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Clinician Perspectives on Cardiovascular Risk–Based Use of DPP-4 and SGLT2 Inhibitors in Type 2 Diabetes Mellitus in Indian Settings

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Abstract

Objective: The survey aimed to assess clinicians' perspectives and preferences in managing type 2 diabetes mellitus (T2DM), with particular emphasis on cardiovascular risk–based decision-making and the use of dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium-glucose co-transporter-2 (SGLT2) inhibitors in routine clinical practice.

Methodology: This cross-sectional study was conducted among clinicians across India to assess clinical perspectives in the management of T2DM with cardiovascular risk, heart failure (HF), and chronic kidney disease (CKD). A structured 22-item, multiple-response questionnaire was distributed via digital platforms, and responses were analyzed using descriptive statistics to summarize clinician preferences and experiences.

Results: A total of 366 clinicians participated in the survey. Nearly 34% of clinicians identified the combination of a DPP-4 inhibitor, an SGLT2 inhibitor, and metformin as their preferred initiation therapy for newly diagnosed individuals with T2DM and cardiovascular risk. Approximately 80% of respondents reported sitagliptin as their preferred DPP-4 inhibitor. Around 70% of clinicians favored switching to a triple combination of metformin, a DPP-4 inhibitor, and an SGLT2 inhibitor in patients inadequately controlled on sulphonylurea plus metformin therapy. Among newly diagnosed individuals with T2DM and HF, 49% preferred the combination of a DPP-4 inhibitor, an SGLT2 inhibitor, and metformin as the oral antidiabetic regimen. Nearly 86% of participants favored dapagliflozin as the preferred SGLT2 inhibitor in patients with established HF.

Conclusion: This survey indicates that clinicians frequently encounter individuals with T2DM presenting with cardiovascular risk. Physicians predominantly favor combination regimens incorporating DPP-4 inhibitors and SGLT2 inhibitors due to their perceived benefits in achieving glycemic targets, reducing glycemic variability, and providing cardiovascular and renal protection.

Introduction

Approximately 589 million adults (1 in 9) are currently living with diabetes globally, a figure with a rapidly increasing global prevalence, projected to rise to 853 million by 2050. Type 2 diabetes mellitus (T2DM) accounts for nearly 90-95% of all diabetes cases and disproportionately affects low- and middle-income countries, where approximately 81% of individuals with diabetes reside.[1] In 2024, India, one of the most affected countries, has an estimated adult population of 947.3 million, with a diabetes prevalence of 10.5%, accounting for approximately 89.8 million adults living with diabetes. [2]

In addition to chronic hyperglycemia, T2DM is characterized by substantial microvascular and macrovascular complications, with cardiovascular disease representing the leading cause of morbidity and mortality. Among individuals with diabetes, cardiovascular disease accounts for approximately 80% of all mortality and 75% of all hospitalizations.[3] Patients with T2DM have a two- to four-fold increased risk of atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and diabetic kidney disease (DKD), emphasizing the need for comprehensive cardiometabolic risk management.[4]

In recent years, large cardiovascular outcome trials have reshaped treatment strategies in T2DM. Sodium-glucose co-transporter-2 (SGLT2) inhibitors have demonstrated significant reductions in hospitalization for HF and favorable renal outcomes, while dipeptidyl peptidase-4 (DPP-4) inhibitors continue to be widely used for their glycemic efficacy, low risk of hypoglycemia, and weight neutrality.[5] These developments have influenced clinical guidelines, which now recommend tailoring therapy based on the presence of cardiovascular disease, HF, and renal impairment.[6-8]

SGLT2 inhibitors represent a unique class of glucose-lowering therapies that reduce plasma glucose through an insulin-independent mechanism by inhibiting renal glucose reabsorption at the proximal tubule (S1 segment), thereby promoting glucosuria. Beyond glycemic control, they exert multisystem benefits including osmotic diuresis, natriuresis, reduction in preload and afterload, improvement in lowering of blood pressure, and weight reduction. These effects have been associated with significant reductions in hospitalization for HF and delayed progression of kidney disease, and the class is increasingly recognized for its role in preventing and treating HF, with or without T2DM.[9,10] DPP-4 inhibitors are antihyperglycemic agents that enhance endogenous incretin activity by preventing degradation of glucagon-like peptide-1 (GLP-1), thereby improving glucose-dependent insulin secretion and suppressing glucagon release. Although major cardiovascular outcome trials have largely demonstrated cardiovascular neutrality for this class, DPP-4 inhibitors are widely used due to their favorable safety profile, low risk of hypoglycemia, weight neutrality, and suitability across a broad spectrum of patients. [11,12]

