

URINARY TRACT INFECTION (UTI) IN POSTMENOPAUSAL WOMEN WITH TYPE 2 DIABETES MELLITUS USING SODIUM-GLUCOSE CO TRANSPORTER 2 INHIBITORS (SGLT-2 I)

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ABSTRACT

Objective: To determine the frequency of urinary tract infection in postmenopausal women with type 2 diabetes mellitus using sodium-glucose co-transporter 2 inhibitors.

Material And Methods: This descriptive cross-sectional study was performed on 101 postmenopausal patients with type 2 diabetes mellitus using sodium-glucose co-transporter 2 inhibitors. Samples of blood and urine were sent to the hospital laboratory for analysis. Data was analyzed using SPSS version 20. The Chi-square test was performed after stratification.

RESULTS: The mean and standard deviation for age was 60.9 ± 4.4 . 24.8% of post-menopausal women with type 2 diabetes mellitus using sodium-glucose co-transporter 2 inhibitors were having urinary tract infections. The majority of these patients were illiterate or had primary education and the duration of diabetes was more than 10 years.

Conclusion: Urinary tract infection is a common problem in postmenopausal women with type 2 diabetes mellitus using sodium-glucose co-transporter 2 inhibitors. Patients with poorly controlled diabetes and increased duration of menopause have an increased risk of urinary tract infection.

Keywords: Urinary tract infection (UTI), Post-menopausal, type 2 diabetes mellitus (DM), sodium-glucose co-transporter 2 inhibitors (SGLT2Is).

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INTRODUCTION

Diabetes Mellitus type 2 is a metabolic disorder caused by a combination of two factors: inadequate insulin secretion and the decreased sensitivity of the tissues to the action of insulin.¹ DM predisposes to various infections by modifying the body's innate and adaptive immune systems.² Infections are more common and severe in patients with diabetes mellitus.³ Urinary tract infection is one of the most common bacterial infections in Pakistan. Presentation of urinary tract infection varies from cystitis to pyelonephritis to septicemia.⁴ There is emergent resistance to the commonly used antibiotics and locally conducted studies showed resistance to ciprofloxacin approaching to almost 50%.⁵

Patients with diabetes are susceptible to infections and their relapses. Diabetes mellitus with HbA_{1c} more than 6.5% are linked with the possibility of community

and hospital-acquired infections.⁶ Urinary tract infections (UTIs) are common in patients with diabetes mellitus, often caused by resistant bacteria and associated with increased severity and unfavorable prognosis.⁷

Cardiovascular diseases are one of the leading causes of death in women, increase radically after menopause, which can be attributed predominantly to the scarcity of estrogen and its cardioprotective properties.^{8,9} SGLT2 inhibitors are commonly associated with beneficial cardiovascular and renal effects.¹⁰ SGLT2 inhibitors have been described to decrease the risk of major adverse cardiovascular events and advancement of kidney disease in patients with diabetes mellitus.¹¹ The most commonly encountered adverse effects reported in a study conducted in Agha Khan University Hospital Pakistan were genitourinary infections with the frequency of urinary tract infections at 7% and genital tract infections at 3%.¹² Diabetes mellitus is linked with a greater risk of Urinary Tract Infections in post-menopausal women. The anatomy of the female urinary tract and menopause in women predispose to Urinary Tract Infections in diabetes.¹³

This study aimed to find out the frequency of urinary tract infections in diabetic postmenopausal women taking SGLT2 inhibitors and resistance to antibiotics in these patients. As both menopause and SGLT2 inhibitors are risk factors for UTIs in diabetic patients, this study will emphasize the judicious use of SGLT2 inhibitors in post-

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menopausal women.

