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Impact of Tirzepatide on Body Weight and Metabolic Parameters in Obesity

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Abstract **Original Research Article**

Background: Obesity is a chronic multifactorial disease associated with excess adiposity, metabolic dysfunction, and increased risk of cardiovascular and other obesity-related complications. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist, has emerged as an effective pharmacological treatment for obesity. However, assessment of its effects on body composition, including fat mass, lean mass, skeletal muscle, and body water compartments, is important for understanding the overall clinical impact of therapy. ***Objective:*** To evaluate the impact of tirzepatide therapy on body weight, BMI, body composition, and selected metabolic parameters among adults with overweight or obesity. ***Methods:*** This prospective observational study was conducted at the Department of Medicine, Tairunnessa Memorial Medical College, Gazipur, Bangladesh, from June 2024 to July 2025. A total of 45 adults with overweight or obesity who initiated once-weekly tirzepatide therapy were enrolled by consecutive sampling and followed prospectively. Baseline and follow-up assessments included body weight, BMI, body fat percentage, fat mass, fat-free mass, skeletal muscle mass, SMM-to-age index, dry lean mass, total body water, extracellular water, intracellular water, and ECW: TBW and ECW: ICW ratios. Tirzepatide was initiated at a low dose and gradually escalated according to clinical response and tolerability. Changes in body composition were evaluated overall and according to sex and initial BMI category. ***Results:*** The mean age of participants was 53 years. Following tirzepatide therapy, the proportion of participants with BMI ≥35 kg/m² decreased from 55.6% to 4.4%, while those with BMI <35 kg/m² increased from 44.4% to 95.6%. Body weight decreased by 28.2% and BMI by 27.9%. Body fat and fat mass declined by 37.6% and 54.2%, respectively, while fat-free mass, skeletal muscle mass, SMM-to-age index, and dry lean mass decreased by 7.3%, 8.2%, 8.3%, and 6.1%, respectively. Total body water, extracellular water, and intracellular water decreased by 7.6%, 9.4%, and 7.5%, respectively, whereas ECW: TBW and ECW:ICW ratios remained essentially stable. Females demonstrated greater reductions in body weight, BMI, fat mass, lean tissue parameters, and body water compartments than males. Participants with higher baseline BMI experienced greater reductions in body weight, BMI, body fat, fat mass, lean tissue measures, and body water compartments compared with those in the lower-BMI group. ***Conclusion:*** Tirzepatide therapy was associated with substantial reductions in body weight, BMI, and adiposity, with the majority of weight loss reflected by a marked reduction in fat mass. Although modest reductions in lean mass and skeletal muscle mass were observed, relative fluid distribution remained largely stable. Greater reductions were observed among female participants and individuals with higher baseline BMI. These findings support the effectiveness of tirzepatide for weight and fat reduction while highlighting the importance of monitoring lean mass and implementing strategies to preserve skeletal muscle during treatment.

Keywords: Tirzepatide; obesity; body weight; body composition.

INTRODUCTION

Obesity is a chronic, progressive, and multifactorial disease characterized by excessive accumulation of adipose tissue and is associated with substantial morbidity and mortality worldwide. Beyond its effects on body weight, obesity contributes to insulin resistance, type 2 diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, metabolic dysfunction-associated steatotic liver disease, and impaired quality of life. Despite the availability of lifestyle interventions and pharmacological therapies,

achieving and maintaining clinically meaningful weight loss remains challenging for many individuals. The chronic nature of obesity and the high rate of weight regain following conventional interventions highlight the need for effective and sustainable therapeutic strategies. [1-2]

The pathophysiology of obesity involves complex interactions between genetic, environmental, metabolic, neuroendocrine, and behavioral factors. Although lifestyle modification, including dietary changes and increased physical activity, remains the foundation of obesity management, the magnitude of weight loss achieved with lifestyle intervention alone is often modest and difficult to sustain. Consequently, pharmacological treatment is increasingly recognized as an important component of comprehensive obesity management, particularly for individuals with severe obesity or obesity-related metabolic complications. [3] Modern anti-obesity medications that target physiological pathways regulating appetite, satiety, glucose metabolism, and energy balance have significantly expanded therapeutic options.

