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Self-Reported Symptoms of Empagliflozin Discontinuation – An Online Survey

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ABSTRACT:

Background and Aim: Sodium-glucose cotransporter 2 inhibitors (SGLT2i) represent a new class of antidiabetic medications that offer benefits such as weight reduction and a decreased risk of cardiovascular diseases. Nevertheless, the use of SGLT2i is associated with a range of potential side effects. The present study aimed to analyze the rate of discontinuation for empagliflozin and investigate the incidence of its side effects.

Patients and Methods: This study employed a cross-sectional design using an online survey to collect data from 567 patients on post-withdrawal symptoms of empagliflozin. Adults (≥ 18 years) who had taken empagliflozin for at least three months and had discontinued for any reasons included. Participants were recruited through online platforms, including social media and online forums. The survey collected demographic information, empagliflozin use and discontinuation, reasons for discontinuation, and post-withdrawal symptoms. SPSS version 26 was used for statistical analysis.

Results: Out of 567 patients, the majority of patients were prescribed Jardiance for diabetes, 75% (n=425), and heart failure, 25% (n=142). Genital infections 27% (n=109) and UTIs 22% (n=90) were the leading reasons for discontinuation, followed by dry mouth/frequent urination 17% (n=70), Lack of efficacy 14% (n=55), low blood pressure 11% (n=45), and Ketoacidosis 9% (n=35). About 67% (n=231) of cases withdrew due to adverse effects. Headache 20% (n=60) and swelling 17% (n=50) were the most common post-withdrawal symptoms. The majority of patients, 68% (n=200), chose not to resume Jardiance, while 19% (n=55) considered restarting it.

Conclusion: While empagliflozin demonstrates clinical efficacy in managing both type 2 diabetes and heart failure—improving glycemic control, promoting weight loss, and reducing cardiovascular mortality—the occurrence of adverse effects remains a key factor in discontinuation. Awareness of these side effects and proactive management strategies may improve adherence and therapeutic outcomes.

Keywords: Empagliflozin, Diabetes, SGLT2 Inhibitors, Empagliflozin side effects

INTRODUCTION:

Heart failure is a common comorbidity in individuals with diabetes, affecting more than 20% of patients aged 65 years and older[1]. The prognosis for patients with both diabetes and heart failure remains poor, with a median survival of approximately four years [2,3]. Evidence from meta-analyses suggests that intensive glycemic control does not significantly reduce hospitalizations for heart failure or overall mortality when compared to standard glucose management 4. Furthermore, many glucose-lowering agents have not demonstrated a significant improvement in heart failure outcomes and may be associated with adverse effects [5].

Empagliflozin is a highly selective sodium-glucose cotransporter 2 (SGLT2) inhibitor approved for the treatment of type 2 diabetes. It lowers blood glucose levels by inhibiting renal glucose reabsorption and enhancing urinary glucose excretion [6]. In addition to its glycemic benefits, empagliflozin is associated with osmotic diuresis, weight loss, and reductions in blood pressure—achieved without increasing heart rate [7]. Other favorable effects include reductions in serum uric acid levels, vascular resistance, albuminuria, and atrial stiffness, all of which contribute to its cardioprotective profile [8]. When administered alongside standard care, empagliflozin has been shown to significantly reduce the risk of major adverse cardiovascular events in patients with type 2 diabetes compared to placebo [9].

Given the high prevalence of obesity and overweight in patients with type 2 diabetes, SGLT2 inhibitors have attracted considerable interest for their cardiometabolic benefits. However, despite these advantages, concerns over potential side effects have limited their broader adoption. Misconceptions about the safety profile of SGLT2 inhibitors have contributed to hesitancy among healthcare providers, even though recent evidence suggests that the incidence of adverse events may be lower than previously reported [10-12].

In this context, our study aimed to evaluate the discontinuation rate of empagliflozin within three months of initiation and to investigate the frequency and nature of adverse effects leading to its discontinuation.

