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ORIGINAL RESEARCH

Understanding Indian Clinicians' Perspectives on Glipizide & Metformin Combination in the Management of Resource-Challenged Type 2 Diabetes Mellitus(T2DM) Patients in India- A DESERVE India Consensus: Part 2

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) affects diverse demographic populations, including resource-challenged (deserving) and rural communities.In India, managing T2DM often involves substantial out-of-pocket expenses, leading to significant health-related financial burdens. Therefore, Indian clinicians should consider affordable, cost-effective, and accessible oral antidiabetic agents (OADs) to optimize T2DM care. **Aim:** DESERVE INDIA CONSENSUS (Diligent Endeavor to Support Deserving T2DM Patients with Individualized Treatment Interventions for Resource-Challenged Settings in India) aimsto address the need for awareness and access to high-quality, affordable, cost-effective interventional approaches for effectively managing resource-challenged (deserving) T2DM patients in India. **Methods:** This mixed-methods study in India involved a quantitative survey of 590 clinicians and qualitative focus group discussions (FGDs) with 60 subject matter experts. The study was conducted between January and March 2024.A structured questionnaire was developed for quantitative data collection regarding clinician management approaches for patients with resource-challenged (deserving) T2DM.Four-day virtual FGDs with subject matter experts for consensus development were organized for qualitative data collection. **Results:** The 590 clinicians surveyed agreed with several critical statements regarding the efficacy, safety, and cost-effectiveness of the fixed-dose combination (FDC) of glipizide + metformin in managing resource-challenged (deserving) T2DM patients.Most clinicians (84.0%) agreed that glipizide + metformin FDC is a clinically preferred SU-based combination, as it has a lower risk of hypoglycemia due to its short half-life.A similar proportion of clinicians agreed that this combination is safe in patients with moderate-to-severe chronic kidney disease and can be used effectively in managing resource-challenged (deserving) T2DM patients.Nearly 65.08% of the clinicians agreed thatglipizide + metformin FDCcould be a first-line consideration in resource-challenged (deserving) T2DM patients.Approximately 90.0% of clinicians agreed that glipizide and metformin FDC, with a monthly cost of < 120 INR, are cost-effective interventions for resource-challenged (deserving) T2DM patients in India.Most (94.0%) cliniciansacknowledged their role in improving the outcomes of resource-challenged (deserving) T2DM patients by improving the awareness, access, availability, and affordability of high-quality medications. **Conclusion:** Indian clinicians favoured prescribing cost-effective OADs, such as glipizide + metformin FDC, as a first-line consideration to improve patient adherence and treatment outcomes in resource-challenged (deserving) T2DM patients.

Keywords: Type 2 Diabetes Mellitus, Glipizide, Sulphonylureas, Secretagogues, Cost-effective, Metformin

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder that has quadrupled worldwide in recent decades [1]. The International Diabetes Federation (IDF) reported a T2DM prevalence of 9.3% in 2019, affecting 463 million people, with projections of a rise to 10.9% (700 million individuals) by 2045 [2]. India is identified as the diabetes capital of the Indian Heart Association, with an expected 109 million T2DM patients by 2035 [2,3].The rapid increase in T2DM cases among India's urban poor, middle-class, and rural populations presents significant management challenges for patients and healthcare providers. Metformin is widely supported as the initial treatment for T2DM [4]. However, there is debate regarding the choice of adjunctive therapy when treatment targets are unmet [5].A comprehensive meta-analysis of nine classes of oral antidiabetic agents (OADs) endorses the recommendation of the American Diabetes Association (ADA), to start with metformin monotherapy, adding adjunctive therapies based on individual patient needs [6].

Although various OADs can effectively manage glycemic control, reducing hypo- and hyperglycemic complications remains a significant challenge in T2DM treatment. Furthermore, medication costs significantly impact disease management in resource-limited countries such as India, affecting drug use and patient adherence. Diabetes exemplifies global inequity, with T2DM patients in high-income countries accessing advanced care more readily. In contrast, low- and middle-income countries (LMICs) such as India encounter substantial barriers and rising costs for OADs [5]. A recent cost variation analysis of OADs in India revealed that SUs exhibited the highest price variation, with Glimepiride at 3450%, followed by metformin (900%), voglibose (571.2%), pioglitazone (300%), and teneligliptin (136.4%).Glibenclamide 5 mg showed the lowest variation (35.4 %).Specifically, Glimepiride 1 mg had the highest variation at 345%, while Glipizide 5 mg had the lowest at 47.6%, with cost ratios ranging from 1.5 (Glipizide 5 mg) to 35.5 (Glimepiride 1 mg) [7].A recent systematic review of the economic evaluation of diabetes treatment in India showed that the mean annual expenditure on diabetes and related complications was INR 15,535 (SD 1.3), with a pooled mean INR 17,080 per year (SD 1.1) [8].A comprehensive pan-India study found a significant difference ($P < 0.05$) in the average monthly expenses between individuals with self-reported diabetes (INR 1,357.65) and those without known diabetes (INR 999.91). Significant cost differences were also noted

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between rural (INR 2,893) and urban (INR 4,162) participants and individuals aged < 40 years (INR 1,996) and > 40 years (INR 5,059) [9]. These data highlight the significantly higher cost of illness (COI) associated with diabetes, emphasizing the need to promote cost-effective medications for resource-limited populations.

