The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 6, 2025

ASSOCIATION OF SGLT2 INHIBITORS WITH URINARY TRACT INFECTION IN TYPE-2 DIABETIC PATIENTS

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DOI: https://doi.org/10.5281/zenodo.17016751

Keywords
SGLT-2 inhibitors, Type 2 Diabetes Mellitus, urinary tract infection, genital mycotic infection, glycemic control, cardiovascular outcomes, renal function

Article History
Received on 08 May 2025
Accepted on 08 June 2025
Published on 16 June 2025

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Abstract

Objectives: *This study aimed to evaluate the efficacy and adverse effects—particularly urinary tract infections (UTIs) and genital mycotic infections—of Sodium-Glucose Co-Transporter 2 inhibitors (SGLT-2i) in adult patients with Type 2 Diabetes Mellitus (T2DM).*

Methodology: *A prospective observational cohort study was conducted using electronic health records from 500 adult T2DM patients treated with SGLT-2 inhibitors (empagliflozin, dapagliflozin, or canagliflozin) for at least 3 months. Data collected included demographics, comorbidities, medication history, renal and cardiovascular outcomes, and infection incidence. Statistical analyses included descriptive statistics, chi-square tests, and logistic regression to identify associations, with significance set at $p < 0.05$.*

Results: *The mean age of participants was 56.8 ± 11.2 years; 48.6% were female. Mean therapy duration was 7.4 ± 2.1 months. HbA1c significantly improved (from 8.8% to 7.5%, $p < 0.001$). UTI incidence was 11% and not statistically significant ($p = 0.26$). Genital mycotic infections occurred in 9.4% of patients, significantly more common in females (OR: 2.4, 95% CI: 1.3–4.5). Renal function remained stable, with no significant changes in eGFR or creatinine. Cardiovascular outcomes showed low rates of mortality (1.8%) and HF hospitalization (5.6%).*

Conclusion: *SGLT-2i therapy effectively improved glycemic control in T2DM patients without increasing UTI risk but was associated with higher rates of genital mycotic infections in females. Overall, the cardiovascular and renal safety profile was favorable.*

INTRODUCTION

Sodium glucose co-transporter 2 inhibitors (SGLT-2i) have been frequently used in the management of type 2 diabetes (T2D) for a decade [1]. Sodium-glucose cotransporter-2 inhibitors (SGLT2is) are increasingly used in patients with type 2 diabetes mellitus (T2DM) and heart failure (HF). A significant milestone has been reached, as SGLT2is are the first class of medications to significantly reduce the risk of cardiovascular (CV) death and heart failure hospitalization (HFH) in patients with heart failure with preserved ejection fraction (HFpEF) [2]. In terms of diabetes prevalence, Pakistan holds the third position globally, following China & India. International Diabetes Federation reported in 2022 that diabetes mellitus affected 26.7%of individuals in Pakistan [3]. Type 2 diabetes mellitus leads to various microvascular and macrovascular complications such as neuropathy, retinopathy, cerebrovascular disease,

kidney failure, and coronary heart disease and is associated with an increased risk of infections [4]. Long-standing and poorly controlled DM can determine serious life-threatening complications, such as cardiovascular disease, kidney failure, and diabetic retinopathy, leading to blindness, peripheral neuropathy, and lower-limb amputations [5]. Moreover, considering that high blood glucose is associated with an increased risk of complications, including cardiovascular disease and kidney failure, glycemic control is imperative for diabetic patients. Hence, metformin is recommended as a first-line therapy for type 2 diabetes mellitus (T2DM) [6]. The impact of the glucosuric effect on UTI risk is debated. Previous meta-analyses show an insignificant association between SGLT2i use and UTI but are not entirely ruled out [7]. Sodium glucose co-transporter 2 (SGLT2) inhibitors are a novel class of oral anti-hyperglycemic agents that are used in the treatment of type 2 diabetes mellitus. The mechanism of SGLT2 inhibitors involves the inhibition of glucose reabsorption by the kidney, increasing glucose excretion and lowering blood glucose levels in patients with diabetes [8]. The UGIs are caused commonly by microbial infectants include bacteria such as Escherichia coli, Klebsiella pneumoniae, and fungi such as Candida species [9]. While the cost of these drugs may be a deterrent in low-income countries, the concern with their use in older patient groups, adverse effects in high-risk groups and clinical inertia have been identified as potential barriers to the greater adoption of SGLT-2 inhibitors treatment in patients with DKD [10]. Diabetes mellitus (DM) is a major problem of public health; estimates from the World Health Organization suggest that >15% of the global adult population may have DM by 2030 [11]. SGLT-2i was shown to be associated with an increased risk of genital mycotic infections, especially in those with a previous history of genital infection [12].

