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Original Research Article

Longitudinal impact of sodium-glucose co-transporter-2 versus dipeptidyl peptidase-4 inhibitors on weight and body mass index in type 2 diabetes: a 12-month comparative analysis

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ABSTRACT

Background: Obesity and elevated body mass index (BMI) are strongly associated with poor glycaemic control and increased cardiometabolic risk in type 2 diabetes mellitus (T2DM). Beyond glycaemic efficacy, contemporary antidiabetic agents are increasingly evaluated for their effects on weight and metabolic outcomes. Sodium-glucose co-transporter-2 (SGLT-2) inhibitors and dipeptidyl peptidase-4 (DPP-4) inhibitors are widely prescribed, yet comparative long-term data on their impact on weight and BMI in Indian populations remain limited.
Methods: This 12-month observational study included 200 T2DM patients 100 each receiving SGLT-2 or DPP-4 inhibitors. Assessments were conducted at baseline and at 3, 6, 9, and 12 months. Primary outcomes were changes in body weight and BMI, analysed using SPSS v31.0 with paired t-tests, repeated measures ANOVA, and Bonferroni/Sidak post hoc tests. Statistical significance was set at $p<0.05$.
Results: Patients on SGLT-2 inhibitors exhibited consistent and significant reductions in both parameters: mean body weight declined from 91.61±4.09 kg to 77.63±4.61 kg (Δ=-13.98 kg, $p<0.001$), and BMI from 29.57±2.68 to 23.13±2.09 (Δ=-6.44, $p<0.001$). Conversely, DPP-4 users showed negligible changes (Δ=+0.14 kg and -0.10, both $p>0.3$). The SGLT-2 group's weight loss was progressive and sustained throughout 12 months. Although gender distribution was similar ($p=0.744$), younger age in the SGLT-2 group may have influenced outcomes.
Conclusions: SGLT-2 inhibitors produced significant, durable reductions in weight and BMI versus DPP-4 inhibitors, highlighting their dual metabolic advantage in comprehensive T2DM management.

Keywords: SGLT-2 inhibitors, DPP-4 inhibitors, Type 2 diabetes mellitus, Weight reduction

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycaemia resulting from insulin resistance and progressive pancreatic β-cell dysfunction. Globally, T2DM represents a major public health burden, with over 537 million adults affected as of 2021, and projections indicate this number will rise to 783 million by 2045 if current trends continue.[1] India, known as the "diabetes capital of the world," is witnessing an alarming increase in T2DM prevalence due to rapid urbanization, sedentary lifestyles, unhealthy dietary patterns, and genetic predisposition.[2]

Beyond glycaemic control, T2DM is intricately associated with multiple comorbidities, notably dyslipidemia, which significantly contributes to the increased cardiovascular morbidity and mortality observed in this population.[3]

Dyslipidemia in T2DM is typically characterized by elevated triglycerides, low HDL-C, and the presence of small dense LDL particles-a triad commonly referred to as diabetic dyslipidemia.[4] Addressing lipid abnormalities is therefore a cornerstone of comprehensive diabetes management, aimed at reducing the risk of atherosclerotic cardiovascular disease (ASCVD).[5]

In recent years, the management of T2DM has undergone a paradigm shift, moving beyond glucose-centric targets to include cardio-metabolic risk reduction.[6] Two important classes of oral anti-diabetic agents SGLT-2 inhibitors and DPP-4 inhibitors have emerged as popular second-line therapies after metformin.[7] SGLT-2 inhibitors, including empagliflozin, dapagliflozin, and canagliflozin, exert their glucose-lowering effect by inhibiting renal glucose reabsorption in the proximal tubule, resulting in glycosuria and osmotic diuresis.[8] In contrast, DPP-4 inhibitors such as sitagliptin and vildagliptin enhance endogenous incretin levels, thereby improving insulin secretion and suppressing glucagon release.[9]

Beyond glycaemic control, SGLT-2 inhibitors have demonstrated multiple pleiotropic benefits, including reductions in body weight, blood pressure, uric acid, and most notably, cardiovascular and renal protection[10]. These agents have shown to favourably influence lipid metabolism by reducing triglycerides and modestly increasing HDL-C.[11] Conversely, the effects of DPP-4 inhibitors on lipid parameters remain largely neutral or marginally beneficial.[12] Therefore, a detailed head-to-head evaluation of these drug classes in terms of their impact on lipid profiles in real-world settings is warranted.

