



Frequency of Urinary Tract Infections in Diabetic Patients Taking SGLT-2 Inhibitors

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ABSTRACT

Background: Sodium-glucose cotransporter 2 (SGLT-2) inhibitors are widely prescribed for type 2 diabetes mellitus due to their glucose-lowering, cardiovascular, and renal benefits. However, concerns remain regarding an increased risk of urinary tract infections (UTIs), particularly in diabetic patients already predisposed to infections. Evidence from local populations is limited, necessitating focused evaluation. **Objective:** To determine the frequency of urinary tract infections in diabetic patients taking SGLT-2 inhibitors. **Study Design:** Descriptive cross-sectional study. **Duration and Place of Study:** This study was conducted from February 2025 to May 2025 in the Department of Medicine, Shaikh Zayed Federal Postgraduate Medical Institute, Lahore. **Methodology:** A total of 193 patients aged 20–70 years with type 2 diabetes mellitus receiving SGLT-2 inhibitors for at least three months were enrolled through non-probability consecutive sampling. Demographic characteristics, clinical history, and anthropometric measures were recorded. UTIs were identified based on clinical symptoms such as fever or dysuria within four weeks and confirmed through urine analysis and culture. **Results:** The mean age was 56.01±9.07 years, with females representing 54.4% of the cohort. The overall frequency of UTIs was 10.9% (n=21). Female gender (p=0.038) and SGLT-2 therapy exceeding 12 months (p=0.010) were significantly associated with higher infection rates. No significant association was found with age, BMI, or residence. **Conclusion:** UTIs were observed in approximately one-tenth of diabetic patients on SGLT-2 inhibitors, with higher risk in females and long-term users.

INTRODUCTION

Diabetes mellitus is among the most frequent chronic metabolic disorders that are on the rise throughout the whole world.¹ It is defined as chronic increased glucose levels in the blood as a result of defective insulin secretion, defective insulin action, or an amalgamation of both.² Unless adequately controlled, diabetes mellitus can generate serious issues in the eyes, kidney, nerves, and cardiovascular system.³ Plans of therapy are constructed with the intention of maintaining the blood glucose concentrations in a desirable limit and include dietary and physical activity modifications and oral antidiabetic drugs and injections of insulin as therapeutic options.⁴ These are very important not only to improve the quality of existence but also to prevent issues related to diabetes mellitus.⁴

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors are a recent development in type 2 diabetes therapies.⁵ Through the action of inhibiting glucose reabsorption in renal proximal tubules, the medication leads to glucose excretion in the urine and reduction of glucose levels in the blood.⁶ Due to their insulin independence, the drugs are able to work in patients with insulin resistance.⁶ SGLT-2

inhibitors also lead to weight reduction, reduction of blood pressure, cardiovascular and renal protection, as evident in numerous clinical trials.⁷ Due to their beneficial effects, SGLT-2 inhibitors have emerged as a first-line therapeutic measure among the majority of type 2 diabetes patients.⁷

Despite such virtues, SGLT-2 inhibitors are also subject to certain side effects, and the most dominant one is an increased risk of urinary tract infection.⁸ With the higher glucose concentration in urine offering an ideal medium upon which to grow, patients are therefore susceptible to infection.⁹ In diabetic patients already in an increased susceptibility for infection secondary to compromised immunity, added risk is therefore apparent clinically. Severity and frequency of urinary tract infection vary and may be as mild infection with response to therapy and recurrent infection with patient noncompliance.¹⁰ Prescribers therefore, while providing SGLT-2 inhibitors as a prescription, must walk delicately and balance their virtues against urinary tract infection peril and regard patients correspondingly.

Wazir ZM et al.¹¹ reported a frequency of urinary tract infections (UTIs) of 6.0% in diabetic patients receiving

SGLT-2 inhibitors. Similarly, Aziz A et al.¹² documented a UTI frequency of 8.8% in this patient group. In contrast, Tanriverdi M et al.¹⁰ observed a much higher rate, with 54.9% of patients developing UTIs while on SGLT-2 inhibitor therapy. Furthermore, Ashfaq M et al.¹³ highlighted that the occurrence of UTIs among patients using dapagliflozin and empagliflozin was 10.1% and 14.7%, respectively.