Current clinical guidelines now emphasize individualized treatment strategies based not only on glycemic status but also on the presence of ASCVD, HF, and chronic kidney disease. In this

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context, drug class selection and molecule preference are increasingly influenced by cardiovascular comorbidities and safety profiles.[13] Understanding clinicians' preferences and practices in patients with cardiovascular risk is important to characterize current treatment patterns and inform clinical practice. Therefore, the present study aims to assess clinicians' preferences in managing T2DM, particularly in the context of cardiovascular risk and HF, with emphasis on DPP-4 inhibitors and SGLT2 inhibitors.

Methodology

A cross-sectional study was carried out among clinicians specialized in managing T2DM in the major Indian cities from June 2025 to December 2025.

Questionnaire

The questionnaire booklet titled SYMPHONY (Sitagliptin and combinations in Type 2 Diabetes Management: Expert Perspectives on efficacy and tolerability) study was sent to the doctors (cardiologists, diabetologists, general physicians, and consulting physicians) who were interested in participating in the study. A 23-item structured, multiple-response questionnaire aimed to assess clinicians' preferences, cardiovascular risk–based treatment strategies, and the use of DPP-4 inhibitors and SGLT2 inhibitors in routine clinical practice. The study was performed after obtaining approval from Bangalore Ethics, an Independent Ethics Committee (ECR/355/Indt/KA/2022), which was recognized by the Indian Regulatory Authority, the Drug Controller General of India.

Participants

A convenient sampling technique was used, and an invitation was sent to professionals across India based on their expertise and experience in treating T2DM in the month of March 2025 for participation in this Indian survey. About 366 clinicians from major cities of all Indian states, representing the geographical distribution, shared their willingness to participate and provide necessary data. Clinicians were instructed to complete the questionnaire independently without consulting colleagues. Written informed consent was obtained from each participant before the study began.

Statistical analysis

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to clearly illustrate their distribution. As an exploratory perception-based survey, the analysis was limited to descriptive statistics. The frequency of occurrence and corresponding percentages were employed to represent the distribution of each variable. Graphs were created to visualize the distribution of the categorical variables, using Microsoft Excel (version 16.0.18025.20030).

Results

The study included 366 clinicians, of whom 57% stated that 21-40% of patients with T2DM have more than one comorbidity, such as ASCVD, HF, and DKD. Approximately 61% of clinicians reported that 21–40% of newly diagnosed individuals with T2DM are at cardiovascular risk. Around 44% of respondents indicated that the most common cardiovascular risk factors observed among newly diagnosed individuals with T2DM are older age (>45 years in males and >55 years in females), a history of hypertension, and smoking or tobacco use. Nearly half of the respondents (50.55%) reported that male individuals have major ASCVD risk factors, whereas 44% indicated that both males and females have an equal risk of major ASCVD factors. More than half of the clinicians (51.91%) reported that high glycemic variability is often observed in patients with T2DM and ASCVD, while 43% indicated that it is observed sometimes.

The majority of respondents (82.24%) opined that high glycemic variability increases the risk of composite major adverse cardiovascular events (MACE), atrial fibrillation (AF), non-infarct-related artery (non-IRA) revascularization, and end-stage kidney disease (ESKD) in individuals with T2DM. Approximately 34% of the clinicians reported that the preferred initiation therapy in newly diagnosed T2DM individuals with cardiovascular risk is DPP4i + SGLT2i + metformin (Table 1).

