International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Cost Effective Analysis of DPPIV Inhibitors and Glucosidase Inhibitors as add on Therapy With Metformin in Type 2 DM Patients At Tertiary Care Hospital

Ketan Avinash Patil[1], Amreen Saba[2], Savithri Desai[3]

[1]Associate professor, Department of Pharmacology, Mahavir Institute of Medical Sciences, Shivareddypet, Vikarabad, Ranga Reddy - 501 102, Telangana, India.
[2]Associate professor, Department of Pharmacology, Faculty of Medical Sciences, Khaja Bandanawaz University, Kalaburagi, - 585 104, Karnataka, India.
[3]Associate professor, Department of Pharmacology, Mahavir Institute of Medical Sciences, Shivareddypet, Vikarabad, Ranga Reddy - 501 102, Telangana, India.

OPEN ACCESS

Corresponding Author:

Dr. Savithri Desai
Associate professor, Department of Pharmacology, Mahavir Institute of Medical Sciences, Shivareddypet, Vikarabad, Ranga Reddy - 501 102, Telangana, India.

Received: 04-01-2026
Accepted: 23-01-2026
Available online: 01-02-2026

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a long-term metabolic disease with a rapidly rising burden; pooled estimates suggest an overall prevalence of about 11.4%. While initiating early oral combination therapy can improve glycaemic control, medication choices should also account for affordability, as ongoing treatment can create a substantial financial load for patients and health systems.

Objectives: To assess and compare the cost-effectiveness of adding DPP-4 inhibitors versus α-glucosidase inhibitors to metformin in individuals with T2DM, using changes in HbA1c, fasting plasma glucose (FPG), and post-prandial plasma glucose (PPG) as indicators of clinical effectiveness.

Methods: A cost-effectiveness evaluation was carried out in a tertiary care hospital, comparing two add-on strategies to metformin. Ethical approval was obtained and all participants provided written informed consent. Only direct drug acquisition costs were included. For each treatment arm, the total cost over 3 months was calculated from the daily drug cost multiplied by the duration of therapy. Cost-effectiveness was reported as the cost required to achieve a 0.1% reduction in HbA1c and a 1 mg/dL reduction in FPG and post-prandial blood glucose at 12 weeks. The DPP-4 inhibitor group included teneligliptin, sitagliptin, and vildagliptin, while the α-glucosidase inhibitor group included acarbose and voglibose.

Results: There were 34 patients in the DPP-4 inhibitor arm (teneligliptin 12, sitagliptin 15, vildagliptin 7) and 31 in the α-glucosidase inhibitor arm (acarbose 13, voglibose 18). Most participants (92%) had associated comorbidities, including hypertension and ischaemic heart disease. Mean age was similar between groups (57.32 ± 13.99 vs 56.88 ± 12.89 years). At 3 months, HbA1c reduction was higher with DPP-4 inhibitors (0.71). Overall, the DPP-4 inhibitor arm demonstrated lower cost per unit improvement in glycaemic indices, whereas α-glucosidase inhibitors were noted to be particularly beneficial for lowering post-prandial glucose.

Conclusion: Over 12 weeks as add-on therapy to metformin, DPP-4 inhibitors provided greater HbA1c reduction and better cost-effectiveness per unit glycaemic improvement than α-glucosidase inhibitors, while α-glucosidase inhibitors showed a relative advantage for post-prandial glucose control.

Keywords*: Type 2 diabetes mellitus; metformin add-on therapy; DPP-4 inhibitors; α-glucosidase inhibitors; cost-effectiveness analysis; HbA1c; fasting plasma glucose; post-prandial glucose..*

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a progressive, lifelong metabolic disorder characterised by chronic hyperglycaemia resulting from insulin resistance with a gradual decline in pancreatic β-cell function. It contributes substantially to premature cardiovascular morbidity, microvascular complications, disability, and avoidable health-care utilisation. In India, population-based data show a high and heterogeneous prevalence of diabetes and prediabetes across states, reflecting rapid epidemiological transition and lifestyle change [1]. Globally, contemporary estimates continue to demonstrate a steep rise in diabetes prevalence, with projections indicating a sustained increase in the coming decades, particularly in low- and middle-income countries where health systems face dual burdens of infectious and non-communicable disease care [2]. Against this backdrop, improving glycaemic control is not only a clinical priority but also a public health imperative.

Long-term glycaemic exposure is strongly associated with both microvascular and macrovascular outcomes in T2DM. Large prospective evidence has demonstrated a graded relationship between increasing HbA1c and complications, supporting the clinical objective of achieving and maintaining durable glycaemic control as early as feasible [4]. However, T2DM is inherently progressive, and many patients fail to achieve targets on monotherapy over time. Current standards of care therefore emphasise timely treatment intensification, individualisation of therapy based on comorbidity profile and hypoglycaemia risk, and selection of agents that balance efficacy, safety, and patient-centred factors [3]. In newly diagnosed T2DM, early combination therapy has also been shown to improve glycaemic durability compared with a stepwise approach in suitable patients, indicating that therapeutic inertia can be harmful when glycaemia remains above target [5].

Metformin remains the foundational pharmacotherapy for most adults with T2DM, but a substantial proportion require add-on therapy to address fasting and post-prandial hyperglycaemia. Post-prandial glucose (PPG) excursions, in particular, contribute significantly to overall glycaemic burden in many patients, especially those with near-target fasting plasma glucose (FPG). Post-prandial hyperglycaemia has been linked to oxidative stress, endothelial dysfunction, and cardiovascular risk pathways; therefore, therapies that attenuate PPG may offer clinically meaningful advantages in selected phenotypes [6]. Clinical trial data also highlight that targeting prandial glycaemia alone does not automatically translate into cardiovascular benefit, reinforcing the need to select therapy based on both glycaemic endpoints and broader risk context [7,8].

