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ORIGINAL RESEARCH

Real-World Effectiveness and Safety of Tirzepatide, Semaglutide, and Liraglutide in Adults with Overweight or Obesity without Diabetes: A Comparative Study

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Video abstract

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Background: Obesity is a chronic metabolic disease associated with substantial cardiometabolic risk and long-term morbidity. Although randomized controlled trials have demonstrated the efficacy of incretin-based therapies, real-world comparative data in adults with overweight or obesity without diabetes remain limited. Real-world studies provide complementary evidence by capturing treatment effectiveness, tolerability, dose escalation, and adherence in routine clinical practice.

Methods: This single-center, retrospective, real-world observational study was conducted at a private internal medicine clinic in Istanbul, Turkey, using electronic medical records of consecutively treated patients between September 2023 and September 2024. Adults aged 18–75 years with overweight or obesity without diabetes who received liraglutide, semaglutide, or tirzepatide for at least 36 weeks were included. Treatment allocation was based on routine clinical decision-making. Insulin resistance was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR). The primary outcome was percent change in body weight from baseline to week 36. Secondary outcomes included changes in waist circumference, lipid profile, liver enzymes, pancreatic enzymes, HbA1c, insulin resistance, and adverse events. Between-group comparisons were performed using appropriate parametric or non-parametric tests and multivariable models. Baseline hepatic steatosis was assessed by ultrasonography. Lipid-lowering therapies were recorded and considered in analyses. Adverse events were systematically collected during follow-up; mild elevations in amylase and lipase were defined as ≤3 times the upper limit of normal.

Results: All three treatments were associated with significant reductions in body weight and waist circumference at week 36 ($p < 0.01$). Weight loss was greater in the tirzepatide group compared with the liraglutide and semaglutide groups. Improvements in lipid parameters were observed across all groups, with greater triglyceride reduction in the tirzepatide group. Liver enzyme levels improved similarly between groups. Gastrointestinal adverse events were common, particularly with liraglutide, and no clinically confirmed pancreatitis was observed.

Conclusion: In this real-world cohort, liraglutide, semaglutide, and tirzepatide were effective and generally well tolerated in adults with overweight or obesity without diabetes. Tirzepatide was associated with greater weight loss; however, these findings are observational and hypothesis-generating, supporting the need for prospective or randomized comparative studies.

Keywords: tirzepatide, semaglutide, liraglutide, obesity, real-world study, GLP-1 receptor agonist

Introduction

The global prevalence of overweight and obesity continues to rise at an alarming rate, affecting nearly 2 billion individuals worldwide, corresponding to approximately 30% of the global population.[1] According to the World Health Organization, as of 2016, more than 1.9 billion adults were overweight, and over 650 million were classified as obese.[2] In Turkey, obesity prevalence has increased steadily, with data from the Turkey Nutrition and Health Survey (2017)

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reporting an overall obesity prevalence of 31.5% among individuals aged ≥15 years, reaching 39.1% in women and 24.6% in men.[3] Although more recent nationwide data are lacking, the growing burden of obesity underscores the urgent need for effective and well-tolerated pharmacological treatment strategies in routine clinical practice.

Obesity is a chronic metabolic disease that imposes a substantial burden on individuals and healthcare systems worldwide and is associated with numerous complications, including type 2 diabetes mellitus, hypertension, obstructive sleep apnea, osteoarthritis, depression, non-alcoholic fatty liver disease, and cardiovascular disease.[4–6] Lifestyle modification remains the cornerstone of obesity management; however, pharmacological therapies are increasingly recommended as adjunctive treatment options for individuals who fail to achieve adequate weight loss with lifestyle interventions alone. Current international guidelines generally define inadequate weight loss as <5% total body weight reduction after 3–6 months of structured lifestyle intervention, supporting escalation to anti-obesity pharmacotherapy in eligible individuals.[6,7]

In recent years, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual incretin-based therapies have emerged as highly effective pharmacological agents for obesity management.[8,9] While randomized clinical trials provide high internal validity under controlled conditions, real-world studies capture treatment effectiveness, tolerability, dose escalation, adherence, and prescribing patterns in routine clinical practice, where patient characteristics and treatment decisions are more heterogeneous. Liraglutide and semaglutide are GLP-1 RAs that promote weight loss primarily through appetite suppression, delayed gastric emptying, and improved metabolic regulation.[10] Semaglutide differs pharmacokinetically from liraglutide due to amino acid substitutions that confer resistance to dipeptidyl peptidase-4 (DPP-4) degradation, thereby extending its half-life to approximately one week and allowing for once-weekly administration.[11,12]

Tirzepatide, the first dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist, represents a novel therapeutic approach in obesity treatment.[13,14] Initially approved for the treatment of type 2 diabetes mellitus, tirzepatide has recently emerged as one of the latest clinically approved and commercially available pharmacological options for obesity management, with growing evidence supporting its efficacy and safety in adults with obesity without diabetes.[15] Tirzepatide exhibits high affinity for the GIP receptor and lower affinity for the GLP-1 receptor compared with native GLP-1; nevertheless, concurrent activation of both incretin pathways has been shown to exert synergistic effects on energy balance and weight reduction. Preclinical studies have demonstrated that combined GIP and GLP-1 receptor activation results in greater weight loss than GLP-1 receptor monoagonism alone.[15]

Despite the expanding use of incretin-based therapies, real-world head-to-head comparative data evaluating the effectiveness and safety of liraglutide, semaglutide, and tirzepatide remain scarce, particularly in adults with overweight or obesity without diabetes. To our knowledge, this study represents the first real-world experience from Turkey directly comparing these agents in adults with overweight or obesity without diabetes managed in an internal medicine setting.

Methods

Study Design and Setting

This real-world, retrospective observational study was conducted at a single-center private internal medicine clinic in Istanbul, Turkey. Clinical data were retrieved from electronic medical records of eligible patients evaluated between September 2023 and September 2024. No direct contact with patients was required, as all data were obtained retrospectively from existing medical records. The study protocol was approved by the local ethics committee, and written informed consent was obtained from all participants prior to inclusion in the study.

Study Population

Adults aged 18–75 years with a body mass index (BMI) ≥30 kg/m^2, or BMI ≥27 kg/m^2 accompanied by obesity-related comorbidities (including hypertension and hyperlipidemia), were included in the study. Only individuals who continued treatment for at least 36 weeks (9 months) were eligible for analysis. This retrospective analysis therefore represents a completer cohort, as patients who discontinued treatment before week 36 were not included in the study. Patient selection, exclusion, and inclusion in the final analysis are summarized in Figure 1.

