



## Research Article

# Study Of Diabetic Complication Of Urinary Tract Infection: A Review

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### ABSTRACT

Urinary tract infections are more common in the diabetic patients. Diabetic patients are severely affected with urinary tract infection. Treatment of UTI without proper diagnosis may lead to antimicrobial drug resistance. Treatment with antimicrobial agents should be started on the basis of culture reports. Only bacteriuria with symptoms of UTI should be treated with antibiotics to avoid the spread of drug resistant pathogens in the society. This practice can reduce the morbidity and mortality in diabetic patients suffering from urinary tract infection. The multidrug resistant pathogens are a challenge to society. Urinary tract infection may present as asymptomatic bacteriuria, acute uncomplicated urinary tract infection in women (acute cystitis or acute non obstructive pyelonephritis), complicated urinary tract infection in men or women with underlying abnormalities of the genitourinary tract and, in men, acute or chronic bacterial prostatitis. Infection is often recurrent, either as relapse when an organism persists within the genitourinary tract and recurs following treatment, or reinfection with new organisms introduced into the genitourinary tract.

### INTRODUCTION

Clinical observations suggest an association between diabetes mellitus and an increased susceptibility to and severity of infections. [1] Urinary tract infection is one of the most common infections. It occurs with increased frequency and severity in diabetic populations, and is more likely to be associated with complications. [2] This review summarizes the current understanding of this important infection in diabetic patients. Type 2 diabetes mellitus is a heterogeneous group of

disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Patients with type 2 diabetes mellitus are at increased risk of infections, with the urinary tract being the most frequent infection site. [3,4] Diabetes is also associated with worse outcomes of UTI, including longer hospitalizations and increased mortality. The increased risk of UTI among diabetic patients, coupled with the increase in the incidence of type

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2 diabetes mellitus worldwide in recent years, may impose a substantial burden on medical costs. [5] In addition, the high rates of antibiotic prescription, including broad-spectrum antibiotics, for UTI in these patients may further induce the development of antibiotic-resistant urinary pathogens. In this review, we will focus on the various types of UTI in this population, their frequency, risk factors, diagnosis, prognosis, and when and what treatment should be administered. [6]

## DIABETES

Diabetes is a disease that occurs when your blood glucose also called blood sugar, is too high. Blood glucose is your main source of energy and comes from the food you eat. Diabetes is a persistent disease. This disease is characterized by increase of blood glucose level. The reasons of increase of blood glucose level may be either insufficient production of insulin, a hormone that regulates the blood glucose level, or the insulin produced cannot be used properly. Frequent urination, increased thirst, and increased hunger are the common symptoms of diabetes. Uncontrolled blood sugar level can cause many complications. These complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the eyes, diabetic ketoacidosis, etc. Diabetes mellitus can be described as group of metabolic disorders causing increase in blood sugar level due to defect in insulin secretion, insulin action, or both. [7] The digestive system breaks carbohydrates, sugars, and starches found in many foods into glucose, which is a type of sugar that enters the bloodstream. [8] By the action of the hormone insulin, cells throughout the body absorb glucose and use it for energy. Diabetes develops when the body does not produce enough insulin or is unable to use insulin effectively or both. Insulin is produced in the pancreas. Clusters of cells found in the pancreas are called islets. Pancreas having

islets, which contain beta cells, produces insulin and releases it into the blood.

## Types of Diabetes

- Type 1 diabetes also called as insulin-dependent diabetes mellitus (type I diabetes occurs due to  $\beta$ -cell destruction, usually leading to absolute insulin deficiency).
- Type 2 diabetes also called as noninsulin-dependent diabetes mellitus (type II diabetes occurs due to a progressive loss of insulin secretion).
- Gestational diabetes mellitus (GDM) (diabetes detected in the second or third trimester of pregnancy that is not clearly overt diabetes).

