

The Link between Diabetes and Urinary Tract Infections

Sunil Kumar[#], Dinesh Nalage^{\$}, Mohammad Aslam[@], Shoorvir Singh[#] and Umesh Kumar^{%,*}

[#]Department of Biotechnology, GLA University, Mathura, Uttar Pradesh - 281 406, India

^{\$}Department of Biotechnology, Maulana Azad College of Arts, Science & Commerce, Aurangabad,
Maharashtra - 431 003, India

[@]Department of Surgery, JN Medical College, Aligarh Muslim University, Aligarh,
Uttar Pradesh - 202 001, India

[%]Chandigarh University, NH-5, Chandigarh-Ludhiana Highway, Gharuan, Mohali, Punjab - 140 413, India

*Email: umeshkumar82@gmail.com

ABSTRACT

People having diabetes mellitus, urinary tract infections are more prevalent, more serious, and have worse consequences. The presence of resistant microbes is a common factor in their occurrence. Urinary Tract Infections (UTI) are more common in these patients for a variety of reasons, including autonomic neuropathy, impaired immune system function, inadequate metabolic regulation, and incomplete bladder emptying. The present review is an amalgamation of existing literature to understand link between diabetes and UTI and the microorganisms responsible for Urinary Tract Infection (UTI) and colonisation in diabetic patients, as well as natural treatments effective in treating and preventing urological problems. For solving the purpose, A review of existing literature on UTIs in diabetic patients was conducted, with a focus on the microorganisms responsible for UTI and colonisation, as well as natural treatments for urological problems. It was observed from the literatures that the UTIs are more common in diabetic patients due to impaired immunity and incomplete emptying of the bladder. The prevention depends on the severity and extent of the infection. Apparently, antibiotics are resistant to urinary tract infections, making treatment more difficult. Upper urinary tract infections are common in diabetics. Natural treatments have shown promise in treating and preventing UTIs in diabetic patients, although more research is needed to confirm their efficacy. UTIs are a serious issue for diabetics, who are susceptible to infections due to a weakened immune system and bladder failure. Effective treatment is becoming more challenging due to increasing antimicrobial resistance. Natural treatments may offer a promising alternative, but further research is needed to explore their potential benefits for UTIs in diabetic patients.

Keywords: Anti-microbial; Diabetes; Microorganisms; Pathogens; Urinary tract infection

1. INTRODUCTION

The prevalence of Diabetes Mellitus (DM) is a significant and growing global public health concern, especially in developing countries such as India¹. Patients with DM are at an augmented risk for Urinary Tract Infections (UTIs) due to various factors². Clinicians must be aware of the potential for DM to cause damage to multiple organs, including the nervous system, blood vessels, and the retina, leading to complications such as heart attacks, strokes, blindness, neuropathy, low blood pressure, foot ulcers, and kidney failure³⁻⁴. Hyperglycaemia can inhibit antimicrobial function through glucose phosphate dehydrogenase⁵. Additionally, defective immunity, including impaired cell-mediated immunity, complement function defect and defective neutrophil function, can increase the adherence of microorganisms to the urinary tract, promoting their growth and increasing the risk of infection⁶. In individuals

with diabetes, cellular pathology, age, metabolic syndrome, and long-term consequences all increase the risk of UTI⁷. UTIs can present in various forms, including asymptomatic bacteriuria, cystitis, pyelonephritis, and severe urosepsis⁸. Community-acquired, catheter-associated, and post-renal transplant UTIs are most commonly caused by Diabetes Mellitus (DM), and patients with DM are more likely to develop infections with increasingly resistant microbes, including fungal pathogens such as *Candida*⁹. Urinary glucose in diabetic patients is associated with compromised immune and bladder function, increasing the risk of UTI¹⁰. *Escherichia coli* (*E. coli*) is the most commonly isolated microorganism in diabetic and non-diabetic patients with UTI. Multidrug-resistant strains of UTI-causing pathogens are increasing in prevalence worldwide. In addition to evaluating multiple risk factors for UTI in individuals with type 1 and type 2 diabetes, this review identifies the most common bacterial causes of UTI and their treatment in patients with DM.