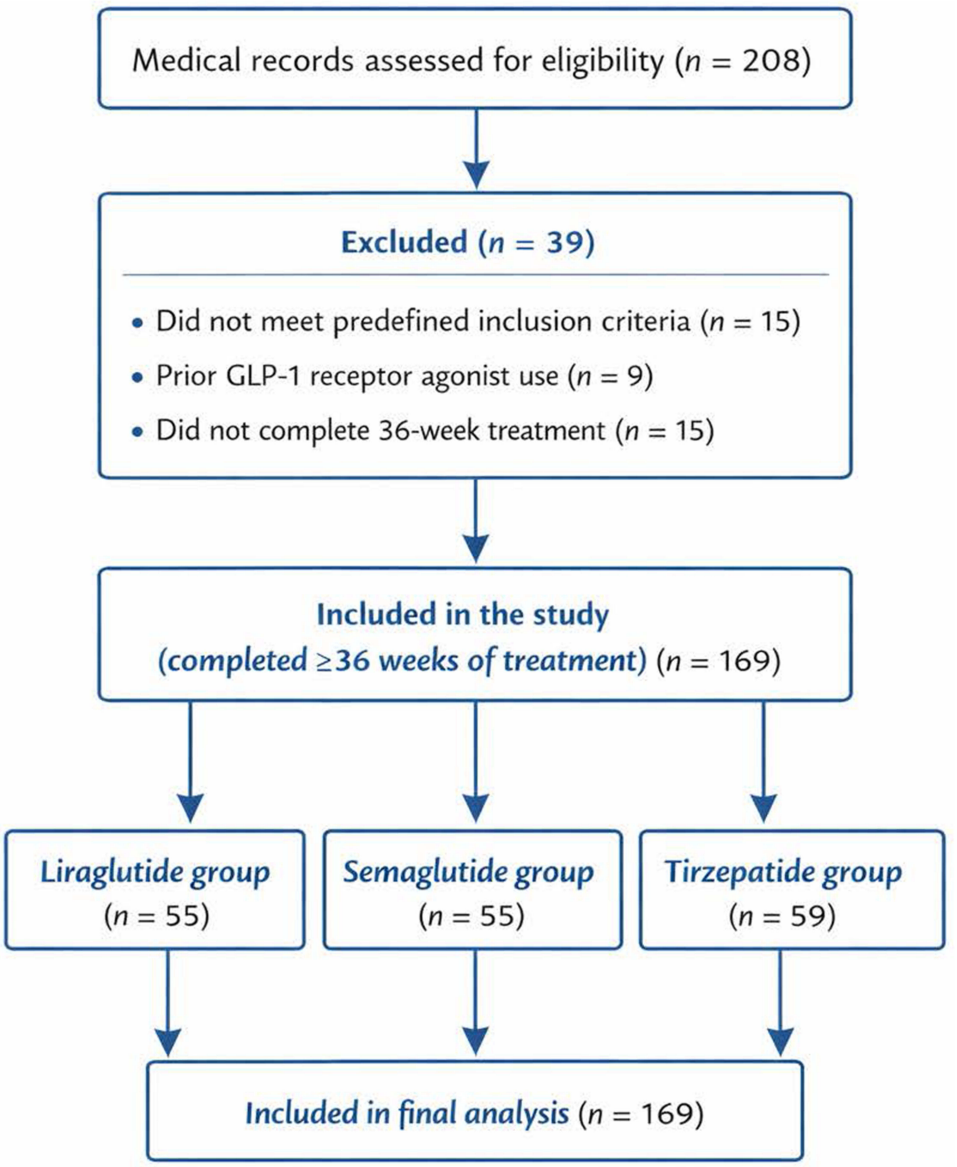

Figure 1 Participant flow diagram illustrating patient screening, exclusion based on predefined criteria, and inclusion of patients who completed at least 36 weeks of treatment in the final analysis.

Exclusion criteria comprised prior use of GLP-1 receptor agonists, history of bariatric surgery, renal failure, and medical conditions associated with unintentional weight loss, such as malignancy or chronic infections.

Treatment Protocol

All were self-administered subcutaneously following standardized patient education provided by the treating medications physician or trained nursing staff. Patients were instructed on proper injection technique, subcutaneous injection site rotation (abdomen, thigh, or upper arm), and adherence to the prescribed dosing schedule. Dose escalation followed standard label-based titration schedules; however, escalation was individualized according to tolerability, gastrointestinal side effects, and clinical response. Deviations from the planned titration schedule, dose delays, or inability to reach the target maintenance dose were documented and reflected in the achieved maintenance dose for each patient.

Adherence to self-administered therapy was assessed indirectly through patient self-report during routine follow-up visits and review of medical records, including documentation of missed doses or temporary treatment interruptions when available.

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All patients received standardized lifestyle counseling, including recommendations for a hypocaloric diet and physical activity consistent with routine clinical practice. Dietary intake was not quantitatively monitored, but dietary recommendations were reinforced at follow-up visits across all treatment groups.

All patients included in the analysis completed a minimum of 36 weeks of continuous treatment; therefore, exposure duration was uniform across groups (Table 1).

Data Collected

Body weight measurements were performed under standardized conditions during clinic visits, with patients wearing light clothing and no shoes, using the same calibrated digital scale throughout the study period.

Waist circumference was measured at the midpoint between the lowest rib and the iliac crest using a non-elastic measuring tape.

All biochemical measurements were obtained from fasting blood samples collected after an overnight fast of at least 8 hours. Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), calculated as fasting insulin (μIU/mL) × fasting glucose (mg/dL) / 405.

All laboratory analyses were performed in accredited laboratories using standardized assay platforms. To ensure analytical consistency, the same laboratory and assay methods were used for baseline and follow-up measurements throughout the study period.

Data extraction from electronic medical records was performed using a standardized data collection form by the study investigators. Extracted data were cross-checked for completeness and plausibility prior to analysis.

Hepatic steatosis was evaluated using abdominal ultrasonography and graded semi-quantitatively (grade 0–3) based on standard echogenicity criteria, including hepatorenal contrast, liver brightness, deep beam attenuation, and visualization of intrahepatic vessels, as previously described.[16]

Adverse events were recorded during routine clinical visits and documented in medical records throughout the treatment period. Reported adverse events primarily included gastrointestinal symptoms such as nausea, vomiting, constipation, diarrhea, and heartburn.

Statistical Analysis

Statistical analyses were performed using SPSS software version 27.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables with a normal distribution are presented as mean ± standard deviation (SD), whereas non-normally distributed variables are presented as median with interquartile range (IQR, Q1–Q3). Categorical variables are expressed as frequencies and percentages.

Within-group comparisons between baseline and week 36 were performed using paired *t*-tests for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables. Between-group comparisons were conducted using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test, as appropriate. When significant differences were detected, post hoc pairwise comparisons were performed with Bonferroni correction.

Table 1 Treatment Exposure, Titration Schedule, and Achieved Maintenance Doses

Parameter	Liraglutide (n = 55)	Semaglutide (n = 55)	Tirzepatide (n = 59)
Starting dose	0.6 mg once daily	0.25 mg once weekly	2.5 mg once weekly
Titration schedule	Weekly dose escalation	Dose increased every 4 weeks	Dose increased every 4 weeks
Achieved maintenance dose	3.0 mg once daily	1.7–2.4 mg once weekly	10–15 mg once weekly
Treatment duration	≥36 weeks	≥36 weeks	≥36 weeks
Treatment discontinuation	Not applicable*	Not applicable*	Not applicable*

Notes: *Treatment discontinuation was not captured, as only patients who completed at least 36 weeks of treatment were included in the analysis.

To address potential confounding, multivariable adjusted analyses were performed using clinically relevant prespecified covariates, including age, sex, baseline body mass index, and baseline values of the outcome of interest. Sensitivity analyses using alternative model specifications yielded results consistent with the primary analysis. A two-sided p value <0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 169 participants were included in the study, of whom 58% (n = 98) were women and 42% (n = 71) were men. Among the participants, 32.5% (n = 55) were treated with liraglutide, 32.5% (n = 55) with semaglutide, and 34.9% (n = 59) with tirzepatide. Baseline demographic, anthropometric, and biochemical characteristics, including age, body weight, body mass index (BMI), fasting blood glucose, insulin levels, and degree of hepatosteatosis, are summarized in Table 2.

