

## URINARY TRACT INFECTION IN POSTMENOPAUSAL WOMEN - A REVIEW

Sarada Satyamoorthy Garg<sup>1</sup> & S Ramalakshmi<sup>2</sup>

<sup>1</sup>Gynaecologist, Senior Clinical Research Coordinator, Sri Ramchandra Institute of Higher Education & Research  
(Deemed to be University), Porur, Chennai, Tamil Nadu, India 600116

<sup>2</sup>Professor & Senior Consultant, Department of Nephrology, Sri Ramchandra Institute of Higher Education & Research  
(Deemed to be University), Porur, Chennai, Tamil Nadu, India 600116

### ABSTRACT

Urinary Tract Infection (UTI) is very common among women, with incidence of bacteriuria increasing with age. Changes in the urinary tract due to decrease in oestrogen levels, anatomical defects, prior urogynecological surgery, post-void urinary retention, indwelling catheter, non secretors of histo-blood group P1 antigens and Vitamin D deficiency predispose women to infection, due to changes in the urinary biome. New onset dysuria is one of the best indicators of symptomatic UTI. Presence of leucocyte esterase and nitrites in urine are used to screen for infection in symptomatic women. Urine culture still remains the test for diagnosis of UTI. E. coli is the commonest organism isolated. Many associations around the world have revised the guidelines for treatment in past few years. Asymptomatic women with bacteriuria do not need screening or treatment with antibiotics. Uncomplicated UTI as well as recurrent UTI with symptoms of cystitis is treated with a short course of antibiotics for 3 to 6 days. Self-start antibiotics for 3 days with onset of symptoms are an option for patients with recurrent UTI. Continuous low dose antibiotic may be prescribed if other measures fail. Fluid intake must not be restricted, especially in women with incontinence. Vaginal oestrogen may be used for prevention of UTI. Various other non-antibiotic therapies including cranberry, ascorbic acid, D-mannose, lactobacilli and immunotherapy have been tried in the prevention of UTI, though more evidence is required. This article highlights the latest guidelines for diagnosis, management and prevention of UTI in postmenopausal women.

**KEYWORDS:** Urinary Tract Infection (UTI), Women

---

### Article History

**Received: 18 Aug 2020 | Revised: 20 Aug 2020 | Accepted: 28 Aug 2020**

---

### INTRODUCTION

Urinary tract infection (UTI) is one of the commonest infections in women. In young to middle aged women, the prevalence is <5%. However, bacteriuria rises to 15-20% by the age of 70 years and up to 20-50% in women >80 years of age (1). UTI affects about 40% of women in their lifetime and approximately 25% of women with an isolated UTI have recurrence within the next 6-12 months (2, 3). However, symptoms due to genitourinary syndrome of menopause are similar to those of UTI and may lead to overuse and misuse of antibiotics and antibiotic resistance. It is hence very important to use guidelines for diagnosis and treatment of UTI in postmenopausal women (4).

## CHANGES AT MENOPAUSE PREDISPOSING TO UTI

Menopause is associated with a decrease in serum estrogen levels. Estrogen receptors are expressed in the epithelium of the urethra and vagina, in the trigone of the bladder and in the levator ani muscle of the pelvic floor (5). Due to decrease in estrogen the vulval, vaginal and lower urinary tract epithelium atrophies, the detrusor function deteriorates, bladder wall shows fibrosis, post void residual urine increases, the pelvic floor musculature loses its strength and the sensory threshold of the distending bladder decreases with an increased sensitivity to neurotransmitters, especially norepinephrine (6). The urethral closure pressure and Valsalva leak-point pressure decrease, contributing to urinary urgency (4). The vaginal pH increases to  $\geq 5$  due to decrease in epithelial glycogen levels. The flora changes from a predominantly *Lactobacillus* spp to an abundance of *Anaerococcus*, *Peptoniphilus* and *Prevotella* and gram negative fecal flora (4, 7, 8). All these changes lead to the genitourinary syndrome of menopause and women may have symptoms including frequency, urgency, postvoid dribbling, nocturia, stress/urge incontinence, dysuria, hematuria, dyspareunia and vulvovaginal itching and become susceptible to UTI (9).

## DEFINITION OF UTI AND CLASSIFICATION

UTI is broadly defined as a microbial infection, usually bacterial, that affects any part of the urinary tract. Various terms used to describe UTI are given in Table 1.

