INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

FREQUENCY OF URINARY TRACT INFECTIONS IN PATIENTS TAKING SODIUM-GLUCOSE COTRANSPORTER-2 (SGLT-2) INHIBITORS

Original Research

Kainat Shaikh[1]*, Abdul Mannan Junejo[2], Asif Nawaz[3], Muhammad Ali[4], Sabih Ahmed[5], Raja Taha Yaseen Khan[6], Syeda Maryam Mehdi[7], Abdullah Nasir[8]

[1]Resident Trainee, Department of Nephrology, Jinnah Sindh Medical University, Karachi, Pakistan.
[2]Professor, Department of Nephrology, Jinnah Sindh Medical University, Karachi, Pakistan.
[3]Resident Trainee, Jinnah Sindh Medical University, Karachi, Pakistan.
[4]Associate Professor, Department of Nephrology, Jinnah Sindh Medical University, Karachi, Pakistan.
[5]Medical Officer, Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan.
[6]Assistant Professor, Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan.
[7]Medical Student, Ziauddin Medical University, Karachi, Pakistan.
[8]Medical Student, Sohail University, Karachi, Pakistan.

Corresponding Author: Kainat Shaikh, Resident Trainee, Department of Nephrology, Jinnah Sindh Medical University, Karachi, Pakistan. Kainat.shaikh98@yahoo.com

Acknowledgement: The authors acknowledge the support of Jinnah Sindh Medical University, Karachi, for facilitating this study.

Conflict of Interest: None

Grant Support & Financial Support: None

ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is a globally prevalent metabolic disorder associated with significant morbidity. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors have emerged as effective antihyperglycemic agents, enhancing renal glucose excretion to improve glycemic control. Despite their benefits, concerns have arisen regarding an increased risk of urinary tract infections (UTIs) in patients using these medications. This study aimed to determine the frequency of UTIs in T2DM patients using SGLT-2 inhibitors at a tertiary care hospital in Karachi.

Objective: To assess the incidence of UTIs and identify associated risk factors in T2DM patients receiving SGLT-2 inhibitors.

Methods: A descriptive cross-sectional study was conducted at Jinnah Sindh Medical University, Karachi, including 215 T2DM patients aged 30–65 years who had been on SGLT-2 inhibitors for over one month. Patients were selected using non-probability consecutive sampling. Exclusion criteria included type 1 diabetes, pregnancy, recurrent UTIs, severe renal impairment, and immunosuppressive therapy. Data collection involved structured interviews, medical record reviews, and urine culture analysis. Variables assessed included gender, glycemic control (HbA1c), comorbidities, hemoglobin levels, and duration of diabetes. Statistical analysis was performed using SPSS version 27.0, with a p-value <0.05 considered significant.

Results: Among the 215 participants, 32 (14.9%) were diagnosed with UTIs. Female patients had a significantly higher incidence of UTIs compared to males (62.5% vs. 37.5%, $p = 0.02$). Poor glycemic control (HbA1c > 8%) was strongly associated with UTI occurrence (96.9% vs. 87.9%, $p = 0.01$). The mean duration of diabetes was 7.5 ± 3.2 years, and patients with UTIs had significantly lower hemoglobin levels (10.3 ± 1.7 g/dL) compared to those without UTIs (10.7 ± 1.2 g/dL, $p = 0.027$).

Conclusion: The study identified a substantial incidence of UTIs in T2DM patients on SGLT-2 inhibitors, with female gender and poor glycemic control being significant risk factors. These findings underscore the importance of monitoring and preventive strategies to mitigate UTI risks in high-risk populations.