Table 2 Baseline Demographic, Anthropometric, and Clinical Characteristics of the Study Population

Parameter	Total (n=169)	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)
Sex, n (%)				
Female	98 (57.9)	31 (56.3)	33 (60.0)	34 (57.6)
Male	71 (42.1)	24 (43.7)	22 (40.0)	25 (42.4)
Age (years)				
Mean ± SD	40.78 ± 11.13	41.89 ± 11.00	41.11 ± 11.18	39.42 ± 11.27
Median (Q1–Q3)	42 (32–48)	43 (35–50)	43 (32–49)	41 (31–48)
Height (cm)				
Mean ± SD	167.77 ± 9.40	166.22 ± 9.98	166.91 ± 8.18	170.02 ± 9.64
Median (Q1–Q3)	168 (160–174)	165 (158–172)	167 (160–173)	171 (163–175)
Weight (kg)				
Mean ± SD	97.58 ± 20.21	100.08 ± 24.96	93.11 ± 15.64	99.41 ± 18.62
Median (Q1–Q3)	92.2 (82.3–108.0)	96.0 (79.2–113.0)	90.0 (81.2–105.0)	95.9 (84.0–109.1)
BMI (kg/m^2)				
Mean ± SD	34.56 ± 5.83	36.08 ± 7.83	33.37 ± 4.39	34.25 ± 4.43
Median (Q1–Q3)	33.4 (30.4–37.0)	34.0 (30.0–40.0)	32.8 (30.1–35.8)	33.9 (30.4–35.7)
FBG (mg/dL)				
Mean ± SD	98.92 ± 15.62	100.71 ± 19.54	98.17 ± 12.65	97.95 ± 14.06
Median (Q1–Q3)	95 (91–102)	95 (92–102)	96 (91–102)	94 (89–101)
Fasting insulin (µIU/mL)				
Mean ± SD	17.42 ± 9.99	20.96 ± 11.85	16.46 ± 9.03	15.00 ± 8.00
Median (Q1–Q3)	15.4 (10.9–20.5)	17.0 (13.5–26.0)	13.5 (10.2–20.1)	13.7 (9.6–18.0)
HOMA-IR (baseline)				
Mean ± SD	4.28 ± 2.69	5.36 ± 3.45	3.95 ± 2.23	3.58 ± 1.90
Median (Q1–Q3)	3.6 (2.6–4.8)	4.3 (3.2–7.1)	3.4 (2.7–4.8)	3.1 (2.4–4.5)

(*Continued*)

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Table 2 (Continued).

Parameter	Total (n=169)	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)
HbA1c (%) baseline				
Mean ± SD	5.56 ± 0.43	5.56 ± 0.47	5.64 ± 0.42	5.49 ± 0.39
Median (Q1–Q3)	5.5 (5.2–5.9)	5.5 (5.2–5.9)	5.6 (5.3–5.9)	5.4 (5.2–5.8)
Hepatic steatosis, n (%)				
None	49 (29.0)	15 (27.3)	17 (30.9)	17 (28.8)
Grade 1	54 (32.0)	21 (38.2)	15 (27.3)	18 (30.5)
Grade 2	56 (33.1)	13 (23.6)	21 (38.2)	22 (37.3)
Grade 3	10 (5.9)	6 (10.9)	2 (3.6)	2 (3.4)

Notes: Values are presented as mean ± SD for normally distributed variables and median (Q1–Q3) for non-normally distributed variables. Categorical variables are presented as n (%).Between-group comparisons were performed using one-way ANOVA or Kruskal–Wallis test for continuous variables, and Pearson's chi-square test for categorical variables.
Abbreviations: BMI, body mass index; FBG, fasting blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance; HbA1c, glycated hemoglobin.

With respect to hepatic steatosis, 29.0% (n = 49) of participants had no hepatosteatosis, while 32.0% (n = 54) had grade 1, 33.1% (n = 56) had grade 2, and 5.9% (n = 10) had grade 3 hepatosteatosis at baseline (Table 2). Baseline demographic and clinical characteristics were generally comparable across treatment groups.

Comparison of Weight Loss and Waist Circumference

Weight Loss

Weight loss differed significantly among treatment groups at week 36 ($p < 0.01$). Mean absolute weight loss was significantly greater in the tirzepatide group compared with both the liraglutide and semaglutide groups ($p < 0.01$ for both comparisons).

Categorical analysis of percentage weight loss demonstrated significant differences across treatment groups (χ^2, p = 0.001), with a moderate effect size (Cramer's V = 0.37). Modest weight loss (5–10%) occurred more frequently in the liraglutide group, whereas higher degrees of weight loss were increasingly observed with semaglutide and tirzepatide (Table 3 and Figure 2).

A weight loss of >15% and >20% was observed more frequently in the tirzepatide group compared with liraglutide ($p < 0.05$). The proportion of patients achieving very high weight loss (>25%) was numerically greater in the tirzepatide group than in the other treatment groups; however, this difference did not reach statistical significance ($p > 0.05$) (Figure 2).

After adjustment for sex, age, baseline body mass index, and hepatic steatosis using ANCOVA, weight loss remained significantly different across treatment groups (F = 12.960, p = 0.001) (Table 4). Adjusted mean weight loss was highest in the tirzepatide group (19.52 ± 0.70 kg), followed by semaglutide (16.63 ± 0.73 kg) and liraglutide (13.18 ± 0.74 kg). Post hoc Bonferroni analyses showed that weight loss was significantly greater with tirzepatide compared with both

Table 3 Distribution of Percentage Weight Loss Across Treatment Groups at Week 36

Percentage Weight Loss	Total (n = 169)	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n = 59)
5–10%	30 (17.8)	17 (30.9)	10 (18.2)	3 (5.1)
10–15%	48 (28.4)	17 (30.9)	20 (36.4)	11 (18.6)
15–20%	50 (29.6)	13 (23.6)	14 (25.5)	23 (39.0)
>20%	41 (24.3)	8 (14.5)	11 (20.0)	22 (37.3)

Notes: Overall comparison: χ^2-test, **p = 0.001. Effect size**: Cramer's V = **0.37** (moderate effect). Values are presented as n (%).Pearson's chi-square test was used for overall group comparisons.

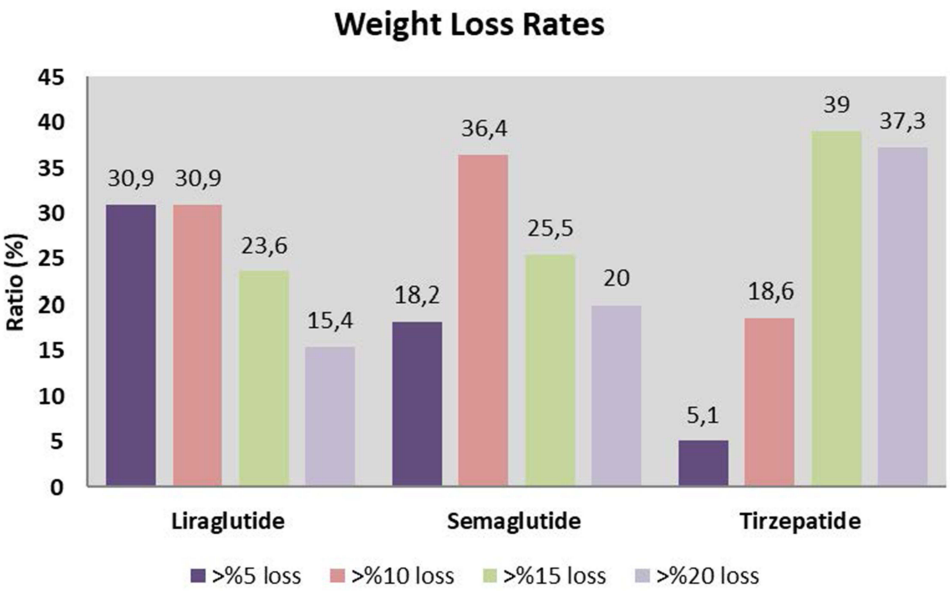

Figure 2 Distribution of categorical weight loss thresholds at week 36 by treatment group. Bar graph illustrating the proportion (%) of patients achieving >5%, >10%, >15%, >20%, and >25% weight loss at week 36 in the liraglutide, semaglutide, and tirzepatide groups. Tirzepatide was associated with a higher proportion of patients achieving ≥15% and ≥20% weight loss compared with liraglutide and semaglutide. Values are presented as percentages of patients within each treatment group.

liraglutide (p = 0.001) and semaglutide (p = 0.014), and greater with semaglutide compared with liraglutide (p = 0.004). The effect size for treatment group was large (partial $\eta^2 = 0.191$) (Table 4).

Sensitivity analyses using alternative model specifications yielded results consistent with the primary analysis.

Waist Circumference

Waist circumference decreased significantly from baseline to week 36 in all treatment groups (within-group comparisons, p < 0.01 for all). In the liraglutide group, mean waist circumference decreased by 12.42 ± 6.81 cm; in the semaglutide group by 12.29 ± 4.89 cm; and in the tirzepatide group by 14.81 ± 7.25 cm, all corresponding to large within-group effect sizes (Cohen's d > 1.8).