Among the commonly used oral add-on options after metformin, dipeptidyl peptidase-4 (DPP-4) inhibitors and α-glucosidase inhibitors (AGIs) have distinct and complementary pharmacological profiles. DPP-4 inhibitors enhance endogenous incretin activity, improving glucose-dependent insulin secretion and suppressing glucagon, thereby reducing HbA1c with a low intrinsic risk of hypoglycaemia and generally neutral weight effects. Cardiovascular outcomes evidence for at least one widely used DPP-4 inhibitor (sitagliptin) supports cardiovascular safety in high-risk T2DM populations, which is relevant when choosing long-term therapy in routine practice where comorbid hypertension and ischaemic heart disease are common [9]. AGIs (e.g., acarbose, voglibose) delay intestinal carbohydrate absorption, thereby primarily targeting post-prandial hyperglycaemia; their utility is often greatest in individuals with prominent PPG excursions, high carbohydrate dietary patterns, or where avoidance of hypoglycaemia is important. Evidence from trials in impaired glucose tolerance has also shown that acarbose can reduce progression to diabetes, supporting the physiological rationale for its prandial mechanism [11]. Further, in coronary heart disease patients with impaired glucose tolerance, acarbose has been evaluated for cardiovascular and diabetes outcomes, indicating sustained interest in its broader clinical implications beyond glucose lowering alone [12].

Head-to-head clinical comparisons between DPP-4 inhibitors and AGIs are directly relevant to decision-making in settings where both classes are accessible. In Japanese patients with T2DM inadequately controlled on sulfonylurea, sitagliptin demonstrated non-inferior glycaemic efficacy compared with an AGI, while class-specific differences remained apparent in post-prandial control and tolerability patterns [10]. Such comparative effectiveness evidence informs rational sequencing and combination choices in real-world clinics, particularly when intensification is constrained by tolerability, pill burden, or patient preference.

In parallel, adherence and persistence are increasingly recognised as determinants of real-world effectiveness. Patients commonly require multiple agents over time, and discontinuation or suboptimal persistence diminishes expected glycaemic benefit. Nationwide data indicate that persistence varies across modern antidiabetic classes and influences long-term outcomes and resource utilisation, underscoring why “best” therapy in trials may not translate into “best value” in practice if patients cannot continue treatment consistently [14]. This consideration is especially important in chronic diseases such as T2DM, where therapy is typically lifelong and comorbidity-driven polypharmacy is common.

The economic dimension is therefore central to therapy selection, particularly in tertiary care hospitals serving mixed socioeconomic populations. Direct drug acquisition costs represent a substantial component of diabetes care expenses, and in many Indian settings these costs are paid out-of-pocket. Pharmacoeconomic evaluation helps quantify value by linking the cost of therapy to measurable clinical benefit. Cost-effectiveness analysis (CEA) typically compares the incremental costs of competing strategies against incremental effectiveness, and best practice reporting is guided by internationally

accepted standards (e.g., CHEERS) to improve transparency and reproducibility [15]. A pragmatic approach used in short-term hospital-based evaluations is to express "cost per unit glycaemic improvement," such as cost per 0.1% HbA1c reduction or cost per 1 mg/dL reduction in FPG/PPG. While such outcomes do not substitute for long-term modelling with quality-adjusted life years, they can provide actionable evidence for formulary decisions and bedside counselling in resource-limited contexts.

Indian pharmacoeconomic data further reinforce the relevance of affordability when selecting add-on therapies. For example, comparative analyses in Indian outpatient practice have evaluated the cost-effectiveness of metformin plus teneligliptin relative to metformin plus glimepiride, demonstrating that treatment choice can materially alter "value for money" even over a short horizon [13]. However, direct cost-effectiveness comparisons between DPP-4 inhibitors and AGIs as add-on therapy to metformin remain limited in many tertiary care settings, despite both classes being routinely prescribed.

Accordingly, the present study is positioned to address a practical, policy-relevant question: in patients with T2DM receiving metformin, how does the cost-effectiveness of adding DPP-4 inhibitors compare with adding α-glucosidase inhibitors when effectiveness is assessed using HbA1c, fasting plasma glucose, and post-prandial plasma glucose over a defined follow-up period? By focusing on direct drug costs and clinically interpretable glycaemic endpoints, the study aims to generate context-specific evidence to support rational, patient-centred, and economically sustainable prescribing in tertiary care practice, where high comorbidity burden and long-term medication needs make "affordable effectiveness" as important as efficacy alone [1–3,10,13–15].

MATERIALS AND METHODS

Study design and setting

This work was conducted as a hospital-based comparative cost-effectiveness evaluation in a tertiary care teaching hospital, focusing on routine clinical management of adults with T2DM. The study was planned to compare two commonly prescribed oral add-on strategies to metformin—DPP-4 inhibitors and α-glucosidase inhibitors—because both are frequently used in day-to-day practice, yet differ in mechanism, glycaemic profile (fasting vs post-prandial control), tolerability, and cost. The analysis followed patients for a fixed period of 12 weeks (approximately 3 months), which was considered adequate to capture short-term changes in glycaemic indices, particularly HbA1c and plasma glucose levels, after initiation or continuation of add-on therapy.

Study duration

Participants were evaluated over a 3-month treatment window. Baseline data were captured at the time of enrolment (or at the time the add-on therapy was recorded as part of routine care), and follow-up values were obtained at the end of 12 weeks. The 12-week interval was selected to align with routine clinic follow-up schedules and to allow for measurable changes in HbA1c, which reflects average glycaemia over the preceding 8–12 weeks. Where follow-up visits varied slightly due to practical reasons, data were taken from the closest available visit within the routine outpatient follow-up pattern.

Ethical approval and consent

Before commencement, the study protocol was reviewed and approved by the Institutional Ethics Committee. The study was conducted in accordance with ethical principles for biomedical research involving human participants. All eligible individuals were informed about the nature and purpose of the evaluation in a language they could understand, including that participation would not alter their ongoing clinical care. Written informed consent was obtained from each participant prior to inclusion, and confidentiality of patient information was maintained throughout by limiting access to identifiers and using coded data for analysis.

