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A Comparative Study Between Tirzepatide and Semaglutide in The Management of Obesity and Type 2 Diabetes Mellitus

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Abstract

Introduction: Obesity and type 2 diabetes mellitus (T2DM) are major public health concerns worldwide, requiring effective treatment strategies. Tirzepatide and Semaglutide are novel therapeutic agents that have shown efficacy in managing both conditions. This study aimed to compare the efficacy and metabolic outcomes of Tirzepatide versus Semaglutide in obese patients associated with T2DM.

Methods: This retrospective observational study was conducted in the Department of Cardiology, Labaid Cancer Hospital & Super Speciality Centre, Labaid Diagnostics Center, Uttara Adhunik Medical College Hospital, Dhaka, Bangladesh, from January 2023 to December 2023. In this study, we included 100 patients with obesity who attended the cardiology department of our institution. The patients were divided into two groups -Group A (Patients who were treated with Tirzepatide) and Group B (Patients who were treated with Semaglutide).

Result: At baseline, the groups were comparable in age (31.73 ± 9.59 years for Tirzepatide vs. 32.96 ± 12.32 years for Semaglutide) and BMI (32.67 ± 6.24 kg/m² vs. 33.41 ± 5.47 kg/m², p = 0.529). By the third follow-up, the mean weight reduction was greater in the Tirzepatide group (77.32 ± 10.63 kg) compared to the Semaglutide group (79.24 ± 9.91 kg), with a statistically significant difference in the percentage reduction in weight (11.4% vs. 10.3%, p < 0.001). FBS and HbA1c levels also showed greater reductions in the Tirzepatide group, with significant differences at the third follow-up (FBS: 5.45 ± 0.41 mg/dl vs. 5.63 ± 0.32 mg/dl, p = 0.016; HbA1c: 4.6 ± 0.4% vs. 4.8 ± 0.3%, p = 0.005). Minor adverse effects were common in both groups, with nausea/vomiting being the most frequent (38% in Group A and 44% in Group B). Unique to the Tirzepatide group were injection site itching (32%) and feeling feverish (12%), while dizziness occurred only in the Semaglutide group (12%).

Conclusion: The study findings show that both Tirzepatide and Semaglutide effectively reduced weight, BMI, FBS, and HbA1c in patients with obesity. Overall, Tirzepatide demonstrated a greater reduction in weight, BMI, fasting blood sugar, and HbA1c compared to Semaglutide, with a statistically significant advantage in (%) change in weight and FBS.

Keywords: Obesity; T2DM; Weight loss; Tirzepatide; Semaglutide

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Introduction

Obesity is a major global health concern, with current estimates indicating that over 650 million adults and approximately 340 million children and adolescents are living with obesity. [1,2] Overweight and obesity are recognized as primary risk factors for the development of type 2 diabetes mellitus (T2DM), which, in turn, drives the excess morbidity and mortality observed in this population. [3] According to a systematic review and meta-analysis done by Akhtar et al. reported that about 10.1% of the adult population in Bangladesh have prediabetes. [4] The economic burden of diabetes is significant, with the total direct and indirect costs of diagnosed diabetes exceeding $410 billion, much of which is attributed to diabetes-related complications. [5] Obesity is associated with numerous comorbidities, including T2DM, hypertension, nonalcoholic fatty liver disease (NAFLD), malignancies, and cardiovascular disease (CVD). [6] Evidence suggests that achieving a 5%-10% reduction in body weight can significantly improve health outcomes and quality of life. [7,8] This weight loss has been associated with improved insulin sensitivity and a reduction in obesity-related complications like backache, nausea, anorexia, weakness, etc.

