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ORIGINAL ARTICLE

Safety and efficacy of liraglutide in patients with obesity; A retrospective observational study across glycemic status groups

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ABSTRACT

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as liraglutide, have demonstrated efficacy in weight reduction and glycemic control. However, comparative data across obese individuals with differing metabolic states non-diabetic (ND), prediabetic (pre-DM), and type 2 diabetes mellitus (T2DM) remain limited, particularly regarding hepatic, lipid, and safety outcomes. This study aimed at evaluating liraglutide's efficacy in reducing body weight and improving metabolic parameters (HbA1c, lipid profile, liver enzymes) and its safety in obese individuals across these groups.

Methods: A prospective study was conducted on 120 obese patients receiving Liraglutide for six months (ND: n=7; pre-DM: n=16; T2DM: n=97). Baseline demographic, anthropometric, and biochemical parameters were recorded. Outcomes assessed at 3 and 6 months included weight, BMI, HbA1c, blood pressure, liver enzymes (ALT, AST), lipid profile, and adverse events. Between-group comparisons were performed using ANCOVA, adjusting for age, disease duration, and baseline metabolic variables.

Results: At baseline, patients with T2DM were older and had significantly higher HbA1c, ALT, total cholesterol (TC), and triglycerides (TG) compared with ND and pre-DM groups ($p<0.05$). Over six months, weight and BMI decreased significantly in all groups, with the greatest mean reduction observed in T2DM (–13.28 ± 8.22 kg), followed by pre-DM (–13.19 ± 9.34 kg), and ND (–6.43 ± 6.53 kg). Higher baseline HbA1c predicted greater weight loss in T2DM and pre-DM ($p<0.001$). Liraglutide was associated with reductions in ALT and AST across all groups, particularly in those with elevated baseline levels. Lipid improvements were most pronounced in T2DM, with significant reductions in LDL and TG.

Conclusion: Liraglutide therapy in obese patients led to significant weight loss and favorable effects on glycemic, hepatic, and lipid parameters across ND, pre-DM, and T2DM groups, supporting the broader role of Liraglutide in obesity and metabolic disease management.

Keywords: Glycemic Control, GLP-1 Receptor Agonist, Liraglutide, Obesity, Prediabetes, Type 2 Diabetes Mellitus, Weight Loss

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Introduction

Dysglycemia and obesity are the two inter connected aspects of the global metabolic crisis that significantly impact type 2 diabetes mellitus (T2DM), cardiovascular disease, and premature mortality (1, 2). The World Health Organization estimates that over 890 million adults worldwide suffer from obesity, and a

significant number of these individuals also have impaired glucose regulation (3-7). This continuum which includes individuals with prediabetes, diagnosed diabetes, and those who are overweight but not diabetic offers an opportunity for early and effective intervention, as metabolic deterioration is largely preventable and manageable(8).

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A glucagon-like peptide-1 receptor agonist (GLP-1 RA), Liraglutide has become a versatile treatment that treats weight gain, dyslipidemia, and hyperglycemia (9, 10). High blood sugar levels are linked to both of these conditions. Although initially developed and approved for the treatment of T2DM, Liraglutide has demonstrated benefits beyond glycemic control (11). These advantages include favorable lipid profile modulation and notable weight loss (12). The GLP-1 agonist Liraglutide, used for weight management in obese non-diabetic and prediabetic individuals, is associated with significant weight loss in morbidly obese patients without diabetes (13). While substantial evidence supports the efficacy of Liraglutide in specific populations, including individuals with T2DM, prediabetes, and non-diabetic obesity, there remains a significant gap in understanding its therapeutic impact across the entire glycemic spectrum when administered under standardized treatment conditions (10). GLP-1RA has also been found to significantly reduce liver enzyme markers, while also decreasing liver fat content (14).

The available clinical data is inconsistent and mostly focuses on the effects of Liraglutide in populations with or without diabetes (13, 15, 16). Comparative studies assessing the effects of Liraglutide across the glycemic spectrum normoglycemia, prediabetes, and T2DM are limited, hindering the optimization of tailored interventions. This study aims to evaluate liraglutide's efficacy in reducing body weight and improving metabolic parameters (HbA1c, lipid profile, liver enzymes) and its safety in obese individuals across these groups. Identifying differential responses could guide personalized therapy. If effective, Liraglutide use in normoglycemia populations may prompt guideline revisions and improve long-term outcomes in cardio metabolic disease prevention.