Study population

The study included adult patients diagnosed with T2DM who were receiving metformin and for whom an additional oral antidiabetic agent was prescribed as part of usual clinical practice. Patients were recruited from outpatient and/or inpatient services of the hospital, depending on the availability of follow-up records and laboratory measurements. The target population reflected a real-world tertiary care cohort, where many patients typically present with coexisting conditions such as hypertension and ischaemic heart disease. This approach was intended to generate findings that are clinically practical and relevant to routine prescribing in similar settings.

Inclusion criteria (operational): Adult patients with established T2DM who were on metformin therapy and received add-on treatment with either a DPP-4 inhibitor or an α-glucosidase inhibitor were eligible. For inclusion, participants were required to have baseline and 12-week measurements for HbA1c, fasting plasma glucose (FPG), and post-prandial plasma glucose (PPG), enabling consistent assessment of effectiveness across both treatment strategies.

Exclusion criteria (operational): Patients were excluded if they had diabetes types other than T2DM (such as type 1 diabetes, gestational diabetes, or secondary diabetes), or if major therapeutic modifications occurred during follow-up that could confound the attribution of glycaemic change to the studied add-on class (for example, switching between the

comparator drug classes, starting insulin, or adding multiple additional glucose-lowering agents). Patients with incomplete outcome data at either baseline or 12 weeks were also excluded from the primary analysis to preserve interpretability of the cost-effectiveness comparisons.

Treatment groups (comparators)

Participants were grouped based on the class of add-on therapy prescribed with metformin. The DPP-4 inhibitor group included patients receiving teneligliptin, sitagliptin, or vildagliptin. The α-glucosidase inhibitor group included patients receiving acarbose or voglibose. The choice of drug and dose was determined by the treating physician according to routine clinical judgment, patient profile, and availability in the hospital setting; the study did not impose a fixed regimen or alter prescriptions. This pragmatic grouping was used to reflect real-world decision-making and to enable comparison of "class-based" cost-effectiveness, which is often how formulary and procurement decisions are made.

Data collection and measurements

Data were collected from patient case records, prescription details, and laboratory reports. Baseline demographic information such as age and sex, along with relevant clinical details including comorbidity status (e.g., hypertension and ischaemic heart disease), were documented to describe the study cohort and to ensure comparability between treatment groups. Glycaemic effectiveness was assessed using three routinely measured parameters: HbA1c (%), fasting plasma glucose (FPG, mg/dL), and post-prandial plasma glucose (PPG, mg/dL). Measurements were recorded at baseline and again at 12 weeks. The change in each glycaemic parameter over the follow-up period was calculated as the baseline value minus the 12-week value; a positive value therefore represented improvement. These outcomes were selected because they are clinically interpretable, widely available in hospital settings, and align with therapeutic goals in T2DM management.

Costing method (direct drug acquisition cost)

The economic evaluation was performed from the perspective of direct medication expenditure, restricting costs to drug acquisition only, as described in the PPT approach. Drug prices were obtained from the hospital pharmacy records or standard purchase pricing used in the institution. For each participant, the daily drug cost was calculated based on the prescribed dose and the unit price of the medicine. The total drug cost over the 3-month period was then estimated by multiplying the daily cost by the number of treatment days within the 12-week follow-up. Costs were summed within each group to generate total group expenditure. By restricting analysis to direct drug costs, the study aimed to produce a clear and practical estimate that is directly relevant to patient affordability and hospital procurement, while acknowledging that broader costs (such as investigations, travel, productivity loss, and complication-related admissions) were beyond the scope of this short-term evaluation.

Cost-effectiveness analysis

Cost-effectiveness was expressed as the cost required to achieve a defined unit of improvement in glycaemic outcomes. For HbA1c, cost-effectiveness was presented as the expense incurred for a 0.1% reduction, allowing fine-grained comparison between groups even when absolute changes were modest. For fasting and post-prandial glucose, cost-effectiveness was expressed as the cost for a 1 mg/dL reduction. For each treatment group, the total drug cost over 3 months was divided by the corresponding improvement in the glycaemic parameter (scaled appropriately for HbA1c). This resulted in three primary cost-effectiveness estimates per group: cost per 0.1% HbA1c reduction, cost per 1 mg/dL FPG reduction, and cost per 1 mg/dL PPG reduction. The two add-on strategies were then compared across these estimates; lower cost per unit improvement was interpreted as greater cost-effectiveness for that specific endpoint. In addition, the analysis considered the expected clinical pattern that DPP-4 inhibitors may provide broader HbA1c lowering while α-glucosidase inhibitors may show comparatively stronger effects on post-prandial glucose, which was taken into account when interpreting the endpoint-specific results.

Outcomes (primary and secondary)

The primary outcome of interest was cost-effectiveness expressed as cost per 0.1% reduction in HbA1c over 12 weeks, since HbA1c is the most widely accepted marker of overall glycaemic control and reflects average glucose exposure. Secondary outcomes included cost per 1 mg/dL reduction in FPG and PPG, and the comparative effectiveness of each add-on strategy in improving these parameters over the same period. Together, these outcomes were intended to provide a practical framework for selecting add-on therapy in tertiary care settings by balancing glycaemic benefit with direct medication cost, particularly in patients where long-term affordability strongly influences adherence and sustained disease control.

Statistical analysis

Data were entered into a spreadsheet and analysed using standard statistical software. Continuous variables were summarised as mean with standard deviation when distribution was approximately normal; non-normally distributed variables were summarised using median and interquartile range. Categorical variables were presented as frequencies and percentages. Within each treatment group, baseline and 12-week glycaemic values were compared using paired statistical tests (paired t-test for normally distributed data or Wilcoxon signed-rank test for non-normal data). Between-group comparisons of baseline characteristics and the magnitude of change in HbA1c, FPG, and PPG were performed using

independent t-tests or Mann–Whitney U tests, as appropriate. A two-sided p value of <0.05 was considered statistically significant. Where relevant, results were interpreted alongside clinical relevance and cost-effectiveness estimates to provide a balanced understanding of both efficacy and affordability.