Effective obesity management is multifactorial and typically involves a combination of behavioral interventions, dietary modification, increased physical activity, pharmacological therapies, and metabolic or bariatric surgery. [9] Among these, surgical interventions offer the most substantial and sustained weight loss; however, barriers to access, risks associated with anesthesia, surgical complications, and postoperative challenges often limit their widespread use. [10]

Pharmacological therapies play a critical role in managing obesity and its associated conditions. The relationship between obesity and T2DM is characterized by a complex interplay of insulin resistance, progressive pancreatic beta-cell dysfunction, and visceral adipose tissue accumulation. These factors heighten cardiometabolic risks, including CVD and NAFLD. [11] Consequently, there is a pressing need for pharmacological interventions that not only control T2DM but also promote weight loss.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as first-line therapies due to their dual efficacy in glycemic control and weight reduction. Semaglutide, a prominent GLP-1 RA, has shown impressive clinical outcomes, including mean reductions in glycated hemoglobin (HbA1c) of 1.5%-2.0%, sustained weight loss of 6%-10% over 52 weeks, and a 26% reduction in the risk of major adverse cardiovascular events (MACE) in high-risk patients. [12,13]

In addition to GLP-1 RAs, newer therapies, such as the dual GLP-1 RA/gastric inhibitory polypeptide (GIP) agonist tirzepatide, have demonstrated substantial weight loss in patients with obesity, with or without T2DM, in randomized clinical trials (RCTs).[13-16] Tirzepatide has shown superior weight reduction compared to semaglutide in patients with T2DM.[17]

However, direct head-to-head comparisons between these therapies in patients with obesity or overweight remain unavailable. Therefore, in this study, we aimed to compare the effectiveness of Tirzepatide and Semaglutide in managing obesity and type 2 diabetes mellitus among obese patients.

Methodology and Materials

This retrospective observational study was conducted in the Department of Cardiology, Labaid Cancer Hospital & Super Speciality Centre, Labaid Diagnostics Center, Uttara Adhunik Medical College Hospital, Dhaka, Bangladesh, from January 2023 to December 2023. This study included 100 patients with obesity associated with type 2 DM who attended the cardiology department and received Tirzepatide and Semaglutide. The patients were divided into two groups: Group A (Patients who were treated with Tirzepatide) and Group B (Patients who were treated with Semaglutide).

These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged above 18 years; b)Patients with obesity; c) Patients with DM, HTN, dyslipidemia, hypothyroidism & PCOS as comorbidity; d) Patients with Body Mass Index (BMI) ≥30 kg/m² (or ≥27 kg/m² with obesity-related comorbidities) were included in the study and a) Patients who were ever prescribed any GLP-1 RA or pramlintide; b) Patients with pregnancy & showing any allergic reaction to study drugs; c) Patients with any history of acute illness (e.g., renal or pancreatic diseases, ischemic heart disease, asthma etc.); d) Patients who were unwilling to participate were excluded from our study.

Drug Dosage: Patients with or without T2DM in group A received Tirzepatide 2.5 mg, 5 mg, and 7.5 mg weekly for at least 3 months. Patients in group B received Semaglutide. Semaglutide has two formations- Plain Semaglutide (Designed to control blood sugar levels and obesity) and Concentrated Semaglutide form (Designed to manage obesity). Patients with T2DM were given 0.25 mg and 0.5 mg of plain Semaglutide, and patients without T2DM were given 0.25 mg, 0.5 mg,1 mg,1.7 mg, and 2.4 mg of concentrated form of Semaglutide per week for at least 3 months.

Data Collection: Informed verbal consent was taken from the patients. Baseline Characteristics like age, sex, comorbidities, and medication history were collected from case records, and the data of BMI, HbA1c, Fasting blood sugar (FBS) & SGPT were collected from the blood test report of the patient. Primary outcomes were the percentage change in body weight from baseline and decreased HbA1c levels.

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Secondary outcomes were the changes in FBS, improvement in weight-related backache, adverse effects, and satisfaction level of treatment.

Statistical Analysis: All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation; qualitative data was expressed as frequency distribution and percentage. The data were analyzed using the t-test, chi-square (X2) test, and Fisher's exact test. A p-value <0.05 was considered as significant. Statistical analysis was performed by using SPSS 22 (Statistical Package for Social Sciences) for Windows version 10. The study was approved by the ethical review committee of Uttara Adhunik Medical College Hospital, Dhaka, Bangladesh.

