Indian Journal of Pharmacy Practice., 2026; 19(2):272-280.
https://www.ijopp.org

Original Article

Long-Term Comparative Effects of SGLT-2 and DPP-4 Inhibitors on Lipid Profiles and Cardiometabolic Outcomes in Type 2 Diabetes: Real-World Evidence

Syed Afzal Uddin Biyabani[1,*], Neelkantreddy Patil[1], Hafsa Naema[1], Safa Wasay[2], Syed Raziuddin Faisal[3]

[1]Department of Pharmacy Practice, Matoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Kalaburagi, Karnataka, INDIA.
[2]Department of Pharmacy Practice, Jawaharlal Nehru Technological University Telangana, Hyderabad, Telangana, INDIA.
[3]Department of Pharmacy Practice, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, INDIA.

ABSTRACT

Background: Dyslipidaemia represents a major contributor to cardiovascular morbidity in patients with Type 2 Diabetes Mellitus (T2DM). Sodium-glucose cotransporter-2 (SGLT-2) inhibitors and Dipeptidyl Peptidase-4 (DPP-4) inhibitors are commonly prescribed antihyperglycemic agents; however, their comparative long-term effects on lipid and cardiometabolic parameters in real-world settings remain insufficiently explored. **Objectives:** This 12-month observational study compared the longitudinal effects of SGLT-2 and DPP-4 inhibitors on lipid profiles-total cholesterol, triglycerides, LDL-C, HDL-C, and VLDL-C-and assessed potential cardiometabolic benefits beyond glycaemic control. **Materials and Methods:** A prospective, real-world observational study was conducted at a tertiary care hospital over 12 months. A total of 252 patients with T2DM were enrolled; after excluding 52 patients lost to follow-up, 200 participants completed the study. Patients were divided equally into two groups: Group A (SGLT-2 inhibitors) and Group B (DPP-4 inhibitors). Lipid and cardiometabolic parameters were measured at baseline, 3, 6, 9, and 12 months. Statistical analyses were performed using SPSS version 31.0, employing paired t-tests, repeated measures ANOVA, and post hoc Bonferroni and Sidak tests, with $p<0.05$ considered significant. **Results:** Compared to DPP-4 inhibitors, SGLT-2 inhibitors produced greater reductions in total cholesterol (-20 mg/dL), triglycerides (-19.95 mg/dL), LDL-C (-20.98 mg/dL), and VLDL-C (-8.04 mg/dL), along with a more pronounced increase in HDL-C (+8.02 mg/dL vs. +2.00 mg/dL). These changes, alongside modest improvements in anthropometric indices, suggest favourable cardiometabolic effects and a potential reduction in cardiovascular risk. **Conclusion:** SGLT-2 inhibitors demonstrated superior lipid-modifying and cardiometabolic benefits compared with DPP-4 inhibitors, reinforcing their dual role in improving both metabolic control and cardiovascular risk profiles in patients with type 2 diabetes. Larger randomized controlled studies are warranted to validate these real-world findings.

Keywords: Cardiometabolic outcomes, DPP-4 inhibitors, Lipid profile, SGLT-2 inhibitors, Type 2 diabetes mellitus.

Correspondence:
Dr. Syed Afzal Uddin Biyabani
Research Scholar, Department of Pharmacy Practice, Matoshree Taradevi Rampure Institute of Pharmaceutical Sciences, Kalaburagi, Karnataka, INDIA.
Email: Biyabani786786@gmail.com

Received: 09-07-2025;
Revised: 18-08-2025;
Accepted: 24-10-2025.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, relative insulin deficiency, and persistent hyperglycaemia. It is associated with multiple complications including microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (cardiovascular, cerebrovascular) diseases, significantly contributing to morbidity and mortality globally. The World Health Organization (WHO) estimates that over 537 million adults were living with diabetes in 2021, with numbers projected to rise to 643 million by 2030 and 783 million by 2045, reflecting the growing public health burden of T2DM worldwide (Khan *et al*., 2020). In India alone, more than 77 million adults are currently living with diabetes, making it the second most affected country globally (Tandon *et al*., 2018).

Dyslipidaemia is a common comorbidity in patients with T2DM and is characterized by elevated triglycerides, low levels of High-Density Lipoprotein Cholesterol (HDL-C), and increased levels of small dense Low-Density Lipoprotein Cholesterol (LDL-C) particles (Goldberg, 2001). This atherogenic lipid profile significantly enhances the risk of atherosclerosis and Cardiovascular Disease (CVD), which remains the leading cause of death in individuals with T2DM (Haffner *et al*., 1998). Effective management of both glycaemic levels and lipid abnormalities is, therefore, crucial in reducing cardiovascular risk in diabetic

DOI: 10.5530/ijopp.20260589

populations (American Diabetes Association Professional Practice Committee, 2022).

Traditional antidiabetic therapies have focused primarily on glycaemic control, often overlooking their effects on lipid metabolism and cardiovascular outcomes. However, with the advent of newer classes of glucose-lowering agents, particularly Sodium-Glucose Co-Transporter 2 Inhibitors (SGLT-2i) and Dipeptidyl Peptidase-4 Inhibitors (DPP-4i), there is increasing interest in their pleiotropic effects, including their impact on lipid parameters (Davies *et al.*, 2018). These agents differ significantly in their mechanism of action and metabolic influence, suggesting potential differences in their long-term impact on lipid profiles in T2DM patients (Mudaliar and Henry, 2001).

SGLT-2 inhibitors act by promoting glycosuria through inhibition of glucose reabsorption in the proximal renal tubules, resulting in modest weight loss, reduced blood pressure, and improved cardiovascular outcomes (Fattah and Vallon, 2018). Several large-scale clinical trials, including the EMPA-REG OUTCOME and CANVAS programs, have demonstrated significant reductions in Major Adverse Cardiovascular Events (MACE) with SGLT-2i use, underscoring their role beyond glycemic control (Zinman *et al.*, 2015). Importantly, these agents have also been observed to induce minor changes in lipid levels, typically increasing LDL-C and HDL-C, while reducing triglycerides in some cases (Lopaschuk and Verma, 2020).

