



## Clinical assessment of the urinary tract infection in patients diagnosed with type 2 diabetes

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### Abstract

DM and urinary tract infections are closely associated with each other for over centuries. The incidence of UTIs is high in DM due to the change in the host defence mechanism, a microvascular disease in the kidney and the presence of diabetic cystopathy. High glucose concentrations in urine flow allow urinary colonization microorganisms. Incidence of UTIs is associated with various factors like age, duration of diabetes, sexual intercourse, glycaemic control and complications of diabetes. Hence based on above findings the present study was planned for Clinical Assessment of the Urinary Tract Infection in Patients Diagnosed with Type 2 Diabetes.

The present study was planned in Department of General Medicine, IGIMS, Patna, Bihar, India. Total 30 cases of the patients suffered from the diabetes and found positive for the UTI infections were enrolled in the present study. All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

The data generated from the present study concludes that the patients are at high risk with UTIs with uncontrolled glucose levels in type 2 DM patients. Therefore, continuous screening for UTIs among Type 2 DM patients is recommended to reduce the further complications.

**Keywords:** urinary tract infection, diabetes, UTI, infection, etc

### Introduction

Urinary tract infection (UTI) is an infection involving the kidneys, ureters, bladder, or urethra. Urine is one of the waste products of your body. Urine is made in the kidneys and travels down the ureters to the bladder. The bladder stores the urine until it is emptied by urinating through the urethra, a tube that connects the bladder to the skin. The opening of the urethra is at the end of the penis in a male and above the vaginal opening in a female.

The kidneys are a pair of fist-sized organs in the back that filter liquid waste from the blood and remove it from the body in the form of urine. Kidneys balance the levels of many chemicals in the body (sodium, potassium, calcium, phosphorous and others) and check the blood's acidity. Certain hormones are also made in the kidneys. These hormones help control blood pressure, boost red blood cell production and help make strong bones.

Normal urine has no bacteria in it, and the one-way flow helps prevent infections. Still, bacteria may get into the urine through the urethra and travel up into the bladder.

Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time. Symptoms often include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, and damage to the eyes.

Diabetes is due to either the pancreas not producing enough

insulin, or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus:

Type 1 diabetes results from the pancreas's failure to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The loss of beta cells is caused by an autoimmune response. The cause of this autoimmune response is unknown.

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise.

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels <sup>[1]</sup>.

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure, maintaining proper foot care, and eye care are important for people with the disease. Type 1 diabetes must be managed with insulin injections. Type 2 diabetes may be treated with medications with or without insulin. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes. Gestational diabetes usually resolves after the birth of the baby <sup>[2]</sup>.

The classic symptoms of untreated diabetes are unintended

weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. Other symptoms of diabetes include weight loss and tiredness.

Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurred vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Long-term vision loss can also be caused by diabetic retinopathy. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes [3].

People (usually with type 1 diabetes) may also experience episodes of diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. A rare but equally severe possibility is hyperosmolar hyperglycemic state (HHS), which is more common in type 2 diabetes and is mainly the result of dehydration [4].

Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies. Effects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behavior such as aggressiveness, seizures, unconsciousness, and (rarely) permanent brain damage or death in severe cases. Rapid breathing, sweating, and cold, pale skin are characteristic of low blood sugar but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in sugar. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon [5].

All forms of diabetes increase the risk of long-term complications. These typically develop after many years (10–20) but may be the first symptom in those who have otherwise not received a diagnosis before that time.

The major long-term complications relate to damage to blood vessels. Diabetes doubles the risk of cardiovascular disease and about 75% of deaths in people with diabetes are due to coronary artery disease. Other macrovascular diseases include stroke, and peripheral artery disease.

The primary complications of diabetes due to damage in small blood vessels include damage to the eyes, kidneys, and nerves. Damage to the eyes, known as diabetic retinopathy, is caused by damage to the blood vessels in the retina of the eye, and can result in gradual vision loss and eventual blindness. Diabetes also increases the risk of having glaucoma, cataracts, and other eye problems. It is recommended that people with diabetes visit an eye doctor once a year. Damage to the kidneys, known as diabetic nephropathy, can lead to tissue scarring, urine protein loss, and eventually chronic kidney disease, sometimes requiring dialysis or kidney transplantation. Damage to the nerves of the body, known as diabetic neuropathy, is the most common complication of diabetes. The symptoms can include numbness, tingling, pain, and altered pain sensation, which can lead to damage to the skin. Diabetes-related foot

problems (such as diabetic foot ulcers) may occur, and can be difficult to treat, occasionally requiring amputation. Additionally, proximal diabetic neuropathy causes painful muscle atrophy and weakness [6].

