

A review on prevalence of bacteria in urinary tract infection

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Abstract

Worldwide, Urinary tract infections are the most common infections. Which can involve the urethra, bladder and kidney and are caused by Gram-negative bacteria, followed by Gram-positive bacteria or fungi. Most commonly by Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Enterococcus faecalis and Staphylococcus saprophyticus. Women are at greater risk of developing a UTI than men are. Antibiotics are the typical treatment for a UTI. But you can take steps to reduce your chance of getting a UTI in the first place. Antibacterial agents are a major part of the treatment for UTI. Antimicrobial resistance patterns vary from time-to-time and across different regions. In this Review, we discuss how basic science studies are elucidating the molecular details of the crosstalk that occurs at the host–pathogen interface, as well as the consequences of these interactions for the pathophysiology of UTIs. We also describe current efforts to translate this knowledge into new clinical treatments for UTIs. A recent study says that infection rate varies among individuals considering their age, immunity, and lifestyle. The pathogens causing UTI are developing resistance against multiple drugs. From this study, we understand that Cranberry is the only plant source for the treatment of UTI in combination with antibiotics. There is a need to understand the importance of improving innate immunity and to know the best treatment regime to treat UTI.

Keywords: Urinary tract infection; Antibiotic; Nanomedicine; Traditional medicine; Alternative Systems of Medicine.

1. Introduction

Urinary tract infections (UTIs) are some of the most common bacterial infections, affecting 150 million people each year. Urinary tract infections (UTIs) are the inflammatory disorders of the urinary tract caused by the abnormal growth of pathogens[1]. Urinary tract infections are infections of the urethra, bladder, ureters, or the kidneys, which comprise the urinary tract. E. coli bacteria cause the majority of UTIs, but many other bacteria, fungi, and parasites may also cause UTIs. Females have a higher risk for UTIs than most males[2]. Clinically, UTIs are categorized as uncomplicated or complicated. Uncomplicated UTIs typically affect individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities [3]. These infections are differentiated into lower UTIs (cystitis) and upper UTIs (pyelonephritis) [3]. Complicated UTIs are defined as UTIs associated with factors that compromise the urinary tract or host defense, including urinary obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy and the presence of foreign bodies such as calculi, indwelling catheters or other drainage devices[3].

UTI is a bacterial infection affecting urinary tract. When bacteria from the rectal area enter the urinary tract via the urethra to the bladder and multiply in the urine, an infection occurs. In many cases bacteria first travel to the urethra. When bacteria multiply an infection can occur. An infection limited to the urethra is called urethritis. If bacteria move to the bladder and multiply, a bladder infection called cystitis. If the infection is not treated promptly, bacteria may then travel further up the ureters to multiply and infect the kidneys, called pyelonephritis [4].

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There is general agreement that sexual intercourse can cause a UTI. This is mostly thought to be a mechanical process whereby bacteria are introduced into the urinary tracts during the sexual act. There is no dispute about the transmission of UTIs caused by sexually transmitted disease (STD) organisms; these infections (for example, gonorrhoea and Chlamydia) are easily transmitted between sex partners[4]. Treatment of UTIs varies according to age, sex, living region, underlying disease, etiologic agent and site of infection[5].

2. Causes of UTIs

Most infections arise from one type of bacteria, E.coli which normally lies in the colon. The organisms most commonly responsible for catheter-associated UTIs are E.coli, Proteus mirabilis, P.aeruginosa and Streptococcus faecalis, Staphylococcus aureus, Klebsiella pneumonia, Mycobacterium tuberculosis, Actinomycetes, Nocardia, Candida etc. can cause UTI. In addition Mycoplasma and Chlamydia may be associated with sexually transmitted UTI [4].

