REVIEW ARTICLE

Knowledge, Attitude and Practice in Managing Chronic Kidney Disease with SGLT2 Inhibitors

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ABSTRACT

Background and objective: Chronic kidney disease (CKD), and its increasing global burden, is associated with significant morbidity and mortality. This survey-based study aims to capture the knowledge, attitude and practices (KAP) amongst practicing physicians in considering sodium-glucose co-transporter 2 inhibitors (SGLT2i) for the prevention and progression of CKD in diabetic or nondiabetic individuals. **Methodology**: An online questionnaire-based survey was conducted among 262 health care practitioners (HCPs) who manage people with CKD with or without diabetes. The survey was prepared as a Google form and circulated through email to different HCPs. The survey consisted of 6 knowledge-based questions, 4 attitude-based questions and 4 practice-based questions. The forms were filled up voluntarily by the participants and the authors had no control over the response provided. All the responses were consolidated using Microsoft Excel and analyzed. **Results**: A total of 262 HCPs from different regions of the country participated in the survey. About 87% to 94% of the participants were aware that SGLT2i, specifically dapagliflozin, is approved for use in CKD patients with or without diabetes. About three-fourths of the HCPs accepted that an initial drop in estimated glomerular filtration rate (eGFR) occurs upon initiation of dapagliflozin treatment. Almost 90% of them acknowledged the importance of screening for CKD in diabetic patients, and the majority were aware of the renal benefits of SGLT2i. Almost 96% of HCPs consider that dapagliflozin could be used in all patients with CKD irrespective of their diabetes status. Major determining factors with respect to a setback in practice are fear of side effects (54%) and hesitation in switching to newer medications when older medications work fine (34%). **Conclusion**: SGLT2i have demonstrated significant clinical benefits in patients with CKD with or without diabetes. This survey has shown good awareness among clinicians of the beneficial role of SGLT2i in CKD.

Keywords: KAP, health care practitioners, survey, diabetic kidney disease, SGLT2i, diabetes, dapagliflozin

Introduction

Chronic kidney disease (CKD), and its increasing global burden, is associated with significant morbidity and mortality.[1] In addition to the distressing effects of decreased renal function, the treatment burden also severely impaired the quality of life of affected individuals.[2,3] With the alarming global prevalence of comorbidities, including diabetes, hypertension and obesity, there is a corresponding significant surge in the prevalence of CKD.[4,5] Diabetic kidney disease co-existing in 30% and 40% of individuals with type 1 and type 2 diabetes (T2DM) remains a grave concern, highlighting the need to prevent CKD and its progression.[6]

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There are no new medicines that have shown to decelerate the progression of CKD to kidney failure in the last two decades. Surprisingly, sodium-glucose co-transporter 2 inhibitors (SGLT2i) came out as reno protective agents due to their potential to treat diabetes and kidney dysfunction.[7,8] Various clinical trials and consensus guidelines have recommended the use of SGLT2i in individuals with T2DM to reduce risks for CKD and cardiovascular disease (CVD).[9-12] The mechanisms of nephroprotective effects of SGLT2i extend beyond glucose-lowering, weight-lowering and blood pressure-lowering effects that accompany their glucosuric action in people with diabetes. They protect the glomeruli by reducing intraglomerular pressure, improving tubular oxygenation and metabolism and reduction in renal inflammation and fibrosis.

Among the class of SGLT2i, dapagliflozin is the first drug to be approved by the Food and Drug Administration (FDA) in April 2021 for use in CKD patients irrespective of their diabetes status.[13]

The results of DECLARE-TIMI 58 suggested a role for SGLT2i in the prevention of diabetic kidney disease. Dapagliflozin had demonstrated a favorable effect on urinary albumin-to-creatinine ratio (UACR) and renal-specific outcome across baseline UACR categories, including patients with normal albumin excretion.[14] In 2020, generic and affordable versions of dapagliflozin were made available by various manufacturers. Despite supporting evidence and improved affordability, the usage of dapagliflozin is still inadequate by the Indian practitioners who manage CKD based on treatment audit.[9]

Experts certainly follow guidelines based on high-quality evidence from landmark studies. However, when it comes to the practical application of the guidance, they must go through certain adaptations that consider the newer evidence and clinical practice guidelines and patient's context, such as comorbidities, economic status, education status and ability to comply with the proposed management. So, the real-world usage or complete adherence to guidelines may not be exactly reflective of a randomized clinical trial setting. Ultimately, real-world usage is based on evidence, expert guidelines and experience-based applications.