Diabetes mellitus is classified into four broad categories: type 1, type 2, gestational diabetes, and "other specific types". The "other specific types" are a collection of a few dozen individual causes. Diabetes is a more variable disease than once thought and people may have combinations of forms. The term "diabetes", without qualification, refers to diabetes mellitus [7].

Type 1 diabetes is characterized by loss of the insulin-producing beta cells of the pancreatic islets, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, in which a T cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin [8]. It causes approximately 10% of diabetes mellitus cases in North America and Europe. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. Although it has been called "juvenile diabetes" due to the frequent onset in children, the majority of individuals living with type 1 diabetes are now adults.

"Brittle" diabetes, also known as unstable diabetes or labile diabetes, is a term that was traditionally used to describe the dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used. Still, type 1 diabetes can be accompanied by irregular and unpredictable high blood sugar levels, and the potential for diabetic ketoacidosis or serious low blood sugar levels. Other complications include an impaired counterregulatory response to low blood sugar, infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrinopathies (e.g., Addison's disease) [9]. These phenomena are believed to occur no more frequently than in 1% to 2% of persons with type 1 diabetes.

Type 2 diabetes is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type of diabetes mellitus. Many people with type 2 diabetes have evidence of prediabetes (impaired fasting glucose and/or impaired glucose tolerance) before meeting the criteria for type 2 diabetes. The progression of prediabetes to overt type 2 diabetes can be slowed or reversed by lifestyle changes or medications that improve insulin sensitivity or reduce the liver's glucose production.

Type 2 diabetes is primarily due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio [10].

Dietary factors also influence the risk of developing type 2

diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk. The type of fats in the diet is also important, with saturated fat and trans fats increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice also may increase the risk of diabetes, whereas substitution of brown rice or other whole grains for white rice may lower the risk of diabetes. A lack of physical activity is believed to cause 7% of cases [11].

Diabetes Mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [12].

DM and urinary tract infections are closely associated with each other for over centuries. The incidence of UTIs is high in DM due to the change in the host defence mechanism, a microvascular disease in the kidney and the presence of diabetic cystopathy. High glucose concentrations in urine flow allow urinary colonization microorganisms. Incidence of UTIs is associated with various factors like age, duration of diabetes, sexual intercourse, glycaemic control and complications of diabetes. Hence based on above findings the present study was planned for Clinical Assessment of the Urinary Tract Infection in Patients Diagnosed with Type 2 Diabetes.

**Methodology**

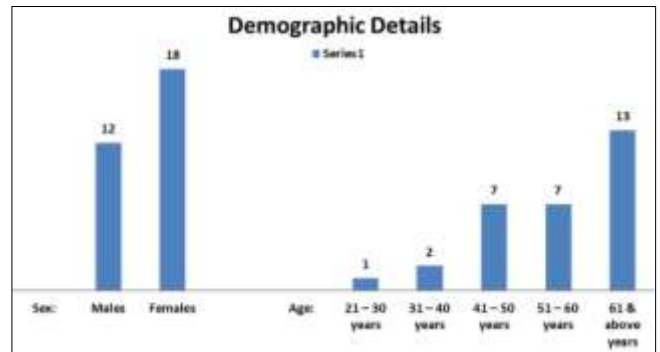
The present study was planned in Department of General Medicine, IGIMS, Patna, Bihar, India. Total 30 cases of the patients suffered from the diabetes and found positive for the UTI infections were enrolled in the present study. All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

The Diabetic patients of both sex males and female with age from 18 years and above with Urine culture positive cases were enrolled in the present study.

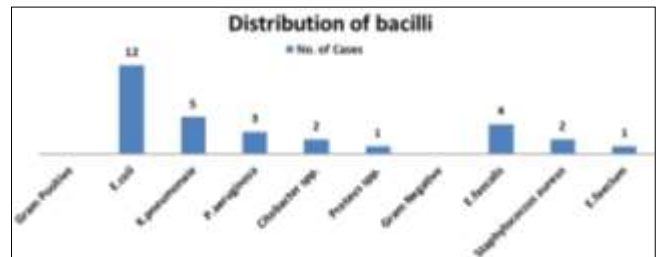
The cases of Non-diabetics, Pregnancy, Known congenital/acquired urogenital anomaly, Patients on chronic catheterization, and Candiduria were excluded from the present study.

**Results & Discussion**

Diabetics are more prone to infections than their nondiabetic counterparts. The urinary tract is the most common site of infection in diabetic patients. Most of the urinary tract infections (UTIs) in diabetic patients are relatively asymptomatic, which can lead to severe kidney damage and renal failure. Bacteriuria is more common in diabetics than in non-diabetics due to a combination of host and local risk factors [13]. Disturbances (low complement factor 4, decreased cytokine response) in humoral innate immunity have been described in diabetic patients. Improved control of the diabetes mellitus (DM) can lead to an improvement in these cellular functions. As well, some microorganisms become more virulent in a high glucose environment [14]. Therefore, screening for UTI in diabetic patients is very important to enable bacteriuria to be properly treated and prevent the development of renal complications of diabetes and eventually severe renal damage and failure [15].