RESULTS

Study participants and baseline profile

A total of 65 participants were evaluated, comprising 34 patients in the DPP-4 inhibitor (DPP4i) group [teneligliptin (n=12), sitagliptin (n=15), vildagliptin (n=7)] and 31 patients in the α-glucosidase inhibitor (AGi) group [acarbose (n=13), voglibose (n=18)]. Most participants (92%) had associated comorbidities such as hypertension and ischaemic heart disease (Table 1).

The mean age was comparable between groups: 57.32 ± 13.99 years in the DPP4i group versus 56.88 ± 12.89 years in the AGi group, and the difference was not statistically significant on an independent (Welch) t-test (p = 0.895). Sex distribution was also similar between the two groups; based on the counts shown in the presentation charts (DPP4i: 21 males, 13 females; AGi: 19 males, 10 females), the association between treatment group and sex was not significant on chi-square testing ($\chi^2 = 0.002$, p = 0.963) (Figure 1).

Table 1: Baseline demographic and clinical profile

Variable			DPP4i group	AGi group	Statistical test
Total participants (n)	34	31	—		
Age (years), mean ± SD	57.32 ± 13.99	56.88 ± 12.89	Welch t-test, **p = 0.895**		
Sex distribution (M/F)*	21 / 13	19 / 10	$\chi^2 = 0.002$, **p = 0.963**		
Comorbidities (HTN/IHD/others)	92% overall	92% overall	Not group-stratified in PPT		

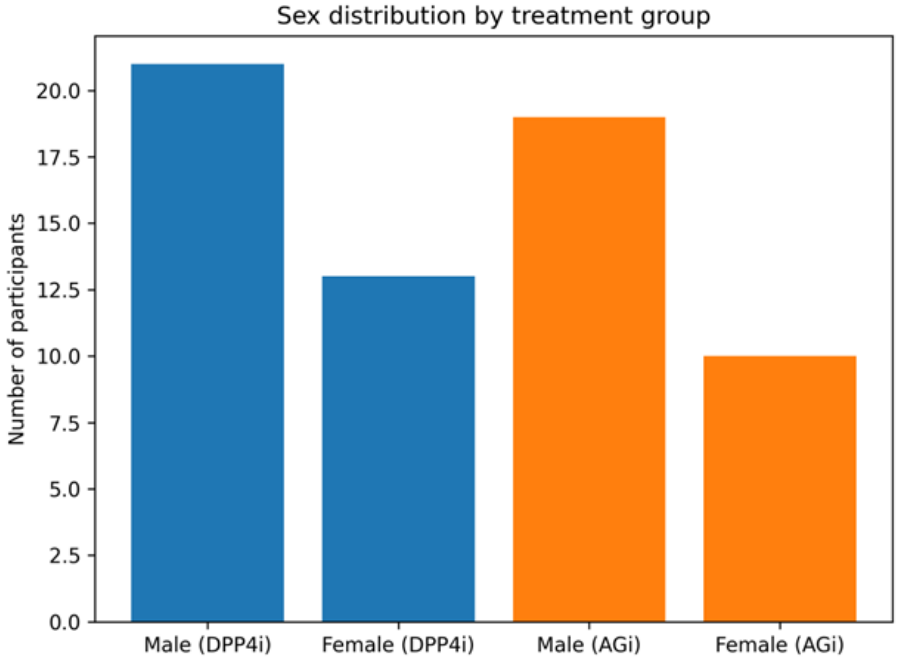

Figure 1: Sex distribution by group

Glycaemic outcomes at 12 weeks (3 months)

Across 12 weeks, both treatment strategies improved glycaemic indices, with distinct patterns in HbA1c and glucose reductions.

HbA1c: At baseline, mean HbA1c was 7.27% in the DPP4i group and 7.48% in the AGi group. At 3 months, HbA1c reduced to 6.56% in the DPP4i group and 6.99% in the AGi group. The absolute HbA1c reduction was therefore 0.71% with DPP4i and 0.49% with AGi, indicating a comparatively larger HbA1c improvement with DPP4i (Table 2 & Figure 2).

Fasting blood glucose (FBS/FPG): Baseline fasting glucose was 166.70 mg/dL in the DPP4i group and 161.32 mg/dL in the AGi group. At 3 months, it decreased to 133.52 mg/dL in DPP4i and 144.86 mg/dL in AGi. The reduction was 33.18 mg/dL in the DPP4i group compared with 16.46 mg/dL in the AGi group (Table 2 & Figure 3).

Post-prandial blood glucose (PPBS/PPG): Baseline post-prandial glucose was 281.52 mg/dL in DPP4i and 283.30 mg/dL in AGi. At 3 months, it reduced to 251.52 mg/dL in DPP4i and 240.94 mg/dL in AGi. The reduction was 30.00 mg/dL with DPP4i and 42.36 mg/dL with AGi, supporting the observation that AGi produced a comparatively stronger reduction in post-prandial glucose (Table 2 & Figure 3).

Table 2: Glycaemic parameters at baseline and 3 months

Parameter	Time point	DPP4i	AGi
HbA1c (%)	Baseline	7.27	7.48
	3 months	6.56	6.99
	Reduction	**0.71**	**0.49**
Fasting glucose (mg/dL)	Baseline	166.70	161.32
	3 months	133.52	144.86
	Reduction	**33.18**	**16.46**
Post-prandial glucose (mg/dL)	Baseline	281.52	283.30
	3 months	251.52	240.94
	Reduction	**30.00**	**42.36**