Table 4 Multivariable ANCOVA Analysis of Absolute Weight Loss at Week 36

Source	F	df	p-value	Partial η^2
Sex	8.908	1	0.003**	0.052
Age	0.100	1	0.753	0.001
Baseline BMI	32.859	1	0.001**	0.169
Hepatic steatosis	4.874	1	0.029*	0.029
Treatment group	19.185	2	0.001**	0.191
Model statistics: F = 12.960; p = 0.001; R^2 = 0.324**				
Treatment group	**Adjusted mean ± SD (kg)**			
Liraglutide	13.18 ± 0.74			
Semaglutide	16.63 ± 0.73			
Tirzepatide	19.52 ± 0.70			

Notes: Covariates included sex, age, baseline BMI, and hepatic steatosis. ANCOVA with Bonferroni post-hoc correction. *p < 0.05; **p < 0.01. Partial eta squared (η^2) values indicate effect size.

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Table 5 Changes in Waist Circumference from Baseline to Week 36 by Treatment Group

Parameter	Statistic	Total (n=169)	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p/Effect size
Waist circumference (cm)	**Baseline – Mean ± SD**	102.22 ± 15.50	104.36 ± 19.35	98.36 ± 11.15	103.81 ± 14.52	[a] p = 0.035* η^2 = 0.030
	Week 36 – Mean ± SD	89.01 ± 14.00	91.95 ± 16.24	86.07 ± 11.91	89.00 ± 13.18	[a] p = 0.088 η^2 = 0.029
	Change (Δ) – Median (Q1–Q3)	–	−11 (−17 to −7)	−12 (−15 to −9)	−14 (−18 to −10)	[c] p = 0.078 η^2 = 0.033
Within-group change	**Mean ± SD (cm)**	–	−12.42 ± 6.81	−12.29 ± 4.89	−14.81 ± 7.25	–
	Paired test (p)	–	[b] p = 0.001**	[b] p = 0.001**	[b] p = 0.001**	–
	Effect size (Cohen's d)	–	1.825	2.515	2.043	–

Notes: Statistical tests: [a]one-way ANOVA with Bonferroni post hoc test; [b]paired samples *t*-test; [c]Kruskal–Wallis test with Dunn–Bonferroni correction. *p < 0.05; **p < 0.01.
Abbreviations: Q1, 25th percentile; Q3, 75th percentile; η^2, eta-squared; d, Cohen's d.

At baseline, waist circumference differed significantly between groups (p = 0.035), with higher values observed in the liraglutide group compared with the semaglutide group. However, waist circumference values at week 36 were comparable across treatment groups, and no statistically significant between-group differences were detected at follow-up (p > 0.05).

The magnitude of waist circumference reduction from baseline to week 36 did not differ significantly between treatment groups (p > 0.05), indicating that all three agents were similarly effective in reducing central adiposity over the study period (Table 5 and Figure 3).

Comparison of Biochemical Parameters

Liver Enzymes (AST, ALT, and GGT)

Baseline levels of AST, ALT, and GGT did not differ significantly between treatment groups (all p > 0.05). At week 36, significant within-group reductions in AST, ALT, and GGT levels were observed across all treatment groups (all p < 0.01). However, no significant between-group differences were detected in enzyme levels at follow-up or in the magnitude of change from baseline (all p > 0.05).

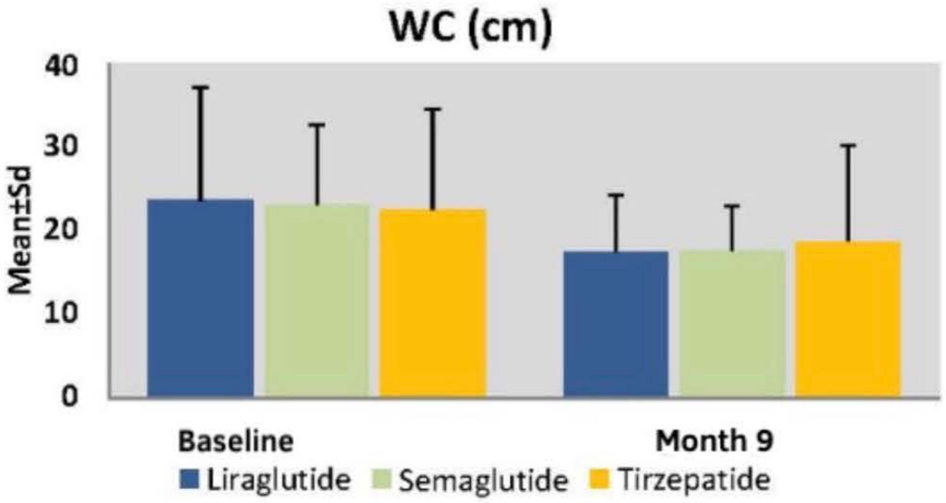

Figure 3 Distribution of waist circumference at baseline and at week 36 by treatment group. Mean (± SD) waist circumference values at baseline and at week 36 for the liraglutide, semaglutide, and tirzepatide groups. All treatment groups demonstrated significant reductions in waist circumference from baseline to week 36 (within-group comparisons, p < 0.01). Although baseline waist circumference differed between groups, no significant between-group differences were observed at week 36. Error bars represent standard deviations.

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Table 6 Changes in Liver Enzyme Levels (AST, ALT, and GGT) from Baseline to Week 36

Parameter	Time point	Total	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p-value / η^2
AST (U/L)	Baseline	20 (16–26)	20 (16–26)	20 (17–29)	20 (16–24)	0.859 / 0.002
	Week 36	16 (14–20)	16 (13–20)	17 (14–21)	17 (14–20)	0.702 / 0.005
	Δ Change	—	−4 (−9 to −1)	−3 (−9 to −1)	−3 (−7 to −0.6)	0.577 / 0.008
ALT (U/L)	Baseline	24 (16.4–39)	22 (16–42)	22 (15–38)	26 (18–39)	0.506 / 0.008
	Week 36	16.7 (12.5–24)	15.6 (12–24)	16 (12–21)	17 (13–24)	0.514 / 0.011
	Δ Change	—	−6 (−13 to −2)	−7.9 (−18 to −3)	−9 (−17 to −3)	0.611 / 0.005
GGT (U/L)	Baseline	26 (15.2–45)	33 (15–53.7)	24 (14–50)	24 (18–37)	0.461 / 0.003
	Week 36	18 (12–28)	19 (13–35)	17.2 (10.8–34)	15 (12–23)	0.219 / 0.010
	Δ Change	—	−6 (−15 to −2)	−6.2 (−21 to −1.6)	−8 (−13 to −4)	0.725 / 0.012

Notes: Values are presented as median (Q1–Q3). η^2 indicates effect size. Between-group comparisons were performed using the Kruskal–Wallis test with Dunn–Bonferroni correction. Within-group comparisons were assessed using the Wilcoxon signed-rank test.
Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyltransferase.

The effect sizes for within-group reductions ranged from small to moderate, whereas between-group effect sizes were uniformly small. These findings indicate that liraglutide, semaglutide, and tirzepatide were each associated with significant improvements in liver enzyme levels over the 36-week treatment period, without evidence of differential effects between agents (Table 6 and Figure 4).

Lipid Profile

At week 36, significant within-group reductions were observed in total cholesterol, LDL cholesterol, and triglyceride levels across all treatment groups, whereas HDL cholesterol did not change significantly.

Total Cholesterol: Mean total cholesterol levels decreased significantly from baseline to week 36 in all groups (all $p < 0.01$).

However, no statistically significant differences were observed between treatment groups at baseline or at week 36 ($p > 0.05$).

Between-group differences in change from baseline were also not statistically significant ($p = 0.241$; $\eta^2 = 0.009$) (Figure 5 and Table 7).

