Real-world Insights into Glimepiride–Metformin Fixed-dose Combinations for Type 2 Diabetes and Hypertension: An Indian Survey

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is frequently complicated by hypertension, which significantly increases cardiovascular and renal risk. In India, where the burden of T2DM is high, real-world insights into integrated management strategies remain limited. Glimepiride–Metformin fixed-dose combinations (FDCs) are widely used for glycemic control, yet their role in patients with comorbid hypertension warrants further exploration.

Objective: This study aimed to evaluate clinician perspectives on the use of Glimepiride–Metformin FDCs in T2DM patients with hypertension, focusing on comorbidity patterns, antihypertensive initiation thresholds, adjunctive therapy preferences, titration practices, and perceived therapeutic benefits.

Methods: A cross-sectional survey of 21 healthcare professionals (HCPs) across India was conducted using a structured questionnaire. The responses were analyzed descriptively and contextualized against current guidelines and published evidence.

Results: Hypertension was the most frequently reported comorbidity in T2DM (58%), followed by neuropathy (25%) and coronary artery disease (CAD) (8%). Most HCPs estimated hypertension prevalence in 25%–50% of their patients with T2DM. Antihypertensive therapy was commonly initiated at >140/90 mmHg (33%), with 25% using the tougher >130/80 mmHg threshold. Low-dose diuretics and calcium channel blockers were frequently preferred as adjuncts to RAAS inhibitors. For Glimepiride–Metformin titration, 38% preferred a conservative "start low, go slow" approach, with lower-dose strengths (1–2 mg Glimepiride + 500 mg Metformin) being most prescribed. Clinicians reported benefits beyond glycemic control, including improved blood pressure (BP), lipid profile, weight, and cardiovascular outcomes.

Conclusion: Glimepiride–Metformin FDCs are widely utilized in Indian practice for T2DM with hypertension. Clinicians emphasized their efficacy, safety, cost-effectiveness, and cardiovascular benefits, highlighting their value as part of comprehensive cardiometabolic risk reduction strategies.

Keywords: Type 2 diabetes mellitus; Hypertension; Glimepiride–Metformin fixed-dose combination; Cardiovascular risk; India.

Introduction

Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by chronic hyperglycemia resulting from a combination of insulin resistance and progressive β-cell dysfunction.[1] Globally, T2DM represents a major public health burden, affecting more than 589 million people in 2025 and expected to increase to 853 million by 2050.[2] South Asia, particularly India, contributes disproportionately to this burden, with earlier onset,

higher prevalence of complications, and clustering of cardiovascular risk factors compared to Western populations.[3] India has the second-highest number of adults (20–79 years) with diabetes in the world, with 156 million people to be affected by 2050.[4]

Among the many comorbidities of T2DM, hypertension is the most prevalent and clinically significant. The overall prevalence of hypertension with diabetes in India was 35.5%, with significantly higher rates in urban compared to rural areas (40.7% vs. 33.0%). Men demonstrated a higher prevalence than women (38.7% vs. 32.6%). Notably, when more stringent American College of Cardiology (ACC)/American Heart Association (AHA) criteria were used, the prevalence of hypertension increased significantly to 66.3%, underscoring the substantial impact of diagnostic thresholds on estimated disease burden.[3] The coexistence of these two conditions substantially increases the risk of both microvascular and macrovascular complications, including nephropathy, retinopathy, stroke, and coronary artery disease (CAD).[5,6]

Hypertension not only accelerates vascular injury but also worsens the prognosis of established diabetes complications, making integrated management of glycemic and blood pressure (BP) targets essential.[5,6]

A. Importance of Hypertension Control in T2DM

The relationship between hypertension and diabetes is synergistic and bidirectional. Insulin resistance contributes to vascular dysfunction and activation of the renin-angiotensin-aldosterone system (RAAS), promoting elevated BP, whereas chronic hypertension exacerbates endothelial dysfunction and vasculopathy of diabetes.[6,7] Clinical trials such as the UK Prospective Diabetes Study (UKPDS 38) demonstrated that intensive BP control in T2DM reduced the risk of diabetes-related endpoints, including microvascular complications, by 37%.[8]

Recently, the ACCORD-BP trial confirmed that intensive BP lowering (<120 mmHg systolic) did not significantly reduce the rate of major cardiovascular events overall but did reduce the risk of stroke. This highlights the complexity of target setting in this population.[9]