The objective of our study was to determine the frequency of urinary tract infections in postmenopausal women with type 2 diabetes mellitus using sodium-glucose transporter 2 inhibitors.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted on 101 post-menopausal patients with type 2 diabetes mellitus in the endocrinology and diabetes department Lady Reading Hospital Peshawar from September 2022 to March 2023, after approval from hospital's ethical committee. Written informed consent was taken from all the patients. Sample size was calculated through the WHO sample size calculator using a 7 % frequency of urinary tract infection in type 2 diabetes mellitus patients using SGLT2Is, 95 % confidence interval, and 5 % margin of error.¹² Nonprobability consecutive sampling techniques were used. Patients with Symptoms of hyperglycemia i-e; polyuria, polydipsia with random blood glucose of more than 200 mg/dl or HBA1C of more than 6.5% were labeled as having diabetes mellitus. Symptomatic patients (urinary frequency, urgency, fever, and burning micturition) with more than 6 to 10 pus cells per high power field on urine microscopy and growth of microorganisms on urine culture were labeled as having UTI. SGLT2Is are oral anti-diabetic drugs used for the treatment of type 2 diabetes mellitus. Examples include empagliflozine, dapagliflozine, canagliflozine etc. Menopause is a point in time 12 months after a woman's last menstrual period. It usually occurs between 45 and 55 years of age. Postmenopausal Type 2 diabetes mellitus patients with or without complications, using sodium glucose co-transporter 2 inhibitors (irrespective of duration of use) were included in the study. Patients with active UTI, recurrent UTI, and Genital tract infection, functional and anatomical abnormalities of the urogenital tract were excluded from the study. Samples of blood were taken from all the patients and sent to the hospital laboratory for measurement of LH, FSH, and HBA1c. Samples of urine were sent to the hospital laboratory for microscopy and culture (Urine culture for fungus growth was not specifically mentioned but the positive cultures showing growth of bacteria did not show candida growth). All information was recorded in pro forma. Data was analyzed using SPSS version 20. Mean and standard deviation were calculated for continuous variables like age, HBA1c, LH, and FSH. Frequencies and percentages were calculated for categorical variables like urinary tract infection, residence, socioeconomic status, and education. Urinary tract infection was stratified against residence, socioeconomic status, and education to see effect modification. Post-stratification chi square test was applied keeping p value less than 0.05 as significant. Results were presented in tables

RESULTS

This study included 101 postmenopausal diabetic patients. The results are as follows,

The mean and standard deviation for age was 60.9 ± 4.4 , for HBA1c was 9.3 ± 1.6 , for LH was 34.5 ± 4.0 , for FSH was 62.3 ± 10.3 and for diabetes duration was 9.7 ± 3.0 . Urinary tract infection was present in 25 (24.8%) patients while 76 (75.2 %) patients did not have urinary tract infection (table no 1). However, 46 (45.5 %) patients had a duration of menopause of less than 5 years, 33(32.7%) patients had a menopause duration of 5 to 10 years while 22(21.8%) patients had a duration of menopause of more than 11 years. 31 (30.7%) patients had monthly incomes less than Rs.15000, 47(46.5 %) patients had monthly incomes between Rs.16,000 to 35,000, and 23(22.8%) patients had monthly income of more than Rs.36,000. 52(51.5%) patients belonged to urban areas while 49(48.5 %) patients belonged to rural areas. 28 (27.7%)patients were illiterate,42(41.6%) patients had primary education,22(21.8%) patients had intermediate education and 9(8.9%) patients were having qualification of secondary level and above. 12(48%) patients with urinary tract infections had duration of menopause of more than 11 years with p value less than 0. 001. Therefore, with the increase in postmenopausal duration, urinary tract infection in patients taking SGLT2I increased with significant p-value (table 2).

There was no significant difference in urinary tract infection among patients with different education classes with p p-value of 0.09 (table no 2). There was a significant difference in urinary tract infection among patients with different socioeconomic classes with p-value of 0.01(Table no 2). There was no significant difference in urinary tract infection among those belonging to rural or urban areas (Table no 2).

24.8 % of post-menopausal type 2 diabetic patients who were using sodium glucose co-transporter 2 inhibitors suffered from urinary tract infection. The majority of these patients had a duration of menopause of more than 11 years were illiterate had primary education or belonged to the socioeconomic middle class.

