

# Urinary Tract Infections – A Review

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Urinary tract infections (UTI) are the second most common medical problem next to URI in adolescents & adults. It is also common at extremes of ages.

It is described as a disease caused by microbial invasion of genito urinary tract that extends from renal cortex to the urethra.<sup>(1)</sup>

Normally urine is sterile. Hence invasion of urine by microorganisms can occur in a variety of ways.<sup>(2)</sup> These include

1. Asymptomatic bacteriuria: - Multiplication of organisms in urine is difficult to distinguish from actual tissue involvement. This is because the host may not exhibit any response to invasion & the patient does not have any symptoms.
2. Urethritis: - Characterized by involvement of urethra.
3. Cystitis- Characterized by involvement of urinary bladder.
4. Pyelonephritis: - Characterized by involvement of pelvis & medulla of kidneys. This can be either acute or chronic pyelonephritis.

## Etiopathogenesis of UTI: -

For the complete understanding of UTI, the physician should be able to answer four questions in UTI. These are

- 1) Who enters the urinary tract: - i.e. what are the different microorganisms that invade the urinary tract.
- 2) How do they enter the urinary tract: - i.e. what are the various routes of entry.
- 3) When do they enter: - i.e. what are the various predisposing factors
- 4) Why do they enter urinary tract: - i.e. what are the various host factors responsible for entry of microorganisms in urinary tract.

## What are the various Microorganisms?

Genito urinary tract is invaded by a variety of microorganisms. The nature of organisms depends upon whether infection is acquired in the hospital or outside

the hospital.<sup>(3)</sup> The various organisms are  
**Gram-negative bacilli:** - these include E. Coli noticed in 70-80% cases in general population & in 50% cases with Hospital acquired infections. The specific strains are 02,04,06,07,08, & 075.

Others are  
Klebsiella species  
Proteus Mirabilis  
Enterobacter  
Pseudomonas aeruginosa  
Serratia

## Gram positive cocci: -

Includes Enterococci including E. fecalis  
Staphylococcus saprophyticus  
Staphylococcus Epidermis  
Staphylococcus aureus

## Miscellaneous: -

Mycobacterium tuberculosis  
Citrobacter  
Salmonella species  
Streptococcus pyogenes  
Streptococcus agalactiae  
Gardinerella vaginalis

## Fungi: -

Candida albicans

## Routes of Entry: -

There are two important routes of entry in genito urinary tract<sup>(2)</sup>

- a) Ascending route: - In this organisms migrate from anal & perianal region to per urethral region & from there enter urinary bladder thro urethra. This is the most common route in females due to short urethra & E. Coli is the most common organism. Other organisms are proteus, klebsiella, staphylococcus aureus, staph. Epidermis, Group B streptococci, pseudomonas species & candida species.
- b) Hematogenous route: - The organisms enter the blood stream thro the primary source of infection site like osteomyelitis, empyema, endocarditis etc & the resultant bacteriemia also involves urinary tract. The specific organisms isolated in such cases are salmonella species, Mycobacteria species, Schistosoma Hematobicum, Histoplasma, CMV virus and Adenovirus II

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**Predisposing factors: -**

The mere bacterial invasion does not precipitate UTI unless any one or multiple predisposing factors are present. These predisposing factors are

I. **Age & Sex:** - UTI is more common in females than males.

In females UTI is common at four distinct age groups.

i) **At Infancy:** The incidence of UTI in girls is 2.2% in first 24 months of life. In such cases urinalysis is

82% sensitive. The risk factors at this age are

- Family history of UTI in mother
- Family history Vesico ureteric reflux (VUR)
- Dysfunctional voiding patterns
- Constipation

Dysfunctional voiding is caused by unstable bladder. This has strong contractions at the volume of 50% -75% of capacity. These cause frequency & incontinence of urine. Girls sit on feet in an attempt to prevent voiding (called as vincent's curtsy). The girls tighten external sphincter during bladder contraction causing high bladder pressure & U.T.I.

ii) **At pre school or school going age:** - This is due to faulty habits, curiosity & putting stones or foreign bodies in urethral & periurethral areas.

iii) **Adolescent or pubertal age:** - due to exposure to sexual activities. In India incidence UTI in such group is maximum after marriage and is termed as Honeymoon cystitis. Voiding after intercourse reduces incidence of UTI in females.

iv) **Child bearing period:** - The gravid uterus presses on the ureters & leads to obstruction & infection.