LDL Cholesterol: Mean LDL cholesterol levels decreased significantly within each treatment group at week 36 (all $p \leq 0.002$). There were no statistically significant differences between groups at baseline or at week 36 ($p > 0.05$). Changes in LDL cholesterol did not differ significantly among groups ($p = 0.633$; $\eta^2 = 0.011$) (Figure 5 and Table 7).

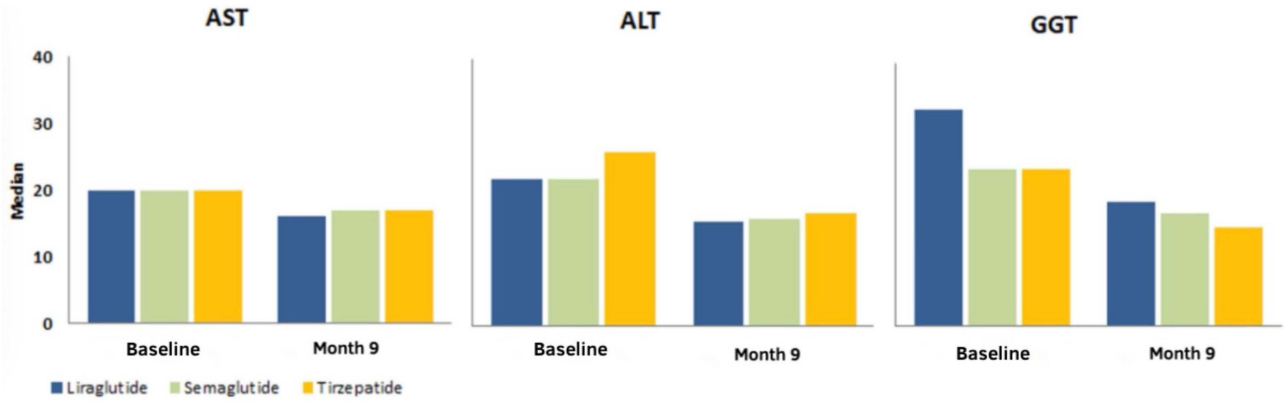

Figure 4 Changes in AST, ALT, and GGT levels from baseline to week 36 by treatment group. Median values are shown. All treatment groups demonstrated significant within-group reductions in liver enzyme levels ($p < 0.01$), with no significant between-group differences.

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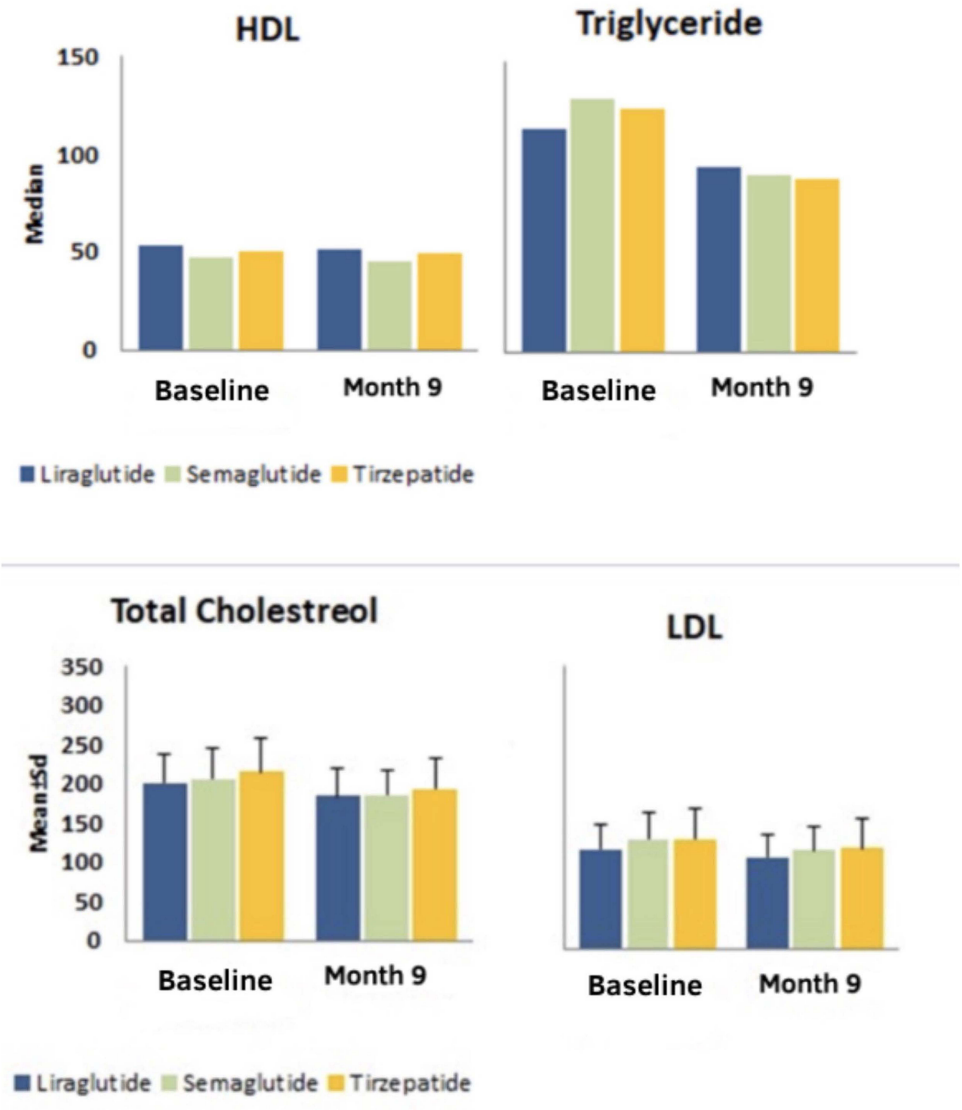

Figure 5 Changes in lipid parameters (total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and triglycerides) from baseline to week 36 according to treatment group.

HDL Cholesterol: Median HDL cholesterol levels did not change significantly from baseline to week 36 in any treatment group (all $p > 0.05$). No significant differences were observed between groups at baseline, week 36, or in change from baseline ($p > 0.05$) (Figure 5 and Table 7).

Triglycerides Median triglyceride levels decreased significantly within each treatment group at week 36 (all $p < 0.01$). Between-group comparison of change from baseline demonstrated a statistically significant difference ($p = 0.009$; $\eta^2 = 0.027$), indicating a modest effect size (Figure 5 and Table 7).

Pancreatic Enzymes

Baseline amylase levels did not differ significantly among treatment groups ($p > 0.05$). At week 36, mean amylase levels increased in the liraglutide and semaglutide groups, whereas no statistically significant change was observed in the tirzepatide group. Within-group analyses demonstrated a significant increase in amylase levels in the liraglutide group (+15.80 ± 29.03 U/L, $p < 0.01$) and in the semaglutide group (+6.02 ± 17.33 U/L, $p < 0.05$), while the change in the tirzepatide group was not statistically significant ($p > 0.05$). Between-group comparison of amylase change revealed a statistically significant difference ($p = 0.006$; $\eta^2 = 0.071$), with a greater increase observed in the liraglutide group compared with the tirzepatide group.