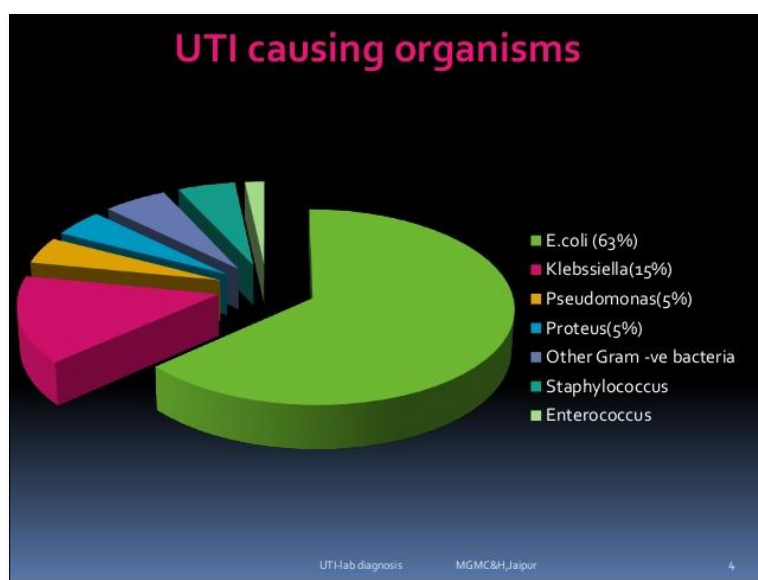


Figure 1 Causes of UTIs

Figure.1. Diagram showing contribution of various microbes for causing the UTI: E. coli 79%, S. Saprophyticus 11%, Klebsiella 3%, Mixed 3%, Proteus 2%, Enterococcus 2%, others 2%.

3. Symptoms of UTIs

- Urge to urinate frequently, often in small amounts
- Burning with urination
- Cloudy urine
- Strong unpleasant smell of urine (not as reliable in children)
- Dark or bloody urine
- Abdominal pain
- Fever
- Vomiting
- Pelvic pain
- Rectal pain (kidney infection)
- Flank or back pain (kidney infection) [4].

4. Risk factors for UTIs

- Infrequent voiding
- Incomplete voiding

- Personal Hygiene
- Sexual Activity
- Use of spermicidal contraception
- Genetics
- Hormonal Status
- Diabetes
- Immunosuppression [4].

5. Etiology

Pathogenic bacteria ascend from the perineum and rectum, predisposing women to urinary tract infections. Women also have shorter urethras than men, which further contributes to their increased susceptibility to UTIs. Blood-borne bacteria cause very few uncomplicated UTIs. *Escherichia coli* is the most common organism in uncomplicated UTIs by a large margin, followed by *Klebsiella*[7].

A major risk factor for UTIs is the use of a urinary catheter. Manipulation of the urethra is also a risk factor. Sexual intercourse and the use of spermicides and diaphragms are also risk factors for UTIs. Frequent pelvic exams and the presence of anatomical abnormalities of the urinary tract can also predispose one to a UTI[7].

UTIs are very common after a kidney transplant. The two triggers include the use of immunosuppressive drugs and vesicoureteral reflux. Other risk factors include the use of antibiotics and diabetes mellitus [7].

6. Epidemiology

Urinary tract infections are very frequent bacterial infections in women. They usually occur between the ages of 16 and 35 years, with 10% of women getting an infection yearly and more than 40% to 60% having an infection at least once in their lives. Recurrences are common, with nearly half getting a second infection within a year. Urinary tract infections occur at least four times more frequently in females than males [7].

The geriatric community is frequently affected by these infections. Notably, these infections often do not cause symptoms [6].

