



## Real-world effectiveness of glimepiride-metformin-dapagliflozin triple therapy in type 2 diabetes mellitus: insights from the western region of India

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### Abstract

**Background:** Type 2 diabetes mellitus (T2DM) often requires treatment intensification, and the metformin-glimepiride-dapagliflozin combination provides complementary glycaemic and cardiometabolic benefits. This study assessed real-world healthcare practitioners' perspectives on the effectiveness and clinical utility of triple therapy of metformin, glimepiride, and dapagliflozin in patients with T2DM in Western India.

**Methods:** A questionnaire-based, cross-sectional observational study was conducted among HCPs managing T2DM in the western region of India. A structured 32-item questionnaire captured data from the last 10 patients treated with triple therapy, including glycaemic outcomes, cardiometabolic effects, safety, prescribing patterns, adherence, and patient acceptance. Descriptive statistics were used to summarise responses as frequencies and percentages.

**Results:** A total of 81 HCPs participated. The most commonly reported HbA1c reduction was 0.5-1% (35.80%) and 1-1.5% (24.69%), with maximum improvement typically observed at 6 months. Triple therapy was considered more effective than dual therapy by 64.20% of HCPs. Weight loss and improvements in blood pressure were frequently reported following initiation of dapagliflozin. Cardiovascular benefit (38.27%) and inadequate glycaemic control (30.86%) were the main reasons for therapy initiation. Renal monitoring was commonly performed every 3-6 months. Non-adherence (44.44%) and side effects (30.86%) were the main barriers to optimal control. Hypoglycaemia (35.80) and genital infections (29.63) were the most commonly reported adverse events. Overall, 70.37% of HCPs reported satisfaction with clinical outcomes of triple therapy.

**Conclusion:** Real-world data from Western India indicate that triple therapy (metformin, glimepiride, and dapagliflozin) provides significant glycaemic and cardiometabolic benefits with tolerability, supporting its use in patients with inadequately controlled T2DM.

**Keywords:** Glycaemic control, HBA1C reduction, cardiometabolic outcomes, treatment adherence, safety, hypoglycaemia

### Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterised by chronic hyperglycaemia resulting from insulin resistance and relative insulin deficiency [1]. It has emerged as a major global public health challenge, with prevalence rising rapidly in both developed and developing countries. According to the World Health Organization, diabetes contributes substantially to premature mortality and increasing healthcare expenditure worldwide [2]. The International Diabetes Federation estimates that 537 million adults were living with diabetes in 2021, a number projected to reach 643 million by 2030 [3]. India alone accounts for more than 77 million people with diabetes, ranking second globally and underscoring the urgent public health burden in the region [4]. The T2DM represents the predominant form of diabetes worldwide. It is strongly associated with increased morbidity and mortality due to microvascular complications such as nephropathy, neuropathy, and retinopathy, as well as macrovascular conditions including coronary artery disease and stroke [5]. Achieving and maintaining optimal glycaemic control is therefore essential to delay disease progression and prevent long-term complications.

Achieving optimal glycaemic control remains the cornerstone of T2DM management to reduce long-term complications and improve quality of life. Metformin is

widely recommended as the first-line therapy because of its proven efficacy, favourable safety profile, and cost-effectiveness. However, its long-term effectiveness often declines as  $\beta$ -cell dysfunction progresses and insulin resistance increases, necessitating the addition of other agents [6]. Consequently, clinical guidelines recommend combining metformin with additional drug classes such as sulfonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and glucagon-like peptide-1 receptor agonist achieve improved glycaemic control and better overall clinical outcomes [7, 8].

