

## Short Communication

### Physicians Experience with SGLT-2 Inhibitors In Type 2 Diabetic Patients

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#### Abstract

**Background:** Approximately, 104 (55%) physicians reported hypertension (HTN), obesity, chronic kidney disease (CKD) and hyperuricemia as the most prevalent comorbidities in diabetic patients.

**Objectives:** This study investigates the experience of Pakistani physicians regarding the use of Sodium-glucose Cotransporter-2 (SGLT2) inhibitors in the management of Type 2 Diabetes (T2D).

This cross-sectional survey study was conducted from 1<sup>st</sup> October to December 31<sup>st</sup>, 2023, enrolled 189 physicians.

**Methods:** The data was collected by self-administered structured questionnaire which was distributed among physicians across various specialties involved in diabetes care, assessing their views on the efficacy, safety, and economic considerations of SGLT2 inhibitors.

**Results:** Approximately, 104 (55%) physicians reported hypertension (HTN), obesity, chronic kidney disease (CKD) and hyperuricemia as the most prevalent comorbidities in diabetic patients. Empagliflozin was the most prescribed among SGLT-2 inhibitor in patients with heart failure. Approximately, 50% of the physicians advise SGLT-2 inhibitor frequently to their patients. Approximately, 81% of the physicians considered efficacious medicine with cost- benefits for their patients and also 89% of them agreed that the cost and quantity of daily diabetes medications impact a patient's overall diabetes management.

**Conclusion:** The study emphasizes the importance of addressing these economic challenges to enhance the accessibility and utilization of SGLT2 inhibitors, potentially improving health outcomes for patients with T2D. By highlighting physicians' perspectives, this research contributes to the ongoing conversation on optimizing diabetes treatment in Pakistan.

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#### Introduction

Over half a billion people are living with diabetes globally as of 2023, and by 2050 it is predicted to be at 1.3 billion. Pakistan has shown a yearly increase in diabetes since reported data in 2016, reaching a 26.7% prevalence in 2021, which approximates to 33 million



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diagnosed adults.<sup>1</sup> The rising global prevalence of Type 2 Diabetes (T2D) worldwide requires the exploration and utilization of effective treatment strategies. Sodium-glucose Cotransporter-2 (SGLT2) inhibitors have emerged as a promising choice. SGLT2 promotes urinary excretion of glucose by reducing the reabsorption of filtered glucose in the renal proximal convoluted tubules.<sup>2</sup> This class of medication, exemplified by drugs like dapagliflozin, offers multiple benefits: a low risk of hypoglycemia, improved renal efficiency, reduced cardiovascular complications, significant weight loss, blood pressure reduction, and can be used without insulin in many patients.<sup>3</sup> Studies have particularly highlighted the long-term efficacy and safety of SGLT2 inhibitors in individuals with chronic kidney disorders, both with and without T2D.<sup>4</sup>

A notable property of SGLT2 inhibitors is their cardio-protective effect. They have been shown to offer superior defense against cardiovascular events, especially atrial fibrillation/atrial flutter (AF/AFL), in high-risk patients. This finding is crucial given the common co-occurrence of cardiovascular diseases and T2D.<sup>5</sup> When compared with Dipeptidyl Peptidase 4 (DPP-4) inhibitors in these patients, SGLT2 inhibitors demonstrated greater effectiveness in reducing weight and improving glycemic control while simultaneously lowering the risk of hyperglycemia.<sup>6</sup>

The usage of SGLT2 inhibitors in combination with metformin in T2D patients has gained favorable views among physicians, particularly due to the reduction in heart failure, hospitalizations, and cardiovascular deaths.<sup>7</sup> Furthermore, the sequential addition of SGLT2 inhibitors to DPP-4 inhibitors has been suggested as a cost-effective alternative in the United States, potentially improving the quality of life for patients.<sup>8</sup>

Despite these promising findings, the use of SGLT2 inhibitors in T2D management requires careful consideration and monitoring to minimize systemic adverse effects. They should be used cautiously in certain populations, such as elderly patients and those with chronic kidney disease, due to risks like genital infections and rare cases of euglycemic ketoacidosis.<sup>4</sup> A thorough understanding of the therapeutic nature of SGLT2 inhibitors is essential for evaluating the most effective and affordable treatment options for T2D, and for reducing the extent of secondary complications.<sup>8</sup>

Previous research has identified a knowledge gap among primary healthcare providers in Pakistan regarding the use of SGLT2 inhibitors in T2D management. Assessing physicians' awareness of these inhibitors is vital to early

examination and prevention of associated consequences in T2D patients.

This study aims to contribute to the understanding of physicians' experience regarding SGLT2 inhibitor use for T2D in Pakistan. Additionally, it seeks to evaluate physician's opinions on cost-effectiveness considerations that may influence medication adherence.