Methods

This prospective observational study was conducted at the Department of Endocrinology, Northwest General Hospital & Research Center, Peshawar, from November 2020 to April 2022, following ethical approval from the Institutional Review Board via letter no IRC&EC 2025-GH/0249.Adult patients (≥18 years) of either gender with obesity, defined as a body mass index (BMI) ≥30 kg/m², were enrolled after providing written informed consent. Participants were categorized into three groups based on glycemic status: normoglycemic, prediabetic, and type 2 diabetic, as defined by American Diabetes Association (ADA) criteria (17). individuals less than 18 years of age, those with a diagnosis of type 1 diabetes mellitus, history of pancreatitis, thyroid carcinoma, or severe gastrointestinal disease, significant hepatic impairment (ALT or AST >3x upper normal limit not due to fatty liver), renal

impairment (eGFR <30 mL/min/1.73 m²), pregnant or lactating women and patient's already receiving Liraglutide therapy prior to study enrollment were excluded.No formal sample size calculation was performed due to the observational nature of the study; instead, all eligible patients presenting during the study period were consecutively enrolled.

Baseline data were collected using a standardized proforma, including demographics, duration of diabetes (if applicable), and history of comorbid conditions such as hypertension, ischemic heart disease, thyroid disorders, chronic kidney disease, and dyslipidemia. Clinical parameters recorded at baseline included BMI, blood pressure, fasting blood glucose (FBG), random blood glucose (RBG), glycated hemoglobin (HbA1c), liver enzymes (ALT, AST), and a full lipid profile (total cholesterol, triglycerides, HDL, LDL). Hepatic steatosis was assessed and staged using abdominal ultrasonography performed by trained radiologists.

The most common indication for initiating Liraglutide therapy was non-alcoholic fatty liver disease (NAFLD), followed by obesity-related weight reduction, with some patients citing both diabetes and weight concerns. All patients were receiving standard oral antidiabetic agents, with or without insulin, prior to Liraglutide initiation. Treatment with Liraglutide was started at a dose of 0.6 mg/day, titrated up to 1.2 mg/day after one week, and further increased to 1.8 mg/day based on individual patient tolerance and physician discretion.

Patients were followed up at 3 months and 6 months after treatment initiation. At each follow-up visit, assessments were repeated for body weight, FBG, RBG, HbA1c, liver enzymes, lipid profile and adverse effects to evaluate treatment efficacy and safety.

Statistical analyses were performed using SPSS v 21. Continuous variables are presented as Mean ± Standard Deviation/Standard error (SD/SE), while categorical variables are expressed as n (%). For continuous variables, differences between the ND, T2DM, and Pre-DM groups were assessed using either one-way ANOVA or the Kruskal-Wallis test (based on distribution of data). For categorical variables, comparisons were conducted using the Chi-square test. To account for potential baseline differences, Analysis of Covariance (ANCOVA) was performed to compare outcomes between groups while adjusting for key covariates, including age, duration of diabetes, baseline HbA1c, TC, TG, and ALT. Pairwise group comparisons were conducted using Bonferroni-adjusted post-hoc tests to identify specific intergroup differences while controlling for multiple comparisons. A p-value < 0.05 was considered statistically significant.

Results

A total of 120 patients with obesity were enrolled and stratified into three groups based on glycemic status: normoglycemic (ND) (n = 7), prediabetic (Pre-DM) (n = 16), and type 2 diabetic (T2DM) (n = 97). Baseline demographic and clinical characteristics are summarized in Table 1. Patients had a mean age of 46.11 ± 10.46 years, with a higher proportion of females. Most participants were categorized as having grade III obesity. The groups were comparable in terms of age and gender distribution. Mean BMI was highest among T2DM patients, while obesity grade distribution was similar across groups. The

prevalence of comorbidities such as hypertension and dyslipidemia was greater in the T2DM group.