IDF 2017, ADA 2020, Research Society for the Study of Diabetes in India (RSSDI) 2020, and the World Health Organization (WHO) 2018 recommend fixed-dose combination (FDC) therapy with two or more drugs for T2DM management.These guidelines suggest adding sulfonylureas (SUs) to patients who do not achieve glycemic control with metformin alone [10-13].SUs are commonly prescribed OADs in LMICs, such as in Asia and Africa, either alone or with metformin, and they stimulate insulin release from β-cells, which helps reduce hyperglycemia and glycated hemoglobin (HbA1c) levels in T2DM patients.SUs are listed as essential OADs in the National List of Essential Medicines (NLEM) of several African countries, the Middle East, and Southeast Asian regions [1]. The ADA, European Association for the Study of Diabetes (EASD), and WHO recommend SUs as second-line agents after metformin, especially when cost is a concern [14,15].First-generation sulfonylureas (SUs), such as chlorpropamide, tolazamide, tolbutamide, and acetohexamide, cause side effects such as headache, dizziness, paresthesia, abdominal discomfort, and nausea.Therefore, they have mainly been replaced by more potent second-generation agents such as glyburide (glibenclamide), glipizide, glimepiride, and gliclazide, which are often administered at lower once-daily doses [16,17].

Modern second-generation SUs are favored for optimal glycemic control because of their enhanced efficacy, cost-effectiveness, reduced risk of hypoglycemia, minimal weight gain, cardiovascular safety, and additional benefits [18].The Core Curriculum in Nephrology addresses glycemic control targets, diabetes medication use, and management strategies for type 1 and type 2 diabetes patients with chronic kidney disease (CKD), noting that glipizide, which lacks kidney-cleared active metabolites, does not require dose adjustments and is preferred for CKD patients with T2DM.However, caution is advised while prescribing [19]. According to RSSDI guidelines, shorter-acting SU-like glipizide, metabolized in the liver, is recommended for those with moderate to severe renal impairment [12].The DGenius Group Diabetes India expert consensus advises using second-generation short-acting SUs (glipizide and gliclazide) at lower doses to manage hypoglycemia in T2DM patients [20]. A review in India found that glipizide and metformin FDC cost INR 2 per tablet, with an annual cost of INR 1,460 for twice-daily use, which is significantly cheaper than other T2DM medications [21].Thus, affordable treatment is crucial for enhancing adherence among resource-constrained T2DM patients, and glipizide + metformin FDC can be a viable therapeutic option.

Although glipizide and metformin FDC are effective in T2DM management, the prescription often depends on the clinician's decision.Limited evidence exists on Indian clinicians' prescription patterns and rationale for using glipizide + metformin FDC, especially in resource-challenged T2DM patients.Thus, this study aimed to build a consensus on the clinical use of glipizide + metformin FDC for T2DM management in resource-challenged T2DM patients, termed DESERVE INDIA CONSENSUS (Diligent Endeavor to Support Deserving T2DM Patients with Individualized Treatment Interventions for Resource-Challenged Settings in India).

MATERIALS AND METHODS

This nationwide study,whichincluded Indian clinicians, followed a mixed-method approach.The mixed-methods study design included a quantitative surveyand qualitative focus group discussions (FGDs) conducted during the first quarter (January to March) of 2024.Clinicians included endocrinologists, diabetologists, and medicine physicians experienced in managing resource-challenged (deserving) T2DM patients in routine clinical practice.All 590 clinicians participated in the quantitative survey, and 60 subject matter experts who participated in the qualitative FGDs provided informed consent. Measures were taken to ensure the confidentiality and anonymity of the collected data.Convenience sampling was used to recruit the clinicians. To enhance the generalizability of the findings, efforts were made to ensure their representation from diverse geographical regions and healthcare settings.

Quantitative phase

Data Collection: We developed a structured questionnaire for quantitative data collection. The questionnaire was designed to comprehensively assess clinicians' KAP towards utilizing a combination of glipizide and metformin for managing resource-challenged (deserving) T2DM patients.

Questionnaire Development: The development process involved a thorough literature review of T2DM management in resource-challenged patients and seeking input from diabetes management clinical experts. The final version comprised nine questions and statements covering various aspects of T2DM management and opinions regarding the combination of glipizide and metformin.The final questionnaire was reviewed and approved by a research-experienced endocrinology clinician (the principal investigator).The questionnaire incorporated closed-ended questions and Likert-scale items for quantitative analysis and was circulated to 590 clinicians in India via Google Forms**.**

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Questionnaire Assessment: A Likert scale consisting of a five-point response scale: "Strongly Agree," "Agree," "Neutral," "Disagree," and "Strongly Disagree" was used to assessclinicians'responses. This format allows clinicians to express their agreement or disagreement with statements concerning various aspects of T2DM management in resource-challenged (deserving) patients. Likert-scale items were crafted, covering multiple topics related to glipizide and metformin combinations in light of the current therapy landscape, cost-effectiveness, and their use as first-line therapy.Each item presented a relevant statement or assertion, and clinicians were required to select the response that best reflected their agreement or disagreement.The Likert-scale responses were then numerically coded for quantitative analysis, with higher scores indicating agreement with the statement**.**

Data Analysis: After completing the survey, the data were transferred to a Microsoft Excel spreadsheet for analysis. Descriptive statistics, including frequencies and percentages, were used to summarize the distribution of survey responses. Cross-tabulations and chi-square tests were used to explore associations. A significance level of $P < 0.05$ was applied. Descriptive and inferential statistics were calculated using the SPSS Version 29.