Keywords: Diabetes mellitus, Glycemic control, Gender differences, Sodium-glucose cotransporter-2 inhibitors, Type 2 diabetes, Urinary tract infections, UTI prevention.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become a global health challenge, accounting for approximately 90–95% of all diabetes cases and characterized by insulin resistance and relative insulin deficiency (1). The burden of diabetes is particularly high in Pakistan, where its prevalence is estimated at 16.98%, posing a significant threat to the healthcare system (2). These alarming statistics underscore the importance of exploring effective pharmacological interventions, including sodium-glucose cotransporter-2 (SGLT-2) inhibitors, which have emerged as a cornerstone in the management of T2DM. SGLT-2 inhibitors are a class of oral antihyperglycemic agents that function by inhibiting glucose reabsorption in the renal tubules, promoting glucose excretion through urine. Beyond their primary role in glycemic control, these drugs offer additional therapeutic benefits, including weight reduction and cardioprotective effects, making them a valuable option for managing T2DM (3–9). However, their mechanism of action raises safety concerns, as glucosuria may create a favorable environment for bacterial growth, potentially increasing the risk of urinary tract infections (UTIs) in patients receiving these drugs (10–12).

UTIs are common infections, particularly in individuals with diabetes, who are predisposed due to immune dysfunction and a hyperglycemic milieu that fosters bacterial colonization (3,13). The glucose excretion promoted by SGLT-2 inhibitors may further elevate this risk. Although these drugs have demonstrated efficacy in managing blood glucose levels, their safety profile has come under scrutiny due to reports of an increased frequency of urogenital infections, including UTIs (14). The association between SGLT-2 inhibitors and UTIs remains a topic of debate in the literature. While some studies suggest a higher incidence of UTIs in patients using these drugs compared to other antidiabetic agents (15), others report only a modest increase in risk, which may be outweighed by their overall benefits in diabetes management (16,17). Given the growing use of SGLT-2 inhibitors and the concerns surrounding their potential to increase UTI incidence, there is a critical need to evaluate the actual frequency of UTIs in specific populations. This study aims to establish the frequency of UTIs in patients with T2DM who are being treated with SGLT-2 inhibitors and are currently presenting at Jinnah Sindh Medical University, Karachi. By focusing on this population, the study seeks to provide relatable and actionable data to guide clinical decision-making and optimize the management of T2DM patients. The objective is to determine the frequency of UTIs in this patient population and contribute valuable insights for balancing the benefits and risks of SGLT-2 inhibitor therapy.

METHODS

The study was a cross-sectional analysis conducted at the Department of Nephrology, Jinnah Sindh Medical University, Karachi, from January 2024 to June 2024, following approval from the Institutional Review Board (IRB). Patients of either gender, aged 30 to 65 years, with a diagnosis of type 2 diabetes mellitus (T2DM) and receiving treatment with sodium-glucose cotransporter-2 (SGLT-2) inhibitors (dapagliflozin, empagliflozin, or canagliflozin) for at least one month were included in the study. Exclusion criteria comprised patients with type 1 diabetes mellitus, pregnant females, those with a prior history of recurrent urinary tract infections (UTIs) before initiating SGLT-2 inhibitors, individuals with severe renal impairment (eGFR < 30 mL/min/1.73 m^2), and those on immunosuppressive therapy. A total of 215 patients meeting the inclusion criteria were enrolled using a non-probability consecutive sampling technique. Data collection involved obtaining written informed consent from all participants before enrollment. Demographic and clinical data, including age, gender, body mass index (BMI), duration of diabetes, HbA1c levels, and comorbidities such as hypertension, were recorded. Symptoms indicative of UTIs, including dysuria, increased urinary frequency, urgency, and fever, were documented. Urine samples were collected from all participants for urinalysis and urine culture to confirm the diagnosis of a UTI. Patients with positive urine cultures were categorized as having a UTI.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 27.0. Descriptive statistics were employed to summarize demographic and clinical characteristics. Continuous variables, such as age and duration of diabetes, were presented as means and standard deviations, while categorical variables, including gender and UTI status, were presented as frequencies and percentages. Associations between UTI occurrence and demographic or clinical factors, such as gender, duration of diabetes, and HbA1c levels, were assessed using chi-square tests for categorical variables and Student's t-tests for continuous variables. A p-value of less than 0.05 was considered statistically significant. Efforts to control confounding variables included ensuring all participants met

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

strict inclusion criteria, such as consistent SGLT-2 inhibitor use and absence of prior recurrent UTIs. Standardized protocols for urine sample collection were implemented, instructing participants on proper midstream clean-catch methods. Samples were promptly processed to ensure accuracy and minimize contamination risks.