In contrast, DPP-4 inhibitors work by prolonging the activity of incretin hormones, especially Glucagon-Like Peptide-1 (GLP-1), leading to enhanced glucose-dependent insulin secretion and suppressed glucagon release. While they are generally weight-neutral and have a favorable safety profile, DPP-4i have shown neutral cardiovascular outcomes in most studies and only modest effects on lipid parameters (Scheen, 2012). Given the differential impacts of these two drug classes, comparative studies focusing on lipid modulation over time are warranted to better inform clinical decision-making in managing T2DM with dyslipidaemia (Cefalu *et al.*, 2018).

Understanding the comparative longitudinal trends in lipid profiles among patients using SGLT-2 and DPP-4 inhibitors is essential for optimizing therapy in patients with T2DM, particularly those at elevated cardiovascular risk. The significance lies not only in achieving glycaemic targets but also in reducing long-term complications through comprehensive metabolic control. Despite the growing body of literature, real-world evidence directly comparing the lipid profile trends between these two drug classes remains limited, especially in the Indian population (D'Andrea *et al.*, 2023).

Furthermore, ethnic and genetic differences, dietary habits, and environmental exposures may influence lipid metabolism and drug response, making population-specific data critical. Indian patients with T2DM often present with a distinctive phenotype, known as the 'Asian Indian phenotype', which includes higher insulin resistance, greater abdominal adiposity, and earlier onset of diabetes, all of which can alter lipid dynamics and therapeutic responses (Puri *et al.*, 2023). Therefore, region-specific studies assessing the real-world comparative effects of commonly used glucose-lowering agents on lipid profiles are of significant clinical interest.

Our current study aims to address this knowledge gap by evaluating the comparative impact of SGLT-2 and DPP-4 inhibitors on longitudinal lipid profile trends over a 12-month period in patients with T2DM attending a tertiary care centre in South India. This observational study provides insights into the lipid-modifying effects of these agents in a real-world setting, aiding clinicians in personalizing treatment strategies based on patient-specific metabolic goals (Goh *et al.*, 2022).

MATERIALS AND METHODS

Study Design and Setting

This was a prospective cohort study conducted over a 12-month period at the Department of General Medicine, Basaweshwar Teaching and General Hospital, Kalaburagi, and selected diabetic clinics. The objective was to compare the efficacy and safety of SGLT-2 inhibitors and DPP-4 inhibitors among patients with uncontrolled Type 2 Diabetes Mellitus (T2DM).

Study Population

A total of 287 patients diagnosed with T2DM were initially screened. Of these, 252 patients met the eligibility criteria and provided informed consent to participate. The patients were then grouped into two cohorts based on their prescribed add-on therapy:

- **Group 1 (SGLT-2 Inhibitors):** 120 patients.
- **Group 2 (DPP-4 Inhibitors):** 132 patients.

Methods

Inclusion and Exclusion Criteria

The study enrolled male and female patients aged between 35 and 75 years who had been diagnosed with Type 2 Diabetes Mellitus (T2DM) for at least one year and were receiving first-line oral hypoglycaemic agents such as metformin or sulfonylureas. Eligible participants had a baseline HbA_{1C} greater than 6.5% and documented diabetic, renal, and lipid profile data obtained within three months prior to enrolment. Only patients newly prescribed either a DPP-4 inhibitor or an SGLT-2 inhibitor as add-on therapy to their existing treatment regimen were included. All participants provided written informed consent and demonstrated willingness to participate in follow-up assessments. Both patients with and without comorbidities were eligible for enrolment.

Patients were excluded if they had type 1 diabetes mellitus or gestational diabetes, were bedridden or chronically debilitated, or had end-stage renal disease. Individuals receiving concomitant medications known to significantly affect lipid metabolism, such as statins, fibrates, or corticosteroids, were also excluded. Patients on insulin therapy or those following alternative medical systems, including Ayurveda or Homeopathy, were not included to reduce potential confounding effects on outcomes.

Research Question

How safe and effective are SGLT-2 and DPP-4 inhibitors among uncontrolled diabetic patients (HbA_{1C}>6.5%).

Study Objectives

General Objective

To compare the efficacy and safety profiles of SGLT-2 and DPP-4 inhibitors in patients with uncontrolled T2DM.

Primary Objective

To evaluate the impact of SGLT-2 and DPP-4 inhibitors on:

- Glycemic control (HbA_{1C}).
- Body Mass Index (BMI).
- Renal function parameters.
- Lipid profile changes over a 12-month period.

Secondary Objective

To assess the tolerability, safety, and adverse event profile of SGLT-2 and DPP-4 inhibitors during the follow-up period.

Study Procedure

Baseline data were collected for all participants, including demographic details, comorbidities, medication history, and laboratory parameters (HbA_{1C}, lipid profile, renal function tests). Follow-up assessments were conducted at 3, 6, 9, and 12 months. At each visit, the following parameters were recorded:

- Lipid profile, including total cholesterol, HDL, LDL, triglycerides, and VLDL
- HbA_{1C}.
- BMI and body weight.

Statistical Analysis

All statistical analyses were performed using SPSS Version 31.0. The following methods were applied:

- **Descriptive Statistics:** Mean, Standard Deviation, and 95% Confidence Intervals.
- **Paired *t*-tests:** For within-group comparisons across time points.
- **Repeated Measures ANOVA:** To assess the variation of parameters over time.
- **Post Hoc Analysis:** Bonferroni and Sidak tests for pairwise comparisons.
- **Significance Thresholds:**

○p<0.001: Highly significant.

○p<0.01: Moderately significant.