Triple therapy combining glimepiride (a sulfonylurea that enhances insulin secretion), metformin (which reduces hepatic gluconeogenesis and improves insulin sensitivity), and dapagliflozin (an SGLT2 inhibitor that promotes glycosuria, weight loss, and cardiorenal protection) offers a complementary, mechanism-based approach to address the heterogeneity of T2DM [9]. Clinical guidance from the American Diabetes Association/European Association for the Study of Diabetes and National Institute for Health and Care Excellence (ADA/EASD) supports the use of such combinations in patients with HbA1c levels >1.5% above target or >9% at baseline, emphasizing the cardiorenal benefits of SGLT2 inhibitors alongside cost-effective generics such as sulfonylureas, particularly in resource-

limited settings [8]. Fixed-dose combinations (FDCs) further simplify pharmacological treatment by combining multiple agents into a single dosage form, thereby reducing pill burden and improving adherence, an important consideration in India, where out-of-pocket healthcare costs remain high [10, 11]. Recent evidence also supports the clinical benefits of this regimen, including a 2025 phase III Indian study evaluating a triple FDC (dapagliflozin 10 mg, glimepiride 1 mg, and metformin ER 1000 mg) compared with dual therapy in patients with inadequately controlled T2DM [9].

Given the progressive nature of T2DM and the growing emphasis on individualized, mechanism-based treatment strategies, evaluating the real-world effectiveness of triple therapy is clinically important. Therefore, the present study aimed to assess the role of the combination of glimepiride, metformin, and dapagliflozin in patients with T2DM, with a focus on glycaemic outcomes and overall therapeutic effectiveness in routine clinical practice.

## Methods

### Study design

A questionnaire-based study was conducted to evaluate real-world clinical practice patterns regarding the use of triple oral therapy (metformin, glimepiride, and dapagliflozin) in the management of T2DM in the West region of India. All responses reflected healthcare practitioners' (HCPs) direct clinical experience with their patient populations. The survey captured insights into treatment initiation, prescribing behaviour, dosing and monitoring practices, treatment effectiveness, safety profile, treatment adherence, and patient acceptance. *Survey instrument*

The study questionnaire was developed based on current clinical practice patterns, published literature, and expert HCP's input. It comprised 32 structured questions focusing on patient demographics, glycaemic efficacy, dosing strategies, cardiovascular (CV) and renal outcomes, safety profile, treatment adherence, weight changes, and overall clinical satisfaction in patients with T2DM receiving triple therapy with glimepiride, metformin, and dapagliflozin. Key areas included reductions in HbA1c and glucose, adverse events, CV benefits, renal monitoring practices, and patient acceptance. The questionnaire

Specifically captured data from the last 10 patients treated by each HCP in routine clinical practice, and the study protocol was reviewed and approved by an Central Independent Ethics Committee (CIEC), Pune (IEC No: CIEC/2025/066), dated 29 April 2025.

### Data collection

Participating HCPs received information regarding the study purpose and instructions for completing the questionnaire. The questionnaires were distributed electronically based on each HCP's preferred mode of communication. Only anonymised clinical information was recorded, and no identifiable patient data were collected at any stage.

### Data analysis

Completed responses were compiled in Microsoft Excel. A descriptive statistical approach was applied, and results were summarised as frequencies and percentages.

## Results

### Survey overview

A total of 81 HCPs from the Western region of India participated in the survey on the use of triple oral therapy (metformin, glimepiride, and dapagliflozin) in the management of T2DM. The highest representation was from Maharashtra (76.54%), followed by Gujarat (13.58%) and Madhya Pradesh (9.88%).

### Clinical effectiveness of triple therapy in T2DM

Healthcare practitioners reported their real-world experience based on their last 10 patients treated with triple oral therapy. Regarding glycaemic control, the most commonly observed HbA1c reduction was 0.5-1% (35.80%), followed by 1-1.5% (24.69%). Improvements in postprandial glucose were observed in 0-2 patients by 53.09% of HCPs, while 20.99% reported improvement in 6-8 patients. Achievement of the HbA1c target (<7%) within 3 months was reported in 0-2 patients by 53.09% of HCPs, while 22.22% observed target achievement in ≥6 patients. For fasting plasma glucose reduction, nearly half of the HCPs (49.38%) reported a reduction of <30 mg/dL, while 22.22% and 20.99% observed reductions of 30-60 mg/dL and 61-90 mg/dL, respectively.