Despite all the affirmative findings and guideline statements and regulatory approvals, continuing medical education (CME) programs, the question remains to what extent the physicians are really applying this knowledge. If this knowledge does not translate into practice, it undermines all the efforts and the actual benefits are never reaped. Therefore, the current survey was conducted to capture the knowledge, attitude and practices (KAP) amongst practicing physicians in considering SGLT2i for the prevention and progression of CKD in diabetic or nondiabetic individuals. Through this study, the authors try to identify and highlight the gaps and eventually hope that the practitioners would reduce these gaps and pass on the benefits of SGLT2i based on recent evidence and guideline recommendations in the management of CKD.

Materials and Methods

An online questionnaire-based survey was conducted among 262 health care practitioners (HCPs) who manage people with CKD with or without diabetes. The HCP practicing in different geographical locations were selected based on random sampling method. The survey was prepared as a Google form and circulated through email to different HCP. The survey consisted of 6 knowledge-based questions, 4 attitude-based questions and 4 practice-based questions.

The forms were filled up voluntarily by the participants had no control over the response provided. All the responses were consolidated using Microsoft Excel and analyzed.

Results

A total of 262 HCPs from different regions of the country participated in the survey.

Two-third of the HCPs were correct in their responses of the patient group included in the DECLARE-TIMI trial (Fig. 1A) and almost 90% were aware that dapagliflozin was the drug studied in the clinical trial including patients with CKD and heart failure with reduced ejection fraction (HFrEF) (Fig. 1B).

About 87% to 94% of the participants were aware that SGLT2i, specifically dapagliflozin, is approved for use in CKD patients with or without diabetes and is considered a first-line treatment choice for diabetes in patients with diabetes and CKD (Table 1). About three-fourths of the HCP accepted the initial drop of estimated glomerular filtration rate (eGFR) upon initiation of dapagliflozin treatment.

Almost 90% of the HCPs acknowledged the importance of screening for CKD in diabetic patients, and the majority were aware of the renal benefits of SGLT2i. Three-fourths of the respondents were aware about the use of dapagliflozin in CKD patients irrespective of the glycated hemoglobin (HbA1c) status.

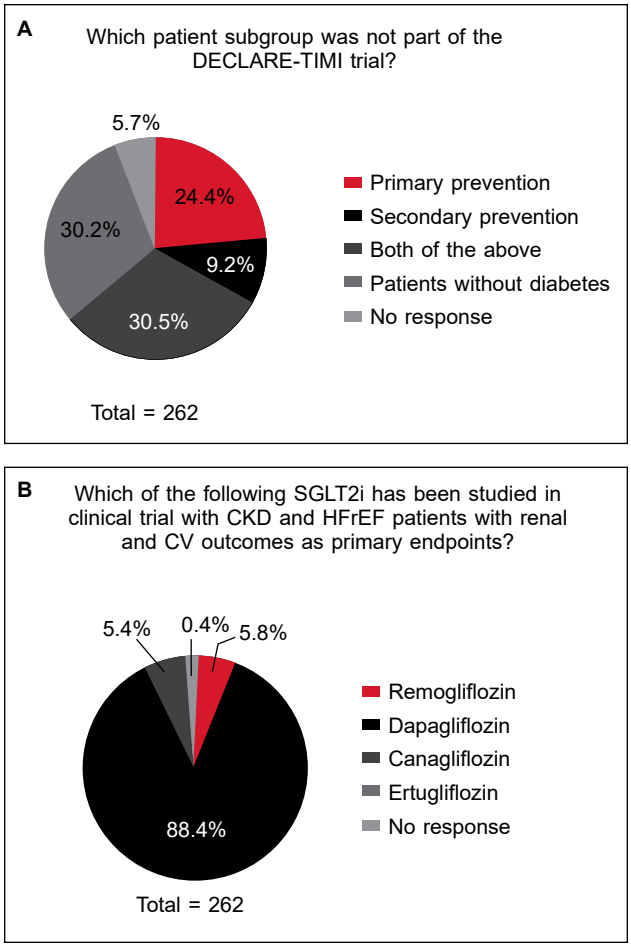


Figure 1. Knowledge-based responses to questions on clinical trials.

Table 1. Responses to Knowledge-based Questions

Questions to map the knowledge gaps	No. of responses	True/Yes
SGLT2i are recently approved for the management of CKD with or without diabetes	245	94.3%
Dapagliflozin reduced the long-term decline of eGFR?	245	92.2%
In patients with DKD, SGLT2i is indicated as first-line agent of T2DM with CKD	241	87.1%
There will be an initial drop of eGFR upon initiation of dapagliflozin. Is it acceptable?	242	74%

Majority of the HCPs opined that people with diabetes must be screened for CKD and consider SGLT2i for management (Fig. 2A and 2B). Almost 96% of HCPs consider that dapagliflozin could be used for management in all patients with CKD irrespective of their diabetes status (Fig. 2C and 2D).