Tirzepatide is a novel once-weekly injectable medication that acts as a dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. Through simultaneous activation of these incretin pathways, tirzepatide enhances glucose-dependent insulin secretion, suppresses inappropriate glucagon secretion, delays gastric emptying, and influences central appetite-regulating mechanisms. [4-5] These combined effects may result in reduced energy intake, improved glycemic control, and substantial reductions in body weight. The dual incretin mechanism of tirzepatide distinguishes it from conventional GLP-1 receptor agonists and has generated considerable interest in its potential role in the treatment of obesity and associated metabolic disorders. [6]

Clinical trials have demonstrated that tirzepatide can produce substantial and sustained weight loss in individuals with obesity or overweight, with the magnitude of weight reduction generally increasing with dose and duration of treatment. In addition to changes in body weight, treatment with tirzepatide has been associated with improvements in several important metabolic parameters, including fasting blood glucose, glycated hemoglobin, insulin resistance, blood pressure, and lipid profiles. These metabolic benefits are particularly clinically relevant because obesity-related complications are driven not only by excess adiposity but also by abnormalities in glucose and lipid metabolism. Therefore, assessment of the effects of tirzepatide should extend beyond weight loss alone to include its broader influence on metabolic health. [7-8]

The response to tirzepatide may vary according to baseline body weight, degree of obesity, presence of type 2 diabetes, treatment dose, duration of therapy, adherence, and individual metabolic characteristics. Although randomized clinical trials have established the efficacy of tirzepatide, real-world data remain important for evaluating its effectiveness in routine clinical practice. Monitoring changes in body weight and metabolic parameters during treatment may help clarify the practical benefits of tirzepatide and identify patient groups most likely to achieve favorable outcomes. Furthermore, evaluation of treatment-associated adverse effects and tolerability is essential for understanding the overall clinical utility of this therapy. [9]

Despite the increasing use of tirzepatide as an important pharmacological option for obesity management, further evaluation of its effects on body weight and metabolic health is warranted in different clinical populations and healthcare settings.

Objective

Therefore, the present study was undertaken to assess the impact of tirzepatide therapy on body weight and selected metabolic parameters among individuals with obesity, with particular emphasis on changes in anthropometric measures, glycemic control, lipid profile, and other relevant metabolic indicators during the treatment period.

METHODOLOGY

Study Design and Setting

This prospective observational study was conducted in the Department of Medicine at Tairunnessa Memorial Medical College, Gazipur, Bangladesh, from June 2024 to July 2025. The study was designed to evaluate the effects of tirzepatide therapy on body weight, body composition, and selected metabolic parameters among adults with overweight or obesity. The study protocol was reviewed and approved by the Institutional Ethics Committee of Tairunnessa Memorial Medical College. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment.

Study Population

A total of 45 adults with overweight or obesity who initiated tirzepatide therapy during the study period were included using consecutive sampling. Participants were enrolled based on predefined eligibility criteria and were followed prospectively from baseline assessment through scheduled follow-up. All patients received routine counseling regarding dietary modification, physical activity, and lifestyle measures as part of comprehensive obesity management.

Baseline Assessment and Data Collection

At baseline, demographic and clinical information was collected using a structured data collection form. Recorded variables included age, sex,

body weight, height, body mass index (BMI), relevant medical history, comorbidities, and baseline metabolic parameters. Body weight was measured using a calibrated clinical weighing scale, while height was measured at baseline and BMI was calculated as weight in kilograms divided by height in meters squared.