In comparison with dual therapy, 64.20% of HCPs considered triple therapy to be more effective in reducing HbA1c (29.63% much more effective; 34.57% slightly more effective). Weight loss was reported sometimes by 38.27% of HCP, while very often by 32.10 % of HCP, and 66.67% observed improvements in blood pressure after initiation of dapagliflozin (25.93% consistently; 40.74% in some patients). Maximum HbA1c reduction was most commonly observed at 6 months (41.98%), followed by 3 months (27.16%). Weight loss of >2 kg was observed in 0-2 patients by 35.80% of HCPs and in ≥6-10 patients by 29.62% (Table 1).

**Table 1:** Clinical effectiveness of triple therapy in T2DM: Real-world HCPs' experience

| Question                                                                                                          | Options | Response of HCPs (N=81) |
|-------------------------------------------------------------------------------------------------------------------|---------|-------------------------|
| Based on the last 10 patients treated, what was the average reduction in HbA1c (%) after starting triple therapy? | <0.5%   | 19 (23.46)              |
|                                                                                                                   | 0.5-1%  | 29 (35.80)              |
|                                                                                                                   | 1-1.5%  | 20 (24.69)              |
|                                                                                                                   | >1.5%   | 13 (16.05)              |
| Based on the last 10 patients, how many showed improvements in postprandial glucose levels?                       | 0-2     | 43 (53.09)              |
|                                                                                                                   | 3-5     | 13 (16.05)              |
|                                                                                                                   | 6-8     | 17 (20.99)              |
|                                                                                                                   | 9-10    | 8 (9.88)                |
| In the past 10 patients, how many achieved an HbA1c target of <7% after 3 months of this therapy?                 | 0-2     | 43 (53.09)              |
|                                                                                                                   | 3-5     | 20 (24.69)              |
|                                                                                                                   | 6-8     | 9 (11.11)               |
|                                                                                                                   | 9-10    | 9 (11.11)               |

|                                                                                                                 |                             |            |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------|------------|
| Based on the last 10 patients, what was the observed average fasting plasma glucose reduction (mg/dL)?          | <30 mg/dL                   | 40 (49.38) |
|                                                                                                                 | 30-60 mg/dL                 | 18 (22.22) |
|                                                                                                                 | 61-90 mg/dL                 | 17 (20.99) |
|                                                                                                                 | >90 mg/dL                   | 6 (7.41)   |
| In your opinion, how effective is triple therapy in reducing HbA1c compared to dual therapy?                    | Much more effective         | 24 (29.63) |
|                                                                                                                 | Slightly more effective     | 28 (34.57) |
|                                                                                                                 | No significant difference   | 17 (20.99) |
|                                                                                                                 | Less effective              | 12 (14.81) |
| In your practice, how often do you observe weight loss as a beneficial outcome of triple therapy?               | Very often (>70% patients)  | 26 (32.10) |
|                                                                                                                 | Sometimes (30-70% patients) | 31 (38.27) |
|                                                                                                                 | Rarely (<30% patients)      | 16 (19.75) |
|                                                                                                                 | Very often (>70% patients)  | 8 (9.88)   |
| Have you observed improvements in blood pressure after starting dapagliflozin?                                  | Yes, consistently           | 21 (25.93) |
|                                                                                                                 | Yes, in some patients       | 33 (40.74) |
|                                                                                                                 | Rarely                      | 22 (27.16) |
|                                                                                                                 | No                          | 5 (6.17)   |
| What is the typical duration after which you observe maximum HbA1c reduction post initiation of triple therapy? | 3 months                    | 22 (27.16) |
|                                                                                                                 | 6 months                    | 34 (41.98) |
|                                                                                                                 | 9 months                    | 11 (13.58) |
|                                                                                                                 | 12 months                   | 14 (17.28) |
| In the past 10 patients, how often was weight loss (>2 kg) observed after therapy initiation?                   | 0-2 patients                | 29 (35.80) |
|                                                                                                                 | 3-5 patients                | 28 (34.57) |
|                                                                                                                 | 6-8 patients                | 12 (14.81) |
|                                                                                                                 | 9-10 patients               | 12 (14.81) |
| Data represented as n (%).                                                                                      |                             |            |
| HbA1c, glycated haemoglobin; HCP, healthcare practitioners; T2DM, type 2 diabetes mellitus.                     |                             |            |