Qualitative Phase

Data collection: Approximately 60 subject matter experts in India were selected based on purposive sampling.The panel consisted of endocrinologists, diabetologists, and internal medicine physicians, all chosen for their experience and expertise in managing resource-challenged (deserving) T2DM patients.This study adopted a virtual FGDs format with a moderator to facilitate discourse among experts.Virtual FGDs, conducted on various dates, included experts from diverse regions of India—north, south, east, and west–from Tier I to IV cities, ensuring generalizability.The primary objective was to gain insights and viewpoints on prescribing cost-effective combinations of glipizide and metformin for managing resource-challenged (deserving) T2DM patients. Throughout the discussions, the moderator directed questions to the group, stimulating dialogue and allowing participants to share their perspectives and experiences. The virtual format of meetings potentially facilitates broader participation and offers scheduling flexibility. The moderator consistently encouraged the involvement of all the panel members, ensuring the representation of diverse viewpoints. The panel members addressed standardizing various antidiabetic treatments that are affordable, cost-effective, and accessible while also maintaining favorable safety profiles for managing resource-challenged (deserving) T2DM patients.The key recommendations from the expert consensus were integrated to align with the prevailing best practices and clinical guidelines. This process ensured that the study's findings were applicable in real-world clinical settings, making a tangible difference forresource-challenged (deserving) T2DM patients.

Data analysis: Direct content analysis was used to analyze the FGDs. All four virtual FGDs were recorded and transcribed word-by-word, and each transcript was checked against the corresponding audio recording.The data analysis involved listening to the audio video recording three times to engage with the content thoroughly, followed by analyzing the data line-by-line to capture and interpret the concept accurately.

RESULTS

Quantitative Findings

The final analysis included 590 clinicians enrolled from different clinics, hospitals, and outpatient centers from various geographic locations in India.

Baseline Characteristics of Clinicians

The 590 clinicians were recruited from various regions of India.The western region contributed the most, with 245 (41.5%) clinicians, 143 (24.2%) from the north, 114 (19.3%) from the south, and 88 (14.9%) from the east (Fig 1a).Nearly 347 (58.8%) clinicians were from non-metropolitan areas (Fig 1b). The survey included clinicians from different city tiers: 201 (34.1%) from Tier I, 231 (39.2%) from Tier II, 23.6% from Tier III, and 3.2% from Tier IV (Fig 1c). Approximately 300 (50.8%) clinicians were medical physicians, 224 (38%) were diabetologists, and 66 (11.2%) were endocrinologists (Fig 1d).

Questionnaire Analysis on Prescribing Practises of Clinicianson Glipizide & Metformin Combination in the Management of Resource-Challenged T2DM Patients

Most clinicians agreed with nearly all the statements of the questionnaire.Almost 145 (24.5%) clinicians 'strongly agreed, and 355 (60.1%) agreed that glipizide + metformin FDC can be optimally used in the treatment of resource-challenged (deserving) T2DM patients (Fig 2a).More than half, 384 (65.08%] clinicians) agreed that glipizide and metformin FDC could be a first-line consideration in eligible resource-challenged (deserving) T2DM patients owing to their efficacy, safety, and cost-effectiveness (Fig 2b).

About 123 (20.84%) clinicians 'strongly agreed, and 396 (62.54%) clinicians 'agreed' to prefer glipizide + metformin FDC, as it has a lower risk of hypoglycemia due to its short half-life.Around 127 (21.52%) clinicians strongly 'agreed, ' and 373 (63.22%) clinicians 'agreed' for preferring glipizide and metformin FDC owing to its safety in moderate to severe (stage 3-5) CKD.Nearly 101 (17.11%) clinicians strongly agreed, and 359 (60.84%)agreed that glipizide was non-inferior to sitagliptin in reducing HbA1c levels over 52 weeks.Similarly, 105

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(17.79%) clinicians strongly agreed and 355 (60.33%) agreed that glipizide was non-inferior to dapagliflozin in reducing HbA1c levels over 52 weeks.Approximately 127 (21.52%) clinicians strongly agreed and 374 (63.55%)agreed that glipizide 5 mg + metformin 500 mg FDC provided an average HbA1c reduction of 1.06% among T2DM patients (Table 1).

Nearly 208 (35.25%) clinicians strongly agreed that glipizide + metformin FDC, with a monthly cost of less than INR 120/−, is a cost-effective intervention for resource-challenged (deserving) T2DM patients in India (Fig 2c).Finally, 231 (39.15%) clinicians strongly agreed, and 320 (54.23%) agreed on their role in improving the patient outcomes of people with T2DM by improving awareness, access, availability, and affordability of high-quality medications (Fig 2d).