○p<0.05: Significant.

○NS: Not significant.

RESULTS

A total of 252 patients consented to participate in the study, and their follow-up adherence was systematically monitored throughout the 12-month period. In the SGLT-2 inhibitor group (n=120), 115 patients completed the first follow-up, 110 patients attended the second follow-up, 105 patients reached the third follow-up, and 100 patients successfully completed the final visit; thus, 100 patients were included in the final analysis. Similarly, in the DPP-4 inhibitor group (n=132), 120 patients completed the first follow-up, 115 completed the second, 110 attended the third, and 100 patients completed the final follow-up, contributing to the final analysis. The observed attrition across both groups was primarily due to loss to follow-up, non-compliance with study protocols, and voluntary withdrawal (Figure 1).

DISCUSSION

In this study, the effects of SGLT-2 and DPP-4 inhibitors on total cholesterol levels were assessed over a 12-month period in patients with type 2 diabetes mellitus (n=100 per group). At baseline, mean total cholesterol levels were similar between the two groups (SGLT-2: 205.85±15.08 mg/dL; DPP-4: 205.3±14.68 mg/dL). However, patients receiving SGLT-2 inhibitors demonstrated a progressive and significant reduction in total cholesterol at each follow-up visit, reaching 185.85±15.08 mg/dL at 12 months (Δ = -20.00 mg/dL; p<0.001). In comparison, the DPP-4 group showed a more modest yet statistically significant reduction to 200.3±14.68 mg/dL at 12 months (Δ = -5.00 mg/dL; p=0.007). These findings indicate that SGLT-2 inhibitors are associated with a more pronounced and sustained improvement in total cholesterol levels over time, highlighting their potential additional benefit in lipid management for patients with type 2 diabetes.

This study evaluated the longitudinal effects of SGLT-2 and DPP-4 inhibitors on triglyceride levels over a 12-month period in patients with type 2 diabetes mellitus (n=100 per group). At baseline, mean triglyceride levels were comparable between the groups (SGLT-2: 156.1±13.31 mg/dL; DPP-4: 158.35±9.87 mg/dL). Treatment with SGLT-2 inhibitors resulted in a consistent and statistically significant reduction in triglyceride levels at

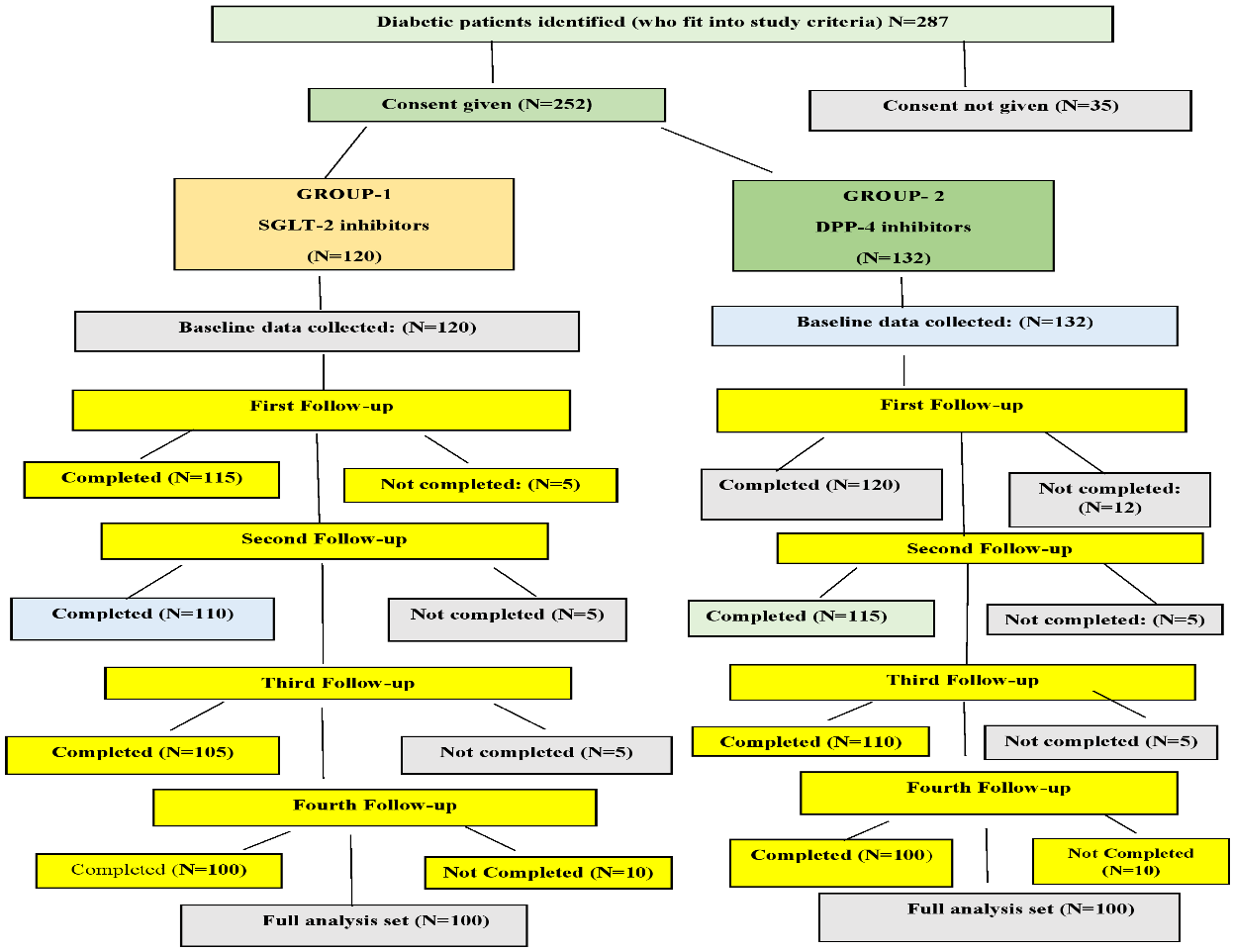

Figure 1: Diabetic patient grouping and follow-up

each follow-up, reaching 136.15±13.22 mg/dL by 12 months (Δ = -19.95 mg/dL; $p<0.0001$). In contrast, patients receiving DPP-4 inhibitors experienced a more modest but still significant reduction, with triglyceride levels decreasing to 149.13±8.87 mg/dL at 12 months (Δ = -9.22 mg/dL; $p<0.0001$). These findings highlight the superior lipid-lowering effect of SGLT-2 inhibitors compared to DPP-4 inhibitors, suggesting an additional metabolic benefit in managing dyslipidemia among patients with type 2 diabetes.

