infection in children, a positive urinary culture is required. Contamination poses a frequent challenge depending on the



method of collection used, thus a cutoff of 105 CFU/mL is used for a "clean-catch" mid stream

sample, 104 CFU/mL is used for catheter-obtained specimens, and 102 CFU/mL is used for suprapubic aspirations (a sample drawn directly from the bladder with a needle). The use of "urine bags" to collect samples is discouraged by the World Health Organization due to the high rate of contamination when cultured, and catheterization is preferred in those not toilet trained. Some, such as the American Academy of Pediatrics recommends renal ultrasound and voiding cystourethrogram (watching a person's urethra and urinary bladder with real time x-rays while they urinate) in all children less than two years old who have had a urinary tract infection. However, because there is a lack of effective treatment if problems are found, others such as the National Institute for Health and Care Excellence only recommends routine imaging in those less than six months old or who have unusual findings.[13]

12. DIFFERENTIAL DIAGNOSIS

In women with cervicitis (inflammation of the cervix) or vaginitis (inflammation of the vagina) and in young men with UTI symptoms, a Chlamydia trachomatis or Neisseria gonorrhoea infection may be the cause.[9] These infections are typically classified as a urethritis rather than a urinary tract infection. Vaginitis may also be due to a yeast infection. Interstitial cystitis (chronic pain in the bladder) may be considered for people who experience multiple episodes of UTI symptoms but urine cultures remain negative and not improved with antibiotics. Prostatitis (inflammation of the prostate) may also be considered in the differential diagnosis.

Hemorrhagic cystitis, characterized by blood in the urine, can occur secondary to a number of causes including: infections, radiation therapy, underlying cancer, medications and toxins. Medications that commonly cause this problem include the chemotherapeutic agent cyclophosphamide with rates of 2 to 40%. Eosinophilic cystitis is a rare condition where eosinophiles are present in the bladder wall.[14] Signs and symptoms are similar to a bladder infection. Its cause is not entirely clear; however, it may be linked to food allergies, infections, and medications among others.

13. PREVENTION

A number of measures have not been confirmed to affect UTI frequency including: urinating immediately after intercourse, the type of underwear used, personal hygiene methods used after urinating or defecating, or whether a person typically bathes or showers. There is similarly a lack of evidence surrounding the effect of holding one's urine, tampon use, and douching. In those with frequent urinary tract infections who use spermicide or a diaphragm as a method of contraception, they are advised to use alternative methods. In those with benign prostatic hyperplasia urinating in a sitting position appears to improve bladder emptying which might decrease urinary tract infections in this group.[15] Using urinary catheters as little and as short of time as possible and appropriate care of the catheter when used prevents catheter-associated urinary tract infections. They should be inserted using sterile technique in hospital however non-sterile technique may be appropriate in those who self catheterize. The urinary catheter set up should also be kept sealed. Evidence does not support a significant decrease in risk when silver-alloy catheters are used.[16]

14. MEDICATIONS

For those with recurrent infections, taking a short course of antibiotics when each infection occurs is associated with the lowest antibiotic use. A prolonged course of daily antibiotics is also effective. Medications frequently used include nitrofurantoin and trimethoprim/sulfamethoxazole (TMP/SMX). Methenamine is another agent used for this purpose as in the bladder where the acidity is low it produces formaldehyde to which resistance does not develop. Some recommend against prolonged use due to concerns of antibiotic resistance. In cases where infections are related to intercourse, taking antibiotics afterwards may be useful. In post-menopausal women, topical vaginal estrogen has been found to reduce recurrence. As opposed to topical creams, the use of vaginal estrogen from pessaries has not been as useful as low dose antibiotics.[17] Antibiotics following short term urinary catheterization decreases the subsequent risk of a bladder infection. A number of vaccines are in development as of 2018.

15. CHILDREN

The evidence that preventive antibiotics decrease urinary tract infections in children is poor. However recurrent UTIs are a rare cause of further kidney problems if there are no underlying abnormalities of the kidneys, resulting in less than a third of a percent (0.33%) of chronic kidney disease in adults. Whether routine circumcision prevents UTIs has not been well studied as of 2011.[18]

16. ALTERNATIVE MEDICINE

Some research suggests that cranberry (juice or capsules) may decrease the number of UTIs in those with frequent infections. A Cochrane review concluded that the benefit, if it exists, is small. Long-term tolerance is also an issue with gastrointestinal upset occurring in more than 30%. Cranberry juice is thus not currently recommended for this indication.[19] As of 2015, probiotics require further study to determine if they are beneficial. The role of the urinary microbiome in maintaining urinary tract health is not well understood as of 2015.[20]

17. TREATMENT

The mainstay of treatment is antibiotics. Phenazopyridine is occasionally prescribed during the first few days in addition to antibiotics to help with the burning and urgency sometimes felt during a bladder infection. However, it is not routinely recommended due to safety concerns with its use, specifically an elevated risk of methemoglobinemia (higher than normal level of methemoglobin in the blood).[21] Acetaminophen (paracetamol) may be used for fevers. There is no good evidence for the use of cranberry products for treating current infections.

18. ASYMPTOMATIC BACTERIURIA

Those who have bacteria in the urine but no symptoms should not generally be treated with antibiotics. This includes those who are old, those with spinal cord injuries, and those who have urinary catheters. Pregnancy is an exception and it is recommended that women take 7 days of antibiotics. If not treated it causes up to 30% of mothers to develop pyelonephritis and increases risk of low birth weight and preterm birth.[22] Some also support

treatment of those with diabetes mellitus and treatment before urinary tract procedures which will likely cause bleeding.