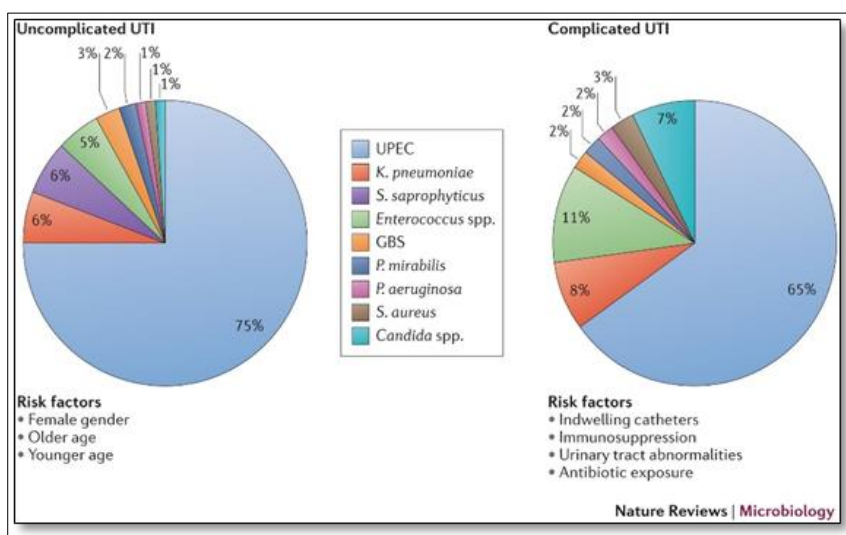


Figure 2 Epidemiology of UTIs

The pediatric population is also affected by UTIs. Bacteriuria is present in 2.7% of boys and 0.7% of girls. Uncircumcised males have a higher incidence of infection. Uncircumcised infants younger than 6 months have a higher incidence of gram-negative uropathogens. The rate of hospital admission is higher in uncircumcised boys, since this population has a 12-fold increased UTI risk. A study by Nuutinen and Uhari found that 35% of boys and 32% of girls who had their first UTI before age 1 contracted a recurrent UTI during the next three years. Other risk factors for exposure in infants are

hospitalization and catheterization. Children between ages 1 and 5 years have a 4.5% increased incidence of bacteriuria [6].

7. Pathophysiology

An uncomplicated UTI usually only involves the bladder. When bacteria invade the bladder mucosal wall, an inflammatory reaction called cystitis is produced. The majority of organisms causing a UTI are enteric coliforms that typically inhabit the periurethral vaginal introitus. These organisms ascend the urethra into the bladder and cause UTIs. Sexual intercourse is a common cause of a UTI as it promotes the migration of bacteria into the bladder. People who frequently void and empty the bladder tend to have a lower risk of a UTI.

Urine is an ideal medium for bacterial growth. Factors that make it less favorable for bacterial growth include a pH of less than 5, the presence of organic acids, and high urea levels. Frequent urination and high urinary volumes are also known to decrease the risk of UTIs.

Bacteria that cause UTIs tend to have adhesions on their surface, which allow the organism to attach to the urothelial mucosal surface. In addition, a short urethra also makes it easier for the uropathogen to invade the urinary tract. Premenopausal women have large concentrations of lactobacilli in the vagina and an acidic pH, preventing colonization with uropathogens. However, the use of antibiotics can erase this protective effect [7].

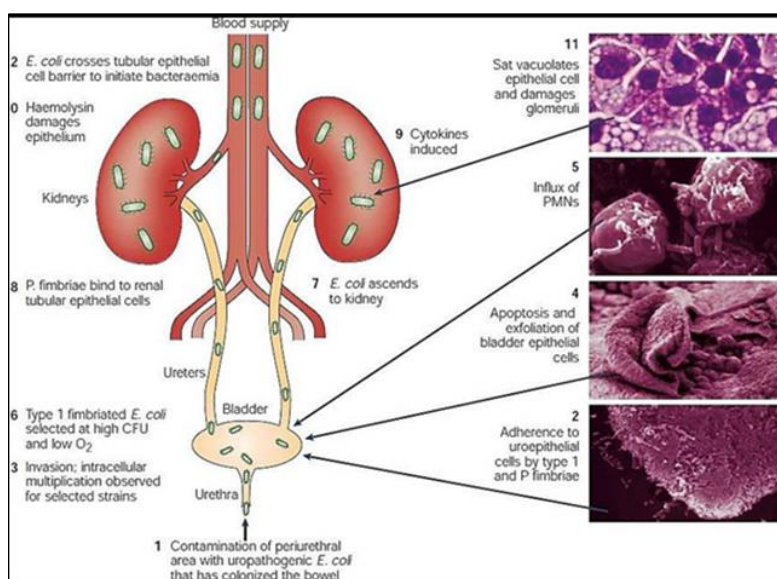


Figure 3 Pathogenesis of UTIs

8. Diagnosis

The diagnoses for acute pyelonephritis, cystitis, and asymptomatic bacteriuria are made by the presence of bacteria in the urine, usually based on a clean midstream urine sample. There must be a minimum of 10⁵ colony-forming units per milliliter (cfu/mL) of uropathogens for diagnosis of acute pyelonephritis and asymptomatic bacteriuria but only 10³ cfu/mL for the diagnosis of cystitis. Up to one third of cystitis cases would be missed if the criterion for diagnosis were the same as that for upper tract infections [6].

