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RESEARCH ARTICLE

A Prospective Observational Study of Anthropometric Parameters in Patients with Type 2 Diabetes Mellitus Receiving Dipeptidyl Peptidase-4 Inhibitors

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Abstract: The confluence of obesity and Type 2 Diabetes Mellitus (T2DM) constitutes a major clinical challenge, where excess adiposity exacerbates insulin resistance and accelerates cardiovascular deterioration. Pharmacological interventions that offer glycemic efficacy without precipitating weight gain are therefore paramount in the management of T2DM. This prospective observational study investigated the longitudinal trajectory of anthropometric parameters in patients newly initiated on dipeptidyl peptidase-4 (DPP-4) inhibitors. Over a six-month period, seventy patients receiving add-on DPP-4 inhibitor therapy were monitored for changes in body weight and Body Mass Index (BMI). Contrary to the traditional classification of these agents as strictly weight-neutral, the analysis revealed a statistically significant, albeit modest, reduction in both mean body weight and BMI at three- and six-months post-initiation compared to baseline values. These results suggest that in real-world clinical settings, DPP-4 inhibitors may offer anthropometric benefits beyond mere weight neutrality, potentially driven by improved metabolic control and the absence of anabolic effects associated with other oral antidiabetic agents. The study validates the utility of DPP-4 inhibitors as a strategic therapeutic option for T2DM patients where weight management is a critical component of the holistic treatment regimen.

Keywords: Type 2 Diabetes Mellitus; Dipeptidyl Peptidase-4 Inhibitors; Anthropometry; Insulin Resistance; Pharmacotherapy.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) represents a complex, multifactorial metabolic disorder characterized by chronic hyperglycemia, insulin resistance, and progressive beta-cell failure. The epidemiological trajectory of T2DM has reached critical proportions globally. According to the International Diabetes Federation (IDF) Diabetes Atlas (11th Edition), approximately 592 million adults are projected to live with diabetes by 2035, a surge driven principally by aging populations, urbanization, and obesogenic environments [1]. India, often termed the diabetes capital of the world, faces a unique challenge; the recent ICMR-INDIAB national cross-sectional study estimates the prevalence of diabetes to affect over 101 million individuals, with a substantial proportion remaining undiagnosed [2].

The pathophysiology of T2DM is intrinsically linked to adiposity. Visceral adipose tissue acts as an endocrine organ, secreting pro-inflammatory adipokines that impair insulin signaling and promote atherogenesis [3]. Consequently, modern therapeutic guidelines, such as the American Diabetes Association (ADA) Standards of Care 2024, emphasize a patient-centered approach that prioritizes weight management and cardiovascular risk reduction alongside glycemic control [4]. Traditional oral antidiabetic agents, particularly sulfonylureas and thiazolidinediones, although effective in lowering HbA1c, are frequently limited by adverse effects such as hypoglycemia and weight gain, which can compromise long-term adherence and cardiovascular health [5, 6].

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Dipeptidyl Peptidase-4 (DPP-4) inhibitors (gliptins) have emerged as a cornerstone of second-line therapy. These agents function by inhibiting the enzymatic degradation of incretin hormones Glucagon-Like Peptide-1 (GLP-1) and Glucose-Dependent Insulinotropic Polypeptide (GIP) thereby potentiating glucose-dependent insulin secretion and suppressing glucagon release [7]. Unlike GLP-1 receptor agonists, which are associated with significant weight loss, DPP-4 inhibitors are clinically classified as weight-neutral [8]. However, their safety profile is robust; landmark cardiovascular outcome trials such as TECOS (Sitagliptin), SAVOR-TIMI 53 (Saxagliptin), and EXAMINE (Alogliptin) have demonstrated that DPP-4 inhibitors do not increase the risk of Major Adverse Cardiovascular Events (MACE) [9, 10, 11].

Despite the "weight-neutral" consensus, real-world evidence remains heterogeneous, with some observational data suggesting modest weight reduction in specific subpopulations [12]. Given the high prevalence of "diabesity" in the Indian phenotype, characterising the anthropometric impact of these agents is clinically relevant. This study aims to provide a rigorous longitudinal assessment of DPP-4 inhibitors on body weight and Body Mass Index (BMI) in an Indian cohort, verifying their suitability in a population where avoiding iatrogenic weight gain is imperative.