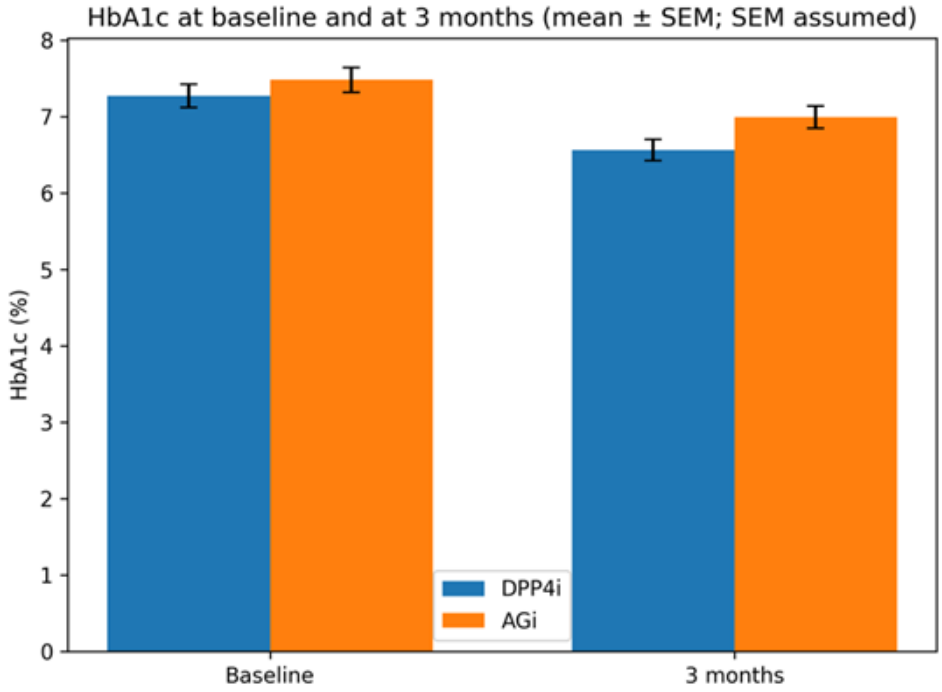

Figure 2: HbA1c at baseline vs 3 months

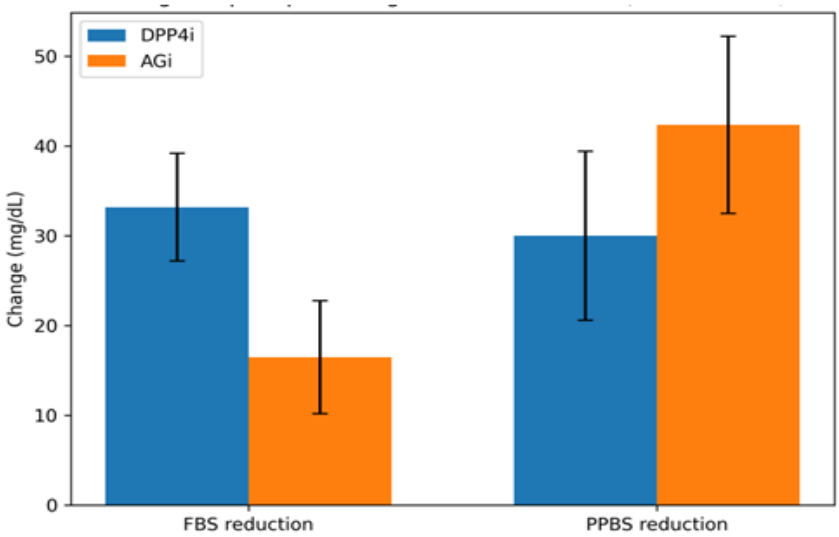

Figure 3: Reduction in fasting and post-prandial glucose

Cost and cost-effectiveness outcomes

Direct drug acquisition costs were used to estimate the expense required to achieve unit improvement in prespecified glycaemic endpoints. Across endpoints, DPP4i showed lower cost per unit improvement in all three parameters, whereas AGi demonstrated a relative advantage for post-prandial glucose reduction clinically.

Fasting glucose: The cost to reduce fasting glucose by 1 mg/dL was ₹30.91 for DPP4i versus ₹140.24 for AGi, indicating markedly better cost-effectiveness for fasting control in the DPP4i group (Table 4).

Post-prandial glucose: The cost per 1 mg/dL reduction in PPBS/PPG was ₹34.19 for DPP4i and ₹54.49 for AGi. Although DPP4i remained less expensive per unit change, AGi achieved a larger absolute PPBS reduction (Table 2), consistent with better post-prandial glycaemic effect (Table 4).

HbA1c: The cost per 0.1% HbA1c reduction was ₹144.47 for DPP4i compared with ₹471.09 for AGi, demonstrating superior HbA1c-related cost-effectiveness with DPP4i over 12 weeks (Table 4).

Table 3: Cost-effectiveness (expense incurred for unit reduction, 12 weeks)

Outcome (unit improvement)	**DPP4i (₹)**	**AGi (₹)**
Cost per **1 mg/dL** reduction in fasting glucose	30.91	140.24
Cost per **1 mg/dL** reduction in post-prandial glucose	34.19	54.49
Cost per **0.1%** reduction in HbA1c	144.47	471.09

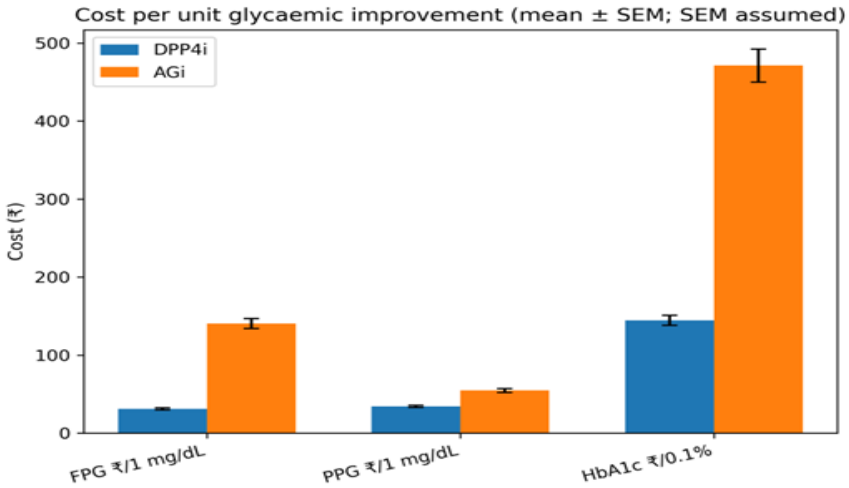

Figure 4: Cost per unit glycaemic improvement

Summary of key findings

Over 12 weeks as add-on therapy to metformin, DPP4 inhibitors produced a larger HbA1c reduction (0.71% vs 0.49%) and greater fasting glucose reduction (33.18 vs 16.46 mg/dL) compared with α-glucosidase inhibitors. In contrast, α-glucosidase inhibitors achieved a larger post-prandial glucose reduction (42.36 vs 30.00 mg/dL). From a pharmacoeconomic standpoint, the cost per unit reduction for HbA1c, fasting glucose, and post-prandial glucose was consistently lower with DPP4 inhibitors, indicating better short-term cost-effectiveness on the endpoints assessed.