Consensus guidelines now advocate for lower BP thresholds in patients with diabetes compared with the general population, typically recommending targets <130/80 mmHg when tolerated.[10,11]

In India, the 2024 guidelines of the Association of Physicians of India also emphasize <130/80 mmHg for high-risk individuals, while allowing <140/90 mmHg for patients unable to achieve stricter control.[5]

B. Antihypertensive Strategies in T2DM

RAAS inhibitors (angiotensin-converting enzyme [ACE] inhibitors and angiotensin II receptor blockers [ARBs]) are considered first-line antihypertensive therapy in T2DM due to their proven renoprotective and cardioprotective benefits.[12] However, RAAS blockers are associated with drug interactions with commonly used medications, including sulfonylurea.[13] Despite the availability of effective therapies, a substantial proportion of patients with T2DM fail to achieve optimal BP control. This treatment gap emphasizes the need for combination strategies, patient-tailored titration, and early intensification of therapy.

Sulfonylureas remain widely prescribed in India due to their effectiveness, cost-efficiency, and established use.[14] Glimepiride, a second-generation sulfonylurea, stimulates pancreatic insulin secretion and enhances peripheral insulin sensitivity, achieving significant reductions in glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), and postprandial glucose (PPG).[15] Compared with older sulfonylureas, such as Glibenclamide, Glimepiride carries a lower risk of hypoglycemia and has a safer cardiovascular profile, as it does not interfere with ischemic preconditioning.[16]

C. Glimepiride–Metformin Fixed-dose Combinations

Given the progressive nature of T2DM, combination therapy is often required early. The Glimepiride–Metformin fixed-dose combination (FDC) is among the most frequently prescribed in India and other resource-limited settings.[17] Real-world evidence shows that these FDCs are effective across all age groups and stages of diabetes, with Glimepiride 2 mg + Metformin 500 mg and Glimepiride 1 mg + Metformin 500 mg being the most commonly prescribed strengths.[17] The use of FDCs improve adherence, simplifies titration, and supports consistent achievement of glycemic targets.[14,18,19] In addition to glycemic control, clinicians frequently combine Glimepiride–Metformin with antihypertensive medications in patients with comorbid hypertension.[17] This dual approach has been observed to not only improve glycemic outcomes but also enhance BP control, reduce dyslipidemia, lower the risk of CAD, and mitigate weight gain in some patients.[20]

D. Rationale for the Present Study

Despite abundant trial evidence, real-world practice patterns in India remain underreported. The association of T2DM with hypertension and dyslipidemia, combined with cultural, dietary, and healthcare system factors, makes it essential to understand how clinicians initiate, combine, and titrate therapies in practice. Surveys of healthcare professionals (HCPs) provide valuable insights into prevailing patterns, areas of adherence to or divergence from guidelines, and perceived benefits of specific therapies.

The present study therefore aimed to evaluate clinician perspectives on the use of Glimepiride–Metformin FDCs in T2DM patients with hypertension, including comorbidity patterns, thresholds for antihypertensive initiation, adjunctive therapy preferences, titration schedules, and perceived benefits. By situating these findings within the context of evolving guidelines and real-world evidence, the study contributes to optimizing integrated management strategies for diabetes and hypertension in the Indian setting.

Methods

This cross-sectional survey collected responses from 24 HCPs across India regarding the management of T2DM with comorbid hypertension. A structured questionnaire was designed to collect information on comorbidity prevalence, BP thresholds for initiating antihypertensive therapy, preferred pharmacologic strategies, and titration practices for Glimepiride–Metformin FDCs. Both multiple-choice and open-ended questions were included to assess clinical decision-making patterns and perceived therapeutic benefits. The responses were analyzed descriptively and presented as proportions, supported by figures summarizing clinician perspectives. The findings were contextualized with reference to current guidelines and existing evidence from the literature to highlight consistencies and gaps in real-world practice.

Results and Discussion

In line with the study objectives, the following findings illustrate how HCPs approach integrated glycemic and BP management in clinical practice, with particular focus on the role of Glimepiride–Metformin FDCs.

