

Comparative efficacy of sitagliptin/metformin versus dapagliflozin/metformin on glycemic control in patients with type 2 diabetes mellitus; an open-ended, randomized, and parallel-group clinical trial study

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a metabolic disorder requiring combination treatment for achieving and maintaining adequate glycemic control. Both combination treatments, including dipeptidyl peptidase-4 (DPP-4) inhibitors such as sitagliptin and sodium-glucose co-transporter 2 (SGLT2) inhibitors such as dapagliflozin, are frequently prescribed as add-on agents to metformin; however, relative effectiveness when used in fixed combinations remains an area of active investigation.

Objectives: This study was conducted to compare the efficacy of sitagliptin/metformin and dapagliflozin/metformin on glycemic control in patients with T2DM.

Materials and Methods: This randomized, open-label, clinical trial was conducted on T2DM patients recruited from two central teaching hospitals in Iraq from June to December 2025. Eligible and consenting patients were randomly allocated in a 1:1 ratio to receive either sitagliptin/metformin (50/500 twice daily) or dapagliflozin/metformin (10/1000 daily) and were followed prospectively for 12 weeks. Baseline and follow-up assessments included demographic and clinical data and measurement of glycemic indices (HbA1c, fasting blood sugar [FBS], and 2-hour postprandial blood sugar [2hPP-BS]), and efficacy analyses compared changes in these parameters between and within treatment groups using standard statistical tests at a two-sided significance level of 0.05.

Results: The results showed that both treatment groups showed significant improvements in glycemic parameters compared with baseline. However, the dapagliflozin plus metformin group demonstrated consistently greater reductions across all glycemic parameters, including HbA1c (↓1.48% versus ↓0.80%), FBS (↓50.64 versus 34.19 mg/dL), and postprandial BS (↓77.93 versus ↓35.86 mg/dL), compared to the sitagliptin/metformin combination after 12-week follow-up, indicating superior efficacy relative to the sitagliptin-based regimen.

Conclusion: Dapagliflozin demonstrated a more significant improvement in glycemic control parameters compared to sitagliptin, although both treatment regimens were effective. These findings support the preferential consideration of a dapagliflozin-based treatment regimen for improved glycemic management.

Trial Registration: The trial protocol was registered at the Iraqi Clinical Research Registry (Registration No: ICRR-2025-121) and approved by the Medicine College of Baghdad University and the Pharmacy College of Al-Mustansiriyyah University in Iraq.

Implication for health policy/practice/research/medical education:

In this study, the results indicated that both treatment regimens, including a combination of dapagliflozin/metformin and sitagliptin/metformin, were associated with notable improvements in glycemic control. The pattern of response to treatment of patients who received dapagliflozin/metformin was more significant, where the decline in all measured parameters appeared consistently greater. Overall, the results point toward a more robust glycemic control with dapagliflozin therapy, while still supporting the effectiveness of both treatment strategies.

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Introduction

Type 2 diabetes mellitus (T2DM) has risen in recent decades (1) and emerged as one of the most common metabolic diseases, placing an enormous strain on global health systems (2,3). According to the international diabetes federation declaration, in 2021, almost 537 million people around the world were living with diabetes, a pattern projected to be more than 780 million by 2045 (4-6). The epidemiological pattern of T2DM is affected by urbanization and inactive lifestyles, growing ageing populations, and increasing obesity, all of which conspire to sustain an unrelenting upward trend in disease prevalence across different income-level nations (2). Cardiovascular disease (CVD) outcome is one of the particularly alarming dimensions related to this burden; a systematic review study including data from 57 countries indicated that about one-third of individuals with T2DM are affected by CVD, with coronary artery disease and stroke accounting for approximately half of all diabetes-related mortality (7).

Prolonged hyperglycemia is one of the leading causes of both microvascular and macrovascular complications in T2DM patients, and rigorous glycemic management remains the cornerstone of disease management (8,9). Evidence from a study in the United Kingdom confirmed that intensive diabetic control confers durable benefits in reducing myocardial infarction and all-cause death (10). Beyond mean glucose levels, glycated hemoglobin (HbA1c) variability has independently been shown to predict major cardiovascular events in patients with T2DM, even among those who appear to be at target glycemic levels, underscoring the need for stable and consistent glycemic control rather than merely achieving short-term targets (11-13). Metformin, a biguanide with well-established efficacy and a favorable safety and cost profile, has long held its position as the recommended first-line pharmacological agent for T2DM; however, the majority of patients require additional antidiabetic agents over time owing to the progressive nature of beta-cell decline (14,15).