Results

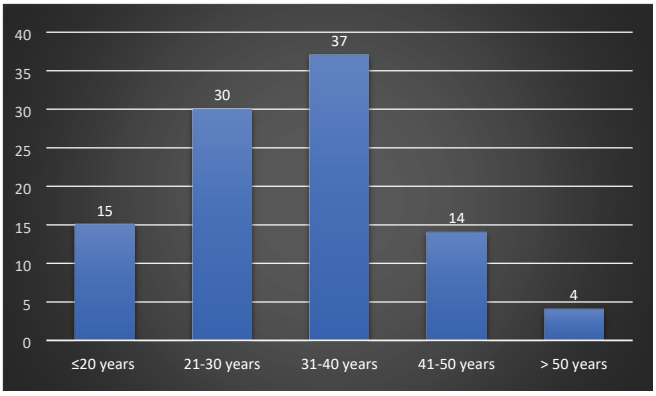
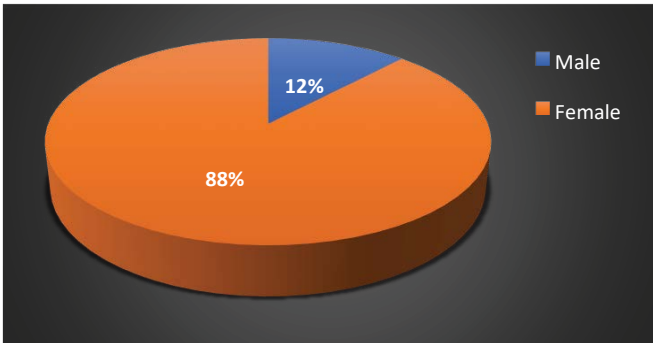


Figure 1: Age distribution of our study patients (n=100).

Figure 1 shows that the majority (37%) of our patients were in the age group of 31-40 years, followed by 30% of them aged 21-30 years, 15% of them aged 20 years or younger, and 14% of patients were in the 4150 years age group. Only a small percentage (4%) of patients were aged more than 50 years.



The pie chart shows that most of our study patients (88%) were female and 12% were male. The male and female ratio was 1:7.33 in our study.

Figure 2: Gender distribution of our study patients (n=100).

Table 1: Baseline characteristics of our study subjects.

Baseline	Group A		Group B	
Mean age (years)	31.73±9.59		32.96±12.32	
Mean Height (cm)	151.34 ± 2.64		150.24 ± 3.64	
Mean Weight (kg)	87.26±13.69		88.36±12.69	
BMI (kg/m²)	32.67±6.24		33.41±5.47	
Systolic blood pressure (mm Hg)	131.90 ± 7.78		132.24 ±6.51	
Diastolic blood pressure (mm Hg)	84.34 ± 4.38		85.4 ± 4.69	
Fasting Blood Sugar (mg/dl)	6.45 ± 0.58		6.63 ± 0.43	
HbA1c (%)	5.5 ± 0.7		5.4 ± 0.7	
SGPT (U/L)	46.25 ± 26.47		46.38 ± 28.93	
Obesity stage				
Class I (30 to 34.9 kg/m²)	29	58.0	32	64.0
Class II (35 to 39.9 kg/m²)	14	28.0	12	24.0
Class III (≥40 kg/m²)	7	14.0	6	12.0
Physical activity				
Sedentary	11	22.0	12	24.0
Moderate	29	58.0	32	64.0
Active	10	20.0	6	12.0
Comorbidities				
Hypertension	19	38.0	17	34.0
DM	18	36.0	15	30.0
Hypothyroidism	15	30.0	16	32.0
Dyslipidemia	9	18.0	7	14.0
PCOS	6	12.0	8	16.0

Table 1 shows the mean age was 31.73 ± 9.59 years in the Tirzepatide group and 32.96 ± 12.32 years in the Semaglutide group. The mean BMI was 32.67 ± 6.24 kg/m² for Tirzepatide and 33.41 ± 5.47 kg/m² for Semaglutide.

