International Journal of Basic & Clinical Pharmacology
Singh RS et al. Int J Basic Clin Pharmacol. 2026 Jul;15(4):718-722
https://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20261960

Original Research Article

Comparative glycemic efficacy and safety of sitagliptin versus gliclazide in uncomplicated type 2 diabetes mellitus: a 6-month prospective study

Ravi Shekhar Singh[1]*, Shilpa Shankarrao Ingle[1], Manisha Rajkumar Dehankar[2]

[1]Department of Pharmacology, Dr. P. D. M. Medical College and Hospital, Amravati, Maharashtra, India
[2]V. Y. W. S. Dental College, Amravati, Maharashtra, India

Received: 28 April 2026
Revised: 04 June 2026
Accepted: 05 June 2026

***Correspondence:**
Ravi Shekhar Singh,
Email: ravi.singh30@rediffmail.com

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder requiring effective glycemic control while minimizing adverse effects such as hypoglycemia. Sitagliptin and gliclazide are commonly used oral antidiabetic agents with different mechanisms of action and safety profiles, but comparative data in uncomplicated T2DM are limited.

Methods: This prospective, open-label, observational cohort study was conducted from July 2024 to August 2025 in patients aged 18-70 years with uncomplicated T2DM. A total of 291 patients were included and allocated into two groups based on treating physician's discretion. Group A received sitagliptin (100 mg once daily) and group B received gliclazide (30 mg once daily). Patients were followed for six months. Glycemic parameters including fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c) were assessed at baseline, 3 months and 6 months. Adverse drug reactions were recorded. Intra-group comparisons were performed using paired t-tests and inter-group comparisons were analyzed using unpaired t-tests, with $p<0.05$ considered statistically significant.

Results: Both groups showed significant reduction in FBG and PPBG over six months ($p<0.05$). At 6 months, FBG decreased from 162.3±18.5 to 138.2±14.7 mg/dl in the sitagliptin group and from 164.1±19.2 to 124.5±13.9 mg/dl in the gliclazide group ($p<0.05$). PPBG decreased from 248.6±26.4 to 198.7±20.3 mg/dl in the sitagliptin group and from 251.2±27.1 to 175.8±19.6 mg/dl in the gliclazide group ($p<0.05$). HbA1c reduction was greater in the gliclazide group (8.3±1.0 to 6.8±0.6) compared to the sitagliptin group (8.2±0.9 to 7.5±0.7) ($p<0.01$). The incidence of hypoglycemia was significantly lower in the sitagliptin group (2.05%) compared to the gliclazide group (8.28%) ($p<0.05$).

Conclusions: Gliclazide provides superior glycemic control, whereas sitagliptin offers a better safety profile with a lower risk of hypoglycemia. Treatment should be individualized based on patient characteristics and clinical priorities.

Keywords: Type 2 diabetes mellitus, Sitagliptin, Gliclazide, Glycemic control, HbA1c, Hypoglycemia, Oral antidiabetic drugs

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by impaired insulin secretion, defective insulin action, or both, resulting in persistent hyperglycemia and disturbances in carbohydrate, fat and protein metabolism.[1-4] Over time, uncontrolled diabetes contributes to the development of microvascular and macrovascular complications affecting the eyes, kidneys, nerves, and cardiovascular system. The prevalence of diabetes has increased substantially worldwide, making it one of the most important public health challenges of the twenty-first century.[5-8] India bears a significant proportion of the global diabetes burden. Rapid urbanization, sedentary lifestyle, dietary changes, obesity and genetic

susceptibility have contributed to the increasing prevalence of type 2 diabetes mellitus (T2DM) in the Indian population.[5,6,8] Effective long-term glycemic control remains essential for preventing complications and improving quality of life in patients with T2DM.[9,10]

Despite the availability of multiple antidiabetic agents, achieving and maintaining optimal glycemic control remains challenging because of progressive β-cell dysfunction, insulin resistance and treatment-related adverse effects. Among oral antidiabetic drugs, sulfonylureas continue to be widely prescribed because of their potent glucose-lowering efficacy and cost-effectiveness. Gliclazide, a second-generation sulfonylurea, stimulates pancreatic insulin secretion and has been associated with a lower risk of hypoglycemia compared with older sulfonylureas.[11,12]