### Healthcare practitioners' prescribing patterns and treatment optimization strategies

Healthcare practitioners reported that the most common reason for initiating triple therapy in patients with T2DM was CV benefit (38.27%), followed by inadequate glycaemic control (30.86%) (Figure 1). The preferred initial dosing strategy for glimepiride was predominantly low dose (1-2 mg) in 58.02% of HCPs, while 32.10% preferred a moderate dose and 9.88% a high dose. Triple therapy was most commonly prescribed to patients aged 30-45 years (46.91%), followed by 46-60 years (35.80%). Most HCPs reassessed patients after 1 month (40.74%), while renal function monitoring after dapagliflozin initiation was typically performed every 6 months (37.04%) or every 3 months (32.10%).

During follow-up, the therapy component most frequently adjusted was glimepiride (55.56%), followed by metformin (28.40%). The HCPs preferred an alternative SGLT2 inhibitor mainly when cost was an issue (46.91%), followed by low eGFR (23.46%). Cardiovascular comorbidities were considered always or sometimes by 71.60% of HCPs when choosing dapagliflozin, and 58.02% routinely counselled patients about hydration. The most important factor influencing long-term continuation of triple therapy was HbA1c control (54.32%), followed by side-effect profile

(19.75%). Regarding real-world utilisation, 65.43% of HCPs reported that  $\leq 30\%$  of their patients were on triple therapy, while 11.11% used it in more than half of their patients. Based on the last 10 patients treated, 44.44% of HCPs reported no need for glimepiride dose adjustment, while 41.98% required adjustment in up to five patients (Table 2).

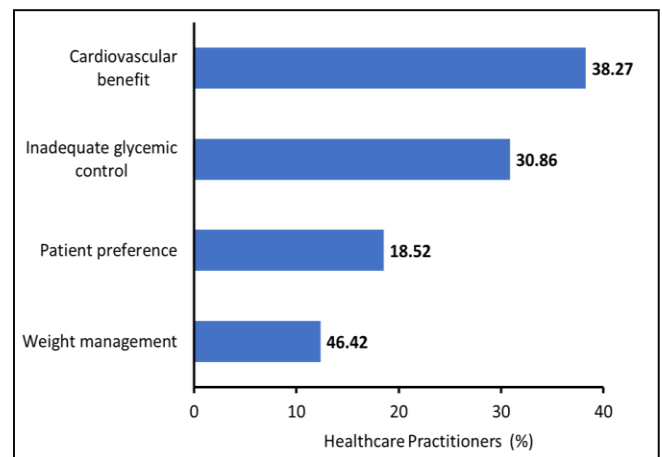


Fig 1: Primary reason for initiating triple therapy in T2DM Patients

Table 2: Healthcare practitioners' prescribing patterns and treatment optimization strategies

| Question                                                                          | Options                | Response of HCPs (N=81) |
|-----------------------------------------------------------------------------------|------------------------|-------------------------|
| What is your preferred initial dosing strategy for glimepiride in triple therapy? | Low dose (1-2 mg)      | 47 (58.02)              |
|                                                                                   | Moderate dose (3-4 mg) | 26 (32.10)              |
|                                                                                   | High dose (5-6 mg)     | 8 (9.88)                |
| Which age group do you most commonly prescribe triple therapy to?                 | 30-45 years            | 38 (46.91)              |
|                                                                                   | 46-60 years            | 29 (35.80)              |
|                                                                                   | >60 years              | 14 (17.28)              |
| How soon do you typically reassess patients after starting triple therapy?        | 2 weeks                | 19 (23.46)              |
|                                                                                   | 1 month                | 33 (40.74)              |
|                                                                                   | 3 months               | 13 (16.05)              |
|                                                                                   | 6 months               | 16 (19.75)              |
| How often do you monitor renal function after initiating dapagliflozin?           | Every 3 months         | 26 (32.10)              |