METHODOLOGY:

This study employed a cross-sectional design using an online survey to collect data from 567 individuals regarding post-withdrawal symptoms of empagliflozin. Adults aged 18 years or older who had taken empagliflozin for a minimum of three months and had subsequently discontinued the medication for any reason were eligible for inclusion. Individuals who were currently using

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empagliflozin or who failed to complete the survey were excluded.

Participants were recruited through various online platforms, including social media and health-related online forums. They were invited to complete a structured online questionnaire designed to assess their experience with empagliflozin use and discontinuation. The survey collected demographic data, details of empagliflozin use, reasons for discontinuation, and post-withdrawal symptoms.

The questionnaire included the following key questions:

1. Why were you prescribed Jardiance (empagliflozin)?
2. Why did you stop using Jardiance?
3. Do you believe Jardiance withdrawal adversely affected your health?
4. What was the worst symptom you experienced after stopping Jardiance?
5. Have you considered or attempted restarting Jardiance?

Statistical analysis was performed using SPSS version 26. Descriptive statistics were used to summarize demographic characteristics, empagliflozin usage patterns, and the frequency and severity of post-withdrawal symptoms. Associations between empagliflozin use characteristics and post-withdrawal symptoms were evaluated using the Chi-square test.

RESULTS:

A total of 567 patients participated in the survey. Of these, 75% (n = 425) were prescribed empagliflozin (Jardiance) for type 2 diabetes, while 25% (n = 142) received it for heart failure.

Among those who discontinued empagliflozin (n = 404), the most commonly reported reasons were genital infections (27%, n = 109) and urinary tract infections (UTIs) (22%, n = 90). Other reasons included dry mouth and frequent urination (17%, n = 70), perceived lack of efficacy (14%, n = 55), low blood pressure (11%, n = 45), and ketoacidosis (9%, n = 35).

Approximately 67% (n = 231) of participants believed that discontinuation of Jardiance adversely affected their health. The most commonly reported post-withdrawal symptoms included headache (20%, n = 60) and swelling (17%, n = 50). Other symptoms reported were anxiety (12%), palpitations (11%), shortness of breath (11%), excessive urination (9%), blurred vision (8%), difficulty concentrating (7%), and tremors (6%).

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When asked about resuming Jardiance, 68% (n = 200) stated they had not resumed the medication, 19% (n = 55) were considering restarting it, 9% (n = 28) reported improvement in symptoms upon resuming, and 4% (n = 13) had resumed but experienced persistent symptoms.