Body composition was assessed using bioelectrical impedance analysis (BIA) according to the manufacturer's standardized instructions. The assessment included body fat percentage (BF%), fat mass (FM), fat-free mass (FFM), skeletal muscle mass (SMM), total body water (TBW), extracellular water (ECW), intracellular water (ICW), and other relevant body composition parameters where available. Participants were instructed to maintain usual hydration and to avoid strenuous exercise and food intake for an appropriate period before body composition assessment to improve measurement consistency.

Tirzepatide Treatment

Following the baseline assessment, participants initiated once-weekly subcutaneous tirzepatide therapy as part of routine clinical management. Treatment was generally initiated at 2.5 mg once weekly, with subsequent dose escalation according to individual clinical response, tolerability, and physician judgment. Dose escalation was performed gradually, and the maximum dose was determined according to treatment response and the occurrence of adverse effects. All participants continued to receive lifestyle counseling throughout the treatment period.

Follow-up and Outcome Assessment

Participants were followed prospectively through regular clinical visits. During follow-up, treatment adherence, tolerability, adverse effects, dose modifications, body weight, and metabolic parameters were assessed. The primary outcome was the change in body weight and BMI from baseline to follow-up. Secondary outcomes included changes in body composition and selected metabolic parameters, including fasting blood glucose, glycated hemoglobin (HbA1c), lipid profile, blood pressure, and other clinically relevant biochemical measurements where available.

Follow-up assessments were performed at predefined clinical visits during the study period. Changes in body weight, BMI, body composition, and metabolic parameters were compared between baseline and subsequent follow-up assessments. Any clinically significant adverse effects or treatment-related complications were documented during follow-up.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range, as appropriate, while categorical variables were presented as frequencies and percentages. The distribution of continuous variables was assessed before statistical analysis. Changes in body weight, BMI, body composition, and metabolic parameters between baseline and follow-up were analyzed using the paired-samples t-test for normally distributed variables or the Wilcoxon signed-rank test for non-normally distributed variables. Categorical variables were analyzed using the chi-square test or Fisher's exact test, where appropriate.

Where appropriate, subgroup analyses were performed according to baseline BMI category, sex, and other clinically relevant characteristics. The association between baseline characteristics and the magnitude of weight loss or metabolic improvement was assessed using appropriate comparative or regression analyses. All statistical tests were two-tailed, and a p-value of <0.05 was considered statistically significant. Statistical analysis was performed using appropriate statistical software.

RESULTS

As shown in Table 1, substantial improvements in body composition were observed following tirzepatide therapy. The proportion of participants with BMI ≥35 kg/m² decreased from 55.6% before treatment to 4.4% after therapy, while those with BMI <35 kg/m² increased from 44.4% to 95.6%. Body weight decreased by 28.2% and BMI by 27.9%, while body fat and fat mass declined by 37.6% and 54.2%, respectively. Lean tissue parameters also showed modest reductions, including fat-free mass (7.3%), skeletal muscle mass (8.2%), SMM-to-age index (8.3%), and dry lean mass (6.1%). Total body water, extracellular water, and intracellular water decreased by 7.6%, 9.4%, and 7.5%, respectively. In contrast, the ECW: TBW and ECW:ICW ratios remained essentially stable, showing only minimal increases of 0.2% and 0.3%, respectively. Overall, the findings indicate that tirzepatide therapy was associated with marked reductions in body weight, adiposity, and BMI, with the majority of weight reduction primarily attributable to loss of fat mass, while fluid distribution remained relatively stable.