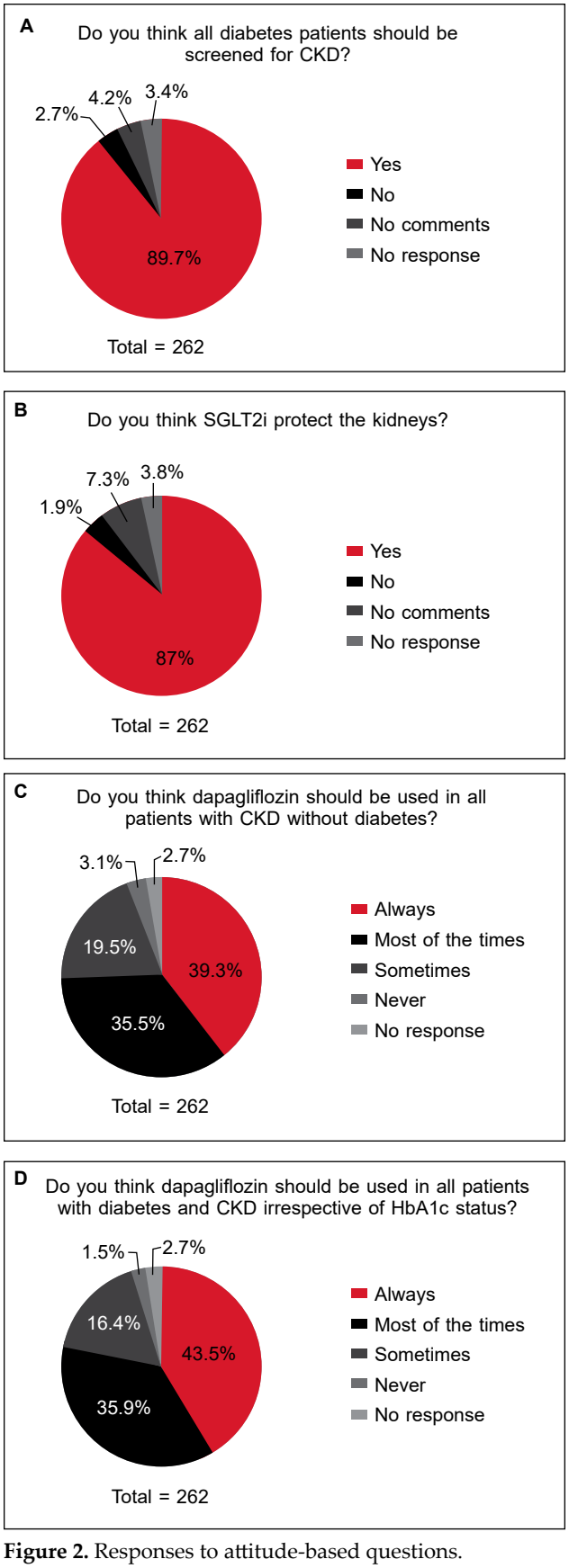


Figure 2. Responses to attitude-based questions.