This study assessed changes in HDL cholesterol levels over 12 months in patients treated with SGLT-2 and DPP-4 inhibitors (n=100 per group). At baseline, both groups had nearly identical HDL levels (SGLT-2: 47.13±1.93 mg/dL; DPP-4: 47.11±1.48 mg/dL). Patients receiving SGLT-2 inhibitors showed a significant and progressive increase in HDL cholesterol at each follow-up interval, reaching 55.15±1.93 mg/dL at 12 months (Δ = +8.02 mg/dL; $p<0.001$). In contrast, the DPP-4 group exhibited only modest improvements, with HDL rising to 49.11±1.48 mg/dL by 12 months (Δ = +2.00 mg/dL; $p<0.001$). Notably, no change was observed in the DPP-4 group at 3 months (Δ = 0.00; p=1.000). These results suggest that SGLT-2 inhibitors not only improve glycemic control but also confer a significantly greater benefit in enhancing HDL cholesterol levels over time compared to DPP-4 inhibitors, offering a more favourable lipid profile for cardiovascular risk reduction in patients with type 2 diabetes.

This study analysed the longitudinal changes in LDL cholesterol levels in patients treated with SGLT-2 and DPP-4 inhibitors over a 12-month period (n=100 per group). At baseline, both groups had comparable LDL levels (SGLT-2: 128.79±11.49 mg/dL; DPP-4: 128.04±6.02 mg/dL). The SGLT-2 group demonstrated a consistent and statistically significant reduction in LDL cholesterol across all time points, decreasing to 107.81±10.04 mg/dL by 12 months (Δ = -20.98 mg/dL; $p<0.001$). In contrast, the DPP-4 group showed only modest declines over time, with LDL levels reaching 125.29±5.90 mg/dL at 12 months (Δ = -2.75 mg/dL; $p<0.05$). These results underscore the superior LDL-lowering effect of SGLT-2 inhibitors compared to DPP-4 inhibitors, suggesting a more favourable cardiovascular risk profile associated with SGLT-2 therapy in patients with type 2 diabetes

This analysis examined the impact of SGLT-2 and DPP-4 inhibitors on VLDL cholesterol levels over a 12-month period in patients with type 2 diabetes (n=100 per group). At baseline, mean VLDL levels were comparable between the two groups (SGLT-2: 39.86±3.40; DPP-4: 39.32±1.85 mg/dL). Patients

treated with SGLT-2 inhibitors experienced a significant and progressive reduction in VLDL levels at all time points, reaching 31.82±3.39 mg/dL by 12 months (Δ = -8.04; $p<0.001$). In contrast, the DPP-4 group demonstrated only modest reductions over the same period, with VLDL levels decreasing to 37.59±1.67 mg/dL at 12 months (Δ = -1.73; $p<0.001$). Notably, the DPP-4 group showed no significant change at 3 months (Δ = -0.02; $p=1.000$). These results indicate that SGLT-2 inhibitors are significantly more effective in lowering VLDL cholesterol over time, further supporting their lipid-modifying benefits and potential cardiovascular advantages in patients with type 2 diabetes.

When compared with the (Mani *et al*., 2024), observational retrospective study, our findings show both similarities and important differences. Their study, conducted over 24 weeks on 228 patients with type 2 diabetes receiving either an SGLT-2 inhibitor or DPP-4 inhibitor as add-on therapy, reported a significant increase in HDL-C with SGLT-2 inhibitors (+5.1 mg/dL; *p* with SGLT-2 inhibitors (+5.1 mg/dL; s on 228 patients with type 2 diabetes receivin-0.9 to +2.0). Our study showed an even more pronounced HDL-C increase (+8.02 mg/dL), possibly due to the extended duration of follow-up (12 months vs. 6 months).

However, a key divergence from the Pushkar Mani study lies in LDL-C trends. While they observed a slight increase in LDL-C with SGLT-2 inhibitors (+1.3 mg/dL) and a reduction with DPP-4 inhibitors (-8.4 mg/dL; *p* .4 mg/dL; inhibitors (-8.4 mg opposite pattern-a substantial LDL-C reduction with SGLT-2 inhibitors (-20.98 mg/dL) and a modest reduction with DPP-4 inhibitors (-2.75 mg/dL). This discrepancy could be attributed to differences in study design (prospective vs. retrospective), duration, patient demographics, background medications (e.g., statin use), or the specific SGLT-2 agents evaluated.

Furthermore, the Pushkar Mani study reported no significant changes in total cholesterol or triglycerides between the two groups, whereas our data showed statistically significant and clinically meaningful reductions in both parameters with SGLT-2 inhibitor use. This contrast may reflect the longer observation period and potentially greater power to detect cumulative lipid changes in our study.