There is a growing prescription of SGLT-2 inhibitors among diabetic patients in Lahore, yet there is limited local data about their relationship with urinary tract infections. There are differences in lifestyle, hygiene practices, and medical care availability that may decide the prevalence of such infection among people living in the city. To create location-specific evidence, safer prescriptive advice for doctors, and improve patient care through ascertaining the size of the problem in the immediate locality, it is best to conduct research in Lahore.

METHODOLOGY

This descriptive cross-sectional study was carried out in the Department of Medicine at Shaikh Zayed Federal Postgraduate Medical Institute, Lahore, from February 2025 to May 2025. The study population consisted of patients with type 2 diabetes mellitus who had been receiving SGLT-2 inhibitor therapy for at least three months. Approval for the study was obtained from the institutional ethical review committee and the College of Physicians and Surgeons Pakistan before the commencement of data collection. The sample size was calculated to be 193 using the WHO sample size calculator for a single proportion, with a 95% confidence level, 4% margin of error, and an expected frequency of urinary tract infections of 8.8% in diabetic patients on SGLT-2 inhibitors.¹² A non-probability consecutive sampling technique was employed. Eligible participants included male and female patients aged 20–70 years with a confirmed diagnosis of type 2 diabetes mellitus, defined as random blood sugar ≥ 200 mg/dl, fasting blood sugar ≥ 126 mg/dl, or HbA1c $\geq 6.5\%$ on more than one occasion, and who had been continuously taking an SGLT-2 inhibitor for the last three months. Patients with culture-proven urinary tract infections within one month of initiating dapagliflozin, current catheter users, those with a history of urinary tract infection within two weeks prior to enrollment, as well as individuals with chronic kidney disease (estimated GFR < 45 mL/min), on renal replacement therapy, or post-renal transplantation were excluded.

Written informed consent was obtained from all participants prior to enrollment. Demographic details including age, gender, place of residence (rural or urban), duration of diabetes, height, weight, and type of SGLT-2 inhibitor in use (dapagliflozin or empagliflozin) were documented. Height was measured using a wall-mounted scale, and weight was measured using a weighing machine. Body mass index was calculated using the formula weight (kg)/height (m²), with values above 30 classified as obese and ≤ 30 classified as non-obese. Clinical history was recorded, and patients underwent relevant laboratory testing to assess urinary tract infection status. Urine samples were analyzed in the institutional laboratory by

pathologists with a minimum of five years of experience. A urinary tract infection was defined as the presence of fever $\geq 38^\circ\text{C}$ or dysuria within the last four weeks, in addition to laboratory confirmation. Laboratory confirmation included a positive midstream urine sample for nitrite or leukocyte esterase, the presence of ≥ 10 white blood cells per high-power field on urine microscopy, and a positive urine culture for any organism. Patients meeting these criteria were labeled as having urinary tract infection.

Data were analyzed using IBM SPSS version 25. Normality of quantitative variables was tested using the Shapiro-Wilk test. Mean and standard deviation or median with interquartile range were computed for continuous variables. Categorical variables were expressed as frequencies and percentages. Potential effect modifiers were controlled through stratification. The chi-square test was applied for post-stratification analysis, and a p-value ≤ 0.05 was considered statistically significant.

RESULTS

Based on the comprehensive data analysis, this study examined 193 diabetic patients taking SGLT-2 inhibitors with a mean age of 56.01 ± 9.07 years and diabetes duration of 8.41 ± 7.09 years, who had been receiving SGLT-2 treatment for an average of 13.42 ± 7.08 months (as shown in Table I). The cohort had a mean height of 1.67 ± 0.10 meters, weight of 75.14 ± 13.24 kg, and BMI of 27.20 ± 5.49 kg/m², with females comprising 54.4% (n=105) and males 45.6% (n=88) of participants. Urban residents constituted 61.7% (n=119) while rural residents made up 38.3% (n=74), and empagliflozin was used by 54.4% (n=105) of patients compared to 45.6% (n=88) using dapagliflozin (as shown in Table I).

