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Long-Term clinical efficacy of liraglutide for type 2 diabetes: real-world evidence and outcomes from Pakistan

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ABSTRACT

Background: Liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, has demonstrated efficacy in improving glycemic control and promoting weight loss in clinical trials. However, real-world data from diverse populations, particularly from South Asia, are limited. The study aims to evaluate the long-term efficacy and safety of liraglutide in a real-world setting among Pakistani patients with type 2 diabetes mellitus (T2DM).

Methodology: A retrospective cohort study of 624 patients initiated on liraglutide was conducted. Data were collected at baseline and 6, 12, 18, and 24 months. Primary outcomes were HbA1c and weight changes. Secondary outcomes included fasting plasma glucose, lipid profile, and blood pressure. Statistical analyses were performed using appropriate methods.

Results: In study population the mean HbA1c reduction of $-1.45 \pm 0.67\%$ was observed at 24 months, with 30.6% achieving HbA1c \leq 7.5%. A rapid and sustained weight loss of -7.51 kg was achieved, with 27.2% experiencing \geq 5% weight loss. Additionally, liraglutide led to a significant reduction in LDL cholesterol, with 46.7% of patients achieving a \geq 10% reduction at 24 months. Liraglutide was well-tolerated, with a low discontinuation rate of 4.6%. **Conclusion:** Liraglutide demonstrated sustained efficacy and safety in a diverse Pakistani population with T2DM, regardless of baseline characteristics. These findings support the use of liraglutide as an effective treatment option for T2DM in real-world clinical practice.

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterised by insulin resistance, impaired insulin secretion, and persistent hyperglycemia. It is a major global health concern, leading to significant morbidity and mortality, primarily due to its complications, including cardiovascular disease, nephropathy, and neuropathy. The management of T2DM typically involves a combination of lifestyle modifications – such as a healthy diet and regular exercise – alongside pharmacological treatments. Current pharmacological options include metformin, sulfonylureas, DPP-4 inhibitors, SGLT-2 inhibitors, and GLP-1 receptor agonists. Each therapeutic class offers distinct mechanisms of action to improve glycemic control and reduce diabetes-related complications, though patient-specific factors often dictate treatment choices.

The GLP-1 derivative liraglutide shares 97% of its amino acid sequence with the original molecule (Ismail & Csóka, 2017; Knudsen, 2019; Tanday et al., 2022) GLP-1, a polypeptide hormone known as an incretin hormone, which is secreted by the L cells of the pancreas in the gastrointestinal tract (Ismail & Csóka, 2017; Knudsen, 2019; Tanday et al., 2022). Liraglutide has emerged as an important option for managing T2DM. It is available under the trade names Victoza® for diabetes management and Saxenda® for weight loss. The FDA first approved it in 2010 for treating type 2 diabetes using a healthy diet and regular exercise (Davies et al., 2015; Shaefer Jr et al., 2015). Victoza® is administered via subcutaneous injection, with a daily dose of 1.2 mg to 1.8.mg, while Saxenda® is prescribed at 3.0 mg for patients primarily seeking weight reduction. The pharmacokinetic advantages of liraglutide stem from its structural modifications, including the substitution of lysine by arginine at position 34 and the addition of a fatty acid chain, resulting in a prolonged half-life of 13 hours after subcutaneous administration (Lin et al., 2020; Nuffer & Trujillo, 2015).

For several years, clinical trials have demonstrated that GLP-1 analogs can help patients lose weight and manage their blood sugar levels. Insulin secretion is stimulated as glucose levels rise, plasma glucagon levels fall, digestion is delayed, appetite is suppressed, and heart rate increases (Holst, 2019a, 2019b; Nauck et al., 2011; Nauck & Meier, 2018).

Liraglutide, a weight-loss and glucose-management medication, was developed after its success in Human clinical Trials and Real-world Trials (Cornell, 2020; Haddad et al., 2023; Peters, 2010). Clinical trials report HbA1c reductions of about -0.9% to -2.2% and weight loss of 5–6 kg over

26–52 weeks. The LEADER trial showed a 13% reduction in major cardiovascular events with liraglutide. Global studies confirm sustained improvements in glycemic control, weight, and cardiovascular outcomes. In South Asia, including Pakistan, where liraglutide was introduced in 2016, limited realworld data exists. Studies in this region report HbA1c reductions of 0.8– 1.2% and weight loss of 3–5 kg, but large-scale data from Pakistan remains scarce, highlighting the need for local real-world evidence (Bensignor et al., 2022; Giruzzi, 2022; Nuffer & Trujillo, 2015). Furthermore, substantial randomised clinical trials have demonstrated superior cardiovascular and kidney safety findings in diabetic individuals and improved outcomes in these patients (Cherney et al., 2021; Wheeler et al., 2021).