Table 1: Body Composition Changes Before and After Tirzepatide Therapy

Variable	Mean (95% CI)	Pre-therapy (%)	Post-therapy (%)	Change (%)
Age	**53 (50, 56)**			
Weight status				
BMI ≥35 kg/m²		55.6	4.4	−51.2
BMI <35 kg/m²		44.4	95.6	+51.2

Variable	Mean (95% CI)	Pre-therapy (%)	Post-therapy (%)	Change (%)
Age	**53 (50, 56)**			
Body weight		100.0	71.8	−28.2
BMI		100.0	72.1	−27.9
Body fat		100.0	62.4	−37.6
Fat mass		100.0	45.8	−54.2
Fat-free mass		100.0	92.7	−7.3
Skeletal muscle mass		100.0	91.8	−8.2
SMM-to-age index		100.0	91.7	−8.3
Dry lean mass		100.0	93.9	−6.1
Total body water		100.0	92.4	−7.6
Extracellular water		100.0	90.6	−9.4
Intracellular water		100.0	92.5	−7.5
ECW:TBW ratio		100.0	100.2	+0.2
ECW:ICW ratio		100.0	100.3	+0.3

The analysis of body composition changes according to sex showed that both male and female participants experienced substantial improvements following tirzepatide therapy. The proportion of participants with BMI ≥35 kg/m² decreased from 45.5% to 6.7% among males and from 40.0% to 0.0% among females, while the proportion with BMI <35 kg/m² increased from 54.5% to 93.3% in males and from 60.0% to 100.0% in females. Females demonstrated greater reductions in body weight (31.5% vs. 22.2%), BMI (31.3% vs. 22.6%), fat mass (56.9% vs. 50.5%), fat-free mass (9.9% vs. 3.5%), skeletal muscle mass (11.4% vs. 3.9%), SMM-to-age index (11.5% vs. 3.9%), dry lean mass (9.0% vs. 2.4%), total body water (10.2% vs. 4.2%), extracellular water (13.5% vs. 3.8%), and intracellular water (9.6% vs. 4.6%) compared with males. Reductions in body fat were comparable between females and males (37.0% vs. 38.7%), while the ECW: TBW and ECW:ICW ratios showed minimal changes in both sexes, with a slight decrease among males and a slight increase among females. Overall, tirzepatide therapy was associated with greater relative reductions in body weight and most body composition parameters among female participants.

Table 2: Body Composition Changes According to Sex

Variable	Male Pre (%)	Male Post (%)	Male Change (%)	Female Pre (%)	Female Post (%)	Female Change (%)
Weight status						
BMI ≥35 kg/m²	45.5	6.7	−38.8	40.0	0.0	−40.0
BMI <35 kg/m²	54.5	93.3	+38.8	60.0	100.0	+40.0
Body weight	100.0	77.8	−22.2	100.0	68.5	−31.5
BMI	100.0	77.4	−22.6	100.0	68.7	−31.3
Body fat	100.0	61.3	−38.7	100.0	63.0	−37.0
Fat mass	100.0	49.5	−50.5	100.0	43.1	−56.9
Fat-free mass	100.0	96.5	−3.5	100.0	90.1	−9.9
Skeletal muscle mass	100.0	96.1	−3.9	100.0	88.6	−11.4
SMM-to-age index	100.0	96.1	−3.9	100.0	88.5	−11.5
Dry lean mass	100.0	97.6	−2.4	100.0	91.0	−9.0
Total body water	100.0	95.8	−4.2	100.0	89.8	−10.2
Extracellular water	100.0	96.2	−3.8	100.0	86.5	−13.5
Intracellular water	100.0	95.4	−4.6	100.0	90.4	−9.6
ECW:TBW ratio	100.0	99.1	−0.9	100.0	100.8	+0.8
ECW:ICW ratio	100.0	98.7	−1.3	100.0	101.4	+1.4