RESULTS

A total of 215 patients with type 2 diabetes mellitus receiving treatment with sodium-glucose cotransporter-2 (SGLT-2) inhibitors were included in the study. The mean age of the participants was 54 years, with a standard deviation of 9.8 years. The majority of patients were male (63.7%), while 36.3% were female. The mean duration of diabetes was 7.5 years (SD ± 3.2). Hypertension was present in 36.3% of patients, while 27.9% of the study population had a body mass index (BMI) equal to or greater than 30 kg/m². The mean hemoglobin level was 10.28 g/dL (SD ± 1.8), mean serum urea was 34.8 mg/dL (SD ± 24.9), and mean serum creatinine was 0.9 mg/dL (SD ± 0.8). Among the participants, 83.2% had an HbA1c level equal to or greater than 8%, while 16.8% had an HbA1c level below 8%.

Table: Baseline characteristics of patients taking Sodium-Glucose Cotransporter-2 Inhibitors

Study population		**N (%)**
Gender	Male	137 (63.7)
	Female	78 (36.3)
History of hypertension	Yes	78 (36.3)
	No	137 (63.7)
HbA1c	≥ 8%	109 (83.2)
	< 8%	23 (16.8)
BMI (kg/m2)	≥ 30	60 (27.9)
	< 30	155 (72.1)
UTI	Present	32 (14.9)
	Absent	183 (85.1)
Age (years± S.D)		56.4±3.6
Duration of Diabetes (years± S.D)		7.5 ± 3.2
Hemoglobin (g/dL)		10.28 ± 1.8
Serum Urea (mg/dl)		34.8 ± 24.9
Serum Creatinine (mg/dl)		0.9 ± 0.8