All analyzed statements were statistically significant (P <0.001) (Supplementary Table 1).

Supplementary Tables 2-3 demonstrate the variations in the prescribing practices of the glipizide + metformin FDC in resource-challenged (deserving) T2DM patients across specialties, regions, metros, and cities.The trends were similar across all specialty, region, metro, and tier city categories, with statistical significance (P<0.001), indicating a consistent pattern of views among all clinicians.

Qualitative Findings

The following practical insights were derived from the perspectives of 60 panelists who participated in qualitative FGDs

Glipizide + metformin FDC is cost-effective and safe

Most panel members recommend prescribing glipizide + metformin FDC,supported by evidence of its efficacy and safety in managing T2DM patients.

Glipizidenon -inferior with Sitagliptin and Dapagliflozin

The panelistsconcurred on the superiority of glipizide, non-inferior to dapagliflozin and sitagliptin, over gliclazide and glimepiride.

HbA1c Reduction and Dosing Insights(Glipizide 5mg + metformin 500mg)

The panelistsconsideredglipizide 5mg + metformin 500mg as the optimal prescribing dose with 1.06% HbA1c reduction in moderate T2DM resource-challenged patients (deserving)

Efficacy and safety of glipizide in patients with CKD

The majority agreed to prescribe the glipizide + metformin FDCin CKD patients owing to its renal safety

Affordability and Accessibilityofglipizide + metformin FDC

Glipizide + metformin FDC remain underutilized for unknown reasons.Owing to their cost-effectiveness, clinicians opined that better drug availability in all pharmacies or remote areas of the country significantly impacted medication adherence and improved patient outcomes.

Patient Outcomes can be improved through communication and education

Many panel members agree that clinicians' intervention by communicating with the patient in detail from the initial visits about T2DM complications is paramount for improving long-term outcomes. Such strategies could include educating patients about T2DM-related complications and the importance of medication adherence.

The Supplementary File contains profiles of the panelists who participated in the qualitative FGDs and verbatim quotes from the interviewed experts.

Summary of Expert Findings: The expert panel agreed to recommend a combination of short-acting SUs,such as glipizide + metformin FDC, as the primary course of action, citing their cost-effectiveness and potential long-term advantages. There was agreement on prescribing glipizide + metformin FDC during initial consultations for patients with moderate T2DM and CKD and making the drug accessible in the country's remote areas.

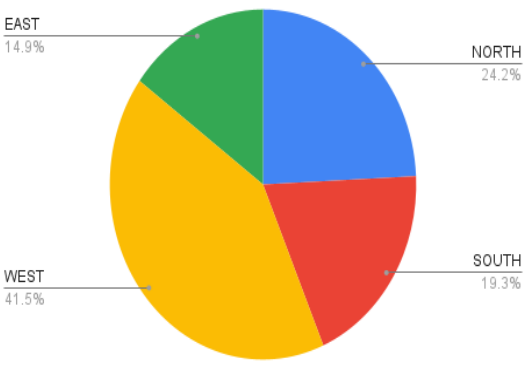

Fig 1a: Zone

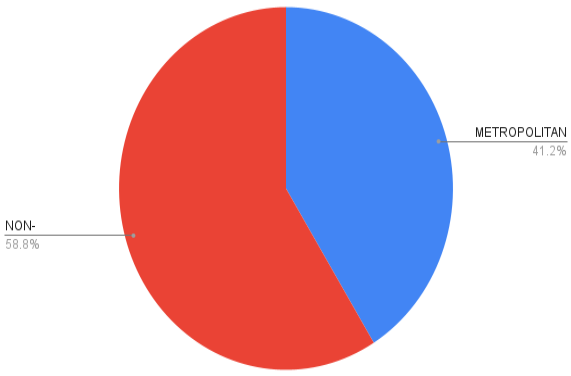

Fig 1b: Metropolitan and Non-metropolitan Region

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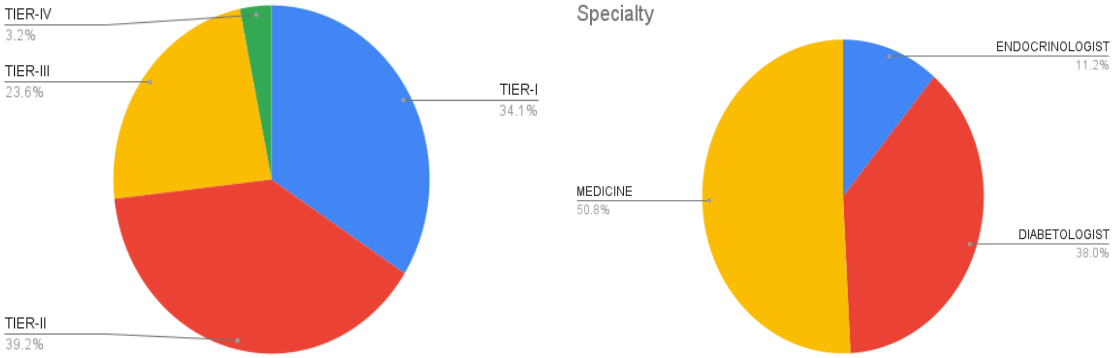