2. Materials and Methods

2.1. Study Design and Setting

A prospective observational study was conducted to evaluate the anthropometric effects of DPP-4 inhibitors over a six-month duration. The investigation was carried out at Basaweshwar Teaching and General Hospital in Kalaburagi, Karnataka, alongside selected specialized diabetes clinics. The study protocol adhered to ethical guidelines for human research, and the observational nature ensured that therapeutic decisions remained at the discretion of the treating physicians, reflecting real-world clinical practice.

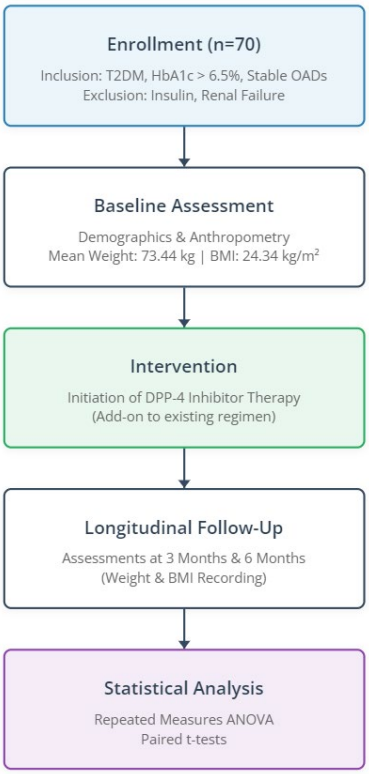

Figure 1. Study Design and Patient Flow

2.2. Study Population

The study cohort comprised patients aged between 35 and 75 years with a confirmed diagnosis of T2DM. Participants were eligible for inclusion if they had an HbA1c level greater than 6.5%, were on a stable background regimen of oral antidiabetic drugs (OADs), and were newly prescribed a DPP-4 inhibitor as add-on therapy. Written informed consent was obtained from all participants prior to enrollment. Rigorous exclusion criteria were applied to eliminate confounding variables affecting body weight. Patients with Type 1 Diabetes Mellitus, gestational diabetes, or severe renal impairment (End-Stage Renal Disease) were excluded. Individuals receiving

insulin therapy or concurrent medications known to significantly alter body weight such as corticosteroids or specific anti-obesity agents were not included in the analysis.

Table 1. Summary of Study Inclusion and Exclusion Criteria

Criteria Category	Characteristics
Inclusion Criteria	Diagnosis of Type 2 Diabetes Mellitus (T2DM) Age 35–75 years HbA1c > 6.5% Newly prescribed DPP-4 inhibitor as add-on therapy Complete baseline clinical data available
Exclusion Criteria	Type 1 Diabetes Mellitus Gestational Diabetes End-Stage Renal Disease (ESRD) Current Insulin therapy Concurrent use of weight-altering medications

2.3. Data Collection and Statistical Analysis

Anthropometric data, specifically body weight (kg) and height (m), were recorded at baseline (initiation of therapy), followed by assessments at three months and six months. Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Data management and statistical analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD). To assess longitudinal changes, repeated-measures Analysis of Variance (ANOVA) and paired t-tests were employed to compare follow-up values against baseline. A p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 70 patients completed the six-month follow-up period and were included in the final statistical analysis. The demographic profile of the cohort indicated a male predominance, with 47 males (67.1%) and 23 females (32.9%), reflecting the gender distribution often observed in tertiary care presentations of metabolic disorders in this region (Figure 2).

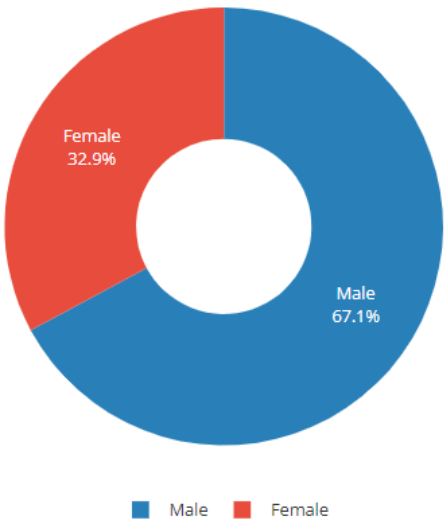

Figure 2. Gender distribution of the study population (n=70).