Fasting blood sugar and HbA1c levels were slightly higher in the Semaglutide group (6.63 ± 0.43 mg/dl and 5.4 ± 0.7%) compared to the Tirzepatide group (6.45 ± 0.58 mg/dl and 5.5 ± 0.7%). Most participants were in the class I obesity, accounting for 58% in the Tirzepatide group, and 64% in the Semaglutide group. Moderate physical activity was the most common lifestyle pattern, reported by 58% of Tirzepatide users and 64% of Semaglutide users. Hypertension affected 38% of the Tirzepatide group and 34% of the Semaglutide group, while DM was present in 36% & 30%, and hypothyroidism was present in 30% & 32%, respectively. Other common comorbidities included dyslipidemia and polycystic ovary syndrome (PCOS).

Table 2 shows that at baseline, the mean weight was 87.26 ± 13.69 kg for the Tirzepatide group and 88.36 ± 12.69 kg for the Semaglutide group (p = 0.678). By the third follow-up, the mean weight decreased to 77.32 ± 10.63 kg for the Tirzepatide group and 79.24 ± 9.91 kg for the Semaglutide

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Table 2: Distribution of our study subjects by their treatment outcome.

Treatment Outcome	Group A	Group B	P-value
Weight (kg)			
At baseline	87.26 ± 13.69	88.36 ± 12.69	0.678
At 1st follow-up	83.45 ± 12.82	85.12 ± 11.93	0.502
At 2nd follow-up	79.68 ± 11.75	81.45 ± 10.88	0.436
At 3rd follow-up	77.32 ± 10.63	79.24 ± 9.91	0.352
(%) Change in weight	**-11.4 %**	**-10.3 %**	**<0.001**
BMI (kg/m²)			
At baseline	32.67 ± 6.24	33.41 ± 5.47	0.529
At 1st follow-up	31.24 ± 5.93	32.18 ± 5.14	0.399
At 2nd follow-up	29.88 ± 5.56	30.75 ± 4.92	0.409
At 3rd follow-up	28.65 ± 5.21	29.48 ± 4.68	0.404
Fasting Blood Sugar (mg/dl)			
At baseline	6.45 ± 0.58	6.63 ± 0.43	0.051
At 1st follow-up	5.98 ± 0.52	6.25 ± 0.39	0.004
At 2nd follow-up	5.62 ± 0.47	5.84 ± 0.35	0.009
At 3rd follow-up	5.45 ± 0.41	5.63 ± 0.32	0.016
HbA1c (%)			
At baseline	5.5 ± 0.7	5.4 ± 0.7	0.476
At 1st follow-up	5.1 ± 0.6	5.2 ± 0.6	0.406
At 2nd follow-up	4.8 ± 0.5	4.9 ± 0.5	0.319
At 3rd follow-up	4.6 ± 0.4	4.8 ± 0.3	0.005
Backache	Group A	Group B	
At baseline	7(14%)	9(18%)	
At 3rd follow-up	2(4%)	3(6%)	
Obstructive sleep apnea			
At baseline	3(6%)	4(8%)	
At 3rd follow-up	0	2(4%)	

Group A= Patients who received Tirzepatide; Group B= Patients who received Semaglutide

group (p = 0.352). The percentage reduction in weight was 11.4% for Tirzepatide and 10.3% for Semaglutide, with a statistically significant difference between the groups (p < 0.001). At baseline, the BMI was 32.67 ± 6.24 kg/m² for Tirzepatide and 33.41 ± 5.47 kg/m² for Semaglutide (p = 0.529). By the third follow-up, BMI reduced to 28.65 ± 5.21 kg/m² and 29.48 ± 4.68 kg/m², respectively, although the difference was not statistically significant (p = 0.404). At baseline, the mean FBS was slightly lower in the Tirzepatide group (6.45 ± 0.58 mg/dl) compared to the Semaglutide group (6.63 ± 0.43 mg/dl) but was not statistically significant (p = 0.051). By the third follow-up, FBS was 5.45 ± 0.41 mg/dl for Tirzepatide and 5.63 ± 0.32 mg/dl for Semaglutide, with the difference being statistically significant (p = 0.016). Baseline HbA1c levels were comparable between the groups (p = 0.476). At the third follow-up, HbA1c levels dropped to 4.6 ± 0.4% in the Tirzepatide group and 4.8 ± 0.3% in the Semaglutide group, with a statistically significant difference (p = 0.005). At baseline, 14% of participants in Group A and 18% in Group B reported experiencing backache. By the third follow-up, there was substantial improvement in backache in both groups. For obstructive sleep apnea, 6% of individuals in Group A and 8% in Group B had the condition at baseline. By the third follow-up, no participants in Group A reported obstructive sleep apnea, while the prevalence in Group B slightly decreased to 4%.