Among the drug classes used in combination with metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium-glucose cotransporter-2 (SGLT2) inhibitors have attracted considerable clinical interest because of their complementary mechanisms of action, low hypoglycemia risk, and well-characterised safety profiles (16,17). Sitagliptin, an extensively studied DPP-4 inhibitor, works by prolonging endogenous incretin activity, thereby enhancing glucose-dependent insulin secretion and suppressing glucagon, and has demonstrated consistent HbA1c reductions when added to metformin across large-scale trials (18). Dapagliflozin, a selective SGLT2 inhibitor, reduces plasma glucose by promoting urinary glucose excretion in an insulin-independent manner and has proven effective as an add-on to metformin in patients with inadequate glycemic control (19). Head-

to-head comparisons of the two agents are relatively limited; a randomized clinical trial demonstrated that sitagliptin achieved superior glycemic improvement over dapagliflozin in patients with T2DM and mild renal insufficiency (20), while a Japanese prospective randomized study reported a greater benefit of dapagliflozin on cardiometabolic risk factors compared with sitagliptin in patients with early-stage, inadequately controlled T2DM (21). These contrasting findings highlight the need for further head-to-head evidence, particularly in open-label, parallel-group randomized designs that reflect real-world clinical practice. The present study was therefore conducted to compare the glycemic efficacy of the sitagliptin/metformin combination against the dapagliflozin/metformin combination in patients with T2DM.

Objectives

This study aimed to compare the effects of sitagliptin/metformin versus dapagliflozin/metformin combination therapy on glycemic control, evaluated by changes in HbA1c, fasting blood sugar (FBS), and postprandial BS levels, in patients with T2DM over a 12-week treatment period.

Materials and Methods

Study design and participants

This randomized clinical trial used a parallel-group, open-label design to compare the effects of sitagliptin/metformin versus dapagliflozin/metformin on glycemic control in adults with T2DM. The study was carried out from June to December 2025 at two central teaching hospitals in Iraq, both of which provide routine outpatient care for patients with diabetes and follow similar standardized management protocols.

Inclusion criteria and exclusion criteria

Adult patients with a confirmed diagnosis of T2DM were considered eligible if they had been on stable antidiabetic therapy, including metformin, for at least three months before enrollment. Patients were required to have suboptimal glycemic control at screening, defined as an HbA1c level between 7.0% and 10.0%, despite ongoing treatment. Individuals had to be willing and able to attend follow-up visits over the 12-week study period and to provide written informed consent after a full explanation of the study procedures and potential risks. Patients were excluded if they had voluntarily withdrawn from the study, or did not adhere to the study protocol, used other DPP-4 and SGLT2 inhibitors during the study period, and patients with incomplete glycemic laboratory tests at 12-week follow-up.

Sample size

The samples were collected by the simple randomized sampling method. The sample size calculation was based

on the primary endpoint, defined as the between-group difference in change in HbA1c from baseline to week 12. Drawing on previously published trials of metformin-based combination therapy, we assumed a more conservative expected mean difference of 0.5 percentage points in HbA1c, with a pooled standard deviation of 1.0. Under these assumptions, a minimum of 27 patients per group was required to detect the specified difference with a two-sided alpha level of 0.05 and 80% power, using an independent samples t-test implemented in G*Power version 1.3.1. To account for an anticipated attrition rate of approximately 10%, whether due to withdrawal or protocol violations, we planned to recruit a total of 60 participants, allocated in equal numbers to the sitagliptin–metformin and dapagliflozin–metformin treatment arms.

Randomization/allocation

Once eligibility had been confirmed and baseline assessments completed, participants were randomly assigned in a 1:1 ratio to receive either sitagliptin/metformin or dapagliflozin/metformin. Randomization was performed using a computer-generated allocation sequence with a fixed block size of four to maintain balance between the treatment arms over the course of recruitment. Treatment codes were placed into consecutively numbered, opaque, sealed envelopes to ensure concealment of group allocation. At the initial study visit, the investigator opened the next envelope in numerical order and prescribed the corresponding study regimen, without prior knowledge of the upcoming assignment.

Blinding

Blinding in this trial was limited due to the open-label design. Because the two treatment regimens differed in dosing schedules and packaging, patients and treating caregivers were aware of group allocation. However, the laboratory staff who analyzed HbA1c, FBS, and postprandial BS samples were not involved in clinical care and were kept unaware of treatment assignment. Outcome data were coded before analysis, and the statistician performed the primary efficacy analyses using anonymized group labels.