The longitudinal analysis of anthropometric parameters demonstrated a consistent downward trajectory. At baseline, the mean body weight of the cohort was 73.44 ± 12.35 kg. Following three months of therapy with DPP-4 inhibitors, the mean weight decreased to 71.19 ± 12.05 kg. This reduction was sustained and progressed further at the six-month interval, with a mean weight of 67.90 ± 11.73 kg. The reduction in body weight at both follow-up time points was statistically significant compared to baseline ($p < 0.001$), indicating a robust effect over the study duration. Table 3 shows the changes in body weight with 95% Confidence Intervals (CI).

Table 2. Longitudinal Changes in Mean Body Weight (kg) in Patients Receiving DPP-4 Inhibitors

Time Point	Mean Weight (kg) ± SD	95% Confidence Interval (CI)	p-value (vs Baseline)
Baseline	73.44 ± 12.35	70.55 – 76.33	—
3 Months	71.19 ± 12.05	68.37 – 74.00	< 0.001
6 Months	67.90 ± 11.73	65.16 – 70.64	< 0.001

Correspondingly, the analysis of BMI revealed similar statistically significant improvements. The baseline mean BMI was 24.34 ± 2.14 kg/m², indicative of a population bordering on overweight status according to Asian-Indian specific criteria. At three months, the mean BMI decreased to 23.73 ± 1.50 kg/m², and by six months, it had further declined to 23.50 ± 1.40 kg/m². The changes in BMI mirrored the weight data, achieving statistical significance ($p < 0.001$) at both intervals. These results suggest that the introduction of DPP-4 inhibitors contributed to a measurable and progressive reduction in overall adiposity in this patient population (Table 3).

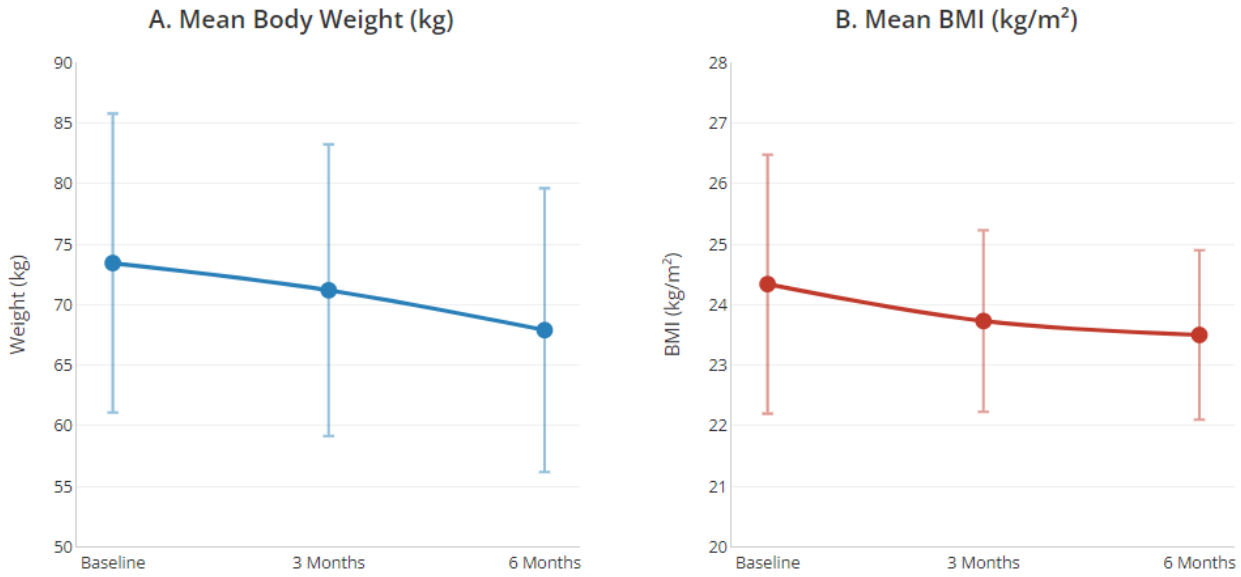

Figure 3. Longitudinal changes in Body Weight and BMI over 6 months (Error bars = SD).
($p < 0.001$ compared to baseline for all time points (3 months and 6 months))