Table 1: Baseline comparison of demographic and clinical characteristics

Variables		ND (n=7)	T2DM (n=97)	Pre-DM (n=16)	p-value
Age (years), **Mean±SD**		30.14±8.59	48.24±9.22	40.19±10.40	<0.001
Duration of condition (years)		-	7.29(5.58)	1.56(2.5)	<0.001
Obesity, n (%)	Grade I	1(14.29)	14(14.43)	2(12.5)	0.846
	Grade 2	1(14.29)	31(31.96)	4(25)	
	Grade 3	5(71.43)	52(53.61)	10(62.5)	
Gender, n (%)	Male	1(14.29)	19(19.59)	3(18.75)	0.942
	Female	6(85.71)	78(80.41)	13(81.85)	
Hypothyroid, n (%)	No	5(71.43)	88(90.72)	13(81.25)	0.196
	Yes	2(28.57)	9(9.28)	3(18.75)	
Weight (kg)		107.43(23.9)	105.98(15.98)	113.56(23.21)	0.281
BMI(kg/m^2)		43.2(8.34)	40.63(5.58)	43.28(7.34)	0.173
DBP (mmHg)		82.71(12.09)	90.37(10.9)	87.38(14.87)	0.177
SBP (mmHg)		129.71(13.91)	139.14(20.17)	137.13(14.14)	0.422
HBA1c%		4.76(0.48)	9.13(1.9)	5.71(0.2)	<0.001
ALT U/L		39.14(20.27)	60.26(27.15)	45.81(23.01)	0.025
AST U/L		38.71(20.83)	54.52(27.02)	40.88(19.29)	0.061
TC (mg/dL)		160(26.22)	205.63(48.17)	193.25(38.96)	0.034
TGs (mg/dL)		124.43(32.4)	277.33(162.12)	182.13(82.48)	0.005
HDL (mg/dL)		43.86(13.87)	39.36(5.8)	46.44(5.67)	0.097
LDL (mg/dL)		101.43(30.65)	127.68(37.64)	122.06(36.54)	0.187

Baseline laboratory investigations are presented in Table 2. T2DM patients exhibited significantly higher HbA1c and ALT levels compared to ND and Pre-DM groups. Lipid profile differences were also evident, with higher triglycerides and total cholesterol in the T2DM group.

Table 2: Baseline laboratory investigations across study groups

Variables	ND (n=7)	T2DM (n=97)	Pre-DM (n=16)	p-value
HBA1c%	4.76(0.48)	9.13(1.9)	5.71(0.2)	<0.001
ALT U/L	39.14(20.27)	60.26(27.15)	45.81(23.01)	0.025
AST U/L	38.71(20.83)	54.52(27.02)	40.88(19.29)	0.061
TC (mg/dL)	160(26.22)	205.63(48.17)	193.25(38.96)	0.034
TGs (mg/dL)	124.43(32.4)	277.33(162.12)	182.13(82.48)	0.005

HDL (mg/dL)	43.86(13.87)	39.36(5.8)	46.44(5.67)	0.097
LDL (mg/dL)	101.43(30.65)	127.68(37.64)	122.06(36.54)	0.187

Table 3 presents a comparative analysis of changes in anthropometric and laboratory parameters across the three groups at 3-month and 6-month follow-up visits. These assessments evaluate the longitudinal effects of Liraglutide treatment on main clinical outcomes. At both 3-month and 6-month follow-ups, a progressive reduction in body weight and BMI was observed in all groups, with the greatest decline among T2DM patients. By 6 months, mean body weight in the T2DM group had decreased from 99.13 kg to 92.61 kg and BMI from 37.78 kg/m² to 35.16 kg/m². Reductions were less pronounced in the ND and Pre-DM groups. HbA1c levels remained relatively stable across groups, with T2DM patients maintaining the highest mean values throughout follow-up. Blood pressure showed minimal change, though the Pre-DM group demonstrated consistently higher systolic values. Liver enzymes (ALT and AST) and lipid profiles showed modest but significant improvements, particularly in LDL and triglyceride levels among T2DM patients.

Table 3: Longitudinal changes in weight, BMI, HbA1c, ALT, and lipid profile at 3 and 6 months