DISCUSSION

Sodium-glucose co-transporter 2 inhibitors are among the commonly prescribed oral antidiabetic medications nowadays due to their efficacy and cardiorenal protective benefits. However, it has been observed that patient especially post-menopausal women who are using sodium-glucose co-transporter 2 inhibitors are at risk of urinary tract infections. This study suggests that 24.8 % of post-menopausal type 2 diabetic patients who were on sodium-glucose co-transporter 2 inhibitors developed urinary tract infections. A study done in Hayatabad Medical Complex Peshawar showed that 5.3 % of type 2 diabetes mellitus patients who were using sodium-glucose co-transporter 2 inhibitors got urinary tract infection.76 % of them were female and more than 86 % of patients were of age above 50 years¹⁴.In this study urinary tract infection was common in women with a duration of menopause of

Table No 1: Urinary tract infection

	Frequency	Percent
yes	25	24.8
no	76	75.2
Total	101	100.0

Table No 2. Stratification of UTI with respect to duration of menopause, education status, socioeconomic status and residence.

URINARY TRACT INFECTION		YES	NO	P-VALUE
DURATION OF MENOPAUSE	LESS THAN 5 YEARS	7 (28%)	39 (51.3%)	0.001%
	6-10 YEARS	6 (24%)	27 (35.5%)	
	> 11 YEARS	12 (48%)	10 (13.2%)	
EDUCATION STATUS	ILITERATE	5 (20%)	23 (30.3%)	0.09%
	PRIMARY	15 (60%)	27 (35.5%)	
	INTERMEDIATE	5 (20%)	17 (22.4%)	
	SECONDARY AND HIGHER	0 (0%)	9 (11.8%)	
SOCIOECONOMIC STATUS	LESS THAN 15000	4 (16%)	27 (35.5%)	0.01%
	16 TO 35000	18 (72%)	29 (38.2%)	
	MORE THAN 36000	3 (12%)	20 (26.3%)	
RESIDENCE	URBAN	14 (56%)	38 (50%)	0.6%
	RURAL	11 (44%)	38 (50%)	

more than 11 years.

A study performed in Thailand suggested that the incidence of urinary tract infection was 33.3 % among patients with type 2 diabetes who were using sodium-glucose co-transporter 2 inhibitors.

The major risk factors were female gender, old age, and lack of permanent jobs¹⁵. We studied only post-menopausal type 2 diabetic patients using sodium-glucose co-transporter 2 inhibitors. As the duration of menopause increased the frequency of urinary tract infection also increased. We did not specifically study the job, but those whose monthly income was less than Rs.35, 000 had an increased incidence of urinary tract infection. Another study conducted in South Korea showed that sodium-glucose co-transporter 2 inhibitors significantly increased the risk of urinary tract infection in type 2 diabetes mellitus patients when used as an add-on therapy to metformin as compared to sulfonylureas, DPP4 inhibitors, and thiazolidinedione¹⁶.

A meta-analysis of 52 randomized controlled trials revealed that sodium-glucose co-transporter 2 inhibitors increased the risk of genital tract infections in patients with type 2 diabetes. Among SGLT2Is Dapagliflozin significantly amplified the risk of urinary tract infection in a dependent manner¹⁷. Postmenopausal women were not specifically focused on in this meta-analysis. We studied SGLT2Is class in general rather than comparing specific SGLT2Is, regarding increased risk of urinary tract infection.

This study was conducted in Peshawar on post-menopausal women, therefore; it lacks generalizability of the results to the rest of the province, pre-menopausal

women, and male patients.

CONCLUSION

Urinary tract infections are frequently seen in post-menopausal women with type 2 diabetes mellitus who use sodium glucose co transporter 2 inhibitors. Patients with poorly controlled diabetes and longer menopausal periods encounter an increased risk of urinary tract infection.

Care must be taken while prescribing sodium-glucose co-transporter 2 inhibitors to post-menopausal women with type 2 diabetes mellitus. Baseline urine microscopy should be done to rule out preexisting urinary tract infections. Further studies are needed to find out the risk factors of urinary tract infection in post-menopausal women on SGLT2Is.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ubaid M	✓	✓	✓	✗	✓	✗
Khan S	✓	✓	✗	✓	✓	✗
Wazir N	✗	✓	✗	✓	✗	✓
Ullah I	✓	✗	✓	✓	✗	✗
Rehman MU	✓	✓	✗	✓	✗	✗
Ahmed I	✗	✓	✗	✓	✓	✗

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Lady Reading Hospital, Peshawar. Vide No. 664/LRH/MTI.

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