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A review on urinary tract infection

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A B S T R A C T

A urinary tract infection (UTI) is defined as the presence of microorganisms that have the potential to invade the tissue of the urinary tract and adjacent structure. Based on the site of infection, UTI can be classified into lower tract infections include cystitis, urethritis, prostatitis and upper tract infections including pyelonephritis. nitrofurantoin and fosfomycin are drug of choice of acute cystitis and piperacillin – tazobactam and ertapenem for acute pyelonephritis. Some Indian studies have reported E. coli as the most common isolated organism followed by Klebsiella species and P. Aeruginosa, while others have reported E. coli as the most causative pathogen followed by S. Aureus. Gram negative bacteria were more likely to cause infection than gram positive bacteria. Nitrofurantoin has a good sensitivity against E. coli and other pathogens, but is the least commonly prescribed medicine. Gender, age, menopause, post menopause, sexual intercourse, indwelling catheters and other co- morbid conditions like diabetes mellitus, urinary stone, and hypertension are the common risk factors of UTI. This review discusses the treatment guideline, common causative agent and risk factors of UTIs.

Keywords: UTI, Urinary tract infection, Antibiotics, Risk factors

Introduction:

Urinary tract infection (UTI) is an infectious disease caused by microorganism like bacteria, fungi, viruses and parasites. It is a condition in which presence of microorganism potential to invade the tissue of the urinary tract, adjacent structure and growth of microorganism.[1] UTI arises via 3 possible routes. The ascending pathway, descending pathway and lymphatic pathways. In ascending pathway, colonization of the bacteria starts at the periurethral area then bacteria enter in to bladder and multiply quickly and reach to the kidney through ureters. [2] In the hematogenous pathway there is blood-borne spread of infections. It is also known as descending pathway [2, 3] while increased pressure on the bladder leads to lymphatic flow in to the kidney resulting in UTI.[4] The size of inoculum, virulence of the microorganisms and immunity of the host are the factors that regulate the onset of UTI.

Epidemiology:

Urinary tract infections (UTIs) are the second most common bacterial infection in community practice, affecting 150 million people each year worldwide. In the United States alone, there were an estimated 10.5 million office visits for UTI symptoms and 2–3 million emergency department visits. The societal costs of these infections, including health care costs and time missed from work, are approximately US$3.5 billion per year in the United States alone. [5,6]

Types

UTI classify in to the two types upper tract infection and lower tract infection. Pyelonephritis is the type of upper tract infection while cystitis, urethritis and prostatitis are the types of lower tract infection.[1]

Anamika Chalise et al., 2017, found that most of the patients (72%) were suffering from cystitis, 14% were suffering from pyelonephritis and remaining 14% patient's types of UTIs was unspecified. They also found that females were more prone to lower tract infection and men tend to suffer more from upper tract infection.[6]

Etiology

UTIs are caused by gram positive bacteria, gram negative bacteria as well as fungi. The most common cause of complicated and uncomplicated UTIs are E. coli., Klebsiella pneumoniae, Staphylococcus saprophyticus, Enterococcus faecalis, group of B Streptococcus (GBS), Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus and Candida spp is common causative agent of uncomplicated UTIs and Enterococcus spp., S. aureus, K. pneumonia, P. mirabilis, Candida spp., for complicated UTIs.[5]

Study carried out by Anamika Chalise et al., in 2017 in southern zone at Bangalore found that E. coli (71.17%) was most common causative agent followed by K. Pneumonia (17.39%), P. Aeruginosa and found that E. coli which was more in males than females followed by klebsiella pneumonia and pseudomonas aeruginosa that were more in females than males.[6] Study carried out by Parastoo Abdolmalaki et al., in 2022 in similar zone reported similar results that E. coli (54.76%) was most common causative agent followed by K. Pneumonia (19.05%) and P. Aeruginosa (11.9%).[7]