Numerous clinical trials and meta-analyses have supported the cardioprotective and renoprotective effects of SGLT-2 inhibitors, including EMPA-REG OUTCOME, CANVAS, and DECLARE-TIMI 58, which collectively underscored their superiority in reducing major adverse cardiovascular events (MACE), heart failure hospitalizations, and progression of renal disease.[13] While DPP-4 inhibitors have demonstrated cardiovascular safety in trials such as TECOS and SAVOR-TIMI 53, they have not shown the same level of benefit regarding hard cardiovascular outcomes.[14] These interclass differences have profound implications for long-term patient management strategies, particularly in individuals with concomitant dyslipidemia and high ASCVD risk.

Furthermore, there is growing clinical interest in the long-term effects of antidiabetic medications on lipid parameters, as optimizing lipid profiles is essential in minimizing cardiovascular risks in T2DM patients.[15] Despite their established role in glycaemic management, real-world data directly comparing the longitudinal impact of SGLT-2 and DPP-4 inhibitors on lipid profiles remains sparse in the Indian population. Most available evidence is derived from short-term studies, randomized trials with strict inclusion criteria, or international populations, limiting their generalizability to diverse and routine clinical practice.[16]

The present 12-month observational study was designed to bridge this evidence gap by comparatively analyzing the effects of SGLT-2 and DPP-4 inhibitors on longitudinal trends in lipid profile parameters among patients with T2DM in a real-world clinical setting. The primary objective was to assess changes in total cholesterol, LDL-C, HDL-C, triglycerides, and VLDL levels, while secondary objectives included evaluating changes in glycaemic parameters, BMI, and body weight. This study is expected to provide clinically relevant insights to inform evidence-based therapeutic decision-making in diabetes care in India.

METHODS

Study design and setting

This was a 12-month, prospective, observational, comparative study conducted at the outpatient endocrinology and diabetic clinics of a tertiary care teaching hospital in South India between August 2023 and August 2024. The study aimed to evaluate and compare the longitudinal effects of SGLT-2 inhibitors and DPP-4 inhibitors on weight and BMI in patients with T2DM.

Study site

Department of general medicine Basaweshwar teaching and general hospital Kalaburagi and selected diabetic clinics.

Study population and eligibility criteria

A total of 200 patients diagnosed with T2DM were enrolled and divided into two matched cohorts, group A (SGLT-2 inhibitors group) included 100 patients who received either empagliflozin, dapagliflozin, or canagliflozin, while group B (DPP-4 inhibitors group) included 100 patients who received either sitagliptin, teneligliptin, or linagliptin.

Inclusion criteria were adults aged 30-65 years diagnosed with T2DM as per the American diabetes association (ADA) 2023 guidelines were included in the study. Eligible participants were those initiating therapy with either SGLT-2 or DPP-4 inhibitors as part of their oral antidiabetic regimen, having a baseline BMI of ≥25 kg/m², and willing to participate after providing informed consent.

Exclusion criteria included the study excluded patients with T1DM, those receiving insulin or GLP-1 receptor agonists, and individuals with a history of recent hospitalization or major surgery within the past three months. Patients with chronic kidney disease (eGFR <45 mL/min/1.73 m²), hepatic failure, or malignancy were also excluded. Additionally, pregnant or lactating women, and

patients with poor medication adherence or unwillingness to attend regular follow-ups, were not included in the study.

Intervention and follow-up

Participants were initiated on either SGLT-2 or DPP-4 inhibitors according to clinical indication and physician discretion. Both groups received standard care for diabetes management, including metformin, lifestyle advice, dietary modifications, and regular exercise counselling. No crossover was permitted during the study period.

Patients were followed up at baseline, 3 months, 6 months, 9 months, and 12 months. At each visit, anthropometric measurements and laboratory parameters were recorded.

Data collection

The following parameters were assessed, wherein primary outcomes where body weight (kg) and BMI (kg/m²), and secondary parameters where fasting blood sugar (FBS), postprandial blood sugar (PPBS), and glycated haemoglobin (HbA1c), although not part of the primary endpoint, were also collected to monitor glycaemic trends.

Anthropometric measurements

Weight was measured using a calibrated digital weighing scale with patients in light clothing and without shoes, height was measured to the nearest 0.1 cm using a stadiometer at baseline whereas, BMI was calculated using the formula: BMI=weight (kg)/height² (m²).