2. EPIDEMIOLOGY

2.1 Prevalence and Incidence

Compared to patients without Diabetes Mellitus (DM), those with DM have a higher incidence of asymptomatic bacteriuria (ASB) and other bacterial infections, such as UTIs. Women with DM had 26 % of ASB compared with 6 % of women without DM. Several studies have shown that patients with diabetes have a higher incidence of UTIs¹⁰. The Canadian study shows that in patients with DM, the range of relevant risk lies between When compared to patients without diabetes, the corresponding confidence intervals were 1.39 (99 % CI 1.36-1.43) and 1.43 (99 % CI 1.39-1.46). The odds ratio for patients with type I diabetes in the cohort Dutch study was 1.56 (95 % CI 1.13-2.15), for type 2 diabetes in patients 1.21 (95 % CI 1.07-1.38), and for postmenopausal women with diabetes it was 2.2 (95 % CI 1.6-3.0) compared to the control group.

2.2 Complications

Patients with DM are at an more risk of infections such as emphysematous pyelonephritis. A Spanish study found that patients with DM are more prone to developing bacteraemia infections, with UTIs being the most common type of infection in patients with DM compared with those without DM¹¹. The incidence rate of bacteraemia per 1000 admissions was 26.8 in patients with DM and 15.5 in those without DM. In 8.7 out of 1000 DM patients and 2.2 out of 1000 non-DM patients, the urinary tract was

the site of infection. The etiology of *E.coli* was 8.9 in patients with DM and 3.4 in patients without DM. The Spanish and Canadian cohort studies both showed higher mortality rates in patients with DM outside the hospital associated with those inside the hospital¹².

2.3 Pathogenesis

The risk of UTI is elevated in due to specific mechanisms associated with diabetes. High glucose levels in urine create an environment conducive to the growth of pathogenic bacteria, which can lead to UTI¹³. Studies have shown that the risk of UTI in diabetic patients is not associated with HbA1c levels representing glycosuria. Inhibitors of sodium glucose transporter 2, which increase urinary glucose levels, are also not associated with an increased incidence of UTI. Pyelonephritis and associated renal disorders, including emphysematous pyelonephritis, can be caused by proliferation of pathogenic microorganisms due to elevated glucose levels in renal tissue Impaired immunity in diabetics also contributes does not cause UTI. Patients with diabetes and ASB have lower levels of cytokines such as IL-6 and IL-8 than those without diabetes. Autonomic neuropathy can result in urine retention and bladder dysfunction, which hinders bacterial clearance through micturition, leading to bacterial growth in urine.

Multiple factors include glucose in urine, neutrophil dysfunction, and bacteria adhering to uroepithelial cells more effectively contribute to UTI in diabetic patients.

Table 1. Complications and pathogenicity related to UTI in diabetic patient

S. No.	Complication	Pathogenicity
1.	Variable su-prapubic pain accompanied by dysuria, malodorous urine, and abdominal pain	Because of their virulence factors, bacteria begin to colonise in the urethra and migrate upward. Here, the bacterial colonies attach to the uroepithelium's surface, grow in quantity, and induce infection.
2.	impairment of the heart, kidney, nerves, eyes, blood vessels, and other body organs	Patients with immunocompromised and long-term sick conditions are more susceptible to bacteremia due to increased bacterial adhesion and decreased antibiotic susceptibility from glucose 6-phosphate dehydrogenase.
3.	cystitis, pyelonephritis, and abdominal pain.	High glucose levels in diabetics promotes bacterial growth. Decreased humoral, cellular, and innate immunity are important factors in urinary tract infections, and increased cross-enzymal glucose provides favorable conditions for bacterial growth and dissemination.
4.	Emphysematous pyelitis, emphysematous pyelonephritis, xanthogranulomatouspyelonephritis, renal or perirenal abscess, renal parenchymal necrosis, and emphysematous cystitis.	The urethral opening becomes colonised by the gastrointestinal tract, which also contaminates the periurethral area. The bacteria travel from the urethra to the bladder, where they settle on the superficial cells through pili. Adhesins trigger the immune system, but some bacteria manage to get past them. Here, bacteria grow and produce biofilm, and the host cells are destroyed by the protease and toxins these bacteria release. They travel to the kidney, where they colonise and induce pyelonephritis, and they release some helpful nutrients to encourage the growth of the bacteria.
5.	It is usually asymptomatic and can sometimes irritate the nervous system.	Urinary tract infections (UTIs) associated with catheter use are caused by the colonisation of the bladder by organisms that enter through urethral catheters. This colonisation creates an environment that is conducive to bacterial adhesion and mucosal irritation. The presence of a urinary catheter is the main risk factor for bacteriuria.