In males, the incidence of UTI is common at two age groups<sup>(4)</sup>.

i) **In young adults** between the age group of 20-40 years. This is due to acute infection of prostate as gonococcal or nongonococcal prostatitis. Stricture urethra can develop secondary to the prostatitis.

ii) **In old age** benign prostatic hypertrophy or malignancy of prostate leads to obstructive uropathy & secondary infection.

2. **Socioeconomic status:** - Poor socioeconomic status associated with poor hygiene along with increased malnutrition predispose to UTI in all age groups.

3. **Instrumentation:** - urinary catheterizations, operations on urethra or urinary bladder predispose the urinary tract to bacterial colonization. Careful & complete sterilization is essential to overcome this.

Neurogenic bladder dysfunctions secondary to spinal cord injury or in Diabetes mellitus & other diseases lead to UTI. Infection is initiated by catheterization & then favored by prolonged stasis of urine in urinary bladder.

4. **Obstruction of urinary tract:** - The urinary tract obstruction due to any cause leads to stasis of urine & UTI. The obstruction can be due to

- 1) Multiple renal calculi
- 2) Pregnancy & tumors arising from pelvis
- 3) Prostatic enlargement
- 4) Urethral strictures
- 5) Retroperitoneal tumors
- 6) Malignancy obstructing genito urinary tract.

5. **Vesico ureteric reflux:** - This is one of the common causes of UTI in children & babies upto 2 years of age. Stage III or IV VUR commonly predisposes to UTI due to backflow of urine in pelviccalceal system.

6. **Congenital abnormalities of urinary & pelviccalceal system:** - This leads to obstruction to urinary flow & UTI. The various abnormalities are

1. Hypoplasia of kidneys
2. Hypospadias
3. Phymosis & paraphymosis
4. Pin hole meatus
5. Diverticulas of urinary bladder.
6. Abnormalities of renal parenchyma
7. Polycystic disease of kidneys
8. Previous scarring of kidneys
9. Duplex pelviccalyceal system
7. **Systemic disorders:** - The UTI is very common in systemic disorders with non leukopenic compromised hosts like DM, Hypertension, SLE, Analgesic abuse, Hypokalaemia, ATN etc. Asymptomatic bacteriuria is very common in these cases & hence routine examination of urine is essential in such cases.

**Host factors:**

The various host factors physiologically help to prevent UTI in most cases. The various host factors are

a. **Urethra:** - Incidence of UTI is more with short or deformed urethra. In females urethra is very short (~ 4 mm) Proximity of urethra to anus & its termination beneath Labia in females further increases the incidence.

b. **Bladder Mucosa & Bladder emptying:** - The lining of bladder has high bactericidal activity. Organisms are destroyed when they come in contact

with bladder mucosa. Hence frequent emptying leads to less accumulation of urine in bladder & lowered incidence of UTI<sup>(2)</sup>.

In females the frequency of bladder emptying is much less compared to males & hence more chances of UTI.

#### c. Urine:

Slightly acidic urine helps to destroy the bacteria in urine. Urine itself is a good culture media & hence if it is allowed to remain in bladder for longer time (as with infrequent emptying in females), the incidence of UTI rises. The presence of glucose in urine further perpetuates the growth.

#### d. Milieu interior of Kidney:

High ammonia load, hypertonicity of medulla & altered blood flow of medulla all adversely affect the incidence of UTI

#### e. Prostatic fluid:

The prostatic fluid has natural antibacterial activity & hence normally eliminates all infections. This antibacterial activity is compromised in inflammations of prostate & hence increased incidence in BHP or prostatitis.

#### f. Genetic factors:

Genetic factors influencing UTI are maternal history of UTI, nonsecretors of blood group & mutation in host genes integral to immune response all increase incidence of UTI.

#### Clinical picture:

The acute attack of UTI is characterized by high-grade fever with rigors. The fever is continuous 38.5° to 40°C. General constitutional symptoms like fatigue, body ache, and loss of appetite may also be present. These symptoms are more commonly seen with Acute Pyelonephritis than lower UTI.