Intervention

Sitagliptin/metformin treatment group: Participants randomized to the DPP-4 inhibitor arm received SITAVIA Plus® tablets, each containing sitagliptin 50 mg and metformin hydrochloride 500 mg (Pioneer Pharmaceutical Industries, Iraq). The starting regimen was one tablet taken twice daily, in the morning and evening, corresponding to a total daily dose of sitagliptin 100 mg and metformin 1,000 mg. For individuals who had been taking more than 1,000 mg/d of metformin before enrollment, additional immediate-release metformin 500

mg tablets were prescribed, as needed, to maintain their pre-study metformin dose up to a maximum of 2,000 mg/d, provided that gastrointestinal tolerance was acceptable and renal function remained adequate. Dose adjustment of metformin was permitted at the week-4 visit, guided by FBS values, reported gastrointestinal symptoms, and the treating investigator's clinical judgment. The sitagliptin dose was fixed at 100 mg/d in line with the product labeling, whereas metformin could be titrated in 500-mg increments to a maximum of 2,000 mg/d. Participants were advised to take all study medication with meals to help minimize gastrointestinal adverse effects.

Dapagliflozin in combination with metformin group: Participants who were allocated to the SGLT2 inhibitor group received DIAZAC M ER®, a fixed-dose combination tablet containing dapagliflozin 10 mg and metformin hydrochloride extended-release 1,000 mg (Ajanta Pharma Ltd., India). The standard regimen was one tablet taken once daily with the evening meal, providing a total daily dose of dapagliflozin 10 mg and metformin 1,000 mg. In line with the approach used in the comparator arm, additional metformin tablets were prescribed when necessary to match each patient's pre-study metformin dose, up to a maximum total daily metformin dose of 2,000 mg. Dose adjustments were considered at the week-4 visit for patients who maintained FBS values above 180 mg/dL despite good gastrointestinal tolerability, with background metformin titrated to the highest permitted dose. Dapagliflozin was not increased beyond 10 mg/d. Participants were advised to maintain adequate hydration throughout treatment and were counseled regarding the signs and symptoms of genitourinary infections, with instructions to report such complaints promptly.

Data collection

For each eligible patient after having taken informed written consent, baseline demographic characteristics were obtained at the time of enrollment through a brief face-to-face interview and review of the medical record. Demographic data (age, sex), diabetes duration, and anthropometric indices, including weight and height for calculation of body mass index (BMI) were recorded by the study nurse using a standardized case-report form. Fasting venous blood samples were taken after an overnight fast to measure FBS and HbA1c, and a postprandial blood sample was collected 2 hours after the main meal to determine 2-hour postprandial blood sugar. Participants were then assigned to receive either sitagliptin/metformin or dapagliflozin/metformin according to the study protocol and were followed for 12 weeks with no modification in background lifestyle advice. At the end of the 12 weeks, the same set of clinical and laboratory parameters was reassessed, using identical procedures and equipment, to minimize measurement variability. All data were entered into a predesigned electronic database by trained personnel, and numerical entries were checked against the

original paper forms by a second investigator to reduce transcription errors before statistical analysis.

Outcomes measurement

The outcomes were comparing the glycemic parameters, including HbA1c, FBS, and postprandial BS between the two treatment groups of sitagliptin/metformin versus dapagliflozin/metformin.

Statistical analysis

Data were analyzed by SPSS version 27 (IBM Corp., USA). The normality status was assessed by the Shapiro-Wilk. Comparison between the two treatment groups was assessed by the independent-samples t-test for continuous variables and the chi-square test for categorical variables. Comparison of glycemic parameters within groups between the times of 12 weeks and baseline was conducted by the paired T-test. The parametric tests were conducted for their higher statistical efficiency, considering the issue that parametric and nonparametric tests had similar *P* values. A *P* < 0.05 was considered significant.

Results

Initially, 78 T2DM patients enrolled in the eligibility assessment; 15 of them were excluded (10 patients met no inclusion criteria, and 5 declined to participate). After that, 63 patients were randomly assigned into two

treatment groups; 31 T2DM patients were assigned to the dapagliflozin/metformin group, and 32 were assigned to the sitagliptin/metformin group. In the sitagliptin/metformin group, 2 patients lost follow-up (one because of non-adherence to treatment and the other due to voluntary withdrawal); finally, 30 patients were analyzed in the final analysis. In the dapagliflozin/metformin treatment group, 1 patient lost follow-up due to voluntary withdrawal, resulting in 30 patients being included in the final analysis (Figure 1).

This study included 60 T2DM patients with a mean age of 51.62 ± 8.87 years, with equal assignment of 30 patients to each sitagliptin/metformin and dapagliflozin/metformin treatment group. The comparative analysis indicated that the frequency distribution of gender, age, BMI, and diabetes duration was comparable between the two treatment groups and showed no statistically significant difference (Table 1).