## Methods

This was a prospective cross-sectional study conducted from 1<sup>st</sup> October to December 31<sup>st</sup>, 2023. It assessed physicians' knowledge and perceptions regarding the use of SGLT2 inhibitors for the treatment of T2D in Pakistan. The study was done in accordance with the Declaration of Helsinki. Approval for the study protocol has been obtained from the Institutional Review Board (IRB) of Ameen medical center (Reference no.ERC-CIRS-2023-625). All physicians who were treating diabetes patients in endocrine, medicine or any other departments were included in this study. A convenience sampling method was used to approach physicians.

Data collection involves a structured questionnaire based on the Knowledge, Attitude, and Perception (KAP) survey model. This questionnaire targets physicians in Pakistan, focusing on their approach to treating T2D with SGLT2 inhibitors, either as monotherapy or in combination with other treatments. The questionnaire, comprising 31 questions, is divided into four sections. The "Demographics" section included variables such as age and designation.

Questions such as prescription frequency, confidence in combination therapy, and drug knowledge followed in the section called "Knowledge, Attitude, and Perception". The third section, "Cost-effectiveness", covered opinions on costs.

The reliability of the questionnaire has been validated through a pilot study on 25 participants, yielding a Cronbach's alpha coefficient of 0.885, indicative of high reliability.

The sample size was determined using the OpenEpi online calculator, based on a previously published knowledge index among pharmacists regarding SGLT2 inhibitors as there was no study available on physicians<sup>14</sup>. Accounting for a 95% confidence interval and an 80% power, the minimum sample size required is 95 participants. To enhance the robustness of our findings, we plan to exceed this number.

Data analysis was conducting using SPSS software, version 26. Descriptive statistics were utilized to summarize demographic information, knowledge, attitudes,

and perceptions of the participants. The normality of the data was checked by using Shapiro Wilk test. The Chi-square test was applied for comparing different demographic groups and their responses to the KAP

questions. A P-value less than 0.05 was considered statistically significant.

**Table 1:** Physicians' Experience About SGLT- 2 Inhibitors

	Frequency (n)	Percentage (%)
<b>Which SGLT2 inhibitors do you typically prescribe in patients of Heart Failure?</b>		
Canagliflozin	11	5.8
Empagliflozin	141	74.6
Dapagliflozin	30	15.9
Ertugliflozin	7	3.7
<b>How often do you prescribe SGLT2 inhibitors to patients with Type 2 Diabetes?</b>		
Very Frequently (more than 75% of the time)	43	22.8
Frequently (50-75% of the time)	94	49.7
Occasionally (less than 50% of the time)	41	21.7
Rarely/ Never	11	5.8
<b>What factors do you consider when deciding whether to prescribe SGLT2 inhibitors to a patient?</b>		
Patient's glycemic control	4	2.1
Cardiovascular risk factors	8	4.2
Renal function	6	3.2
Presence of Heart Failure	7	3.7
All of the above	145	76.7
Patient weight	4	2.1
Renal function and glycemic control	3	1.6
Presence of heart failure and cardiovascular risk factors	2	1.1
Presence of heart failure, renal function and cardiovascular risk factors	2	1.1
Cardiovascular risk factors and renal function	3	1.6
Presence of heart failure, cardiovascular risk factors and patient weight	2	1.1
Cardiovascular risk factors and glycemic control	3	1.6
<b>How confident are you in the combination therapy of Empagliflozin and Metformin as a treatment option for T2DM in kidney and cardiac compromised patients?</b>		
Very confident	46	24.3
Confident	106	56.1
Neutral	30	15.9
Not confident	7	3.7
<b>Empagliflozin is the most effective treatment option available especially a patient with weak cardiac activity?</b>		
Agreed	169	89.4
Not Agreed	20	10.6
<b>What is the superiority of SGLT2 inhibitors over other OADs?</b>		
Unique mechanism of action	33	17.5
Weight loss	22	11.6
Cardiovascular and renal benefits	116	61.4
Lower hyperglycemia risk	12	6.3
Cost	6	3.1

## Results

The mean age of all participating physicians was 40.83  $\pm$  11.88 with 135 (71.4%) were male and 54 (28.6%) females. Approximately, 104 (55%) physicians reported hypertension (HTN), obesity, chronic kidney disease (CKD) and hyperuricemia (50%) as the most prevalent comorbidities in diabetic patients. Approximately, 111 (58.7%) physicians reported that both genders with diabetes have comorbidity disease burden. However, 47 (24.9%) of them reported its higher in female. 163 (86.2%) physicians considered dual therapy as preferred treatment for Diabetes and 13 (6.8%) preferred monotherapy and triple therapy respectively.

Regarding Knowledge, Attitude and Perception About SGLT-2 Inhibitors, Empagliflozin was the most prescribed SGLT-2 inhibitor in patients with heart failure. Approximately, 49.7% of the physicians advise SGLT-2 inhibitor frequently to their patients. Most physicians considered patient's glycemic control, cardiovascular risk factors, renal function and presence of Heart Failure while choosing SGLT-2 for the patients with diabetes. Approximately, 56% of the physicians were confident to prescribe SGLT-2 inhibitor in combination with Metformin a treatment option for T2DM in kidney and cardiac compromised patients. However, 89% of the physicians were agreed on the effectiveness of Empagliflozin for diabetic patients with weak cardiac activity. Approximately, 61.4% of physicians considered that SGLT-2 inhibitor is superior than other oral anti-diabetic drugs due to its cardiovascular and renal benefits. All details regarding knowledge, attitude and perception of physicians about SGLT-2 are presented in Table. 1.