## URINARY TRACT INFECTION IN DIABETICS

Infections are frequent causes of morbidity and mortality in diabetic patients. Evidence suggesting that urinary tract infection (UTI) is the most common bacterial infections among diabetic patients. High glucose concentration in the urine can provide a rich source of nutrients for bacteria. [9-10] Therefore, bacteria can multiply and make foundation for infection; also, high glucose concentration in the urine can allow urinary colonization by microorganisms. Moreover, some of the immunological defects like impaired neutrophil function, reduced T cell-mediated immune response, low levels of prostaglandin E, thromboxane B<sub>2</sub>, and leukotriene B<sub>4</sub> may contribute to the increased risk for infection. Other conditions such as bladder dysfunction (incomplete bladder emptying) caused by autonomic neuropathy also may contribute to the increased risk for infection. [11,12] UTI in diabetes can lead to severe complications including bacteremia, renal abscess, and renal papillary necrosis. In some cases, diabetes modifies the genitourinary system and may cause damage to the organ, which leads to pyelonephritis. This type of UTI occurs 15 times

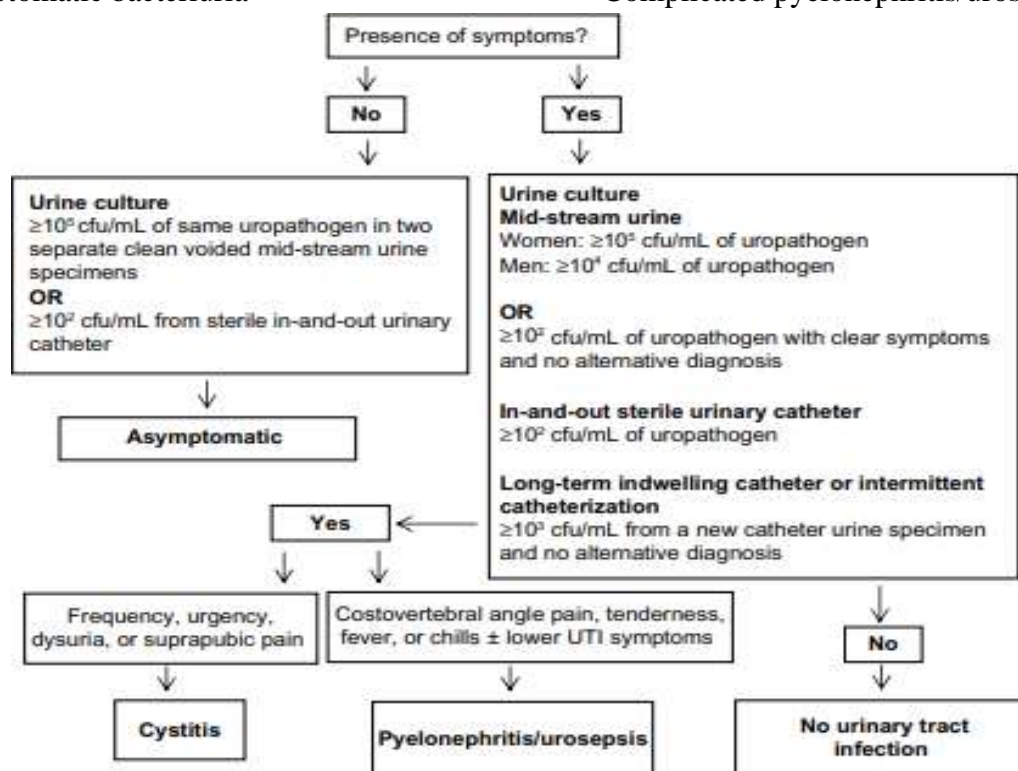


more frequently in diabetic patients. Therefore, early diagnosis and correct treatment are very important for diabetes patients with UTI. [13,14]

### Various types of UTI in patients with diabetes

- Asymptomatic bacteriuria

- Acute cystitis
- Complicated lower UTI (including catheter-associated UTI)
- Uncomplicated pyelonephritis
- Complicated pyelonephritis/urosepsis