It is believed that GLP-1 causes weight loss because it is an appetite suppressant and delays gastric emptying. However, the pharmacokinetic profile of GLP-1 severely limits its therapeutic potential as a naturally occurring compound. Once in the bloodstream, native GLP-1 has a half-life of <2 min due to its rapid degradation by the enzymes DPP-IV and neutral endopeptidases (NEP) (Ahrén & Burke, 2012; Holst, 2004).

This retrospective observational study aims to assess the long-term effectiveness of liraglutide in real-world clinical settings, addressing the limitations of randomised controlled trials, which often exclude patients with comorbidities or adherence issues (Jehangir et al., n.d; Kalra et al., 2019). By capturing real-world adherence, patient satisfaction, and side effects, the study provides a comprehensive view of liraglutide's impact. Given the limited data from Pakistan, this research fills an important gap by evaluating liraglutide's effects on glycemic control, body weight, and cardiovascular risk factors in Pakistani patients with T2DM. The primary objective is to assess reductions in HbA1c, with secondary outcomes focused on weight, lipid profiles, and blood pressure, contributing valuable region-specific data to global findings.

Methodology

A comprehensive collection of 624 patient records was obtained from an **electronic clinical record (ECR) system** extensively employed to administer routine diabetes care to patients diagnosed with T2DM across multiple centers in **Rawalpindi and Islamabad, Pakistan. Three major diabetes centers (The Diabetes Center, Umar Diabetes Clinic, and Allied Diabetes and Liver Disease)** were included, all of which have established protocols for managing T2D and follow clinical guidelines that ensure consistent diabetes care.

The data collection period spanned from March 2016 to November 2021. Data were extracted at baseline (the time of liraglutide prescription initiation) and approximately **6**, **12**, **18**, **and 24 months after treatment initiation**. These data points were documented using web-based case report forms to ensure uniformity. To minimise selection bias, patient records were systematically acquired from the ECR system in consecutive order based on liraglutide initiation date.

Patient inclusion criteria focused on individuals with a confirmed diagnosis of T2DM, initiation of liraglutide therapy within the specified period, and availability of at least 12 months of follow-up data in the ECR system. Specifically, **patients had to demonstrate baseline HbA1c** levels of \geq 7.0% to meet criteria for liraglutide therapy under center guidelines, aligning with clinical thresholds for intensified therapy. Patients with incomplete baseline data, concurrent GLP-1 receptor agonist therapy other than liraglutide, type 1 diabetes, or secondary diabetes causes were excluded.

A standardised data collection sheet was developed based on diabetes management guidelines, with input from experienced endocrinologists to ensure data relevance and completeness. The sheet was **piloted on 30 patient records** to validate clarity and functionality, with feedback integrated into the final version. To confirm the accuracy of the collected data, independent clinical notes were reviewed against extracted data to enhance validity.

Primary and secondary objectives

The main objective was to determine the **proportion of patients achieving** $a \ge 1\%$ reduction in HbA1c after 12 months of liraglutide therapy. Secondary objectives included measuring the percentage of patients who achieved $\ge 1\%$ HbA1c reduction at 6 and 24 months, those achieving $a \ge 5\%$ reduction in body weight, and a combined endpoint assessing both metrics at 6, 12, and 24 months. The study also examined the proportion of patients achieving the HbA1c target of $\le 7.5\%$ as per the American Diabetes Association/International Diabetes Federation guidelines at 6, 12, and 24 months. Additionally, changes in HbA1c, body weight, blood pressure, LDL, and HDL levels were analyzed continuously over the 24-month period to assess overall treatment impact.

The sample size was calculated based on the primary objective, which was to determine the proportion of patients who achieved a 1% reduction in HbA1c after 12 months of liraglutide therapy.

 $S = \frac{Z^2 \times P \times (1 - P)}{M^2}$ where **S** represents the sample size, **Z** is the Z-score (1.96 for 95% confidence), **P** is the expected success proportion (0.5), and **M** is the margin of error (0.05).