Dipeptidyl peptidase-4 (DPP-4) inhibitors represent a newer therapeutic approach for T2DM management. Sitagliptin enhances endogenous incretin activity, thereby promoting glucose-dependent insulin secretion and suppressing glucagon release. This mechanism provides effective glycemic control with a lower risk of hypoglycemia and neutral effects on body weight.[11,12] Recent studies and real-world evidence have demonstrated the clinical utility of sitagliptin-based therapy in diverse patient populations, including Indian patients with T2DM.[13-15]

Although both gliclazide and sitagliptin are commonly used in clinical practice, differences in their mechanisms of action may influence glycemic outcomes and safety profiles. Comparative evidence from routine clinical settings remains limited, particularly among patients with uncomplicated T2DM. Therefore, the present study was undertaken to compare the glycemic efficacy and safety of sitagliptin and gliclazide in patients with uncomplicated T2DM and to evaluate their relative benefits in real-world clinical practice.

METHODS

This prospective, open-label, observational cohort study was conducted at a tertiary care teaching hospital from July 2024 to August 2025. Adult patients aged 18-70 years with a confirmed diagnosis of uncomplicated type 2 diabetes mellitus (T2DM) were enrolled consecutively after obtaining written informed consent. A total of 291 patients were included in the study. Each enrolled patient was followed for a period of six months from the initiation of treatment. The study protocol was approved by the Institutional Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki.

Patients were allocated into two treatment groups according to routine clinical practice and the treating physician's discretion; no randomization was performed. Group A received sitagliptin (100 mg once daily), while group B received gliclazide (30 mg once daily). Patients receiving combination antidiabetic therapy were excluded to maintain homogeneity.

Exclusion criteria included patients with type 1 diabetes mellitus, pregnant or lactating women, individuals with significant hepatic or renal impairment, known hypersensitivity to the study drugs and those with severe comorbid conditions.

Baseline demographic and clinical data, including age, sex, duration of diabetes, and prior treatment history, were recorded. Glycemic parameters, namely fasting blood glucose (FBG), postprandial blood glucose (PPBG), and glycated hemoglobin (HbA1c), were assessed at baseline, 3 months and 6 months. Blood glucose levels were measured using the glucose oxidase method in the central laboratory. Patients were followed at regular intervals throughout the study period. Adverse drug reactions, including hypoglycemic episodes and gastrointestinal symptoms, were recorded and evaluated.

The primary outcome measures were changes in FBG, PPBG, and HbA1c levels over time. Secondary outcome measures included the incidence of hypoglycemia and other adverse drug reactions. Statistical analysis was performed using SPSS software. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables as percentages. Intra-group comparisons were performed using paired t-tests, while inter-group comparisons were analyzed using unpaired t-tests. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 291 patients with T2DM completed the study. The patients were allocated into two groups: Group A received sitagliptin and group B received gliclazide. Both groups were comparable with respect to baseline demographic and clinical characteristics.

No statistically significant difference was observed between the two groups at baseline ($p>0.05$), indicating comparability. The primary outcomes assessed were glycemic control and the incidence of adverse drug reactions. Glycemic control was evaluated within groups over a period of six months and between groups at the end of the study period. Both treatment groups demonstrated a statistically significant reduction in fasting and postprandial blood glucose levels following initiation of therapy. In Group A (sitagliptin), a significant reduction in blood glucose levels was observed when compared with baseline values ($p<0.05$). In group B (gliclazide), a more pronounced and consistent reduction in glycemic parameters was observed over the six-month period ($p<0.01$). On intergroup comparison, gliclazide demonstrated a greater reduction in mean fasting and postprandial blood glucose levels compared to sitagliptin ($p<0.05$).

Table 1: Baseline demographic and clinical characteristics.