**Table 1: Terms used to Describe UTI (2, 9)**

Criteria	Definition
Asymptomatic bacteriuria	Presence of $\geq 10^5$ Colony forming units(CFU)/mL of the same organism in voided midstream clean-catch urine sample or at least 100 CFU/mL of urine from a catheterized specimen BUT patient does not have any symptoms or signs of UTI
Symptomatic UTI	Symptoms of UTI present along with presence of $\geq 10^5$ CFU/mL of one organism in urine sample
Uncomplicated UTI	When urinary tract is normal, both structurally and physiologically, with no associated disorder to impair the host defence mechanisms
Complicated UTI	Infection occurs within an abnormal urinary tract e.g. in presence of renal disease or calculi, vesicoureteric reflux, indwelling catheters or ureteric obstruction or with other concomitant immune compromising diseases like diabetes
Isolated UTI	First episode of UTI, or episodes are $>6$ months apart
Unresolved UTI	When therapy fails due to bacterial resistance or due to infection by two different bacteria with equally limited susceptibilities
Reinfection	When urine culture is sterile after therapy but the same organism regrows after two weeks of therapy OR when a different microorganism grows at any point in time
Relapse	When the same microorganism causes a UTI within 2 weeks of therapy – difficult to distinguish from a reinfection
Bacterial persistence	Therapy is impaired by accumulation of microorganism in a location not reached by antibiotics e.g. infected stones, urethral diverticula
Recurrent UTI	$\geq 3$ symptomatic and medically diagnosed UTIs in the previous 12 months, with resolution in between episodes
Urosepsis	Life threatening sepsis due to UTI
Cystitis	Infection of the bladder
Pyelonephritis	Infection of the upper urinary tract- kidneys and ureters

## Risk Factors for UTI

Risk factors for UTI are given in Table 2. Increasing age, women with cystocele, uterovaginal prolapse, prior urogynecological surgery, a postvoid residual urine of  $>30$ -50ml, diabetics and women with a history of recurrent UTI are at an increased risk for UTI (1, 2, 3, 9, 10). Non secretors of histo-blood group P1 antigens have increased risk due to

increased adherence of uropathogenic *Escherichia coli* (1, 11, 12). Dysfunctional voiding interrupts laminar flow of urine through the urethra permitting ascending infection (12). In older and institutionalized women, bladder catheterization and functional status deterioration are strongly associated with bacteriuria (1, 13). Chronic constipation leading to overflow fecal incontinence increases the risk of ascending infection (13). Vitamin D aids in antimicrobial activities of macrophages. Women with deficiency of Vitamin D may be at risk for UTI (14).

**Table 2: Risk Factors for UTI**

Risk Factors for UTI
Increase in age
Anatomical defects- Cystocele, prolapse, prior urogynecological surgery, filling defects
Dysfunctional voiding - postvoid residual urine >30-50ml, incontinence, prolonged catheterization
Non secretors of histo-blood group P1 antigens
Functional status deterioration- Alzheimer's disease, Parkinson's disease, stroke
Immunodeficiency
Chronic constipation
Vitamin D deficiency

Persistence of symptoms between UTI episodes and nocturia are negative predictors for recurrent UTI (15). Factors not proven to be associated with UTI are douching, bubble baths, caffeine consumption, non-cotton underwear, sexual activity and postcoital voiding habits (1, 11).

### Organisms Causing UTI

UTI is caused by diverse gram-negative and/or gram positive bacteria and rarely by fungi or viruses (16). Pathogens isolated frequently include gram negative bacteria like *Escherichia coli* (commonest), *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* and gram positive organisms like *Staphylococcus* spp, *Enterococcus faecalis* and group B *Streptococcus* (13, 16). *P. mirabilis* and *Pseudomonas* infections or poly-microbial bacteriuria are common in older women, diabetics or those with long term indwelling catheters (13, 17). Occasionally, fungiuria, caused by *Candida*, *Cryptococcus* or *Aspergillus* or haemorrhagic cystitis caused by BK virus, adenovirus or cytomegalovirus may be seen in immune compromised patients (18, 19).

### Pathogenesis of Recurrent UTI

The urinary biome is formed by a unique community of bacteria. Its disruption predisposes to UTI (20). Antibiotics may render the urine sterile, but there may be recolonization post treatment (20). Bacterial virulence factors (VF) encoded by genes, like adhesins, toxins, protectins and iron acquisition systems, antibiotic resistance and host factors play a role in causing recurrent infections (21, 22, 23). Stimulation of host inflammation occurs due to urothelial bacteria invasion. *E. coli* causing persistence or relapse of UTI has been shown to have a higher biofilm formation capacity in vitro (22, 23). Patients with pyelonephritis were found to have bacteria with the most virulent VFs (23).

