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Original Article

Frequency of UTI in Diabetic Patients taking SGLT2 Inhibitors

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Abstract

Objective: The objective of this study is to evaluate the frequency of UTI in diabetic patients taking SGLT2 inhibitors.

Methods: It was a cross-sectional study in which 125 diabetic patients from Arif Memorial Teaching Hospital, Lahore were enrolled. Data was gathered from individuals with Type 2 diabetes who were undergoing treatment with SGLT2i, either as monotherapy or in combination with other medications, over a span of three months. Data was entered and analyzed through computer software SPSS version 25.0.

Results: Among 125 diabetic patients, 45.6 were males and 54.4% were females and the mean age was 46.19+8.718 years. Association of UTI with age was found statistically significant while association of UTI with gender, family history of diabetes, duration of diabetes and SGLT2 inhibitors was found statistically insignificant.

Conclusion: Study concluded that frequency of UTI among diabetic patients taking SGLT2i was 8.8%.

Keywords: Frequency, urinary tract infection, diabetes, SGLT2 inhibitors

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Introduction

Diabetes mellitus (DM) is the most prevalent chronic metabolic disorder that affects individuals aged 20-79 years with 9.3% prevalence rate globally.[1] Asian countries contribute to more than 60% of all the diabetic patients in the world and its prevalence is still rising at a very high rate.[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] This burden will drastically increase if appropriate measures are not taken in time.[4]

Typical therapeutic choices for managing diabetes mellitus type 2 comprise medications like metformin, sitagliptin, sulfonylureas, insulin and glucagon-like peptide-1 receptor agonists.[5] The SGLT2 inhibitors represent a novel category of oral antidiabetic medications employed both as stand-alone therapy and in combination with other treatments for patients with diabetes. The drugs only approved by FDA are dapagliflozin, canagliflozin, ertugliflozin and empagliflozin. These medications boast an outstanding safety as well as tolerance profile without hypoglycemia risk. These medications demonstrate promising effects on the blood glucose levels, HbA1c, blood pressure, lipid profile and body weight. Furthermore, these drugs exhibit cardioprotective properties by enhancing endothelial function.[6-9]

Nevertheless, there have been safety concerns raised about the enhanced risk of UTI and genital infections linked to the elevated glucose level in urinary tract caused by SGLT2i.10-12 During 2015, the United States Food & Drug Administration issued a cautionary warning regarding the potential for severe urinary tract infections associated with SGLT2 inhibitors.[13,14]

Multiple meta-analysis studies have indicated that individuals with type-2 DM who utilized SGLT2i faced a significantly elevated risk for UTIs compared to those who received placebo or some other oral anti-diabetic medications.[15,16] Conversely, certain meta-analysis studies have determined that there is no significant difference in the UTI risk between patients using SGLT2 inhibitors and those receiving a placebo.[17-19] Consequently, the association between SGLT2 inhibitors and the risk of UTIs remains a topic of debate and controversy.[20]

Not many studies have been done about the prevalence of UTIs due to SGLT2i in Pakistan. Thus, it is pertinent to conduct a study to find out the frequency of urinary tract infections among diabetic patients taking SGLT2 inhibitors.

Methods

It was a cross-sectional study conducted at Arif Memorial Teaching Hospital, Lahore. Approval for the study was granted by the institutional review board and written informed consent was obtained from all participants prior to commencing the study. Data was gathered from individuals with Type 2 diabetes who were undergoing treatment with SGLT2i, either as monotherapy or in combination with other medications, over a span of three months. Individuals who did not have diabetes, had gestational diabetes only or a history of urinary tract infections were excluded from study.

The patients were advised to collect midstream urine sample in a sterile urine bottle for microbiological analyses.

A questionnaire was designed for recording the patients' history and demographic data.

Data was entered and analyzed through computer software SPSS version 25.0. The quantitative variable like age was presented as mean±SD. The qualitative variables like gender, family history of diabetes, duration of diabetes, symptoms and frequency of UTI were presented as frequency and percentages. Data was presented in tables and graphs for both quantitative and qualitative variables. Chi-square test was used to estimate the association of UTI with SGLT2 inhibitors and other variables. P-value <0.05 was considered significant. Confidentiality of data was ensured that data will not be utilized except for academic purpose.

Results

Table-1 depicts that among 125 diabetic patients, 94 (75.2%) were up to 50 years of age and 31(24.8%) were above the age of 50 years while mean age was 46.19+ 8.718 years. Among these patients, 57 (45.6%) were males and 68 (54.4%) were females.

