Type 2 Diabetes: Existence of Genitourinary Infections with Sodium-Glucose Cotransporter-2 (Sglt2) Inhibitors

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Abstract

Background: Diabetes mellitus is a well-known chronic metabolic issue characterized by persistently elevated glucose levels brought on by absent/inadequate or improperly functioning insulin. There are many drugs available to control hyperglycemia among them SGLT2 inhibitors are one. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are oral antidiabetic drugs used to reduce blood sugar levels by blocking glucose reabsorption in the kidney's proximal convoluted tubule. People with diabetes are more likely to develop genitourinary infections, and these infections could be brought on by either drug-related or non-drug-related causes. **Objective:** To determine the frequency of Genitourinary tract infection in people with type 2diabetes Mellitus who are treated with SGLT2 inhibitors. **Study design:** Cross-sectional study **Place and Duration:** This study was conducted at Pak Emirates Military Hospital Rawalpindi from February 2022 to February 2023 **Methodology:** Overall, a total of 550 people were selected to be a part of this research. Patients with diabetes who had been using SGLT-2 inhibitors for at least three months, either in combination or as monotherapy, were included in this study.Patients were questioned about any symptoms &signs of Genital infection or urinary symptoms during their therapy with SGLT-2 inhibitors by medical assistants using a structured proforma.Patients who had a positive urine/genital swab culture were classified as having a genitourinary infection. **Results:** There were a total of 374 men and 176 women. The meanage was 38.2 years. Patients were divided into 2 groupsbased on dapa or empagliflzin. Group A contained 264 people who were on dapagliflozin. Group B contained 286 people who took empagliflozin for the glycemic control. In Empagliflozin group the frequency of Urinary infection was 6.4% and gentital infection 4.1%, whereas in dapagliflozin group GU infection frequency was 3%, & 4.1% respectively. **Conclusion:** Patients with type 2 diabetes who take SGLT-2 inhibitors whether empagliflozin or Dapagliflozin do not have an increased risk of genitourinary infection.

Keywords: Type 2 diabetes mellitus, adults, genital infection, urinary tract infections, dapagliflozin, empagliflozin

1. Introduction

Diabetes mellitus is a metabolic disorder in which blood sugar levels remain abnormally high for an extended period of time [1,2].People with diabetes are at twice the risk of contracting infections in comparison to those without the diabetes [3].

According to therecent IDF data, Pakistan' become the 1st country in diabetes prevalence [4, 21].If no measures will be taken to cure diabetes or if diabetes is no to be taken as a serious issue, it is expected that diabetes will increase to 11 million by 2030. The lack of resources in the healthcare system could make this problem worse. Anti-diabetic medication categories have so far been divided into seven groups, on which several studies are already been done [5]. Sodium-glucose co-transporter-2 (SGLT2) inhibitors are a novel class of oral anti-diabetes medications that can be used alone or in combination [6]. The medications in this class that are approved by FDA are the following; ertugliflozin, empagliflozin, dapagliflozin, and canagliflozin. These medicines have good safety

and tolerability profiles. These drugs have positive impact not only on the control of blood sugar levels but also help in regulating blood pressure, lipid profile, HbA1c, and body weight [7]. Additionally, they enhance endothelial function, which gives them cardio-protective qualities.[8].

People with diabetes are more likely to get genitourinary infections, and these infections could be brought on by either drug-related or non-drug-related causes. Females with diabetes are more at risk of developing genitourinary tract infections compared to males because of short urethra. According to a study done in India, vulvovaginal candidiasis (VVC) is the most common genital infection among females who are diagnosed with diabetes. Among men, Candida balanitis occurs more frequently, particularly in uncircumcised diabetic males [22].

About 3% of uncircumcised males are diagnosed with Candida balanoposthitis each year [9]. The warm, wet environment under the foreskin in uncircumcised males is ideal for the growth of bacteria and other microbes [10].

The purpose of this study is to investigate the relationship between type 2 diabetes and Genitourinary infections in patients on sodium-glucose cotransporter-2 inhibitors (SGLT2).

2. Methodology

In total, 550 participants were chosen to participate in the study. An informed written consent was taken before study, and data was collected on predesigned questionnaire containing itching, discomfort, throbbing pain, redness, urgency, discharge, and some other sensory symptoms.

All people with diabetes who used SGLT2 inhibitors alone or in combination were included in study, Participants with type 1 diabetes & female with gestastional diabetes excluded from study along with those participants who had history of recurrent UTI, structural genito urinary tract defect, history of neurogenic bladder and stroke patients, because they are at increased risk of GU tract infections

Their regular laboratory test results, such as HbA1c, was noted. Urine culture advised to those with symptoms and signs suggestive of infection. Genitourinary infections diagnosed in in those patients who had positive urine/ genital culture.

In order to analyze the data, SPSS version 23 was used. Categorical variables such as gender and history of previous UTI were expressed in frequencies and percentages whereas numerical data such as BMI, and HbA1C were analysed by chi-square test. It was considered statistically significant if the p value less than 0.05.