18.1 UNCOMPLICATED

Uncomplicated infections can be diagnosed and treated based on symptoms alone.[4] Antibiotics taken by mouth such as trimethoprim/sulfamethoxazole (TMP/SMX), nitrofurantoin, or fosfomycin are typically first line. Cephalosporins, amoxicillin/clavulanic acid, or a fluoroquinolone may also be used. However, resistance to fluoroquinolones among the bacterial that cause urinary infections has been increasing. The FDA recommends against the use of fluoroquinolones when other options are available due to higher risks of serious side effects. These medications substantially shorten the time to recovery with all being equally effective. A three-day treatment with trimethoprim, TMP/SMX, or a fluoroquinolone is usually sufficient, whereas nitrofurantoin requires 5–7 days. Fosfomycin may be used as a single dose but has been associated with lower rates of efficacy. With treatment, symptoms should improve within 36 hours.[17] About 50% of people will recover without treatment within a few days or weeks. Fluoroquinolones are not recommended as a first treatment. The Infectious Diseases Society of America states this due to the concern of generating resistance to this class of medication. Amoxicillin-clavulanate appears less effective than other options. Despite this precaution, some resistance has developed to all of these medications related to their widespread use.[4] Trimethoprim alone is deemed to be equivalent to TMP/SMX in some countries.[23] For simple UTIs, children often respond to a three-day course of antibiotics. Women with recurrent simple UTIs are over 90% accurate in identifying new infections.[4] They may benefit from self-treatment upon occurrence of symptoms with medical follow-up only if the initial treatment fails.[4]

18.2 COMPLICATED

Complicated UTIs are more difficult to treat and usually requires more aggressive evaluation, treatment and follow-up. It may require identifying and addressing the underlying complication.[24]

Increasing antibiotic resistance is causing concern about the future of treating those with complicated and recurrent UTI.

19. PYELONEPHRITIS

Pyelonephritis is treated more aggressively than a simple bladder infection using either a longer course of oral antibiotics or intravenous antibiotics. Seven days of the oral fluoroquinolone ciprofloxacin is typically used in areas where the resistance rate is less than 10%. If the local resistance rates are greater than 10%, a dose of intravenous ceftriaxone is often prescribed. Trimethoprim/sulfamethoxazole or amoxicillin/clavulanate orally for 14 days is another reasonable option.[25] In those who exhibit more severe symptoms, admission to a hospital for ongoing antibiotics may be needed. Complications such as urinary obstruction from a kidney stone may be considered if symptoms do not improve following two or three days of treatment.

20. EPIDEMIOLOGY

Urinary tract infections are the most frequent bacterial infection in women.[17] They occur most frequently between the ages of 16 and 35 years, with 10% of women getting an infection yearly and more than 40–60% having an infection at some point in their lives. Recurrences are common, with nearly half of people getting a second infection within a year. Urinary tract infections occur four times more frequently in females than males. Pyelonephritis occurs between 20–30 times less frequently.[4] They are the most common cause of hospital acquired infections accounting for approximately 40%.[26] Rates of asymptomatic bacteria in the urine increase with age from two to seven percent in women of child bearing age to as high as 50% in elderly women in care homes. Rates of asymptomatic bacteria in the urine among men over 75 are between 7–10%. Asymptomatic bacteria in the urine occurs in 2% to 10% of pregnancies. Urinary tract infections may affect 10% of people during childhood.[6] Among children, urinary tract infections are most common in uncircumcised males less than three months of age, followed by females less than one year.[20] Estimates of frequency among children, however, vary widely. In a group of children with a

fever, ranging in age between birth and two years, two to 20% were diagnosed with a UTI.[20]

21. HISTORY

Urinary tract infections have been described since ancient times with the first documented description in the Ebers Papyrus dated to c. 1550 BC.[18] It was described by the Egyptians as "sending forth heat from the bladder".[27] Effective treatment did not occur until the development and availability of antibiotics in the 1930s before which time herbs, bloodletting and rest were recommended.[18]

22. PREGNANCY

Urinary tract infections are more concerning in pregnancy due to the increased risk of kidney infections. During pregnancy, high progesterone levels elevate the risk of decreased muscle tone of the ureters and bladder, which leads to a greater likelihood of reflux, where urine flows back up the ureters and towards the kidneys. While pregnant women do not have an increased risk of asymptomatic bacteriuria, if bacteriuria is present they do have a 25–40% risk of a kidney infection. Thus if urine testing shows signs of an infection even in the absence of symptoms treatment is recommended. Cephalexin or nitrofurantoin are typically used because they are generally considered safe in pregnancy.[28] A kidney infection during pregnancy may result in premature birth or pre-eclampsia (a state of high blood pressure and kidney dysfunction during pregnancy that can lead to seizures). [29] Some women have UTIs that keep coming back in pregnancy and currently there is not enough research on how to best treat these infections.

23. CONCLUSION

This study finding showed that Bacterial UTIs can involve the urethra, prostate, bladder, or kidneys. Symptoms may be absent or include urinary frequency, urgency, dysuria, lower abdominal pain, and flank pain. Systemic symptoms and even sepsis may occur with kidney infection. Diagnosis is based on analysis and culture of urine. Treatment is with antibiotics and removal of any urinary tract catheters and obstruction. Among adults aged 20 to 50 yr, UTIs are about 50-fold more common in women. In

women in this age group, most UTIs are cystitis or pyelonephritis. In men of the same age, most UTIs are urethritis or prostatitis. The incidence of UTI increases in patients > 50 yr, but the female:male ratio decreases because of the increasing frequency of prostate enlargement and instrumentation in men.. As drug resistance among bacterial pathogens is an evolving process, routine surveillance and monitoring studies should be conducted to provide physicians knowledge on the updated and most effective empirical treatment of UTIs.

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