



Frequency of UTI in Patients Taking Empagliflozin Versus Dapagliflozin in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Individuals with diabetes are more likely than those without the disease to get a UTI. Determining the prevalence of genitourinary infections in individuals with type 2 diabetes receiving treatment with two SGLT-2 inhibitors (dapagliflozin and empagliflozin) was the aim of the current investigation. Future recommendations for medications that lessen UTIs will be made in order to lower morbidity in these people. **Study Design:** Randomized Controlled Trail. **Settings:** Department of Medicine, Aziz Fatima Hospital, Faisalabad. **Materials & Methods:** There were 90 (45 in each group) type 2 diabetes individuals of either gender who were older than 18 and using SGLT-2 inhibitors as monotherapy or combination therapy. Participants were excluded if they had gestational diabetes, had a UTI within the last three months, were pregnant or nursing. Those in group B received 25 mg of empagliflozin for three months, while those in group A received 10 mg of dapagliflozin. The patients were told to collect their urine midstream in a sterile urine bottle for analysis. Three months later, the results were documented in terms of UTI. **Results:** Patients in groups A and B had mean ages of 39.51 ± 10.22 and 40.31 ± 8.36 years, respectively. The majority of the 47 patients (52.22%) were in the 19–40 age range. With a male to female ratio of 1:1.4, 37 (41.11%) of the 90 patients were men and 53 (58.89%) were women. Three patients (6.67%) in Group A (dapagliflozin group) and fifteen (33.33%) in Group B (empagliflozin group) had UTIs on average (p -value = 0.0016). **Conclusion:** According to this study, people with type 2 diabetes mellitus who take empagliflozin have a higher incidence of UTIs than those who take dapagliflozin.

INTRODUCTION

Patients with type II diabetes mellitus (T2DM) are more likely to have infectious disorders, such as urinary tract infections (UTIs). Immune dysfunctions such as humoral immunity diseases, neutrophil dysfunction, and antioxidant defense system impairment are brought on by hyperglycemia.¹ Urinary retention and UTIs can be caused by bladder dysfunction, which is encouraged by diabetic neuropathy. Elevated urine glucose levels may encourage the growth of bacteria, one of the numerous factors that raise the risk of UTI.² Sodium-glucose co-transporter-2 (SGLT2) inhibitors are a more recent class of antihyperglycemic medications that have demonstrated cardiovascular (CV) safety in addition to decreasing systolic blood pressure, body weight, and blood glucose.³ The safety of these medications is of great importance to doctors who treat patients with type II diabetes. SGLT2 inhibitor use has been linked to common adverse effects (AEs), including polyuria, UTIs, and vaginal infections.⁴ Canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin are the

FDA-approved medications in this category.⁴

Dapagliflozin is a highly selective SGLT2 inhibitor that increases urine glucose excretion and inhibits renal glucose reabsorption to reduce blood glucose levels without the need for insulin. In both the early and late phases of type 2 diabetes, dapagliflozin was effective and well tolerated in phase III studies.⁵ T2DM can be treated with empagliflozin, a strong and specific SGLT2 inhibitor. In terms of fewer adverse events, empagliflozin performed well when compared to groups receiving conventional therapy.⁶ According to a study on the prevalence of UTIs in patients with type 2 diabetes on dapagliflozin, the incidence was 5.3%.⁷ A study on the frequency of UTI in individuals with type II diabetes mellitus using SGLT2 inhibitors found that the prevalence of UTI was 33.03% for empagliflozin.⁸

Compared to people without diabetes, people with diabetes are more likely to get a UTI. In order to ascertain the frequency of genitourinary infections

caused by two SGLT-2 inhibitors (dapagliflozin and empagliflozin) in patients with type 2 diabetes, the current investigation was carried out. In the future, a medication with a lower UTI will be suggested to lessen morbidity in these patients.

MATERIALS AND METHODS

The Department of Medicine at Aziz Fatima Hospital in Faisalabad conducted this randomized controlled experiment from Feb 2024 to August 2024. With a 90% research power, a 5% significance level, an expected proportion of 5.3%⁷ in dapagliflozin and 33.03%⁸ in empagliflozin (P1 and P2, respectively), a sample size of 90 (45 in each group) was obtained. To determine the sample size, the non-probability, sequential sampling technique was employed. We included all patients with Type II diabetes aged 18–60 years who were using SGLT-2 inhibitors as monotherapy or combination therapy for 3 months, irrespective of gender. Women with gestational diabetes, a UTI within the preceding three months, or those who were pregnant or breastfeeding were excluded.

Patients were enrolled following approval by the hospital's ethical review committee. Patients gave their written informed permission. All demographic information was recorded, including age, gender, and BMI, as well as clinical information such the length of diabetes mellitus and the HbA1C level. Using a lottery, the patients were split into two groups. For three months, patients in group A received 10 mg of dapagliflozin, whereas patients in group B received 25 mg of empagliflozin. For analysis, the patients were instructed to collect their pee midstream in a sterile urine bottle. After three months, the outcome was recorded in terms of UTI. Every piece of information was entered into a pre-made proforma.