Age, metabolic control, autonomic neuropathy, diabetic nephropathy, and vascular complications are other factors that increase the risk of UTI in diabetic patients¹³. Despite the high glucose concentrations in urine, studies have not found a correlation between HbA1C levels and UTI infections in diabetic patients^{14,15}. Pyelonephritis and other renal problems like emphysematous pyelonephritis are caused by microorganisms growing and multiplying in the renal parenchyma due to the high glucose level in the parenchyma^{16,17}. One possible factor in the development of UTIs in diabetic patients is immune system dysfunction, which can manifest in various ways, including cellular, humoral, and innate dysfunctions¹⁸. When the genitourinary tract is affected by autonomic neuropathy, it can lead to problems with voiding and retention of urine. Additionally, micturition, the physical process of removing bacteria from the body, is reduced, making it easier for bacteria to grow. (Table 1; Figure 1).

Bacteria and fungi are examples of microorganisms that can inhabit aquatic environments and survive in water. These microorganisms require pathogenic factors to infect and thrive in a protective environment¹⁹. Infections can arise when bacteria establish a presence in the urethra, leading to the urinary bladder infection. If left untreated, urinary tract infections can progress to cystitis²⁰. *E. Coli* is the most common cause of cystitis and, if left

untreated, can enter the bladder through the bladder and cause pyelonephritis. Adverse effects of pyelonephritis may include renal failure, viral infections, and urosepsis. *E. coli* can form in drains and other contaminated environments despite the presence of the human immune system. The harmful effects of *E. coli* are believed to be facilitated by its adhesions, flagella, toxins and fimbriae which help to adhere, stabilize and infect.

Among uropathogens, *Enterococci*, *Proteus mirabilis*, and *Klebsiella* are the most common, and fungi play a significant role in urinary tract infections.

2.4 Pathogens

The most prevalent causative agents of UTIs in diabetic patients are Bacteria such as *Escherichia coli*, *Klebsiella*, *Proteus*, *Enterobacter*, etc.

Diabetics often have resistant bacteria, such as Enterobacteriaceae that test positive for extended-spectrum β -lactamase, uropathogens resistant to fluoroquinolones, Enterobacteriaceae resistant to carbapenems, and vancomycin-resistant enterococci. Possible increased incidence in UTIs, which is also associated with microbial resistance, and multiple antibiotics given to diabetic patients with silent or symptomatic UTIs often associate type 2 diabetes with fungal UTI²¹.

2.5 Fungal Infection

Fungal Urinary Tract Infections (UTIs) are frequently caused by the colonisation of the urinary tract by fungi, particularly *Candida* species. Such infections are more common in elderly individuals who may experience difficulty in fully emptying their bladder due to urethral narrowing. As urine acts as an enriching medium for fungi, colonisation can lead to the proliferation of these microorganisms. Additionally, catheter-associated UTIs are another source of fungal infections. When patients are catheterised and catheters are not removed or changed at appropriate intervals, fungal colonisation can occur, leading to catheter-associated UTIs²².