**Fig 1:** Demographic Details



**Fig 2:** Distribution of gram-negative bacilli

**Table 1:** Treatment taken for diabetes

Treatment	No. of Cases
Insulin	7
Oral hypoglycaemic agents	15
Both	8
No treatment	0
Total	30

Bahl AL *et al.* (1970) found significant correlation between duration of diabetes and the prevalence of bacteriuria [16]. The prevalence of bacteriuria increased 1.9-fold for every 10 years of diabetes duration. This is probably due to higher prevalence of autonomic neuropathy and subsequent incomplete bladder emptying in longstanding diabetes [17]. However, such a correlation was not observed in our study. Zhanel GG *et al.* (1995) noted that the prevalence of UTI was significantly higher among patients on oral hypoglycaemic agents [18].

It has been established that women with diabetes are about two to three times more likely to have urinary tract infections than women without diabetes. Interestingly, the same does not appear true for men. This gender-based difference may be because of shorter urethra and closer proximity to the anus among women [19]. In our study, incidence of bacteriuria was significantly higher among female patients, which is in agreement with almost all previous studies [20].

All types of UTI are more frequent in patients with type 2 diabetes. Various studies have reported the overall incidence of UTI among these patients. An observational study of all patients with type 2 diabetes in the UK general practice research database found that the incidence rate of UTI was 46.9 per 1,000 person-years among diabetic patients and 29.9 for patients without diabetes [21]. Women with previously diagnosed diabetes had a higher risk of UTI than those with recently diagnosed diabetes (within 6 months) (91.9/1,000 person-years; 95% confidence interval [CI] 84.3–99.4, vs 70.5/1,000 person-years; 95% CI 68.2–72.8) [21]. A cohort study of over 6,000 patients enrolled in ten

clinical trials found an incidence rate of 91.5 per 1,000 person-years in women and 28 per 1,000 person-years in men, and a cumulative incidence of 2% during 6 months [22]. A recent American study performed on a health service data base with more than 70,000 patients with type 2 diabetes found that 8.2% were diagnosed with UTI during 1 year (12.9% of women and 3.9% of men, with incidence increasing with age). Another American database study from 2014 found that a UTI diagnosis was more common in men and women with diabetes than in those without diabetes (9.4% vs 5.7%, respectively) among 89,790 matched pairs of patients with and without type 2 diabetes mellitus [23].

ASB is more prevalent in women, due to a short urethra that is in proximity to the warm, moist, vulvar, and perianal areas that are colonized with enteric bacteria. ASB increases with age and is also associated with urinary tract abnormalities or foreign bodies (urethral catheters, stents, etc) [24, 25]. Many studies have reported an increased prevalence of ASB in diabetic patients, with estimates ranging from 8%–26% [26, 27]. A meta-analysis of 22 studies, published in 2011, found a point prevalence of 12.2% of ASB among diabetic patients versus 4.5% in healthy control subjects. The point prevalence of ASB was higher both in women and men, was higher in patients with a longer duration of diabetes, and was not associated with glycemic status, as evaluated by glycosylated hemoglobin A1c (HbA1c) [28]. A recent prospective study of inpatients at an Indian hospital found a 30% prevalence rate of ASB among diabetic patients [29].

The major limitations of our study include observational study design, which denies any conclusion on causation of bacteriuria in elderly diabetic patients. In addition, the role of common antibiotic medications in the management of these patients was not considered in the analysis. Our study also lacks subgroup comparisons of clinical and laboratory profiles for men vs. women, early vs. late elderly, or young, middle, and late elderly due to the small sample size. The small sample size of our study population and non-parametric nature of the data may limit the generalization of the results. Despite these limitations, we strongly believe that present study provides important insights about urinary tract infections in 'elderly', for which data are rare.

### Conclusion

The data generated from the present study concludes that the patients are at high risk with UTIs with uncontrolled glucose levels in type 2 DM patients. Therefore, continuous screening for UTIs among Type 2 DM patients is recommended to reduce the further complications.