Statistical analysis

Data were entered and analyzed using IBM SPSS Statistics version 31.0. Descriptive statistics were used to summarize baseline characteristics.

Continuous variables were expressed as mean±standard deviation (SD), and categorical variables as frequencies and percentages.

Intergroup comparisons of weight and BMI changes were performed using independent t-tests, while intragroup changes across time points were analyzed using repeated measures ANOVA followed by Bonferroni correction and a $p<0.05$ was considered statistically significant.

RESULTS

Of 252 enrolled patients, 100 in each group completed all follow-up visits and were included in the final analysis. In the SGLT-2 group (n=120), 115, 110, and 105 patients completed the first, second, and third follow-ups, respectively. In the DPP-4 group (n=132), 120, 115, and 110 patients completed the corresponding follow-ups. Dropouts were due to loss to follow-up, non-compliance, or voluntary withdrawal (Figure 1).

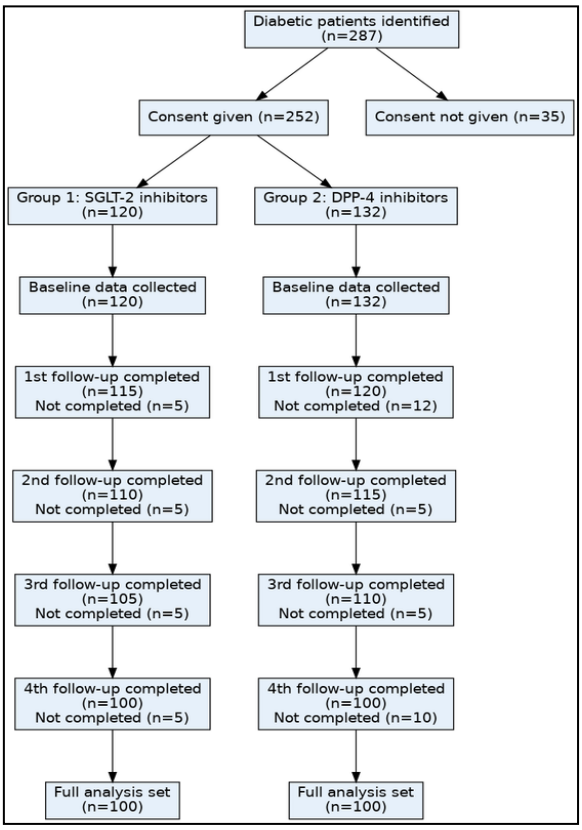

Figure 1: Study criteria.

Gender distribution was comparable between groups (p=0.744), indicating no significant difference. However, age distribution varied, with a higher proportion of younger patients (46-55 years) in the SGLT-2 group and more older patients (56-65 years) in the DPP-4 group. This demographic variation may have contributed to differences in metabolic outcomes between the two groups.

Both groups were comparable in average age and diabetes duration (p>0.05). Baseline HbA1c levels showed no significant difference, indicating similar glycaemic status. However, the SGLT-2 group had a significantly higher baseline BMI (p=0.001), suggesting greater initial obesity among these patients.

Over 12 months, patients on SGLT-2 inhibitors showed a progressive and significant reduction in both body weight (-13.98 kg) and BMI (-6.44 kg/m²), with steady improvement at each follow-up. In contrast, the DPP-4 group demonstrated negligible changes in weight and BMI throughout the study. These results confirm the superior and sustained weight-reducing effect of SGLT-2 inhibitors compared to DPP-4 inhibitors. After 12 months, SGLT-2 group showed markedly greater reductions in weight (-13.98 kg) and BMI (-6.44 kg/m²) compared to the DPP-4 group, which showed minimal change. HbA1c reduction was also significantly higher with SGLT-2 inhibitors (-1.87% vs. -1.05%, p=0.002). Overall, SGLT-2 inhibitors demonstrated superior efficacy in improving both metabolic and glycaemic parameters.

Table 1: Baseline demographic characteristics of patients on SGLT-2 and DPP-4 inhibitors, (n=200).