Fig 1c: Tier/ cities **Fig 1d: Speciality of Practice**

Fig 1: Distribution of Cliniciansacross Zones, Regions, Tiers and Speciality of Practice

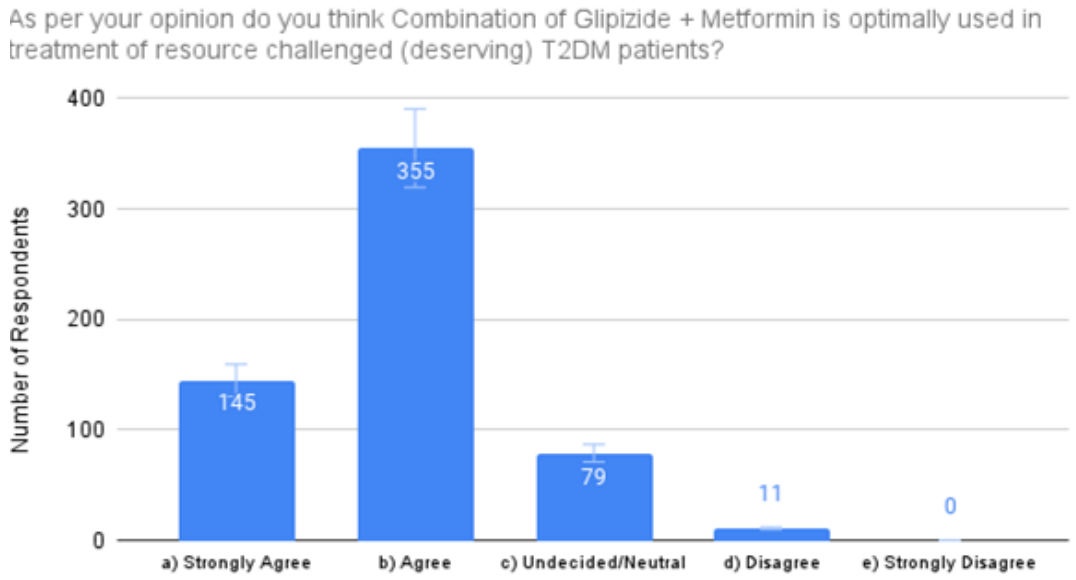

Fig 2a: Clinicians' agreement on the optimal use of Glipizide & Metformin combination in resource-challenged (deserving) T2DM patients

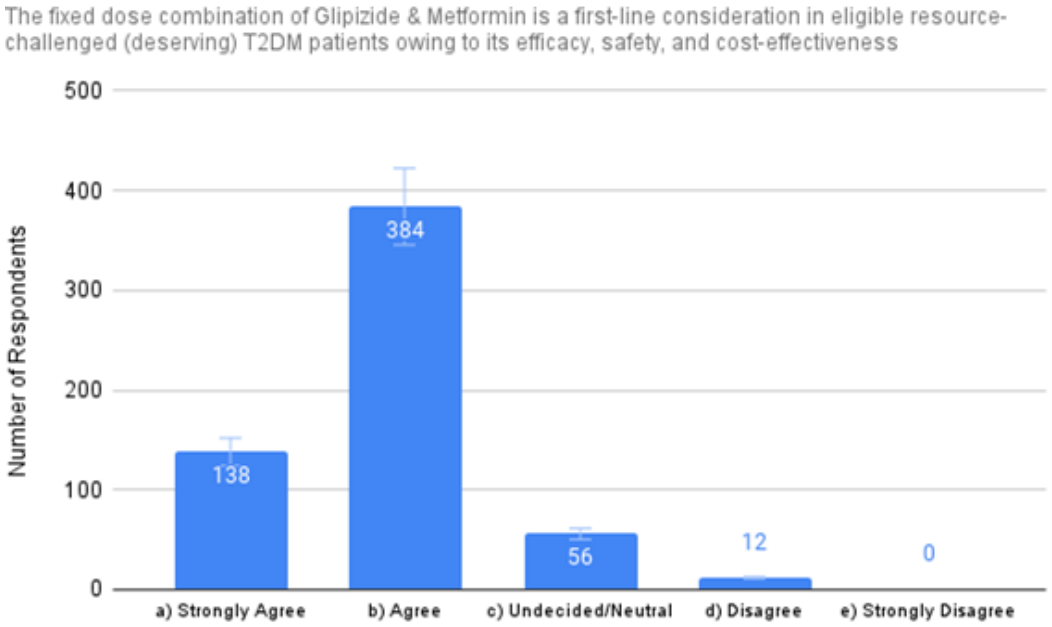

Fig 2b: Clinicians agreement on Glipizide & Metformin as first-line consideration in resource-challenged (deserving) T2DM patients