Dipstick urinalysis has become the most frequently used test due to its cost and fast results. Studies have shown that dipstick urinalysis, in combination with clinician judgment, greatly improves diagnostic accuracy in the patient with nonspecific symptoms. Urine dipstick is positive if there is a presence of nitrate and/or if there is a positive reaction greater than or equal to trace leukocyte esterase [6].

Sometimes blood in the urine is assign of a UTI but it may also indicate other problems, such as a urinary calculus or –stone. In young children, infants, and some elderly patients, the best urine specimen is obtained by catheterization, as they are unable to deliver a –clean catch" urine sample as described above [4].

8.1. Differential Diagnosis

- Pyelonephritis
 - Renal stone
 - Vaginitis
 - PID
 - Herpes simplex
 - Renal infarction[7].
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9. Prognosis

Even with proper antibiotic treatment, most UTI symptoms can last several days. In women with recurrent UTIs, the quality of life can be poor. About 25% of women experience such recurrences within six months. Factors that indicate a poor outlook include:

- Poor overall health
 - Advanced age
 - Presence of renal calculi
 - Diabetes (especially if poorly controlled)
 - Sickle cell anaemia
 - Presence of malignancy
 - Urethral catheterization
 - Ongoing chemotherapy
 - Incontinence
 - Chronic diarrhoea[7].
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10. Complication

Complications of urinary tract infections include:

- Persistent lower urinary tract symptoms
 - Staghorn urinary calculi
 - Pyelonephritis
 - Emphysematous pyelonephritis and cystitis
 - Incontinence
 - Focal renal nephronia
 - Renal abscess
 - Hypertension
 - Renal failure[7].
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11. Treatment

Treatment for a UTI should be designed for each patient individually and is usually based on the patient's underlying medical conditions, what pathogen(s) are causing the infection, and the susceptibility of the pathogen(s) to treatments. Patients who are very ill usually require intravenous (IV) antibiotics and admission to a hospital; they usually have a kidney infection (pyelonephritis) that may be spreading to the bloodstream. Other people may have a milder infection (cystitis) and may get well quickly with oral antibiotics. Still others may have a UTI caused by pathogens that cause STDs and may require more than a single oral antibiotic [4].

The treatment has varied historically from 3 days to 6 weeks. There are excellent cure rates with "mini-dose therapy," which involves three days of treatment. *E. coli* resistance to common antimicrobials varies in different areas of the country, and if the resistance rate is greater than 50%, choose another drug [7].

Trimethoprim/Sulfamethoxazole for three days is good mini-dose therapy, but resistance rates are high in many areas. It should not be used if local resistance is >20%. First-generation cephalosporin's are good choices for mini-dose

therapy. Nitrofurantoin is a good choice for uncomplicated UTIs, but it is bacteriostatic, not bactericidal, and must be used for 5 to 7 days. Fluoroquinolones have high resistance but are a favorite of urologists because of high tissue penetration levels, especially in the prostate. For this reason, fluoroquinolones are not preferred except for complicated infections and those involving the prostate. Recent precautions from the FDA about fluoroquinolone side effects should be heeded [7].

11.1. Most commonly used Antibiotics for UTIs and its possible side effects

- Macrodantin (Macrobid or nitrofurantoin) –Side effects of long-term use may include fibrosis or scarring of the lungs and peripheral neuropathy. Generally, the medication is considered safe during pregnancy, except with rare genetic metabolic deficiencies.
- Bactrim (Septra or sulfa/TMP) –This drug should not be taken early during pregnancy and may affect the effectiveness of oral contraceptives.
- Trimethoprim –It should not be taken during pregnancy.
- Quinolones (Levaquin, Levofloxacin, or Cipro) - This drug should not be taken during pregnancy.
- Cephalosporin (Keflex) – This may affect the effectiveness of oral contraceptives.
- Doxycycline –It is not safe during pregnancy or breastfeeding [4].