Legends: BMI: Body Mass Index; UTI: Urinary tract infection

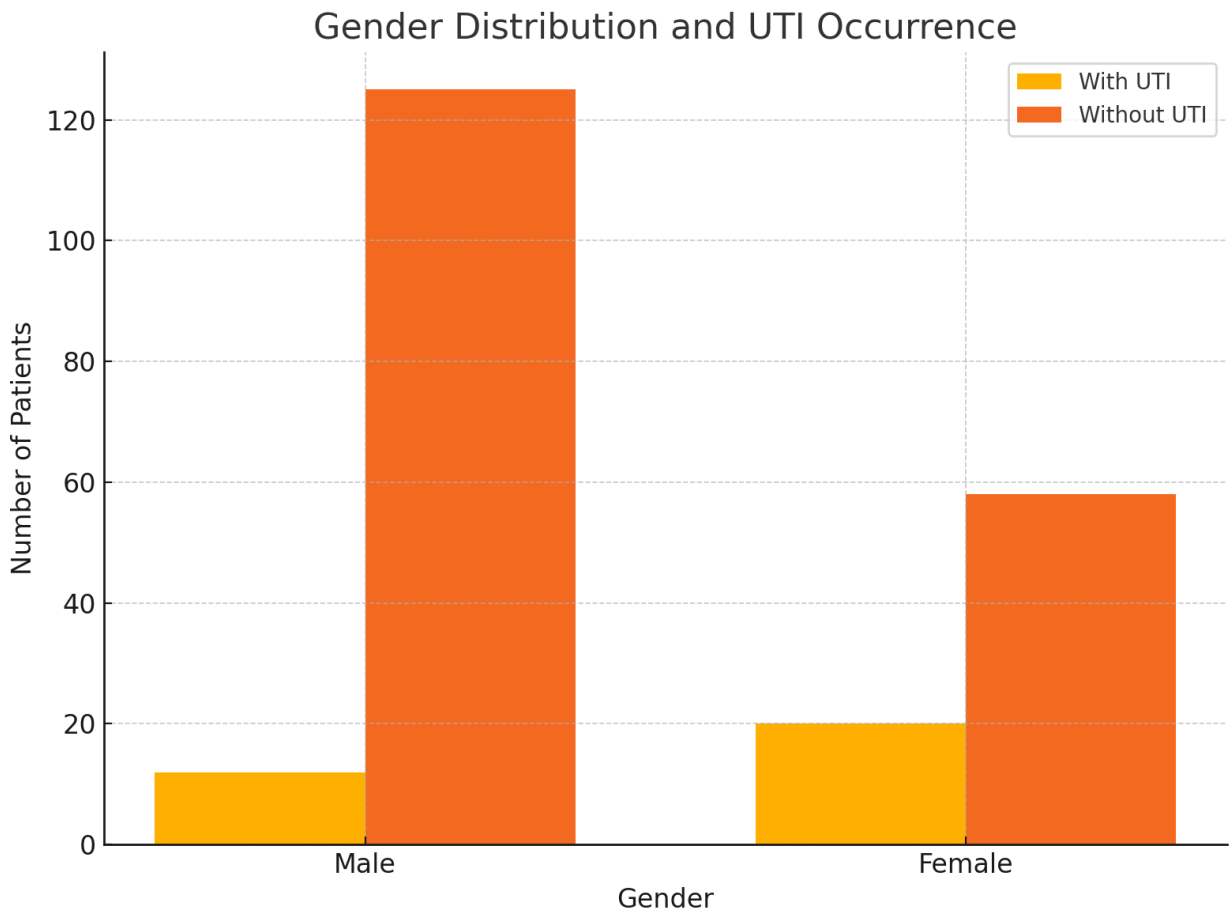
Out of the total patients, 32 (14.9%) were diagnosed with urinary tract infections (UTIs) based on positive urine culture results, while 183 (85.1%) showed no evidence of infection. On comparing patients with and without UTIs, female patients were found to have a significantly higher incidence of UTIs (62.5% of UTI cases were female, $p = 0.02$). Patients with an HbA1c level greater than 8% were also more likely to develop UTIs compared to those with lower HbA1c levels (96.9% vs. 87.9%, $p = 0.01$). No significant differences were observed in terms of duration of diabetes, BMI, age, serum creatinine, or serum urea levels between patients with and without UTIs ($p > 0.05$ for all variables).

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Table: Clinical and demographic variables of patients with and without UTI (n-215)

Variables		Present (N-32)	Absent (N-183)	p-value
Gender	Male	12 (37.5)	125 (68.3)	0.02
	Female	20 (62.5)	58 (31.7)	
HbA1c	≥ 8%	31 (96.9)	161 (87.9)	≤ 0.01
	< 8%	1 (3.1)	22 (12.1)	
Duration of Diabetes		8.4 ± 4.5	7.6 ± 3.1	0.24
BMI (kg/m2)		28.4 ± 3.9	27.7 ± 4.9	0.46
Age (years)		56.4 ± 8.2	53.8 ± 9.5	0.34
Hemoglobin (g/dL)		10.3 ± 1.7	10.7 ± 1.2	0.027
Serum Creatinine (mg/dl)		0.75 ± 0.42	0.69 ± 0.71	0.733
Serum urea levels (mg/dl)		34 ± 6.3	45 ± 8.3	0.694

These findings suggest that female gender and poor glycemic control, as indicated by elevated HbA1c levels, are significant risk factors for the development of UTIs in patients receiving SGLT-2 inhibitors. Additional investigations may further elucidate other potential risk factors and mechanisms contributing to this association.



