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Prevalence of Genital Mycotic Infections with Sodium-Glucose Co-Transporter 2 Inhibitors among Type 2 Diabetic Patients

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ABSTRACT

Background and Aim: Sodium-glucose co-transporter 2 (SGLT2) inhibitors have emerged as an effective oral antidiabetic agents for glycemic control in patients with type 2 diabetes mellitus (T2DM). However, the mechanism of their action - promoting glycosuria - is associated with increasing risk of genital mycotic infections. The purpose of this study was to determine the prevalence of genital mycotic infections among T2DM patients using SGLT2 inhibitors. **Patients and Method:** A cross-sectional observational study investigated 300 T2DM patients receiving SGLT2 inhibitors in the Diabetes Management Center of Services Hospital, Lahore during January 16, 2025 to April 15, 2025. Clinical data, including the type and duration of demographic characteristics, SGLT2 inhibitors therapy, collected through structured interviews and medical records to the history of clinical data, HBA1C level, personal hygiene practices, and genital infections. The diagnosis of genital mycotic infection based on clinical symptoms and confirmed by laboratory findings where necessary. SPSS version 26 used for data analysis. **Results:** Of the 300 patients, 78 (26%) developed genital mycotic infections. The prevalence in women was much higher (38%) than men (17%) ($p < 0.01$). Poor glycemic control (HBA1C> 8%) and inadequate hygiene important risk factor were found ($P < 0.05$). The highest prevalence of was seen within the first 6 months of initiating SGLT2 inhibitor therapy, especially with dapagliflozin. 12 patients had recurrent infections, and most cases responded well to antifungal therapy without discontinuation of SGLT 2 obstructions.**Conclusion:** Genital mycotic infections have common but manageable side effects of SGLT2 inhibitors in T2DM patients, especially in women and those with poor glycemic control. Early patient's education on genital hygiene and close monitoring can reduce the incidence and improve treatment adherence during the initial months of therapy.

INTRODUCTION

Genital fungi infections such as Balanopostitis in men and vulvovaginal candidiasis in women are often observed in individuals with poor controlled diabetes [1]. Factors such as glycosuria, because of hyperglycemia, increase bacterial rearing in the uroepithelium, and compromised immune functions contribute to sensitivity to these infections [2-4]. Candida Albicans is the most implicated pathogen [5]. These infections are especially prevalent among the uncircumcised men, as the warm, moist environment under the foreskin can encourage fungal development, especially in cases of inadequate genital hygiene [6]. The presence of glucose-rich urine that can encounter glans and foreskin facilitates the development of yeast and bacteria. Common symptoms include itching, redness of external genitals, irritation, a yellow-white discharge, painful urination (dysuria), and pain during sexual intercourse (dyspareunia). Management involves maintaining optimum blood sugar levels with the use of topical antifungal creams and/or systemic antifungal drugs [7].

Sodium-glucose cum-transporter 2 inhibitors (SGLT2I) represent a new class of oral antibiotic drugs approved for management of type 2 diabetes (T2D). They work through an insulin-independent pathway by preventing glucose reabsorption in proximal renal tubes, increasing urine glucose excretion and lowering blood sugar levels [8, 9]. The induced Glycosuria communal associated with the use of SGLT2I creates a favorable environment for the proliferation of genital microorganisms, leading to the risk

of genital mycrotic infections and urinary tract infections (UTIs) [10]. Clinical testing data indicates that the use of SGLT2 inhibitors is associated with 3- to 5 times the risk of genital infections, which is likely to be caused by glucose levels in the genitourinary tract [11]. In older adults, such infections can significantly reduce the quality of life. Although SGLT2 inhibitors have also been linked to an increased risk of urinary tract infection (UTI). Many clinical trials and studies have highlighted the increasing risk of genital infections in patients with SGLT2i inhibitors. Incidents estimated to be 2 to 5 times more in patients using SGLT2 inhibitors compared to placebo or other antidiabic drugs [12, 13]. Reports suggest that about 8–10% of individuals on SGLT2i experience genital fungi infections, while compared to 3–5% in control groups. These infections, while generally are mild and responsible for topical antifungal treatment, can give rise to complications such as non-adhering, treatment discontinuation, and rare cases such as severe balanitis, cellulitis, or Fournier's gangrene.

