RESEARCH PAPER

Therapeutic Outcomes of Metformin Alone Versus Metformin Plus Saxagliptin in Newly Diagnosed Type 2 Diabetes

Dhafer Rahman Abed Al-Janabi[1], Rusul Mushtaq Talib[8], Alaa Hadi Shakir[8], Nawras Noori Mohammad Hussain[8], Hadeel Maan Rashied[2], Thualfiqar Ghalib Turki[3], Hussein Ali Salih[4], Mustafa S Khudhur[5], Qasim Abbas Muhammad Muhail[6], Asseel Majeed Al Amery[7] and Haider Abbas Hadi Al-Mhanaa[8]

[1]The Islamic University of Najaf, College of Medical Technology, Department of Medical Laboratory Technology, Iraq and Al-Hakim General Hospital, Haemodialysis Centre, Najaf, Iraq., Laboratory department
[2,3,4,5,6] The Islamic University of Najaf, College of Medical Technology, Department of Medical Laboratory Technology, Iraq
[7]Jabir ibn Hayyan University for Medical and Pharmaceutical Sciences / College of Pharmacy, Iraq
[8]Laboratories Techniques Department, College of Health and Medical Techniques, Al-Mustaqbal University, 51001, Babylon, Iraq
*[*]**Corresponding Author:** Dhafer Rahman Abed Al-janabi*
Email id: dhafer.rahmaan@iunajaf.edu.iq
ORCID id: 0000-0001-7576-0555

Received: 26th Feb, 2025; Revised: 8th March 2026; Accepted: 12th April, 2026; Available Online: 20th April, 2026

ABSTRACT
Background: As a progressive metabolic disease, type 2 diabetes mellitus (T2DM) necessitates early and efficient glycemic control to avoid long-term consequences. The first-line medication for type 2 diabetes is metformin; however, many patients require combination therapy since metformin alone is insufficient to provide good glycemic control.
Aim: The purpose of this study was to assess the effects of metformin alone versus metformin plus saxagliptin on body mass index (BMI) and glycemic control in individuals with type 2 diabetes mellitus who had just received a diagnosis.
Methods: Eighty newly diagnosed T2DM patients in the Najaf Governorate were divided into two groups for a comparative study: metformin monotherapy (n = 40) and metformin plus saxagliptin (n = 40). BMI, glycated hemoglobin (HbA1c), and fasting blood glucose were assessed at baseline, 30 days, and 60 days of treatment. SPSS software was used for statistical analysis, and a p-value of less than 0.05 was deemed statistically significant.
Results: Over the course of the 60-day follow-up period, both treatment regimens produced substantial decreases in fasting serum glucose, HbA1c, and BMI ($p < 0.05$). However, patients receiving metformin combined with saxagliptin showed significantly greater improvements in glycemic parameters and BMI compared with those receiving metformin alone, particularly after 60 days of treatment.
Conclusion: In newly diagnosed individuals with type 2 diabetes, metformin with saxagliptin was more effective than metformin alone at lowering BMI and improving glycemic control. For this patient population, early combination therapy may be a useful tactic for enhancing metabolic outcomes and attaining quick glycemic control.
Keywords: Type 2 diabetes mellitus, Metformin, Saxagliptin, Glycaemic, HbA1c.
How to cite this article: Al-Janabi DRA, Talib RM, Shakir AH, Hussain NNM, Rashied HM, Turki TG, Salih HA, Khudhur MS, Muhail QAM, Al Amery AM, Al-Mhanaa HAH. Therapeutic Outcomes of Metformin Alone Versus Metformin Plus Saxagliptin in Newly Diagnosed Type 2 Diabetes. Int J Drug Deliv Technol. 2026;16(31s):149-154. DOI: 10.25258/ijddt.16.31s.18
Source of support: Nil.
Conflict of interest: None

