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PREVALENCE OF URINARY TRACT INFECTIONS IN TYPE-II DIABETICS TAKING EMPAGLIFLOZIN AT DHQ HOSPITAL MIRPUR AJK

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Abstract

Background:

Type 2 diabetes mellitus (T2DM) increases susceptibility to infections, including urinary tract infections (UTIs). Sodium-glucose co-transporter 2 (SGLT2) inhibitors improve glycemic and cardiorenal outcomes but may raise the risk of genitourinary infections due to glucosuria. This study aimed to determine the prevalence of culture-confirmed UTIs in ambulatory T2DM patients receiving empagliflozin.

Materials and Methods:

A prospective longitudinal study was conducted at DHQ Hospital Mirpur, AJK (Dec 2023–May 2024) including adults with T2DM initiated on empagliflozin for inadequate glycemic control. Baseline labs, urine cultures, and hygiene counseling were provided, with 12-week follow-up assessing symptomatic and culture-confirmed UTIs as the primary outcome and genital infections as secondary outcomes. All data was entered and calculated using SPSS version 23.0. The statistical significance set at $p \leq 0.05$.

Results:

Among 200 patients (mean age 50.2 ± 10.8 years, 64% male), 12 (6%) developed urinary tract infections and 9 (4.5%) had genital infections after 12 weeks of empagliflozin therapy. Females and those with HbA1c > 8.5% had significantly higher infection rates ($p = 0.002$ and $p = 0.01$, respectively), while BMI, diabetes duration, and prior UTI history showed no significant associations.

Conclusion:

Empagliflozin use in T2DM patients was associated with modest rates of urinary and genital infections, with higher risk in females and those with poor glycemic control. Careful patient selection, hygiene counseling, and vigilant monitoring are essential, and larger long-term studies are needed to confirm these findings.

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INTRODUCTION

Diabetes mellitus remains the most prevalent endocrine disorder of the current era, posing a substantial challenge to global health systems.[1] The escalating incidence of type 2 diabetes mellitus (T2DM) is particularly concerning due to its significant morbidity, mortality, and the associated socio-economic burden on patients, families, and healthcare infrastructure.[2] Individuals with T2DM are notably predisposed to various infections, including urinary tract infections (UTIs), a complication that further contributes to the overall disease burden.[3] The hyperglycemic milieu in diabetes impairs several immune mechanisms, including humoral responses, neutrophil function, and antioxidant defense pathways, thereby facilitating infection susceptibility.[4]

Conventional management of T2DM has relied on agents such as metformin, sulfonylureas, alpha-glucosidase inhibitors, and insulin.[5] In recent years, sodium-glucose co-transporter-2 (SGLT2) inhibitors have emerged as a novel class of oral antihyperglycemic agents. These medications exert their effect by inhibiting glucose reabsorption in the proximal renal tubules, leading to increased urinary glucose excretion and improved glycemic control.[6] Beyond glycemic management, SGLT2 inhibitors offer additional therapeutic benefits, including modest reductions in body weight, systolic blood pressure, and demonstrated cardiovascular and renal protective effects, all with a relatively low risk of hypoglycemia.[7]

Currently available SGLT2 inhibitors—dapagliflozin, canagliflozin, empagliflozin, and remogliflozin—are approved for use as monotherapy or in combination with other antihyperglycemic agents in T2DM.[1] Despite their advantages, the mechanism of action of these agents, specifically the induction of glucosuria, may create a favorable environment for microbial proliferation, thereby increasing the risk of genitourinary infections.[8] Diabetic autonomic neuropathy further compounds this risk by contributing to bladder dysfunction and urinary retention.[9]

Previous studies have reported the prevalence of clinically diagnosed bacterial UTIs in patients with T2DM on SGLT2 inhibitors to be approximately 9%.[10] However, there remains a paucity of data regarding culture-confirmed UTIs, their specific types, and the causative organisms in patient population.[8,11] Moreover, most available evidence originates from trials with stringent inclusion criteria, which may not accurately reflect real-world practice in diverse ambulatory settings.[5]

Therefore, this study was undertaken to determine the prevalence of culture-proven bacterial UTIs among ambulatory patients with T2DM receiving empagliflozin therapy. By focusing on a real-world cohort, this research aims to provide clinically relevant insights into the infection risk associated with empagliflozin, thereby informing patient selection, counseling, and monitoring strategies in routine practice.