The analysis of body composition changes according to initial BMI category showed that participants in both groups experienced reductions in body weight and body composition parameters following tirzepatide therapy, with greater relative changes observed in the upper-BMI group. Body weight decreased by 22.5% in the lower-BMI group compared with 35.6% in the upper-BMI group, while BMI declined by 22.6% and 35.2%, respectively. Similarly, reductions in body fat were 35.2% in the lower-BMI group and 41.0% in the upper-BMI group, whereas fat mass decreased by 49.9% and 60.6%, respectively. The upper-BMI group also demonstrated greater reductions in fat-free mass (11.5% vs. 4.4%), skeletal muscle mass (13.2% vs. 5.0%), SMM-to-age index (13.3% vs. 4.9%), dry lean mass (10.3% vs. 3.5%), total body water (12.2% vs. 4.8%), extracellular water (16.5% vs. 4.9%), and intracellular water (11.9% vs. 4.5%) compared with the

lower-BMI group. In contrast, ECW: TBW and ECW:ICW ratios remained essentially stable in both groups, with only minimal changes. Overall, participants with higher initial BMI experienced greater relative reductions in body weight, adiposity, lean tissue measures, and body water compartments following tirzepatide therapy.

Table 3: Body Composition Changes According to Initial BMI Category

Variable	Lower BMI Pre (%)	Lower BMI Post (%)	Change (%)	Upper BMI Pre (%)	Upper BMI Post (%)	Change (%)
Body weight	100.0	77.5	−22.5	100.0	64.4	−35.6
BMI	100.0	77.4	−22.6	100.0	64.8	−35.2
Body fat	100.0	64.8	−35.2	100.0	59.0	−41.0
Fat mass	100.0	50.1	−49.9	100.0	39.4	−60.6
Fat-free mass	100.0	95.6	−4.4	100.0	88.5	−11.5
Skeletal muscle mass	100.0	95.0	−5.0	100.0	86.8	−13.2
SMM-to-age index	100.0	95.1	−4.9	100.0	86.7	−13.3
Dry lean mass	100.0	96.5	−3.5	100.0	89.7	−10.3
Total body water	100.0	95.2	−4.8	100.0	87.8	−12.2
Extracellular water	100.0	95.1	−4.9	100.0	83.5	−16.5
Intracellular water	100.0	95.5	−4.5	100.0	88.1	−11.9
ECW:TBW ratio	100.0	100.3	+0.3	100.0	99.9	−0.1
ECW:ICW ratio	100.0	100.5	+0.5	100.0	99.8	−0.2

DISCUSSION

The present study demonstrated substantial improvements in body weight and body composition following tirzepatide therapy. The overall 28.2% reduction in body weight and 27.9% reduction in BMI were accompanied by marked decreases in body fat (37.6%) and fat mass (54.2%), indicating that the principal effect of treatment was a substantial reduction in adiposity. These findings are consistent with the body-composition substudy of SURMOUNT-1, in which tirzepatide produced significantly greater reductions in body weight, fat mass, and lean mass than placebo over 72 weeks. However, the magnitude of weight reduction in the present cohort was greater than that reported in SURMOUNT-1, where body weight decreased by approximately 21.3%. This difference may be related to the longer treatment duration, differences in dose exposure, patient selection, lifestyle counseling, or the use of bioelectrical impedance analysis rather than DXA in the present study. [10]

A particularly important finding was that the reduction in body weight was predominantly associated with loss of fat mass, while reductions in lean tissue were comparatively modest. Fat mass decreased by 54.2%, whereas fat-free mass, skeletal muscle mass, and dry lean mass declined by 7.3%, 8.2%, and 6.1%, respectively. This pattern supports the favorable adiposity-reducing effect of tirzepatide, although the observed reduction in lean tissue emphasizes the importance of monitoring muscle mass during pharmacological weight loss. The SURMOUNT-1 body-composition analysis similarly demonstrated substantial reductions in fat mass but also reported a measurable reduction in lean mass, with approximately three-quarters of weight loss attributable to fat mass and one-quarter to lean mass. A systematic review of randomized controlled trials has likewise concluded that tirzepatide consistently reduces total and visceral fat, although the effect on fat-free mass remains less consistent across studies. [11]