**Figure 1: Flow chart for the diagnosis of urinary tract infection in patients with type 2 diabetes mellitus.**

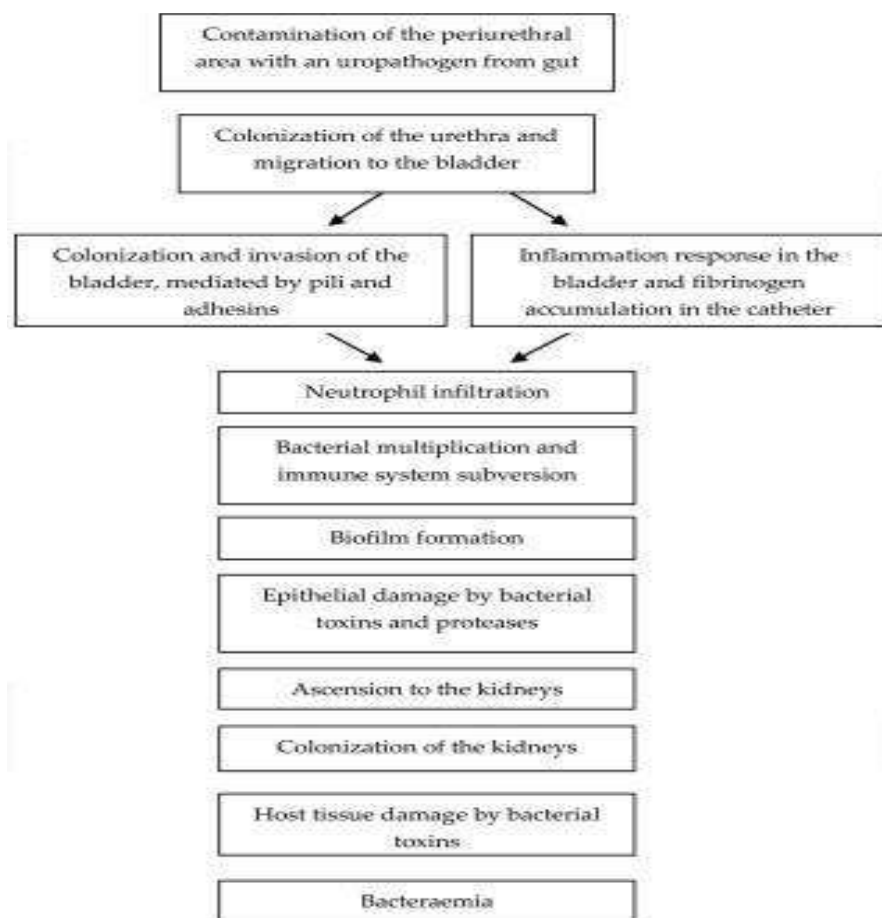
### PATHOGENESIS

The chance of occurrence of UTIs in diabetic patients used to increase many folds due to several factors. Multiple potential mechanisms unique to diabetes may cause increased risk of UTI in diabetic patients. Elevated renal parenchymal glucose levels create a positive environment for the growth and multiplication of microorganisms, which is one of the precipitating factors of pyelonephritis and renal problem such as emphysematous pyelonephritis. Several problems in the immune system, including humoral, cellular,

and innate immunity, may help in the pathogenesis of UTI in diabetic patients. [15,16] Lower urinary interleukin-6 and interleukin-8 levels were found in diabetic patients with UTI. An outline of process involved in pathogenesis of urinary tract infection in diabetic patients is mentioned in Figure.

Some suggested host related mechanisms include. [17]

- Presence of glycosuria
- Increased adherence to uroepithelial cells
- Immune dysfunction



**Figure 2: Process involved in pathogenesis of UTI in patients with diabetes**

## EPIDEMIOLOGY

Asymptomatic bacteriuria occurs in 8-26% of diabetic women a prevalence estimated to be 2-3 times higher than nondiabetic women. [18] There is limited, if any, increased frequency of asymptomatic bacteriuria for diabetic men. In a cohort of over 6,000 patients with diabetes mellitus enrolled into ten clinical trials of diabetes therapies [19]. In a cohort of over 6,000 patients with diabetes mellitus enrolled into ten clinical trials of diabetes therapies, the incidence of urinary infection was 91.5/1,000 person-years for women and 28.2/1,000 for men; the cumulative risk over 6 months was 3.5% of women and 1.1% of men. [19] In the Dutch National Survey of General Practice, patients with Type 1 diabetes mellitus were 1.96 times more likely to experience urinary infection (95% confidence intervals (CI) 1.49 -

2.58), and with Type 2 diabetes 1.24 times more likely (95% CI 1.10 - 1.39) .

## Classification of urinary tract infection

UTIs are classified based on laboratory data, clinical symptoms, and microbiological findings. Practically, UTIs have been divided into uncomplicated and complicated UTIs and sepsis. The present guidelines give an outline of a tentative improved system of -

Classification of UTI based on various factors as follows :- (Guidelines on Urological Infections by European Association of Urology)

- Grade of severity of infections and symptom
- Underlying risk factors
- Anatomical level of infection
- Microbiological findings

## Sign and Symptoms

Urinary tract infections don't always cause signs and symptoms, but when they do they may include

- A strong, persistent urge to urinate
- A burning sensation when urinating
- Passing frequent, small amounts of urine
- Urine that appears cloudy
- Urine that appears red, bright pink or cola-coloured a sign of blood in the urine
- Strong-smelling urine
- Pelvic pain, in women especially in the center of the pelvis and around the area of the pubic bone.