A. Clinical Profile of T2DM Patients with Hypertension

Figure 1A illustrates the comorbidities most frequently observed in patients with T2DM. Hypertension was the most common comorbidity, reported by 58% of HCPs, followed by diabetic neuropathy (25%) and CAD (8%). These findings reflect the clustering of cardiometabolic risk factors in Indian patients with T2DM, which is consistent with epidemiological data showing that hypertension occurs in nearly half of diabetics and significantly increases cardiovascular and renal risk. Figure 1B presents HCP estimates of the prevalence of hypertension among their T2DM patients. The majority (71%) reported a prevalence of 25%–50%, followed by 21% who estimated 51%–75%, and 8% who estimated <25%. This aligns with Indian studies, where hypertension prevalence among T2DM patients ranges from 41% to 58%, with urban populations showing even higher

clustering due to sedentary lifestyles and obesity.[5] Figure 1C highlights the most common stage of hypertension observed in patients with T2DM.

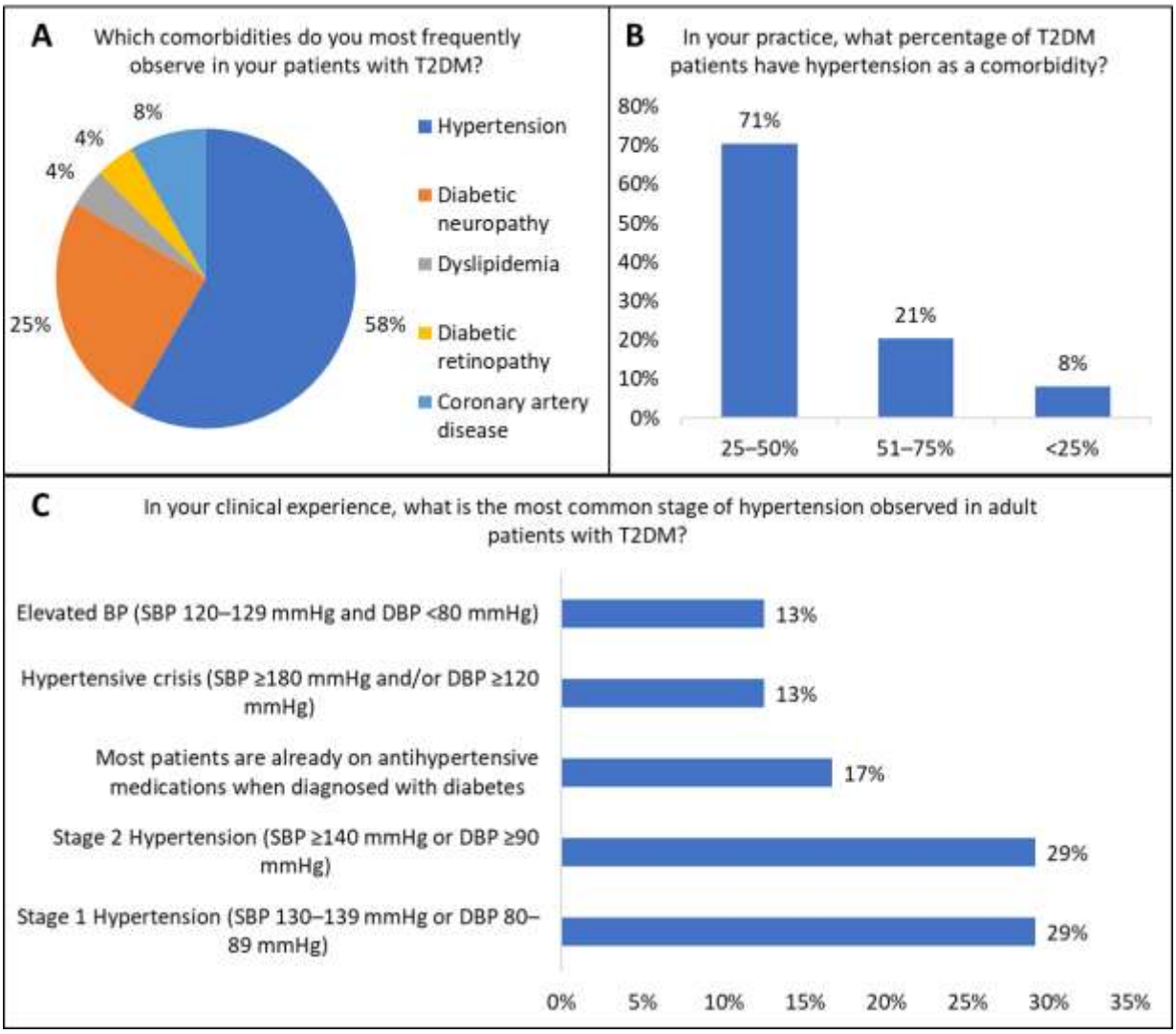

Figure 1: Responses of HCPs regarding the clinical profile of T2DM patients with hypertension