### Biomarkers for Diagnosis of UTI

Various biomarkers have been studied to aid in accurate diagnosis, prediction of disease severity and progression and prevention of overtreatment and unnecessary hospitalization.

Leucocyte esterase and nitrite are commonly used as a dipstick test in urine. Leucocyte esterase is found in white blood cells and shows as positive in presence of >5-15 white blood cells/high power field (WBC/hpf). Nitrite indicates presence of bacteria containing enzymes that reduce nitrates to nitrites (24). These tests are good screening tests for UTI in

symptomatic women (25). Uropathogens like *Staphylococcus saprophyticus* do not reduce nitrates and result in false negative result (24).

Serum procalcitonin is a sensitive biomarker to predict renal parenchymal disease (25). However, Stalenhosf JE et al compared the values of mid-regional proadrenomedullin (MR-proADM), procalcitonin (PCT) and C-reactive protein (CRP) and they found that using a cut off of MR-proADM values of 0.8nmol/L was better than procalcitonin and CRP in predicting a severe course in patients with febrile UTI (26).

Urinary heparin-binding protein has been found to have high sensitivity and specificity to differentiate between cystitis and pyelonephritis. Uromodulin, xanthine oxidase, myeloperoxidase and urinary lactoferrin are promising markers to predict bacteriuria (25, 27). Increased levels of granulocyte colony-stimulating factor, macrophage colony-stimulating factor, interleukins 5 and 8 and immunoglobulins(M, G and A) and decreased levels of nerve growth factor and neutrophil gelatinase-associated lipocalin levels have been studied as predictors for recurrent UTI (21). More clinical trials are necessary to confirm their predictive efficacy.

Cell-free DNA have been isolated from urine samples and found to be informative about bacterial and viral composition of the microbiome, antimicrobial sensitivity and host response to infection (28). This may in future be a single test for UTI.

## **DIAGNOSIS OF UTI**

The incidence of asymptomatic bacteriuria increases with age (9, 29). Patients may present with non-specific storage symptoms (polyuria, nocturia, incontinence, urgency and nocturnal enuresis), voiding difficulties (weak or intermittent stream, hesitation or straining) and post micturition symptoms (feeling of incomplete emptying, dribble) (5, 30). Fever, malodorous urine and hematuria may be present (2). There may be associated symptoms of other disorders, e.g. flank pain in ureteric calculus, pelvic prolapse. Very elderly patients with neurological problems, dementia, catheterization or other comorbidity may present without clear symptoms (2, 29).

Symptomatic UTI is diagnosed in patients who present with acute dysuria or fever with the presence of new urinary tract symptoms such as frequency, urgency, new incontinence or costovertebral angle or suprapubic tenderness along with laboratory evidence for urinary infection (9, 29). New onset dysuria is one of the best indicators of symptomatic UTI in older women (9). UTI should be suspected in the presence of non-localizing symptoms and no signs of any other infection (e.g. Pneumonia). In older adults with suspected UTI, a history of infection with multi drug resistant organisms (MDRO) and antibiotic exposure may indicate infection with resistant bacteria (9). In a cognitively impaired patient, a change in character of urine not responding to other interventions like hydration indicates a need for urine tests (9).

A physical examination should be performed to detect any masses or tenderness in suprapubic or costovertebral angle, pelvic organ prolapse and the status of the vaginal epithelium.

## **INVESTIGATIONS FOR UTI**

Urine dipstick test for leucocyte esterase and nitrites is a screening test to detect bacteriuria in patients with symptoms suggestive of UTI. If patients have a high pretest probability of UTI, a negative test needs to be followed up with urine microscopy and urine culture which are standard methods in the diagnosis of UTI (24). Collection of a clean catch mid-urine sample after spreading the labia is advised. In incontinent women, one may do a single in-out catheterization, but this

may cause significant discomfort (4). Urine microscopy should show  $\geq 10$  (WBC/hpf) for diagnosis of UTI. In urine culture, a growth of a single microorganism with  $\geq 10^5$  CFU/mL in an un-catheterized patient or  $10^3$  CFU/mL in a catheterized patient is diagnostic. In symptomatic women, an uropathogen concentration of  $\geq 10^2$  may be sufficient for diagnosis (15, 24). Sensitivity tests help to choose the appropriate antibiotic. Bacteriuria with absence of pyuria is usually due to colonization or contamination(24).