The results demonstrated that the two treatment groups showed broadly similar patterns of glycemic control at baseline, with no statistically significant imbalance in their initial indices of glucose regulation between the two groups. Over the course of a 12-week follow-up, both regimens led to clear within-group improvements in HbA1c status as well as fasting and postprandial glucose levels. However, the two treatment groups indicated significant differences in the glycemic parameters at 12-

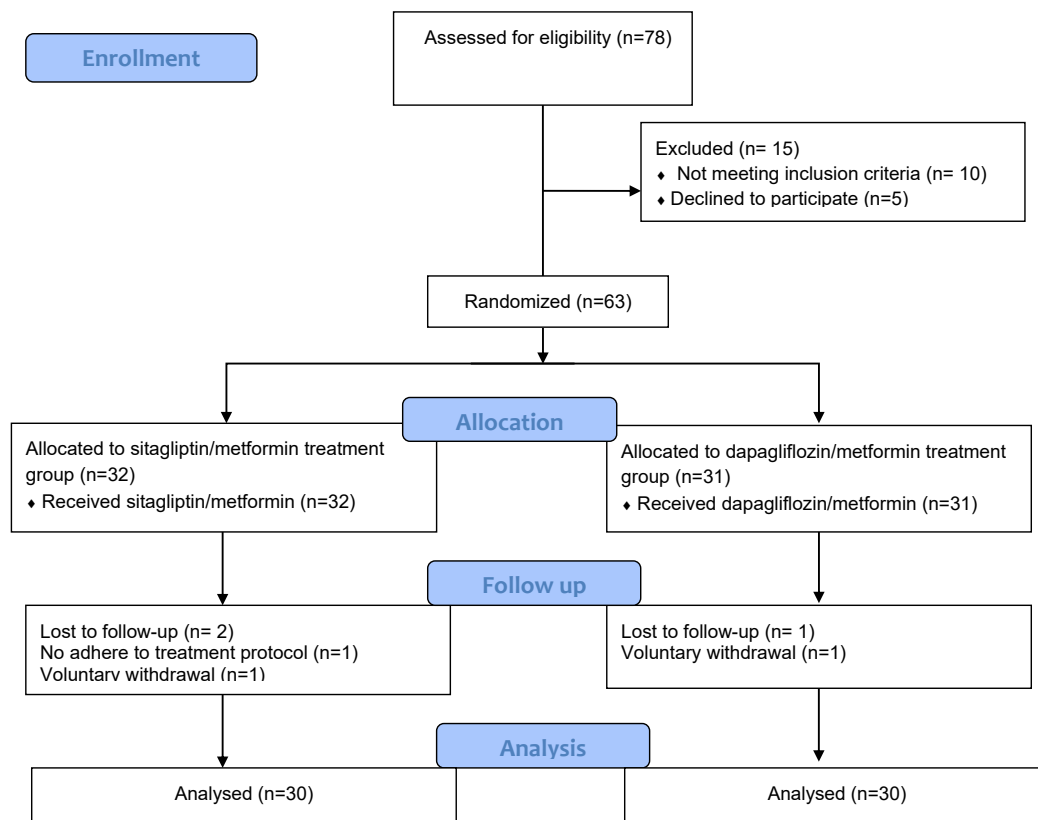


Figure 1. CONSORT flow diagram of the study.

Table 1. Comparison of demographic profile at baseline time among the sitagliptin/metformin and dapagliflozin/metformin treatment groups

Qualitative variables	Treatment group		Total (N = 60)	P value*
	Sitagliptin/metformin (n = 30)	Dapagliflozin/metformin (n = 30)		
Gender N (%)	Male	17 (54.8)	14 (45.2)	0.438
	Female	13 (44.8)	16 (55.2)	
Quantitative variables	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	P value**
Age (year)	52.15 $\pm$ 7.36	51.1 $\pm$ 10.26	51.62 $\pm$ 8.87	0.651
Diabetes duration (year)	7.16 $\pm$ 2.64	6.70 $\pm$ 2.79	6.93 $\pm$ 2.71	0.522
BMI (kg/m ²)	30.81 $\pm$ 3.65	31.15 $\pm$ 3.42	30.95 $\pm$ 4.12	0.723

BMI: Body mass index, SD: Standard Deviation, *Chi-square, **Independent T-test.