### References

1. "Diabetes Fact sheet N°312". WHO. October 2013. Archived from the original on 26 August, 2013. Retrieved 25 March 2014.
2. Cash Jill. Family Practice Guidelines (3rd ed.). Springer, 2014, p. 396. ISBN 978-0-8261-6875-7. Archived from the original on 31 October 2015.
3. Rockefeller JD. Diabetes: Symptoms, Causes, Treatment and Prevention, 2015. ISBN 978-1-5146-0305-5.
4. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. "Hyperglycemic crises in adult patients with diabetes". *Diabetes Care*. 2009; 32(7):1335-43. doi:10.2337/dc09-9032. PMC 2699725. PMID 19564476. Archived from the original on 2016-06-25.
5. "Glucagon–Injection side effects, medical uses, and drug interactions". *Medicine Net*. Retrieved 2018-02-05.
6. "Diabetes Programme". World Health Organization. Archived from the original on 26 April, 2014. Retrieved 22 April 2014.
7. "Definition of Diabetes mellitus". *MedicineNet*. Retrieved 2019-11-04.
8. Rother KI. "Diabetes treatment--bridging the divide". *The New England Journal of Medicine*. 2007; 356(15):1499-501. doi:10.1056/NEJMp078030. PMC 4152979. PMID 17429082.
9. "Diabetes Mellitus (DM): Diabetes Mellitus and Disorders of Carbohydrate Metabolism: Merck Manual Professional". Merck Publishing. April, 2010. Archived from the original on 2010-07-28. Retrieved 2010-07-30.
10. Shoback DG, Gardner D, eds. "Chapter 17". *Greenspan's basic & clinical endocrinology (9th ed.)*. New York: McGraw-Hill Medical, 2011. ISBN 978-0-07-162243-1.
11. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT, *et al.*. "Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy". *Lancet*. 2012; 380(9838):219-29. doi:10.1016/S0140-6736(12)61031-9. PMC 3645500. PMID 22818936.
12. Fauci AS, Kasper DS, Longo DL, Braunwald E, Hauser SL, Jameson JL, *et al.*. *Harrison's principles of internal medicine*. United States; McGraw Hill, 2008.
13. Patterson JE, Andriole VT. Bacterial urinary tract infections in diabetes. *Infect Dis Clin North Am*. 1997; 11(3):735-50.
14. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus. *FEMS Immunol Med Microbiol*. 1999; 26:259-65.
15. Kunin CM. *Detection, prevention and management of urinary tract infections*. 4th ed. Philadelphia, PA: Lea and Febiger; 1987.
16. Bahl AL, Chugh RN, Sharma KB. Asymptomatic bacteremia in diabetics attending a diabetic clinic. *Indian J Med Sci*. 1970; 24:1-6.
17. Keane EM, Boyko EJ, Reller LB, Hamman RF. Prevalence of asymptomatic bacteriuria in subjects with NIDDM in San Luis Valley of Colorado. *Diabetes Care*. 1988; 11:708-12.
18. Zhanel GG, Nicolle LE, Harding GK. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. The Manitoba Diabetic Urinary Infection Study Group. *Clin Infect Dis*. 1995; 21:316-22.
19. 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*. 2015; 8:129-36.
20. Shill MC, Huda NH, Moain FB, Karmakar UK. Prevalence of uropathogens in diabetic patients and their corresponding resistance pattern: Results of a survey conducted at diagnostic centers in Dhaka, Bangladesh. *Oman Med J*. 2010; 25(4):282-85.
21. Hirji I, Guo Z, Andersson SW, Hammar N, Gomez-Caminero 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):513-516.
22. 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; 19(12):1287-1292.
  23. Fu AZ, Iglay K, Qiu Y, Engel S, Shankar R, Brodovicz K, *et al.*. Risk characterization for urinary tract infections in subjects with newly diagnosed type 2 diabetes. *J Diabetes Complications*. 2014; 28(6):805-810.
  24. Colgan R, Nicolle LE, McGlone A, Hooton TM. Asymptomatic bacteriuria in adults. *Am Fam Physician*. 2006; 74(6):985-990.
  25. Nicolle LE. Asymptomatic bacteriuria. *Curr Opin Infect Dis*. 2014; 27(1):90-96.
  26. Zhanel GG, Nicolle LE, Harding GK. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. The Manitoba Diabetic Urinary Infection Study Group. *Clin Infect Dis*. 1995; 21(2):316-322.
  27. Schneeberger C, Kazemier BM, Geerlings SE. Asymptomatic bacteriuria and urinary tract infections in special patient groups: women with diabetes mellitus and pregnant women. *Curr Opin Infect Dis*. 2014; 27(1):108-114.
  28. Renko M, Tapanainen P, Tossavainen P, Pokka T, Uhari M. Meta-analysis of the significance of asymptomatic bacteriuria in diabetes. *Diabetes Care*. 2011; 34(1):230-235.
  29. Aswani SM, Chandrashekar U, Shivashankara K, Pruthvi B. Clinical profile of urinary tract infections in diabetics and non-diabetics. *Australas Med J*. 2014; 7(1):29-34.