11.2. Antibiotics

UTI treatment currently relies heavily on antibiotics. The antibiotics most preferred for the treatment of UTI are mentioned in Table No. 1. Uropathogenic bacteria isolates from the pregnant woman revealed that the pathogens were sensitive to Gentamycin, Nalidixic acid, Nitrofurantoin, Amikacin and Co-trimoxazole and resistant to Amoxicillin, Norfloxacin and erythromycin [8].

Table 1 Antibiotics and their dosage prescribed against uncomplicated UTI [8].

Sr No.	Drug	Dosage
1.	Nitrofurantoin monohydrate/ macrocrystals	100mg twice daily for 5 days
2.	Trimethoprim-sulfamethoxazole	160/800 mg (1 DS tablet) twice daily for 3 days
3.	Fosfomycin trometamol	3-g single-dose sachet
4.	Ciprofloxacin	500 mg twice daily for 5–7 days
5.	Ciprofloxacin XR	1000 mg once daily for 5–7 days

11.3. Vaccines

For E. coli to cause infection cells must adhere to the urinary tract of the mucosa. E. coli vaccine development has been targeted to disrupt the process of cell adhesion, capsules, toxins, and iron metabolism. Vaccines targeting adhesions invade the epithelial cell membrane inside the bladder and promote irreversible bacterial attachment. Vaccines targeting toxins protect the bladder by preventing toxins from interacting with host epithelial cells. UPEC requires iron for transporting and storing oxygen, vaccines for iron metabolism focuses on reducing the iron availability in the host [8].

11.4. Nanomedicine

Nanoparticles synthesized from various plant extracts are showing promising effects in treating UTI. Zinc nano-particles from *Berberis aristata* & *Passiflora caerulea*, copper-sulfide nanoparticles from *Serratia nematodiphila* silver nanoparticles from *Anogeissus acuminata* are the major nanoparticle components that can be potential drug candidates against UTI [8].

11.5. Cranberry fruit extract as an anti-adhesive agent

The efficacy of fruit extract of cranberry against Tamm-Horsfall Protein in human urine and its anti-adhesive activity against UPEC was investigated. Results indicated inhibition of adhesion of UPEC strain UTI89 to human T24 bladder cells. The chemical constituent of food-grade cranberry dry extract contains flavonoid glycosides, anthocyanidins, A- and B-type proanthocyanidins, phenylpropanoid acid derivatives, benzoic acid derivatives, chlorogenic acid

derivatives, and coumaroyl-tryptophan derivatives have anti-adhesive properties. The oligosaccharide of cranberry also has anti-adhesive properties [8].

11.6. Ayurveda

Ayurveda is one of the major alternative systems of medicine in India, Ayurveda drugs are being used for treating many urinary tract ailments. A review of Ayurveda drugs against UTI Bhokardankar [47] has listed 37 potent plants. UTI is termed as Mutrakrucha in Ayurveda. Trinetrakhya Ras, Varunadilauh, Mutrakruchhantak Ras, Trunpanchmula, Gokshurkwith, Haritakyadiyog Duralabhadikashaya, Eladi Churna, Tarkeshwar Ras, Varundya Lauh and Chandrakala Ras are the Ayurveda formulation which was used for treating UTI. The listed plants and formulations showed their activity against uropathogens along with antipyretic and diuretic properties. The mode of action was similar to the anti-bacterial and anti-adhesive properties of active ingredients in the formulations [8].

11.7. Homeopathy

The homeopathic system of medicine has its origin in Germany is being considered as one of the most effective systems with lesser side effects. Children and pregnant women prefer this system as there are fewer side effects [8].