Table 2. Comparison of glycemic parameters among the sitagliptin/metformin and dapagliflozin/metformin groups during the study period

Glycemic parameters	Treatment group		P value*
	Sitagliptin/metformin (Mean ± SD)	Dapagliflozin/metformin (Mean ± SD)	
	Baseline		
HbA1c (%)	8.49 ± 0.69	8.65 ± 0.62	0.343
FBS (mg/dL)	178.96 ± 29.92	179.92 ± 26.01	0.895
2hPP-BS (mg/dL)	253.33 ± 41.28	244.02 ± 33.03	0.339
12 weeks after intervention			
HbA1c (%)	7.69 ± 0.89	7.17 ± 0.78	0.019
FBS (mg/dL)	144.73 ± 32.86	129.28 ± 26.57	0.049
2hPP-BS (mg/dL)	217.44 ± 54.32	166.09 ± 44.37	<0.001

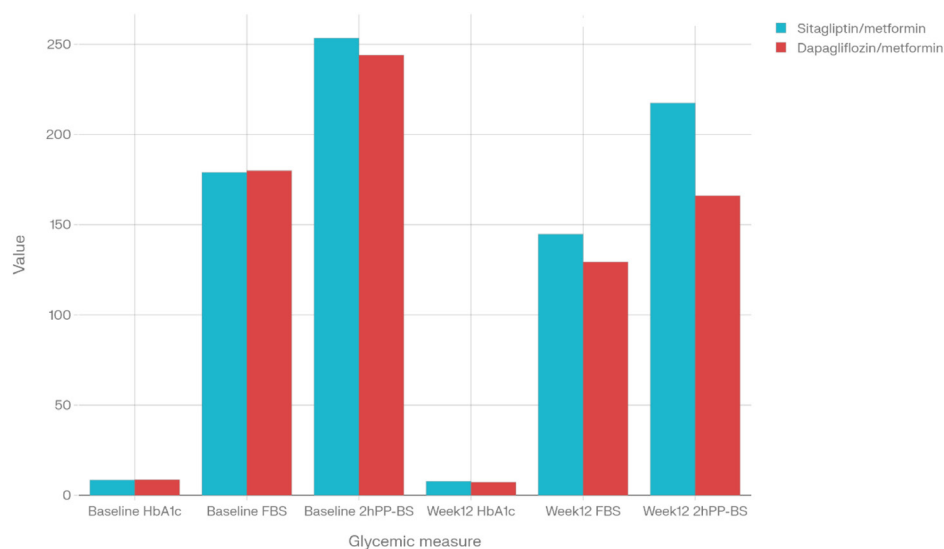
FBS: Fasting blood sugar, 2hPP-BS: 2-hour postprandial blood sugar, SD: Standard Deviation, *Independent T-test.

week follow-up, so that these parameters were significantly lower in the dapagliflozin/metformin group (Table 2 and Figure 2).

The comparative analysis of glycemic indices 12 weeks after the intervention demonstrated that both treatment approaches led to significant improvements from baseline across all measured parameters, although the magnitude of change consistently favored the dapagliflozin combined with metformin regimen. Reductions in HbA1c were more significant in the dapagliflozin-based arm, and a similar pattern was found for FBS, where the decrease

was greater in patients receiving dapagliflozin/metformin compared to those receiving sitagliptin/metformin. This trend became even more evident in postprandial glucose levels, with the dapagliflozin combination demonstrating a substantially larger decline in this glycemic parameter (Table 3 and Figure 3).

Within-group comparison between baseline and 12-week follow-up indicated that both therapeutic regimens were associated with statistically significant improvements in all assessed glycemic parameters. Sitagliptin/metformin combination treatment was accompanied with a consistent

**Figure 2.** Comparison of glycemic parameters at baseline and 12 weeks after intervention between the two treatment groups. FBS: Fasting blood sugar, 2hPP-BS: 2-hour postprandial blood sugar.

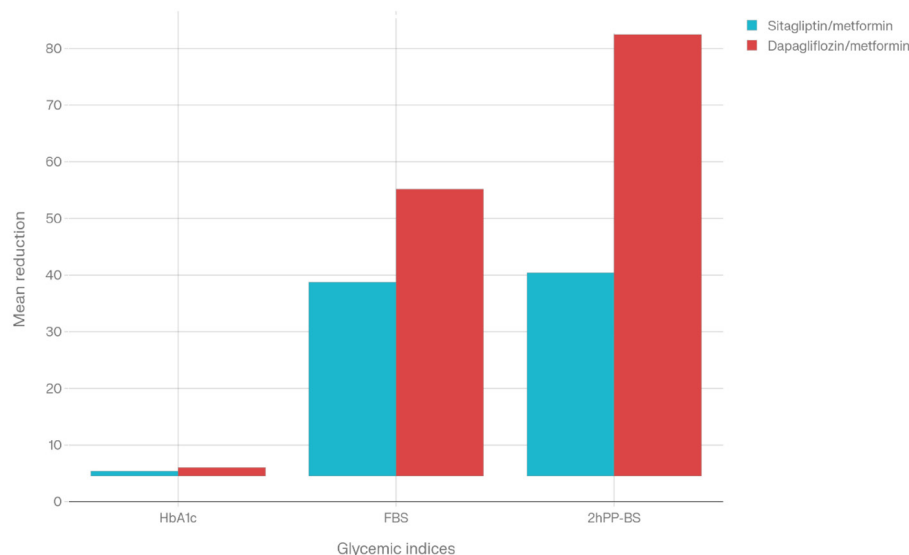


Figure 3. Comparison of changes in glycemic parameters over 12 weeks by treatment groups. FBS: Fasting blood sugar, 2hPP-BS: 2-hour postprandial blood sugar.