|                                                                                                      |                                   |            |
|------------------------------------------------------------------------------------------------------|-----------------------------------|------------|
|                                                                                                      | Every 6 months                    | 30 (37.04) |
|                                                                                                      | Annually                          | 12 (14.81) |
|                                                                                                      | Only if clinically indicated      | 13 (16.05) |
| Which component of the triple therapy do you most commonly adjust during follow-up?                  | Glimepiride                       | 45 (55.56) |
|                                                                                                      | Metformin                         | 23 (28.40) |
|                                                                                                      | Dapagliflozin                     | 13 (16.05) |
|                                                                                                      |                                   |            |
| When would you prefer an alternative SGLT2 inhibitor over dapagliflozin?                             | If cost is an issue               | 38 (46.91) |
|                                                                                                      | If eGFR is low                    | 19 (23.46) |
|                                                                                                      | If patient experiences infections | 15 (18.52) |
|                                                                                                      | Rarely need to switch             | 9 (11.11)  |
| Do you consider cardiovascular comorbidities when choosing dapagliflozin?                            | Always                            | 25 (30.86) |
|                                                                                                      | Sometimes                         | 33 (40.74) |
|                                                                                                      | Rarely                            | 10 (12.35) |
|                                                                                                      | Never                             | 13 (16.05) |
| Do you routinely counsel patients about hydration when prescribing dapagliflozin?                    | Yes                               | 47 (58.02) |
|                                                                                                      | Sometimes                         | 20 (24.69) |
|                                                                                                      | No                                | 14 (17.28) |
| Which factor most influences your decision to continue triple therapy long-term?                     | HbA1c control                     | 44 (54.32) |
|                                                                                                      | Side effect profile               | 16 (19.75) |
|                                                                                                      | Cardiovascular benefits           | 14 (17.28) |
|                                                                                                      | Patient preference                | 7 (8.64)   |
| What percentage of your Type 2 Diabetes patients are currently managed with triple therapy?          | <10%                              | 27 (33.33) |
|                                                                                                      | 10-30%                            | 26 (32.10) |
|                                                                                                      | 30-50%                            | 19 (23.46) |
|                                                                                                      | >50%                              | 9 (11.11)  |
| Based on your last 10 patients, how many needed a glimepiride dose adjustment during triple therapy? | 0 patients                        | 36 (44.44) |
|                                                                                                      | 1-2 patients                      | 17 (20.99) |
|                                                                                                      | 3-5 patients                      | 17 (20.99) |
|                                                                                                      | >5 patients                       | 11 (13.58) |
| Data represented as n (%).<br>HCP, healthcare practitioners.                                         |                                   |            |

### Safety profile, barriers, and patient acceptance of triple therapy

The HCPs identified non-adherence (44.44%) as the most common barrier to achieving optimal glycaemic control despite triple therapy, followed by side effects (30.86%). The CV benefit most commonly associated with dapagliflozin was reduced heart failure (HF) hospitalization (45.68%), followed by reduced stroke risk (35.80%). Genital infections were reported rarely (<5%) by 44.44% of HCPs and occasionally (5-10%) by 34.57%. Most HCPs always educated patients about recognising hypoglycaemia (56.79%), while 20.99% did so sometimes. Patient acceptance of triple therapy was reported as moderate by 50.62% and high by 27.16% of HCPs (Figure 2). Regarding overall tolerability, 45.68% of HCPs reported side effects in

only 1-20% of patients, and 28.40% observed no side effects in their last 10 patients.

Hypoglycaemia was the most common reason for discontinuation (51.85%), followed by genital infections (24.69%). The most frequently reported adverse event was hypoglycaemia (35.80%), followed by genital infections (29.63%) and gastrointestinal upset (20.99%). Medication non-adherence was encountered rarely by 48.15% of HCPs, while 22.22% reported frequent non-adherence. Hypoglycaemia incidence in the last 10 patients was absent in 44.44%, while mild events were reported in up to two patients by 24.69% and severe episodes by 11.11%. Overall, 70.37% of HCPs were satisfied or very satisfied with the clinical outcomes of triple therapy in their practice (Table 3).