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance and relative insulin deficiency (1). Due to its linked morbidity, mortality, and financial cost, type 2 diabetes has become much more common worldwide in recent decades, posing a significant public health concern (2) (3) . In order to lower the risk of long-term microvascular and macrovascular problems and to enhance overall clinical outcomes, it is imperative that newly diagnosed patients achieve early glycemic control (4). Because of its effectiveness in lowering hepatic glucose production, enhancing insulin sensitivity, excellent safety profile, minimal risk of hypoglycemia, and potential cardiovascular advantages, metformin continues to be the cornerstone and first-line pharmacological therapy for type 2 diabetes (5) (6). Despite these benefits, a significant percentage of patients, especially in the early stages of the disease, are unable to attain or sustain optimal glycemic control with metformin monotherapy, requiring the

**Author for Correspondence: dhafer.rahmaan@iunajaf.edu.iq*

addition of additional glucose-lowering medications (7). Saxagliptin and other dipeptidyl peptidase-4 (DPP-4) inhibitors are a significant class of oral antidiabetic medications that increase endogenous incretin activity, resulting in glucose-dependent stimulation of insulin production and reduction of glucagon release (8) . Saxagliptin is a desirable choice for combination therapy with metformin since it is typically well tolerated, weight-neutral, and linked to a low risk of hypoglycemia (9). The effectiveness of metformin in conjunction with DPP-4 inhibitors in improving glycemic indices has been shown in a number of trials, but there is still a dearth of information specifically on newly diagnosed T2DM patients in actual clinical settings, especially in Middle Eastern populations (10)(11). Thus, the purpose of this study was to compare the effects of metformin monotherapy versus metformin plus saxagliptin on glycemic control in newly diagnosed patients with type 2 diabetes mellitus in the Najaf Governorate. Glycemic control was measured by fasting serum glucose and glycated hemoglobin (HbA1c), as well as changes in body mass index (BMI).

METHOD

Study design and setting

A comparative prospective study was conducted in Najaf Governorate, Iraq, from October 2024 to May 2025. The study aimed to evaluate the effects of metformin monotherapy versus metformin combined with saxagliptin on glycemic control and body mass index in newly diagnosed patients with type 2 diabetes mellitus.

Study population and sample size

A total of 80 newly diagnosed patients with type 2 diabetes mellitus were enrolled in the study and allocated into two equal groups (n = 40 each). Patients were recruited from outpatient clinics after confirmation of diagnosis according to standard diagnostic criteria.

Inclusion and exclusion criteria

Inclusion criteria: Age between 40 and 55 years, Newly diagnosed with type 2 diabetes mellitus, Male patients and Not previously treated with antidiabetic medications

Exclusion criteria:Presence of chronic diseases (e.g., cardiovascular, renal, or hepatic disorders), Current use of chronic medications and Body mass index (BMI) > 35 kg/m²

Treatment protocol

Patients were allocated into two treatment groups:

Group 1: Received metformin monotherapy at a dose of 850 mg/day.

Group 2: Received metformin (1000 mg/day) in combination with saxagliptin (2.5 mg/day).

All patients were advised to follow standard lifestyle modifications, including dietary control and regular physical activity, throughout the study period.

Data collection and measurements

Baseline measurements were obtained before initiation of treatment and included age, body mass index (BMI), fasting serum glucose, and glycated hemoglobin (HbA1c). Follow-up measurements were recorded after 30 days and 60 days of treatment.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m²).

Fasting serum glucose was measured after an overnight fast using standard biochemical methods.

Glycated hemoglobin (HbA1c) was measured using high-performance liquid chromatography (HPLC) with a closed system analyzer, which is considered the gold standard method for HbA1c assessment due to its high accuracy and reliability.

Blood sample collection and analysis

Venous blood samples were collected under aseptic conditions. Samples for HbA1c analysis were collected in EDTA tubes and analyzed using a closed HPLC system in accordance with the manufacturer's instructions. This system ensures standardized calibration and minimizes analytical variability.