reduction in HbA1c, FBS, and postprandial BS levels. However, the dapagliflozin/metformin treatment yielded more significant changes across the same parameters, with a greater relative decline in HbA1c and a more substantial reduction in both FBS and postprandial BS levels. Collectively, while both therapeutic regimens improved glycemic status, the dapagliflozin/metformin combination indicated a greater magnitude of response across all measured outcomes (Table 4 and Figure 4).

Discussion

Both treatment groups in the present study demonstrated statistically significant within-group improvements in all three glycemic parameters, HbA1c, FBS, and 2-hour postprandial BS, compared with baseline values. These findings are consistent with the established efficacy of both drug classes as add-on therapies to metformin. Sitagliptin, a competitive inhibitor of the DPP-4 enzyme, exerts its glucose-lowering action by prolonging the activity of

Table 3. Comparison of glycemic parameter changes between 12 weeks after intervention and baseline among the sitagliptin/metformin and dapagliflozin/metformin groups

Glycemic parameters (Mean ± SD)	Treatment group		Mean difference	95% CI	P value*
	Sitagliptin/ metformin	Dapagliflozin/metformin			
HbA1c (%)	↓ 0.80 ± 0.55	↓ 1.48 ± 0.67	0.68	0.36 – 1.01	<0.001
FBS (mg/dL)	↓ 34.19 ± 19.61	↓ 50.64 ± 26.46	16.45	4.41 – 28.49	0.008
2hPP-BS (mg/dL)	↓ 35.86 ± 23.90	↓ 77.93 ± 24.10	42.07	29.66 – 54.47	<0.001

FBS: Fasting blood sugar, 2hPP-BS: 2 hours postprandial blood sugar, CI: confidence interval, SD: Standard Deviation, *Independent T-test.

Table 4. Comparative analysis of glycemic parameters, 12 weeks after the intervention versus baseline, within each of the sitagliptin/metformin and dapagliflozin/metformin groups

Glycemic parameters	Mean difference			Percentage change	P value*
	Mean	Standard Error	95% CI		
Sitagliptin/metformin (n = 30)					
HbA1c (%)	- 0.80	0.10	- 1.01 – [- 0.59]	↓ 9.42%	<0.001
FBS (mg/dL)	- 34.19	3.58	- 41.51 – [- 26.86]	↓ 19.10%	<0.001
2hPP-BS (mg/dL)	- 35.86	4.36	- 44.78 – [- 26.93]	↓ 14.15%	<0.001
Dapagliflozin/metformin (n = 30)					
HbA1c (%)	- 1.48	0.12	- 1.73 – [- 1.23]	↓ 17.10%	<0.001
FBS (mg/dL)	- 50.64	4.83	- 60.52 – [- 40.76]	↓ 28.14%	<0.001
2hPP-BS (mg/dL)	- 77.93	4.40	- 86.93 – [- 68.92]	↓ 31.93%	<0.001

FBS: Fasting blood sugar, 2hPP-BS: 2 hours postprandial blood sugar, CI: confidence interval, *Paired T-test.