Table 3: Distribution of our study subjects by adverse effects and their satisfaction level after treatment.

Adverse effects	Group A		Group B	
	N=50	P(%)	N=50	P(%)
Heartburn	12	24.0	19	38.0
Nausea /Vomiting	19	38.0	22	44.0
General weakness	18	36.0	20	40.0
Itching at the injection site	16	32.0	0	0.0
Feeling feverish on 1st day of injection	6	12.0	0	0.0
Anorexia	2	4.0	8	16.0
Dizziness	0	0.0	6	12.0
Loose motion	2	4.0	1	2.0
Abdominal pain	2	4.0	3	6.0
Others	2	4.0	2	4.0
Patient satisfaction level				
Satisfied	46	92.0	42	84.0
Dissatisfied	4	8.0	8	16.0

Group A= Patients who received Tirzepatide; Group B= Patients who received Semaglutide

Table 3 shows that the most commonly reported side effects in both groups were nausea/vomiting, affecting 38% of Group A and 44% of Group B, followed by general weakness (36% in Group A and 40% in Group B). Heartburn was also frequent, reported by 24% of Group A and 38% of Group B. However, side effects like itching at the injection site (32%) and feeling feverish on the first day of injection (12%) occurred only in Group A, while dizziness occurred only in Group B (12%). Anorexia was more prevalent in Group B (16%) compared to Group A (4%). Less common side effects included loose motion (4% in Group A vs. 2% in Group B), and abdominal pain (4% in Group A vs. 6% in Group B), with other minor effects like increased SGPT reported by 4% of participants in both groups. Despite the adverse effects, most participants (92%) in Group A were satisfied compared to 84% in Group B.

Conversely, 8% of Group A and 16% of Group B were dissatisfied with their treatment.

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Discussion

This study compared the effectiveness and safety of Tirzepatide and Semaglutide in managing obesity and type 2 diabetes mellitus (T2DM). The mean age was 31.73 ± 9.59 years for Tirzepatide vs. 32.96 ± 12.32 years for Semaglutide. Anson et al found the mean age was 47.5 ± 11.8 years and 47.5 ± 11.9 years for the tirzepatide and semaglutide groups respectively. [18] In the present study, most of the patients (88%) were female. Anson et al found that 73% were female in their study. [18]

The findings of this study indicate that Tirzepatide was more effective in promoting weight loss compared to Semaglutide. By the third follow-up, the mean weight in the Tirzepatide group decreased by 11.4%, while the Semaglutide group experienced a 10.3% reduction ($p < 0.001$). Although both treatments resulted in substantial BMI reductions, the difference between the two groups was not statistically significant by the third follow-up ($p = 0.404$).

Enson et al found that weight loss at 1 year was greater in the tirzepatide group (−7.7 kg [95% CI −6.8, −8.5 kg], $p < 0.001$) than the semaglutide group (−4.8 kg [95% CI −3.9, −5.6 kg], $p < 0.001$). Reduction in HbA1c was greater in the tirzepatide (−0.24% [95% CI −0.22, −0.26%], $p < 0.001$) than semaglutide (−0.1% [95% CI −0.13, −0.07%], $p < 0.001$) group. [18]