Some HCPs (17%) reported that most of their patients were already on antihypertensive therapy at the time of diabetes diagnosis, indicating delayed detection of hypertension.[21,22] Among those untreated, 29% most frequently encountered Stage 1 hypertension, followed by 29% reporting Stage 2 hypertension, 13% reporting elevated BP, and 13% experiencing hypertensive crisis (SBP ≥180 mmHg and/or DBP ≥120 mmHg). These results support guideline observations that hypertension in T2DM often presents earlier, progresses rapidly, and is strongly influenced by insulin resistance and vascular dysfunction.[6,7] Hypertension is not only the most prevalent comorbidity in T2DM, but is also often presents at a more advanced stage, reinforcing the need for early detection and integrated cardiometabolic management strategies in Indian patients.[5]

B. Clinical Decision-Making in Hypertension Management among Patients with T2DM

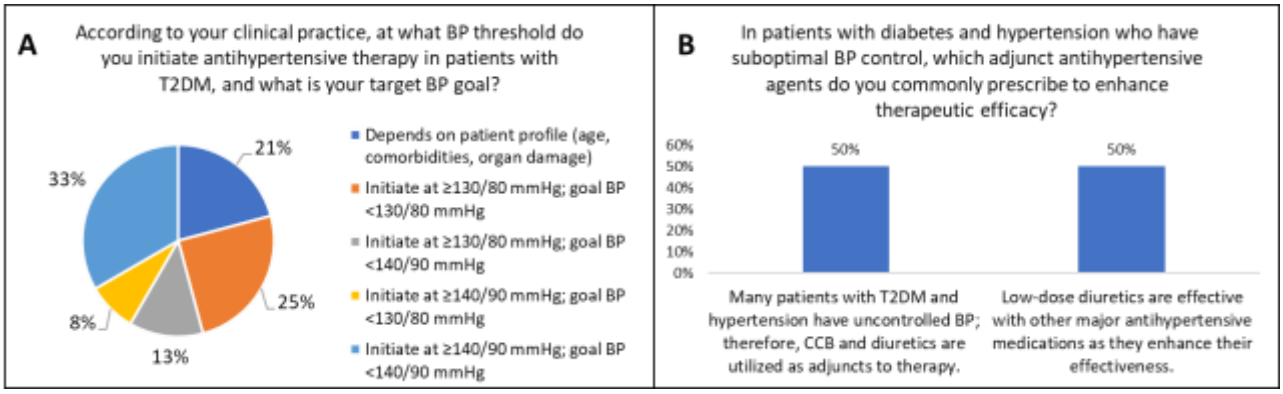

Figure 2: Responses of HCPs on initiation and management strategies for hypertension in patients with T2DM

Figure 2A demonstrates the preferred BP thresholds at which HCPs initiate antihypertensive therapy in patients with T2DM. The majority (33%) indicated initiating therapy at >140/90 mmHg, reflecting persisting reliance on older thresholds.[23] A smaller proportion (25%) reported a threshold of >130/80 mmHg, which is consistent with guideline recommendations advocating stricter BP targets in diabetics compared with the general population.[11,24] This variation highlights the evolving shift in practice patterns as more evidence supports intensive BP control to mitigate cardiovascular risk.

Some of the HCPs (21%) also opined that initiating hypertensive therapy depends on patient profile such as age, comorbidities, organ damage.[25] The 2024 Indian guidelines recommend <130/80 mmHg for high-risk individuals, including those with diabetes, while <140/90 mmHg remains acceptable if stricter control is not tolerated. This reflects a pragmatic approach where individualized therapy balances evidence-based targets with patient safety and adherence.[5]

Figure 2B highlights the preference of HCPs for adjunct antihypertensive agents in patients with diabetes and hypertension who have suboptimal BP control. Around 50% of HCPs believed that low-dose diuretics are effective with other major antihypertensive medications as they enhance their effectiveness. Many patients with T2DM and hypertension have uncontrolled BP; therefore, calcium channel blockers (CCBs) and diuretics are being used as adjuncts to therapy (50% of HCPs). In hypertensive patients with T2DM, RAAS blockers and dihydropyridine CCBs are recommended as first-line agents in the absence of contraindications. Diuretics also play an important role, either as first-line or add-on therapy, particularly for heart failure prevention, though close monitoring of electrolytes and glycemic levels is required at therapy initiation.[26]