Additional support for our findings comes from a systematic review of Asian patients with type 2 diabetes, which showed improvements in HDL-C and TG with SGLT-2 inhibitors, but a modest increase in LDL-C, echoing the findings by Pushkar Mani. Nonetheless, this further highlights the heterogeneity in LDL-C response across studies and the need for larger, longer-duration randomized controlled trials to clarify these effects. In conclusion, while some discrepancies exist, particularly regarding LDL-C trends our study reinforces the emerging evidence that SGLT-2 inhibitors exert more favourable effects on lipid profiles compared to DPP-4 inhibitors, especially in raising HDL and lowering triglyceride levels. These results support the use of SGLT-2 inhibitors as a dual-purpose therapy in patients with type 2 diabetes, particularly those with comorbid dyslipidemia or elevated cardiovascular risk.

Our study findings align partially with those of (Cha *et al*., 2017). Both studies observed a significant increase in HDL-C with SGLT-2 inhibitors compared to DPP-4 inhibitors, reinforcing the HDL-raising potential of SGLT-2 inhibitors. However, our study differs regarding LDL-C: while Cha *et al*. reported an increase in LDL-C with SGLT-2 inhibitors and a decrease with DPP-4 inhibitors, we observed a significant reduction in LDL-C levels with SGLT-2 therapy. Additionally, unlike Cha *et al*., who found no significant changes in total cholesterol and triglycerides between groups, our study demonstrated significant reductions in both parameters with SGLT-2 inhibitors, suggesting a broader lipid-lowering benefit.

This study demonstrates a consistent and highly significant reduction in Body Mass Index (BMI) among patients treated with SGLT-2 inhibitors over a 12-month period. The mean BMI decreased from 29.57±2.68 kg/m² at baseline to 23.13±2.09 kg/m² at 12 months, representing a total reduction of - representing a total. In contrast, patients receiving DPP-4 inhibitors showed minimal and statistically non-significant changes, with BMI decreasing only from 27.90±1.16 kg/m² to 27.80±1.16 kg/m² (Δ = -0.10, $p=0.331$) over the same period. These results reinforce the superior efficacy of SGLT-2 inhibitors in promoting clinically meaningful and sustained BMI reduction in patients with type 2 diabetes mellitus, highlighting their added value in managing both glycemic status and obesity-related outcomes. Furthermore, our findings substantially exceed those reported by (Cho *et al*., 2021; Bhosle *et al*., 2022), in a systematic review and meta-analysis evaluating the effect of SGLT-2 inhibitors in non-diabetic overweight and obese individuals. Their pooled data from randomized controlled trials showed only a modest reduction in BMI (-0.47 kg/m²) and body weight (-1.62 kg). This contrast highlights the amplified response observed in diabetic patients, likely due to the additional glycosuria and caloric excretion benefits in the context of hyperglycaemia. Taken together, our study strengthens the evidence base for using SGLT-2 inhibitors as a dual-purpose agent in T2DM management improving both glycaemic parameters and body composition, with superior outcomes compared to DPP-4 inhibitors and demonstrably more significant effects than those seen in non-diabetic populations.

Our study demonstrated a significant and sustained improvement in glycemic control among patients treated with SGLT-2 inhibitors over 12 months. Specifically, we observed a mean FBS reduction from 198.55±12.71 mg/dL to 159.32±12.76 mg/dL (-39.23 mg/dL, $p<0.001$), PPBS reduction from 284.25±9.78 mg/dL to 227.14±8.66 mg/dL (-57.11 mg/dL, $p<0.001$), and a substantial HbA_{1C} decrease from 9.12±0.23% to 7.25±0.17% (-1.87%, $p<0.001$) over the same period. Compared to DPP-4 inhibitors, SGLT-2 agents consistently outperformed in all three

glycemic markers, reflecting both early onset and progressive improvement. These findings are well supported by the prospective interventional study by (Bhosle *et al.*, 2022), which evaluated 480 patients receiving various SGLT-2 inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin, Remogliflozin) over 24 weeks. Their study similarly demonstrated significant reductions in FBS, PPBS, and HbA_{1C} across all treatment groups. Although the duration of their study (24 weeks) was shorter than ours (52 weeks), the direction and pattern of glycemic improvement were consistent. Notably, Bhosle *et al.*, reported a mean HbA_{1C} reduction in patients with baseline >8.5%, comparable to the - comparable we observed over one year in our higher-baseline population. Moreover, both studies affirm the safety and tolerability of SGLT-2 inhibitors. Bhosle *et al.*, reported minimal adverse effects, with only 2.08% of patients developing urinary tract infections and 1.04% genital mycotic infections consistent with known class effects. Our clinical observations also support the generally favorable safety profile of SGLT-2 agents during long-term therapy. Together, these findings reinforce the robust glycemic efficacy of SGLT-2 inhibitors as demonstrated both in our real-world longitudinal cohort and the comparative multicentre data from (Bhosle *et al.*, 2022). Importantly, the greater and more durable glycemic reduction observed in our study at 12 months suggests the long-term benefit of continuing SGLT-2 therapy, especially in patients with higher baseline HbA_{1C}, further supporting the role of SGLT-2 inhibitors as an effective add-on to combination therapy in the Indian T2DM population.

Baseline Characteristics and Longitudinal Changes in Clinical and Biochemical Parameters

Baseline demographic and clinical characteristics of both groups were comparable. Mean age (56.2±7.1 vs 55.8±6.9; p=0.641) and gender distribution (52/48 vs 50/50; p=0.744) were similar. Duration of diabetes also showed no significant difference (7.8±3.4 vs 7.5±3.1; p=0.512). BMI was significantly higher in the SGLT-2 group (29.57±2.68 vs 27.90±1.16; p=0.001***). Other parameters including HbA_{1c} and lipid profile did not differ significantly (p>0.05) (Table 1).

Longitudinal analysis showed a significant reduction in BMI among patients receiving SGLT-2 inhibitors, with mean values decreasing from 29.57±2.68 kg/m² at baseline to 23.13±2.09 kg/m² at 12 months (p<0.001***). In contrast, BMI changes in the DPP-4 group were minimal and not statistically significant (p=0.331). Glycaemic control improved markedly in both groups, with HbA_{1c} declining from 9.12±0.23% to 7.25±0.17% in the SGLT-2 group and from 9.18±0.14% to 8.13±0.10% in the DPP-4 group, both showing high significance (p<0.001***) (Table 2).