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Table 7 Changes in Lipid Parameters from Baseline to Week 36 by Treatment Group

Parameter	Total (n=169)	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p/Effect size (η^2)
Total cholesterol (mg/dL)					
Baseline (Mean ± SD)	207.6 ± 39.72	200.75 ± 37.14	206.16 ± 39.29	215.32 ± 41.72	0.139/0.023[a]
Week 36 (Mean ± SD)	187.55 ± 36.80	184.27 ± 36.35	185.17 ± 32.87	192.77 ± 40.47	0.399/0.011[a]
Δ Change (Median, Q1–Q3)	—	−10 (−25 – −1)	−18 (−34 – −4)	−25 (−44 – −1)	0.241/0.009[c]
Within-group p/d	—	0.001** / 0.637	0.001** / 0.879	0.001** / 0.718	
HDL (mg/dL)					
Baseline (Median, Q1–Q3)	50 (42–57)	53 (43–60)	47 (41–53)	50 (41–59)	0.072/0.029[c]
Week 36 (Median, Q1–Q3)	48 (41.5–56)	51 (42–60)	45 (38–54)	49 (42–57)	0.116/0.030[c]
Δ Change (Median, Q1–Q3)	—	−2 (−6 – 3)	−0.6 (−4.1–3)	0 (−5 – 5)	0.264/0.003[c]
Within-group p/d	—	0.163 / 0.150	0.431 / 0.120	0.931 / 0.034	
LDL (mg/dL)					
Baseline (Mean ± SD)	131.4 ± 34.5	122.6 ± 29.63	135.85 ± 33.04	135.45 ± 38.79	0.070/0.032[a]
Week 36 (Mean ± SD)	119.70 ± 32.23	113.29 ± 27.21	121.08 ± 29.86	124.39 ± 37.76	0.172/0.021[a]
Δ Change (Median, Q1–Q3)	—	−7 (−18 – 1)	−14 (−27.4 – −5)	−8 (−30.1–6)	0.633/0.011[c]
Within-group p/d	—	0.001** / 0.519	0.001** / 0.765	0.002** / 0.418	
Triglycerides (mg/dL)					
Baseline (Median, Q1–Q3)	125 (90–181)	115 (76–180)	131 (94–172.3)	126 (92–222)	0.424/0.008[c]
Week 36 (Median, Q1–Q3)	95 (70–130)	96 (75–137)	91 (73–128)	89 (65–127)	0.453/0.010[c]
Δ Change (Median, Q1–Q3)	—	−15 (−46 – 9)	−34 (−53 – −9)	−45 (−89 – −7)	0.009**/0.027[c]
Within-group p/d	—	0.001** / 0.339	0.001** / 0.792	0.001** / 0.771	

Notes: [a]One-way ANOVA with Bonferroni post hoc test. [c]Kruskal–Wallis test with Dunn–Bonferroni correction. ** $p < 0.01$.
Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; Q1: 25th percentile; Q3: 75th percentile; η^2: Eta-squared; d: Cohen's d.

Baseline lipase levels were comparable across treatment groups ($p > 0.05$). At week 36, lipase levels differed significantly among groups ($p = 0.022$; $\eta^2 = 0.041$), with higher values observed in the liraglutide group compared with the tirzepatide group. Within-group analyses showed significant increases in lipase levels in all three treatment groups (liraglutide: +11.89 ± 29.28 U/L; semaglutide: +6.73 ± 15.34 U/L; tirzepatide: +7.60 ± 20.28 U/L; all $p < 0.01$). However, the magnitude of change did not differ significantly among groups ($p > 0.05$) (Table 8).

Table 8 Changes in Pancreatic Enzyme Levels (Amylase and Lipase) from Baseline to Week 36

Parameter	Time Point	Total	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p-value/ Effect size
Amylase (U/L)	Baseline (Mean ± SD)	61.09 ± 22.56	59.35 ± 24.02	60.42 ± 21.60	63.33 ± 22.24	0.623/η^2=0.006
	Week 36 (Mean ± SD)	68.78 ± 30.79	75.16 ± 40.78	66.44 ± 24.67	65.02 ± 23.94	0.275/η^2=0.021
	Δ Change (Median Q1–Q3)	—	10 (1–21)	3 (−3.6–16)	3 (−7–12)	0.006**/η^2=0.071
	Within-group p / d	—	0.001**/d=−0.544	0.013*/d=−0.347	0.420/d=−0.106	—

(*Continued*)

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Table 8 (Continued).

Parameter	Time Point	Total	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p-value/ Effect size
Lipase (U/L)	Baseline (Median Q1–Q3)	—	38 (27–57)	33 (24.6–41)	35 (24–40)	0.186/η^2=0.035
	Week 36 (Median Q1–Q3)	—	45 (32–65)	37 (28–53.1)	37 (27–48)	0.022*/η^2=0.041
	Δ Change (Median Q1–Q3)	—	7 (1–19.8)	5 (−1.4–14.1)	6 (−4–13)	0.600/η^2=0.010
	Within-group p/d	—	0.001**/d=−0.406	0.001**/d=−0.439	0.003**/d=−0.374	—

Notes: Values are presented as mean ± SD or median (Q1–Q3), as appropriate. Between-group comparisons were performed using one-way ANOVA or Kruskal–Wallis test, as appropriate. Within-group comparisons were assessed using paired samples *t*-test or Wilcoxon signed-rank test. *p < 0.05; ** p < 0.01.
Abbreviations: η^2, eta-squared (effect size); d, Cohen's d.

HOMA-IR and HbA1c

Results – Insulin Resistance and Glycemic Parameters

Significant improvements in insulin resistance were observed across all treatment groups at week 36. Baseline HOMA-IR values differed significantly among groups (p = 0.006), with higher values in the liraglutide group compared with tirzepatide. At week 36, HOMA-IR levels remained significantly different between groups (p = 0.038), although the effect size was small (η^2 = 0.035).

Within-group analyses demonstrated significant reductions in HOMA-IR from baseline to week 36 in all three treatment groups (all p < 0.001). The magnitude of reduction was greatest in the liraglutide group (Cohen's d = 0.953), followed by semaglutide (d = 0.963) and tirzepatide (d = 0.794), all indicating large effect sizes. Between-group comparison of HOMA-IR change showed a statistically significant difference (p = 0.048; η^2 = 0.068), with a greater reduction in the liraglutide group compared with semaglutide. Regarding glycemic parameters, baseline HbA1c levels did not differ significantly among groups (p > 0.05). At week 36, HbA1c levels differed modestly between groups (p = 0.014; η^2 = 0.050), with slightly higher values observed in the semaglutide group compared with tirzepatide. However, the magnitude of HbA1c reduction from baseline did not differ significantly between groups (p = 0.870). Within-group analyses showed significant reductions in HbA1c in all treatment groups (all p < 0.001), with large effect sizes (Cohen's d ranging from 0.866 to 0.932) (Table 9).

Table 9 Changes in HOMA-IR and HbA1c from Baseline to Week 36

Parameter	Total	Liraglutide (n=55)	Semaglutide (n=55)	Tirzepatide (n=59)	p/Effect size (η^2)
HOMA-IR					
Baseline (Median, Q1–Q3)	3.6 (2.6–4.8)	4.3 (3.2–7.1)	3.4 (2.7–4.8)	3.1 (2.4–4.5)	0.006**/0.081[c]
Week 36 (Mean ± SD)	2.36 ± 1.16	2.60 ± 1.14	2.43 ± 1.13	2.08 ± 1.16	0.038*/0.035[a]
Δ Change (Median, Q1–Q3)	—	−2.0 (−4.3 to −0.7)	−1.2 (−2.0 to −0.5)	−1.3 (−2.5 to −0.3)	0.048*/0.068[c]
Within-group p/Effect size (d)	—	0.001**/0.953[d]	0.001**/0.963[d]	0.001**/0.794[d]	—
HbA1c (%)					
Baseline (Mean ± SD)	5.56 ± 0.43	5.56 ± 0.47	5.64 ± 0.42	5.49 ± 0.39	0.201/0.019[a]
Week 36 (Mean ± SD)	5.23 ± 0.37	5.24 ± 0.42	5.33 ± 0.34	5.13 ± 0.33	0.014*/0.050[a]
Δ Change (Median, Q1–Q3)	—	−0.3 (−0.5 to −0.1)	−0.3 (−0.5 to −0.2)	−0.3 (−0.6 to −0.1)	0.870/0.004[c]
Within-group p/Effect size (d)	—	0.001**/0.870[b]	0.001**/0.932[b]	0.001**/0.866[b]	—

Notes: Statistical tests. [a] One-way ANOVA + Bonferroni. [b] Paired samples *t*-test. [c] Kruskal–Wallis + Dunn-Bonferroni. [d] Wilcoxon signed-rank test. * p < 0.05. ** p < 0.01.
Abbreviations: HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; HbA1c, Hemoglobin A1c; Q1, 25th percentile; Q3, 75th percentile; η^2, Eta-squared.