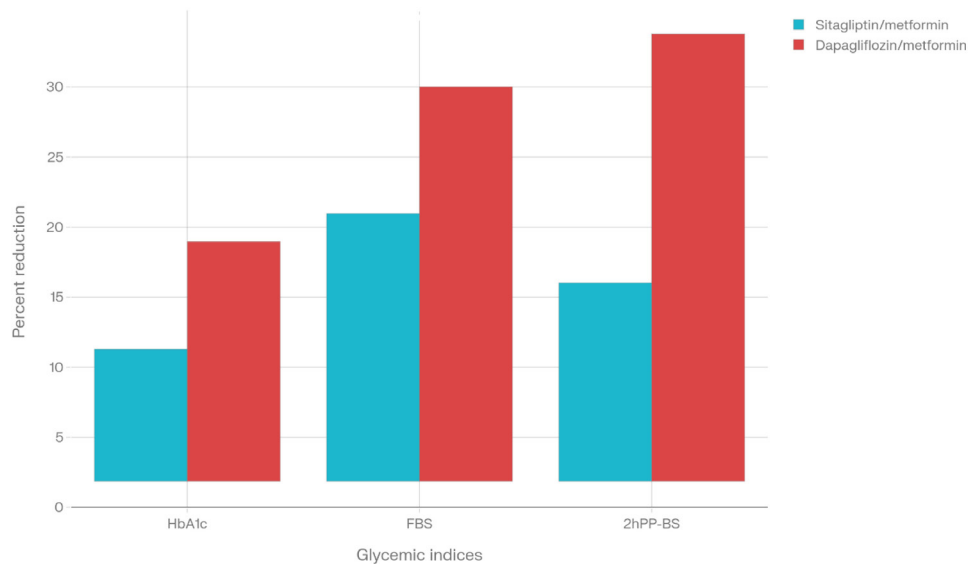


Figure 4. Percentage reduction in glycemic indices over 12 weeks in the treatment groups. FBS: Fasting blood sugar, 2hPP-BS: 2-hour postprandial blood sugar.

endogenous incretin hormones, particularly glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), thereby stimulating glucose-dependent insulin secretion and suppressing glucagon release (18). A randomized clinical trial by Shankar et al has documented that the addition of sitagliptin to ongoing metformin therapy significantly reduces HbA1c by approximately 0.7% from baseline, along with meaningful reductions in FBS and 2-hour postprandial BS (22). In a multicenter study involving Chinese patients with T2DM, initial co-administration of sitagliptin and metformin yielded significant improvement in glycemic control and was generally well tolerated (23). Similarly, dapagliflozin, acting through an insulin-independent renal mechanism, inhibits SGLT2 cotransporters in the proximal tubule, thereby reducing glucose reabsorption, lowering the renal glucose threshold, and inducing sustained glucosuria, resulting in clinically meaningful reductions in HbA1c and FBS (19). Clinical evidence has consistently confirmed that dapagliflozin, whether as monotherapy or in combination with metformin, produces significant HbA1c reductions (24). The within-group improvements observed in the present study for both regimens are therefore in accord with existing pharmacological and clinical evidence.

The most clinically significant finding of the present trial is that the dapagliflozin/metformin combination produced a greater reduction in HbA1c (−1.48%) compared with sitagliptin/metformin (−0.80%) after 12 weeks of treatment. This magnitude of difference aligns with and is broadly supported by a growing body of comparative literature. A prospective, randomized study by Hong et al comparing sitagliptin, dapagliflozin, and lomeglitazone, each added to sulfonylurea and metformin therapy, demonstrated that all three agents achieved significant reductions in HbA1c, with dapagliflozin

conferring additional benefits in body composition (25). The randomized, 24-week trial study by Fuchigami et al, compared the effectiveness of dapagliflozin and sitagliptin on cardiometabolic risk factors, resulting in superior efficacy of dapagliflozin on these risk factors (21). In a separate Japanese investigation, dapagliflozin was reported to exert beneficial effects on glycemic parameters comparable to sitagliptin and metformin monotherapy over 12 weeks in drug-naïve Japanese patients, with the additional advantages of significant body weight reduction and improvement in serum adiponectin levels (26). Furthermore, a comparative effectiveness study involving 144 614 adults with T2DM found that patients initiating SGLT2 inhibitor therapy achieved favorable glycemic and cardiometabolic outcomes across all baseline HbA1c strata when compared with DPP-4 inhibitor initiators (27). A meta-analysis of 14 randomized controlled trials encompassing 4,828 patients demonstrated that the addition of SGLT2 inhibitors to a DPP-4 inhibitor background was associated with significant reductions in HbA1c (−0.71%), FBS (−25.62 mg/dL), postprandial BS (−44.00 mg/dL), and body weight (−2.05 kg) compared with DPP-4 inhibitor-based regimens alone (28). Collectively, the superior HbA1c reduction observed in the dapagliflozin/metformin arm of the present study is consistent with these multiple lines of evidence supporting the stronger glycemic efficacy of SGLT2 inhibitor-based combinations at comparable treatment durations.

The present study revealed that the dapagliflozin/metformin group achieved a markedly greater reduction in FBS (−50.64 mg/dL) compared with the sitagliptin/metformin group (−34.19 mg/dL). Several clinical investigations have shown that dapagliflozin produces greater reductions in FBS than sitagliptin-based regimens. In the CompoSIT-R study, a prospective, randomized trial

in patients with T2DM and mild renal insufficiency on background metformin $\pm$ sulfonylurea, dapagliflozin was associated with a greater reduction in FBS, while sitagliptin achieved superior reductions in HbA1c overall (20). A prospective comparison of dapagliflozin and sitagliptin in patients with early-stage, inadequately controlled T2DM similarly found that dapagliflozin was significantly superior in reducing FBS, insulin levels, and uric acid, and in achieving the composite primary endpoint of cardiometabolic improvement (21). The pronounced reduction in FBS with dapagliflozin/metformin in the present study therefore reinforces prior evidence for the preferential action of SGLT2 inhibitors on fasting glycemia in real-world and clinical trial populations.