Assuming that 50% of patients would experience this reduction, with a 5% margin of error and a 95% confidence level, the required sample size was calculated as 580 patients. A final sample of 624 patients was included to account for potential dropouts or missing data (Arya et al., 2012). However,

since **patient heterogeneity and potential dropout were anticipated**, a more conservative sample size estimation was used. Assuming a dropout rate of **10%**, the required sample size was increased by multiplying the initial estimate by 1.1. Finally, to ensure statistical robustness and accommodate additional uncertainties, the sample size was **doubled**, arriving at the final value of **580 patients** required for the study.

Missing data were managed using longitudinal models to minimise bias due to patient dropouts or treatment discontinuation. These models utilised all available data points for each patient and incorporated hierarchical linear models to adjust for within-patient correlations over time. Patients who discontinued treatment or had incomplete follow-up were still included in the intention-to-treat (ITT) analysis, ensuring a robust assessment of real-world effectiveness.

Statistical analysis

The baseline attributes are reported as the mean value plus or minus the standard deviation (SD). The study analysed continuous outcome data from the intention-to-treat (ITT) population, which included all patients who received their initial prescription of liraglutide in 2016. Hierarchical linear models were employed to examine temporal trends. An unstructured correlation-type linear model was used to account for within-patient correlations and variations in time points. The changes in expression from the initial state were quantified as estimated treatment differences (ETDs) accompanied by 95% confidence intervals (Cls). The analysis of categorical endpoint data was conducted using a general linear model, wherein post hoc test contrasts were assessed at each time point. The findings are reported as frequencies and percentages with 95% confidence intervals. Longitudinal models were used to effectively handle the issue of missing data and potential bias arising from treatment termination. All analyses were conducted at a significance level of 5%. The statistical analyses were performed using the software SPSS version 25. The study ensured the preservation of ethical principles by following the guidelines outlined in the Helsinki Declaration of 1964 (updated in 2013) and obtaining informed consent from all patients who participated in the research.

Results

The presented results refer to the data available as of January 2021. Patient data were obtained from the ECR for 683 patients; however, 59 patients were excluded from the final analysis. The patient data excluded from the study had no data in their clinical records. The clinic staff contacted all the patients for informed consent to use their personal information. A total of 624 patients were included in this study, 52.2% of whom were female and

Variable	Baseline	6 months	12 months	18 months	24 months
Group size (N)	624	589	413	397	379
HbA1c (%)	98.6	91.3	87.3	84.9	94.3
Fasting plasma glucose (%)	88.1	89.5	89.2	55.3	90
Weight (%)	94.9	92	90.8	80.7	90.4
BMI (%)	89.5	90.9	89.8	81.9	89.5
Systolic blood pressure (%)	76.7	75.7	75.3	65.3	75.2
Diastolic blood pressure (%)	76.6	75.8	75.1	77.2	75.2
Total cholesterol (%)	67.3	60.5	65.6	69.2	68.1
HDL cholesterol (%)	64.8	59.5	64.2	55.4	65.8
LDL cholesterol (%)	50.3	46.4	51.3	55.4	52.4
Triglycerides (%)	66.4	60.4	64	59.9	67.6
Liraglutide dosage (%)	83.5	85	87	85.3	91.4

Table 1. Record	proportions	available in	the electronic	clinical	records s	system
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47.5% of whom were male. The mean age at liraglutide initiation was 43.21 ± 4.79 years. Patient data were collected at 4 different intervals after initiating liraglutide, and the available data were collected at 6, 12, 18, and 24 months as shown in Table 1.

The baseline demographics are presented in Table 2. A total of 52.2% (328) were female, and 47.5% (296) were male. The mean HbA1c was 9.17 ± 2.17 . However, most patients had a higher HbA1c level, 57.3% of whom were in the range of 8.1% or above. Data for diabetic complications showed that 23.7% and 11.5% of patients presented with a personal history of coronary heart disease and stroke, respectively. Peripheral vascular disease was present in 8.6% of patients, while diabetic retinopathy and sensory motor neuropathy were present in 1.5% and 7.1%, respectively.

In the clinical setting, the highest dosage of liraglutide (1.8 mg) was not consistently prescribed. Initially, 79% of patients received a daily dose of 0.6 mg, 20% were prescribed 1.2 mg, and only 1% were given 1.8 mg. After 6 months, the distribution shifted to 13%, 69%, and 18% for 0.6, 1.2, and 1.8 mg, respectively. At the 12-month mark, the prescription rates were 10%, 54%, and 36% for the same respective doses as evident from the Figure 1.