### Causes

Urinary tract infections typically occur when bacteria enter the urinary tract through the urethra and begin to multiply in the bladder. Although the urinary system is designed to keep out such microscopic invaders, these defenses sometimes fail. When that happens, bacteria may take hold and grow into a full-blown infection in the urinary tract.

The most common UTIs occur mainly in women and affect the bladder and urethra.

- **Infection of the bladder (cystitis):-**

This type of UTI is usually caused by *Escherichia coli* (*E. coli*), a type of bacteria commonly found in the gastrointestinal (GI) tract. However, sometimes other bacteria are responsible.

- **Infection of the urethra (urethritis) :-**

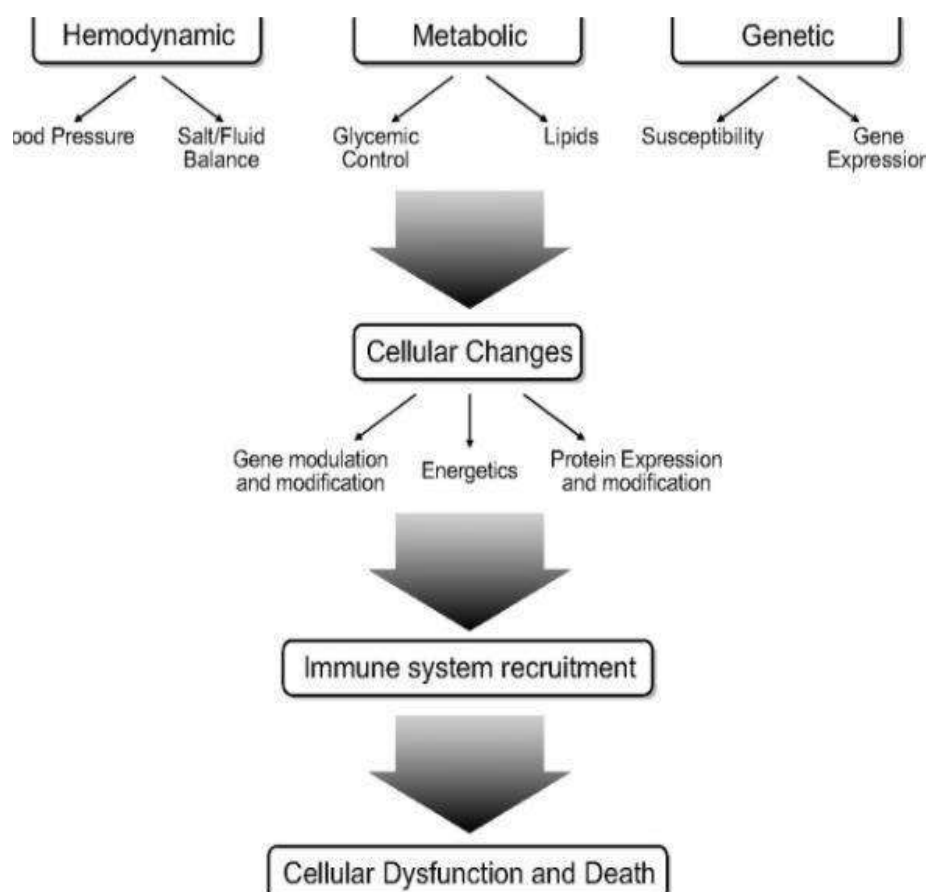
This type of UTI can occur when GI bacteria spread from the anus to the urethra. Also, because the female urethra is close to the vagina, sexually transmitted infections, such as herpes, gonorrhea, chlamydia and mycoplasma, can cause urethritis.