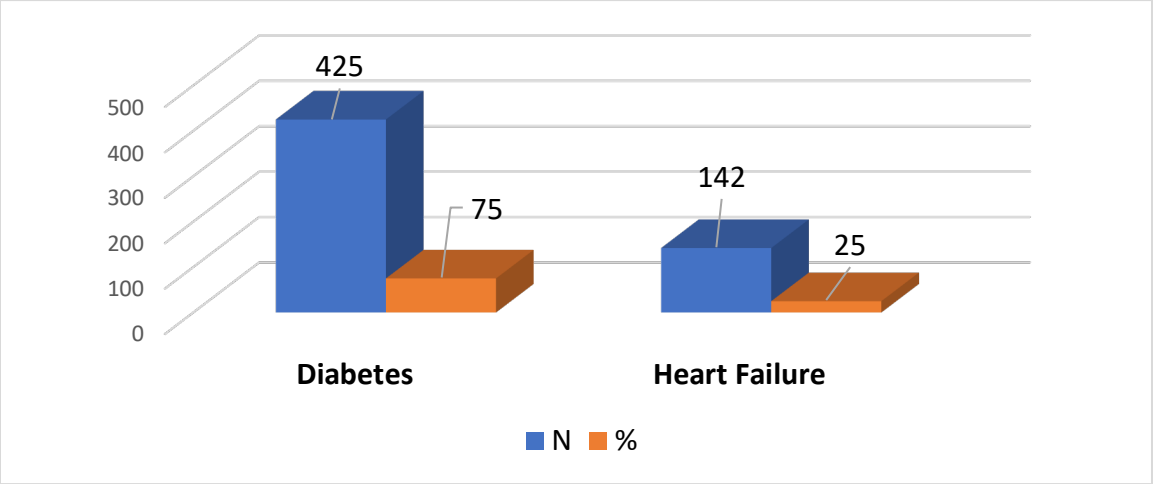

Figure 1 illustrates the reasons for empagliflozin prescription

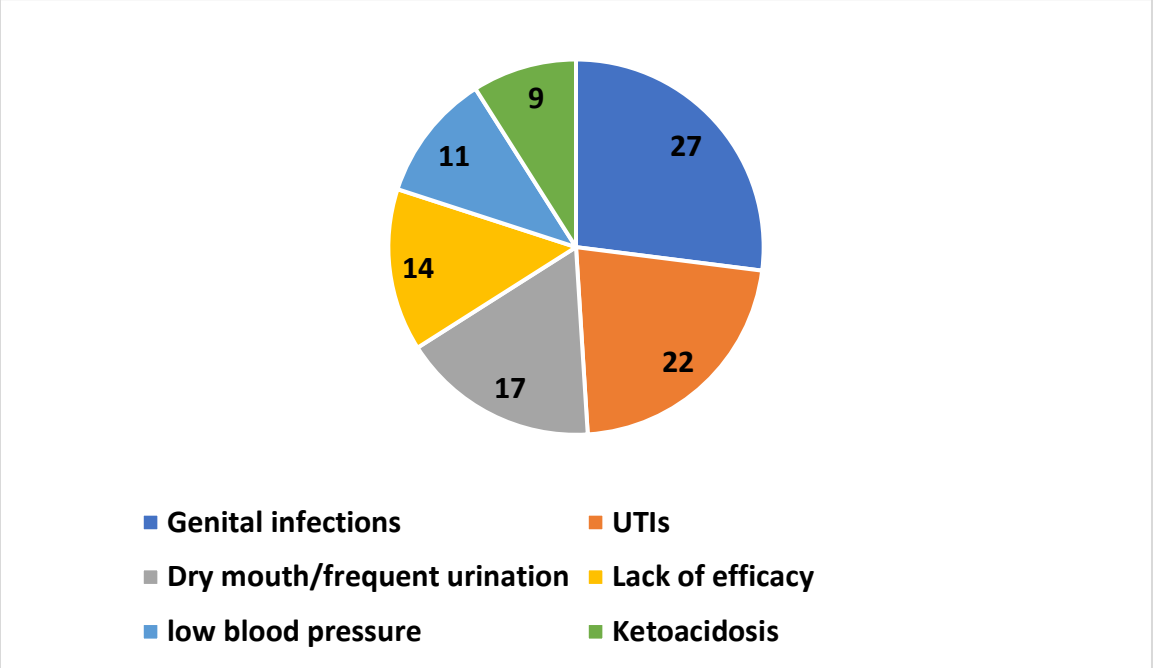

Figure 2 presents the leading causes of discontinuation.