Parameters	SGLT-2, (n=100)	DPP-4, (n=100)	Overall, (n=200)	Percentage difference	P value
Gender					
Male	52 (52%)	50 (50%)	102 (51%)	2%	0.744 (NS)
Female	48 (48%)	50 (50%)	98 (49%)	-2%	-
Age distribution (in years)					
35-45	14 (14%)	30 (30%)	44 (22%)	-16%	-
46-55	44 (44%)	21 (21%)	65 (32.5%)	23%	-
56-65	32 (32%)	46 (46%)	78 (39%)	-14%	-
66-75	10 (10%)	3 (3%)	13 (6.5%)	7%	-

Table 2: Baseline clinical characteristics of patients on SGLT-2 and DPP-4 inhibitors, (n=200).

Parameters	SGLT-2, (n=100)	DPP-4, (n=100)	Overall, (n=200)	Percentage difference	P value
Avg age (in years)	56.2±7.1	55.8±6.9	56.0±7.0	-	0.641 (NS)
Duration of type 2 diabetes (in years)	7.8±3.4	7.5±3.1	7.65±3.25	-	0.512 (NS)
BMI (kg/m²)	29.57±2.68	27.90±1.16	28.74±2.18	1.67	0.001
HbA1c (%)	9.12±0.23	9.18±0.14	9.15±0.19	-0.06	0.216 (NS)

Table 3: Longitudinal changes in weight and BMI over 12 months for SGLT-2 and DPP-4 inhibitors, (n=100 each).

Time point	Group	Weight (kg, mean±SD)	95% CI	Δ weight	BMI (kg/m², mean±SD)	95% CI	Δ BMI
Baseline	SGLT-2	91.61±4.09	90.80-92.42	-	29.57±2.68	29.04-30.10	-
	DPP-4	77.91±4.91	76.94-78.89	-	27.90±1.16	27.65-28.15	-
3 months	SGLT-2	87.00±4.17	86.17-87.83	-4.61	27.96±2.52	27.46-28.46	-1.61
	DPP-4	77.93±5.06	76.93-78.93	0.02	27.88±1.15	27.63-28.13	-0.02
6 months	SGLT-2	83.05±4.40	82.18-83.92	-8.56	26.33±2.39	25.86-26.81	-3.24
	DPP-4	77.90±5.20	76.87-78.93	-0.01	27.85±1.15	27.60-28.10	-0.05
9 months	SGLT-2	80.16±4.58	79.25-81.07	-11.45	24.72±2.23	24.28-25.16	-4.85
	DPP-4	77.92±5.21	76.89-78.95	0.02	27.83±1.15	27.58-28.08	-0.07
12 months	SGLT-2	77.63±4.61	76.72-78.55	-13.98	23.13±2.09	22.72-23.55	-6.44
	DPP-4	78.05±5.32	76.99-79.11	0.14	27.80±1.16	27.55-28.05	-0.10

Table 4: Comparative summary of 12-month changes in weight, BMI, and HbA1c for SGLT-2 vs DPP-4 inhibitors.

Parameters	SGLT-2 Δ (12M-baseline)	DPP-4 Δ (12M-baseline)	Between-group p	Significance
Weight (kg)	-13.98	0.14	<0.001	Significant
BMI (kg/m²)	-6.44	-0.10	<0.001	Significant
HbA1c (%)	-1.87	-1.05	0.002	Significant

DISCUSSION

The longitudinal analysis of body weight and BMI in this study provides compelling evidence for the superior metabolic efficacy of SGLT-2 inhibitors over DPP-4 inhibitors in patients with T2DM. Our findings demonstrated that patients on SGLT-2 inhibitors achieved a mean weight reduction of -13.98 kg over 12 months, in stark contrast to a negligible +0.14 kg gain in the DPP-4 group. These results were statistically significant across all time points ($p<0.001$), reinforcing the robust and sustained weight-lowering effect of SGLT-2 inhibitors observed in real-world settings.