Table 3. Longitudinal Changes in Body Mass Index (BMI) in Patients Receiving DPP-4 Inhibitors

Time Point	Mean BMI (kg/m²) ± SD	95% Confidence Interval (CI)	p-value (vs Baseline)
Baseline	24.34 ± 2.14	23.85 – 24.84	—
3 Months	23.73 ± 1.50	23.35 – 24.10	< 0.001
6 Months	23.50 ± 1.40	23.13 – 23.87	< 0.001

Table 4. Net Changes in Anthropometric Parameters from Baseline to 6 Months

Parameter	Baseline Mean	6-Month Mean	Net Change (Mean)	Statistical Significance
Body Weight (kg)	73.44	67.90	- 5.54 kg	p < 0.001
BMI (kg/m²)	24.34	23.50	- 0.84 kg/m²	p < 0.001

4. Discussion

The findings of this prospective study challenge the rigid classification of DPP-4 inhibitors as solely weight-neutral agents. While pivotal clinical trials established their non-inferiority regarding weight gain compared to placebo, our real-world data indicates a modest but statistically significant weight-reducing potential. The observed reduction in body weight and BMI over six months aligns with emerging viewpoints that in specific phenotypic subgroups, particularly those transitioning from sulfonylureas or engaging in concurrent lifestyle modifications, DPP-4 inhibitors may facilitate weight loss [12, 13].

The mechanism underlying this observation is likely multifactorial. DPP-4 inhibitors elevate the concentration of GLP-1, a potent incretin hormone that delays gastric emptying and promotes central satiety [7]. Although the physiological levels of GLP-1 achieved with DPP-4 inhibition are lower than those seen with pharmacological GLP-1 receptor agonists, they may be sufficient to curb appetite subtly in compliant patients [14]. In contrast with sulfonylureas, which drive lipogenesis and hypoglycemia-induced defensive snacking, DPP-4 inhibitors possess a low risk of hypoglycemia [15]. This safety profile allows patients to adhere to dietary restrictions without the fear of hypoglycemic episodes, indirectly supporting caloric deficit maintenance [13].

When juxtaposed with other modern antidiabetic classes, the magnitude of weight loss observed here is less than that typically seen with Sodium-Glucose Co-transporter-2 (SGLT-2) inhibitors, which induce weight loss through distinct mechanisms of glycosuria and osmotic diuresis [16]. However, SGLT-2 inhibitors are associated with specific risks, such as genitourinary infections and euglycemic diabetic ketoacidosis, which may limit their utility in frail or elderly populations [17]. Similarly, while GLP-1 receptor agonists offer superior weight loss, their injectable nature and gastrointestinal side effects can be barriers to adherence [14].

In this context, DPP-4 inhibitors offer a balanced therapeutic profile: they avoid the weight gain of older agents like sulfonylureas still widely prescribed in developing nations [18, 19] and provide a safer, albeit more modest, weight management benefit compared to SGLT-2 inhibitors. Our results reinforce the positioning of DPP-4 inhibitors as a preferred second-line therapy, particularly for patients where weight stabilization or modest reduction is a clinical priority alongside glycemic control.

5. Conclusion

This six-month observational study substantiates the therapeutic value of DPP-4 inhibitors in the management of Type 2 Diabetes Mellitus. Beyond their established glycemic efficacy, these agents demonstrated a statistically significant capacity to reduce body weight and BMI, effectively countering the weight gain often associated with traditional oral antidiabetics. While the absolute reduction is modest compared to SGLT-2 inhibitors, the favorable safety profile and tolerability of DPP-4 inhibitors make them an indispensable component of the pharmacotherapeutic arsenal. These results show their broader utilization in comprehensive diabetes care plans that aim to harmonize glycemic targets with weight management goals.

Compliance with ethical standards

Acknowledgements

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this manuscript. No external funding was received for this study.

Statement of ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Institutional Ethics Committee prior to the commencement of the study.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study

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