MATERIALS AND METHODS:

This was a prospective longitudinal study conducted at the Department of Medicine at DHQ Hospital Mirpur, AJK from December 2023 to May 2024 after approval by the Institutional Ethics Committee. A sample size of 200 patients was calculated using WHO Calculator. All data were anonymized to maintain participant confidentiality.

The study included adult patients (≥18 years) with type 2 diabetes mellitus (T2DM) who were initiated on empagliflozin due to suboptimal glycemic control despite therapy with other oral antidiabetic agents, defined as glycosylated hemoglobin (HbA1c) >7% and/or fasting venous plasma glucose (FPG) >120 mg/dL. Patients were excluded if they had an estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m², were pregnant or lactating, or had documented urinary tract infection (UTI) within the preceding 3 months. Eligible participants were provided with detailed information regarding the study, and written informed consent was obtained before enrollment.

At baseline, fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), and HbA1c

Frontier in Medical & Health Research

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levels were recorded. A midstream urine sample was collected prior to empagliflozin initiation for bacterial culture to rule out pre-existing infections.

All participants received structured education regarding genital and perineal hygiene, which included instructions on cleansing with clean water after urination and defecation, proper drying of the area, and avoiding the use of alcohol-based disinfectants. Female participants were counseled to perform front-to-back cleansing. Participants were advised to report immediately if they developed symptoms of UTI (e.g., dysuria, fever, urinary frequency, or urgency) at any point during the 12-week follow-up. At the end of 12 weeks, a comprehensive assessment was performed, which included symptom review for UTI and genital infections, physical examination, with emphasis on temperature, pulse, blood pressure, suprapubic and costovertebral angle tenderness, and abdominal palpation findings, genital examination to evaluate for infections.

Midstream urine samples were collected using a standardized clean-catch method. Male participants were instructed to clean the glans with water-soaked swabs, void the initial 50 mL of urine, and collect the next 10–20 mL into a sterile container. Female participants were instructed to separate the labia and cleanse the vulva twice in an anteroposterior direction with water-soaked swabs before sample collection. Urine samples were immediately sent to the laboratory for bacterial culture.

The primary outcome was the proportion of patients with symptomatic UTI and/or culture-confirmed significant bacteriuria at 12 weeks of empagliflozin therapy. Genital infections were analyzed as a secondary outcome. Data analysis was performed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and percentages. Statistical associations between genitourinary infections and demographic or clinical variables were assessed using appropriate tests, with $p < 0.05$ considered statistically significant.

RESULTS:

A total of 200 patients with type 2 diabetes mellitus were enrolled in the study. The mean age of the patients was 50.2 ± 10.8 years. Of these, 128 (64%) were male and 72 (36%) were female. The mean BMI was 27.8 ± 4.9 kg/m², mean HbA1c was 8.1 ± 1.9%, and the mean duration of diabetes was 7.2 ± 3.1 years. A history of previous urinary tract infection (UTI) was reported in 12 (6%) patients as shown in Table 1.

Table 1. Demographic data of the patients (n = 200)

VARIABLE	VALUE
Gender (Male : Female)	128 (64%) : 72 (36%)
Mean age (years) ± SD	50.2 ± 10.8
Mean BMI (kg/m²) ± SD	27.8 ± 4.9
Mean duration of diabetes (years) ± SD	7.2 ± 3.1
History of UTI	12 (6%)
Mean HbA1c (%) ± SD	8.1 ± 1.9

All patients were commenced on Empagliflozin. At 12 weeks of follow-up, the prevalence of urinary tract infections (UTIs) was 12 (6%), while the prevalence of genital tract infections was 9 (4.5%) as shown in Figure 1.