According to 48% of respondents, approximately 41–60% of patients achieve the HbA1c target of 7% within 3 months after the addition of dapagliflozin. A reduction in cardiovascular mortality was reported by 54% of respondents as the most prominent extra-glycemic benefit following the addition of SGLT2 inhibitors in patients with T2DM and HF. More than half of the respondents (51.37%) agreed that dapagliflozin reduces the risk of atrial fibrillation in individuals with T2DM, irrespective of HF status. As reported by 42% of clinicians, the primary beneficial effect observed with the combination of a DPP-4 inhibitor and an SGLT2 inhibitor in individuals with T2DM is a low risk of hypoglycemia. Additionally, 41% of respondents reported observing multiple benefits with this combination therapy, including reduced glycemic variability, modest weight loss, favourable renal effects, moderate reductions in systolic blood pressure, and the convenience of once-daily dosing.

The majority of respondents (52.46%) reported that a lower risk of hypoglycemia is the primary reason for preferring DPP-4 inhibitors over sulfonylureas in elderly patients with T2DM and established cardiovascular disease (eCVD). Approximately 66% agreed that the addition of a DPP-4 inhibitor to SGLT2 inhibitor therapy decreases the frequency of genitourinary infections in patients with T2DM. As reported by 45% of clinicians, approximately 11-20% of patients use the newer single-pill combination of sitagliptin, glimepiride, and metformin. A significant proportion of respondents (83.61%) reported that they have not observed any adverse drug reactions in patients treated with sitagliptin. Regarding glycemic control with sitagliptin, 42.9% of respondents reported marked improvement, while 41% reported moderate improvement.

Table 1: Distribution of responses on the preferred initiation therapy in newly diagnosed T2DM individuals with cardiovascular risk

Drugs	Response rate (n = 366)
DPP4i + Metformin	23.5%
Sulphonylureas + Metformin	8.47%
SGLT2i + Metformin	21.58%
DPP4i + Sulphonylureas + Metformin	11.48%
DPP4i + SGLT2i + Metformin	33.88%
All of the above	1.09%

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A significant proportion (79.78%) reported that sitagliptin is the preferred DPP-4 inhibitor for individuals with T2DM and cardiovascular risk (Table 2). Approximately 43% of participants indicated that established cardiovascular outcome trial (CVOT) evidence and demonstrated cardiovascular benefits, along with good tolerability in patients with nonalcoholic fatty liver disease (NAFLD), a lower risk of hypoglycemia, weight neutrality, and suitability across different stages of T2DM, are key factors influencing their decision to prefer sitagliptin in individuals with cardiovascular risk.

As reported by 58% of the experts, approximately 30–50% of patients with T2DM are inadequately controlled on sulphonylurea plus metformin therapy. More than half of the participants (69.67%) reported that switching to a triple combination of metformin, a DPP-4 inhibitor, and an SGLT2 inhibitor is the preferred add-on strategy for managing patients with T2DM who are uncontrolled on sulphonylurea plus metformin therapy (Table 3).

As indicated by 49% of clinicians, the combination of a DPP-4 inhibitor, an SGLT2 inhibitor, and metformin is the preferred oral antidiabetic drug (OAD) therapy for individuals with T2DM newly diagnosed with HF (Figure 1). The majority of clinicians (86.34%) reported that dapagliflozin is the preferred SGLT2 inhibitor for individuals with T2DM and established HF (Figure 2).

Table 2: Distribution of responses on the most preferred DPP4i for T2DM individuals with cardiovascular risk

Drugs	Response rate (n = 366)
Linagliptin	11.48%
Vildagliptin	7.38%
Sitagliptin	79.78%
Teneligliptin	0.55%
All of the above	0.82%

Table 3: Distribution of responses on the preferred add-on class of drug in the management of T2DM patients uncontrolled with sulphonylureas + metformin therapy

Drug class	Response rate (n = 366)
DPP4i alone	17.49%
SGLT2i alone	11.48%
Switch to metformin + DPP4i + SGLT2i	69.67%
All of the above	1.37%

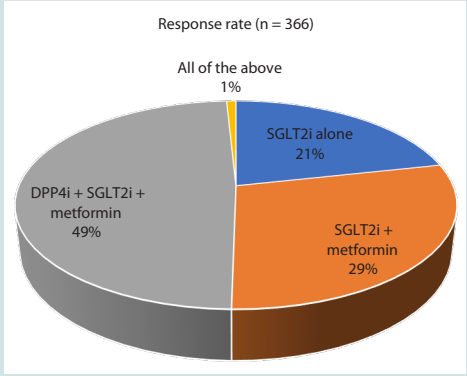

Figure 1: Distribution of responses on the preferred OAD therapy in T2DM individuals newly diagnosed with HF

