

# **THE MANAGEMENT OF POST-CATHETERIZATION URINARY TRACT INFECTION IN PATIENTS WITH UNCONTROLLED DIABETES**

## **ABSTRACT**

Urinary tract infections (UTI) are a frequent complication that follows course after hospitalization in patients. The reason for this lies in the fact that the majority of the patients get catheterized during their stay at the hospital, which adds to the risk of infections ultimately. It was seen that the majority of patients who got infected with UTIs were hospitalized patients with diabetes being the most common ones. In such circumstances, the control of situations in which a patient has an advanced case of diabetes and there are significant obstacles due to the combined effects of the immune weakening features of the disease and catheter-related risks. Patient with uncontrolled diabetes are disposed to UTIs because of their immune status being compromised, neuropathy affecting bladder emptying and high levels of sugar in urine providing a great and conducive environment for bacterial growth. Catheterization provides extra risks as it forms a port for micro-organisms to get to the bladder through where the infection gets a higher chance of infection. For patients with uncontrolled diabetes, the diagnosis of UTI can be different as the body could mask or present atypical symptoms in the off-shoot. In the context of non-traditional signs being less severe (for instance, dysuria and urgency) the diagnosis time will likely be delayed and the treatment deferred. Thus, urine culture and sensitivity are essential as they dictate indecent treatment as a method of management. Optimizing glycemic control is essential in managing post-catheterization UTIs in patients with diabetes. Hyperglycemia compromises immune function and promotes bacterial proliferation, thus exacerbating the risk of infection.

Therefore, aggressive management of blood glucose levels through lifestyle modifications, oral hypoglycemic agents, or insulin therapy is crucial in reducing UTI recurrence rates. This review will explore all the reasons that people with diabetes suffer from the atrocities of UTIs, while at the same time, working to reflect upon the current management strategies to deal with this condition as per the current guidelines and recommendations.

**Keywords:** Urinary tract infections, UTI, diabetes mellitus, immunocompromised, hospitalized patients.

## INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) may manifest in different forms among patients as a result of insulin resistance, insufficient insulin secretion, and excessive glucose production.(1)Diabetes is a chronic metabolic disease characterized by elevated blood sugar levels (hyperglycemia) due to impairment of insulin secretion, insulin action, or both.(2) In diabetes, cells are unable to effectively utilize glucose, leading to increased breakdown of fats and proteins for energy, producing ketones as a byproduct. In type 1 diabetes, this can lead to a dangerous condition called diabetic ketoacidosis (DKA), which is characterized by high ketone levels, acidosis, and dehydration.(3) High blood sugar levels because increased urine production as the kidneys filter out excess glucose from the blood. This can lead to frequent urination, especially at night (nocturia), which can cause sleep problems. Dehydration from frequent urination causes excessive thirst as the body tries to replace lost water.(4) Despite high blood sugar levels, cells cannot effectively utilize glucose for energy, resulting in persistent hunger and weight loss. Lack of energy production due to lack of intracellular glucose contributes to persistent fatigue and weakness. The major complications of T2DM are infections that greatly compromise the quality of life of the affected

patients.(5) Among these complicated infections, the most common ones are urinary tract infections (UTIs). They are seen to affect both males and females, with the elderly age group being the most susceptible due to their compromised immunity. The complex pathogenic mechanisms behind UTIs in patients with T2DM involve impaired immune function, poor metabolic control, and neurogenic or neuropathic bladder dysfunction.(3)

T2DM patients develop higher levels of urinary tract infections because of several related reasons. The immune response of people with diabetes is impeded by the metabolic disorders of the disease itself. UTIs become likely as a result. (6)

Similarly to this, the autonomic neuropathy causing incomplete bladder emptying boosts the likelihood. Among those with diabetes, factors like age, glycemic control, and the presence of long-term complications such as diabetic nephropathy and cystopathy further intensify the risk of urinary tract infections.(7)

The wide range of UTIs in patients with T2DM runs from asymptomatic bacteriuria to severe urosepsis with complications such as emphysematous cystitis, pyelonephritis, renal abscesses, and renal papillary necrosis being more prevalent in these people compared to general population.(8) In addition to this, T2DM raises the risk of many types of UTIs such as; community-acquired, healthcare-associated, catheter-associated, and post-renal transplant-recurrent UTIs.(9)