In a question exploring the clinical factors influencing the initiation of antihypertensive therapy in patients with diabetes, survey results showed that:

- All patients with stage 2 hypertension should start medications (33%), aligning with guidelines that universally recommend drug initiation in stage 2 hypertension regardless of 10-year atherosclerotic cardiovascular disease (ASCVD) risk.
- Patients with stage 1 hypertension and ASCVD risk <10% were recommended lifestyle modifications (25%).
- Patients with T2DM and BP >130/80 mmHg were recommended to start antihypertensive medications (13%).
- Medication initiation in stage 1 hypertension with ASCVD ≥10% was supported by 13%.
- Monotherapy initiation with escalation to combination therapy if required was chosen by 17%.

These findings are consistent with international and Indian guidelines, where therapy initiation depends on hypertension stage, ASCVD risk stratification, and coexistence of T2DM.[5,11] Notably, clinicians' emphasis on early initiation in stage 2 hypertension and in patients with T2DM reflects an understanding that dual disease provides synergistic cardiovascular risk, justifying more aggressive treatment strategies.

Thus, clinicians emphasize that they are increasingly adopting lower BP thresholds and individualized risk-based approaches in managing diabetic hypertension. This aligns with contemporary evidence showing that tighter BP control in diabetics reduces cardiovascular morbidity and mortality, though lifestyle interventions remain integral, especially in lower-risk patients.

In patients with T2DM, initiation of therapy to reduce cardiovascular risk requires a comprehensive approach addressing both BP and glycemic control. At the outset, hypertension should be confirmed, and the 10-year cardiovascular risk assessed to guide treatment intensity. Pharmacological therapy, typically based on RAAS blockers with the addition of CCBs or diuretics as needed, should be initiated alongside lifestyle interventions to achieve BP targets of 120–129/70–79 mmHg, while lower optimal targets (≤120/70 mmHg) remain under investigation. Early therapy selection should also consider antidiabetic agents with proven cardiovascular and renal benefits, ensuring a tailored strategy that addresses both BP control and long-term outcomes.[26]

C. *Advantages of Combining Glimepiride–Metformin with Antihypertensive Therapy*

Metformin remains the cornerstone first-line therapy for T2DM due to its efficacy, safety, affordability, and cardiovascular benefits, and is frequently used in fixed-dose combinations.[1,17] Glimepiride, a second-generation sulfonylurea, enhances insulin secretion and improves peripheral insulin sensitivity, thereby lowering HbA1c, FPG, and PPG.[15] Compared with older sulfonylureas, glimepiride carries a relatively lower risk of hypoglycemia, has a safer cardiovascular profile, and offers a cost-effective option for use either alone or in combination with metformin and other agents, making it a valuable component of T2DM management, particularly in resource-limited settings.[20]

A real-world, multicentric study of 4,858 T2DM patients demonstrated that Glimepiride–Metformin FDCs are widely prescribed across all age groups in India, both in early and long-standing diabetes. Among 11 available strengths, Glimepiride 2 mg with Metformin 500 mg (26.7%) and Glimepiride 1 mg with Metformin 500 mg (24.6%) were the most common prescriptions, with twice-daily dosing being preferred. The combinations were frequently used in patients with comorbid hypertension and dyslipidemia, as well as those with diabetes complications, underscoring the central role of Glimepiride in the management of T2DM in real-world clinical practice.[17]

In response to an open-ended question in the survey, the HCPs favored combining Glimepiride–Metformin with antihypertensives. Combining it with antihypertensive medications has been observed to provide consistent glycemic control (FPG, PPG, and HbA1c), along with better blood pressure management, improvements in dyslipidemia, reduced risk of CAD, weight loss in some patients, and overall cardiovascular benefits, contributing to improved patient well-being. Around 75% of HCPs were 'very satisfied' with Glimepiride-Metformin therapy in patients with coexisting diabetes and hypertension and 25% were 'satisfied'.