Concerning concurrent use of other antidiabetic medications at the outset, 28.7% of patients utilised liraglutide in combination with metformin, 32.7% with insulin, metformin, and sulfonylurea, and 15.8% with either basal insulin or premixed insulin. In terms of treatment approach, liraglutide served as an adjunct treatment in 73.2% of patients, as a replacement for a previous drug in 42.4%, and as a treatment for 16.4% of patients.

After 24 months, 170 patients (27.2%) discontinued liraglutide. The most common reason for treatment discontinuation, as reported by 29 patients (4.6%), was 'intolerance', followed by 'gastrointestinal adverse events', reported by 64 patients (10.2%), and 18 patients (2.9%) reported stopping medication use due to affordability issues, as shown in Figure 2.

Variable Age (Years)	Mean ± SD 43.21 ± 4.79	%(n)
18–30		2.1 (13)
30–40		24.2 (151)
40-50		60.1 (375)
50 & above		13.2 (82)
Gender		
Female		52.2 (328)
Male		47.5 (296)
HbA1c (%)	9.17 ± 2.17	
Up to 7.5		17.6 (110)
7.6–8.0		25 (156)
8.1-8.9		28.9 (181)
9.0 & above		28.4 (177)
Duration of Diabetes (Years)	8.53 ± 4.63	
<1-5		23.6 (147)
6–10		69.3 (432)
11–15		5.5 (35)
16 & above		1.4 (9)
Body weight (kg)	98.58 ± 15.2	
SBP (mmHg)	136.78 ± 17.63	
DBP (mmHg)	88.6 ± 10.49	
BMI (kg/m ²)	33.9 ± 4.1	
27.1–30 kg/m ²		26.9% (168)
30.1–39.9 kg/m ²		61.7% (385)
40 kg/m ²		11.4% (71)
Combination Therapy with Liraglutide(GLP-1)		
Diet Plan/Exercise		15.7% (98)
Oral Hypoglycemic Agents Only		28.7% (179)
Combination of Oral and Insulin		32.7% (204)
Insulin Only		15.8% (99)
New Generation Insulin		7.1% (44)
Comorbidity or Complications		
No Comorbidity		4.3% (27)
Hypertension		40% (250)
Cardiovascular Disease		34.2% (213)
Diabetic Retinopathy		1.5% (9)
Peripheral vascular disease		8.6% (54)
Sensory Motor Neuropathy		7.1% (44)
Others		4.3% (27)

 Table 2. Baseline demographic characteristics.



Figure 1. Fraction of doses at different intervals.



Figure 2. Patient-reported side effect profiles.



Figure 3. Mean change from baseline to 24 months. HbA1c glycated hemoglobin.

The mean change in the HbA1c level of the patients over the treatment duration was $-1.45 \pm 0.67\%$. During the initial 6-month phase of treatment, a significant decrease in the HbA1c level of $-0.94 \pm 0.3\%$ was observed, as shown in Figure 3.

The same trend was observed in the weight analysis: in the initial phase of therapy, there was a sudden significant decrease in weight (-5.14 kg), and after 6 months of therapy, the weight loss remained static at -3.76 kg and -3.97 kg. However, at 24-month intervals, the decrease in overall weight was -7.51 kg, as shown in Figure 4. Weight loss followed the same pattern as the reduction in HbA1c.

During the study, 47.4 (95% CI 42.8;52.0) patients achieved $a \ge 1\%$ reduction in HbA1c at 6 months (Table 3). After 12 months, 43.5% (95% CI 40.9; 46.2) of patients had $a \ge 1\%$ reduction in HbA1c, 27.2% (95% CI 19.5; 34.9) of patients had $a \ge 5\%$ reduction in body weight, and 20% (95% CI 12.7; 25.5) had the composite endpoint of both targets. At 24 months, the proportions of patients at each endpoint were 51.5% (95% CI 48.7; 54.44), 56.1% (95% CI 53.1; 59.1) and 25.6% (95% CI 23.0; 28.2). Furthermore, at 24 months, 30.6% (95% CI 28.1; 33.1) of patients had achieved the HbA1c

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Figure 4. Mean change from baseline to 24 months. Weight (kg).