One of the problems of concern is the development of pathogens resistance in UTIs among T2DM patients here. Such examples comprise ESBL-producing Enterobacteriaceae, fluoroquinolone-resistant uro-pathogens, carbapenem-resistant Enterobacteriaceae, and

vancomycin-resistant Enterococci. Fungal UTIs, most often occurring from Candida species, also risk increases in patients with T2DM.(10)

## **THE PREVALENCE AND RISK OF URINARY TRACT INFECTIONS IN DIABETIC PATIENTS**

People with type 2 diabetes mellitus (T2DM) from different categories of UTIs age have a much higher risk of being infected by UTIs. The studies reveal that T2DM is associated with a lot of UTIs among the individuals who contracted this disease which is why this population constitutes the greatest burden in the region.(8)

Using an observational study carried out among UK health practices through the general practitioner research database, it was shown that diabetic patients had a higher incidence rate of UTIs, with the rate of UTIs among diabetic patients being 46.9 per 1000 patients being generally higher than that for people who were not diabetic, which number being 29.9 per 1000 patients.(11) The longer the duration of the female diabetes was diagnosed, the higher the risk of UTIs was. This might just be possible and it is highly suggested for the subject of the duration and the risk of the UTI.(12)

Another study conducted in the USA on health databases grouped over 70,000 T2DM patients revealed an overall diagnosis of UTI was 8.2% for the previous year, showing women (12.9%) had significantly more index compared to men (3.9%). (13)

The observed incidence of increased age is associated with the disease. In 2014, along with researchers from the US, another similar study enlisted data from clinical associations among Americans that confirmed that UTI was higher both among the men with T2DM and among the women with T2DM than their good non-diabetic counterparts.(14)

A more prevalent asymptomatic bacteriuria (ASB) in women because of their anatomical features and a higher incidence of colonization of enteric bacteria has been observed in patients with diabetes mellitus (DM). (15) Research has indicated the magnitude of ASB among people with diabetes may vary from 8 to 26 percent, providing evidence of the consequence of ASB to be taken in this population. (16)

In case-control studies on local and foreign women with diabetes, a significant rise is observed in the incidence of pyelonephritis, which is a rare but severe form of UTI, in the pre-menopausal group compared to non-diabetic women. (17)

A study conducted in Denmark revealed a threefold increase in the likelihood of hospitalization due to pyelonephritis among patients with diabetes mellitus compared to individuals without diabetes. This further elaborates on the heightened risk of severe renal infections in diabetic populations. (18)

In men, diabetes mellitus is associated with an elevated risk of various urogenital complications. This includes an increased susceptibility to acute bacterial prostatitis, the formation of prostatic abscesses, and a higher likelihood of progression to chronic prostatitis. (19) Moreover, diabetic men are at greater risk of developing infections following prostatic manipulations such as trans-rectal prostate biopsy, highlighting the importance of vigilance and appropriate management strategies in this patient group. (20)

Among the microorganisms contributing to urinary tract infections in diabetic patients, the most common include *E. coli*, other Enterobacteriaceae (for example, *Klebsiella* spp., *Proteus* spp., and *Enterobacter* spp.), and Enterococci. These microbial signatures define the complicated microbiological milieu of diabetes linked with urinary tract infections. (21)(22)(23)

They thus have a higher incidence of infecting microorganisms, which are resistant to medications, adding to the complexity of their treatment. Resistant species often encountered in the urinary tract infections of diabetic patients include ESBL-positive Enterobacteriaceae, fluoroquinolone-resistant uro-pathogens, carbapenem-resistant Enterobacteriaceae, and vancomycin-resistant Enterococci.(24) However, the development of antibiotic resistance in E. coli in diabetic UTIs is due to several factors that could be the result of frequent antibiotic use or taking unnecessary antibiotics. Furthermore, the prevalence of nosocomial UTIs and catheter-associated infections among diabetic patients is considered to be associated with the occurrence of resistant microorganisms.(25)

Besides that, type 2 diabetes burns are a very important risk factor for fungal UTIs which is an example of how this is a pathogen very wide spectrum in diabetic individuals. The multi-methodical character of pathogen resistance addresses the necessity of wise antibiotic usage and proper infection control methods for the management of UTIs in diabetic patients.(26)