Investigations for diabetes and an ultrasound scan for post void residual urine  $> 30$  mL is required in women with pelvic organ prolapse or recurrent UTI. Cystoscopy, ultrasound of the kidneys, an intravenous pyelogram and a computed tomography scan help in detection of structural urogenital abnormalities, acute pyelonephritis or chronic renal insufficiency (15, 17). Urodynamic study is indicated to evaluate bladder outlet obstruction, storage symptoms or incontinence (31).

Due to the known transient and recurring nature of bacteriuria in older women, a test of cure should not be performed (9).

## **TREATMENT**

Antimicrobial therapy depends on various factors depending on the type of organism, age of the patient, comorbidity and pharmacokinetics of the drugs. The challenges that are faced in postmenopausal women are asymptomatic bacteriuria and recurrent UTI. The key in treatment is to decrease the UTI burden in women as well as to prevent antimicrobial resistance.

## **ASYMPTOMATIC BACTERIURIA**

Screening and treatment of asymptomatic bacteriuria in healthy postmenopausal woman is not recommended by the Infectious Diseases Society of America (IDSA), 2019 (strong recommendation moderate quality evidence) (32).

Asymptomatic bacteriuria is not a predictor of symptomatic UTI and treatment does not decrease the frequency of symptomatic UTI or pyelonephritis. In a study by Cai T et al, the results revealed that asymptomatic bacteriuria itself may offer protection in prevention of symptomatic UTI and treatment may be harmful. This is an independent risk factor in development of UTI(33).

A thesis study tried to elucidate the science behind it. In a placebo controlled inoculation study, *E.coli* 83972 bacteriuria was found to be a shield in preventing symptomatic UTI. The level of mucosal host responses to bacterial challenge showed unique inter individual variation and further genetic analysis revealed polymorphisms in specific genes coding for innate immunity. Possibly owing to this protection offered, the UTI recurrences were fewer and delayed in the inoculated compared to controls (34). This phenomenon was highlighted in other clinical studies in which neither did the treatment improve symptoms nor was there a decrease in incidence of symptomatic UTI. On the contrary they developed antibiotic resistant bacteria later and also had adverse reactions to drugs (35). A study done on ambulatory elderly women revealed that screening and treatment of asymptomatic bacteriuria was not warranted and that UTI was not an independent risk factor for mortality (36).

In addition to IDSA guidelines, the US Preventive services task force and European Association of Urology (EAU) guidelines also recommend not to screen and or treat asymptomatic bacteriuria (37, 38).

## TREATMENT OF ACUTE UNCOMPLICATED CYSTITIS

The antibiotics prescribed for UTI are given in Table 3. Tablet Nitrofurantoin 100 mg twice per day for five days, Trimethoprim/sulfamethoxazole 160/800 mg twice per day for three days (if local resistance pattern for E coli <20%) or Fosfomycin (a single 3-gdose) are the first line drugs advised (39).

The most common antibiotic used in outpatient setting is fluoroquinolones. However, recently, concerns have been expressed because of potential drug resistance and side effects particularly in older patients. Hence, its prescription needs to be restricted as a second line drug only. Restricting its use can help in prevention of drug resistance in the future also (40, 41).

### Should Empiric Treatment be Started for Symptoms without Testing?

Postmenopausal women can have symptoms of dysuria and urgency occasionally, which can be due to atrophic vaginitis. These women can be restrained from immediate treatment with empiric antibiotics. If the symptoms suggestive of cystitis continue, urine analysis may be used to identify infection, as an additional aid only as it is not recommended in guidelines. Bradley MS et al showed that urine analysis added to the cost in groups where the post-test probability of positive urine culture was high (40). In case of poor response to treatment or if the patient has recurrent infection, urine culture should be done and infection treated as per sensitivity (42).

The choice of antibiotic, dose and duration of treatment in elderly women are similar to that of younger postmenopausal women (Grade of Recommendation- C)(1). However, frail geriatric women with significant comorbidities can have UTI with more resistant Gram negative organisms and their management should be tailored as per the complicated UTI protocol (1).

### What is the Duration of Treatment?

In a study looking at the optimal duration of treatment, the results showed that antibiotic therapy for 3 days was not inferior in efficacy when compared to 7 days treatment in a group of symptomatic UTI elderly women (43). As the adverse effects of the drugs were higher in longer duration of therapy this seems to be an option as it is also better tolerated in patients (43). 3 to 6 days of therapy can be used to treat uncomplicated UTI (44).