DISCUSSION

In this 12-week, tertiary-care comparison of add-on oral therapy to metformin, patients receiving DPP-4 inhibitors demonstrated a larger improvement in overall glycaemic control, reflected by a greater mean reduction in HbA1c (0.71%) and fasting plasma glucose (≈33 mg/dL) than those receiving α-glucosidase inhibitors (HbA1c ≈0.49%; fasting glucose ≈16 mg/dL). In contrast, α-glucosidase inhibitors produced a larger mean reduction in post-prandial glucose (≈42 mg/dL) than DPP-4 inhibitors (≈30 mg/dL). This "split" outcome profile is clinically coherent: DPP-4 inhibitors tend to yield broader day-long glucose lowering, whereas α-glucosidase inhibitors are particularly effective in attenuating post-meal excursions by delaying carbohydrate absorption [1–5].

From a pragmatic perspective, this pattern is important because the baseline HbA1c range in the cohort (around 7.3–7.5%) typically represents a stage where post-prandial hyperglycaemia still contributes substantially to overall HbA1c. Monnier and colleagues demonstrated that the relative contribution of post-prandial glucose to total hyperglycaemia is higher at lower HbA1c strata and gradually shifts toward fasting hyperglycaemia as HbA1c rises [19]. In the present study, the superior post-prandial improvement in the α-glucosidase inhibitor arm aligns with this physiology, while the stronger

HbA1c and fasting glucose improvement in the DPP-4 inhibitor arm suggests a more consistent reduction across the diurnal glycaemic profile.

DPP-4 inhibitors enhance endogenous incretin action, increasing glucose-dependent insulin secretion and suppressing glucagon in a manner that generally affects both fasting and post-prandial glucose without increasing hypoglycaemia risk when used without sulfonylureas/insulin [2–4]. α-Glucosidase inhibitors (acarbose, voglibose) act locally in the gut to delay enzymatic breakdown and absorption of complex carbohydrates, thereby preferentially blunting post-prandial peaks; their HbA1c reduction is typically modest and often limited by gastrointestinal adverse effects, which can affect adherence over time [6–8,20]. The observed results are therefore consistent with expected class pharmacology, and the larger post-prandial reduction seen with α-glucosidase inhibitors in this cohort supports their role in patients with predominant post-meal dysglycaemia, carbohydrate-heavy diets, or high post-prandial readings despite acceptable fasting glucose [6–8,20].

A key contribution of this work is the focus on affordability at the point of prescribing. The DPP-4 inhibitor group showed a lower cost per unit improvement across all three prespecified endpoints (HbA1c, fasting glucose, and post-prandial glucose) over 12 weeks, indicating superior short-term cost-effectiveness based on direct drug acquisition costs alone. In many Indian tertiary-care settings, medication affordability strongly influences persistence and adherence; therefore, the "cost per glycaemic gain" approach used here is clinically relevant for both patients and institutional procurement committees [11–15].

At the same time, cost-effectiveness should not be interpreted as a single "winner" across all patient types. Where post-prandial control is the dominant unmet need—particularly in patients with relatively controlled fasting values but marked post-meal spikes—α-glucosidase inhibitors may deliver clinically meaningful improvements in the parameter most relevant to that individual, even if the cost per unit change is higher overall. The practical message is that glycaemic phenotype (fasting-predominant vs post-prandial-predominant) and economic feasibility should be integrated, rather than choosing add-on therapy solely on class averages [2–6,19].

A substantial proportion of participants (92%) had comorbidities such as hypertension and ischaemic heart disease, which mirrors real-world tertiary-care diabetes clinics. DPP-4 inhibitors as a class have demonstrated cardiovascular safety (non-inferiority) in large outcome trials, although certain agents have raised specific safety signals. Saxagliptin was associated with increased hospitalization for heart failure in SAVOR-TIMI 53 [16], whereas alogliptin in EXAMINE did not show an excess in major adverse cardiovascular events and has been generally interpreted as neutral from a cardiovascular outcomes standpoint [17]. Linagliptin was noninferior to glimepiride for major cardiovascular outcomes in the CAROLINA trial and had less hypoglycaemia than sulfonylurea therapy [18]. Although the present study involved teneligliptin, sitagliptin, and vildagliptin (not saxagliptin or alogliptin), it remains clinically prudent to consider baseline heart failure risk, renal status, and concomitant therapies when selecting a DPP-4 inhibitor, particularly in older patients and those with cardiovascular disease [2–4,16–18].

For α-glucosidase inhibitors, gastrointestinal intolerance (flatulence, abdominal discomfort, diarrhoea) is the principal barrier and may influence persistence; this is relevant when interpreting short-term effectiveness and when counselling patients for long-term therapy [6–8,20].

This evaluation provides practical, short-horizon evidence, but several limitations should be acknowledged when interpreting the findings:

1. **Short duration (12 weeks):** While adequate to detect early HbA1c movement, it does not capture durability, adherence drop-off, or longer-term complication prevention—key drivers of cost-utility in chronic disease [11–15].
2. **Cost perspective restricted to direct drug acquisition:** Indirect costs, monitoring costs, adverse-event costs, productivity loss, and hospitalization/complication costs were not included, which can materially alter economic conclusions [13–15].
3. **Heterogeneity within drug classes:** The DPP-4 arm combined multiple molecules with potentially different acquisition costs and clinical profiles; similarly, the α-glucosidase arm included two agents. Class-level pooling supports pragmatic decisions but may obscure molecule-level differences [2–4,6–8].
4. **Limited inferential statistics for glycaemic change:** If the thesis/PPT provides only group means without dispersion (SD/SEM) for HbA1c, fasting, and post-prandial glucose, formal hypothesis testing and confidence intervals for changes are constrained, and conclusions should remain primarily descriptive [13–15].
5. **Real-world selection effects:** If therapy choice was clinician-driven rather than randomized, baseline diet patterns, symptom burden, post-prandial predominance, tolerability expectations, or affordability could have influenced allocation, potentially biasing comparative outcomes [11–15].