A large clinical analysis of US adults with overweight or obesity by Rodriguez et al found the mean ontreatment change in body weight was −5.9% (95% CI, −6.0% to −5.8%) for tirzepatide vs −3.6% (95% CI, −3.7% to −3.4%) for semaglutide at 3 months, −10.1% (95% CI, −10.4% to −9.9%) vs −5.8% (95% CI, −6.0% to −5.5%) at 6 months, and −15.3% (95% CI, −16.0% to −14.5%) vs −8.3% (95% CI, −9% to −7.6%) at 12 months. It was initiated that with tirzepatide or semaglutide treatment, those receiving tirzepatide were more likely to achieve 5% or greater, 10% or greater, and 15% or greater weight loss and experienced larger reductions in body weight at 3, 6, and 12 months. [19]

Azuri et al found the estimated weight reduction with tirzepatide was 21.1% of body weight and 2.5% in the control arm, compared with 16.2% versus 3.3% weight loss with semaglutide, respectively. Therefore, the weight reduction for tirzepatide was 18.52% versus 12.95% with semaglutide. [20]

The findings from this study are also consistent with existing evidence from RCTs (randomized controlled trials). Among placebo-controlled trials of patients with overweight or obesity, treatment with tirzepatide at 10 mg per week resulted in 82% and 96% of individuals with and without T2D achieving 5% or more weight loss by 72 weeks, respectively. [15,16] Among similarly designed placebo-controlled trials, treatment with semaglutide at 2.4 mg per week resulted in 73% and 92% of individuals with and without T2D achieving 5% or greater body weight by 68 weeks, respectively. [13,21]

In the present study, we found that by the third follow-up, the mean FBS in the Tirzepatide group decreased to 5.45 mg/dl, compared to 5.63 mg/dl in the Semaglutide group ($p = 0.016$). HbA1c levels also showed a statistically significant improvement in the Tirzepatide group (4.6% vs. 4.8%, $p = 0.005$). These results suggest that Tirzepatide may provide better glucose regulation, making it a potentially more effective option for patients with T2DM who require improved glycemic outcomes. A single study evaluated the glucoselowering effect of tirzepatide (5 mg per week) compared with semaglutide (1 mg per week) in patients with T2D and found that 5% weight loss was achieved by 69% and 58%, respectively. [17] Another study reported that the magnitude of HbA1c reduction with GLP-1 use is greater with a higher starting baseline HbA1c. The SELECT trial, evaluating semaglutide in obesity without diabetes, reported a modest −0.31% reduction in HbA1c, which is similar to Anson et al. [18,22]

A meta-analysis by de Mendonça et al demonstrated that Tirzepatide is significantly more effective than Semaglutide in helping patients with T2DM and obesity achieve weight loss greater than 10%. The results revealed that, on average, 45-60% of patients treated with Tirzepatide achieved >10% weight loss, compared to 25-40% of those treated with Semaglutide. [23] However, it is essential to consider the safety profile, including gastrointestinal adverse effects such as nausea, which may impact treatment adherence. In the current study, nausea/vomiting was the most commonly reported side effect in both groups, affecting 38% of the Tirzepatide group and 44% of the Semaglutide group. General weakness and heartburn were also frequently reported. Moreover, injection site itching (32%) and feeling feverish on the first day (12%) were unique to the Tirzepatide group, while dizziness (12%) occurred only in the Semaglutide group. Despite the occurrence of effects, patient satisfaction was higher among those receiving Tirzepatide, with 92% expressed satisfaction compared to 84% in the Semaglutide group.

Limitations of the study

The study took a small sample size due to the short study period. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

Conclusion and Recommendations

In this comparative study, we found that both medications were effective in reducing weight, BMI, fasting blood sugar (FBS), and HbA1c levels over the follow-up period. However, Tirzepatide showed greater efficacy in achieving weight loss

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and better glycemic control compared to Semaglutide, with a statistically significant difference in the percentage reduction in weight (11.4% vs. 10.3%, $p < 0.001$) and improved FBS and HbA1c levels by the third follow-up. Despite common adverse effects, patient satisfaction remained high in both groups, accounting for 92% and 84% of the Tirzepatide and Semaglutide groups respectively.

Further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate the findings of our study and evaluate the safety & efficacy of Tirzepatide & Semaglutide in obese patients.

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Ethical approval:

This study was approved by the ethical review committee

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