**Table 3: Antibiotics Prescribed in UTI**

Category	Management options	Level of Evidence	Recommendation
Asymptomatic bacteriuria	Screening and treatment not recommended	B*	Strong#
	Nitrofurantoin 100mg twice daily for five days		
Acute uncomplicated cystitis	Trimethoprim/sulfamethoxazole 160/800mg twice daily for three days (if local resistance pattern for E. coli is <20%)		
	Fosfomycin 3g single dose	C	
	Other antibiotics as per local uropathogen resistance		
Recurrent UTI	Nitrofurantoin 100mg twice daily for five days	B	Strong
	Trimethoprim/sulfamethoxazole 160/800mg twice daily for three days (if local resistance pattern for E. coli is <20%)		
	Fosfomycin 3g single dose		
	Parenteral antibiotics as per uropathogen sensitivity for seven days		
	Self start antibiotics for three days		
Recurrent UTI with failure of intermittent therapy	Continuous low dose antibiotics - Nitrofurantoin 100mg once daily or Trimethoprim 100mg once daily or Fosfomycin 3g once every ten days	B	Moderate

# Levels of recommendation: B- Moderate evidence to support recommendation, C-poor evidence

\* Quality of evidence- C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort.xml>

## RECURRENT UTI

Recurrent UTI is a health hazard as it affects the quality of life in postmenopausal women. It causes recurrent discomfort and women need to be treated with alternative agents after the initial antibiotic management to prevent microbial resistance (10).

Treatment regimen includes nitrofurantoin, trimethoprim-sulfamethoxazole [TMP-SMX], fosfomycin for symptomatic UTI (Strong Recommendation; Evidence Level: Grade B). Treatment dosages are similar to that of acute uncomplicated cystitis as mentioned above (45). For recurrent UTI with symptoms of acute cystitis episodes, short duration antibiotic course is preferred for a maximum seven days. (Moderate Recommendation; Evidence Level: Grade B) (45).

In case of recurrent UTI with culture growing organisms resistant to oral antibiotics, parenteral culture sensitive antibiotics may be administered for a short course for not more than 7 days (Expert Opinion) (45).

Self-start antibiotics are a convenient option for patients with recurrent UTI. Patients can start a prescription of a 3 day course of antibiotic as per recommendation once they are symptomatic without testing. If no improvement occurs in 3 days they need to contact their physician (46).

## ANTIBIOTIC PROPHYLAXIS

Continuous low dose antibiotic may be prescribed when all the above measures fail. After explaining the risks benefits of chronic antibiotic usage, clinicians may use antibiotic prophylaxis for a period of time. (Moderate Recommendation; Evidence Level: Grade B)(45, 46).

Antibiotics advised are tablet Nitrofurantoin 50 mg or 100 mg once daily, Trimethoprim 100 mg once daily or Fosfomycin trometamol 3 g every ten days (38).

The duration of therapy is unclear as there no strong evidence and so needs to be tailored as per patients symptoms. But patients need to be educated that there is a similar risk of recurrent UTI after stopping the antibiotic prophylaxis.

Prevention is the key for recurrent UTI. Although we have limited resources for prevention as on date, the new urobiome research for bladder health and the adaptive immune response management may throw some light in this context providing us with new clinical data (47).

## PREVENTION OF UTI

Various non-antibiotic therapies have been used in the prevention of UTI. They include estrogens, cranberry, ascorbic acid, D-mannose, lactobacilli, methenamine hippurate, herbal therapy, Canephron N and immunotherapy. Many elderly who suffer from incontinence may limit fluid intake which is a major problem that should be addressed. Fluid restriction is not recommended as it could increase the risk of UTI. Increasing oral fluid intake to dilute contaminating bacteria has been frequently recommended by clinicians to prevent recurrent UTI (48).

## ESTROGENS

Estrogen deficiency may be an inciting event for UTI in postmenopausal women. The potential role of hormone therapy in prevention has been evaluated in various studies. In a recent meta-analysis of 8 studies with 4702 patients, vaginal oestrogen treatment was found to reduce recurrent UTI and lower vaginal pH in postmenopausal women. But a similar effect not obtained with oral oestrogen. In 3 studies including 2766 patients, there was no significant difference in the number of recurrent UTI in women on oral oestrogen as compared to placebo (RR1.11; 95% CI, 0.92–1.35) (1, 49). This was also noted in a Cochrane review where the topical oestrogen use reduced the UTI recurrence by 50% and oral oestrogen offered additional risk and no benefit (50).

Oestrogen (especially vaginal) can be used for prevention of UTI (Grade of Recommendation C). Vaginal oestrogen delivered via ring or cream with contemporary dosing schedules helps in prevention of UTI in postmenopausal patients (51).