Despite the growing body of evidence, correct circulation of genital fungi infections in diverse population and patterns- especially in lower and middle-income countries where diabetes is increasing- was underestimated. Cultural and social barriers, lack of awareness and reluctance to discuss genital symptoms with healthcare providers can contribute to underdiagnoses and under-trials. In addition, some risk factors such as circumcision conditions, hygiene practices, use of concurrent antibiotic or corticosteroids, and glycemic control conditions can affect sensitivity to these infections, but not always adequately evaluated in clinical tests [14]. Given the widespread use of SGLT2 inhibitors and increasing emphasis on patient-focused care in the management of type 2 diabetes, it is mandatory to understand the scope and impact of adverse events that can affect the compliance with treatment and the quality of life. Genital mycotic infections, although usually non-serious, can be disturbed and stigmatized for patients, especially in conservative societies where genital health is a sensitive subject. In real -world clinical settings, searching for these infections and exploring risk factors will provide valuable insight to both physicians and policy makers. The purpose of this study was to assess the prevalence of genital mycotic infections in patients with type 2 diabetes, which are receiving SGLT2 inhibitors, which contributes to the increasing evidence base on the safety profile of these drugs.

METHODOLOGY

Study Design and Setting

This cross-sectional observation study was conducted in the Diabetes Management Center of Services Hospital, Lahore during January 16, 2025 to April 15, 2025. The primary objective was to assess the prevalence of genital mycotic infections in patients with type 2 diabetes mellitus (T2DM), which were receiving sodium-glucose cum-transporter 2 (SGLT2) inhibitors as part of their antidiabetic therapy.

Study Population

300 patients with T2DM diagnosed and currently undergoing treatment with SGLT2 inhibitors were enrolled. The inclusion criteria included either gender having age ≥18 years), diagnosed with T2DM for at least one year, and receiving SGLT2 inhibitors (such as Empaglifliflozin, Dapagliflozin, or Cannagliflozin) for a minimum period of three months. Patients with type 1 diabetes, recent use of systemic antifungal agents, or other causes of immunosuppression (e.g HIV infection, chemotherapy) excluded.

Data Collection Procedure

Clinical and demographic data collected using a structured interview questionnaire and verified through medical records. Demographic details such as age, gender, marital status, and educational background, clinical characteristics such as duration of diabetes, duration and SGLT2 obstructive therapy duration and types, comorbidities, and glycemic control (as recently measured by HBA1C levels), Personal hygiene practices such as the frequency of genital washing, the use of antiseptic or antifungal hygiene products, circumcision condition in men, and underwear content/type, history of genital infections: genital itching, redness, discharge, dysuria, dyspareunia, and other related symptoms. The genital mycotic infection diagnosed based on clinical presentation, including symptoms such as genital itching, erythema, pain or burning, white or yellow discharge, pain or irritation, and discomfort during intercourse.

Data Analysis

All collected data recorded and analyzed using the SPSS version 26. Descriptive figures used to summarize demographic and clinical characteristics. The range of variables expressed as frequencies and percentage, while continuous variables reported as mean ± standard deviation (SD). The prevalence of genital mycotic infections calculated as a ratio of affected individuals among the total study population. Relations were evaluated between genital mycotic infections and potential risk factors (e.g HBA1C level, SGLT2I therapy period, hygiene practices), which were appropriately appropriate by using the Chi-square tests or Fisher accurate tests. P-Value of less than 0.05 considered as statistically significant.

RESULTS

Of these 300 patients, 78 patients (26%) developed genital mycotic infections (GMI) during the observation period. Genital mycotic infections were much more common in women than men. Among 142 female participants, 54 (38.0%) developed infection, compared to 24 (17.1%) of 140 men (P <0.01). A significant association was found between poor glycemic control (HBA1C> 8%) and the occurrence of genital mycotic infections. GMIs developed in patients with HBA1C> 8%, 49 (33.1%) with HBA1C ≤ 8% (P = 0.014) compared to 29 (18.6%). Inadequate genital hygiene (as a self-report in questionnaire) was significantly associated with GMI development. Among people with poor hygiene, 46 (35.1%) developed an infection compared to 32 (18.8%) in good hygiene group (P = 0.007). The majority of genital mycotic infections occurred within the first six months of the SGLT2 inhibitors therapy. In 78 cases, 55 (70.5%) developed

infection within this period. Dapagliflozin was the most frequent drug (n = 34), followed by Empagliflozin (n = 28) and Canagliflozin (n = 16). Among 78 patients developing genital mycotic infections, 12 (15.4%) experienced recurrent infections. All patients treated with local or systemic antifungal drugs. Importantly, permanent discontinuation of SGLT2 inhibitors due to infection not required. Symptomatic improvement obtained in almost all cases within 7-10 days of starting antifungal therapy.

Table 1

Prevalence of Genital Mycotic Infections by Gender

Gender	Total Patients	GMI Cases	Prevalence (%)	p-value
Male	140	24	17.1%	
Female	142	54	38.0%	
Total	282*	78	26.0%	<0.01

***Note:** 16 patients did not report gender or excluded from gender-specific analysis.

Table 2

Association between HbA1c and Genital Mycotic Infections (N=300).