Table 10 Frequency and Distribution of Adverse Events According to Treatment Group

Adverse Event	Total n (%) (n=169)	Liraglutide n (%) (n=55)	Semaglutide n (%) (n=55)	Tirzepatide n (%) (n=59)	p value	Effect Size (Cramer's V)
Any adverse event					**0.001**	**0.43**
None	45 (26.6)	4 (7.3)	17 (30.9)	24 (40.7)		
Yes	124 (73.4)	51 (92.7)	38 (69.1)	35 (59.3)		
Constipation					0.048	0.22
Yes	40 (23.7)	18 (32.7)	14 (25.5)	8 (13.6)		
Vomiting					**0.001**	**0.49**
Yes	24 (14.2)	20 (36.4)	1 (1.8)	3 (5.1)		
Nausea					0.189	0.16
Yes	39 (23.1)	9 (16.4)	17 (30.9)	13 (22.0)		
Diarrhea					0.071	0.20
Yes	16 (9.5)	2 (3.6)	9 (16.4)	5 (8.5)		
Heartburn					0.661	0.06
Yes	23 (13.6)	9 (16.4)	7 (12.7)	7 (11.9)		
Xerostomia	1 (0.6)	0 (0.0)	0 (0.0)	1 (1.7)	–	–
Headache	3 (1.8)	0 (0.0)	0 (0.0)	3 (5.1)	–	–
Gas	2 (1.2)	0 (0.0)	0 (0.0)	2 (3.4)	–	–
Fatigue	3 (1.8)	0 (0.0)	0 (0.0)	3 (5.1)	–	–

Notes: Pearson's chi-square test was used for between-group comparisons. Cramer's V indicates effect size. Bold values indicate statistical significance ($p < 0.05$).

Adverse Events

Adverse events were reported in 73.4% of participants overall and differed significantly among treatment groups ($p = 0.001$; Cramer's $V = 0.43$). The highest frequency of adverse events was observed in the liraglutide group (92.7%), followed by semaglutide (69.1%) and tirzepatide (59.3%). Nausea and diarrhea rates did not differ significantly between groups ($p > 0.05$). Constipation was more frequently reported in the liraglutide group compared with tirzepatide ($p = 0.048$; $V = 0.22$). Vomiting rates differed significantly among groups ($p = 0.001$; $V = 0.49$), with the highest incidence in the liraglutide group. Heartburn rates did not significantly differ between treatments ($p > 0.05$) (Table 10 and Figure 6).

Gastrointestinal adverse events, including nausea, vomiting, constipation, and diarrhea, were the most frequently reported events across treatment groups and were observed most commonly in the liraglutide group. Because this analysis included only patients who completed 36 weeks of treatment, discontinuations due to adverse events or dose-limiting intolerance were not systematically captured. Therefore, safety findings reflect adverse events reported during ongoing treatment among completers.

Discussion

Obesity has traditionally been managed through lifestyle-based interventions; however, it is now recognized as a complex, multifactorial metabolic disease requiring long-term and individualized treatment strategies.[17] Accordingly, current clinical guidelines, including those from the American Association of Clinical Endocrinology (AACE) and European Association for the Study of Obesity (EASO), recommend pharmacological therapy for individuals with obesity or overweight accompanied by weight-related comorbidities.[7,8,18] Recommendations may vary by region or population, and local clinical judgment should guide therapy.

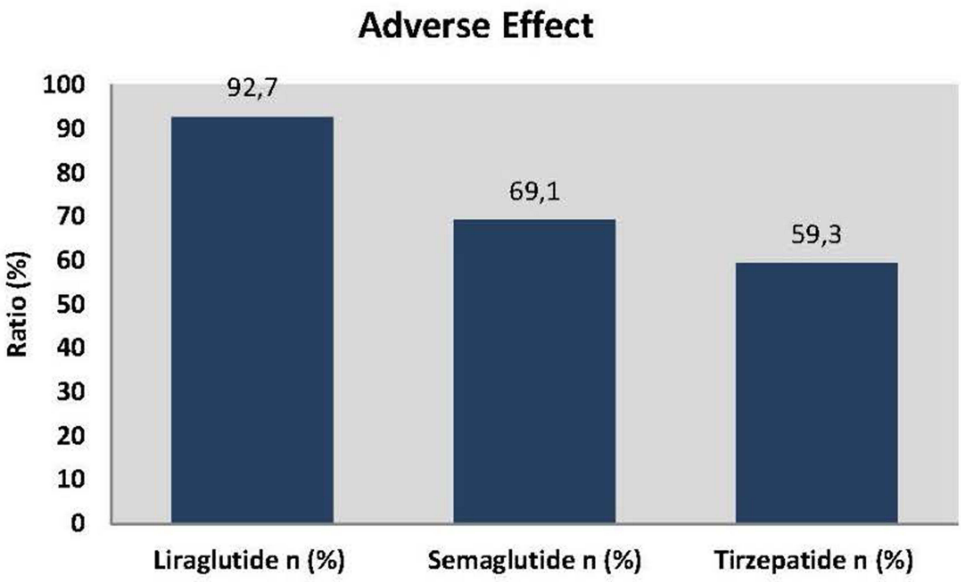

Figure 6 Distribution of gastrointestinal and other adverse events observed during treatment with liraglutide, semaglutide, and tirzepatide.

In this real-world study, we compared the effects of liraglutide, semaglutide, and tirzepatide on weight loss and metabolic parameters over a 36-week period in non-diabetic individuals with overweight or obesity. The primary outcome was percent change in body weight from baseline to week 36, while secondary outcomes included waist circumference, lipid profile, liver enzymes, pancreatic enzymes, HbA1c, and insulin resistance.

Weight loss from baseline to week 36 was greatest in the tirzepatide group compared with the liraglutide and semaglutide groups. While modest weight reduction (≥5%) occurred at similar rates across treatment groups, higher thresholds of weight loss (≥10% and ≥20%) were more frequently achieved with tirzepatide. Although the proportion of patients achieving very high levels of weight loss (≥25%) was numerically greater in the tirzepatide group, these differences did not reach statistical significance, possibly due to limited sample size. These findings are consistent with indirect comparisons from network meta-analyses and systematic reviews, which generally report superior weight-loss outcomes with tirzepatide compared with GLP-1 receptor agonists alone.[19,20]

Results from pivotal randomized controlled trials support these observations. Liraglutide 3.0 mg has been associated with approximately 8% weight loss over 56 weeks,[21] whereas semaglutide 2.4 mg achieved a mean weight loss of 14.9% at 68 weeks in the STEP-1 trial.[22] More recently, the SURMOUNT-5 trial demonstrated that tirzepatide produced significantly greater reductions in body weight and waist circumference than semaglutide.[23] Similar findings have also been reported in populations with type 2 diabetes.[24]

The greater efficacy of semaglutide compared with liraglutide has been attributed to differences in pharmacokinetic and molecular properties, including enhanced albumin binding, prolonged half-life, and increased resistance to dipeptidyl peptidase-4 degradation.[12,25] Tirzepatide, by contrast, exerts its effects through dual agonism of both GIP and GLP-1 receptors, resulting in a distinct pharmacological profile. The synergistic activation of these incretin pathways, together with the role of GIP in central and peripheral energy regulation, may contribute to the superior weight-loss efficacy observed with tirzepatide.[15,26]

Importantly, these findings should be interpreted in the context of the observational study design. Although greater weight reduction was observed in patients receiving tirzepatide, these results reflect associations rather than causal effects and may be influenced by confounding by indication, differences in baseline characteristics, treatment selection, dose escalation, and tolerability in routine clinical practice.

Waist circumference, an established marker of central adiposity and cardiometabolic risk, decreased significantly from baseline to week 36 in all treatment groups. The magnitude of within-group reduction was clinically meaningful across liraglutide, semaglutide, and tirzepatide, with large effect sizes observed for each agent. However, consistent with

the between-group analyses, no statistically significant differences were detected among treatments with respect to waist circumference change. These findings suggest that reductions in central adiposity largely parallel overall weight loss in real-world clinical practice and may contribute to the observed metabolic improvements, without supporting differential effects between agents.