DISCUSSION

The study explored the incidence of urinary tract infections (UTIs) in patients with type 2 diabetes mellitus (T2DM) using sodium-glucose cotransporter-2 (SGLT-2) inhibitors and identified key factors contributing to an increased risk of UTIs. Among the 215 patients included, the overall incidence of UTIs was 14.9%, with female gender and poor glycemic control (HbA1c > 8%) emerging as significant risk factors. These findings are consistent with previous research, which highlights the association between SGLT-2 inhibitors and UTIs due to glucosuria creating a favorable environment for bacterial colonization (14). The observation that female patients had a higher risk of UTIs aligns with existing literature, where anatomical predispositions, such as a shorter urethra, increase the susceptibility to infections. Studies conducted on diabetic populations have similarly reported a higher prevalence of UTIs in females using SGLT-2 inhibitors, emphasizing the need for regular monitoring and preventive measures in this subgroup (20). Poor glycemic control was another prominent risk factor identified, as patients with elevated HbA1c levels had significantly higher rates of UTIs. Hyperglycemia likely contributed to immune suppression and glucosuria, both of which enhance bacterial growth in the urinary tract. This finding supports the importance of maintaining optimal glycemic control to reduce the risk of infections (23, 24).

While SGLT-2 inhibitors are associated with UTIs, some studies suggest that the incidence of these infections may not significantly differ when compared to other antidiabetic agents, such as dipeptidyl peptidase-4 (DPP-4) inhibitors. However, the current study showed a relatively higher UTI frequency, potentially reflecting population-specific factors or differences in study design. Certain studies have also indicated a possible dose-dependent relationship between SGLT-2 inhibitors and UTI risk, particularly with higher doses of dapagliflozin, although this aspect could not be analyzed in the present research due to the lack of dosage stratification (19). The study's major strength lies in its relatively large sample size, which allowed for a comprehensive assessment of UTI risk factors across a diverse patient population. Additionally, the use of urine culture for UTI diagnosis enhanced the accuracy of the findings compared to symptom-based diagnoses. However, the cross-sectional design limits the ability to establish causality or observe long-term trends in UTI incidence. The study was also limited to a single medical center in Karachi, reducing the generalizability of the results to other regions or populations. Furthermore, the lack of stratification by the specific class or dose of SGLT-2 inhibitor may have influenced the observed outcomes.

The findings highlight the importance of personalized treatment approaches for patients using SGLT-2 inhibitors, particularly females and those with poor glycemic control. Regular monitoring, urine cultures, and preventive strategies such as improved hygiene and fluid intake may help mitigate the risk of UTIs in high-risk patients. Optimizing glycemic control should remain a priority in reducing infection risk. Future research focusing on the dose-response relationship and multicenter studies across diverse populations would provide further insight into the safety profile of SGLT-2 inhibitors and inform clinical decision-making. These results reinforce the need for a balanced approach, ensuring the benefits of SGLT-2 inhibitors are maximized while minimizing the risk of adverse effects such as UTIs.

CONCLUSION

The study concluded that the use of SGLT-2 inhibitors in patients with type 2 diabetes mellitus is associated with an increased risk of urinary tract infections, particularly among females and those with poor glycemic control. These findings highlight the importance of personalized management, regular monitoring, and preventive measures to mitigate infection risks in this vulnerable population. Future research should focus on exploring long-term outcomes and strategies to reduce the incidence of UTIs, ensuring the safe and effective use of SGLT-2 inhibitors in clinical practice.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 9th edn. Brussels, Belgium: International Diabetes Federation; 2019.

2. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. BMJ Open. 2018;8:e020961.

3. Pelletier R, Ng K, Alkabbani W, et al. Adverse events associated with sodium glucose co-transporter 2 inhibitors: an overview of quantitative systematic reviews. Ther Adv Drug Saf. 2021;12:2042098621989134.