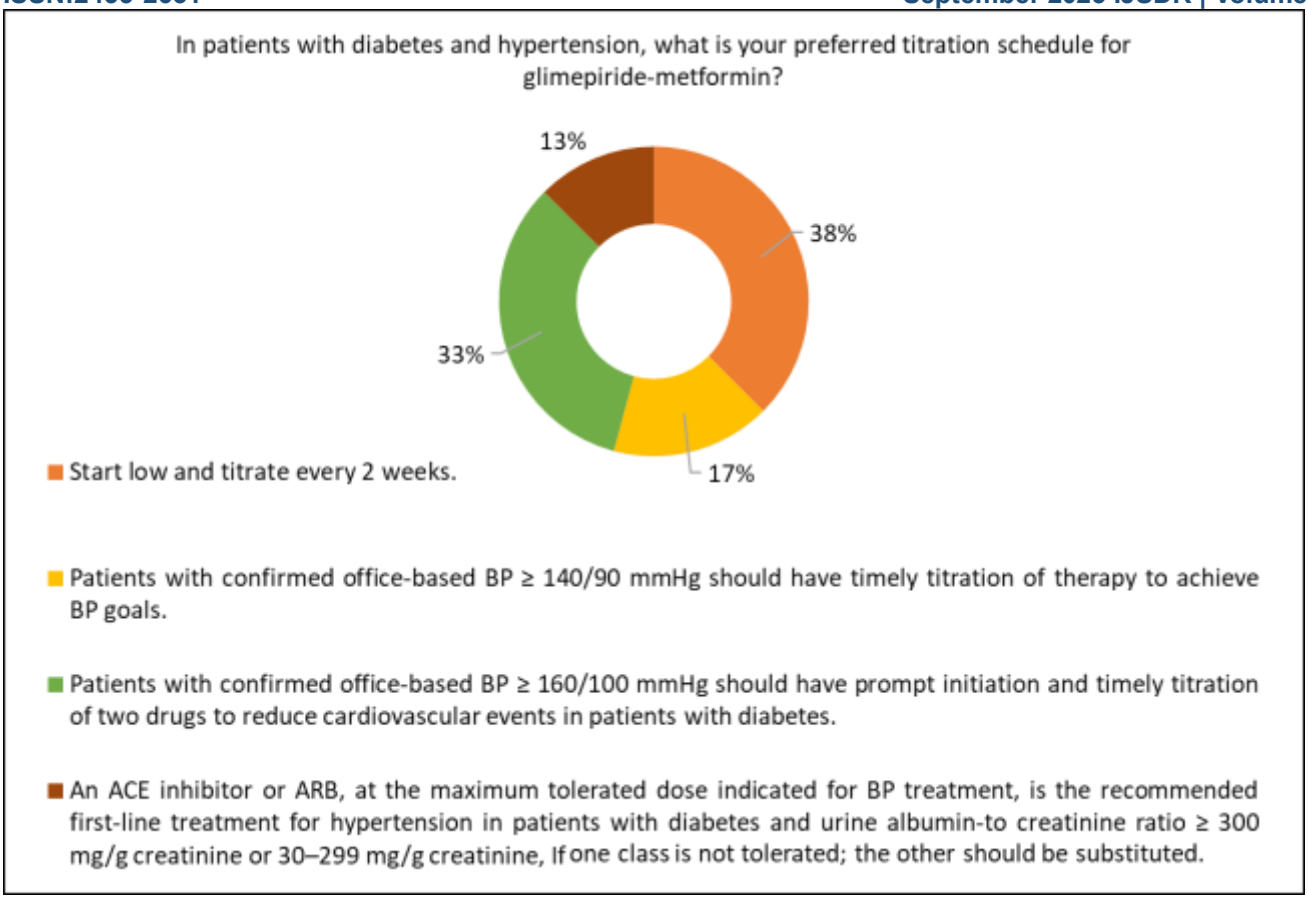

Figure 3: Clinician preferences for titration schedules of Glimepiride–Metformin in patients with type 2 diabetes and hypertension.

When asked about their preferences in the titration schedule for Glimepiride-Metformin in patients with diabetes and hypertension, the largest proportion (38%) favored a conservative approach of starting low and titrating every two weeks, reflecting caution to balance glycemic efficacy with hypoglycemia risk (Figure 3). About one-third (33%) preferred titration in patients with confirmed office-based BP ≥160/100 mmHg, suggesting more aggressive adjustment to reduce cardiovascular risk. Smaller proportions recommended titration based on BP ≥140/90 mmHg (17%) or aligned with ACE inhibitor/ARB initiation guidelines (13%).