According to literature search, the three-study done in the western zone of India at Gujarat (Vadodara, Gandhinagar) and Maharashtra, suggest similar results in this area. In 2015 a study done at Maharashtra found that E. coli (35.9%) was most causative agent followed by Klebsiella species (14.06%) and Pseudomonas aeruginosa (7.8%) [8] and another study done at Gandhinagar in 2020 also found that E. coli was the most common causative agent.[9] In 2021 study done at Vadodara found isolates of E. coli (38%), Klebsiella sp. (24%) and Pseudomonas aeruginosa (7.8%).[10]

Another study done in the eastern part of India at Odisha in 2017 observed that E. Coli (60.29%) was most common causative agent followed by S. aureus (13.23%), Klebsiella species (11.76%) then Candida (5.88%), Pseudomonas (4.41%) and enterococcus (4.41%).[11]

Similarly, a study done in the central region of India at Delhi in 2015 found similar results as eastern zone study and common isolated organisms were E. coli (36.09%), S. Aureus (27.83%), Enterococcus faecalis (7.65%) and pseudomonas aeruginosa (5.5%) and gram-negative bacteria were more likely to cause infection than the gram-positive bacteria.[12]

Treatment

According to ICMR guidelines (Treatment guidelines for antimicrobial use in common syndromes" ICMR Guidelines, 2019) the treatment of UTI based on the types of UTIs (Upper & lower tract infection). But most of the studies found that the types of UTIs was unspecified.**[13]**

Antibiotics are commonly used for the treatment of UTI. Other options available for treating UTI include Ayurvedic, Homeopathy, Herbal medicines, Unani system of medicines, vaccines and home remedies.

Antibiotics:

The choice of antibiotics for the treatment of UTI according to ICMR guidelines 2019 are mentioned in table 1.**[13]**

Table 1: Treatment of UTI as per ICMR guidelines-2019[13]

Antibiotics	Does	Frequency	Duration	ROA
Acute Cystitis				
Nitrofurantoin	**100 mg**	**BD**	**5 days**	**Oral**
Nitrofurantoin	**1.25-1.75 mg/kg (in children)**	**6 hours**	**5 days**	**Oral**
Fosfomycin	**3 gm**	**OD**	**1 day**	**Oral**
Cotrimoxazole	**1 tab**	**BD**	**3 days**	**Oral**
Ertapenem	**1 gm**	**OD**	**3 days**	**IV**
Amikacin	**15 mg/kg/day**	**OD**	**3 days**	**IV or IM**
Acute Pyelonephritis				
Piperacillin – tazobactam	**4.5 gm**	**6 hours**	**-**	**IV**
Ertapenem	**1 gm**	**OD**	**7- 10 days**	**IV**
Imipenem	**1 gm**	**8 hours**	**-**	**IV**
Meropenem	**1 gm**	**8 hours**		**IV**
Amikacin	**g/kg/day**	**OD**	**7-14 days**	**IV / IM**

There were 7 study included in time frame of 2009 to 2022. According to a study done by Hardip Singh et al., 2009 at Punjab that found cephalosporin (67.37%) was most common prescribed class of antibiotics followed by aminoglycoside (16.79%) and penicillin (14.98%).

Eima Fatima et al., in 2013 did a study at New Delhi, that reflects the maximum prescribed antibiotic was the combination of amoxicillin – clavulanic acid (43.33%) followed by nitrofurantoin (38.83%), amikacin (3.05%). They also reported that nitrofurantoin was more sensitive to pathogens than other antibiotics.**[12]**

According to the study of Sunil S.G et al., in 2015, at Maharashtra, cephalosporine (70.37%) was the most commonly used antimicrobial class. Ceftriaxone was most commonly prescribed antibiotics followed by ciprofloxacin, cefixime, azithromycin and amikacin. Ampicillin and ceftriaxone were resistance to the E. coli while amikacin and nitrofurantoin was sensitive to E. coli and other pathogens.**[8]**