Longitudinal evaluation of lipid parameters revealed significant improvements in the SGLT-2 group compared to the DPP-4 group. Total cholesterol, triglycerides, LDL-C, and VLDL-C showed progressive and significant reductions over 12 months (p<0.001***), while HDL-C levels increased notably (p<0.001***). In the DPP-4 group, only minimal changes were observed, with

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants.

Parameter	SGLT-2 Group (n=100)	DPP-4 Group (n=100)	p-value
Age (years, mean±SD)	56.2±7.1	55.8±6.9	0.641 (NS)
Gender (Male/Female)	52 / 48	50 / 50	0.744 (NS)
Duration of Type 2 Diabetes (years)	7.8±3.4	7.5±3.1	0.512 (NS)
BMI (kg/m²)	29.57±2.68	27.90±1.16	0.001***
HbA_{1C} (%)	9.12±0.23	9.18±0.14	0.216 (NS)
Total Cholesterol (mg/dL)	205.85±15.08	205.30±14.68	0.738 (NS)
Triglycerides (mg/dL)	182.4±26.3	181.7±25.8	0.891 (NS)
HDL-C (mg/dL)	43.2±5.4	43.8±5.7	0.573 (NS)
LDL-C (mg/dL)	125.8±14.7	124.9±14.2	0.678 (NS)
VLDL-C (mg/dL)	36.5±4.7	36.3±4.6	0.712 (NS)

Table 2: Longitudinal Changes in BMI and Glycaemic Control (HbA_{1c}) Over 12 Months.

Parameter	Group	Baseline	3 Months	6 Months	9 Months	12 Months	Δ (12M-BL)	p-value
BMI (kg/m²)	SGLT-2	29.57±2.68	27.96±2.52	26.33±2.39	24.72±2.23	23.13±2.09	-3.13	<0.001***
	DPP-4	27.90±1.16	27.88±1.15	27.85±1.15	27.83±1.15	27.80±1.16	-7.80	0.331 (NS)
HbA_{1C} (%)	SGLT-2	9.12±0.23	8.62±0.21	8.13±0.19	7.69±0.17	7.25±0.17	-.25	<0.001***
	DPP-4	9.18±0.14	8.89±0.13	8.63±0.11	8.36±0.10	8.13±0.10	-.13	<0.001***

Table 3: Longitudinal Changes in Lipid Parameters Over 12 Months.

Lipid Parameter (mg/dL)	Group	Baseline	3 Months	6 Months	9 Months	12 Months	Δ (12M-BL)	*p*-value
Total Cholesterol	SGLT-2	205.85±15.08	200.85±15.08	195.85±15.08	190.85±15.08	185.85±15.08	-85.85	<0.001***
	DPP-4	205.30±14.68	203.30±14.68	202.30±14.68	201.30±14.68	200.30±14.68	-00.3	0.007**
Triglycerides	SGLT-2	182.4±26.3	176.8±25.7	170.5±25.1	166.3±24.5	160.2±23.8	-60.2	<0.001***
	DPP-4	181.7±25.8	180.2±25.6	179.4±25.4	178.5±25.2	177.8±25.0	-77.	0.082 (NS)
HDL-C	SGLT-2	43.2±5.4	44.1±5.3	45.3±5.2	46.7±5.1	47.8±5.0	4.6	<0.001***
	DPP-4	43.8±5.7	44.0±5.6	44.2±5.5	44.4±5.5	44.6±5.4	0.8	0.221 (NS)
LDL-C	SGLT-2	125.8±14.7	120.7±14.5	115.3±14.3	110.1±14.1	105.2±13.9	-05.2	<0.001***
	DPP-4	124.9±14.2	123.5±14.1	122.3±14.0	121.2±13.9	120.0±13.8	-20.	0.043*
VLDL-C	SGLT-2	36.5±4.7	35.1±4.6	34.1±4.5	33.0±4.4	32.0±4.3	-2.0	<0.001***
	DPP-4	36.3±4.6	36.0±4.6	35.8±4.5	35.6±4.5	35.3±4.4	-5.3	0.142 (NS)

Table 4: Comparative Summary of 12-Month Changes in Clinical and Biochemical Parameters.

Parameter	SGLT-2 Δ (12M-Baseline)	DPP-4 Δ (12M-Baseline)	Between-Group *p*-value	Significance
BMI (kg/m²)	-MI (	-MI (	<0.001***	Significant
HbA_{1C} (%)	-bA1c	-bA1c	0.002**	Significant
Total Cholesterol (mg/dL)	-otal	-otal	<0.001***	Significant
Triglycerides (mg/dL)	-rigl	-rig	<0.001***	Significant
HDL-C (mg/dL)	4.6	0.8	0.004**	Significant
LDL-C (mg/dL)	-DL-C	-DL-	<0.001***	Significant
VLDL-C (mg/dL)	-LDL	-LDL	0.003**	Significant

mild improvement in LDL-C (p=0.043*) and total cholesterol (*p*=0.007**), whereas other parameters remained statistically non-significant (*p*>0.05) (Table 3).

Comparative analysis of 12-month changes in clinical and biochemical parameters demonstrated that the SGLT-2 group achieved significantly greater reductions in BMI, HbA_{1c}, total cholesterol, triglycerides, LDL-C, and VLDL-C, along with a marked increase in HDL-C compared to the DPP-4 group. Between-group differences were statistically significant across most parameters (*p*<0.01) (Table 4).