Variable	ND (n=7)		T2DM (n=97)		Pre-DM (n=16)	
Follow-up	**3-months**	**6-months**	**3-months**	**6-months**	**3-months**	**6-months**
Weight (kg)	104.29 ± 22.80	101.00 ± 18.73	99.28 ± 14.96	92.70 ± 14.83	107.63 ± 19.57	100.38 ± 16.71
Weight Δ	3.14 ± 3.53	6.43 ± 6.53	6.70 ± 6.05	13.28 ± 8.22	5.94 ± 5.45	13.19 ± 9.34
BMI (kg/m²)	41.69 ± 8.28	40.65 ± 6.80	38.07 ± 5.35	35.48 ± 5.12	40.71 ± 6.02	38.79 ± 5.72
BMI Δ	1.51 ± 1.60	2.55 ± 2.38	2.56 ± 2.09	5.14 ± 2.92	2.56 ± 2.44	4.49 ± 3.51
HbA1c (%)	4.80 ± 0.30	4.80 ± 0.38	7.67 ± 1.40	7.05 ± 1.11	5.43 ± 0.33	5.10 ± 0.34
HbA1c Δ	-0.04 ± 0.51	-0.04 ± 0.49	1.45 ± 1.33	2.07 ± 1.56	0.29 ± 0.26	0.61 ± 0.32
ALT (U/L)	34.71 ± 15.94	30.14 ± 14.09	49.72 ± 17.77	41.85 ± 13.41	34.31 ± 16.99	31.13 ± 9.29
ALT Δ	4.43 ± 16.05	9.00 ± 16.62	10.54 ± 18.11	18.41 ± 19.76	11.50 ± 23.23	14.69 ± 20.83
AST (U/L)	30.71 ± 11.69	29.43 ± 12.20	45.82 ± 17.35	39.03 ± 12.73	31.50 ± 12.94	28.13 ± 7.60
AST Δ	8.00 ± 16.39	9.29 ± 16.79	8.69 ± 16.26	15.48 ± 20.39	9.38 ± 24.03	12.75 ± 19.19
TC (mg/dL)	137.57 ± 12.90	128.86 ± 11.52	177.06 ± 35.71	157.08 ± 35.29	178.25 ± 38.88	158.31 ± 31.10
TC Δ	22.43 ± 15.82	31.14 ± 20.56	28.57 ± 32.55	48.55 ± 36.29	15.00 ± 22.52	34.94 ± 20.58
TGs (mg/dL)	123.00 ± 26.09	112.00 ± 35.32	210.91 ± 111.13	173.62 ± 73.35	165.13 ± 58.12	144.69 ± 37.16
TGs Δ	1.43 ± 24.94	12.43 ± 29.78	66.42 ± 78.95	103.71 ± 105.85	17.00 ± 57.30	37.44 ± 65.58
HDL (mg/dL)	40.86 ± 5.18	41.57 ± 2.44	41.91 ± 4.81	41.82 ± 2.38	44.25 ± 5.63	41.50 ± 3.41
HDL Δ	2.14 ± 11.33	1.43 ± 12.55	-2.55 ± 5.15	-2.46 ± 5.89	-1.81 ± 4.52	0.94 ± 4.19

LDL (mg/dL)	80.86 ± 11.98	79.14 ± 6.82	106.76 ± 27.64	95.29 ± 22.41	106.19 ± 25.36	92.94 ± 17.83
LDL Δ	20.57 ± 25.77	22.29 ± 30.27	20.92 ± 26.18	32.39 ± 30.90	15.88 ± 33.22	29.13 ± 34.03

Table 4: ANCOVA adjusted intergroup comparisons for major outcomes

Variable	**ND (n=7)**		**T2DM (n=97)**		**Pre-DM (n=16)**		**p-value***	**Significant Covariates (p < 0.05)**
Follow-up	***3 Months***	***6 Months***	***3 Months***	***6 Months***	***3 Months***	***6 Months***		
Weight	104.23 ± 7.50	100.55 ± 7.06	99.13 ± 1.80	92.61 ± 1.69	108.53 ± 4.86	101.14 ± 4.57	0.025	Age (p=0.026)
BMI	43.43 ± 2.54	42.47 ± 2.36	37.78 ± 0.61	35.16 ± 0.56	41.71 ± 1.65	39.91 ± 1.53	0.006	HbA1c (p=0.041), TC (p=0.048)
HbA1c	6.996 ± 0.39	6.996 ± 0.39	7.239 ± 0.09	7.239 ± 0.09	7.092 ± 0.25	7.092 ± 0.25	0.816	HbA1c (p=0.019)
SBP	131.01 ± 6.02	131.01 ± 6.02	132.18 ± 1.44	132.18 ± 1.44	142.77 ± 3.90	142.77 ± 3.90	0.027	HbA1c (p=0.019)
DBP	85.29 ± 4.99	85.29 ± 4.99	85.65 ± 1.20	85.65 ± 1.20	85.67 ± 3.23	85.67 ± 3.23	0.997	DM Duration, HbA1c (<0.001)
ALT	44.14 ± 5.95	44.14 ± 5.95	47.96 ± 1.43	47.96 ± 1.43	40.85 ± 3.86	40.85 ± 3.86	0.247	ALT (<0.001)
AST	38.24 ± 4.91	38.24 ± 4.91	44.37 ± 1.18	44.37 ± 1.18	37.04 ± 3.18	37.04 ± 3.18	0.131	ALT (<0.001)
TC	162.14 ± 10.88	162.14 ± 10.88	173.91 ± 2.61	173.91 ± 2.61	186.58 ± 7.05	186.58 ± 7.05	0.055	HbA1c (p=0.038), TC (<0.001)
TGs	207.38 ± 21.69	207.38 ± 21.69	196.02 ± 5.19	196.02 ± 5.19	218.46 ± 14.04	218.46 ± 14.04	0.377	TC (0.021)TG (<0.001)
HDL	43.31 ± 2.21	43.31 ± 2.21	41.58 ± 0.53	41.58 ± 0.53	45.17 ± 1.43	45.17 ± 1.43	0.093	–
LDL	105.36 ± 10.16	87.47 ± 8.96	103.12 ± 2.43	94.08 ± 2.15	117.58 ± 6.58	96.63 ± 5.80	0.129	TC, TG (<0.001)