### **CURRENT MANAGEMENT PROTOCOLS FOR THE TREATMENT OF POST-CATHETERIZATION UTIS IN DIABETIC PATIENTS**

The treatment of urinary tract infections (UTIs) in patients with type 2 diabetes is multifaceted, taking into account various factors that influence the management approach. These factors include the presence of symptoms, the localization of the infection (whether it is limited to the bladder or involves the kidneys), the presence of urologic abnormalities, the severity of systemic symptoms, accompanying metabolic alterations, and renal function. Treatment strategies for UTIs in diabetic patients generally mirror those used for non-diabetic patients.(27)

Antibiotic selection plays a crucial role in the management of UTIs and should be guided by local susceptibility patterns of uro-pathogens. Tailoring antibiotic therapy based on the specific

pathogens prevalent in the local community helps ensure effective treatment while minimizing the risk of antibiotic resistance.(28)

In addition to antibiotic therapy, treatment should address any metabolic complications resulting from the infectious process. This may involve addressing hyperglycemia or other metabolic abnormalities exacerbated by the UTI to promote optimal recovery and prevent complications.(29)

Overall, the treatment of UTIs in patients with type 2 diabetes requires a comprehensive approach that considers the unique needs and characteristics of diabetic individuals while adhering to established principles of UTI management.(29)

Given below is an overview of the different medications that are recommended for the treatment of UTIs in these patients.

For the treatment of different urinary tract infections (UTIs), antibiotics of different types are recommended according to the specific state of the disease in question. Since there are no usual signs of the presence of bacteria in the urinary tract in men and women, treatment of asymptomatic bacteriuria is typically not necessary.

In cases of acute cystitis in women, treatment options include:

- **Nitrofurantoin:** Currently, it is administered orally with a dosage of 100 mg twice or thrice a day for 5 days.
- **Fosfomycin:** Taken with a single 3 g dose orally.
- **TMP-SMX (Trimethoprim-sulfamethoxazole):** Taking a 960 mg dose 2 times a day for 3 days through the oral route.

For complicated lower UTIs, including catheter-associated UTIs, treatment options consist of:

- **Ciprofloxacin:** Administered through oral route 250–500 mg two times a day for 7 to 14 days.
- **Ofloxacin:** Converts to the bloodstream twice a day once a time at the dose of 200 mg for 7-14 days.
- **TMP-SMX:** The treatment is administered through oral route in a dosage of 960 mg taken twice each day for a period of seven to fourteen days.
- **Cefuroxime:** After a 500 mg oral intake twice daily for 7–14 days of treatment.

In cases of uncomplicated pyelonephritis in women, treatment options include:

- **Ciprofloxacin:** Intravenous administration: 400 mg twice daily or a similar regimen for 7 days. Oral administration: A total of 500 mg twice a day for 7 days.
- **Ofloxacin:** Intravenous administration: 400 mg twice daily for 7 days. Oral administration: 400 mg twice a day for 7 days.
- **Gentamicin:** 5 mg/kg of the drug be given intravenously once per day over 7 days.
- **Cefuroxime:** Intravenous administration: take 750 mg, three times per day, for 10–14 days. Oral administration: Take 500 mg twice a day, for 10–14 days.

For complicated pyelonephritis or urosepsis in both men and women, treatment options include:

- **Ciprofloxacin:** Intravenous administration: The dosage schedule is twice a day at 400 mg for 10-14 days.
- **Ofloxacin:** Intravenous injection of disulfiram in the dose of 400 mg b.i.d. times 10-14 days.
- **Gentamicin:** Intravenous injection of 5 mg/kg of the drug daily once. This dosage is given for 10–14 days.

- **Amikacin:** The treatment will be performed intravenously with a dosage of 15 mg/kg once a day for a two-week course of therapy.
- **Piperacillin-tazobactam:** Repeated administration by intravenous route of 4.5 g TDS for 10–14 days.
- **Ertapenem:** Giving a shot of 1 g intravenously, repeated every day for 10–14 days as a single dose is the standard treatment for severe disease.(8)

The optimal duration of antibiotic therapy for catheter-associated urinary tract infections (CAUTI) remains a subject of significant clinical interest. Existing recommendations, largely informed by expert consensus, span a range of durations from 5 to 14 days.(30) Autopsy investigations have provided compelling evidence of the prevalence of occult, chronic pyelonephritis among individuals with prolonged urinary catheterization. (31)

In a trial conducted by Harding et al., the efficacy of single-dose trimethoprim-sulfamethoxazole therapy was comparable to a 10-day course of the same antibiotic in resolving post-catheterization cystitis. However, single-dose therapy demonstrated reduced effectiveness in women over the age of 65. (32)