SPSS V-25 was used to enter all of the data. Every quantitative variable, including age, height, weight, BMI, HbA1C (%), and the length of time with type 2 diabetes (months), had its mean and standard deviation determined. For every qualitative variable, including gender, UTI symptoms, urine examination, and outcome (UTI), frequency and percentage were computed. The UTIs in the two groups were compared using the chi-square test. To account for effect modifiers such age, gender, BMI, HbA1c level, and length of type 2 diabetes, stratification was employed. According to the post-stratification chi-square test, a significant P-value was defined as less than 0.05.

RESULTS

The study's participants ranged in age from >18 to 60, with a mean age of 40.12 ± 9.65 years. Group A patients were 39.51 ± 10.22 years old, while group B patients were 40.31 ± 8.36 years old. 47 patients, or 52.22% of the total, were between the ages of 19 and 40, as shown

in Table I. The male to female ratio was 1:1.4, with 37 (41.11%) of the 90 patients being male and 53 (58.89%) being female, as shown in Table II. On average, DM lasted 11.52 ± 5.01 years. The mean body mass index was 29.16 ± 3.34 kg/m². Height was 14.76 cm ± 165.86 cm on average. The weight was 75.63 ± 8.35 cm on average. The mean hemoglobin A1c level was 8.14 ± 0.40 percent.

According to Figure I, the frequency of UTI was seen in 03 (6.67%) patients in Group A (dapagliflozin group) and 15 (33.33%) patients in Group B (empagliflozin group) (p-value = 0.0016). Table III displays the stratification of UTI by age, gender, BMI, HbA1c level, and duration of type 2 diabetes.

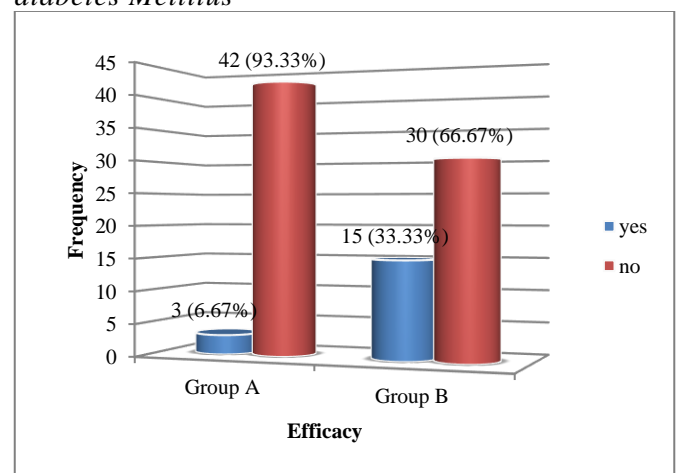
Table I
Distribution of age (n=90).

Age (years)	Group A (n=45)		Group B (n=45)		Total (n=90)	
	Frequency	%age	Frequency	%age	Frequency	%age
19-40	25	55.56	22	48.89	47	52.22
41-60	20	44.44	23	51.11	43	47.78
Mean ± SD	39.51 ± 10.22		40.31 ± 8.36		40.12 ± 9.65	

Table II
Distribution of gender (n=90).

Gender	Group A (n=45)		Group B (n=45)		Total (n=90)	
	Frequency	%age	Frequency	%age	Frequency	%age
Male	18	40.0	19	42.22	37	41.11
Female	27	60.0	26	57.78	53	58.89

Figure I
Frequency of UTI in patients taking Empagliflozin versus Dapagliflozin in patients with type 2 diabetes Mellitus



P-value = 0.0016 which is statistically significant.

Table III*Stratification of UTI with respect to age, Gender, BMI, HbA1c level, Duration of T2DM.*

		Group A (n=45)		Group B (n=45)		P-value
		UTI		UTI		
		Yes	No	Yes	No	
Age (years)	19-40	00 (0.0%)	25 (100.0%)	07 (31.82%)	15 (68.18%)	0.002
	41-60	03 (15.0%)	17 (85.0%)	08 (34.78%)	15 (65.22%)	0.138
Gender	Male	02 (11.11%)	16 (88.89%)	06 (31.58%)	13 (68.42%)	0.131
	Female	01 (3.70%)	26 (96.30%)	09 (34.62%)	17 (65.38%)	0.004
BMI (kg/m ²)	≤30	01 (4.0%)	24 (96.0%)	11 (42.31%)	15 (57.69%)	0.001
	>30	02 (10.0%)	18 (90.0%)	04 (21.05%)	15 (78.95%)	0.339
Duration (years)	≤10	00 (0.0%)	15 (100.0%)	05 (27.78%)	13 (72.22%)	0.027
	>10	03 (10.0%)	27 (90.0%)	10 (37.04%)	17 (62.96%)	0.015
HbA1c levels (%)	≤8	01 (5.56%)	17 (94.44%)	04 (30.77%)	09 (69.23%)	0.059
	>8	02 (7.41%)	25 (92.59%)	11 (34.38%)	21 (65.62%)	0.013