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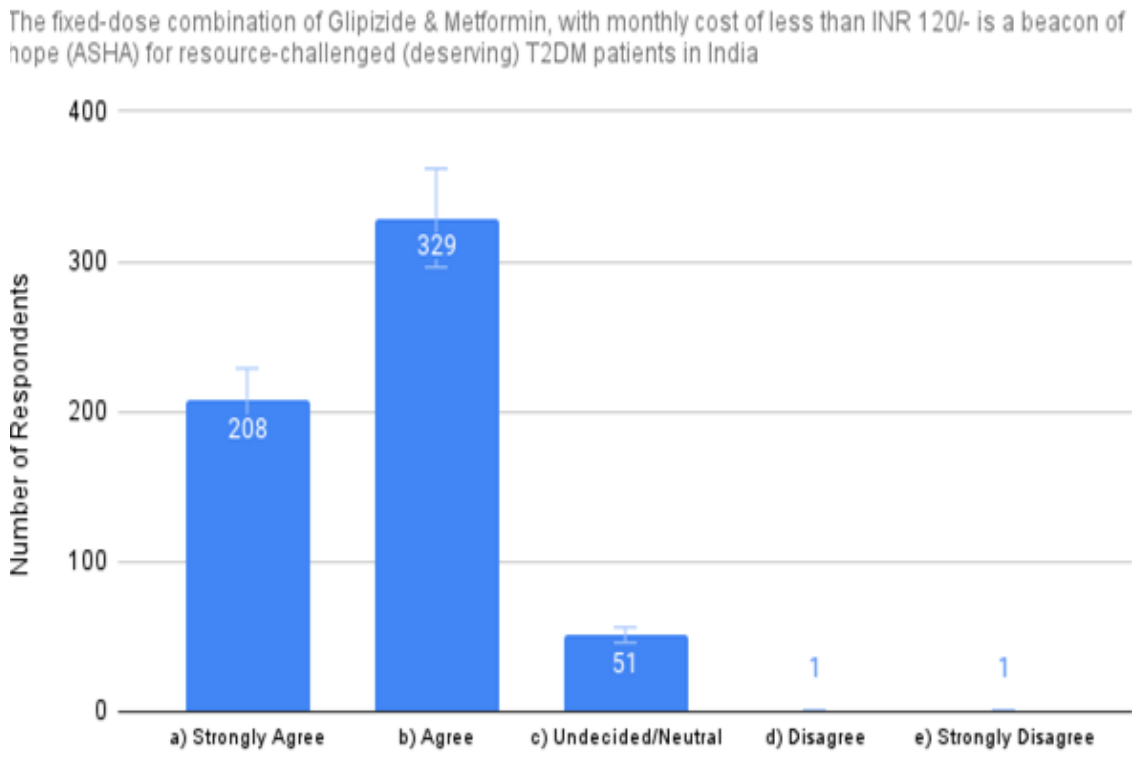

Fig 2c: Clinicians agreement on prescribing Glipizide & Metformin owing to its cost-effectiveness in resource-challenged (deserving) T2DM patients

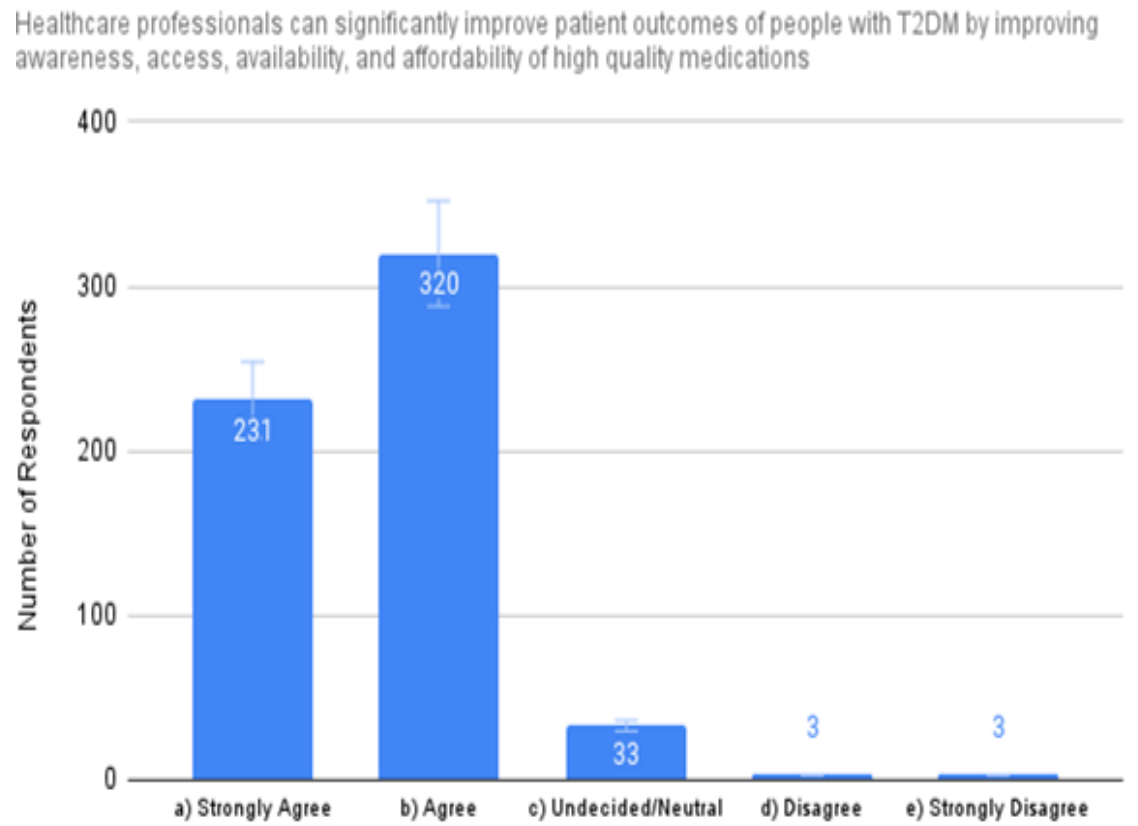

Fig 2d: Clinicians agreement on their role in improving patient outcomes by prescribing Glipizide & Metformin in combination in resource-challenged (deserving) T2DM patients