These findings align with guidelines emphasizing individualized titration strategies in T2DM with comorbid hypertension, where cardiovascular and renal risks are amplified.[11] Evidence demonstrates that low-dose combination therapy with glimepiride and metformin provides synergistic benefits: metformin enhances insulin sensitivity, while glimepiride stimulates insulin secretion, supporting durable glycemic control.[20,27]

Traditional recommendations advocate stepwise addition of agents to Metformin to maintain target A1c, allowing clearer assessment of benefits and adverse effects of each drug while minimizing side effects and cost.[28] Importantly, in patients with hypertension, optimal glycemic management may indirectly improve BP outcomes, while antihypertensive therapy provides additional cardiovascular protection.[6] Overall, the figure illustrates that most physicians prefer a stepwise titration approach for Glimepiride–Metformin, consistent with evidence-based guidelines balancing efficacy, safety, and long-term cardiovascular outcomes.

The survey findings also highlighted the perceived benefits and prescribing patterns of Glimepiride–Metformin FDCs in patients with T2DM and hypertension. As shown in Figure 4A, the majority of clinicians (47%) reported controlled blood glucose as the most significant advantage of combination therapy over monotherapy, whereas 33% observed a delay in diabetes progression and related complications, and 20% noted improvements in body

weight and BP control. In terms of dosing preferences (Figure 4B), the most commonly prescribed strength was Glimepiride 2 mg + Metformin 500 mg (50%), followed by Glimepiride 1 mg + Metformin 500 mg (29%), and Glimepiride 2 mg + Metformin 1000 mg (21%). These trends were further reflected in overall practice patterns (Figure 4C), where Glimepiride 2 mg + Metformin 500 mg accounted for 54% of prescriptions, Glimepiride 1 mg + Metformin 500 mg for 33%, and Glimepiride 2 mg + Metformin 1000 mg for 13%.