This observed efficacy is attributable to the unique mechanism of action of SGLT-2 inhibitors, which induce urinary glucose excretion, leading to caloric loss, natriuresis, and mild diuresis all of which contribute to progressive weight reduction.[17] These findings echo results from earlier landmark trials such as the EMPA-REG outcome trial and the CANVAS program, both of which highlighted weight loss as a consistent secondary benefit among SGLT-2i users.[18,19]

In our Indian cohort, the 13.98 kg mean weight reduction far exceeds the clinically meaningful threshold of 3-5% weight loss, typically associated with improved cardiovascular and metabolic outcomes.[20] This contrasts sharply with weight-neutral/modestly weight-increasing profile of DPP-4 inhibitors, which act via incretin modulation without promoting glycosuria or caloric loss.[21]

The findings of our study align with those of Danpanichkul et al who reported that 45.6% of T2DM patients on SGLT-2i achieved >3% weight loss within 6 months.[22] They also identified higher baseline BMI, older age, and concomitant sulfonylurea use as predictors of favourable weight response factors prevalent in our cohort. Furthermore, Tuli et al in Delhi found a -2.16 kg weight reduction over 6 months in SGLT-2i-treated patients, compared to a gain of +0.7 kg in those on other oral hypoglycaemics.[23] While the magnitude of weight loss was lower than in our 12-month analysis, their study supports the direction and early onset of benefits, particularly in Indian T2DM populations.

It is noteworthy that our study revealed not just statistical but clinical significance, with weight reduction sustained and progressive throughout year. The durability of this effect underscores the potential of SGLT-2i to offer lasting benefit in obese and overweight T2DM patients a population increasingly prevalent in India.[24] Given India's high diabetes burden compounded by high obesity rates, this dual-action mechanism becomes even more clinically valuable.

In parallel, the impact on BMI was equally noteworthy. Patients on SGLT-2 inhibitors exhibited a mean BMI decrease of -6.44 kg/m² (from 29.57 to 23.13 kg/m²), representing a shift from obese to near-normal ranges. In contrast, the DPP-4 group experienced a minimal and statistically non-significant change (-0.10 kg/m², $p=0.331$). These data are unprecedented in magnitude, especially when compared to published trials in non-diabetic populations.

For instance, Cho et al conducted a systematic review and meta-analysis in overweight but non-diabetic adults and found that SGLT-2i led to only modest BMI reductions (-0.47 kg/m²) and body weight loss (-1.62 kg).[25] The contrast underscores the amplified effect in diabetic individuals, likely due to the presence of hyperglycaemia, which enhances glucose excretion and increases caloric loss.

Moreover, the enhanced response in our study could be partly attributed to baseline characteristics such as higher BMI, dietary factors, and genetic predispositions known to affect weight loss pharmacodynamics in South Asian populations.[26] Also, unlike many randomized trials, our real-world design reflects routine clinical practice and adherence patterns, increasing external validity of our results.

From a comparative pharmacological standpoint, DPP-4 inhibitors, while well tolerated and neutral in weight effect, lack the robust metabolic benefits offered by SGLT-2 inhibitors. Their incretin-based mechanism improves glycaemic control modestly but does not translate into body weight or BMI reduction.[27] Therefore, in patients where obesity co-exists with T2DM, SGLT-2 inhibitors provide a clear therapeutic advantage.

Our study also extends the findings from international evidence to Indian diabetic population, cohort historically underrepresented in global trials. It provides much-needed data on the long-term weight-modulating effects of SGLT-2 inhibitors in this demographic. Importantly, the longer follow-up (12 months) allows for assessment of sustainability and not just short-term efficacy, as seen in studies like Ridderstråle et al and Wilding et al.[28,29]

Overall, present study highlights the clinical and practical implications of favouring SGLT-2 inhibitors in overweight or obese T2DM patients. Their consistent weight-lowering, BMI-reducing, and glycaemic benefits suggest they should be considered frontline agents when weight reduction is a treatment goal alongside glucose control.

Limitations

This single-center study with a 12-month follow-up limits generalizability and long-term outcome assessment. Medication adherence was self-reported, and lifestyle factors were not fully controlled, which may have influenced results.

CONCLUSION

This 12-month longitudinal study provides compelling evidence supporting the superior efficacy of SGLT-2 inhibitors over DPP-4 inhibitors in managing weight and

BMI among patients with T2DM. Patients treated with SGLT-2 inhibitors exhibited consistent and statistically significant reductions in both body weight and BMI throughout the study period, highlighting the class's potential as a dual-purpose agent for glycaemic and weight management. In contrast, patients on DPP-4 inhibitors showed only minimal or non-significant changes in these anthropometric parameters. These findings reinforce the clinical value of SGLT-2 inhibitors not only in improving metabolic control but also in addressing obesity-related concerns in T2DM management. Future studies with larger cohorts and longer follow-up durations are warranted to further validate these outcomes and explore associated cardiovascular and renal benefits.

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