2.6 Immune-Suppression

In individuals with compromised immune systems, bacteria and fungi can cause infections due to the weakened immunity of the host. This is especially evident in children, the elderly, cancer patients, kidney transplant recipients, and other immunocompromised individuals who are unable to effectively combat urinary tract infections due to their weakened immune response. When bacteria or fungi invade the urinary tract of these patients, they can overcome the weakened immune defences. While immunological factors such as phagocytic cells, natural killer cells, and antibody production do play a role in fighting off pathogenic agents in the urinary tract, they are not as effective in immunocompromised individuals as they are in healthy individuals²³. As a result, the immunity of immunocompromised patients is weakened against bacterial and fungal infections.

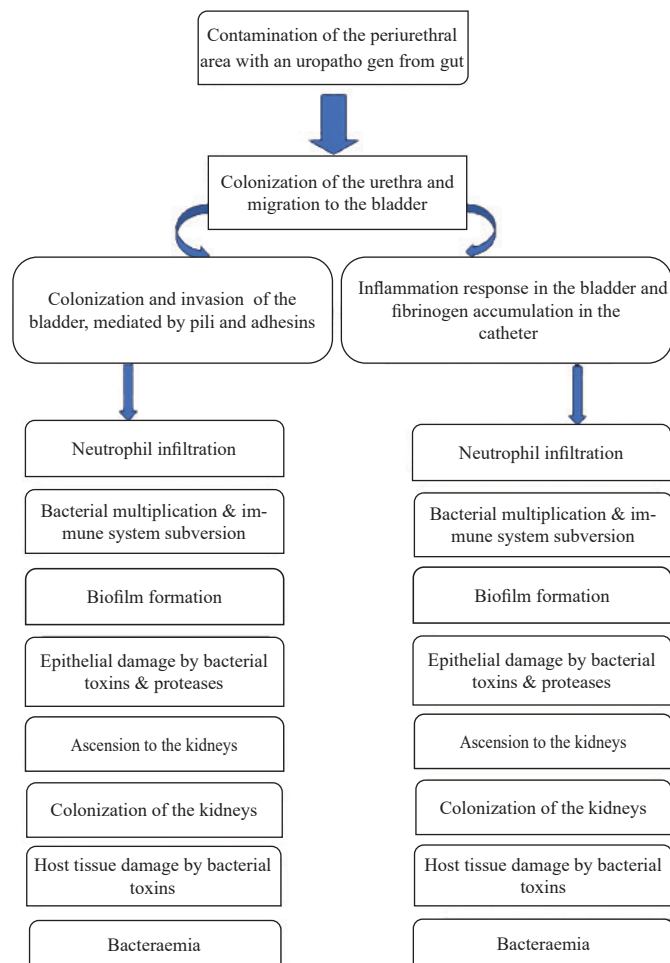


Figure 1. Schematic representation of the colonisation of symptomatic bacteriuria and pathological changes.

2.7 Risk Factor

In our country, females have a high odd of developing Urinary Tract Infection (UTI) compared with males due to various factors such as having a shorter urethra, changes in vaginal pH, and hygiene practices., sexually active women are also more vulnerable to UTI. Prolonged use of antibiotics can cause the colonisation of resistant pathogenic strains in the urinary tract. Other factors that contribute to UTI are defects in host defense mechanisms such as impaired activation of neutrophils, prolonged diabetes, metabolic disorders, bladder dysfunction, and advanced age of patients.

2.7.1 Old Age

As individuals age, the urethra may become narrower, which can lead to difficulty in fully emptying the urinary bladder. When urine remains in the bladder, it can provide a favourable environment for the growth of pathogenic bacteria, allowing them to colonize and cause infection. Additionally, older patients may have weakened immune defences against the colonisation and growth of these pathogens in the urethra.

2.7.2 Women

Compared to males, women have a smaller urethral structure, which leads to a lack of flushing of microorganisms from the urinary tract. As a result, some bacteria might not be able to be eliminated and instead attach themselves to the urethral cavity, where they might colonise and lead to an infection of the urinary tract. a neutral or basic gut pH can promote the growth of harmful diseases, which can lead to infection in the urinary tract.