3. Results

Overall, 550 people were a part of this research, among them 374 men, representing 68% of the total sample size. On the other hand, there were a total of 176 women, representing 32% of the total sample size. The mean age was 38.2 years. . The study population divided into two groups based on whether they were taken Dapaglilozin or Empagliflozin Table 1 shows basic characteristics of study participants.

Table No. 1: various characteristics of study participants (n=550)		
Parameters	N	%
Mean Age (years)	38.2	-
Gender		
Male	374	68
Female	176	32
Mean Body Mass Index	28.5	-
Urban area	401	72.9
Private clinic	407	74
Government Hospital	143	26
Mean time period of treatment with SGLT-2 (months)	4	-
Mean time period of diabetes (years)	6	-
Mean HbA1C	7.6	-
History of previous UTI	30	5

Table No. 2: Comparison between Group A and B regarding genitourinary infections (n=550)				
Parameters	Group A (dapagliflozin) (n=264)		Group B (empagliflozin) (n=286)	
	N	%	N	%
Urinary infection	11	4.1	19	6.4
Male	4	36.4	6	31.6
Female	7	63.6	13	68.4
Genital infection	8	3	12	4.1
Male	2	25	4	33.3
Female	6	75	8	66.7

Table No. 3: Table 3 shows association of different parameters with genitourinary tract infections	
Parameters	Genitourinary urinary infections (n=50)
HbA1C (%)>8.5%	70% (n=35)
Body Mass Index (kg/m2) >30	16% (n=8)
Female sex	68% (n=34)
History of previous UTI	12% (n=6)
The time period of diabetes (years)>5	14% (n=7)

4. Discussion

It has been hypothesized that the increased glucose in the urine produced by SGLT-2 inhibitors provides a fertile environment for the growth of bacteria and fungus. As a result, several studies have looked at how this medicine class fares against genital and urinary tract infections.

Our findings suggest that dapagliflozin use is associated with an increased risk of genital and urinary tract infections (3.0% and 4.1%, respectively). However, various studies yield different estimates of the prevalence of genitourinary infections. The risk of

urinary tract infections with dapagliflozin was 6.6% and 3.3%, respectively, compared to the placebo, which was 2.2% and 0%, [11]. In another research the risk of urinary and vaginal infections due to dapagliflozin was between 3.9% and 6.9%, respectively, compared to placebo, which was 6.2%and 6.6% [12].

A higher dose of dapagliflozin increases urinary excretion of glucose and would theoretically increase the risk of UTIs by providing a good flourishing environment for the bacteria.

In a 48-week placebo-controlled experiment, it was discovered that adding dapagliflozin to pioglitazone for Uncontrolled type 2 diabetic patients, increases the risk of genital infection by 8.6-9.2% and the risk of urine infection was also increased by 5.0-8.5% [13]. In a 2nd placebo controlled trial (dapa combined with sitagliptin) noted increase risk of genital and urineraytract infection in dapagliflozin group as compared to placebo [14]. In another study, it was discovered that taking dapagliflozin at doses of 5 mg and 10 mg increased the risk of urinary tract infection by 8.0–13.3% and the risk of genital infection by 11.7–14.6% compared to the placebo group, which increased these risks by 8.0% and 5.1%, respectively [15].

Our data show that 4.1% of women and 6.5% of men whotook empagliflozin develop genital or urinary tract infections. Empagliflozin was associated with a 4% increase in the risk of urinary tract infections and a 4% increase in the risk of genital tract infections compared to placebo in a 12-week study of people with unsatisfactory diabetes management [16]. In a 12-week phase 1b trial, 480 people with type 2 diabetes who took empagliflozin had a 2% increase in the rate of genital tract infections compared to 0% on placebo, and a 1.6% increase in the rate of urinary tract infections. Future trials will evaluate risk factors that may predispose a patient to develop one of these infections. Adding varying doses of empagliflozin to metformin and sulfonylurea in type 2 diabetes patients was the focus of another 24-week, placebo-controlled research[17]. As compared to placebo, the incidence of urinary tract infection was 10.3% (with 10 mg dosage) and 8.3% (25 mg dose), while the risk of genital tract infection was 2.7% (10 mg dose) and 2.3% (25 mg dose) as compared to 0.9%. In our investigation, female patients had greater infection rates than male patients.

Schernthaner et al. conducted a study to assess the effectiveness and safety of empagliflozin over a 78-week period in type 2 diabetes patients, [18]. According to this study, the prevalence of urinary tract infections varied between 3.8% and 12.7% in patients taking SGLT2 inhibitors. Empagliflozin (SGLT2 inhibitors) was shown to have a 3.0% to 5.5% prevalence of vaginal infections.

5. Conclusion

Patients with diabetes are at increased risk for genitourinary infections. Infections of the urinary tract are more common in patients on SGLT-2 inhibitors especially in female patients with poorly managed diabetes were at high risk to develop infections

6. Funding

7. Conflict

No conflict of interest

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