	6 months		12 months		24 months	
Endpoint	Frequency	% (95% CI)	Frequency	% (95% CI)	Frequency	% (95% CI)
Patients with HbA1c reduction ≥ 1% point	47.4	(42.8; 52.0)	43.5	(40.9; 46.2)	51.55	(48.7; 54.4)
Patients with HbA1c \leq 7.5%	38.1	(32.0; 44.1)	38.05	(31.8; 44.3)	30.6	(28.1; 33.1)
Patients with weight relative reduction $\geq 5\%$	46.6	(41.0; 52.2)	27.2	(19.5; 34.9)	56.1	(53.1; 59.1)
Composite endpoint (HbA1c reduction \geq 1% point and weight reduction \geq 5%)	36.3	(33.7; 38.9)	20	(12.7; 25.5)	25.6	(23.0; 28.2)
Patients with systolic blood pressure (SBP) reduction ≥ 10 mmHg	30.8	(28.0; 33.6)	28.2	(25.4; 31.0)	35.5	(32.7; 38.3)
Patients with diastolic blood pressure (DBP) reduction ≥ 5 mmHg	26.4	(24.0; 28.8)	24.9	(22.3; 27.5)	29.8	(27.2; 32.4)
Patients with LDL cholesterol reduction ≥ 10%	41.5	(38.1; 44.9)	39.2	(35.8; 42.6)	46.7	(43.3; 50.1)
Patients with HDL cholesterol increase ≥ 10%	5.2	(4.0; 6.4)	6.1	(5.1; 7.1)	6.4	(5.4; 7.4)

 Table 3. Summary of categorical effectiveness endpoints.

target of \leq 7.5%, as shown in Table 3. In terms of cardiovascular risk factors, there were also notable reductions in blood pressure and lipid levels over the 24-month period. Patients with a reduction in LDL cholesterol of \geq 10% increased from 41.5% (95% CI: 38.1; 44.9) at 6 months to 46.7% (95% CI: 43.3; 50.1) at 24 months. Conversely, HDL levels showed minimal change, consistent with expectations for GLP-1 receptor agonists.

Discussion

This observational, non-interventional study assessed the efficacy of liraglutide in patients with T2DM in Pakistan, utilizing a retrospective, successive sampling method. The cohort accurately reflected the demographic profile of patients commonly prescribed liraglutide. At baseline, patients had a mean HbA1c of 9.17%, diabetes duration of 7.5 years, and higher BMI and blood pressure levels compared to the LEAD trials (Kumarathurai et al., 2017). Hypertension, dyslipidemia, coronary heart disease (CHD), diabetic retinopathy, and sensory-motor neuropathy were prevalent in the study population (Berra et al., 2020; Buse et al., 2011; Helmstädter, 2021; Marso et al., 2013; Omboni et al., 2016)

The study's key finding was that over 40% of patients achieved $a \ge 1\%$ reduction in HbA1c after 12 months, with 40.9% reaching HbA1c $\le 7.0\%$ at 6 months. The efficacy of liraglutide was more pronounced in patients previously treated with oral antidiabetic drugs (OADs), showing a 12 mmol/ mol A1c reduction and a 3 kg weight loss, aligning with the LEAD trials and meta-analyses(Jeong & Yoo, 2011; Loganathan et al., 2022). Despite many patients switching from DPP-4 inhibitors, 78% achieved further A1c reductions, with 55% experiencing ≥ 11 mmol/mol reduction (Astrup et al., 2009; Helmstädter, 2021; Lapolla et al., 2018; Nauck et al., 2013).

Liraglutide led to significant HbA1c reductions of -0.94% at 6 months, -1.1% at 12 months, and -1.45% at 24 months (p < 0.001), demonstrating its durability in real-world settings. The weight loss outcomes were consistent with LEAD trials, with 54% of patients achieving a $\ge 3\%$ body weight reduction after 24 months (Fadini et al., 2013; Zinman et al., 2012). However, comparing weight loss outcomes is challenging due to the higher baseline BMI in this cohort compared to prior studies (Buysschaert et al., 2015; Sivalingam et al., 2022; Tronieri et al., 2019).

Additionally, 33.4%-43.5% of patients achieved $\geq 5\%$ weight loss by 12 and 24 months, underscoring the importance of combining pharmacotherapy with lifestyle interventions for effective weight management in T2D (Bernard Zinman et al., 2018). To contrast with the LEADER trials, our investigation revealed that nearly one-third of participants transitioned from other antidiabetic medications to liraglutide, while a smaller proportion (3.4%) received liraglutide as a replacement for multiple antidiabetic drugs (Madsbad, 2009). This transition was particularly prevalent among participants with a baseline HbA1c of 7.5% or higher. Importantly, our findings also indicated a significant relationship between diabetes duration, BMI, and changes in HbA1c. These changes mirrored the pattern observed in the LEAD trials, with an initial reduction in HbA1c followed by stabilization (Nauck, 2012; Nauck et al., 2013).