The specific urinary symptoms include burning in micturition, frequency, passing cloudy urine & hematuria. Hematuria usually indicates cystitis & is associated with suprapubic tenderness. It is also associated with unilateral pain at costovertebral area (CVA) & is more suggestive of Pyelonephritis. Foul smell to urine usually indicates cystitis by staphylococci saprophyticus<sup>(5)</sup>.

#### Acute urethral syndrome:

This is characterized by symptoms of dysuria, urgency & frequency that are unaccompanied by significant bacteriuria.

#### UTI in females: - Usually occurs in 1-3% cases<sup>(2)</sup>.

Adult women are most commonly affected. The various clinical modes of presentations are

##### 1. Cystitis / pyelonephritis:

This is characterized by dysuria & frequency of micturition. Unilateral costovertebral angle pain, fever of >38.9° C and significant bacteriuria of > 10<sup>5</sup> bacterias/ml indicates pyelonephritis<sup>(6)</sup>.

##### 2. Dysuria Pyuria syndrome:

This usually occurs in sexually active ladies. In them the signs & symptoms of cystitis are present with negative urine culture, or urine culture yields low organism count as *E. coli* <10<sup>3</sup> bacterias/ml of urine. Chlamydia Trachomonalis organisms usually cause it.

##### 3. Catheter associated bacteriuria (CAB):

Occurs in women who are catheterized for long time. Pyuria due to indwelling catheter usually occurs as UTI or CAB. Bacterial colonization without infection is noticed in more than 95% cases. Thus Bacteriuria without pyuria signifies colonization of urinary tract while pyuria without bacteriuria signifies inflammation of Urinary tract<sup>(6)</sup>.

##### 4. Benign Bacteriuria of Elderly:

Because of varying degree of relaxation of pelvic muscles associated with cystocele or rectocele changes the anatomic relationship and angularity of ureters & predisposes to colonization. Elderly women without any signs or symptoms with presence of bacteriuria or pyuria on routine urine analysis indicate Benign Bacteriuria of Elderly.

#### UTI in Males:

This also occurs at various age groups<sup>(6,7)</sup>.

- During infancy: - vesicoureteric reflux leads to UTI in 34% of infants. Presence of foreskin is associated with higher risk of neonatal UTI.
- In young males: - In adults of < 35 years age, epididymitis because of sexual activity or outlet obstruction leads to increased incidence of UTI. *N. Gonorrhoeae*, Chlamydia, *Trachomonas vaginalis* & *Ureaplasma urealyticum* are common

Pathogens while *E. coli* are commonest after 35 years of age. Epididymitis is more common in homosexual than heterosexuals.

#### c. Prostatitis

This causes UTI in young males. There are 4 types of prostatitis<sup>(7,8,9)</sup>.

- Acute bacterial prostatitis – characterized by fever

with chills.

2. Chronic bacterial prostatitis – characterised by recurrent UTI
3. Chronic pelvic pain syndrome – characterized by pelvic perineal, penile & periscrotal pain.
4. Asymptomatic inflammatory prostatitis.

#### Investigations: -

For the diagnosis of UTI evidence of infection & inflammation both need to be documented. Evidence of infection is growth of invading organisms on culture and inflammation is demonstration of pus cells in urine<sup>(4)</sup>.

- a. **Collection of sample:** - The external part should be thoroughly cleaned with wet swab & always mid stream specimen is collected in wide mouth sterile bottle. Early morning sample yields maximum positivity but is not mandatory.

In catheter samples, tip of catheter should be cleaned before collection. Suprapubic aspiration of urine for collection sample is needed only in infants or unconscious patients or with gross obstruction of lower urinary tract. This is however the best method of collection of sample.

- b. **Transport of sample:-** The sample should be transported to laboratory as early as possible. If this is not possible, sample can be stored in refrigeration at 4<sup>o</sup> C<sup>(4)</sup>.
- c. **Gross Urine Examination:-** Turbid urine usually indicates UTI while foul smell to urine indicates cystitis with staph. saprophyticus infection. Presence of proteinuria indicates upper UTI especially as chronic pyelonephritis.
- d. **Microscopic Examination:-** Presence of > 5 puscells / HPF in females & > 2 p.c. /HPF in males in uncentrifuged specimen suggests UTI. Presence of RBCs indicates cystitis.
- e. **Urine Culture & Sensitivity:-** Significant bacterial growth is said to be present when the bacterial count is > 10<sup>5</sup> bacteria/ml. However in symptomatic individuals the bacterial count of 10<sup>2</sup> – 10<sup>5</sup> bacteria/ml may also be significant.