Table I

Patient Demographics

Demographics	Mean \pm SD
Age (years)	56.01 \pm 9.07
Duration of Diabetes (years)	8.41 \pm 7.09
Duration of SGLT-2 Treatment (months)	13.42 \pm 7.08
Height (m)	1.67 \pm 0.10
Weight (kg)	75.14 \pm 13.24
BMI (kg/m ²)	27.20 \pm 5.49
Male n(%)	88 (45.6%)
Female n(%)	105 (54.4%)
Residence	
Rural n (%)	74 (38.3%)
Urban n (%)	119 (61.7%)
SGLT-2 Inhibitor Type	
Dapagliflozin n (%)	88 (45.6%)
Empagliflozin n (%)	105 (54.4%)

The overall frequency of urinary tract infections was 10.90% (n=21), while 89.10% (n=172) of patients remained infection-free (as shown in Table II).

Table II

Frequency of Urinary Tract Infections Among Diabetic Patients Taking SGLT-2 Inhibitors

Urinary Tract Infection	Frequency	% age
Yes	21	10.90%
No	172	89.10%
Total	193	100%

Stratified analysis revealed significant associations between UTI occurrence and several demographic factors (as shown in Table III): females demonstrated a

significantly higher UTI rate of 15.2% (n=16) compared to males at 5.7% (n=5) with p=0.038, and patients receiving SGLT-2 treatment for more than 12 months had a significantly elevated UTI frequency of 16.3% (n=17) versus 4.5% (n=4) in those treated for ≤12 months with p=0.010. Age stratification showed UTI rates of 9.7% (n=3) in patients ≤45 years versus 11.1% (n=18) in those >45 years (p=1.000), while diabetes duration analysis revealed 8.3% (n=11) UTI frequency in patients with ≤10 years duration compared to 16.7% (n=10) in those >10 years duration (p=0.083). BMI analysis demonstrated UTI rates of 9.9% (n=7) in patients with BMI ≤25 kg/m² versus 11.5% (n=14) in those with BMI >25 kg/m² (p=0.728), residence showed 16.2% (n=12) UTI frequency in rural areas compared to 7.6% (n=9) in urban areas (p=0.061), and SGLT-2 inhibitor type revealed 6.8% (n=6) UTI rate with dapagliflozin versus 14.3% (n=15) with empagliflozin (p=0.097), with statistical significance determined using Fischer Exact Test where applicable (as shown in Table III).

Table III

Association of Urinary Tract Infections with Demographic Factors

Demographic Factors	Urinary Tract Infections		p-value
	Yes n(%)	No n(%)	
Age (years)	≤45	3 (9.7%) 28 (90.3%)	1.000*
	>45	18 (11.1%) 144 (88.9%)	
Sex	Male	5 (5.7%) 83 (94.3%)	0.038*
	Female	16 (15.2%) 89 (84.8%)	
Diabetes Duration (years)	≤10	11 (8.3%) 122 (91.7%)	0.083
	>10	10 (16.7%) 50 (83.3%)	
SGLT-2 Duration (months)	≤12	4 (4.5%) 85 (95.5%)	0.010*
	>12	17 (16.3%) 87 (83.7%)	
BMI (Kg/m ²)	≤25	7 (9.9%) 64 (90.1%)	0.728
	>25	14 (11.5%) 108 (88.5%)	
Residence	Rural	12 (16.2%) 62 (83.8%)	0.061
	Urban	9 (7.6%) 110 (92.4%)	
SGLT-2 Type	Dapagliflozin	6 (6.8%) 82 (93.2%)	0.097
	Empagliflozin	15 (14.3%) 90 (85.7%)	

*Fischer Exact Test

DISCUSSION

The present study demonstrates that urinary tract infections occur in approximately one in ten diabetic patients receiving SGLT-2 inhibitor therapy, with significant demographic variations influencing infection susceptibility. The observed 10.90% UTI prevalence aligns with the known mechanism of SGLT-2 inhibitors, which increase urinary glucose excretion and create a favorable environment for bacterial growth in the genitourinary tract. The significantly higher UTI frequency in females (15.2% versus 5.7% in males) reflects well-established

anatomical and physiological differences, including shorter urethral length, proximity to the anal opening, and hormonal influences on urogenital flora that predispose women to ascending bacterial infections. The notable association between prolonged SGLT-2 treatment duration (>12 months) and increased UTI risk (16.3% versus 4.5%) suggests a cumulative effect of sustained glycosuria, where prolonged exposure to elevated urinary glucose concentrations progressively alters the urogenital microenvironment and potentially compromises local immune defenses. While not statistically significant, the trend toward higher UTI rates with longer diabetes duration (16.7% versus 8.3%) likely reflects progressive diabetic complications including autonomic neuropathy affecting bladder function, compromised immune response, and chronic hyperglycemic states that impair neutrophil function and cellular immunity. The numerically higher UTI frequency with empagliflozin compared to dapagliflozin, though not reaching statistical significance, may relate to differential pharmacokinetic properties and varying degrees of glucosuria between these agents, warranting further investigation in larger cohorts.