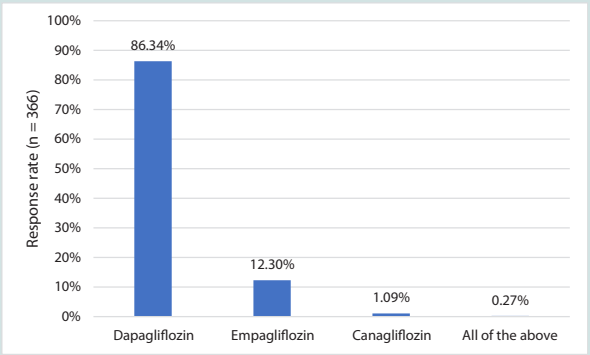

Figure 2: Distribution of responses on the most preferred SGLT2i for T2DM individuals with established HF

Discussion

The study highlights current cardiovascular-focused treatment practices for T2DM in Indian clinical settings, with particular emphasis on the use of DPP-4 inhibitors and SGLT2 inhibitors. In the present study, the majority of participants reported that the preferred initiation therapy in newly diagnosed individuals with T2DM and cardiovascular risk was the combination of a DPP-4 inhibitor, an SGLT2 inhibitor, and metformin. This preference reflects a shift toward early combination therapy aimed at achieving comprehensive metabolic and cardiovascular risk management rather than glucose-centric management alone.

These findings are consistent with previously published Indian data. Bafna et al. reported that 74% of clinicians strongly recommended the triple fixed-dose combination of an SGLT2 inhibitor (dapagliflozin) with a DPP-4 inhibitor (sitagliptin) and metformin for patients with T2DM and cardiovascular or renal risk. [14] A prior survey conducted by the current authors similarly highlighted that the majority of physicians prescribed sitagliptin and dapagliflozin (DPP-4 inhibitor + SGLT2 inhibitor) specifically for newly diagnosed individuals with T2DM and cardiovascular risk.[15] Furthermore, Sahay et al. concluded that the preferred initiation therapy in newly diagnosed individuals with T2DM and cardiovascular risk in India includes DPP-4 inhibitors and SGLT2 inhibitors, particularly in those inadequately controlled on metformin monotherapy.[16] Likewise, Das et al. demonstrated that for newly diagnosed individuals with T2DM and HbA1c >7.5%, the preferred initiation therapy was a combination of DPP-4 inhibitors and metformin, based on expert consensus among diabetes specialists.[17]

A significant proportion of respondents in the current survey reported that sitagliptin is the most preferred DPP-4 inhibitor for individuals with T2DM and cardiovascular risk. Consistent with prior observational studies and expert consensus statements, sitagliptin appears to be widely favored because of its established efficacy, favorable cardiovascular safety profile, and overall tolerability across diverse patient populations.[18–20] Kumar et al. concluded that sitagliptin was the most preferred DPP-4 inhibitor for individuals with T2DM and cardiovascular risk in India.[18] Similarly, Kalra et al. reported that sitagliptin is a preferred DPP-4 inhibitor for T2DM management in India due to its efficacy and safety when used as monotherapy, in combination, or as an add-on therapy.[20]

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The preference for triple combination therapy comprising metformin, a DPP-4 inhibitor, and an SGLT2 inhibitor, as noted in the present survey, reflects evolving cardiometabolic treatment strategies in routine clinical practice. Clinical studies, and meta-analyses have consistently demonstrated that this combination provides superior glycemic control compared with dual therapy, along with additional benefits such as reductions in body weight and blood pressure, without compromising safety.[21–23] A recent phase 3 study by Singh et al. showed that a fixed-dose triple combination of dapagliflozin, sitagliptin, and metformin is effective and well tolerated, offering improved glycemic control compared with dual therapy.[21] In addition, a meta-analysis by Li et al. reported that the addition of an SGLT2 inhibitor to a DPP-4 inhibitor plus metformin (triple therapy) resulted in significantly greater reductions in blood glucose levels, body weight, and blood pressure compared with dual therapy.[23]