Parameters	Sitagliptin (n=146)	Gliclazide (n=145)	P value
Age (years)	52.4±8.6	51.8±9.1	0.62
Male/female (N)	78/68	75/70	0.78
Duration of diabetes (years)	5.8±2.7	6.1±2.9	0.41
Fasting blood glucose (mg/dl)	162.3±18.5	164.1±19.2	0.48
Postprandial blood glucose (mg/dl)	248.6±26.4	251.2±27.1	0.52
HbA1c (%)	8.2±0.9	8.3±1.0	0.57

Table 2: Glycemic parameters over time.

Parameters	Time point	Sitagliptin (mean±SD)	Gliclazide (mean±SD)	P value
FBG (mg/dl)	Baseline	162.3±18.5	164.1±19.2	0.48
	3 months	148.6±16.2	140.3±15.8	0.01
	6 months	138.2±14.7	124.5±13.9	0.001
PPBG (mg/dl)	Baseline	248.6±26.4	251.2±27.1	0.52
	3 months	220.4±22.8	205.6±21.5	0.01
	6 months	198.7±20.3	175.8±19.6	0.001
HbA1c (%)	Baseline	8.2±0.9	8.3±1.0	0.57
	3 months	7.8±0.8	7.2±0.7	0.01
	6 months	7.5±0.7	6.8±0.6	0.001

Table 3: Adverse effects.

Adverse effects	Sitagliptin (n=146)	Gliclazide (n=145)	P value
Hypoglycemia (%)	3 (2.05)	12 (8.28)	0.01
Nausea (%)	4 (2.74)	6 (4.14)	0.52
Vomiting (%)	2 (1.37)	4 (2.76)	0.41
Abdominal discomfort (%)	1 (0.68)	3 (2.07)	0.31
Weight reduction (%)	12 (8.22)	2 (1.38)	0.01

HbA1c was assessed as an indicator of long-term glycemic control. In group B, a statistically significant reduction in HbA1c levels was observed at both three and six months compared to baseline ($p<0.01$). In contrast, a significant reduction in HbA1c levels was observed in the sitagliptin group; however, the magnitude of reduction was less pronounced compared to the gliclazide group. Between-group comparison showed superior improvement in HbA1c levels with gliclazide. Both treatment groups demonstrated a statistically significant reduction in fasting and postprandial blood glucose levels over the six-month study period. The reduction was more pronounced in the gliclazide group compared to the sitagliptin group at both 3 months and 6 months ($p<0.05$).

Figure 1 illustrates the trend in fasting and postprandial blood glucose levels over the 6-month study period, with a more pronounced reduction observed in the gliclazide group. HbA1c levels showed a significant reduction in the gliclazide group at 3 and 6 months ($p<0.01$), whereas the reduction in the sitagliptin group was comparatively modest. Intergroup comparison revealed superior glycemic control with gliclazide at the end of the study period. With respect to safety, hypoglycemic episodes were reported in 2.01% of patients in the sitagliptin group and 8.06% in the gliclazide group, and this difference was statistically significant ($p<0.01$). Gastrointestinal adverse effects, including nausea, vomiting and abdominal discomfort, were reported in both groups, with a slightly higher incidence in the gliclazide group (6.1%) compared to the sitagliptin group (4.69%).

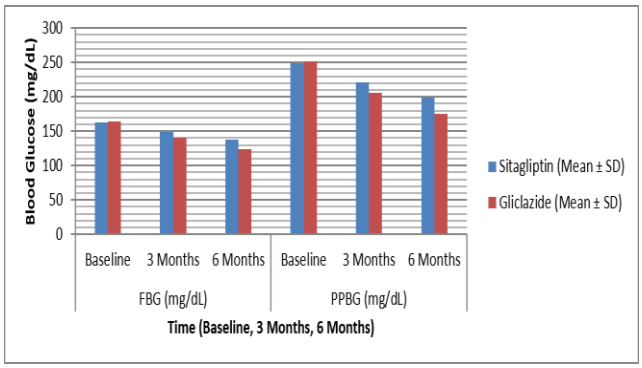

Figure 1: Comparison of trends in fasting blood glucose (FBG) and postprandial blood glucose (PPBG) at baseline, 3 months and 6 months in sitagliptin and gliclazide groups. Values are expressed as mean±standard deviation (SD) in mg/dl.