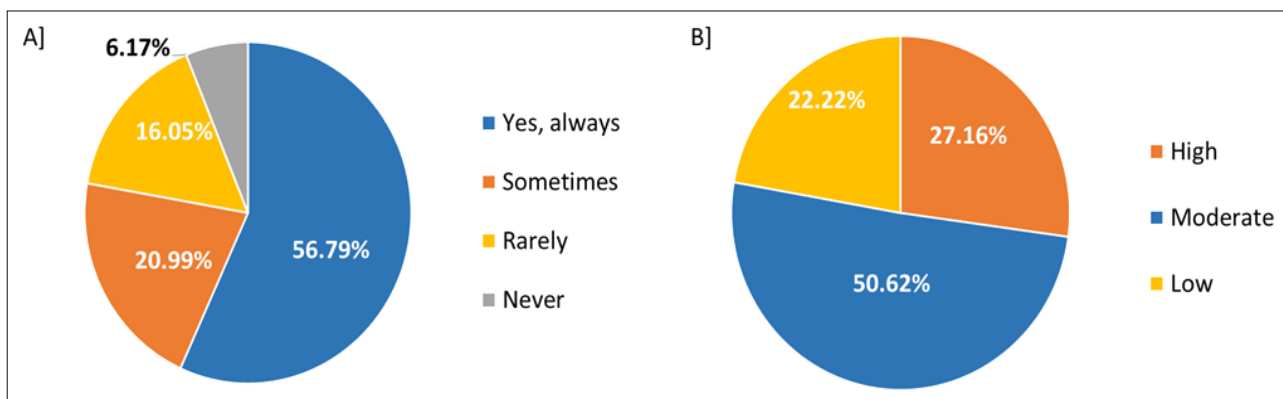


**Fig 2:** Healthcare practitioners' reported patient education and acceptance of triple therapy in T2DM patients  
A) Hypoglycaemia education before therapy B) Patient acceptance of triple therapy

**Table 3:** Safety profile, barriers, and patient acceptance of triple therapy

| Question                                                                                       | Options                               | Response of HCPs (N=81) |
|------------------------------------------------------------------------------------------------|---------------------------------------|-------------------------|
| What is the most common barrier to achieving optimal glycaemic control despite triple therapy? | Non-adherence                         | 36 (44.44)              |
|                                                                                                | Side effects                          | 25 (30.86)              |
|                                                                                                | Inadequate dosing                     | 8 (9.88)                |
|                                                                                                | Progression of disease                | 12 (14.81)              |
| Which cardiovascular benefit do you most associate with dapagliflozin use?                     | Reduced heart failure hospitalization | 37 (45.68)              |
|                                                                                                | Reduced stroke risk                   | 29 (35.80)              |
|                                                                                                | Blood pressure reduction              | 10 (12.35)              |
|                                                                                                | No cardiovascular benefit observed    | 5 (6.17)                |
| How frequently do you observe genital infections with dapagliflozin?                           | Rarely (<5%)                          | 36 (44.44)              |
|                                                                                                | Occasionally (5-10%)                  | 28 (34.57)              |
|                                                                                                | Frequently (>10%)                     | 7 (8.64)                |
|                                                                                                | Very frequently (>20%)                | 10 (12.35)              |
| In your last 10 patients, what percentage reported any side effects related to this therapy?   | None                                  | 23 (28.40)              |
|                                                                                                | 1-20%                                 | 37 (45.68)              |
|                                                                                                | 21-50%                                | 17 (20.99)              |
|                                                                                                | >50%                                  | 4 (4.94)                |
| In your experience, which side effect leads most often to discontinuation of triple therapy?   | Hypoglycemia                          | 42 (51.85)              |
|                                                                                                | Genital infections                    | 20 (24.69)              |
|                                                                                                | Weight gain                           | 14 (17.28)              |
|                                                                                                | GI upset                              | 5 (6.17)                |
| Based on the last 10 patients, what was the most commonly reported adverse event?              | Hypoglycaemia                         | 29 (35.80)              |
|                                                                                                | Genital infections                    | 24 (29.63)              |
|                                                                                                | Gastrointestinal upset                | 17 (20.99)              |
|                                                                                                | No adverse event                      | 11 (13.58)              |
| How often do you encounter medication non-adherence among patients on triple therapy?          | Rarely (<10%)                         | 39 (48.15)              |
|                                                                                                | Occasionally (10-30%)                 | 24 (29.63)              |
|                                                                                                | Frequently (>30%)                     | 18 (22.22)              |
| In the past 10 patients, what was the observed incidence of hypoglycaemia?                     | None                                  | 36 (44.44)              |
|                                                                                                | Mild in 1-2 patients                  | 20 (24.69)              |
|                                                                                                | Mild in >2 patients                   | 16 (19.75)              |
|                                                                                                | Severe in any patient                 | 9 (11.11)               |
| Overall, how satisfied are you with the clinical outcomes of triple therapy in your practice?  | Very satisfied                        | 28 (34.57)              |
|                                                                                                | Satisfied                             | 29 (35.80)              |
|                                                                                                | Neutral                               | 15 (18.52)              |
|                                                                                                | Dissatisfied                          | 9 (11.11)               |
| Data represented as n (%).<br>HCP, healthcare practitioners.                                   |                                       |                         |