Ethical considerations

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was obtained from all participants prior to enrollment. Patient confidentiality was strictly maintained throughout the study. Clinical trial number: Not applicable.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS), version 20. Continuous variables were expressed as mean ± standard deviation (SD). Comparisons within groups over time were performed using repeated-measures analysis, while comparisons between groups were conducted using appropriate parametric tests. A p-value < 0.05 was considered statistically significant.(12)

RESULTS

Eighty newly diagnosed patients with type 2 diabetes mellitus were involved in the trial. They were split equally into two groups: metformin monotherapy (Group 1, n = 40) and metformin plus saxagliptin (Group 2, n = 40). Table 1 displays the baseline clinical and demographic features of both groups. Age, body mass index (BMI), fasting serum glucose, and baseline HbA1c levels did not significantly differ between the two groups ($p > 0.05$), suggesting that the groups were similar before to starting treatment.Both groups' BMI, fasting serum glucose, and HbA1c levels significantly improved after therapy over the 60-day follow-up period (Table 2). BMI, fasting serum glucose, and HbA1c levels significantly decreased after 30 days and continued to improve after 60 days as compared to baseline in Group 1 (metformin monotherapy) ($p < 0.05$). Similarly, at all follow-up time periods, Group 2 (metformin + saxagliptin) showed substantial decreases in all measured parameters, with more noticeable benefits shown after 60 days of treatment. After 60 days, a

comparison of the two groups showed that patients taking metformin with saxagliptin had significantly lower BMI, fasting blood glucose, and HbA1c levels than patients on metformin alone ($p < 0.05$). These results show that in newly diagnosed individuals with type 2 diabetes mellitus, combination treatment improved metabolic and glycemic outcomes better than metformin monotherapy .After 60 days, a comparison of the two groups showed that patients taking metformin with saxagliptin had significantly lower BMI (Figure 1), fasting blood glucose (Figure 2), and HbA1c levels (Figure 3) than patients on metformin alone ($p < 0.05$).

Table 1 Baseline demographic and clinical characteristics of newly diagnosed type 2 diabetes mellitus patients in the two study groups

Description	Group 1 - 40 Patients	Group 2 - 40 Patients	P value	Significant
Sex	only Male	only Male		No
Age	48.34 ± 2.7317	49.07 ± 3.216	0.549	No
BMI (kg/m)	34 ± 8.7	33 ± 9.5	0.1962	No
fasting Serum glucose	170 ± 8.7	172 ± 10.3	0.7133	No
HbA1cValues	12.3 ± 3.2	12.4 ± 3.4	0.5534	No

Table 2 Effects of metformin monotherapy and metformin plus saxagliptin on body mass index, fasting serum glucose, and HbA1c levels during the 60-day follow-up period

		-A-	-B-	-C-	(P < 0.05)	
		Before treatment	After 30 days	After 60 days	A&B	B&C
BMI (kg/m)	Group 1	34 ± 8.7	32 ± 5.5	31 ± 6.3	0.0227*	0.0157*
	Group 2	33 ± 9.5	31 ± 6.7	28 ± 8.7	0.00423*	< 0.0001**
fasting Serum glucose	Group 1	170 ± 8.7	126 ± 6.5	120 ± 6.2	< 0.001*	< 0.0001**
	Group 2	172 ± 10.3	120 ± 7.8	115 ± 4.3	0.0213*	< 0.0001**
HbA1cValues	Group 1	12.3 ± 3.2	10.7 ± 2.9	9.8± 1.8	0.0098*	0.0013*
	Group 2	12.4 ± 3.4	9.6 ± 2.3	8.3± 2.1	0.0188*	< 0.0001**