### Other Non-Antibiotic Therapies

Cranberries contain a compound proanthocyanidin which can reduce bacteriuria by preventing colonisation of *E. coli* in the vaginal mucosa. They also help in reducing the urine pH and thereby decreasing UTI symptoms. Various studies have been conducted, particularly in recurrent UTI and have shown promising results in prevention of UTI. But most of the studies are underpowered with variable population (52).

Ascorbic acid may help in acidification of urine and thus prevent UTI. It is a frequently prescribed home remedy but studies have not shown promising results (52).

D-mannose is an antagonist of the bacterial adhesion FimH. It prevents UTI by stopping the FimH-mediated bacterial adhesion to the uroepithelial cells through a competitive inhibition mechanism. Some studies have shown that D-mannose is a good alternative for treatment and prevention for uropathogenic *E.coli* (53). However, more studies are needed before prescribing D-mannose for postmenopausal women with recurrent UTI.

Methanamine hippurate prevents UTI by helping in acidification of urine. It has shown promising results in the elderly and in catheter related UTI in small studies (54).

Deficiency of *Lactobacillus* species in the vaginal epithelium in postmenopausal women may lead to recurrent UTI. Use of both oral and intravaginal lactobacillus can increase vaginal colonisation of lactobacillus. We need more studies to use it as an alternative treatment to help reduce antibiotic resistance (55).

### Recommendations for Non-Antibiotic Therapies

Good evidence and Level of Evidence A-1 for vaginally applied oestriol cream or oestrogen containing silicone rings to prevent postmenopausal UTI in women >45years (56).

Recommendations level C from a randomized controlled trial with poor evidence to support the recommendation for cranberry capsules at a dose of 500 mg twice daily for prevention of UTI for women >45 years of age (56).

No recommendations for or against have been made for ascorbic acid, cranberry juice or cranberry capsules with high proanthocyanadin content, D-mannose, lactobacilli, methanamine hippurate made as per the article (56).



## IMMUNOTHERAPY

With further evidence on urobiome and immunopathogenesis in recurrent UTI, immunotherapy has been gaining significance. OM-89 (*E. coli* lyophilized lysate) is an active immunostimulant. In a murine model of lipopolysaccharide-induced cystitis, OM-89 induced significant change in vesical Interleukin-6 and interferon gamma levels. This in turn helped in reduction of inflammation in bladder. This technique may be a viable alternative to prevent cystitis but more human studies are needed (57).

## CONCLUSIONS

UTI is very common in postmenopausal women. Many women have recurrence of symptoms in their lifetime, which can be quite debilitating. There has been a lot of research in recent years to understand the pathogenesis of UTI and for biomarkers to aid in early diagnosis of UTI and prognosticating its severity. No treatment is recommended for asymptomatic bacteriuria. Many antibiotic and non-antibiotic medications are being used for treatment and prevention of recurrence. Short courses of antibiotics are effective in cystitis as well as recurrent infections. Continuous low dose antibiotics are recommended only in women non responsive to intermittent therapy. Topical oestrogen is useful in prevention of UTI. More studies are being done to gather evidence for use of other medicines to prevent UTI and they will hopefully be used to improve the quality of life in the post-menopausal elderly women soon.

## REFERENCES

1. Raz, Raul. *Urinary Tract Infection in post menopausal women. Korean J Urol* 2011;52:801-808
2. Hamid R and Losco G. *Pelvic organ prolapse-associated cystitis. Curr Bladder Dysfunct Rep* (2014); 9:175-180.
3. Toz E, Kurt S, Sahin C and Canda MT. *Frequency of recurrent urinary tract infection in patients with pelvic organ prolapse. Research and reports in Urology* 2015;7:9-12
4. Gandhi J, Chen A, Dagur Get al. *Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation and management. Am J Obstet Gynecol* 2016;704-711
5. Henn EW. *Menopause and its effect on the female lower urinary tract. SA Fam Pract* 2010;52(5):405-408
6. Siroky MB. *The aging bladder. Reviews in Urology* 2004; Vol6 Suppl 1, S3- S7
7. Brotman RM, Shardell MD, Gajer Pet al. *Association between the vaginal microbiota, menopause status and signs of vulvovaginal atrophy. Menopause* 2014;21(5):450-458.
8. Gliniewicz K, Schneider GM, Ridenhour BJ et al. *Comparison of the vaginal microbiomes of premenopausal and postmenopausal women. Front. Microbiol.* 2019; 10.193.
9. Mody L and Juthani-Mehta M. *Urinary tract infections in older women: A clinical review. JAMA.* 2014;311(8):844-854.
10. Jung C and Brubaker L. *The etiology and management of recurrent urinary tract infections in postmenopausal women. Climacteric* 2019;22(3):242-49.
11. Ishitoya S, Yamamoto S, Mitsumori K, Ogawa O and Terai A. *Non-secretor status is associated with female uncomplicated pyelonephritis. BJU International* 2012;89:851-854