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Table 1: Knowledge, Attitude, and Practices of Cliniciansin Prescribing Glipizide &Metformin Combination in the Management of Resource-Challenged T2DM

S.No	Questions	Strongly Agree n (%)	Agree n (%)	Neutral n (%)	Disagree n (%)	Strongly disagree n (%)
1.	The fixed-dose combination of Glipizide & Metformin is a clinically preferred SU-based combination as it has a lower risk of hypoglycemia due to its short half-life	3 (20.84%)	9 (62.54%)	86(14.5%)	12 (2%)	NA
2.	The fixed-dose combination of Glipizide & Metformin is a clinically preferred SU-based combination owing to its safety in moderate to severe (stage 3-5) chronic kidney disease (CKD)	7 (21.52%)	3 (63.22%)	77(13.05%)	12(2.03%)	1(0.16%)
3.	Scientific evidence has indicated that Glipizide is non-inferior to Sitagliptin in the reduction of glycated haemoglobin (HbA1c) over 52 weeks	1 (17.11%)	9 (60.84%)	109(18.1%)	19 (3.22%)	2(0.33%)
4.	Scientific evidence has indicated that Glipizide is non-inferior to Dapagliflozin in the reduction of glycated haemoglobin (HbA1c) over 52 weeks	5 (17.79%)	5 (60.33%)	106(18.13%)	20(3.55%)	1 (0.16%)
5.	Glipizide 5 mg / Metformin 500 mg provides an average HbA1c reduction of 1.06% among T2DM patients	7 (21.52%)	4 (63.55%)	81(13.72%)	5(0.84%)	2(0.3%)

Abbreviations: n-number of patients, CI-Confidence interval, T2DM-Type 2 diabetes mellitus.

DISCUSSION

The authors critically evaluated clinicians' KAPs in utilizing glipizide + metformin FDC in India's resource-challenged (deserving) T2DM patients. The current study demonstrates that clinicians possess robust and favorable knowledge of the efficacy and safety of glipizide + metformin FDC.Clinicians' attitudes and practice patterns reflect their willingness to prescribe cost-effective combination therapies, such as glipizide + metformin FDC, indicating a positive outlook toward improving patient care.Given its cost-effectiveness, efficacy, safety, and renal safety profile, clinicians agree that glipizide + metformin FDC is optimal for the treatment of resource-challenged (deserving) T2DM patients.There is a consensus on prescribing cost-effective OADs such as glipizide + metformin FDC from initial visits to improve adherence and outcomes in resource-challenged (deserving) T2DM patients.

Our unique focus on resource-challenged (deserving) T2DM patients constrained the comparison of our survey findings with those of previous or similar studies. However, we assume that our findings align with the similar global challenges reported in other low-resource settings. The current findings from the quantitative and qualitative analyses of clinician responses indicate that modern SUs are widely prescribed across India. There is consensus among clinicians and experts on prescribing modern short-acting SUs as the first-line therapy for resource-challenged (deserving) T2DM patients because of their demonstrated safety, efficacy, and cost-effectiveness.This consensus aligns with a consensus in India that underscores the substantial advantages of SUs and emphasizes their role in managing T2DM, alone or in combination with other treatments.

Experts recommend SUs as one of the most prescribed OADs [22]. Their established efficacy and safety make them an integral part of T2DM pharmacotherapy. The selection of SUs should be highly individualized, coupled with careful monitoring of patients at a high risk of hypoglycemia. Based on available evidence, modern SUs should be favored over conventional SUs for T2DM management because of their superior efficacy, cardiovascular safety, lower hypoglycemic risk, and weight-neutralizing effects. These advantages have positioned modern SUs as a first-line treatment option in the early management of T2DM. To ensure the practical and prudent use of SUs, it is essential to focus on appropriate patient selection, comprehensive patient education, physician training, and meticulous drug and dose selection [22].

In the present study, most clinicians agreed on the necessity of widespread availability of glipizide + metformin FDCacross all pharmacies in India, particularly in remote regions. This aligns with epidemiological data, underscoring the availability of essential OAD medications in low-income and middle-income countries compared to their high-income counterparts. Moreover, metformin was available in 65% of pharmacies, whereas insulin was only available in 10% [23]. Clinicians in the current study agreed on the safety of prescribing glipizide +

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metformin FDC for T2DM patients with CKD.This consensus is consistent with the recommendations outlined in the RSSDI guidelines, where glipizide and gliclazide are the preferred SUs classes of OADs in patients with moderate-to-severe renal impairment [12].