Non-alcoholic fatty liver disease affects approximately 30% of the general population and is substantially more prevalent among individuals with obesity.[27,28] In the present cohort, more than two-thirds of participants exhibited ultrasonographic evidence of hepatic steatosis at baseline, consistent with previous epidemiological data. Weight loss has been consistently associated with improvements in NAFLD,[16,29] and emerging evidence suggests potential beneficial effects of GLP-1 receptor agonists and dual GIP/GLP-1 receptor agonists on hepatic steatosis and inflammatory markers.[30,31] In our study, significant reductions in AST, ALT, and GGT levels were observed across all treatment groups. However, no significant intergroup differences were detected. These findings should be interpreted cautiously, as changes in liver enzyme levels do not necessarily reflect histological improvement.[32,33] Moreover, hepatic steatosis was assessed using ultrasonography rather than histological or advanced imaging techniques, which may limit sensitivity for detecting subtle changes in liver fat content. Longer-term studies incorporating quantitative imaging or histological endpoints are therefore warranted.

Improvements in lipid parameters were observed across all treatment groups at week 36. Reductions in total cholesterol, LDL cholesterol, and triglyceride levels were evident with liraglutide, semaglutide, and tirzepatide, whereas HDL cholesterol levels remained largely unchanged. Although overall lipid improvements were broadly comparable among treatments, triglyceride reduction appeared more pronounced with tirzepatide in this cohort. These findings suggest that incretin-based therapies may confer favorable lipid effects in routine clinical practice, although the magnitude of benefit may vary across agents. Previous studies have reported modest and variable lipid-lowering effects with liraglutide,[34,35] whereas semaglutide has been associated with small but favorable changes in lipid profiles.[36,37] Tirzepatide appears to provide broader improvements across lipid parameters.[38] In the present real-world cohort, although numerical reductions were generally greater with tirzepatide, statistically significant superiority was observed only for triglyceride reduction. Lipid-lowering therapies were considered in the analyses; however, residual confounding related to diet, weight loss magnitude, or lifestyle modification cannot be entirely excluded. These lipid changes may be partly mediated by weight reduction rather than direct lipid-modifying mechanisms, and their long-term cardiovascular implications require further investigation.

Mild increases in pancreatic enzymes have been reported with GLP-1 receptor agonists, without a proven increase in the risk of acute pancreatitis.[39,40] In the present study, modest increases in amylase and lipase levels were observed, particularly in the liraglutide group, whereas changes in the tirzepatide group were less pronounced. These enzyme elevations were generally mild and did not exceed clinically significant thresholds. One case of acute pancreatitis occurred in the liraglutide group; however, given the observational design and the absence of systematic adjudication, causality cannot be established.

These findings are consistent with large randomized clinical trials and post-marketing surveillance data, which have not demonstrated a clear association between incretin-based therapies and pancreatitis.[41,42] The relatively greater enzyme elevations observed with liraglutide may relate to its daily administration and continuous receptor stimulation.[43] However, because this analysis was restricted to patients who completed 36 weeks of treatment, potential early discontinuations due to intolerance may not have been captured, and safety findings should therefore be interpreted cautiously.

Significant improvements in insulin resistance and HbA1c levels were observed across all treatment groups, despite the non-diabetic status of the participants. Although the absolute reduction in HOMA-IR appeared numerically greater in the liraglutide group, this finding should be interpreted cautiously. Baseline HOMA-IR values were significantly higher in the liraglutide group, which may have contributed to a greater magnitude of reduction over time due to regression toward the mean or a greater potential for metabolic improvement. Moreover, treatment allocation was not randomized and may have been influenced by baseline metabolic severity, thereby introducing potential confounding by indication. Accordingly, the greater observed reduction in HOMA-IR with liraglutide likely reflects baseline differences rather than intrinsic superiority of the agent. Importantly, all three incretin-based therapies demonstrated clinically meaningful improvements in insulin resistance, consistent with their established metabolic effects.

Gastrointestinal adverse events were common across all treatment groups, with the highest frequency reported in the liraglutide group. These findings are consistent with prior studies and meta-analyses comparing incretin-based therapies.[44,45] Differences in tolerability may be related to dosing frequency, pharmacokinetic profiles, and receptor selectivity, underscoring the importance of individualized dose escalation and careful monitoring in routine clinical practice.[46,47] Given the observational and completer-based design of the present study, these findings should be considered exploratory and hypothesis-generating. Prospective studies with balanced baseline metabolic characteristics and robust confounding control are warranted to further clarify potential differential effects of these agents on insulin sensitivity and tolerability.

From a clinical perspective, these findings suggest that incretin-based therapies can be effectively implemented in routine practice for weight management in adults with overweight or obesity without diabetes. The observed differences in weight loss and metabolic outcomes across agents underscore the importance of individualized treatment selection, considering patient characteristics, tolerability, dose escalation, dosing feasibility, and overall treatment goals.

These results should be interpreted in light of study limitations, including the exclusion of patients who discontinued treatment early, non-randomized treatment allocation, unmeasured adherence to dietary and physical activity recommendations, and variability in dose escalation and intensity. Given the observational design and completer-based analysis, these findings are primarily hypothesis-generating. Future prospective comparative studies and large-scale real-world registries with robust control of confounding factors are warranted to define optimal treatment strategies and long-term clinical outcomes.

Limitations

Several limitations of this study should be acknowledged. First, the retrospective design limits causal inference. Prospective studies with larger sample sizes and longer follow-up periods, particularly beyond the first year of treatment, are needed to provide more robust evidence regarding long-term metabolic outcomes. Second, hepatic steatosis was assessed primarily using ultrasonography rather than histological evaluation or advanced imaging techniques, which may limit sensitivity for detecting subtle changes in liver fat content. Therefore, future studies incorporating quantitative imaging or biopsy-based assessments are warranted to better clarify the hepatic effects of incretin-based therapies.

This was a single-center study, which may limit the generalizability of the findings. Furthermore, treatment allocation was not randomized, and residual confounding cannot be fully excluded despite multivariable adjustment. In addition, the study cohort was derived over a defined time period during which prescribing practices for incretin-based therapies may have evolved. Although all three agents were prescribed within the same center, temporal changes in clinical experience, drug availability, and physician preference may have influenced treatment selection. This may have introduced prescription bias, particularly given the relatively balanced group sizes.

Moreover, because the analysis was restricted to patients who completed 36 weeks of treatment, the findings may not be generalizable to individuals who discontinued therapy earlier. This selection may also have influenced the observed adverse event rates, as treatment tolerability and physician familiarity with specific agents may have varied over time, potentially affecting both reporting and management of side effects.

Finally, the effects of liraglutide, semaglutide, and tirzepatide on blood pressure could not be reliably evaluated, as patients with pre-existing hypertension and those receiving antihypertensive treatment were included, potentially confounding blood pressure measurements. These factors should be considered when interpreting between-group differences, particularly for safety outcomes.

Conclusions

In this real-world cohort of adults with overweight or obesity without diabetes, liraglutide, semaglutide, and tirzepatide were all associated with clinically meaningful weight loss and favorable metabolic effects over 36 weeks of treatment. Among these agents, tirzepatide was associated with greater weight reduction compared with liraglutide and semaglutide. However, given the retrospective observational design and completer-based analysis, these findings should not be interpreted as evidence of comparative effectiveness or causal superiority. Rather, they highlight the feasibility of incretin-based therapies in routine clinical practice and support their potential role in individualized obesity management. Future prospective controlled studies and large-scale real-world registries with robust confounding control are warranted to confirm these observations and to better inform optimal treatment selection.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Bakırköy Sadi Konuk Training and Research Hospital (Approval No: 2024/267, Date: 02 September 2024).

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Informed Consent Statement

Written informed consent was obtained from all participants included in the study.

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Author Contributions

The author gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work. S.C: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Supervision.

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The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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