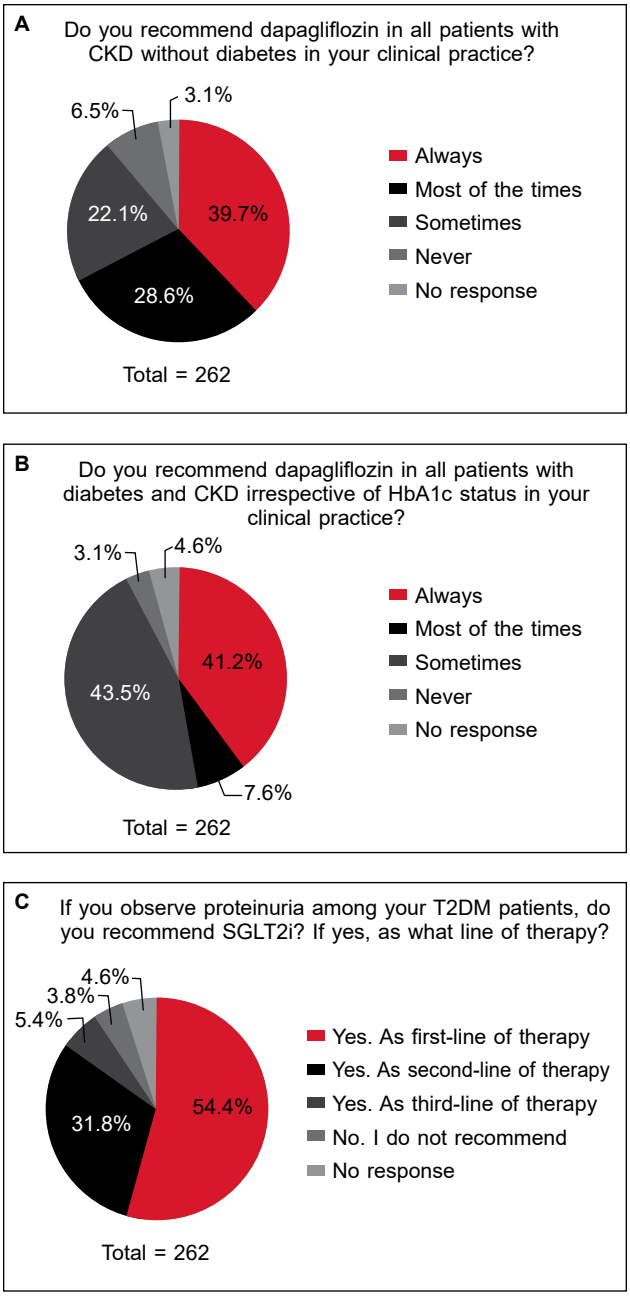


Figure 3. Extent of recommendation of dapagliflozin **A**) in patients with CKD with or without diabetes, **B**) All patients with diabetes, CKD and **C**) T2DM patients with proteinuria.

Practice-based Questions

Only about 40% to 50% of the respondents always recommend the use of SGLT2i in patients with proteinuria or dapagliflozin for CKD patients with or without diabetes (Fig. 3A-3C). Major determining factors with respect to a setback in practice are fear of side effects (54%) and hesitation in switching to newer medications when older medications work fine (34%) (Fig. 4).

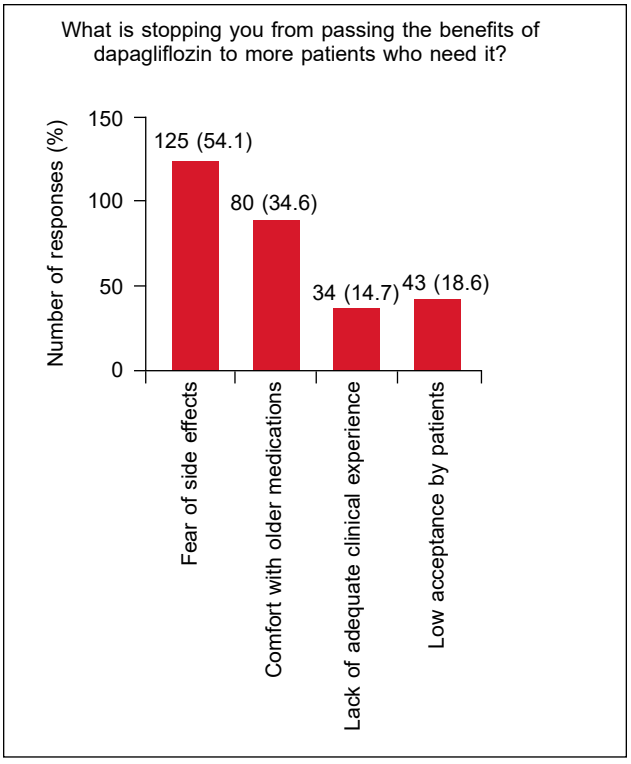


Figure 4. Factors affecting practice of passing the benefits of dapagliflozin to more patients.

Discussion

Knowledge among HCPs about SGLT2i and the efficacy of dapagliflozin to prevent the decline of eGFR is noteworthy (Fig. 1). Based on the responses to different types of questions, it was seen that there is a high level of awareness on the pertinent aspects on the usage of SGLT2i for the management of people with CKD. Various clinical trials and consensus guidelines have recommended the use of SGLT2i in individuals with T2DM to reduce the risks of CKD and CVD.[9] The KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease recommends the administration of SGLT2i in patients with T2DM and CKD with an eGFR ≥20 mL/min/1.73 m^2.[10] However, for people with type 2 diabetes and diabetic kidney disease, use of an SGLT2i in individuals with eGFR ≥20 mL/min/1.73 m^2 and UACR ≥200 mg/g creatinine is recommended to reduce CKD progression and cardiovascular events. This is a change in eGFR from previous recommendations that suggested an eGFR level ≥25 mL/min/1.73 m^2.[11] Among SGLT2i, dapagliflozin was the first drug to be approved by the FDA in April 2021 for use in CKD patients irrespective of their diabetes status based on the findings of the DAPA-CKD trial.[12] NICE has also recommended dapagliflozin as a treatment option for certain people

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