Dow et al examined the efficacy of 3 days versus 14 days of ciprofloxacin treatment in individuals with spinal cord injury and suspected lower urinary tract infection. Notably, the majority of participants in this study utilized intermittent catheterization, with none having indwelling catheters.(33)

## CONCLUSION

While recent guidelines and publications have heightened awareness regarding catheter-associated urinary tract infections (CAUTI), significant knowledge gaps remain. The lack of recent evidence supporting current treatment strategies for CAUTI underscores the need for new

trials focusing on symptomatic CAUTI to determine optimal treatment duration. Additionally, the challenge of diagnosing CAUTI in catheterized patients highlights the necessity for validated diagnostic algorithms and clinical markers of UTI. Further research into the pathogenesis of ASB transitioning to CAUTI may provide insights into relevant laboratory parameters. While efforts to reduce urinary catheter use are commendable, addressing the needs of patients requiring catheterization remains a critical question, given their heightened risk for CAUTI.

## REFERENCES

1. Azeem S, Khan U, Liaquat A. The increasing rate of diabetes in Pakistan: A silent killer. *Ann Med Surg* [Internet]. 2022 Jul [cited 2024 Mar 18];79. Available from: [https://journals.lww.com/annals-of-medicine-and-surgery/fulltext/2022/07000/the\\_increasing\\_rate\\_of\\_diabetes\\_in\\_pakistan\\_\\_a.13.aspx](https://journals.lww.com/annals-of-medicine-and-surgery/fulltext/2022/07000/the_increasing_rate_of_diabetes_in_pakistan__a.13.aspx)
2. Sapra A, Bhandari P. Diabetes. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Apr 6]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK551501/>
3. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 2010 Jan;33(Suppl 1):S62–9.
4. Genuth SM, Palmer JP, Nathan DM. Classification and Diagnosis of Diabetes. In: Cowie CC, Casagrande SS, Menke A, Cissell MA, Eberhardt MS, Meigs JB, et al., editors. *Diabetes in America* [Internet]. 3rd ed. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018 [cited 2024 Apr 6]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK568014/>
5. Goyal R, Singhal M, Jialal I. Type 2 Diabetes. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Mar 19]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK513253/>
6. Banday MZ, Sameer AS, Nissar S. Pathophysiology of diabetes: An overview. *Avicenna J Med*. 2020 Oct 13;10(4):174–88.
7. Ahmed AE, Abdelkarim S, Zenida M, Baiti MAH, Alhazmi AAY, Alfaifi BAH, et al. Prevalence and Associated Risk Factors of Urinary Tract Infection among Diabetic Patients: A Cross-Sectional Study. *Healthcare*. 2023 Mar 15;11(6):861.

8. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. *Diabetes Metab Syndr Obes Targets Ther.* 2015 Feb 26;8:129–36.
9. Al Qurabiy HE, Abbas IM, Hammadi ATA, Mohsen FK, Salman RI, Dilfy SH. Urinary tract infection in patients with diabetes mellitus and the role of parental genetics in the emergence of the disease. *J Med Life.* 2022 Aug;15(8):955–62.
10. Ahmad S, Hussain A, Khan MSA, Shakireen N, Ali I. Diabetes mellitus and urinary tract infection: Causative uropathogens, their antibiotic susceptibility pattern and the effects of glycemic status. *Pak J Med Sci.* 2020;36(7):1550–7.
11. Hirji I, Guo Z, Andersson SW, Hammar N, Gomez-Camirero A. Incidence of urinary tract infection among patients with type 2 diabetes in the UK General Practice Research Database (GPRD). *J Diabetes Complications.* 2012;26(6):513–6.
12. Hammar N, Farahmand B, Gran M, Joelson S, Andersson SW. Incidence of urinary tract infection in patients with type 2 diabetes. Experience from adverse event reporting in clinical trials. *Pharmacoepidemiol Drug Saf.* 2010 Dec;19(12):1287–92.
13. Yu S, Fu AZ, Qiu Y, Engel SS, Shankar R, Brodovicz KG, et al. Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S. *J Diabetes Complications.* 2014;28(5):621–6.
14. Fu AZ, Iglay K, Qiu Y, Engel S, Shankar R, Brodovicz K. Risk characterization for urinary tract infections in subjects with newly diagnosed type 2 diabetes. *J Diabetes Complications.* 2014;28(6):805–10.
15. Colgan R, Nicolle LE, McGlone A, Hooton TM. Asymptomatic bacteriuria in adults. *Am Fam Physician.* 2006 Sep 15;74(6):985–90.
16. Nicolle LE. Asymptomatic bacteriuria. *Curr Opin Infect Dis.* 2014 Feb;27(1):90–6.
17. Papazafiropoulou A, Daniil I, Sotiropoulos A, Balampani E, Kokolaki A, Bousboulas S, et al. Prevalence of asymptomatic bacteriuria in type 2 diabetic subjects with and without microalbuminuria. *BMC Res Notes.* 2010 Jun 17;3:169.
18. Renko M, Tapanainen P, Tossavainen P, Pokka T, Uhari M. Meta-analysis of the significance of asymptomatic bacteriuria in diabetes. *Diabetes Care.* 2011 Jan;34(1):230–5.
19. Chávez-Reyes J, Escárcega-González CE, Chavira-Suárez E, León-Buitimea A, Vázquez-León P, Morones-Ramírez JR, et al. Susceptibility for Some Infectious Diseases in Patients With Diabetes: The Key Role of Glycemia. *Front Public Health.* 2021 Feb 16;9:559595.
20. Wen SC, Juan YS, Wang CJ, Chang K, Shih MCP, Shen JT, et al. Emphysematous prostatic abscess: case series study and review. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis.* 2012 May;16(5):e344-349.