Clinical and policy implications

Within the constraints of a 3-month hospital-based comparison, the findings support a pragmatic approach:

- **DPP-4 inhibitors** appear preferable when the clinical priority is broader HbA1c improvement with relatively favourable short-term cost per unit glycaemic gain, especially in patients needing better fasting control and an adherence-friendly regimen [2–5].
- **α-Glucosidase inhibitors** remain valuable when **post-prandial glucose control** is the primary gap, particularly in patients with near-target fasting glucose but marked post-meal excursions and diet patterns that predispose to post-prandial spikes [6–8,19,20].

For tertiary-care systems, these results can inform formulary decisions, counselling strategies, and personalised add-on selection—linking clinical phenotype to economic feasibility, which is essential for sustained glycaemic control in routine practice [11–15].

Future directions

A logical next step would be a longer follow-up with molecule-specific costing, inclusion of adverse-event and monitoring costs, and presentation of incremental cost-effectiveness (ICER) or cost-utility (QALY-based) analyses with sensitivity testing, consistent with pharmacoeconomic reporting standards [13–15]. Subgroup analyses based on baseline HbA1c, fasting vs post-prandial predominance, and comorbidity burden would also strengthen decision-making relevance.

CONCLUSION

In this 12-week tertiary care evaluation of add-on therapy to metformin in adults with type 2 diabetes, DPP-4 inhibitors demonstrated a more favourable overall glycaemic profile, with greater improvement in HbA1c and fasting glucose compared with α-glucosidase inhibitors. In contrast, α-glucosidase inhibitors produced a comparatively stronger reduction in post-prandial glucose, consistent with their primary mechanism of action.

From a pharmacoeconomic perspective based on direct drug acquisition costs, DPP-4 inhibitors showed lower cost per unit improvement across the assessed glycaemic outcomes, indicating better short-term cost-effectiveness in this setting. However, treatment choice should remain individualised: DPP-4 inhibitors may be preferred when the goal is broader HbA1c and fasting control with better value for money, whereas α-glucosidase inhibitors may be particularly useful when post-meal hyperglycaemia is the dominant clinical concern.

Overall, the findings support a pragmatic, patient-centred approach that integrates glycaemic phenotype with affordability to optimise sustained diabetes control in routine tertiary care practice.

Acknowledgements

The authors express their sincere gratitude to all patients who consented to participate in this study. We thank the Department of Medicine for clinical support and guidance during patient enrolment and follow-up. We also acknowledge the Department of Pharmacology for academic supervision and assistance in protocol execution and data compilation. We are grateful to the hospital laboratory staff for timely processing and reporting of HbA1c and plasma glucose investigations. The support extended by the hospital pharmacy in providing drug price information/records required for the pharmacoeconomic analysis is also acknowledged. Finally, we thank the Institutional Ethics Committee for review and approval of the study and all colleagues who provided constructive inputs during the conduct and write-up of the work.

Funding statement

This study did not receive any external funding from government agencies, commercial entities, or not-for-profit organisations. The work was carried out as part of routine academic and clinical activities within the institution.

Conflict of Interest (COI) statement

The authors declare that they have no conflicts of interest, financial or non-financial, that could have influenced the conduct of this study or the interpretation of its findings.

Author Contributions

All authors contributed substantially to the conception and design of the study. Patient recruitment and clinical data collection were performed by the clinical team. Drug cost data were compiled from institutional pharmacy records, and effectiveness outcomes were extracted from laboratory reports. Data entry, verification, and statistical analysis were performed by the primary investigator with support from the co-investigators. All authors participated in interpretation of the results, drafting of the manuscript/thesis sections, critical revision for intellectual content, and approval of the final version.

Ethical approval statement

The study protocol was reviewed and approved by the Institutional Ethics Committee. The study was conducted in accordance with applicable ethical principles. Written informed consent was obtained from all participants prior to inclusion.

Consent to participate
Written informed consent was obtained from each participant after explaining the study purpose, procedures, and confidentiality safeguards in an understandable language.

Data availability statement
The dataset generated and analysed during the present study is available from the corresponding author on reasonable request, subject to institutional policies and ethical safeguards to protect participant confidentiality.