Samira Kumar Naik et al., in a study carried out at Odisha in 2016, reported that found that most common prescribed antibiotic was Ceftriaxone (43.75%), Ofloxacin (17.70%) and Cefixime (16.67%). Nitrofurantoin and cotrimoxazole were sensitive to E. coli but still was the least prescribed medicine.[11]

Another study done at Bangalore in 2017, that found that most common prescribed antibiotics were Norfloxacin (25.54%), ciprofloxacin (16.06%), cefixime (13.13%), ceftriaxone (11.68%) and amikacin (8.03%). Sensitivity and resistance pattern of antibiotics was similar to the results of Sunil S.G et al (2015) that ampicillin, ceftriaxone and cefotaxime were resistant to E. coli and amikacin, nitrofurantoin were sensitive towards the E. coli. [6,8]

Janki Patel et al., in 2019 did a study in Gandhinagar and found that most common prescribed antibiotics were Levofloxacin (75.8%), Ceftriaxone (33.33%), Amoxicillin (25.8%), Moxicillin (25.8%) and piperacillin – tazobactam (18.3%). Resistance was seen towards Levofloxacin.[9]

In a study done in Bangalore in 2022 by Parastoo Abdolmalaki et al., found common prescribed antibiotics were cefotaxime (31.33%) Ceftriaxone (24%), Ciprofloxacin (12%), Norfloxacin (8%) and Nitrofurantoin (6.67%).[7]

From the results of the abovementioned studies, it can be concluded that cephalosporin class of antibiotics was most commonly prescribed although E. coli and other pathogens were resistant to cephalosporins. Nitrofurantoin is sensitive to most of the pathogenic organism but was less prescribed medicine. Another aspect worth mentioning is that antibiotics were not prescribed as per ICMR guidelines. There is need for the prescribers to follow the standard guidelines for treatment of UTI.

Other systems of medicines:

5.2.1 Herbal Medicine:

Bachu, Cougrass, Cranberry and Echinacea are plants that have been used for the prevention of recurrent UTI. They can also be used along with antibiotics.[14]

The clinical benefits of cranberry juice in preventing UTI have been reported. Specially in sexually active adult women and previous UTI history of UTI. It is also beneficial in high risk of UTI (Neurogenic bladder, Diabetes) and bacteuria.[15] Cranberry is safe, less expensive, effective as alternative to long term preventive antibiotics.

5.2.2 Ayurveda

In the traditional systems for treatment and prevention of disease. A review by Prashant Bhokardankar, suggested 11 formulations for treatment of UTI (Mutrakrucha). Trinetrakhya Ras, Varunadi lauh, Mutrakruchhantak Ras, Trunpanchamula, Gokshur kwath, Haritakyadi yog, Duralabhadi Kashaya, Eladi churna, Tarkeshwar Ras, Varundya lauch, Chandrakala Ras are the formulation for treat UTI.[16]

Dr. Niraml Bhusal et al., in 2017 have reported the benefit of Chandraprabhavati, Gokshuradi – Guggulu, Syrup Neeri, Shita Sudha, Gokshra and Shatavari, in improvement in UTI.[17]

5.2.3 Homeopathy

This method originated from Germany which is effective and with lesser side effects. Abhijeeth S. Badiger et al., 2021 has described the use of Thuja occidentalis, Lycopodium clavatum, Sepia ocinalis, Pulsatilla pratensis, Hepar Sulphur, Nux vomica, Arnica Montana, Tuberculinum bovinum (Kent), Natrium muriaticum, Carbo vegetabilis, Calcarea carbonica, Cantharis vesicatoria, Staphisagria, Rhus Toxicodendron and Berberis vulgaris integrated with antibiotics can show significant effect against pathogens.[18]

Risk factors of UTI:

There are the many risk factors for UTI and recurrent UTI. Females are prone to the infection due to the shorter urethra than the male.[19]