2.7.3 Diabetes

Diabetics often suffer from urinary tract infections due to a weakened immune system caused by nerve and blood vessel damage. Diabetes juice contains a lot of sugar, which gives pathogens more energy and faster growth. In people with diabetes, pathogens can spread into the stool, causing infection and possibly clinical symptoms.

2.7.4 Catheterisation

Due to the presence of *Candida* on the catheter, prolonged catheterisation increases the risk of UTI. Through the catheter, pathogens can enter the urethra and cause disease.

2.7.5 Impaired Host Defence

People with weakened immune systems, neutrophil dysfunction, cancer patients, kidney transplant recipients, and HIV patients are at risk for cancer. Due to their weakened immune system, they are less capable of fighting off the virulent factors of infectious bacteria, making them more vulnerable to infection by pathogenic agents²⁴.

2.7.6 Antibiotics Resistance

Long-term use of antibiotics increases the risk of developing urinary tract infections caused by antibiotic-resistant strains of microorganisms²⁵⁻²⁶.

2.8 Symptoms of Urinary Tract Infection

The symptoms of UTI include prolonged urination. During urination, there is a burning feeling Pain in the abdomen. Urine that is reddish-brown in colour and smells awful. There is also an increased number of pus cells and beta-carcinoma.

2.9 Techniques

The identification of urinary tract infections is carried out using the culture technique. Agar lacking cysteine lactose electrolyte was used for the culture of waterborne pathogens. Water samples were filled using a standardised loop. Culture plates are tested after incubation at 37 °C for 24 to 48 hours.

2.10 Diagnosis

To diagnose the presence of urinary tract infections, it is necessary to count a single bacterial colony with 100,000 CFU/ml or more. Leukocyte counts are especially important when diagnosing urinary tract infections; A value greater than five indicates pyuria. Results from culture plates are also evaluated in conjunction with patient age, sex, history, and diabetic status. A positive result is indicated by the presence of bacteria in a urine sample during microscopic examination, while a negative result may occur when bacterial counts are low or when bacteria are unable to convert nitrate to nitrite. Obtaining a urine culture before starting antibiotic treatment is crucial in diagnosing urinary tract infections. Symptoms experienced by diabetic patients due to impaired excretory system function may also be indicative of urinary tract infection.

2.11 Use of Medicinal Plants

The use of medicinal plants and their products for therapeutic purposes dates back to ancient times. Humans likely learned this skill from animals, which have natural remedies for various health issues. Medicinal plants are a rich source of bioactive compounds that can be used to create novel medications. The use of these plants has many advantages, including reduced side effects, increased patient acceptance, cost savings, and biochemical regeneration. Studies show that phytochemicals can improve antibiotic efficacy by modifying or inhibiting multidrug resistance.

Certain diuretic plants, such as *Urtica dioica*, the fruit of *Petroselinum crispus*, the root of *Levisticum officinale*, and *Solidago* spp. herb, increase urine volume and can aid in flushing out potential hazards in both healthy individuals and those with urinary diseases. *Vaccinium macrocarpon* seeds, leaves of the genus *Juniperus*, and *Arctostaphylos uva-ursi* are associated antibacterial plants

that produce antibiotics that can kill microorganisms or prevent their adhesion to epithelial cells, and prevents both acute and chronic UTIs for example. Berberine, found abundantly in the roots of *Mahonia aquifolium* and *Hydrastis canadensis* L., is effective against various bacteria as well as *Proteus* and *E. coli*. *Coli* strains can prevent infection by releasing cell adhesion by reducing the number of RBCs, tumor cells, and crystals in urine, corn (*Zea mays* L.) and silk (outer fiber fragments) soaking mixed inclusion significantly reduced UTI symptoms in patients without adverse effects. Plants from several families, including Apiaceae, Asteraceae, Cucurbitaceae, Fabaceae, and Malvaceae, have had potent anti-UTI properties^{27,28}. Table 2 lists some plants' ethnomedicinal uses for treating persistent and recurrent UTI.