12. Minardi D, d'Anzeo G, Cantoro Det al. Urinary tract infections in women: etiology and treatment options. *Int J Gen Med* 2011;4:333-343
13. Ariathianto Y. Asymptomatic bacteriuria- Prevalence in the elderly population. *Australian Family Physician* 2011;40(10): 805-808
14. Haghghi M, Shoaee S, Moghaddam MA et al. The association between serum level of Vitamin D and asymptomatic bacteriuria in pre and post menopausal women evaluated between 2011-2016. *Arch clin Infect Dis* 2017;12(3):e62134.
15. Kodner CM and Gupton EKT. Recurrent urinary tract infection in women: diagnosis and management *Am Fam Physician* 2010;82(6):638-643
16. De Nisco NJ, Neugent M, Mull Jet al. Direct detection of tissue-resident bacteria and chronic inflammation in bladder wall of post menopausal women with recurrent urinary tract infection. *J of Molecular biology* 2019;431:4368-4379
17. Al-Badr A and Al-Shaikh G. Recurrent urinary tract infections management in women: A review. *SQU Medical Journal* 2013; 13(3): 359-367
18. Sobel JD, Vazquez JA. Fungal infections of the urinary tract. *World J Urol.* 1999;17(6):410-414.
19. Paduch DA. Viral lower urinary tract infections. *Curr Urol Rep.* 2007;8(4):324-335.
20. Cortes-Penfield NW, Trautner BW and Jump RLP. Urinary tract infection and asymptomatic bacteriuria in older adults. *Infect Dis Clin N Am* 2017;31:673-688
21. Jhang J-F, Kuo H-C. Recent advances in recurrent urinary tract Infection from pathogenesis and biomarkers to prevention. *Tzu Chi Medical Journal* 2017;29(3): 131-137
22. Ejrnæs K. Bacterial characteristics of importance for recurrent urinary tract infections caused by *Escherichia coli*. *Dan Med Bull.* 2011;58(4):B4187.
23. Timothy Kudinha (July 12th 2017). *The Pathogenesis of Escherichia coli Urinary Tract Infection.* 2107, Jul. *Recent Advances on Physiology, Pathogenesis and Biotechnological Applications*, Amidou Samie, IntechOpen,
24. Chu CM and Lowder JL. Diagnosis and treatment of urinary tract infections across age groups. *Am J Obstet Gynecol* 2018;219(1):40-51
25. Masajitas-Zagajewska A and Nowicki M. New markers of urinary infection. *Clinica Chimica Acta* 471 2017;286-291.
26. Stalenhoef JE, van Nieuwkoop C, Wilson DC et al. Biomarker guided triage can reduce hospitalization rate in community acquired febrile urinary tract infection. Open access article, 2018 may, Elsevier Ltd, on behalf of The British Infection Association.
27. Garimella PS, Bartz TM, Ix JH et al. Urinary uromodulin and risk of urinary tract infections : The cardiovascular health study. *Am J Kidney Dis* 2017;69(6):744-751.
28. Burnham P, Dadhania D, Heyang M et al. Urinary cell-free DNA is a versatile analyte for monitoring infections of the urinary tract. *Nature Communications* Open article. DOI:10/1038/s41467-018-04745-0.