The sex-specific analysis revealed greater relative reductions in body weight and most body-composition parameters among females than males. Women experienced greater reductions in body weight, BMI, fat mass, fat-free mass, skeletal muscle mass, the SMM-to-age index, dry lean mass, and total and extracellular body water. In contrast, the reduction in body fat percentage was broadly comparable between sexes. These findings are consistent with recent real-world evidence suggesting that female sex may be independently associated with greater weight loss during tirzepatide treatment. [12] However, they differ somewhat from the SURMOUNT-1 body-composition substudy, which did not identify significant sex-based differences in the percentage treatment effect for body weight, fat mass, or lean mass. The discrepancy may reflect differences in sample size, treatment duration, baseline characteristics, dosing, and the observational nature of the present study. [13]

The greater reduction in lean tissue observed among females in the present study should be interpreted carefully. Although women experienced greater absolute percentage reductions in skeletal muscle mass and fat-free mass, this may partly reflect differences in baseline body composition and the relatively greater overall weight loss achieved by female participants. Importantly, the reduction in fat mass was also substantial, and the overall pattern remained one of predominantly fat-oriented weight loss. Nevertheless, the findings highlight the importance of strategies to preserve lean mass during tirzepatide therapy, including adequate dietary protein intake and resistance exercise, particularly in patients

experiencing rapid or substantial weight reduction. The observed sex-related differences also suggest that individualized monitoring of body composition may provide more clinically meaningful information than body weight alone. [14]

Participants with a higher baseline BMI demonstrated greater relative reductions in body weight, BMI, body fat, and fat mass than those in the lower-BMI group. Weight decreased by 35.6% in the upper-BMI group compared with 22.5% in the lower-BMI group, while fat mass declined by 60.6% and 49.9%, respectively. The upper-BMI group also showed greater reductions in fat-free mass, skeletal muscle mass, dry lean mass, and body water compartments. These findings suggest that patients with greater initial adiposity may experience a larger absolute and relative response to tirzepatide. The pattern is broadly consistent with subgroup findings from SURMOUNT-1, which demonstrated clinically meaningful reductions across different baseline and weight-loss subgroups. However, the greater loss of lean tissue and body water in the higher-BMI group may partly reflect the larger overall magnitude of weight loss rather than a specific adverse effect of higher BMI. [15]

Finally, the stability of the ECW: TBW and ECW:ICW ratios in the overall cohort and across sex and BMI categories is noteworthy. Although absolute extracellular and intracellular water decreased, the relative distribution of body water remained largely unchanged. This suggests that the reductions in body water were proportionate to overall body mass loss rather than indicating a major disturbance in fluid compartment balance. Taken together, the present findings indicate that tirzepatide was associated with marked and clinically meaningful reductions in body weight and adiposity, with most weight loss arising from fat mass and relatively smaller reductions in lean tissue and body water. The findings also demonstrate potentially important differences according to sex and baseline BMI. However, because the study was based on a relatively small observational cohort and body composition was assessed using bioelectrical impedance analysis, the results should be interpreted cautiously and confirmed in larger prospective studies using standardized imaging-based methods such as DXA. [11, 4]

Conclusion

In conclusion, the present study demonstrated that tirzepatide therapy was associated with substantial improvements in body weight and metabolic body composition among adults with overweight and obesity. Treatment resulted in marked reductions in body weight, BMI, body fat, and fat mass, with the majority of weight loss attributable to fat mass, while reductions in fat-free mass and skeletal muscle mass were comparatively modest. Female participants showed greater reductions in body weight and several body-composition parameters than males, whereas participants with higher baseline BMI experienced greater overall reductions in adiposity and body weight than those with lower BMI. Despite decreases in absolute total, extracellular, and intracellular body water, the ECW: TBW and ECW:ICW ratios remained largely stable, suggesting preservation of relative fluid distribution. Overall, these findings support tirzepatide as an effective pharmacological treatment for substantial weight and fat reduction, while emphasizing the importance of monitoring lean mass and incorporating strategies to preserve skeletal muscle during treatment.

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