HbA1c Level	Total Patients	GMI Cases	Prevalence (%)	p-value
≤ 8%	154	29	18.6%	
> 8%	146	49	33.1%	
Total	**300**	**78**	**26.0%**	**0.014**

Table 3

Hygiene and Genital Mycotic Infections (N=300)

Hygiene Status	Total Patients	GMI Cases	Prevalence (%)	p-value
Good	170	32	18.8%	
Poor	130	46	35.1%	
Total	**300**	**78**	**26.0%**	**0.007**

Table 4

Distribution of GMIs by SGLT2 Inhibitor Type and Duration of Use (N=300)

SGLT2i Type	<6 Months	≥6 Months	Total GMI Cases
Dapagliflozin	26	8	34
Empagliflozin	20	8	28
Canagliflozin	9	7	16
Total	**55**	**23**	**78**

DISCUSSION

The current study examined sodium-glucose cum-transporter 2 inhibitors (SGLT2I) in patients with Type 2 Diabetes Mellitus (T2DM). The findings highlight a remarkable burden of GMI, in which 26% of the study population develops such infections during the observation period. This aligns with pre -published data that reports the increasing risk of genital infections associated with the use of SGLT2I due to pharmacologically induced glycosuria, which promotes microbial overcrowding in the genitourinary tract [15].

Our results revealed much more prevalence of GMI between women (38%) compared to men (17.1%), which were in consistence with the findings of earlier studies [16, 17]. The female anatomy, which involves a shorter urethra and proximity to the vaginal and anal areas, possibly contributes to an increase in sensitivity. In addition, factors such as hormonal effects and hygiene practices can further increase the risk in women. Statistically significant differences (P <0.01) strengthen the need for increased monitoring and patient education, especially among the female SGLT2 I users.

Poor glycemic control (HBA1C> 8%) emerged as an important risk factor for the development of GMI. Among people with high HBA1C, 33.1% developed infection compared to better glycemic control (P = 0.014) than 18.6%. Chronic hyperglycemia leads to glycosuria and impaired immune response, creating a favorable environment for fungal proliferation. This underlines the importance of maintaining optimal glycemic goals not only to prevent long -term complications of diabetes, but also to reduce the risk of infections associated with new antidiabic therapy. Similar results reported in an earlier study [18].

The study also identified inadequate genital hygiene as an independent risk factor. Patients reporting poor hygiene practices had much higher infection rate (35.1%) than people with good hygiene (18.8%, P = 0.007). This finding is clinically relevant, as it exposes an easily convertible risk factor. Educating patients about proper genital care on SGLT2I therapy can serve as a simple and cost -effective strategy to reduce GMI events. Earlier study reported similar results [19].

Most infections (70.5%) occurred within the first six months of the SGLT2 inhibitors therapy. This early onset documented in pre-literature and can be attributed to a sudden and continuous increase in urine glucose excretion immediately after treatment initiation. In various agents, Dapagliflozin was associated with the highest number of GMI cases (n = 34), followed by Empagliflozin (n = 28) and canagliflozin (n = 16). Although it can reflect patterns that determine the pattern can reflect, it further examines through head-to-head tests to determine if specific SGLT2I agents take the risk for infection. Similar findings reported in earlier clinical trials [20, 21].

Approximately 15.4% of patients experienced the recurrent GMI, a discovery that reflects the recurrent nature of candidate infection in susceptible individuals. Despite this, it is convinced that all cases gave a favorable response to antifungal therapy - either topical or systemic - and SGLT2i does not require any necessary dissection of inhibitory therapy. This emphasizes that GMIs, although common, are manageable complications and should not stop the use of SGLT2I, especially in patients who receive the benefits of the heart or kidney from these agents [22].

Given the widespread use of SGLT2 inhibitors in T2DM management, physicians should be cautious about the risk of GMI. Early symptoms can assist in timely management of glycemic control and hygiene practices along with patient education on recognition. Importantly, the risk of GMI should be weighed against the benefits of the kidney of proven metabolism, heart and SGLT 2 inhibitors. Routine screening is not necessary, but active counseling and initial intervention can help maintain the patient's compliance and reduce adverse results.

CONCLUSION

Genital Mycotic Infections are a relatively common but manageable complication among T2DM patients on SGLT2 inhibitor therapy, particularly in women, those with poor

glycemic control, and inadequate hygiene. Most infections occur within the early months of treatment and react well to antifungal therapy without the need for drug dissection. These findings highlight the importance of individual patient consultation and initial identification strategies to reduce risks by maximizing therapeutic benefits.

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