REFERENCES

1. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. Lancet Diabetes Endocrinol. 2017 Aug;5(8):585-596. doi: 10.1016/S2213-8587(17)30174-2. Epub 2017 Jun 7. Erratum in: Lancet Diabetes Endocrinol. 2017 Aug;5(8):e5. doi: 10.1016/S2213-8587(17)30199-7. PMID: 28601585.
2. 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 Jan;183:109119. doi: 10.1016/j.diabres.2021.109119. Epub 2021 Dec 6. Erratum in: Diabetes Res Clin Pract. 2023 Oct;204:110945. doi: 10.1016/j.diabres.2023.110945. PMID: 34879977; PMCID: PMC11057359.
3. American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178. doi: 10.2337/dc24-S009. Erratum in: Diabetes Care. 2024 Jul 1;47(7):1238. doi: 10.2337/dc24-er07a. PMID: 38078590; PMCID: PMC10725810.
4. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000 Aug 12;321(7258):405-12. doi: 10.1136/bmj.321.7258.405. PMID: 10938048; PMCID: PMC27454.
5. Matthews DR, Paldánius PM, Proot P, Chiang Y, Stumvoll M, Del Prato S; VERIFY study group. Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial. Lancet. 2019 Oct 26;394(10208):1519-1529. doi: 10.1016/S0140-6736(19)32131-2. Epub 2019 Sep 18. PMID: 31542292.
6. Ceriello A, Davidson J, Hanefeld M, Leiter L, Monnier L, Owens D, et al. International Prandial Glucose Regulation Study Group. Postprandial hyperglycaemia and cardiovascular complications of diabetes: an update. Nutr Metab Cardiovasc Dis. 2006 Oct;16(7):453-6. doi: 10.1016/j.numecd.2006.05.006. Epub 2006 Aug 24. PMID: 16934443.
7. Raz I, Wilson PW, Strojek K, Kowalska I, Bozikov V, Gitt AK, et al. Effects of prandial versus fasting glycemia on cardiovascular outcomes in type 2 diabetes: the HEART2D trial. Diabetes Care. 2009 Mar;32(3):381-6. doi: 10.2337/dc08-1671. PMID: 19246588; PMCID: PMC2646013.
8. Ceriello A. Postprandial hyperglycemia and cardiovascular disease: is the HEART2D study the answer? Diabetes Care. 2009 Mar;32(3):521-2. doi: 10.2337/dc08-2209. PMID: 19246590; PMCID: PMC2646040.
9. Green JB, Bethel MA, Armstrong PW, Buse JB, Engel SS, Garg J, et al. TECOS Study Group. Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2015 Jul 16;373(3):232-42. doi: 10.1056/NEJMoa1501352. Epub 2015 Jun 8. Erratum in: N Engl J Med. 2015 Aug 6;373(6):586. doi: 10.1056/NEJMx150029. PMID: 26052984.
10. Kobayashi K, Yokoh H, Sato Y, Takemoto M, Uchida D, Kanatsuka A, et al. SUCCESS Study Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin compared with α-glucosidase inhibitor in Japanese patients with type 2 diabetes inadequately controlled on sulfonylurea alone (SUCCESS-2): a multicenter, randomized, open-label, non-inferiority trial. Diabetes Obes Metab. 2014 Aug;16(8):761-5. doi: 10.1111/dom.12264. Epub 2014 Feb 18. PMID: 24447683.
11. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M; STOP-NIDDM Trail Research Group. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet. 2002 Jun 15;359(9323):2072-7. doi: 10.1016/S0140-6736(02)08905-5. PMID: 12086760.
12. Holman RR, Coleman RL, Chan JCN, Chiasson JL, Feng H, Ge J, et al. ACE Study Group. Effects of acarbose on cardiovascular and diabetes outcomes in patients with coronary heart disease and impaired glucose tolerance (ACE): a randomised, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2017 Nov;5(11):877-886. doi: 10.1016/S2213-8587(17)30309-1. Epub 2017 Sep 13. Erratum in: Lancet Diabetes Endocrinol. 2017 Nov;5(11):e7. doi: 10.1016/S2213-8587(17)30335-2. Erratum in: Lancet Diabetes Endocrinol. 2019 May;7(5):e5. doi: 10.1016/S2213-8587(19)30063-4. PMID: 28917545.
13. Tandon T, Dubey AK, Srivastava S, Manocha S, Arora E, Hasan N. A pharmacoeconomic analysis to compare cost-effectiveness of metformin plus teneligliptin with metformin plus glimepiride in patients of type-2 diabetes mellitus. J Family Med Prim Care. 2019 Mar;8(3):955-959. doi: 10.4103/jfmpc.jfmpc_22_19. PMID: 31041232; PMCID: PMC6482796..

14. Jermendy G, Kiss Z, Rokszin G, Abonyi-Tóth Z, Wittmann I, Kempler P. Persistence to Treatment with Novel Antidiabetic Drugs (Dipeptidyl Peptidase-4 Inhibitors, Sodium-Glucose Co-Transporter-2 Inhibitors, and Glucagon-Like Peptide-1 Receptor Agonists) in People with Type 2 Diabetes: A Nationwide Cohort Study. Diabetes Ther. 2018 Oct;9(5):2133-2141. doi: 10.1007/s13300-018-0483-4. Epub 2018 Aug 17. PMID: 30120754; PMCID: PMC6167279.
15. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Research Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value Health. 2022 Jan;25(1):3-9. doi: 10.1016/j.jval.2021.11.1351. PMID: 35031096..
16. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, Hirshberg B, et al. SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. N Engl J Med. 2013 Oct 3;369(14):1317-26. doi: 10.1056/NEJMoa1307684. Epub 2013 Sep 2. PMID: 23992601.
17. White WB, Cannon CP, Heller SR, Nissen SE, Bergenstal RM, Bakris GLet al.EXAMINE Investigators. Alogliptin after acute coronary syndrome in patients with type 2 diabetes. N Engl J Med. 2013 Oct 3;369(14):1327-35. doi: 10.1056/NEJMoa1305889. Epub 2013 Sep 2. PMID: 23992602.
18. Rosenstock J, Kahn SE, Johansen OE, Zinman B, Espeland MA, Woerle HJ, et al.. Effect of Linagliptin vs Glimepiride on Major Adverse Cardiovascular Outcomes in Patients With Type 2 Diabetes: The CAROLINA Randomized Clinical Trial. JAMA. 2019 Sep 24;322(12):1155-1166. doi: 10.1001/jama.2019.13772. Erratum in: JAMA. 2019 Dec 3;322(21):2138. doi: 10.1001/jama.2019.19012. PMID: 31536101; PMCID: PMC6763993.
19. Monnier L, Lapinski H, Colette C. Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycemia of type 2 diabetic patients: variations with increasing levels of HbA(1c). Diabetes Care. 2003 Mar;26(3):881-5. doi: 10.2337/diacare.26.3.881. PMID: 12610053.
20. van de Laar FA, Lucassen PL, Akkermans RP, van de Lisdonk EH, Rutten GE, van Weel C. Alpha-glucosidase inhibitors for patients with type 2 diabetes: results from a Cochrane systematic review and meta-analysis. Diabetes Care. 2005 Jan;28(1):154-63. doi: 10.2337/diacare.28.1.154. PMID: 15616251.