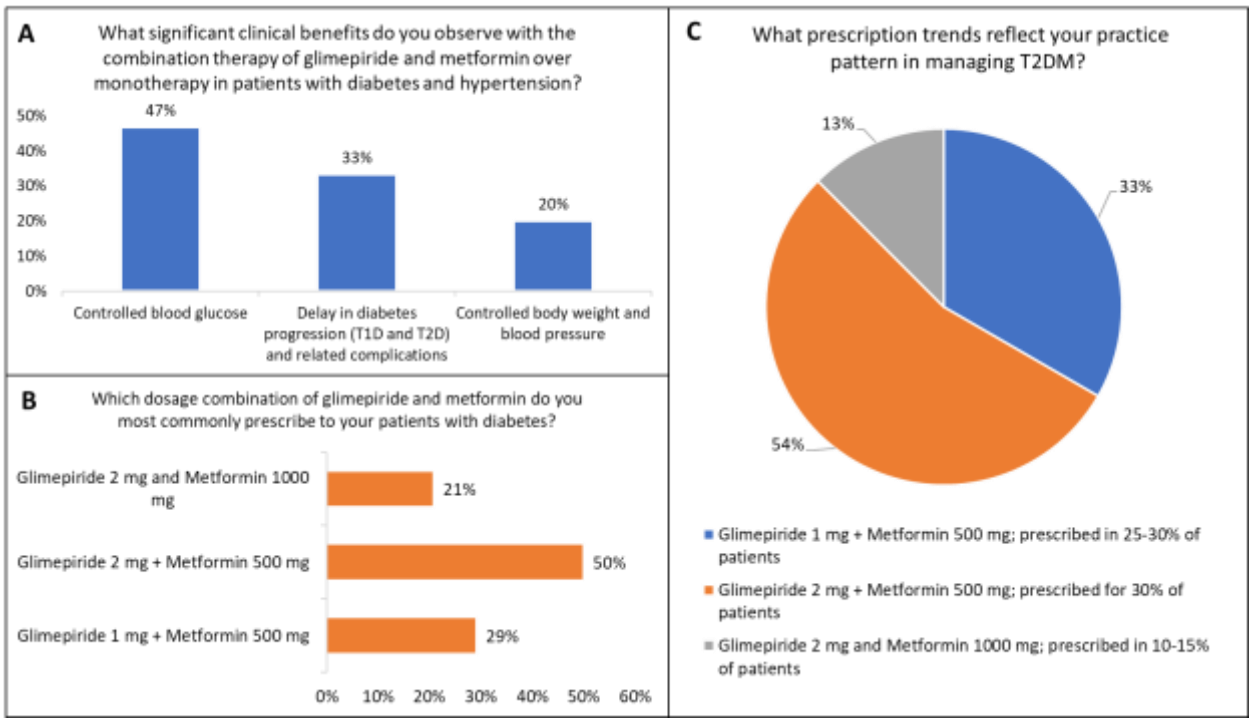

Figure 4: Reported benefits, dosage preferences, and prescription trends of Glimepiride–Metformin FDCs in T2DM.

These real-world observations align closely with broader evidence. A multicenter Indian study highlighted that early initiation of Glimepiride–Metformin FDCs fosters a legacy effect, maintaining long-term glycemic control and potentially mitigating the development of complications linked to "glycemic memory". This is highly relevant given the prevalence of micro- and macrovascular comorbidities in T2DM patients.[17]

Meta-analyses of randomized controlled trials confirm that adding a sulfonylurea to Metformin yields meaningful reductions in HbA1c (typically around 0.9%) as well as improvements in FPG, although gains beyond 1% are uncommon.[29] These benefits, however, come with a modest increase in hypoglycemic events and some weight gain, underscoring the need for careful patient selection and dose titration.[29,30]

Importantly, Glimepiride appears to be safer from a cardiovascular standpoint compared to older sulfonylureas. A large UK cohort study found that Glimepiride was not associated with increased risk of myocardial infarction or stroke, and was actually linked with lower all-cause mortality relative to other second-generation sulfonylureas.[31] Moreover, the CAROLINA cardiovascular outcomes trial showed no significant difference in major adverse cardiovascular events (MACE) between Glimepiride and Linagliptin (a dipeptidyl peptidase-4 [DPP-4] inhibitor), although Glimepiride was associated with higher rates of hypoglycemia and modest weight gain.[32]

Mechanistically, Glimepiride may pose fewer cardiovascular risks than first-generation sulfonylureas because it does *not* interfere with myocardial ischemic preconditioning, a protective heart mechanism, unlike some older sulfonylureas.[33] This distinction may partly explain its comparatively safer profile.

On the broader scale of sulfonylureas, systematic reviews suggest that as a class, they may carry a slightly elevated risk of all-cause mortality and MACE when compared to non-hypoglycemia-inducing agents. However, subgroup analyses reveal that Glimepiride, specifically, often fares better, with no significant increase in mortality risk.[34]

Lastly, avoiding severe hypoglycemia remains critical: pooled analyses link it to significantly higher risks of all-cause mortality, cardiovascular mortality, MACE, stroke, and arrhythmic death.[33] This underscores the importance of patient education, appropriate dosing, and vigilant monitoring when prescribing agents such as Glimepiride, especially in vulnerable populations.

Conclusion

This real-world survey demonstrates that Glimepiride–Metformin FDCs are extensively used in the management of T2DM patients with hypertension and other comorbidities in India. The combination was consistently associated with improved glycemic control, better HbA1c outcomes, and effective maintenance of FPG and PPG levels. Clinicians also highlighted benefits extending beyond glycemia, including smoother BP control, favorable effects on weight, and reduction in dyslipidemia and cardiovascular risk. Among available strengths, lower doses such as Glimepiride 1–2 mg with Metformin 500 mg were most frequently prescribed, often in twice-daily regimens, suggesting a "start low, go slow" approach. The therapy was regarded as suitable across diverse patient groups, from early-stage to long-standing diabetes, reflecting its flexibility in clinical practice. Physicians emphasized cautious titration to balance efficacy with safety, particularly to minimize hypoglycemia risk. The findings also reinforce the role of combining antidiabetic therapy with antihypertensives to achieve comprehensive cardiometabolic risk reduction. Urban-rural prescribing trends indicated wide acceptance of this regimen across settings, supporting its relevance in varied healthcare contexts. Overall, the survey underscores the practicality, cost-effectiveness, and cardiovascular safety of Glimepiride–Metformin FDCs in Indian clinical practice. These insights support guideline-directed use of early combination therapy while highlighting the value of real-world evidence in informing diabetes management strategies.

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