21. Kofteridis DP, Papadimitraki E, Mantadakis E, Maraki S, Papadakis JA, Tzifa G, et al. Effect of diabetes mellitus on the clinical and microbiological features of hospitalized elderly patients with acute pyelonephritis. *J Am Geriatr Soc*. 2009 Nov;57(11):2125–8.
22. Sobel JD, Fisher JF, Kauffman CA, Newman CA. Candida urinary tract infections--epidemiology. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2011 May;52 Suppl 6:S433-436.
23. Lim JH, Cho JH, Lee JH, Park YJ, Jin S, Park GY, et al. Risk factors for recurrent urinary tract infection in kidney transplant recipients. *Transplant Proc*. 2013 May;45(4):1584–9.
24. Inns T, Millership S, Teare L, Rice W, Reacher M. Service evaluation of selected risk factors for extended-spectrum beta-lactamase Escherichia coli urinary tract infections: a case-control study. *J Hosp Infect*. 2014 Oct;88(2):116–9.
25. Venmans LM a. J, Hak E, Gorter KJ, Rutten GEHM. Incidence and antibiotic prescription rates for common infections in patients with diabetes in primary care over the years 1995 to 2003. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis*. 2009 Nov;13(6):e344-351.
26. Yu S, Fu AZ, Qiu Y, Engel SS, Shankar R, Brodovicz KG, et al. Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S. *J Diabetes Complications*. 2014 Sep 1;28(5):621–6.
27. Fünfstück R, Nicolle LE, Hanefeld M, Naber KG. Urinary tract infection in patients with diabetes mellitus. *Clin Nephrol*. 2012 Jan;77(1):40–8.
28. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2005 Mar 1;40(5):643–54.
29. Nicolle LE, Zhanel GG, Harding GKM. Microbiological outcomes in women with diabetes and untreated asymptomatic bacteriuria. *World J Urol*. 2006 Feb;24(1):61–5.
30. Wazait HD, van der Meullen J, Patel HRH, Brown CT, Gadgil S, Miller RA, et al. Antibiotics on urethral catheter withdrawal: a hit and miss affair. *J Hosp Infect*. 2004 Dec;58(4):297–302.
31. Wazait HD, Patel HR, van der Meulen JHP, Ghei M, Al-Buheissi S, Kelsey M, et al. A pilot randomized double-blind placebo-controlled trial on the use of antibiotics on urinary catheter removal to reduce the rate of urinary tract infection: the pitfalls of ciprofloxacin. *BJU Int*. 2004 Nov;94(7):1048–50.
32. Harding GK, Nicolle LE, Ronald AR, Preiksaitis JK, Forward KR, Low DE, et al. How long should catheter-acquired urinary tract infection in women be treated? A randomized controlled study. *Ann Intern Med*. 1991 May 1;114(9):713–9.
33. Dow G, Rao P, Harding G, Brunka J, Kennedy J, Alfa M, et al. A prospective, randomized trial of 3 or 14 days of ciprofloxacin treatment for acute urinary tract infection in patients

with spinal cord injury. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 Sep 1;39(5):658–64.

UNDER PEER REVIEW