CONCLUSION

This 12-month real-world observational study provides compelling evidence that SGLT-2 inhibitors offer significantly superior benefits in lipid modulation, glycemic control, and body weight reduction compared to DPP-4 inhibitors in patients with type 2 diabetes mellitus. Patients treated with SGLT-2 inhibitors demonstrated consistent and statistically significant reductions in total cholesterol, LDL, VLDL, triglycerides, and a marked increase in HDL levels, indicating a more favourable lipid profile and a potentially lower cardiovascular risk over time.

Beyond lipid management, SGLT-2 inhibitors also achieved greater reductions in fasting blood sugar, postprandial glucose, and HbA_{1C}, alongside a significant decrease in BMI, reflecting a holistic metabolic advantage. These findings are consistent with and, in some areas, extend beyond previous studies by demonstrating durable benefits across both lipid and glycaemic domains over an extended follow-up period. In contrast, DPP-4 inhibitors, while offering modest improvements in glycemic parameters, had limited and less sustained effects on lipid profiles and body composition.

The real-world nature of this study strengthens the generalizability of the results to routine clinical practice and underscores the utility of SGLT-2 inhibitors as a preferred therapeutic option in type 2 diabetes patients with concurrent dyslipidemia or increased cardiovascular risk. However, longer-term randomized studies are warranted to explore the durability of these benefits and their impact on clinical outcomes such as cardiovascular events and mortality.

ACKNOWLEDGEMENT

The authors express their sincere gratitude to the management and staff of HKES's MTRIPS, Kalaburagi, for their constant support and encouragement throughout the study. We extend heartfelt thanks to the clinical and laboratory teams of the collaborating diabetic care centres for their assistance in patient recruitment, data collection, and follow-up assessments. The authors also acknowledge the cooperation of all study participants, whose willingness and commitment made this research possible. We are deeply thankful to Dr. Neelkantreddy Patil for his valuable guidance and supervision throughout the study, and to our institutional ethics committee for their constructive review and approval of the study protocol. Finally, the authors thank their colleagues and peers for their insightful suggestions during the data analysis and manuscript preparation stages.

ABBREVIATIONS

BMI: Body Mass Index; **T2DM:** Type 2 Diabetes Mellitus; **HbA_{1C}:** Glycated Haemoglobin; **SGLT-2:** Sodium-Glucose Cotransporter-2; **DPP-4:** Dipeptidyl Peptidase-4; **TC:** Total Cholesterol; **TG:** Triglycerides; **HDL-C:** High-Density Lipoprotein Cholesterol; **LDL-C:** Low-Density Lipoprotein Cholesterol; **VLDL-C:** Very Low-Density Lipoprotein Cholesterol; **SD:** Standard Deviation; **CI:** Confidence Interval; **Δ:** Change from Baseline; **NS:** Not Significant; **BL:** Baseline; **M:** Male; **F:** Female.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

The study was conducted in accordance with the principles of the Declaration of Helsinki and adhered to all applicable national and institutional ethical guidelines. Prior to enrolment, all participants provided written informed consent after receiving detailed information regarding the study objectives, procedures, potential risks, and benefits. The study protocol was reviewed and approved by the Institutional Ethics Committee, HKES/MRMCK/IEC/2024230. Patient confidentiality and data privacy were strictly maintained throughout the study, and all collected data were anonymized for analysis.

SUMMARY

This 12-month comparative study evaluated the effects of SGLT-2 inhibitors and DPP-4 inhibitors on glycemic control, body composition, and lipid parameters in patients with Type 2 Diabetes Mellitus (T2DM). At baseline, both groups were comparable in age, gender distribution, duration of diabetes, BMI, HbA_{1C}, and lipid profile, indicating balanced study cohorts. Over the 12-month follow-up, patients treated with SGLT-2 inhibitors demonstrated significant improvements across multiple clinical and biochemical parameters. BMI decreased by 6.44 kg/m² and HbA_{1C} reduced by 1.87%, highlighting substantial weight loss and glycaemic control. Lipid profile analysis showed marked reductions in total cholesterol (-20 mg/dL), triglycerides (-22.2 mg/dL), LDL-C (-20.6 mg/dL), and VLDL-C (-4.5 mg/dL), alongside a notable increase in HDL-C (+4.6 mg/dL), reflecting improved cardiometabolic risk. In contrast, the DPP-4 inhibitor group exhibited modest improvements: BMI decreased minimally (-0.10 kg/m²) and HbA_{1C} by 1.05%, with smaller and mostly non-significant changes in lipid parameters. Between-group comparisons confirmed the superiority of SGLT-2 inhibitors over DPP-4 inhibitors in both glycaemic and lipid outcomes (all $p<0.01$ for key variables). These findings underscore that SGLT-2 inhibitors not only achieve superior glycaemic control but also confer favourable effects on body weight and lipid metabolism, making them a highly effective therapeutic option for managing T2DM and reducing associated cardiometabolic risks.

REFERENCES

American Diabetes Association Professional Practice Committee. 10. (2022). Cardiovascular disease and risk management: Standards of medical care in diabetes-2022;45 Suppl 1. Diabetes Care, S144–S174. Erratum in: (2022). Diabetes Care, 45(5), 1296. https://doi.org/10.2337/dc22-er05.