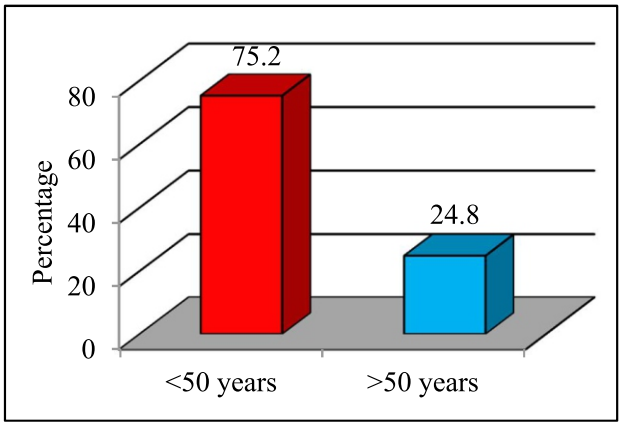

Figure 1: *Age of diabetic patients*

Out of 125 diabetic patients, 49 (39.2%) had family history of diabetes while 76 (60.8%) had no such history.

Result shows that among 125 diabetic patients, 18(14.4%) had duration of diabetes <1 year, 59 (47.2%) had 1-5 years and 32 (25.6%) had 6-10 years while 16 (12.8%) patients had >10 years. Among 125 diabetic patients, 25(20.0%) were taking Empagliflozin while 100 (80.0%) patients were taking Dapagliflozin.

Table-2 asserts that among 94 diabetic patients who were <50 years old, 4 had UTI and 90 had no UTI.

Table 1: *Demographic information of diabetic patients*

	Frequency	Percentage
Age (years)		
≤50	94	75.2
>50	31	24.8
Total	125	100.0
Mean±SD	46.19±8.718	
Gender		
Male	57	45.6
Female	68	54.4
Total	125	100.0
Family history of diabetes		
Yes	49	39.2
No	76	60.8
Total	125	100.0
Duration of diabetes (years)		
<1	18	14.4
1-5	59	47.2
6-10	32	25.6
>10	16	12.8
Total	125	100.0
Drug group		
Empagliflozin	25	20.0
Dapagliflozin	100	80.0
Total	125	100.0

Among 31 diabetic patients who were >50 years old, 7 had UTI and 24 had no UTI.

Among 57 diabetic patients who were males, 2 had UTI and 55 had no UTI. Among 68 diabetic patients who were females, 9 had UTI and 59 had no UTI.

Among 49 diabetic patients who had family history of diabetes, 7 had UTI and 42 had no UTI. Among 76 diabetic patients who had no family history of diabetes, 04 had UTI and 72 had no UTI.

Among 18 diabetic patients who had duration of diabetes <1 year, 1 had UTI and 17 had no UTI. Among 59 diabetic patients who had duration of diabetes 1-5 years, 4 had UTI and 55 had no UTI. Among 32 diabetic patients who had duration of diabetes 6-10 years, 3 had UTI and 29 had no UTI. Among 16 diabetic patients who had

duration of diabetes >10 years, 3 had UTI and 13 had no UTI (P=0.433).

Among 25 diabetic patients who were taking Empagliflozin, 3 had UTI and 22 had no UTI. Among 100 diabetic patients who were taking Dapagliflozin, 8 had UTI and 90 had no UTI.

Table 2: *Factors associated with UTI in diabetic patients*

	UTI		Total	P-value
	Present	Absent		
Age (years)				
≤50	4(3.2%)	90 (72.7%)	94 (75.2%)	0.000
>50	7(5.6%)	24 (19.3%)	31 (24.8%)	
Total	11 (8.8%)	114 (91.2%)	125(100.0%)	
Gender				
Male	2 (1.6%)	55 (44.4%)	57 (45.6%)	0.461
Female	9 (7.2%)	59 (47.6%)	68 (54.4%)	
Total	11 (8.8%)	114 (91.2%)	125(100.0%)	
Family history of diabetes				
Yes	7 (5.6%)	42 (33.9%)	49 (39.2%)	0.128
No	4 (3.2%)	72 (58.1%)	76 (60.8%)	
Total	11 (8.8%)	114 (91.2%)	125(100.0%)	
Duration of diabetes (years)				
<1	1 (0.8%)	17 (13.6%)	18 (14.4%)	0.433
1-5	4(3.2%)	55 (44.4%)	59 (47.2%)	
6-10	3(2.4%)	29 (23.4%)	32 (25.6%)	
>10	3 (2.4%)	10 (8.0%)	16 (12.8%)	
Total	11 (8.8%)	114 (91.2%)	125(100.0%)	
Drug group				
Empagliflozin	3 (2.4%)	22(17.7%)	25 (20.0%)	0.385
Dapagliflozin	8(6.4%)	92 (74.3%)	100 (80.0%)	
Total	11 (8.8%)	114(91.2%)	125(100.0%)	