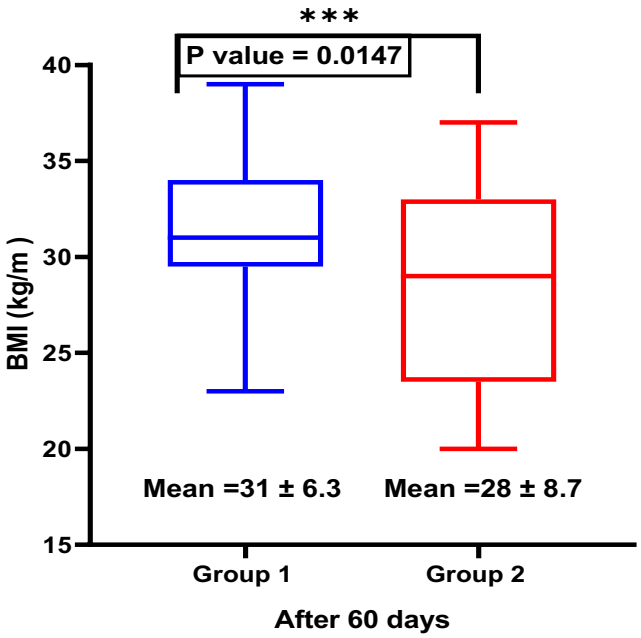

Figure 1 Comparison of body mass index (BMI) between metformin monotherapy and metformin plus saxagliptin groups after 60 days of treatment

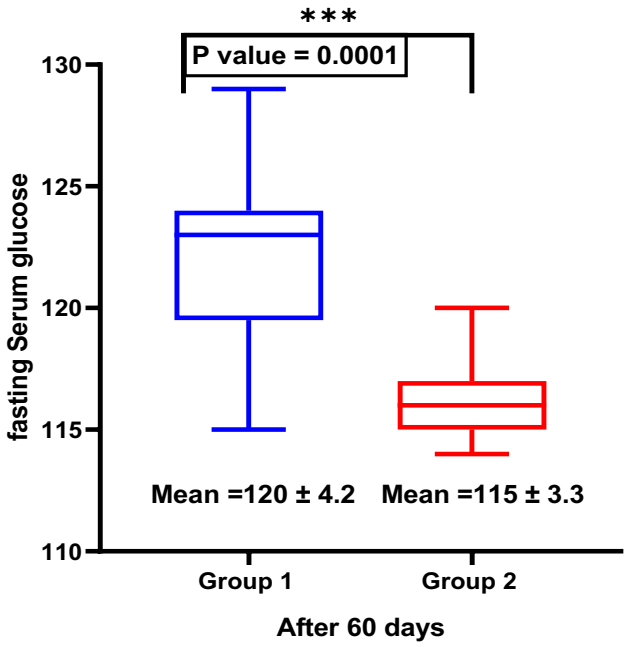

Figure 2 Comparison of fasting serum glucose levels between metformin monotherapy and metformin plus saxagliptin groups after 60 days of treatment

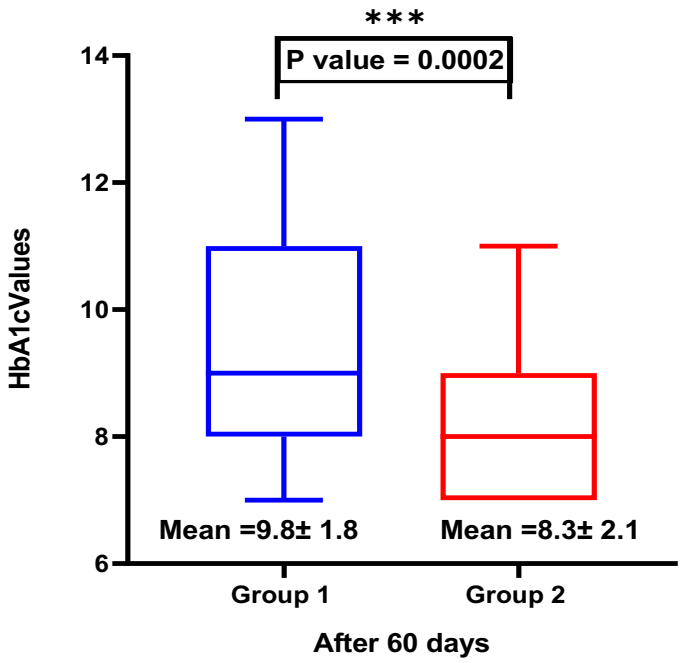

Figure 3 Comparison of HbA1c levels between metformin monotherapy and metformin plus saxagliptin groups after 60 days of treatment