### COMPLICATION

General host factors associated with risk of infection in patients with diabetes include age,

metabolic control, duration of diabetes mellitus, micro vascular complications, urinary incontinence, and cerebrovascular disease or dementia. [20] Over 50% of men and women with diabetes have bladder dysfunction which may impair voiding and facilitate infection. The presence of renal disease is an additional predictor of urinary tract infection[21,22] .Emphysematous pyelonephritis (EPN) is a severe and necrotizing form of multifocal bacterial nephritis along with gas formation within parenchyma of the kidney. So far, more than 200 cases have been reported in literature. Underlying poorly controlled diabetes mellitus is present in up to 90% of affected patients. [23] Diabetes is associated with a number of complications. Acute metabolic complications associated with mortality include diabetic ketoacidosis from exceptionally high blood glucose concentrations (hyperglycemia) and coma as the result of low blood glucose (hypoglycemia). This review will focus on arguably the most devastating consequence of diabetes, its long-term vascular complications. These complications are wide ranging and are due at least in part to chronic elevation of blood glucose levels, which leads to damage of blood vessels. Micro vascular complications include eye disease or “retinopathy,” kidney disease termed “nephropathy,” and neural damage or “neuropathy,” which are each discussed in detail later within this review. The major macrovascular complications include accelerated cardiovascular disease resulting in myocardial infarction and cerebrovascular disease manifesting as strokes.





**Figure 3: Schematic overview of the major areas contributing to diabetic complications**

## MANAGEMENT

Generally, treatment of UTI is similar in both diabetic patients and non-diabetic patients [24]; however, the choice of antibiotics in UTI patients with diabetes is one of the important considerations in the therapeutic management. Possible drug interactions between antimicrobials and anti-diabetics or certain antibiotics may lead to impaired glucose homeostasis.

UTI treatment in diabetes patients depends on various factors including ; [24]

- Presence of symptoms
- Presence of infection in the bladder (lower UTI) or also involves the kidney (upper UTI)
- Presence of urologic abnormalities
- Severity of systemic symptoms
- Occur with metabolic alterations and renal function

Moreover, UTI treatment varies based on patient's age, sex, infecting agent, underlying disease, and

whether there is lower or upper urinary tract involvement.

## DIAGNOSIS

Upper and lower UTI can be suspected in diabetic patients with most common symptoms Symptoms vary in upper and lower UTI.

Diagnosis of urinary tract infection can be done by following methods

- Examination of midstream urine specimen: After the symptomatic identification, a midstream urine sample should be examined for the presence of WBCs, as pyuria is present in almost all cases of UTI.
- Pyuria detection: Pyuria can be detected either by microscopic examination (defined as  $>10$  leukocytes/mm<sup>3</sup> ) or by dipstick leukocyte esterase test (sensitivity of 75–96% and specificity of 94–98%).
- Colonization: An absence of pyuria on microscopic assessment can suggest

colonization, instead of infection, when there is bacteriuria. [25]

- Microscopic examination: Allows for visualizing bacteria in urine.
- Urine culture: Should be done in all cases of suspected UTI in diabetic patients, prior to initiation of treatment (preferred method of obtaining a urine sample for culture is from voided, clean-catch, and midstream urine). [26]

Diabetic patients are prone to have a more severe presentation of UTI. [27] though some patients with diabetic neuropathy may have altered clinical signs. A recent multi-center study from South Korea of women with community-acquired acute pyelonephritis found that significantly fewer of the diabetic patients had flank pain, costovertebral angle tenderness, and symptoms of lower UTI as compared to non-diabetic women. [28] Patients with type 2 diabetes and UTI might present with hypo- or hyperglycemia, non-ketotic hyperosmolar state, or even ketoacidosis, all of which prompt a rapid exclusion of infectious precipitating factors, including UTI. [29,30]

### MECHANISUM

UTI in diabetes can lead to severe complications including bacteremia, renal abscess, and renal papillary necrosis. In some cases, diabetes modifies the genitourinary system and may cause damage to the organ, which leads to pyelonephritis. This type of UTI occurs 15 times more frequently in diabetic patients. Therefore, early diagnosis and correct treatment are very important for diabetes patients with UTI. [31]

### CONCLUSION

Urinary tract infections are more common in the diabetic patients. Diabetic patients are severely affected with urinary tract infection. Treatment of UTI without proper diagnosis may lead to antimicrobial drug resistance. Treatment with antimicrobial agents should be started on the basis of culture reports. Only bacteriuria with symptoms

of UTI should be treated with antibiotics to avoid the spread of drug resistant pathogens in the society. This practice can reduce the morbidity and mortality in diabetic patients suffering from urinary tract infection. The multidrug resistant pathogens are a challenge to society.

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