## Discussion

The present study provides valuable insights into the real-world clinical use of triple therapy with glimepiride, metformin, and dapagliflozin in the Western region of India, focusing on glycaemic outcomes, cardio-renal and metabolic benefits, safety, prescribing patterns, and patient acceptance as reported by HCPs in routine clinical practice. Most HCPs reported an average HbA1c reduction of 0.5-1.5%, indicating meaningful glycaemic improvement in routine practice. Postprandial glucose improvement and achievement of HbA1c <7% within 3 months were observed in a smaller proportion of patients, although some achieved target control in  $\geq 6$  patients. These real-world findings align with evidence from a Phase III Indian FDC trial of dapagliflozin, glimepiride, and metformin ER in patients with uncontrolled DM, demonstrated an HbA1c reduction of -1.64% to -1.98% at 16 weeks, with 52.6% of patients achieving HbA1c <7% and a fasting plasma glucose reduction of -43.4 mg/dL [9]. Similar benefits were reported in a randomized trial by Matthaei *et al.*, who reported FPG reduced to -25.7 mg/dL (1.43 mmol/L) from baseline at 52 weeks [12] and a cohort study by Joaquim *et al.*, showing a 0.86% HbA1c reduction at 12 months with 35% achieving  $\geq 0.5$ -1% drop and 25% achieving 1-1.5% [13]. In comparison with dual therapy, triple therapy was perceived to be more effective in reducing HbA1c. This observation is supported

by a study by Sahay *et al.*, which reported greater HbA1c reduction with triple therapy compared with dual therapy (-1.98% vs -1.64%;  $p=0.0047$ ), with a higher proportion of patients achieving HbA1c <7% (52.6% vs 36.7%), reinforcing its superior glycaemic efficacy [9]. Together, these findings support the effectiveness of triple therapy in improving glycaemic outcomes in both clinical trials and real-world practice.

Weight loss was reported in a proportion of patients, along with improvements in blood pressure after initiation of dapagliflozin, while maximum HbA1c reduction was most commonly observed at 6 months, followed by 3 months. These findings align with a Phase III Indian FDC trial (dapagliflozin 10 mg + glimepiride 1 mg + metformin ER 1000 mg), which demonstrated a mean weight loss of -2.1 kg at 16 weeks ( $p<0.0001$  vs dual therapy), with 68% of patients achieving >2 kg weight loss and a -4.2 mmHg reduction in systolic blood pressure [9]. Consistently, a meta-analysis of dapagliflozin with oral antidiabetic drugs reported >2 kg weight loss in a majority of trials, peak glycaemic effects at 3-6 months, and 3-6 mmHg reductions in blood pressure, supporting the metabolic and cardiometabolic benefits of triple therapy [14]. Cardiovascular benefits emerged as the most common reason for initiating triple therapy in patients with T2DM, followed by inadequate glycaemic control. A real-world

study evaluating dapagliflozin as an add-on to sulfonylurea and metformin similarly identified inadequate glycaemic control as the primary driver for escalation to triple therapy, followed by CV risk reduction [13]. Current guidance from the ADA further supports this dual rationale, emphasising that while inadequate control necessitates treatment intensification, SGLT2 inhibitors such as dapagliflozin are prioritised for their established CV benefits in patients with or without existing CV disease [8]. Overall, these findings reinforce the broader cardiometabolic advantages of this combination beyond glycaemic control.