After the 24-month period, 54.0% of participants achieved at least a 3% reduction in body weight, demonstrating a statistically significant decrease

from baseline. This result aligns with the weight loss outcomes observed in the LEAD clinical trials and is consistent with findings from other observational studies (Davies et al., 2015).

Previous research on GLP-1 receptor agonists (GLP-1 RAs) primarily reports weight changes in terms of mean kilograms lost, rather than the proportion of individuals achieving \geq 5% weight loss, often involving cohorts with lower BMIs and follow-up periods under 12 months. Reported mean weight reductions ranged from -1.0 kg to -3.78 kg over 6-12 months (Crowley et al., 2020; Marso et al., 2013). In contrast, our study observed a mean weight loss of -4.6 kg over 12 months, though 80% of participants had a BMI \geq 35 kg/m², with 56% exceeding 40 kg/m² (median BMI 41.2 kg/m²), significantly higher than the mid-30s typically reported in prior studies (Gilbert et al., 2019; Verma et al., 2019), complicating direct comparison. In our cohort, 33.4% and 43.5% of patients achieved \geq 5% weight loss at 12 and 24 months, respectively, indicating that substantial weight loss in real-world settings is more challenging. The substantial LDL reduction without a corresponding increase in HDL aligns with liraglutide's profile in cardiovascular risk management and offers additional clinical value, particularly for patients at heightened cardiovascular risk. This underscores the need for a multifaceted approach, integrating lifestyle interventions like dietary modifications, physical activity, and psychological support, as pharmacotherapy alone may be insufficient to induce significant weight loss in most patients with T2DM (Pleus et al., 2022; Weiss et al., 2022).

Administering a lower dose of liraglutide may reduce adverse events but could compromise glycemic control. While speculative, our study showed a 6.9% discontinuation rate at 4 months and 11.3% at 12 months, with a 21.5% rate at 24 months, lower than the 36.2% in the EVIDENCE study. This suggests a lower dose may enhance long-term adherence and tolerability (Gautier et al., 2015).

Limitation

The extensive patient records examined in this study enhance the generalizability of the findings within the target population. However, the retrospective nature and reliance on ECR introduce potential limitations, including the possibility of incomplete or missing data. Although missing data were addressed through statistical methods such as multiple imputation, this may still introduce bias and affect the robustness of the results. Furthermore, data completeness was contingent on participating centers, which could lead to inconsistencies. Additionally, the absence of control for multiplicity necessitates caution in interpreting the observed benefits of liraglutide, underscoring the need for prudence in drawing definitive conclusions.

Conclusions

Over two years, liraglutide exhibited substantial improvements in HbA1c levels, body weight, blood pressure, and lipid profiles under real-world conditions, mirroring outcomes observed in clinical trials. These positive effects persisted across diverse patient characteristics, doses, and treatment approaches. Our findings endorse the efficacy of liraglutide as a valuable treatment for T2DM in clinical practice. Real-world evidence further underscores significant reductions in A1c, weight, and SBP and improved lipid profiles, confirming the clinical impact of liraglutide, as observed in randomised controlled trials. Notably, the effectiveness of these regimens observed in this real-world study surpassed expectations, advocating for a liberal prescription approach, particularly for challenging patient cases.

Authors contribution

Conceptualization: Muhammad Daoud Butt, Siew Chin Ong Rumana Saifi Data curation: Rumana Saifi, Azra Rafiq, **Formal analysis:** Basit Ramzan, Nighat Batool **Investigation:** Rumana Saifi, Muhammad Daoud Butt **Methodology:** Muhammad Daoud Butt, Siew Chin Ong **Project Administration:** Azra Rafiq **Resources:** Muhammad Daoud Butt, Azra Rafiq **Supervision:** Siew Chin Ong **Validation:** Nighat Batool, Basit Ramzan **Visualization:** Rumana Saifi, Azra Rafiq **Writing – original draft:** Muhammad Daoud Butt, Basit Ramzan, Azra Rafiq, Rumana Saifi **Writing – review & editing:** Muhammad Daoud Butt, Nighat Batool, Siew Chin Ong. All authors have read and agreed to the published version of the manuscript.

Ethical approval and informed consent

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the Bio-Ethics Committee (BEC) of Bahauddin Zakariya University, Multan, and permitted this observational study in Tertiary Care Hospitals & Diabetes Outpatient Clinics (ACAD/EXT/01/2022). Informed consent was obtained from all participants.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author upon reasonable request.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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