Specific strains of organisms like K,H, serotypes of E-coli should be identified<sup>(3)</sup>.

The antibody coated bacteria be detected by immunofluorescence test & its presence indicates upper UTI. Such bacteria are present only when kidneys are infected with organisms.

- f. Other investigations – These include

1. KFT
2. Blood sugar fasting & post prandial
3. Abdominal & pelvic sonography
4. I.V. urography

#### Relapse & Reinfection:

In cases with recurrent UTI, it is necessary to decide between relapse & reinfection<sup>(10)</sup>.

Relapse means recurrent UTI with same organisms while reinfection indicates infections with new or different organisms.

#### Treatment of UTI: -

The treatment of UTI is prompt use of antibiotics. The choice of antibiotic & duration of treatment varies with site & type of infection<sup>(2,11,12)</sup>. Table I shows various drugs used.

In acute uncomplicated cystitis, microorganisms are sensitive to many antibiotics. Amoxycillin, Septran or cephalosporins are useful but resistant strains are emerging fast. Single dose therapy may be useful but recurrences are common & hence 3-day regimen are usually advocated. However 3 days therapy should not be used for women with pyelonephritis, renal calculi with UTI and antibiotic resistant organisms. In chlamydial infection, Azithromycin 1 Gm single dose or Doxycycline 100 mg BD for 07 days is used.

In acute uncomplicated pyelonephritis, 7-14 days treatment with Fluoroquinolones, Aminoglycosides or third generation cephalosporins is advocated. Oral Septran can follow this for 14 days.

Complicated UTI are usually hospital-acquired infections and many strains are antibiotic resistant. In patients with minimal or mild symptoms, oral fluoroquinolones can be started till culture report is available. In hospitalized & serious patients, parenteral therapy with imipenem, cephalosporin with aminoglycosides or ceftriaxone or ceftazidime can be started. A more specific antibiotic is used after urine culture & sensitivity report.

A treatment is given for 14-21 days & follow up cultures 2-4 weeks after cessation of therapy are done to demonstrate cure.

In CAB, short course of antibiotic is enough to control symptoms.

In pregnancy acute cystitis is managed with 7 days treatment with NFT, amoxycillin or cephalosporin.

Asymptomatic bacteriuria during pregnancy should be treated. Acute pyelonephritis in pregnancy is managed by hospitalization & parenteral cephalosporins. Asymptomatic bacteriuria is treated only when associated with neutropenia, obstruction, renal transplantation or in patients with nonleukopenic

compromised host.

In all cases of pyelonephritis urine cultures should be repeated monthly to ensure complete cure.

Table: - Recommended, Antimicrobial Agents in UTI

Sr. No.	Condition	Pathogens	Mitigating agents	Treatment
1	Acute uncomplicated cystitis in women.	E. Coli St. saprophyticus proteus klebsiella	None	Septan BDx3d Quinolones(any)x 7d Nitrofurantoin (NFT) 100 mg QID x 7d
			D.M. Sympt >7 days Recurrent UTI Age > 65 Pregnancy.	7 days regimen Amoxicillin or NFT TMP – SMX cefodoxime
2	Acute uncomplicated P.N. in women.	E. coli Pro. Mirabilis S. saprophyticus	Mild to mod. illness No nausea or vomiting outpatient treatment	Any quinolone 7-14d Ceftriaxone 1g bd or Inj. Gentamycin 3-5 mg/kg Followed by TMP – SMX x 14 days
			Severe illness Hospitalised patient.	Initial 5-7 d any one Inj. Quinolones Gentamycin Inj. Ampicillin or Inj. Ceftriazone Or Inj. Aztreonam Followed by Oral Quinolones or Cephalosporin IIIrd gen or septran x 14 d
3	Complicated UTI in Men & Women.	E. coli, Proteus Klebsiella, Pseudo monas, Serratia Enterococci staphylococci	Mild to Mod. Illness outpatient treatment	Oral Quinolones 10-14 days
			Severe illness	Any one as Inj. Amp. + Inj. Gentamycin, Inj. Quinolones/Inj. Cifatoxime Ticarcillin Ciavulanate Imipenam Cilastdin followed by oral TMP – SMX or Quinolone x 10-21 d

#### Diagnosis tips:

- It is not possible to predict uropathogens of cystitis from clinical picture except staphylococcus saprophyticus
- Fishy urinary odor indicates infection by staph saprophyticus. It also causes microscopic

hematuria & alkaline PH of urine.