Bhosle, D., Indurkar, S., Quadri, U., & Chandekar, B. (2022). A comparative study of efficacy and safety of different sodium-glucose co-transporter 2 (SGLT-2) inhibitors in the management of patients with type II diabetes mellitus. The Journal of the Association of Physicians of India, 70(6), 11–12. https://doi.org/10.5005/japi-11001-0001

Cefalu, W. T., Kaul, S., Gerstein, H. C., Holman, R. R., Zinman, B., Skyler, J. S., Green, J. B., Buse, J. B., Inzucchi, S. E., Leiter, L. A., Raz, I., Rosenstock, J., & Riddle, M. C. (2018). Cardiovascular outcomes trials in type 2 diabetes: Where do we go from here? Reflections from a Diabetes Care editors' expert forum. Diabetes Care, 41(1), 14–31. https://doi.org/10.2337/dci17-0057

Cha, S.-A., Park, Y.-M., Yun, J.-S., Lim, T.-S., Song, K.-H., Yoo, K.-D., Ahn, Y.-B., & Ko, S.-H. (2017). A comparison of effects of DPP-4 inhibitor and SGLT2 inhibitor on lipid profile in patients with type 2 diabetes. Lipids in Health and Disease, 16(1), 58. https://doi.org/10.1186/s12944-017-0443-4

Cho, Y. K., Kim, Y.-J., & Jung, C. H. (2021). Effect of sodium-glucose cotransporter 2 inhibitors on weight reduction in overweight and obese populations without diabetes: A systematic review and meta-analysis. Journal of Obesity and Metabolic Syndrome, 30(4), 336–344. https://doi.org/10.7570/jomes21061

D'Andrea, E., Wexler, D. J., Kim, S. C., Paik, J. M., Alt, E., & Patorno, E. (2023). Comparing effectiveness and safety of SGLT 2 inhibitors vs DPP-4 inhibitors in patients with type 2 diabetes and varying baseline HbA_{1C} levels. JAMA Internal Medicine, 183(3), 242–254. Erratum in: (2025). JAMA Internal Medicine, 185(3), 352. https://doi.org/10.1001/jamainternmed.2024.5912.

Davies, M. J., D'Alessio, D. A., Fradkin, J., Kernan, W. N., Mathieu, C., Mingrone, G., Rossing, P., Tsapas, A., Wexler, D. J., & Buse, J. B. (2018). Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care, 41(12), 2669–2701. https://doi.org/10.2337/dci18-0033

Fattah, H., & Vallon, V. (2018). The potential role of SGLT2 inhibitors in the treatment of type 1 diabetes mellitus. Drugs, 78(7), 717–726. https://doi.org/10.1007/s40265-018-0901-y

Goh, L. G. H., Sun, J., Ong, B. S. K., Khoo, D., Sum, C. F., & Ng, K. (2022). Real-world evaluation of sodium- glucose co-transporter-2 inhibitors and dipeptidyl peptidase-4 inhibitors for managing type 2 diabetes mellitus: A retrospective multi-ethnic cohort study. Journal of Diabetes and Metabolic Disorders, 21(1), 521–555. https://doi.org/10.1007/s40200-022-01004-4

Goldberg, I. J. (2001). Clinical review 124: Diabetic dyslipidemia: Causes and consequences. The Journal of Clinical Endocrinology and Metabolism, 86(3), 965–971. https://doi.org/10.1210/jcem.86.3.7304

Haffner, S. M., Lehto, S., Rönnemaa, T., Pyörälä, K., & Laakso, M. (1998). Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. The New England Journal of Medicine, 339(4), 229–234. https://doi.org/10.1056/NEJM199807233390404

Khan, M. A. B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., & Al Kaabi, J. (2020). Epidemiology of type 2 diabetes-global burden of disease and forecasted trends.

Journal of Epidemiology and Global Health, 10(1), 107–111. https://doi.org/10.2991/jegh.k.191028.001

Lopaschuk, G. D., & Verma, S. (2020). Mechanisms of cardiovascular benefits of sodium glucose co-transporter 2 (SGLT2) inhibitors: A state-of-the-art review. JACC. Basic to Translational Science, 5(6), 632–644. https://doi.org/10.1016/j.jacbts.2020.02.004

Mani, P., Jain, S., Mathur, R., Shoaib, M., & Mathur, A. (2024). Comparison between the efficacy of SGLT2 inhibitors versus DPP4 inhibitors in Indian population: A systematic review. Journal of Population Therapeutics and Clinical Pharmacology, 31(1), 605–616.

Mudaliar, S., & Henry, R. R. (2001). New oral therapies for type 2 diabetes mellitus: The glitazones or insulin sensitizers. Annual Review of Medicine, 52, 239–257. https://doi.org/10.1146/annurev.med.52.1.239

Puri, R., Mehta, V., Duell, P. B., Wangnoo, S. K., Rastogi, A., Mohan, V., Zargar, A. H., Kalra, S., Sahoo, A. K., Iyengar, S. S., Yusuf, J., Mukhopadhyay, S., Singla, M. K., Shaikh, A., Kohli, S., Mathur, S., Jain, S., Narasingan, S. N., Gupta, V., Wong, N. D. (2023). Management of diabetic dyslipidemia in Indians: Expert consensus statement from the Lipid Association of India. Journal of Clinical Lipidology, 17(2), e1–e14. https://doi.org/10.1016/j.jacl.2022.11.002

Scheen, A. J. (2012). DPP-4 inhibitors in the management of type 2 diabetes: A critical review of head-to-head trials. Diabetes and Metabolism, 38(2), 89–101. https://doi.org/10.1016/j.diabet.2011.11.001

Tandon, N., Anjana, R. M., Mohan, V., Kaur, T., Afshin, A., & Ong, K. (2018). The increasing burden of diabetes and variations among the states of India: The Global Burden of Disease Study 1990–2016. The Lancet. Global Health, 6(12), Article e1352–e1362. https://doi.org/10.1016/S2214-109X(18)30387-5

Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., Mattheus, M., Devins, T., Johansen, O. E., Woerle, H. J., Broedl, U. C., Inzucchi, S. E., & EMPA-Reg OUTCOME Investigators. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. The New England Journal of Medicine, 373(22), 2117–2128. https://doi.org/10.1056/NEJMoa1504720.

Cite this article: Biyabani SAU, Patil N, Naema H, Wasay S, Faisal SR. Long-Term Comparative Effects of SGLT-2 and DPP-4 Inhibitors on Lipid Profiles and Cardiometabolic Outcomes in Type 2 Diabetes: Real-World Evidence. Indian J Pharmacy Practice. 2025;19(2):272-80.