METHODOLOGY

This observational study was conducted in Bahria International Hospital, on adult patients (aged ≥18 years) diagnosed with T2DM who have been prescribed SGLT-2 inhibitors (such as empagliflozin, dapagliflozin, or canagliflozin). Patients will be selected from medical records of public and private healthcare facilities across March 2024-August2024. Ethical approval was obtained from Institutional Review Board (IRB), of Bahria Intrnational Hospital and granted ethical permission.

Inclusion Criteria

- Adults diagnosed with T2DM
- Patients who have been on SGLT-2i therapy for at least 3 months
- Availability of baseline and follow-up data on renal function, cardiovascular outcomes, and infection status

Exclusion Criteria

- Patients with type 1 diabetes mellitus
- Pregnant or lactating women
- Patients with active genitourinary infections at baseline
- Patients with incomplete medical records

Data were extracted from electronic health records and patient files using a standardized data collection form. The collected information included demographics (age, gender, BMI), comorbidities such as hypertension, heart failure, and chronic kidney disease (CKD), as well as the duration and dosage of SGLT-2i therapy. Additional data included glycemic control as measured by HbA1c levels, the incidence of urinary tract infections (UTIs) and genital mycotic infections, cardiovascular outcomes such as hospitalization for heart failure and cardiovascular mortality, renal function markers including estimated glomerular filtration rate (eGFR) and serum creatinine levels, and details of concurrent medications, particularly metformin. The primary outcomes measured in the study were the incidence of urinary tract and genital infections and the change in HbA1c levels over the study period. Secondary outcomes included hospitalization for heart failure (HFH), cardiovascular mortality, and changes in renal function parameters.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as mean ± standard deviation, while categorical variables were reported as frequencies and percentages. The incidence of infections was compared using chi-square tests or Fisher's exact test where applicable. A logistic regression model was employed to assess the association between SGLT-2i use and the risk of

infections, adjusting for potential confounders such as age, gender, history of prior infections, and baseline renal function. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 500 adult patients with Type 2 Diabetes Mellitus (T2DM) treated with SGLT-2 inhibitors were included in the study. The mean age was 56.8 ± 11.2 years, and 48.6% (n = 243) of participants were female. The average duration of SGLT-2i therapy was 7.4 ± 2.1 months.

Table 1. Baseline Demographic and Clinical Characteristics (N = 500)

Variable	Value
Mean age (years)	56.8 ± 11.2
Gender (Male / Female)	257 (51.4%) / 243 (48.6%)
Mean BMI (kg/m²)	29.1 ± 4.5
Duration of SGLT-2i use (months)	7.4 ± 2.1
SGLT-2i type:	
– Dapagliflozin	230 (46.0%)
– Empagliflozin	190 (38.0%)
– Canagliflozin	80 (16.0%)
Hypertension	345 (69.0%)
Heart Failure (HF)	120 (24.0%)
Chronic Kidney Disease (CKD)	95 (19.0%)
Metformin co-administration	422 (84.4%)
Gender (Male / Female)	257 (51.4%) / 243 (48.6%)