2.12 Prevention

- Follow a healthy diet; avoid sugar and the things responsible for bad cholesterol.
- Having an active day schedule
- Avoid chewing tobacco and smoking.
- Always take care of genitals
- Keep foot neat and clean

3. DISCUSSION

The aim of this review aimed to evaluate the incidence of symptomatic and asymptomatic bacteriuria in with poor glucose control, identify the most common bacterial species, and determine the most effective treatments for Urinary Tract Infections (UTIs) in this population²⁹. Studies have suggested that diabetic patients are more susceptible to various infections, as their immune systems are compromised³⁰. Urinary tract infections may be the first manifestation of diabetes and can lead to serious complications such as bloodstream infections. Older age has been identified as a important risk factor for UTIs in diabetic patients. The review summarizes the average incidence of UTIs and prevalent bacterial species in diabetic patients in a particular region, as well as the drug of choice that is effective for many patients with diabetes. However, the efficacy of antibiotics may vary over time due to bacterial mutations, highlighting the importance of ongoing research. Herbal treatments are considered safe but may take longer to work than conventional medications for acute infections. When it comes to avoiding infections and their aftereffects, they work better. Herbal extracts contain therapeutic antioxidants and glycosides that may prevent pathogenic bacteria from attaching to host cells and hindering further pathogenesis. Nevertheless, more research is needed to confirm these findings.

4. CONCLUSION

Urinary Tract Infection (UTI) is a prevalent health issue in patients with diabetes, and catheter-associated urinary tract infections should be prevented by following standard protocols. Proper hygiene practices should be

followed by sexually active women to avoid infections. The best antibiotic should be selected by antibiotic testing isolated from diabetic UTI patients, and UTI treatment may depend on the length and severity of the infection. Antibiotics completion of a thorough evaluation is essential to prevent multidrug resistance.

Furthermore, the molecular activity of various phytochemicals found in medicinal plants against uropathogens and uropathogenesis warrants further investigation. The effectiveness of these traditional remedies can be reinforced through scientific validation, such as positive clinical trial results. This will contribute to the prevention of these widespread and uncomfortable health issues.

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CONTRIBUTORS

Mr. Sunil Kumar is a PhD scholar from Department of Biotechnology, GLA University, Mathura. Kumar has 14 years of experience in microbiology and currently employed in the

Microbiology Lab of Amrita Institute of Medical Science, Faridabad, India.

He has contributed in original draft preparation, and visualisation.

Dr. Dinesh Nalage is working as Assistant Professor at Institute of Biosciences and Technology, MGM University, Aurangabad, India. His field of specialisation is molecular biology and infectious diseases in human. He has been actively involved in research and training organising activities in molecular biology and sequencing for the last 15 years.

He helped in literature review.

Prof. Mohammad Aslam is MS (General Surgery) from JNU Medical College, AMU, Aligarh. He is professor of Surgery in the same department since 2010. He holds his interest in Laparoscopic surgery and Urology.

He has reviewed final manuscript.

Prof. Shoorvir Singh is PhD in Veterinary Microbiology (1998) from Veterinary College Mathura (CSA University of Agriculture & Technology, Kanpur). Currently He is Head, Department of Biotechnology, GLA University, Mathura.

He has contributed by editing and reviewing the final manuscript.

Dr. Umesh Kumar obtained his PhD in Epigenetic Regulation in Breast Cancer from Dr B.R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi. Currently, He is working as Associate Director in Chandigarh University, Mohali, Punjab. His keen interest is in HPV infection, Breast Cancer Epigenetics, Stem Cell Biology & Molecular Medicine.

He has contributed towards conceived the study, manuscript preparation, designed the experiment data collection, assisted in the biochemical analysis experiments and literature analysis.