Triple therapy was most commonly prescribed to patients aged 30-45 years, consistent with Indian observational study data showing the highest use in this age group due to earlier diagnosis and increasing uptake of SGLT2 inhibitors. Patients were most often reassessed after 1 month, while renal function monitoring after dapagliflozin initiation was typically performed every 3-6 month [15], aligning with recommendations from the ADA to reassess and modify therapy regularly to avoid therapeutic inertia [8]. During follow-up, the therapy component most frequently adjusted was glimepiride, followed by metformin. Alternative SGLT2 inhibitors were mainly preferred when cost was a concern, followed by low eGFR. Supporting this, Rashid *et al.* reported substantial price variation for dapagliflozin 10 mg tablets in India (INR 5.9-30), which often leads clinicians to consider more affordable alternatives such as generic empagliflozin or canagliflozin in resource-constrained settings [16].

In the present study, CV comorbidities were commonly considered when choosing dapagliflozin, and patients were routinely counselled about hydration. HbA1c control emerged as the most important factor influencing long-term continuation of triple therapy, followed by the side-effect profile, while real-world utilisation indicated that  $\leq 30\%$  of patients were on triple therapy. A cross-sectional study by Nizamudheen *et al.* in Andhra Pradesh reported non-adherence to antidiabetic therapy driven by forgetfulness, multiple medications, cost, and side effects, consistent with the present study, identifying non-adherence as the most common barrier to achieving optimal glycaemic control, followed by side effects [17]. The most frequently recognised CV benefit of dapagliflozin was reduced HF hospitalisation, supported by major CV outcome trials demonstrating reductions in CV death and HF admissions [18]. Genital infections were reported rarely or occasionally, consistent with findings by Unnikrishnan *et al.*, who reported low rates of urogenital infections and dehydration, supporting the favourable safety profile of this regimen [19].

In the current study, patients were commonly educated on recognising hypoglycaemia, and acceptance of triple therapy was moderate to high. Side effects occurred in only a small proportion of patients. Hypoglycaemia was the main reason for discontinuation, followed by genital infections, while the most reported adverse events were hypoglycaemia, genital infections, and gastrointestinal upset this aligns with previous conducted, a 52-week randomised control trial of dapagliflozin added to sulfonylurea and metformin reported adverse events in 15.6% of patients (genitourinary 8.3%, headache 4.1%), no signal for severe hypoglycaemia, and 84.4% of patients reporting no side effects [12]. Medication non-adherence was reported as infrequent across the study population. Overall, most HCP expressed satisfaction or high satisfaction with the clinical outcomes of triple therapy

in their practice. These findings highlight strong real-world confidence in the effectiveness and acceptability of triple therapy in routine clinical care.

A key strength of this study is its real-world, questionnaire-based design, capturing prescribing patterns, perceived glycaemic and cardiometabolic outcomes, safety, and adherence to metformin–glimepiride–dapagliflozin triple therapy in routine clinical practice across Western India. The inclusion of multiple practitioners managing diverse T2DM profiles enhances the applicability of the findings to everyday practice. However, the study is limited by its cross-sectional observational design, reliance on HCP-reported data, and lack of objective patient-level biochemical measurements and a comparator group, which may introduce reporting bias and limit causal interpretation. Larger prospective, controlled studies are needed to further substantiate these findings and assess long-term outcomes.

## Conclusion

This real-world study indicates that triple oral therapy with metformin, glimepiride, and dapagliflozin offers significant glycaemic improvement, cardiometabolic benefits, and good tolerability in routine practice. Cardiovascular benefit and poor glycaemic control were key reasons for initiation, while hypoglycaemia and genital infections led to discontinuation. High HCP satisfaction supports its role as an effective strategy for inadequately controlled T2DM in India, though larger long-term studies are needed to confirm these findings.

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