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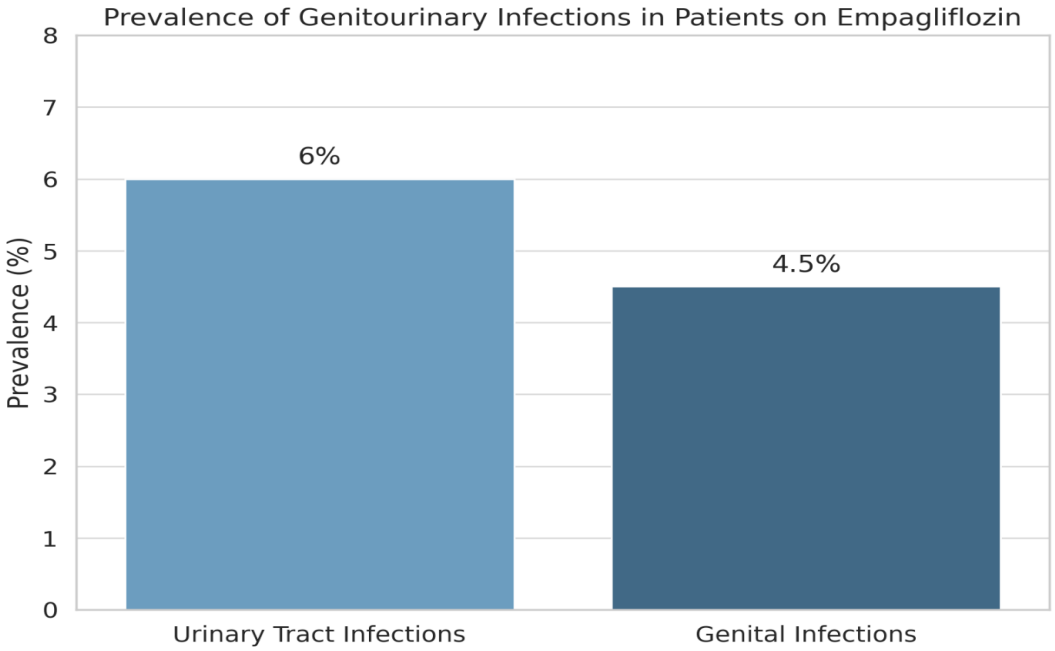
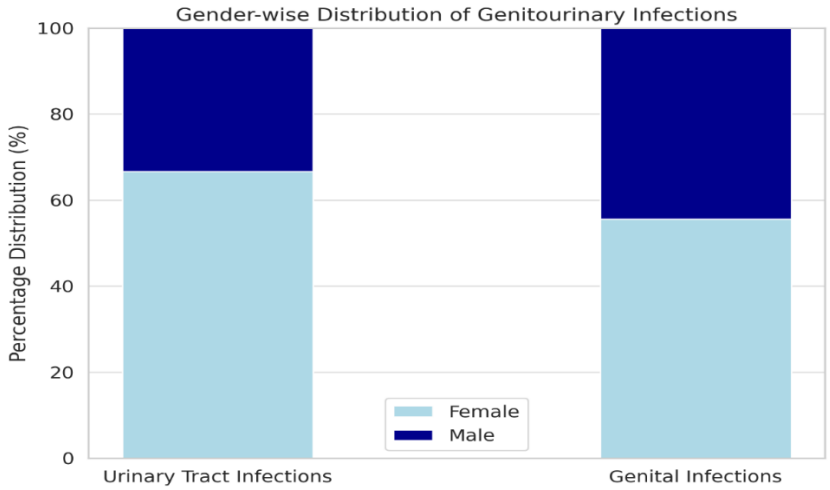
Figure 1. Prevalence of genitourinary infections in patients on Empagliflozin



A gender-wise analysis revealed that females exhibited a higher prevalence of genitourinary infections compared to males as shown in Figure 2.

Figure 2. Gender-wise distribution of infections



Among those who developed UTIs, 8 (66.7%) were female and 4 (33.3%) were male. Similarly, genital infections were more frequent in females (5 [55.6%]) than in males (4 [44.4%]) as shown in Table 2.

Frontier in Medical & Health Research

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Table 2. Prevalence of infections according to gender

TYPE OF INFECTION	TOTAL N (%)	FEMALE N (%)	MALE N (%)
Urinary tract infection	12 (6%)	8 (66.7%)	4 (33.3%)
Genital infection	9 (4.5%)	5 (55.6%)	4 (44.4%)

Correlation analysis demonstrated a statistically significant association between female gender and the occurrence of genitourinary infections ($p = 0.002$) and between HbA1c >8.5% and increased infection risk ($p = 0.01$). Other variables, such as BMI and diabetes duration, did not demonstrate a statistically significant correlation as shown in Table 3.