Discussion

Urinary tract infections most frequently occur among individuals diagnosed with diabetes. The utilization of sodium-glucose cotransporter-2 inhibitors for effective blood sugar management results in elevated levels of glucose in the urine. This condition of glycosuria, in turn, increases the susceptibility to UTIs. Therefore, current study was carried out to know the frequency of UTI in diabetic patients taking SGLT2 inhibitors. To obtain proper results, a group of 125 diabetic patients was included in the study and found that most of them were up to 50 years old and the mean age of the patients was 46.19+8.718 years. The findings of a study conducted by Shrikrishna and coworkers (2023) sowed different scenario that most of the diabetic patients belonged to elderly age group as the mean age was 54.4 ± 7.7 years.[9] Another study carried out by Khan and associates (2022) also highlighted that mean age of the patients was 55.2 ± 6.2 years.[5] However, Hussain and collaborators (2021) reported in their study that average age of the patients was 38±12 years.[6]

As far as gender of the diabetic patients is concerned, study disclosed that most of them (54.4%) were females and 45.6% were males. But a study undertaken by Khan and associates (2022) reported that more than half (56.5%) of the patients were males and 43.5% were females.[5] Similar results were also reported by a study done by Shrikrishna and coworkers (2023) who asserted that 51.7% patients were males and 48.3% were females.[9] The findings of a study performed by Khan and associates (2022) also confirmed that 68.6% patients were males and 31.4% females.[6]

During study duration of diabetes was also identified among patients, study highlighted that majority had diabetes duration 1-5 years. A most recent study performed by Azhar and teammates (2023) indicated that mean diabetes duration among patients was 6.1±2.6 years.[4] The results of another study carried out by Ferwani and fellows (2022) revealed that mean diabetes duration was 8.95±4.84 years.[7]

It was found during study that dapagliflozin was the most frequently utilized SGLT2i among patients (80.0%) while empagliflozin was utilized among only 20.0% patients. But the results of a study conducted by Shrikrishna and coworkers (2023) showed different scenario that empagliflozin was utilized by majority (60.0%) of the patients while remaining proportion (40.0%) was prescribed dapagliflozin or canagliflozin.[9] The results of a study conducted by Azhar and teammates (2023) demonstrated that 48.0% patient were treated with dapagliflozin while 52% patients were treated with empagliflozin.[4] A study performed by Asfaq and collaborators (2023) also confirmed that 48.2% patients were given dapagliflozin while 51.8% were treated with empagliflozin.[8]

The findings of our study further revealed that prevalence of UTI among patients taking SGLT2i was 8.8%. These results are better than the study done by Caro and comrades (2022) who stated that 55.7% patients had urinary tract infection due to utilization of SGLT2i.[11] But the studies performed by Khan et al. (2022)[5], Shrikrishna et al. (2023)[9] and Ferwani et al. (2022)[7] highlighted that prevalence of UTI among patients taking SGLT2i was only 5.3%, 3.3% and 1.3%, respectively. However, in a study Uitrakul and colleagues (2022) elucidated that the prevalence of UTI was 33.5 percent among diabetic patients taking SGLT2 inhibitor.[20]

When the association of UTI with other factors was

evaluated, significant results (P<0.05) were found regarding age and symptoms of UTI but insignificant result (P>0.05) regarding gender, family history of diabetes, duration of diabetes and drug group. A study carried out by Shrikrishna and coworkers (2023) reported insignificant association of UTI with patients age, gender, disease duration, types of SGLT2i used.[9] In a study Khan and associates (2022) found significant association of UTI with age, sex, symptoms of UTI but insignificant association with drug dosage.[5] Another similar study undertaken by Azhar and teammates (2023) demonstrated that there was significant association of UTI with gender but insignificant association with drug dosage.[4]

Conclusion

Study concluded that frequency of UTI among diabetic patients was 8.8%. More studies are needed on a larger scale to assess the frequency of UTI among diabetic patients.

Conflict of Interest: None

Funding Source: None

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