Regarding cost effectiveness of SGLT-2 inhibitor, approximately, 154 (81%) physicians considered effi-

cient medicine with cost- benefits for their patients. Most of the physicians (89%) agreed that the cost and quantity of daily diabetes medications impact a patient's overall diabetes management. Most the physicians (88%) were in the favour of encouraging efforts to make easy access of good quality medicine with safety, efficacy and cost effectiveness in the collaboration with pharmaceutical companies. The physician's perceptions about cost effectiveness of SGLT-2 inhibitors are mentioned in Table.2.

## Discussion

This cross-sectional study provides a comprehensive evaluation of Pakistani physicians' experience regarding the use of SGLT2 inhibitors in T2D management, alongside an assessment of cost-effectiveness implications on patient adherence to these treatments. Our findings reveal that physicians recognize the significant clinical benefits of SGLT2 inhibitors, supporting existing literature that highlights their role in improving glycemic control, and in offering cardiovascular and renal advantages,<sup>9</sup> which is relevant considering the high comorbidity burden observed among the diabetic population in Pakistan as shown in our results.

Our survey highlights the preference for dual therapy by 56% of the physicians, primarily combining SGLT2 inhibitors with metformin. This preference reflects a practical approach toward the management of T2D in low resource settings as supported by international guidelines.<sup>10</sup> Starting treatment with a combination of SGLT2 inhibitor and metformin is relatively safe while providing better control of blood sugar and weight compared to using either medication alone.<sup>11</sup> This is aligning with global treatment trends that favor multi-

**Table 2:** Responses about cost effectiveness of SGLT-2 inhibitor

Cost Effectiveness	Frequency (n)	Percentage (%)
<b>The ultimate need to diabetic patient is:</b>		
Efficacious Medicine	35	18.5
Efficacious Medicine with cost- benefits	154	81.5
<b>Can the cost and quantity of daily diabetes medications impact a patient's overall diabetes management?</b>		
Yes	169	89.4
No	20	10.6
<b>How can pharmaceutical companies and health care professionals work together to ensure that patients have access to affordable and effective diabetes medications like empagliflozin + metformin?</b>		
Quality medicine with safety, efficacy and cost	167	88.4
Quality medicines with safety and efficacy only	22	11.6

faceted interventions to tackle the multifactorial risks associated with diabetes. Our study found 89% of physicians agree on the effectiveness of Empagliflozin, particularly for patients with cardiac vulnerabilities, in line with findings from previous clinical trials and regional studies highlighting Empagliflozin's effectiveness in cardiac-compromised diabetic patients.<sup>12</sup>

However, our study also surfaces a critical barrier to the broader application of SGLT2 inhibitors—cost. Most physicians (81%) agree that efficacious medicine should also offer cost-benefits, reflecting a pragmatic understanding of the socio-economic realities faced by patients. The high proportion of physicians acknowledging the impact of medication costs on management (89.4%) suggests an urgent need to resolve clinical efficacy with affordability to improve adherence. Even in the United States, the patient's socioeconomic status may influence the uptake of the medication due to its cost.<sup>13</sup> Similarly, our findings are also consistent with physician surveys from other low- and middle-income countries (LMICs), such as India and Bangladesh, where barriers like medication cost, limited clinical familiarity, and concerns about adverse effects impact the uptake of SGLT2 inhibitors in routine practice.<sup>13</sup>

This research underscores the necessity for educational programs to enhance physician knowledge and patient awareness of SGLT2 inhibitors. Our study calls for policy interventions and collaborations with pharmaceutical companies to make cost-effective medications more accessible. This is critical in a country where economic barriers pose a significant challenge to the effective management of chronic conditions like T2D.

Furthermore, our study had certain limitations. It was performed in a single geographic region and a specific timeframe, which may affect the generalizability of the findings. Longitudinal studies are recommended to monitor changes in experience over time, particularly as newer medications enter the market and healthcare policies evolve.

## Conclusion

Our study highlights the positive experience of Pakistani physicians towards SGLT2 inhibitors and the broad agreement for cost-effective diabetes care. It advocates for underscoring the need for a multidisciplinary approach involving healthcare providers, policymakers, and pharmaceutical companies to ensure that clinically

effective therapies like SGLT2 inhibitors are also economically accessible.

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## Authors' Contribution:

**ZAK:** Conception & design, acquisition of data, analysis & interpretation of data, drafting of article, critically revision for important intellectual content

**UM:** Conception & design, analysis & interpretation of data, drafting of article, critically revision for important intellectual content

**SFJ:** Acquisition of data, analysis & interpretation of data, drafting of article

**WA:** Conception & design, critically revision for important intellectual content

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