29. Beveridge LA, Davey PG, Philips G and McMurdo MET. Optimal management of urinary tract infection in older people. *Clin Interv Aging* 2011;6:173-180
30. Varella LRD, DaSilva RB, deOliveira MCE et al. Assessment of lower urinary tract symptoms in different stages of menopause. *J. Phys. Ther. Sci.* 2016; 28:3116-3121
31. Choudhury S, Das SK, Jana D and Pal DK. Is urodynamic study a necessity for evaluation of lower urinary tract symptoms in postmenopausal female patients? Results of a prospective observational study. *Urol Ann* 2017;9:239-243
32. Nicolle LE, Gupta K, Bradley SF et al. IDSA 2019 Clinical Practice Guideline for the management of asymptomatic bacteriuria. *Clin Infect Dis* 2019 May 2;68(10):e83-e110 doi:10.1093/cid/ciy1121
33. Cai T, Mazzoli S, Mondaini Net al. The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat? *Clin Infect Dis* 2012;55:771-7
34. Sunden F. Asymptomatic bacteriuria protection against, and differential diagnosis towards symptomatic urinary tract infection. Lund University publication ( thesis published)
35. Kang Cheol-In, Kim J, Park DW et al. Clinical Practice guidelines for antibiotic treatment of community acquired urinary tract infections. *Infect Chemother* 2018;50(1):67-100
36. Abrutyn E, Mossey J, Berlin JA et al. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women. *Ann Intern Med* 1994; 120(10):827-33
37. Owens DK, Davidson KW, Krist AH et al. Screening for asymptomatic bacteriuria in adults. US Preventive services task force recommendations statement. *JAMA* 2019;322(12):1188-94
38. Grabe M, Bartoletti R, Johansen TEB et al. European Association of Urology. EAU guidelines on urological infections 2015
39. Colgan R, Williams M. Diagnosis and treatment of acute uncomplicated cystitis. *Am Fam Physicians* 2011;84(7):771-76
40. Bradley MS, Beigi RH, Shepherd JP. A cost-minimization analysis of treatment options for postmenopausal women with dysuria. *Am J Obstet Gynecol* 2019;221(5):P505.e1-505.e7
41. Kallen AJ, Welch HG, Sirovich BE. Current antibiotic therapy for isolated urinary tract infections in women. *Arch Intern Med* 2006;166(6):635-39
42. Treatment of urinary tract infections in nonpregnant women. Clinical management guideline for obstetrician-gynecologist. *ACOG practice bulletin* 2008; 91
43. Vogel T, Verreault R, Gourdeau Met al. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women: A double blind randomized control trial. *CMAJ* 2004;170(4):469-73
44. Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. *Cochrane Database Syst Rev* 2008;(3):CD001535. Published 2008 Jul 16. Reaffirmed 2016

45. Anger J, Lee U, Ackerman AL et al. Recurrent uncomplicated urinary tract infections in women: AUA/CUA/SUFU guideline. *J Urol* 2019;202(2):282-89
46. Dason S, Dason JT, Kapoor A. Guidelines for the diagnosis and management of recurrent urinary tract infection in women. *Can Urol Assoc J* 2011;5(5):316-322
47. DeNisco NJ, Neugent M, Mull J et al. Direct detection of tissue-resident bacteria and chronic inflammation in the bladder wall of postmenopausal women with recurrent urinary tract infection. *J Mol Biol* 2019;431(21):4368-4379
48. Zeng G, Zhu W, Lam W, Bayramgil A. Treatment of urinary tract infections in the old and fragile. ( Published online ahead of print, 2020 Mr 27) *World J Urol.* 2020;10.1007/s00345-020-03
49. Chen YY, Su TS, Lau HH. Estrogen for the prevention of recurrent urinary tract infections in postmenopausal women: a meta-analysis of randomized controlled trials. [Published online ahead of print, 2020 Jun 20]. *Int Urogynecol J* 2020;10.1007/s00192-020-04397-z
50. Arnold JJ, Hehn LE, Klein DA. Common questions about recurrent urinary tract infections in women. *Am Fam Physician* 2016;93(7):560-69
51. Ferrante KL, Wasenda EJ, Jung CE et al. Vaginal estrogen for the prevention of recurrent urinary tract infection in postmenopausal women: A randomized clinical trial [published online ahead of print, 2019 Jun 19]. *Female Pelvic Med Reconstr Surg.* 2019;10.1097/SPV.0000000000000749
52. Wawrysiuk S, Naber K, Rechberger T and Miotla P. Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance- non-antibiotic approaches: asystemic review. *Arch Gynecol Obstet* 2019;300(4):821-828
53. Scribano D, Sarshar M, Prezioso C et al. d-Mannose treatment neither affects uropathogenic *Escherichia coli* properties nor induces stable FimH modifications. *Molecules* 2020;25(2):316
54. Chwa A, Kavanagh K, Linnebur SA and Fixen DR. Evaluation of methanamine for urinary tract infection prevention in older adults- a review of the evidence. *Ther Adv Drug Saf* 2019;10:1-9
55. Gupta V, Nag D, Garg P. Recurrent urinary tract infections in women: how promising is the use of probiotics? *Indian J Med Microbiol* 2017;35(3):347-354
56. Gill CM, Hughes MSA, LaPlante KL. A review of nonantibiotic agents to prevent urinary tract infections in older women. *JAMDA* 21(2020)46-54
57. Haddad JM, Ubertazzi E, Cabrera OS et al. Latin American consensus on uncomplicated recurrent urinary tract infection-2018. *Int Urogynecol J* 2020;31(1):35-44