Values represent adjusted means (estimated marginal means ± SE) at 3 and 6 months. Between-group comparisons were assessed using **ANCOVA**, with age, diabetes duration, baseline HbA1c, TC, TG, and ALT as covariates.* Group Effect, P-values <0.05 were considered statistically significant. NS = not significant. Significant covariates influencing each outcome are listed.

ANCOVA was conducted across three groups while controlling for covariates. Overall model was highly significant ($F = 39.50$, $p < 0.001$, $R^2 = 0.740$), indicating that covariates strongly predicted HbA1c changes. Baseline HbA1c was the strongest predictor of post-treatment HbA1c levels ($p < 0.001$, $\eta^2 = 0.497$), patients with higher initial HbA1c had greater reductions. Liraglutide significantly improved glycemic control in T2DM and prediabetes, with a trend toward lower HbA1c in prediabetic patients, though no significant between-group differences were observed after adjusting for covariates ($p = 0.816$).

Weight loss was observed across all groups, but between-group differences were not significant after adjusting for covariates ($p = 0.242$ for weight, $p = 0.055$ for BMI). Age was not associated with weight changes ($p = 0.069$, $\eta^2 = 0.029$). Baseline HbA1c and lipid

levels did not significantly influence weight loss, indicating that liraglutide's weight-reducing effects were independent of initial metabolic status.

The overall model was significant ($F = 22.16$, $p < 0.001$, $R^2 = 0.615$), with baseline TC as a strong predictor ($p < 0.001$, $\eta^2 = 0.534$). However, group effects were not significant ($p = 0.055$), indicating that liraglutide had a similar impact across all groups.

Liraglutide significantly reduced TG levels ($F = 62.24$, $p < 0.001$, $R^2 = 0.818$), with baseline TGs being the strongest predictor ($p < 0.001$, $\eta^2 = 0.792$). No significant differences were found between groups ($p = 0.377$). The model was significant ($F = 2.55$, $p = 0.014$, $R^2 = 0.155$), with age significantly affecting HDL levels ($p = 0.010$, $\eta^2 = 0.058$), suggesting that older patients had different HDL responses to Liraglutide. However, diabetes status did not significantly impact HDL improvements ($p = 0.093$).

ALT levels significantly improved across all groups ($F = 17.32$, $p < 0.001$, $R^2 = 0.555$), with baseline ALT strongly predicting final ALT levels ($p < 0.001$, $\eta^2 = 0.473$). AST levels also showed significant reductions ($F = 27.05$, $p < 0.001$, $R^2 = 0.661$), with baseline AST as the primary determinant ($p < 0.001$, $\eta^2 = 0.594$) [**Table 4**].

Adverse events were relatively infrequent: gastrointestinal side effects occurred in 14.17%, injection site reactions in 6.67%, and insufficient efficacy was reported by 17.5% of patients. Cost issues were cited by 24.17% as a barrier. Changes in fatty liver staging from baseline throughout the study period are illustrated Changes in fatty liver staging from baseline throughout the study period are illustrated in Figure 1.