DISCUSSION

The effects of metformin monotherapy and metformin plus saxagliptin on glycemic management and body mass index in newly diagnosed individuals with type 2 diabetes mellitus were examined in this study. Over the course of the 60-day follow-up period, the results showed that both treatment regimens significantly improved fasting serum glucose, HbA1c levels, and BMI. However, compared to those using metformin alone, patients receiving the combined therapy demonstrated a more noticeable decrease in glycemic indices and BMI. Metformin is a proven first-line pharmacological treatment for type 2 diabetes because it can improve peripheral insulin sensitivity and reduce hepatic glucose production without causing weight gain or severe hypoglycemia (13)(14). The current investigation found that metformin monotherapy significantly reduced fasting glucose and HbA1c, which is consistent with previous clinical trials and real-world research demonstrating its efficacy in early-stage T2DM (15)(16). Saxagliptin, a DPP-4 inhibitor, increases

endogenous incretin levels, thereby stimulating glucose-dependent insulin secretion and suppressing glucagon release and addition of saxagliptin to metformin therapy resulted in a greater reduction in HbA1c and fasting serum glucose compared to metformin alone. This enhanced glycemic control can be attributed to the complementary mechanisms of action of the two drugs. (17). This synergistic effect has been reported in several randomized controlled trials, which demonstrated significant improvements in glycemic indices when saxagliptin was added to metformin therapy (18). When compared to metformin alone, the combination medication was linked to a higher decrease in BMI in addition to glycemic control. Improved glycemic management and decreased insulin resistance may indirectly contribute to modest weight loss, even though DPP-4 inhibitors are typically thought to be weight-neutral (19)(20) .Previous studies assessing metformin–DPP-4 inhibitor combos have revealed similar results, with either neutral or slightly beneficial effects on body weight (21) .The current study's findings are especially pertinent to people with recently diagnosed type 2 diabetes. In the early stages of the disease, β-cell activity is crucial, and early combination therapy may assist establish quick glycemic control, minimize glucotoxicity, and maintain it (22)(23). The European Association for the Study of Diabetes and the American Diabetes Association's current guidelines advocate the early use of combination therapy in patients who do not achieve acceptable glycemic control with metformin alone and place an emphasis on personalized treatment methods (24).

Despite these positive results, there are a few things to be aware of. The evaluation of long-term glycemic durability and safety outcomes is restricted by the comparatively short follow-up period. Furthermore, the results may not be as applicable to other groups due to the small sample size and single governorate. To validate these results and assess long-term cardiovascular and renal outcomes, more research with bigger sample sizes, longer follow-up periods, and randomized controlled designs is necessary.

CONCLUSIONS

In conclusion, this study shows that in newly diagnosed individuals with type 2 diabetes mellitus, metformin monotherapy and metformin plus saxagliptin both successfully improve glycemic control and lower body mass index. Crucially, when compared to metformin alone, the combination therapy produced better decreases in fasting glucose and HbA1c levels. These findings demonstrate the potential advantages of early combination therapy in attaining more rapid and noticeable improvements in metabolism. To validate these results and evaluate the sustainability and safety of this therapeutic strategy, more extensive, long-term research is advised.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