DISCUSSION

According to studies, people with diabetes are more likely than people without the disease to get several types of infections. Changes in immunological activities such as adhesion phagocytosis, chemotaxis, and polymorphonuclear leukocyte activity are responsible for this high incidence rate of infections. Acidosis in particular can further impair the function of polymorphonuclear leucocytes. An antioxidant system that is involved in bactericidal activity is compromised in diabetic individuals.⁹ Therefore, diabetes patients' blood glucose levels should be regularly checked and managed for a proper recovery from infections.¹⁰ According to a 14-year follow-up research, 83.8% (3980) of the 4748 diabetes patients experienced an infection-related hospitalization episode. Additionally, during the 1996–2009 study period, there was a 4% yearly rise in the number of diabetic patients admitted to hospitals.¹¹

The purpose of this study was to compare the incidence of UTIs in individuals with type 2 diabetes mellitus who were taking empagliflozin versus dapagliflozin. Participants in the study were between the ages of >18 and 60, with a mean age of 40.12 ± 9.65 years. The male to female ratio was 1:1.4, with 37 (41.11%) of the 90 patients being male and 53 (58.89%) being female. In Group A (dapagliflozin group), three patients (6.67%) and Group B (empagliflozin group), fifteen patients (33.33%) experienced UTIs (p-value = 0.0016). According to a study, the frequency of UTIs was 5.3% among patients on dapagliflozin for type II diabetes.⁷ The prevalence of UTI was 33.03% for empagliflozin, according to a study.⁸

Numerous studies have demonstrated that diabetic patients have a high prevalence of UTIs.¹²⁻¹⁴ Out of 967 patients with diabetic ketoacidosis (DKA), 679 patients (70.2%) had bacterial infections, whereas 198 patients (29.2%) had UTIs, according to a study by Gillani et al. conducted in Malaysia.¹⁵ In patients with DM, UTIs are also more severe and have worse consequences.¹⁶ It has been demonstrated that a lower urine leukocyte cell

count in diabetics is correlated with lower urinary concentrations of interleukin-8 and interleukin-6, which may increase the incidence and worsen the outcomes of UTI in DM. Excessive urine can serve as an ideal habitat for uropathogens, which promote the development of harmful bacteria in the urinary system.¹⁷ Patients with diabetes may have a higher etiology and a higher incidence of bacteriuria because the disease enhances the adherence of bacteria, especially *E. coli* that expresses type-1 fimbriae, to uroepithelial cells.¹⁸

According to Shah et al.¹⁹ UTIs were present in 40.2% DM patients, respectively. High UTI prevalence of 51%, 37%, and 62% were reported by Ijaz et al.²⁰, Yang H et al.¹¹, and Hirji et al.²¹, while 25.2% and 19.5% were discovered by Al-Rubeaan et al.²² and Hamdan et al.²³, respectively. Incidence is higher in females than in males.^{19,23} UTIs are more common in people with uncontrolled glycemia than in those with managed glycemia.^{22,23}

According to a 2014 American database study, those with diabetes were more likely to receive a UTI diagnosis than those without the disease (9.4% vs. 5.7%, respectively).²⁴ 8.2% of the 70,000+ individuals with DM type II in another American study were diagnosed with a UTI within a year (12.9% of females and 3.9% of males, with the prevalence rising with age).²⁵ According to a Canadian study, hospitalization rates for acute pyelonephritis were 3.4–17 times higher for diabetic males and 6–15 times higher for diabetic females than for non-diabetic females. According to reports, asymptomatic bacteriuria is 8% to 25% more common in diabetics and is more common in people who have had diabetes for a longer period of time.²⁶

Hussain and colleagues (2021)²⁷ conducted a study to determine the frequency of vaginal and urinary infections caused by SGLT-2 inhibitors in individuals with type II diabetes. The findings indicated that 319 (52%) and 296 (48%) of the 615 patients were using empagliflozin and dapagliflozin, respectively. Urinary infection risk was 4.3% in the dapagliflozin group and 6.5% in the empagliflozin group. However,

dapagliflozin had a 3% risk of genital tract infection, whereas empagliflozin had a 4.3% risk. Genital infections were more common in females (67%), who were treated with dapagliflozin, and in males (33%), who were treated with empagliflozin, and 4%, who were treated with empagliflozin. In a similar vein, females were more likely to have urinary infections (8, or 62%) by dapagliflozin and 14 (or 67%) by empagliflozin than males, who were more likely to have them (5, or 38%) by dapagliflozin and 7 (or 33%) by empagliflozin. Uncontrolled diabetes and the frequency of genitourinary infections in females were found to be

significantly correlated. According to the study's findings, SGLT2 inhibitors do not raise the risk of genitourinary infections in people with diabetes.²⁷

CONCLUSION

According to this study, people with type II diabetes mellitus who take empagliflozin have a higher incidence of UTIs than those who take dapagliflozin. Therefore, in order to reduce urinary tract infections and patient morbidity, we advise that patients with type 2 diabetes mellitus take dapagliflozin on a regular basis.

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