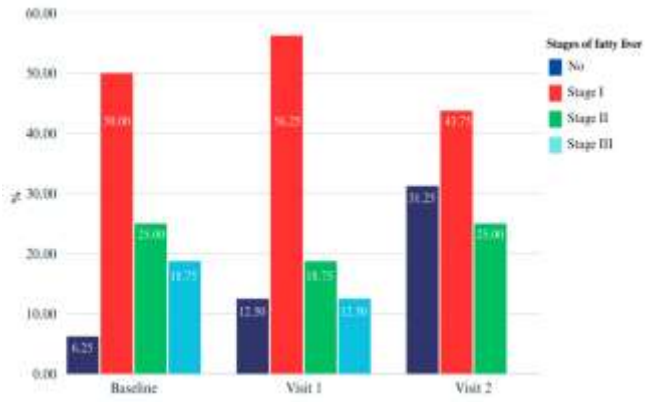

Figure 1: Changes in fatty liver staging from baseline

Discussion

GLP-1 RA has gained widespread recognition for its dual efficacy in managing both hyperglycemia and obesity, making it a promising therapeutic option for metabolic disorders. It has also shown significant benefits in weight management, leading to its use in non-diabetic obese individuals (15, 16).

Our study findings demonstrated significant weight reduction across all groups, with T2DM patients achieving the greatest mean weight loss (13.28 kg at 6 months), aligning with the SCALE Obesity and Prediabetes trial, where Liraglutide 3.0 mg led to a mean 6.1% weight loss over 3 years (16, 18). However, our T2DM cohort exhibited more pronounced reductions than those reported in the LEAD program (-8.4 kg at 56 weeks) (19), potentially due to stricter lifestyle interventions or longer follow-up. HbA1c improvements in our T2DM group (2.07% reduction at 6 months) were consistent with LEAD trials (1.1–1.5% reductions) (19, 20), though greater than the SCALE trial's 0.33% reduction in prediabetes, likely reflecting higher baseline HbA1c in our cohort (9.13% vs. 5.7–6.5% in SCALE) (16, 18).

Our study observed significant LDL reductions in T2DM patients (32.39 mg/dL), surpassing the modest lipid improvements in LEAD trials (e.g., 0.2 mmol/L TG reduction)

(19, 21). These discrepancies may stem from concurrent statin use or dietary modifications in our cohort. Elevated ALT levels improved across all groups corroborating preclinical studies showing liraglutide's hepatoprotective effects, though this outcome was not a primary focus in most RCTs (18, 19).

The high prevalence of fatty liver (74.17% stage I–III) in our cohort underscores the metabolic complexity of obese patients, consistent with SCALE trial populations (16, 18). However, our study's lipid changes were less pronounced than those in the LEADER trial, which reported cardiovascular risk reductions (21), suggesting baseline differences in cardiovascular risk profiles.

Adverse event rates in our study were lower than those in major trials: gastrointestinal side effects (14.17% vs. 30–40% in SCALE) and injection site reactions (6.67% vs. 10–15% in LEAD). This may reflect slower dose titration or improved patient education in our clinical setting. The 24.17% reporting cost-related barriers highlights real-world challenges not typically addressed in RCTs, which often provide subsidized medications (16, 18).

The dose escalation (baseline 0.63 mg to 1.78 mg at 6 months) in our study mirrors the STEP trials' structured titration, though our median final dose (1.8 mg) was lower than the 3.0 mg used in SCALE. Despite this, majority achieved weight loss, comparable to SCALE's 63% at 3.0 mg, suggesting effective adherence and protocol fidelity. The extended visit duration (4.37 to 5.56 months) may have enhanced patient engagement, a factor underreported in RCTs (16, 18).

In contrast, our non-diabetic group showed modest weight loss (6.43 kg vs. 8.4 kg in SCALE), potentially due to smaller sample size (n=7) (18). While SCALE reported 66% reversion to normoglycemia (16, 18), our prediabetic group focused on weight/HbA1c improvements, possibly due to study design differences. Unlike the LEADER trial, which demonstrated cardiovascular risk reduction (21, 22); our study did not assess

Conclusion

Our findings suggest potential of Liraglutide for broader use in early intervention, metabolic disease prevention and personalized treatment strategies.

Limitations and Strengths

Our study reinforce liraglutide's efficacy in weight and glycemic management across glycemic spectrums, consistent with LEAD and SCALE trials. The inclusion of liver-specific outcomes (ALT/AST) addresses an understudied area in Liraglutide research. Real-world data on dosing practices, cost barriers, and heterogeneous metabolic profiles enrich RCT findings. Unique contributions include insights into hepatic benefits, and real-world adherence challenges. This observational design limits causal inferences compared to other large RCTs. Future studies should explore long-term sustainability and cardiovascular outcomes in similar cohorts.

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Conflict of interest: None

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.