Weight reduction was observed in 8.10% of patients treated with sitagliptin, whereas no significant change in body weight was observed in patients receiving gliclazide.

The incidence of hypoglycemia was significantly lower in the sitagliptin group compared to the gliclazide group ($p<0.05$). Gastrointestinal adverse effects such as nausea, vomiting, and abdominal discomfort were observed in both groups, with no statistically significant difference. Weight reduction was more commonly observed in patients treated with sitagliptin, which was statistically significant ($p<0.05$). Overall, gliclazide demonstrated superior glycemic control, while sitagliptin exhibited a more favorable safety profile with a lower incidence of hypoglycemia.

DISCUSSION

Diabetes mellitus is a rapidly increasing global health concern characterized by chronic hyperglycemia and associated metabolic disturbances. Effective management of T2DM requires achieving optimal glycemic control while minimizing adverse effects, particularly hypoglycemia. The present study compared the efficacy and safety of sitagliptin and gliclazide as monotherapy in patients with uncomplicated T2DM. Both treatment groups demonstrated significant reductions in fasting and postprandial blood glucose levels over the six-month study period.[13] However, gliclazide showed a more pronounced and consistent reduction in glycemic parameters compared to sitagliptin.

The greater efficacy of gliclazide can be attributed to its mechanism of action as a sulfonylurea, which directly stimulates insulin secretion from pancreatic β-cells. This results in a stronger glucose-lowering effect, as reflected in the significant reduction in HbA1c levels observed in this study. These findings are consistent with randomized controlled trials and meta-analyses demonstrating comparable glycemic efficacy between sitagliptin and sulfonylureas, with a lower risk of hypoglycemia observed with sitagliptin.[16-18] In contrast, sitagliptin, a DPP-4 inhibitor, enhances incretin hormone activity, leading to glucose-dependent insulin secretion and suppression of glucagon release. While this mechanism contributes to improved glycemic control, the magnitude of reduction is generally lower than that observed with sulfonylureas, which may explain the comparatively modest changes in HbA1c observed in the present study.

With regard to safety, a significantly lower incidence of hypoglycemic episodes was observed in patients treated with sitagliptin compared to those receiving gliclazide. This finding is clinically important and is consistent with the glucose-dependent mechanism of action of DPP-4 inhibitors, which reduces the risk of hypoglycemia. In contrast, sulfonylureas are associated with a higher risk of hypoglycemia due to continuous stimulation of insulin secretion, irrespective of blood glucose levels. Gastrointestinal adverse effects were observed in both groups but were generally mild and comparable between treatments. Weight reduction observed in patients treated with sitagliptin may provide an additional therapeutic advantage, particularly in overweight or obese individuals.

Some earlier studies have reported comparable efficacy between DPP-4 inhibitors and sulfonylureas, highlighting variability in clinical outcomes depending on study design, patient characteristics, and duration of therapy.[14] Recent real-world studies from Indian clinical settings have also demonstrated significant improvement in glycemic parameters with sitagliptin-based therapy.[15] The findings of the present study, however, suggest that gliclazide provides superior glycemic control, whereas sitagliptin offers a more favorable safety profile. The present study has certain limitations, including a relatively short duration of follow-up and resource constraints. Additionally, being an observational study, the potential for confounding factors cannot be entirely excluded. Further large-scale, randomized controlled trials with longer follow-up are required to validate these findings and better define the role of these agents in clinical practice. Overall, the results of this study emphasize the importance of individualized treatment selection in T2DM, balancing efficacy and safety to achieve optimal patient outcomes.

CONCLUSION

The findings of the present study demonstrate that gliclazide provides superior glycemic control compared to sitagliptin in patients with uncomplicated T2DM. This is evidenced by a more consistent and significant reduction in both blood glucose levels and HbA1c. However, this improved efficacy is accompanied by a higher incidence of hypoglycemic episodes, which may limit its use in certain patient populations.