- Voiding after intercourse reduces incidence of UTI in females.
- Acute uncomplicated cystitis is the most common type of UTI in adult women.
- In elderly women cystitis manifests as pyuria &

bacteriuria without fever & dysuria & termed as benign bacteriuria of elderly.

- Dysuria/pyuria syndrome is a variant of cystitis & is also called abacteriuric cystitis.
- Pyelonephritis in women is an uncommon complication of cystitis during pregnancy.
- Cystitis with alkaline urine suggests infection secondary to *S. saprophyticus*, ureaplasma urealyticum or proteus.
- If a patient with cystitis & microscopic Hematuria fail to resolve with antimicrobial therapy, consider alternative diagnosis of renal T.B. or bladder/renal Neoplasm.
- Cystitis with gross hematuria suggest a viral hemorrhagic cystitis or renal lesion.
- Persistent pyuria without bacteriuria should suggest interstitial cystitis or renal T.B.
- In cystitis urine specific gravity is not decreased in contrast to pyelonephritis
- Pyelonephritis is differentiated from cystitis by fever of  $\geq 38.9^{\circ}\text{C}$  & unilateral costo vertebral angle (CVA) tenderness.
- Clinically pyelonephritis is almost always unilateral but may be bilateral pathophysiologically.
- Bilateral CVA tenderness should suggest an alternative diagnosis.
- Urine analysis/ culture findings in pyelonephritis & cystitis are same. Bacterimia frequently occur with pyelonephritis but is not a feature of cystitis in normal hosts.
- In nonleukopenic compromised hosts like DM, SLE, Cirrhosis etc. cystitis may be complicated by pyelonephritis or bacterimia.
- Bilateral normal sized or enlarged kidneys should suggest an alternative diagnosis to pyelonephritis.
- UTI with low bacterial count ( $10^2$ - $10^5$  bacteria/ml) is noticed in suprapubic aspirate samples, water diuresis, patient on antibiotic therapy, high urine osmolarity & acidic urine.
- Sterile pyuria (pyuria in absence of bacterimia) indicates infection with *C. trachomatis*, *U.*

Urealyticum, Myco. TB, fungi & also renal calculi, anatomic abnormality, nephro –calcinosis vesicoureteric reflux, interstitial nephritis & polycystic disease of Kidneys.

- Epididymitis is more common in homosexuals than heterosexual

#### Tips on Therapy:

- Virtually all cases of uncomplicated cystitis initially resolve spontaneously with or without treatments.
- For dysuria of cystitis phenazopyridine (Pyridium) is used. It relieves spasm promptly
- Single dose therapy with Nitrofurantoin, TMP-SMX or Amoxicillin is useful for initial attack of cystitis.
- Cystitis in non-leukopenic compromised host should be treated for 1-2 weeks to prevent bacteremia/ascending infection.
- Ampicillin should be avoided for its high resistance potential. Instead Amoxicillin should be used.
- Nitrofurantoin is useful in cystitis or CAB, but is not used in pyelonephritis bacteremia.
- The problems in relapse UTI are diagnostic & not therapeutic.
- Relapsing UTI has structural abnormality or ureteral shunts that do not permit antimicrobial therapy to be effective.
- The effective treatment in pyelonephritis is for 2-4 weeks.
- Patients with acute pyelonephritis become afebrile within 72 hours with treatment. Persistence of high fever for greater than 72 hours should indicate renal abscess.
- For pyelonephritis, parenteral agents useful against coliforms are cephalosporins, Aztreonam, Aminoglycosides, or renally eliminated quinolones. Against enterococci, Parenteral Ampicillin, Antipseudomonal Penicillins & Meropenem are useful.
- Oral antibiotics useful in pyelonephritis are renally eliminated quinolones, Amoxicillin, TMP-SMX.

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