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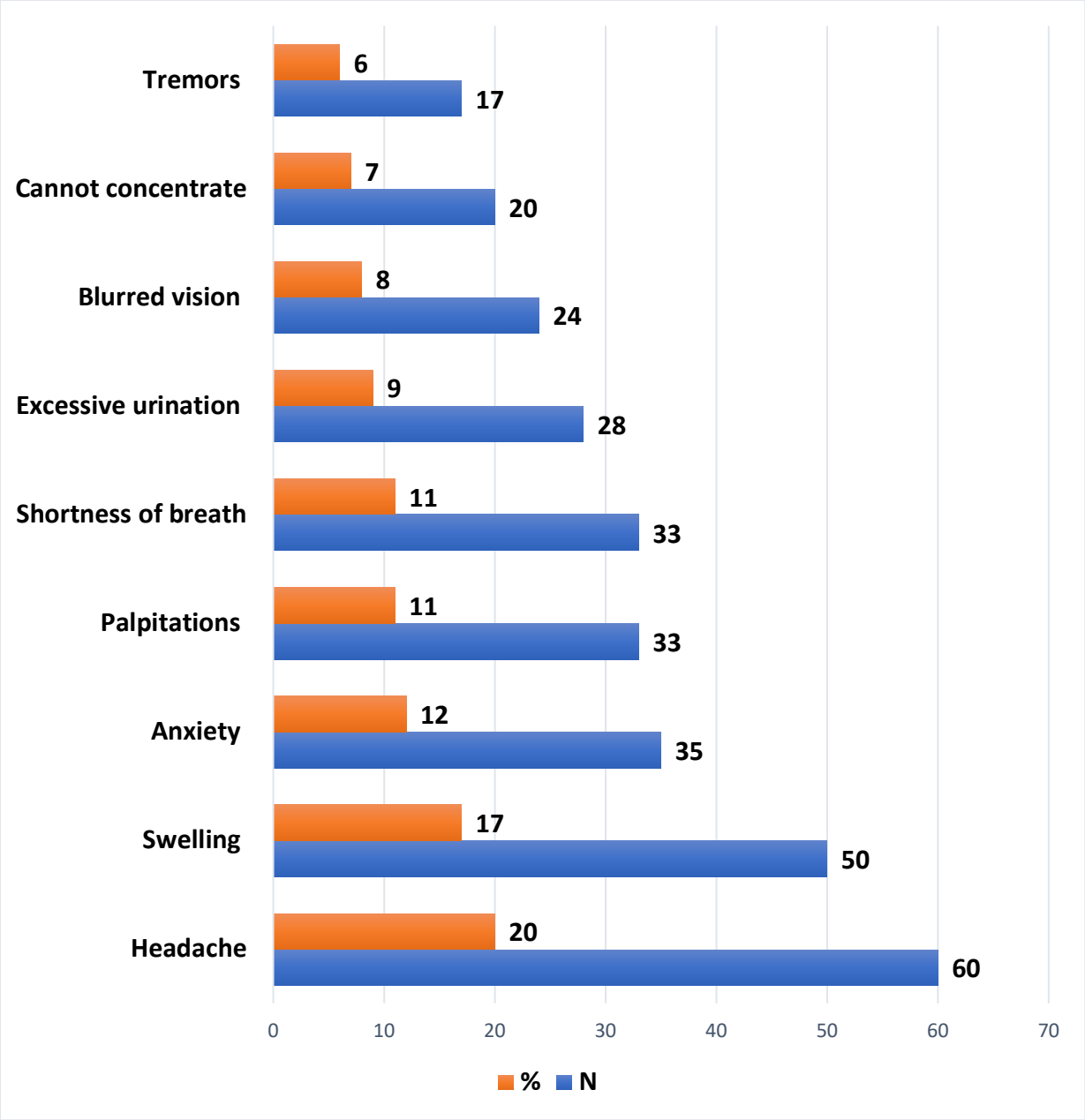

Figure 3 summarizes post-withdrawal symptoms.

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Detailed participant responses to survey questions are provided in Table I.

Question	Response	N	%
Why were you prescribed Jardiance?	Heart Failure	142	25%
	Diabetes	425	75%
Why did you stop using Jardiance?	Genital infection	109	27%
	Urinary tract infection (UTI)	90	22%
	Dry mouth/frequent urination	70	17%
	Lack of efficacy	55	14%
	Low blood pressure	45	11%
	Ketoacidosis	35	9%
Do you think Jardiance withdrawal adversely affected your health?	Yes	231	67%
	No	114	33%
Which symptom was the worst after stopping Jardiance?	Headache	60	20%
	Swelling	50	17%
	Anxiety	35	12%
	Palpitations	33	11%
	Shortness of breath	33	11%
	Excessive urination	28	9%
	Blurred vision	24	8%
	Difficulty concentrating	20	7%
	Tremors	17	6%
Have you tried resuming Jardiance?	Yes, but symptoms persisted	13	4%
	Yes, symptoms improved after resuming	28	9%
	No, but planning to resume	55	19%
	No	200	68%

Table I. Survey Questions and Participant Responses (N = 567)

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DISCUSSION:

This observational study provides valuable insights into the reasons for discontinuation of empagliflozin and the post-withdrawal effects experienced by patients. While the majority of participants were prescribed empagliflozin for the management of type 2 diabetes, a significant proportion were using it to treat heart failure. The clinical benefits of empagliflozin in heart failure have been well documented, including a reduced risk of hospitalization (HR 0.73; 95% CI 0.61–0.88) and a decrease in primary cardiovascular outcomes in both diabetic and non-diabetic populations [13].