4. Kalra S. Sodium glucose co-transporter-2 (SGLT2) inhibitors: a review of their basic and clinical pharmacology. Diabetes Ther. 2014;5(2):355–66.

5. Rieg T, Vallon V. Development of SGLT1 and SGLT2 inhibitors. Diabetologia. 2018;61:2079–86.

6. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2019;380:347–57.

7. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017;377:644–57.

8. Kanie T, Mizuno A, Takaoka Y, et al. Dipeptidyl peptidase-4 inhibitors, glucagon-like peptide 1 receptor agonists and sodium-glucose co-transporter-2 inhibitors for people with cardiovascular disease: a network meta-analysis. Cochrane Database Syst Rev. 2021;10:CD013650.

9. McGill JB, Subramanian S. Safety of sodium-glucose co-transporter 2 inhibitors. Am J Cardiol. 2019;124:45–52.

10. Chandrashekar M, Philip S, Nesbitt A, et al. Sodium glucose-linked transport protein 2 inhibitors: an overview of genitourinary and perioperative implications. Int J Urol. 2021;28(10):984–90.

11. Imai T, Kato N, Kanda N, et al. Risk of urogenital bacterial infection with sodium-glucose cotransporter-2 inhibitors: a retrospective cohort study using a claims database. Diabetes Ther. 2024;15(8):1821–30.

12. Xu B, Li S, Kang B, et al. The current role of sodium-glucose cotransporter 2 inhibitors in type 2 diabetes mellitus management. Cardiovasc Diabetol. 2022;21(1):83.

13. Kaze AD, Zhuo M, Kim SC, et al. Association of SGLT2 inhibitors with cardiovascular, kidney, and safety outcomes among patients with diabetic kidney disease: a meta-analysis. Cardiovasc Diabetol. 2022;21:47.

14. Ashfaq M, Shafique S, Niazi Z, et al. Occurrence of urinary tract infections in type 2 diabetes mellitus patients taking sodium-glucose co-transporter-2 inhibitors to regulate their blood sugar levels. Int J Health Sci. 2023;7(S1):1999–2005.

15. Tanrıverdi M, Baştemir M, Demirbakan H, et al. Association of SGLT-2 inhibitors with bacterial urinary tract infection in type 2 diabetes. BMC Endocr Disord. 2023;23(1):211.

16. FREQUENCY OF URINARY TRACT INFECTIONS IN TYPE 2 DIABETES MELLITUS PATIENTS, USING SGLT-2 INHIBITORS. J Popul Ther Clin Pharmacol. 2024;31(3):2424–29.

17. Berbudi A, Rahmadika N, Tjahjadi AI, et al. Type 2 diabetes and its impact on the immune system. Curr Diabetes Rev. 2020;16(5):442–49.

18. Caparrotta TM, Greenhalgh AM, Osinski K, et al. Sodium-glucose co-transporter 2 inhibitors exposure and outcomes in type 2 diabetes: a systematic review of population-based observational studies. Diabetes Ther. 2021;12:991–1028.

19. Rådholm K, Wu JH, Wong MG, et al. Effects of sodium-glucose cotransporter-2 inhibitors on cardiovascular disease, death, and safety outcomes in type 2 diabetes: a systematic review. Diabetes Res Clin Pract. 2018;140:118–28.

20. Zhang YJ, Han SL, Sun XF, et al. Efficacy and safety of empagliflozin for type 2 diabetes mellitus: meta-analysis of randomized controlled trials. Med (Baltim). 2018;97(43):e12843.

21. 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.

22. Hsia DS, Grove O, Cefalu WT. An update on sodium-glucose co-transporter-2 inhibitors for the treatment of diabetes mellitus. Curr Opin Endocrinol Diabetes Obes. 2017;24(1):73–9.

23. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 diabetes and its impact on the immune system. Curr Diabetes Rev. 2020;16(5):442–49.

24. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med. 2017;377:644–57.