Risk factors for UTIs and recurrent UTIs in female patients

A recurrent UTI refers to the occurrence of more than two symptomatic episodes within 6 months or more than three episodes within 12 months.[19]
Stage of Perimenopause and adult hood, sexual intercourse, change in bacterial flora, history of UTI during childhood, family history of UTI were the risk factors of UTIs during this phase. Specific risk factors related to sexual intercourse were use of spermicides (may alter the vaginal PH), use of condom, use of contraceptive pills, engagement with new sexual partner within the last year. Other factors included lack of postcoital urination, vaginal douches, improper underwear, poor hygienic condition, circumcision status of male partners. [12,19]

Vulvovaginal atrophy, estrogen deficiency, history of UTI during peri menopause were the risk factors at stage of menopause and post menopause, consequent year spent in menopause, rural area of residence, illiteracy, lower socio-economic class, inadequate housing standards, obesity and smoking are some of the other reported risk factors of UTI.[20]

Samreen khan et al., 2016 and Anamika chalise et al., 2017 found the history of hysterectomy as most common risk factor of UTI in female patients. [6, 20]

Pregnancy is also considered a risk factor for UTI, because of physiological changes, increase the level of progesterone, high progesterone causes smooth muscle relaxation so that reduced ureteric peristalsis and increase bladder capacity thus favoring physiological hydronephrosis and urinary stasis.[21]

Risk factors for UTI in male patients:

Male specific risk factors are less than the female factors. Benign prostatic hyperplasia (BPH), prostate cancer and old age are reported to be the risk factors.[6]

Common comorbid condition for males and females:

UTI are more common, more severe and have worse outcomes in patients with diabetes. In diabetic patient's higher glucose concentration create favorable environment for promote the growth of pathogenic bacteria. Diabetes was a common co- morbid condition reported in many studies.[22]

Renal calculi, urinary obstruction, kidney disease and BPH were the factors responsible for the urinary blockage. Syed Aamer Nawa et al., 2021 found that hydronephrosis occurs due to the urinary blockage which results in the swelling of renal calyces and ureter so the chance of infection.[23]

At the time of catheterization poor hand hygiene poor aseptic technique and poor catheter placement and over long catheterization were risk factors for CA-UTI (Catheter associated urinary tract infection). Open drain catheterization has higher risk of ABU (Asymptomatic bacteriuria) than closed drain catheterization.[19]

In cases of neurogenic bladder dysfunction there is altered filling and voiding, as well as detrusor hyperactivity. Management of this situation by the catheterization or nephrectomy also increases the risk of UTI.[19]

Osteoarthritis, anemia, cancer weakens the immune systems and increasing the risk of UTI. Colitis, diarrhea, hernia, recent urinary procedure, spinal cord injury, kidney disease, malaria were co-morbid conditions reported in various studies. Low socio – economic status and poor hygienic conditions were other risk factors reported. [6, 8, 12]

There could be presence of more than one risk factors in UTI patients. Anamika Chalise et al., have reported presence of hypertension + DM in 8.82% patients, post tuberculosis + BPH, bronchitis + BPH, HTN + DM+ COPD in to 2.94% patients.[6]

Conclusion

In the southern and western zone studies the common isolated organisms were E. coli followed by Klebsiella species and P. Aeruginosa. Eastern zone and central zone studies (2015 to 2017) have reported E. coli as the most causative pathogen followed by S. Aureus. Gram negative bacteria were more likely to cause infection than gram positive bacteria. Cephalosporin was the commonly prescribed class of antibiotics. Nitrofurantoin has a good sensitivity against E. coli and other pathogens, but is the least commonly prescribed medicine. Antibiotics were not prescribed as per ICMR guidelines. There is need for the prescribers to follow standard treatment guidelines for the management of UTI. Family history of UTI, history of UTI, sexual intercourse, menopause, post menopause, BPH, old age, diabetes, renal calculi, urinary obstruction, catheterization, neurogenic bladder dysfunction, suppressed immune system were the risk factors of UTI.

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