Numerous studies have examined both the beneficial and adverse effects of SGLT2 inhibitors. However, fewer have specifically focused on reasons for discontinuation. In one such study involving 775 patients, 85 (11%) discontinued therapy. The main reasons for discontinuation included general weakness, over-diuresis, renal dysfunction, and urinary tract infections. Additionally, 31 patients stopped treatment due to cost concerns or side effects such as hypoglycemia and constipation. In contrast, our study found that genital infections (27%) and UTIs (22%) were the most frequently reported reasons for discontinuation, followed by dry mouth/frequent urination (17%), lack of efficacy (14%), low blood pressure (11%), and ketoacidosis (9%). Moreover, 67% of participants perceived that stopping empagliflozin had negatively impacted their health [14].

Saijo et al. similarly reported that frequent urination (19.6%) and genital infections (11.3%) were the leading causes of SGLT2i discontinuation [15]. They also noted that some patients discontinued the drug due to improvements in glycemic control or concerns related to renal function. These findings are generally consistent with our data but emphasize a slightly different prioritization of side effects.

The perception of adverse health outcomes after discontinuation is a key finding of our study. Approximately 67% of respondents reported negative health effects following cessation of therapy. In a prior study, empagliflozin was discontinued in 22.7% of patients within the first three months, 44.3% between three and twelve months, and 33.0% between twelve and twenty-four months [13]. Additionally, the discontinuation of empagliflozin has been associated with increases in fasting blood glucose, N-terminal pro-brain natriuretic peptide, body weight, systolic blood pressure, uric acid, and reductions in hemoglobin and hematocrit—suggesting a potential physiological rebound effect [16]

Post-withdrawal symptoms have not been widely studied. In our cohort, the most commonly reported symptoms after stopping empagliflozin were headache (20%) and peripheral swelling (17%). These findings highlight a need for further

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research to understand the nature and mechanisms of post-withdrawal effects, which remain underrecognized in clinical practice.

Interestingly, a substantial proportion of patients (68%) chose not to resume empagliflozin after discontinuation. This reluctance may be attributed to the severity of side effects experienced or inadequate counseling about the drug's long-term benefits. Conversely, 19% of participants expressed a willingness to consider restarting the medication. This underscores the importance of patient education, shared decision-making, and individualized care in improving medication adherence and treatment outcomes.

Compared to existing literature, our study reinforces the role of genitourinary infections as a leading cause of discontinuation but also provides new data on post-discontinuation symptoms—an area seldom explored. This gap in the literature necessitates further investigation to guide future clinical practice.

Conclusion:

Although empagliflozin offers substantial therapeutic advantages in managing type 2 diabetes and heart failure, discontinuation due to adverse effects—and the ensuing post-withdrawal symptoms—poses significant challenges. Clinicians should proactively monitor for common side effects, educate patients about the risk-benefit profile of the drug, and provide adequate support for those who discontinue therapy. Future research should focus on strategies to minimize side effects and better understand the physiological impact of withdrawal, with the goal of enhancing long-term patient adherence and outcomes.

LIMITATIONS:

The study relied on self-reported data, which may be subjected to bias. The convenient sampling technique restricted the study to smaller size and may not represents the larger population.

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Conflict of Interest:

The authors declare no conflict of interest regarding the publication of this paper.

Data Availability Statement:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Approval:

Institutional Review Board (IRB) approved the study. Written informed consent provided by all the participants who completed the survey. Participants were assured of confidentiality and anonymity.

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