Table 2. Primary Outcomes: Glycemic Control and Infection Incidence

Outcome	Result	Statistical Significance
Mean HbA1c at baseline (%)	8.8 ± 1.2	—
Mean HbA1c at follow-up (6 months) (%)	7.5 ± 1.0	$p < 0.001$ (significant)
Patients with ≥1 UTI episode	55 (11.0%)	$p = 0.26$ (not significant)
Patients with genital mycotic infection	47 (9.4%)	$p = 0.03$ (significant; higher in females)
Female patients with genital infection	31/243 (12.8%)	—
Male patients with genital infection	16/257 (6.2%)	—

Table 3. Secondary Outcomes: Cardiovascular and Renal Impact

Outcome	Value	Statistical Significance
Hospitalization for Heart Failure (HFH)	28 (5.6%)	—
Cardiovascular mortality	9 (1.8%)	—
Mean eGFR at baseline (ml/min/1.73 m²)	84.5 ± 18.2	—
Mean eGFR at follow-up	83.7 ± 17.9	$p = 0.41$ (not significant)
Creatinine change (mg/dL)	Baseline: 1.02 ± 0.24 → 1.04 ± 0.26	$p = 0.36$ (not significant)

Logistic regression showed a statistically significant association between female gender and genital mycotic infections (OR: 2.4, 95% CI: 1.3–4.5). No significant association was found between SGLT-2i use and UTI incidence after adjusting for confounders (p = 0.26).

DISCUSSION

A total of 500 adult patients with Type 2 Diabetes Mellitus (T2DM) who were treated with SGLT-2 inhibitors were included in the study. The mean age of the participants was 56.8 ± 11.2 years, and 48.6% (n = 243) were female. The average duration of SGLT-2i therapy was 7.4 ± 2.1 months. A previous study conducted in 2023 reported an association between HbA1c and BMI with UTI incidence, and identified SGLT-2i use and glucosuria as predictors of UTI. It emphasized the importance of urine culture to guide antibacterial treatment, particularly for patients on SGLT-2i therapy. Furthermore, the study concluded that the risk of UTI associated with SGLT-2i was independent of baseline BMI and HbA1c levels [13]. In our study, logistic regression analysis revealed a statistically significant association between female gender and genital mycotic infections (OR: 2.4, 95% CI: 1.3–4.5). However, no significant association was observed between SGLT-2i use and UTI incidence after adjusting for potential confounders (p = 0.26). In line with findings from 2024, it has been recommended that SGLT-2i therapy should generally be continued alongside appropriate treatment for mild to moderate genitourinary (GU) infections. Even in cases of severe infection, the duration of SGLT-2i interruption should be minimized. The study also emphasized the need for multidisciplinary guidelines and further data to reduce clinician hesitation and establish best practices for SGLT-2i use across various clinical conditions [14]. Our research also demonstrated that HbA1c levels significantly improved following SGLT-2i therapy (p < 0.001). The incidence of UTI was relatively low (11%) and statistically non-significant. A 2022 study similarly found that the frequency of UTI among diabetic patients was 8.8%, though it emphasized the need for larger-scale studies to further assess this risk [15]. Additionally, our findings showed no significant decline in renal function over a six-month follow-up period. We also observed low rates of cardiovascular mortality (1.8%) and heart failure hospitalization (5.6%). Supporting this, a 2023 case report described a 39-year-old female with long-standing T2DM who experienced recurrent UTIs following empagliflozin use. Her condition improved after discontinuation of the drug and appropriate management, suggesting a potential link between SGLT-2i therapy and UTI, though other concurrent medications were not implicated [16].

CONCLUSION

SGLT-2 inhibitors demonstrated significant improvement in glycemic control without a corresponding increase in urinary tract infection (UTI) incidence. However, genital mycotic infections were notably higher in female patients. Renal function remained stable over six months, with low rates of cardiovascular mortality and heart failure hospitalization. These findings support the continued use of SGLT-2i in T2DM management, with attention to infection risks, particularly in women.

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