Beyond FBS, the present trial demonstrated that dapagliflozin/metformin achieved a notably greater reduction in 2-hour postprandial BS (-77.93 mg/dL) than sitagliptin/metformin (-35.86 mg/dL). This finding merits careful contextual discussion, as prior studies have yielded divergent conclusions regarding the postprandial efficacy of each agent class. DPP-4 inhibitors such as sitagliptin are generally believed to confer particular benefit on postprandial BS regulation given their incretin-potentiating mechanism, augmenting meal-stimulated insulin secretion and suppressing inappropriate glucagon responses (18). Nevertheless, data from several trials and systematic reviews suggest that SGLT2 inhibitors, through their continuous renal glucose excretion mechanism, also significantly attenuate postprandial glucose levels when assessed across the full glucose exposure curve. Two systematic review and meta-analysis of 14 and 7 randomized controlled trials confirmed that the combination of SGLT2 and DPP-4 inhibitors achieved greater reductions in both FBS and 2-hour postprandial BS compared with DPP-4 inhibitor monotherapy (28,29). The larger postprandial glucose reduction in the dapagliflozin/metformin arm of the current study may partly reflect the higher baseline glucose burden in that group, the cumulative contribution of continuous glucosuria on overall glucose flux, or the synergistic glucose-lowering actions of SGLT2 inhibition combined with metformin's insulin-sensitizing properties, and should be interpreted with these contextual considerations in mind.

Overall, the findings of this trial indicate that both sitagliptin/metformin and dapagliflozin/metformin are effective therapeutic strategies for the improvement of glycemic control in patients with T2DM. However, the dapagliflozin/metformin combination demonstrated consistently superior reductions across all three glycemic parameters compared with sitagliptin/metformin, with notably greater decreases in HbA1c. These results are broadly concordant with existing clinical evidence supporting the favorable glycemic efficacy of SGLT2 inhibitor-based combinations in renally intact patients with inadequately controlled T2DM. While the superior glycemic profile of dapagliflozin/metformin supports

its preferential consideration in this clinical context, individualized treatment decisions should continue to account for patient-specific factors, including renal function, cardiovascular risk, tolerability, and cost, as both regimens represent evidence-based therapeutic options across the spectrum of T2DM management.

Conclusion

The present study results demonstrated that both sitagliptin/metformin combined treatment and dapagliflozin/metformin combination are effective in improving glycemic control. However, the dapagliflozin-based combination treatment was accompanied by a greater magnitude of improvement across all assessed parameters, including HbA1c, FBS, and postprandial BS levels. These results suggest that, while both therapeutic regimens are beneficial, the dapagliflozin/metformin combination strategy may offer a more potent effect in achieving glycemic control targets. This differential response may have important clinical implications when selecting individualized treatment approaches for patients requiring intensified glycemic management.

Limitations of the study

Our study has several strengths, including its prospective, randomized, parallel-group design, standardized follow-up protocol, and assessment of three complementary glycemic parameters in a clinical trial framework. These design features reduce the risk of selection bias and confounding, enabling a more robust between-group comparison. Nonetheless, the short 12-week period, the open-label design, the modest sample size from only two teaching hospitals in a single country, and medication adherence based primarily on clinical follow-up and patient report rather than objective measures are the most common limitations that should be acknowledged in the case of interpreting these study results.

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Authors' contribution

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Formal analysis: Safa K. Qasim.

Investigation: Safa K. Qasim and Kadhim Ali Kadhim.

Methodology: Safa K. Qasim and Suaad Muhammed Abd-Alqader.

Project management: Kadhim Ali Kadhim.

Resources: All authors.

Supervision: All authors.

Validation: Kadhim Ali Kadhim and Suaad Muhammed Abd-Alqader.

Writing—original draft: All authors

Writing—review and editing: All authors

Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical issues

The research was performed in accordance with the principles of the Declaration of Helsinki. This study was conducted at two central teaching hospitals in Iraq and was approved by the Medicine College of Baghdad University and the Pharmacy College of Al-Mustansiriyah University in Iraq. The study protocol was also registered at the Iraqi Clinical Research Registry (Registration No: ICRR-2025-121). Accordingly, informed written consent was taken from all participants before any intervention. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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