Sitagliptin, although less effective in reducing glycemic parameters, offers a safer profile with a lower risk of hypoglycemia and additional benefits such as weight reduction. Therefore, the choice of therapy should be individualized based on patient characteristics, clinical priorities and risk factors. Gliclazide may be preferred in patients requiring stronger glycemic control, whereas sitagliptin may be more suitable for patients where safety and avoidance of hypoglycemia are of greater concern. Further large-scale and long-term studies are recommended to confirm these findings and guide clinical decision-making.

ACKNOWLEDGEMENTS

The authors sincerely acknowledge the support and facilities provided by the Department of Pharmacology, GMCH, Udaipur, Rajasthan, India, for the successful conduct of this study and also grateful to the Institutional Ethics Committee for granting approval and for their valuable guidance throughout the study. Extending sincere thanks to all the participants for their cooperation and willingness to be a part of this research. The authors also acknowledge the contribution of the clinical and laboratory staff for their assistance in patient management, data collection and biochemical investigations and appreciation to all individuals and colleagues who

contributed directly or indirectly to the completion of this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Kumar P, Clark M. Diabetes Mellitus and Other Disorders of Metabolism. In: Clinical Medicine. 6th ed. London: Saunders WB. 2002;1069-71.
2. American Diabetes Association. Standards of Medical Care in Diabetes—2024. Diabetes Care. 2024;47(1):S1-350.
3. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of T2DM and its complications. Nat Rev Endocrinol. 2018;14(2):88-98.
4. Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, Lafont S, Bergeonneau C, Kassai B, et al. Effect of intensive glucose lowering treatment on all-cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomized controlled trials. BMJ. 2011;343:d4169.
5. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183:109119.
6. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation. 2021.
7. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet. 2017;389(10085):2239-51.
8. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in India: results from the ICMR-INDIAB study. Lancet Diabetes Endocrinol. 2017;5(8):585-96.
9. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359:1577-89.
10. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with T2DM (UKPDS 49). JAMA. 1999;281:2005-12.
11. Deacon CF, Lebovitz HE. Comparative review of dipeptidyl peptidase-4 inhibitors and sulfonylureas in type 2 diabetes. Diabetes Obes Metab. 2016;18(4):333-47.
12. Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, et al. Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. Ann Intern Med. 2016;164(11):740-51.
13. Terauchi Y, Yamada Y, Ishida H, Yokoyama H, Shimomura I, Hirose T, et al. Efficacy and safety of sitagliptin compared with glimepiride in patients with type 2 diabetes (START-J trial). Diabetes Obes Metab. 2017;19(8):1188-92.
14. Gallwitz B. Clinical use of DPP-4 inhibitors. Front Endocrinol (Lausanne). 2019;10:389.
15. Bhat KA, Singh KP, Maddukuri HR, Routray SN, Sharma S, Sharma SK, et al. Clinical profile, comorbidities and therapies in type 2 diabetes patients on sitagliptin-based therapy in an Indian outpatient setting. Cureus. 2024;16(11):e74820.
16. Nauck MA, Meininger G, Sheng D, Terranella L, Stein PP, Sitagliptin Study 024 Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin compared with the sulfonylurea glipizide in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial. Diabetes Obes Metab. 2007;9:194-205.
17. Seck T, Nauck M, Sheng D, Sunga S, Davies MJ, Stein PP, et al. Safety and efficacy of treatment with sitagliptin or glipizide in patients with type 2 diabetes inadequately controlled on metformin: a 2-year study. Int J Clin Pract. 2010;64:562-76.
18. Sharma M, Beckley N, Nazareth I, Heald AH, Cummins E, Bhattacharya D, et al. Effectiveness of sitagliptin compared to sulfonylureas for type 2 diabetes mellitus inadequately controlled on metformin: a systematic review and meta-analysis. BMJ Open. 2017;7:e017260.

Cite this article as: Singh RS, Ingle SS, Dehankar MR. Comparative glycemic efficacy and safety of sitagliptin versus gliclazide in uncomplicated type 2 diabetes mellitus: a 6-month prospective study. Int J Basic Clin Pharmacol 2026;15:718-22.