Nwabudike has prescribed homeopathic preparations of Phosphorus, Platinum metallicum, Collibacillinum, and Causticum were very effective in treating three women with recurrent UTI. Thuja occidentalis, Lycopodium clavatum, Sepia ocinalis, Pulsatilla pratensis, sulfur, Nux vomica, Hepar Sulphur, Rhus toxicodendron, Arnica Montana, Calcarea carbonica, Tuberculinum bovinum (Kent), Natrium muriaticum, Carbo vegetabilis, Cantharis vesicatoria, Staphisagria, and Berberis vulgaris integrated with antibiotics can show significant effect against uropathogens. Rather than acting directly on the pathogens, homeopathic medicine concentrated on boosting innate immunity to eliminate pathogens from the urinary tract [8].

12. Treatment for recurrent UTIs

Recommended treatments for recurrent UTIs include maximizing personal hygiene factors, avoiding spermicides, wiping correctly, using vaginal estrogens if appropriate, etc. The effectiveness of lifestyle changes in personal hygiene in reducing recurrent UTIs has not been conclusively demonstrated [5].

D-mannose has been proposed as an aid in recurrent cystitis due to its ability to bind to bacterial surface ligands, which decrease the adherence of infecting organisms to the urothelial mucosa. While there is some evidence of a reduction in recurrent infections from D-mannose, definitive studies have not yet been done, and optimal dosages are still undetermined [5]. Antibiotic prophylaxis has been quite successful in controlling recurrent UTIs, but using alternative means first is preferable. When other measures fail or there is evidence of multiple rapid recurrences, antibiotic prophylaxis is reasonable. Prophylaxis is never appropriate in patients who have permanent catheters or nephrostomies as this will rapidly lead to highly resistant organisms [5].

If a recurrent UTI patient develops an acute UTI, a urine culture should be obtained, and an alternate antibiotic agent used to treat the infection. The duration of treatment should be no longer than a week. If the urine cultures show resistance to all available oral agents, then parenteral antibiotics will be required. Again, the duration of therapy should generally be no more than one week [5].

12.1. Long Term, Low Dose Prophylaxis

Continuous prophylaxis is typically done with a lower dose than is typically used for acute cystitis therapy. Therefore, this approach is called the long-term, low-dose therapy protocol. The selection of the antibiotic is based on culture and sensitivity results for that individual patient. Initial evaluation of the effectiveness of prophylaxis is suggested at three months. If effective, a six to twelve-month duration is typical. Unfortunately, many individuals will revert to their prior pattern of infections once prophylaxis stops [5]. Overall, long-term, low dose antibiotic prophylaxis for recurrent UTIs substantially decreases recurrent urinary tract infections [5].

12.2. Preferred Agents for Recurrent UTI Prophylaxis

- Nitrofurantoin at 50 to 100 mg daily.
- SMX-TMP at 40/200 mg daily.
- Trimethoprim at 100 mg daily [5].

12.3. Second Line Agents That Are Less Preferred for Prophylaxis

- Cephalexin at 125 mg or 250 mg daily
- Cefaclor at 250 mg daily
- Fosfomycin at 3 gm every 10 days
- Norfloxacin at 400 mg daily [5].

13. Conclusion

Urinary tract infection, UTIs as the name indicates this infection occurs in urinary tract. UTIs involves the urethra, bladder, ureters or the kidneys. Women also have shorter urethras than men, which further contributes to their increased susceptibility to UTIs. So, the urinary tract infection are most common in female than male. Mostly sexually transmission is the reason for urinary tract infection. For the purpose of diagnosis the dipstick method is widely use. Dipstick urinalysis has become the most frequently used test due to its cost and fast result. Treatment for a UTI is usually based on the patients underlying medical conditions. Consumption of antibiotics, vaccinations is the usual treatment regimen for UTI. Also, cranberry juice is the home remedy to get rid of vaginitis and a burning sensation in the genital area due to UTI. Treatment for recurrent UTIs include maximizing personal hygiene factor, avoiding spermicides, wiping correctly. The effectiveness of lifestyle changes in personal hygiene in reducing recurrent UTIs has not been conclusively demonstrated.

Compliance with ethical standards

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Disclosure of conflict of interest

The Authors declares that there is no disclosure of conflict of interest.

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