In the current survey, clinicians agreed that glipizide was as effective and safe as dapagliflozin. Similar to our study, another study in India among 844 physicians responded to a survey questionnaire on the cost-effectiveness of dapagliflozin in resource-challenged (deserving) T2DM patients. This group of physicians included diabetologists, endocrinologists, cardiologists, consulting physicians, and family physicians. Most physicians (53%) believed that only 10%-30% of their patients could afford newer antidiabetic medicines. Approximately 39% of the physicians mentioned that 20%-40% of their patients discontinued their medication owing to the high cost [24].In the current survey, clinicians agreed that glipizide is as effective and safe as sitagliptin.This finding aligns with that of a randomized clinical trial involving patients with T2DM and chronic renal insufficiency.At 54 weeks, sitagliptin and glipizide showed similar HbA1C-lowering efficacy [25].

As per most clinicians in the current survey, the combination of glipizide 5 mg and metformin 500 mg has been found to provide an average HbA1c reduction of 1.06% in T2DM patients. This combination's monthly cost, < INR 120/-, is a cost-effective intervention for resource-challenged (deserving) T2DM patients in India. This finding aligns with that of a comparative study on the safety, efficacy, and cost of glipizide versus glimepiride as an add-on therapy to metformin in India. The study demonstrated that glimepiride 2 mg (Group A) as an add-on therapy with metformin 500 mg was modestly less beneficial than glipizide 5 mg (Group B) in terms of efficacy and cost. The total therapy costs for groups A and B were 508.68 INR and 298.08 INR, respectively, with a difference of 41.28% [26]. Therefore, modern short-acting SUs such as glipizide + metformin FDCs are beneficial in clinical practice as this combination is effective in achieving glycemic control, especially in resource-challenged (deserving) T2DM patients.

Key Practice Insights from the Study

The expert panel convened for this study provided several key insights to address in the management of T2DM in resource-challenged (deserving) patients

- Early combination therapy is recommended when the target glycemic levels are challenging. Cost-effective metformin combinations with SUs are crucial in maintaining glycemic control.
- The utilisation of glipizide + metformin FDC as first-line therapy during initial visits for T2DM patients with HbA1c levels >7.5%, especially in resource-constrained patients (deserving)
- Efforts should be made to enhance the accessibility and affordability of glipizide + metformin FDC in remote areas of the country
- To consider glipizide + metformin FDC in resource-constrained (deserving) T2DM patients with comorbidities such as CKD.
- Patient education to reinforce and regularly monitor medication adherence and glycemic control is valuable.
- Clinicians should actively engage in patient communication and consider glipizide and metformin combination for resource-constrained communities (deserving) when appropriately indicated

The main strength of the survey lies in gathering data from 590 clinicians and approximately 60 experts, allowing for a more robust data analysis. Another major strength is the comprehensive data collection from clinicians across diverse regions, including metropolitan and non-metropolitan cities and Tiers I, II, III, and IV cities in India. This approach allows for a broader understanding of different perspectives and enhances their applicability in clinical decision-making. The strength of this survey lies mainly in addressing the impact of prescribing cost-effective glipizide + metformin FDC to resource-challenged (deserving) patients, thus filling a gap in the existing literature.

The survey was not without its limitations. The survey findings may have reported a self-reporting bias, potentially causing clinicians to overstate their knowledge or adherence to best practices. The survey focused solely on clinicianprescription practices regarding glipizide + metformin FDC.It lacks direct patient outcome data, which could provide a more comprehensive understanding of the impact of glipizide + metformin FDC prescription on T2DM management in resource-challenged (deserving) patients.The survey overlooked confounding variables affecting treatment outcomes, including clinical practice duration, practice type, adherence to guidelines, socioeconomic factors, comorbidities, and concomitant medications, potentially compromising the reliability of the results. However, this was beyond the scope of this study. Therefore, we recommend further prospective longitudinal studies incorporating patient outcome data to better understand the cost-effectiveness and safety of prescribingglipizide + metformin FDC in resource-challenged (deserving) T2DM patients. These data can add clinical outcome evidence to overcome financial resource constraints in T2DM patients. Phase 4 real-world effectiveness and safety studies and health economic outcomes research studies are recommended to ensure the rational use of glipizide + metformin FDC in resource-challenged (deserving) T2DM patients.

CONCLUSION

This study reveals the prescribing trends of glipizide + metformin FDC in managing T2DM in resource-

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constrained patients (deserving).Clinicians favoredprescribing glipizide + metformin FDC for T2DM management under financial constraints, significantly influencing their clinical decisions. Additionally, the clinicians strongly support this combination's efficacy, safety, and cost-effectiveness, with a significant number acknowledging its potential to lower the risk of hypoglycemia and its safety in patients with moderate-to-severe CKD. Thus, the economic burden in resource-challenged (deserving) patients with T2DM can be alleviated by encouraging clinicians to prescribe short-acting modern SUs, such as glipizide + metformin FDC, as a cost-effective first-line therapeutic approach. Considering the high prevalence of T2DM in India, the findings of this study may serve as a valuable resource for clinicians in real-world settings by offering evidence-based recommendations.

Appendices/Supplementary files - Sample of the questionnaire used in the survey /Supplementary results (Tables/figures)

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