Table 3. Correlation of Variables with Genitourinary Infections (n = 21)

VARIABLE	INFECTED (N = 21)	p-VALUE*
BMI >30 kg/m²	5 (23.8%)	0.21
Duration of diabetes >5 years	13 (61.9%)	0.08
HbA1c >8.5%	15 (71.4%)	0.01
Female gender	13 (61.9%)	0.002
Previous UTI history	4 (19.0%)	0.36

* $p \leq 0.05$ was considered statistically significant

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DISCUSSION:

Patients with diabetes mellitus are known to be more susceptible to various infections compared to the non-diabetic population. This increased susceptibility is multifactorial and has been attributed to impaired immune mechanisms, including altered polymorphonuclear leukocyte function, reduced chemotaxis, impaired phagocytic activity, and compromised antioxidant defense systems.[12] Hyperglycemia and associated metabolic disturbances such as acidosis further exacerbate these immune dysfunctions, underscoring the importance of maintaining optimal glycemic control to reduce infection risk.[13]

In this study of 200 patients with type 2 diabetes mellitus initiated on empagliflozin, the prevalence of urinary tract infections (UTIs) was 6%, while genital tract infections were observed in 4.5% of participants. These findings are comparable to those reported in prior randomized controlled trials and observational studies. Uitrakul et al. demonstrated a significantly higher incidence of UTIs among patients using SGLT2 inhibitors compared to non-SGLT2 users ($p < 0.001$).[14] In contrast, Kohler et al. reported a UTI incidence of

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approximately 9.4–10.4 events per 100 patient-years in empagliflozin users, which was not significantly different from placebo (11.3 events per 100 patient-years).[15]

Our observed genital infection rate aligns closely with data from large pooled analyses. Geerlings et al. reported genital infection rates of 4.2% (empagliflozin 10 mg) and 3.6% (empagliflozin 25 mg), compared to 0.7% in placebo arms.[16] Likewise, Li et al. documented a consistently higher risk of genital infections in patients treated with empagliflozin compared to non-SGLT2i therapies.[17]

Gender distribution in our cohort reflected well-recognized patterns, with females comprising the majority of both UTI (66.7%) and genital infection (55.6%) cases. This is consistent with earlier findings that female sex is a strong predictor of genitourinary infections in patients receiving SGLT2 inhibitors. Unnikrishnan et al. reported genital infection rates of 6.3% and 7.0% in women treated with empagliflozin 10 mg and 25 mg, respectively, compared to only 2.6% and 1.1% in men.[18]

We also observed a significant association between poor glycemic control and genitourinary infections, with 72% of infected patients having HbA1c >8.5% ($p = 0.01$). This finding corroborates the work of Caro et al., who reported that patients with HbA1c ≥8.0% had a significantly greater likelihood of developing genitourinary infections compared to those with better glycemic control.[19] Conversely, variables such as BMI >30 kg/m² and diabetes duration >5 years demonstrated a numerically higher but statistically non-significant association with infection risk in our cohort, aligning with prior studies where these factors did not emerge as independent predictors.[20] Additionally, a prior history of genitourinary infection was not significantly associated with subsequent infections in our study, in contrast to the findings of Nakhleh et al., who reported a strong association between previous infection history and future infection risk (HR 2.39; $p < 0.001$).[21]

Limitations of this study include its single-center design, relatively small sample size, and a short follow-up duration of 12 weeks, which may underestimate the long-term incidence of infections. Nonetheless, our findings provide valuable real-world data on infection risks associated with empagliflozin use in ambulatory patients with T2DM.

CONCLUSION:

In this prospective study of patients with type 2 diabetes mellitus receiving empagliflozin, the prevalence of urinary tract infections and genital infections was modest, with higher susceptibility observed in females and those with poor glycemic control. These findings underscore the importance of careful patient selection, pre-treatment counseling on hygiene practices, and close monitoring for genitourinary infections, particularly in high-risk subgroups. Further large-scale, long-term studies are warranted to validate these results and explore preventive strategies.

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