The current study further demonstrated that the combination of a DPP-4 inhibitor, an SGLT2 inhibitor, and metformin was the preferred oral antidiabetic therapy in newly diagnosed T2DM individuals with HF. This finding is clinically relevant, given the established cardiovascular and HF benefits associated with SGLT2 inhibitors and the neutral cardiovascular safety profile of DPP-4 inhibitors. Supporting this observation, Chadha et al. reported that the combination of a DPP-4 inhibitor and an SGLT2 inhibitor is particularly beneficial for individuals with T2DM due to its favorable effects on glycemic parameters and vascular risk.[24]

The present survey results identified dapagliflozin as the preferred SGLT2 inhibitor for individuals with T2DM and established HF. This preference is consistent with the expanding body of evidence supporting its cardiovascular and renal benefits beyond glycemic control. Ghosh et al. reported that dapagliflozin is commonly preferred in Indian clinical practice for patients with T2DM and established HF because of its synergistic effects on glycemic improvement and cardio-renal protection.[25] Similarly, Shaline Rao highlighted that dapagliflozin is a preferred SGLT2 inhibitor for the treatment of HF in patients with and without T2DM, noting that it was the first agent in its class to receive US FDA approval for this indication.[26] Mehta et al. further observed that, among available SGLT2 inhibitors, dapagliflozin was the most frequently preferred option in routine practice, particularly for cardiovascular and renal risk reduction in patients with T2DM.[27] These findings support the prominent role of dapagliflozin in cardiometabolic risk management.

In addition to therapeutic preferences, the current survey also provided insights into tolerability patterns. A substantial proportion of respondents (83.61%) reported not observing any adverse drug reactions in patients treated with sitagliptin. This observation aligns with previously published regional data. Sudhakaran et al. concluded that sitagliptin effectively reduced glycemic parameters in individuals with T2DM and was associated with a low incidence of adverse experiences.[28] Mohan et al. similarly reported that sitagliptin was generally well tolerated in Chinese, Indian, and Korean patients with T2DM, with a low incidence of serious adverse events; most reported events were mild and self-limiting.[29]

This nationwide cross-sectional survey involving 366 clinicians provides valuable insights into contemporary cardiovascular-focused management of T2DM in India, particularly regarding the use of DPP-4 inhibitors and SGLT2 inhibitors. Its strengths include a relatively large and geographically diverse sample, a comprehensive 23-item structured questionnaire capturing initiation strategies, add-on therapy, drug selection rationale, and safety perceptions, and a clear descriptive statistical presentation of findings. The focus on cardiometabolic risk, including ASCVD, HF, and DKD, enhances its clinical relevance in the context of evolving guideline-directed care. However, the study has limitations inherent to survey-based research, including its cross-sectional design, reliance on self-reported physician perceptions rather than audited prescription or patient-level outcome data, potential recall and response bias, and the use of descriptive statistics without inferential analysis. Furthermore, the survey did not include patient-level clinical data, treatment adherence information, or longitudinal cardiovascular and renal outcomes. Therefore, while the findings provide insight into prevailing therapeutic preferences, they do not establish the clinical effectiveness or safety of the reported strategies in the patient population. These limitations should be considered when interpreting the results, and future prospective studies incorporating prescription audits and outcome-based clinical data would help validate and expand upon these observations.

Conclusion

This survey indicates a clear preference among clinicians for early combination therapy incorporating DPP-4 inhibitors and SGLT2 inhibitors, particularly sitagliptin- and dapagliflozin-based regimens, in individuals with cardiovascular risk and heart failure. The strong inclination toward triple therapy with metformin, a DPP-4 inhibitor, and an SGLT2 inhibitor suggests a shift from glucose-centric treatment toward comprehensive cardiometabolic risk reduction. Sitagliptin was reported as the preferred DPP-4 inhibitor due to its perceived efficacy, cardiovascular safety, and tolerability, while dapagliflozin is favored for its established cardio-renal benefits and heart failure outcomes.

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Conflict of Interest

Both authors are employees of Micro Labs Limited. The study was designed and conducted as part of a scientific initiative. The authors declare that no undue influence was exerted on data collection, analysis, or interpretation.

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