REFERENCES

1. Al-Sallami ZHR, Smesim AAA, Al-Janabi DRA, Algenabi AHA. Impact of Vitamin D Status on Irisin Hormone Level in Type 2 Diabetic Iraqi Women. In: BIO Web of Conferences. EDP Sciences; 2024. p. 4002.
2. Kumar A, Gangwar R, Ahmad Zargar A, Kumar R, Sharma A. Prevalence of diabetes in India: A review of IDF diabetes atlas 10th edition. Curr Diabetes Rev. 2024;20(1):105–14.
3. Roglic G. WHO Global report on diabetes: A summary. Int J Noncommunicable Dis. 2016;1(1):3–8.
4. Assessment G. 6. Glycemic targets: Standards of medical care in diabetes—2021. Diabetes Care. 2021;44:S73.
5. Fritsche A. Insulin Secretion Capacity as a Crucial Feature to Distinguish Type 1 From Type 2 Diabetes and to Indicate the Need for Insulin Therapy–A Critical Discussion of the ADA/EASD Consensus Statement on the Management of Type 1 Diabetes in Adults. Exp Clin Endocrinol Diabetes. 2023;131(09):500–3.
6. DeFronzo R, Fleming GA, Chen K, Bicsak TA. Metformin-associated lactic acidosis: Current perspectives on causes and risk. Metabolism. 2016;65(2):20–9.
7. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes? Ther Adv Endocrinol Metab. 2021;12:2042018820980225.
8. Ussher JR, Drucker DJ. Cardiovascular biology of the incretin system. Endocr Rev. 2012;33(2):187–215.
9. Rosenstock J, Hansen L, Zee P, Li Y, Cook W, Hirshberg B, et al. Dual add-on therapy in type 2 diabetes poorly controlled with metformin monotherapy: a randomized double-blind trial of saxagliptin plus dapagliflozin addition versus single addition of saxagliptin or dapagliflozin to metformin. Diabetes Care. 2015;38(3):376–83.
10. Raz I, Riddle MC, Rosenstock J, Buse JB, Inzucchi SE, Home PD, et al. Personalized management of hyperglycemia in type 2 diabetes: reflections from a Diabetes Care Editors' Expert Forum. American Diabetes Association; 2013.
11. Akhras KS, Alsheikh-Ali AA, Kabbani S. Use of real-world evidence for healthcare decision-making in the Middle East: practical considerations and future directions. Expert Rev Pharmacoecon Outcomes Res. 2019;19(3):245–50.
12. Smesim AAA, Al-Sallami ZHR, Al-janabi DRA, Algenabi AHA. Significance of malondialdehyde in Iraqi women patients with iron deficiency anemia. In: BIO Web of Conferences. EDP Sciences; 2024. p.

4001.

13. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 5. Facilitating positive health behaviors and well-being to improve health outcomes: standards of care in diabetes—2023. Diabetes Care. 2023;46(Supplement_1):S68–96.
14. Sundheim B, Hirani K, Blaschke M, Lemos JRN, Mittal R. Pre-type 1 diabetes in adolescents and teens: screening, nutritional interventions, beta-cell preservation, and psychosocial impacts. J Clin Med. 2025;14(2):383.
15. Lin YY, Weng SF, Hsu CH, Huang CL, Lin YP, Yeh MC, et al. Effect of metformin monotherapy and dual or triple concomitant therapy with metformin on glycemic control and lipid profile management of patients with type 2 diabetes mellitus. Front Med. 2022;9:995944.
16. Sulaiman MK. Diabetic nephropathy: recent advances in pathophysiology and challenges in dietary management. Diabetol Metab Syndr. 2019;11(1):7.
17. Bennett WL, Maruthur NM, Singh S, Segal JB, Wilson LM, Chatterjee R, et al. Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Intern Med. 2011;154(9):602–13.
18. Davies MJ. Management of hyperglycaemia in type 2 diabetes: the 2018 consensus report by ADA/EASD Insights from one of the authors. Br J Diabetes. 2018;18(4):137–40.
19. Zhou XD, Lian L, Chen QF, Kim SU, Yip CF, Petta S, et al. Effect of Hypertension on Long-Term Adverse Clinical Outcomes and Liver Fibrosis Progression in Metabolic Dysfunction-Associated Steatotic Liver Disease.
20. Taheri S, Zaghloul H, Chagoury O, Elhadad S, Ahmed SH, El Khatib N, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. lancet Diabetes Endocrinol. 2020;8(6):477–89.
21. Diaz M. Adapting a Culturally Grounded Diabetes Prevention Program to a Family Diabetes Prevention Program. Arizona State University; 2024.
22. LeRoith D, Taylor SI, Olefsky JM. Diabetes mellitus: a fundamental and clinical text. Lippincott Williams & Wilkins; 2004.
23. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia. 2009;52(1):17–30.
24. Association AD. Standards of medical care in diabetes—2011. Diabetes Care. 2011;34(Supplement_1):S11–61.