The present study's UTI prevalence of 10.90% among diabetic patients on SGLT-2 inhibitors demonstrates consistency with several regional investigations, particularly aligning closely with Dayo et al.¹⁴ who reported 10.7% UTI frequency in a Pakistani cohort, and falls within the range observed by Shaikh et al.¹⁵ at 14.9% and Aziz et al.¹² at 8.8%. This convergence of findings across multiple Pakistani centers suggests a relatively stable UTI incidence pattern in South Asian diabetic populations receiving SGLT-2 therapy. However, our results contrast notably with lower rates reported by Wazir et al.¹¹ (6%), Hussain et al.¹⁶ (4.3-6.5%), and Azhar et al.¹⁷ (4.3-6.74%), which may reflect variations in diagnostic criteria, patient selection, or study methodology rather than true epidemiological differences. The significantly higher UTI frequency in females (15.2%) compared to males (5.7%) in our study strongly corroborates findings from multiple investigations, including Hussain et al.¹⁶ Azhar et al.¹⁷ Shaikh et al.¹⁵ and Radi et al.¹⁸ reinforcing the established pattern of female predisposition to SGLT-2 inhibitor-associated urogenital infections across diverse populations. Our observation of increased UTI risk with prolonged SGLT-2 treatment duration (>12 months: 16.3% vs ≤12 months: 4.5%) finds support in the comprehensive analysis by Radi et al.¹⁸ who demonstrated that extended exposure periods correlate with higher infection rates, suggesting a cumulative effect of sustained glycosuria on urogenital bacterial colonization. The trend toward higher UTI rates in patients with longer diabetes duration, though not statistically significant in our cohort, aligns with findings from Dayo et al.¹⁴ who reported 23% UTI frequency in patients with diabetes duration >10 years, and Ubaid et al.¹⁹ who identified prolonged disease duration as a risk factor, likely reflecting progressive diabetic complications affecting immune function and bladder physiology. Interestingly, our numerically higher UTI rates with empagliflozin compared to dapagliflozin mirrors observations from multiple studies including Hussain et al.

¹⁶ (6.5% vs 4.3%), Azhar et al. ¹⁷ (6.74% vs 4.3%), and Dayo et al. ¹⁴ (14.8% vs 9.7%), suggesting potential drug-specific differences in glucosuric effects or pharmacokinetic properties that warrant further mechanistic investigation. The moderate UTI frequency observed in our study also corresponds with Aziz et al. ¹² who concluded that UTI frequency was moderate in their cohort, while Wazir et al. ¹¹ noted that their 6% incidence aligns with previous reports and supports continued clinical vigilance. The lack of significant association between UTI occurrence and age groups in our study contrasts with findings from Dayo et al. ¹⁴ and Aziz et al. ¹² who demonstrated significantly higher infection rates in older patients (>50 years), possibly reflecting differences in cohort characteristics or sample size limitations that may have obscured age-related effects in our population.

Several limitations should be acknowledged in interpreting these findings. The single-center design conducted at one tertiary care facility may limit the generalizability of results to broader populations and different healthcare settings with varying patient demographics, clinical practices, and diagnostic protocols. The cross-sectional nature of the study design restricts the ability to establish temporal relationships between SGLT-

2 inhibitor use and UTI development, precluding definitive causality assessment. The relatively small sample size of 193 patients, while adequate for initial analysis, may have been insufficient to detect significant associations for some variables, particularly given the modest number of UTI events (n=21), which could have led to type II errors in statistical testing.

CONCLUSION

Our study has concluded that urinary tract infections represent a notable complication among diabetic patients receiving SGLT-2 inhibitor therapy, with female gender and prolonged treatment duration emerging as significant risk factors for infection development. The findings demonstrate that SGLT-2 inhibitors are associated with an increased susceptibility to urogenital infections, particularly in women, likely due to the combined effects of glucosuria-induced bacterial growth promotion and gender-specific anatomical predispositions.

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