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Effects of Liraglutide 3.0 mg Injection on Weight Reduction and Metabolic Parameters for Patients Living with Obesity and Type 2 Diabetes Mellitus

Hanadi Alnageeb [a], Aseilah Al Qaidy [a], Ashraf Alakkad [b*], Rania Murad [c], Ibrahim Mahgoub [d], Masah Mardinin [e], Heba Shalabi [e], Ahmad Asmi [e] and Aji Gopakumar [f]

[a] Medical Department, Fujairah Hospital, Obesity Clinic, Fujairah, Emirates Health Services, UAE.
[b] Medical Department, Madinat Zayed Hospital, Al Dhafra Region, UAE.
[c] Endocrine Department, Cure Plus Medical Centre, Al Ain, UAE.
[d] Imperial College London, Diabetic Center, Al Ain, UAE.
[e] Fujairah Hospital, Fujairah, Emirates Health Services, UAE.
[f] Research Section, Emirates Health Services, UAE.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: By 2025, it is projected that one billion adults will be classified as having obesity worldwide. Unfortunately, the disease of obesity remains vastly undertreated. As an example, in the United States, nearly half of the adults meet recommendations for anti-obesity pharmacotherapy (defined as having a BMI ≥ 30, or a BMI ≥ 27 with weight-related diseases).

**Corresponding author: E-mail: ashraf.alaqqad@gmail.com;*

Owing to its impact on weight loss, remission of diabetes mellitus, and metabolic syndrome, treatment of obesity with medical therapy like Liraglutide 3.0 mg injection has offered hope for obese individuals. In recent years, obesity has increased in the UAE and the use of medical treatment for obesity has increased in-line with this trend. However, data regarding medical treatment for obesity outcomes in diabetic and non-diabetic Emirati people is scarce.

Objectives: The primary objective of the study is to evaluate the effect of Liraglutide 3.0 mg injection for weight management in patients with diabetes mellitus. In addition, we evaluated the impact of weight reduction in improving the metabolic parameters (HbA1c and LDL-c for a patient living with type2 diabetes).

Secondary objectives include improvement of infertility in females with PCOS and improvement of psychological well-being, functional capacity and quality of life. Also, we evaluated the response post-bariatric group who received Liraglutide 3.0 mg to treat their post-bariatric weight regain.

Results: In terms of weight changes, the average weight at baseline was 100.98 kg and had decreased to 97.54 kg, 96.00 kg, and 96.37 kg at 3, 6, and 12 months, respectively. Males experienced a greater rate of weight reduction than females, while diabetic patients had a lower percentage of weight loss than non-diabetic patients. Additionally, patients with PCOS were able to conceive after reducing 10% of their body weight after using Liraglutide, while the remaining 15 patients who were married but unable to conceive had an improvement in their menstrual cycle and hirsutism.

Conclusion: The results demonstrated that Liraglutide helps to induce and sustain weight loss in patients with obesity. It is an effective treatment for weight reduction and offers the unique benefit of improved glycaemic control. In addition, the study identified a correlation between weight reduction and improvements in psychological health, quality of life, and fertility in females with PCOS. Additional studies are needed to determine its long-term efficacy and safety profile.

Keywords: Type 2 diabetes; body mass index (BMI); polycystic ovarian syndrome (PCOS).

1. INTRODUCTION

Obesity has become a global epidemic that affects diverse societies across both developed and developing countries. It is a key contributor to numerous adverse conditions that includes, but are not limited to, Type 2 Diabetes Mellitus, cardiovascular disease and stroke [1]. The first line therapy for obesity in order to achieve significant weight loss is lifestyle modification. Clinically relevant weight loss is defined as a loss of more than 5% of one's starting body weight. This typically includes calorie restriction, with a deficit of 500-750kCal/day, as well as 150-180 minutes per week of physical exercise [2]. The obesity treatment guideline highly advocates the usage of pharmacological therapy in adults with refractory obesity, where patients have a BMI ≥ 30 kg/m2 despite attempting lifestyle modification [3]. Pharmacological therapy is also advocated in patients with a BMI ≥ 27 kg/m2 having at least one comorbid condition, such as hypertension, dyslipidaemia, insulin resistance, or type 2 diabetes mellitus [4]. It is essential to counsel the patients about lifestyle changes alongside medical therapy in order to improve outcomes.

Liraglutide is a daily glucagon-like peptide 1 receptor agonist – or GLP-1 analogue – which was initially approved at a lower dose of 1.8 mg for the treatment of type 2 diabetes. It was subsequently FDA- and EMA-approved for obesity treatment at the higher dose of 3 mg daily [5].

The mean total body weight loss with this medication is about 7-8% in excess of placebo.

The dose is titrated up slowly, from 0.6 mg daily subcutaneous injection to 3 mg daily over several weeks, in order to mitigate the side effects.

The most common side effects of GLP-1 analogues are gastrointestinal, and include nausea, diarrhoea, vomiting, or constipation. Often these side effects can be attenuated by slow up titration of the medication. Gallstone formation can also occur in some patients.

This medication is contraindicated in patients who have a history of medullary thyroid cancer or multiple endocrine neoplasia type 2.

Obesity is a heterogeneous disease. The concept of heterogeneity is important, as it helps us to understand why the response to anti-obesity medications is variable.

When we assess the response to an anti-obesity medication, if a patient loses less than 5% of their total body weight, we consider that to be an inadequate response. If the patient loses more than 5% of their total body weight, currently, we consider that medication to be effective. If the patient loses more than 10% of their total body weight, we consider that medication to be highly effective.

5-10% range of weight loss is consistent with reduction of incidence, reversal of severity, and / or remission of many of the major comorbidities related to obesity, like diabetes, hypertension, non-alcoholic fatty liver disease, and gastroesophageal reflux disease.

Each of anti-obesity medication options have allowed us to effectively support our patients by affecting the appetite control centre in the hypothalamus (helping them feel less hungry), the reward mechanisms in other areas of the brain that likely play a role in food cravings, as well as satiety via mechanically filling the stomach. Anti-obesity medications provide the physiological support that patients need to succeed long-term. And we know that for many patients the efficacy of these medications, that ranges from 4-12% total body weight loss depending on patient response and type of medication, is encouraging – and while they lower the risk or severity of many obesity-related comorbidities, 5-10% total body weight also sometimes falls short of both the patient's and the health care provider's expectations and goals for obesity treatment and long-term health.

2. MATERIALS AND METHODS

2.1 Aim of Study

To evaluate the response of patients, with and without type 2 diabetes Mellitus, who received liraglutide 3 mg injection in terms of weight reduction and improvement of metabolic parameters.

2.2 Primary Objective

To assess the reduction of BMI and changes in metabolic parameters. This includes lipid profile, HbA1C in diabetics as well as liver function tests. The parameters were recorded from the day of starting the Liraglutide drug and diet up to 12 months of therapy [6-7].

2.3 Secondary Objectives

To evaluate the effect of weight reduction in the improvement of fertility for females with PCOS. In addition, to evaluate the benefit of weight reduction in the improvement of psychological well-being and improve the quality of life.

Study design: A prospective clinical audit of obese Arab patients with liraglutide 3 mg effective in reducing weight between January 2021 till January 2022 with 200 participants recruited.

All aspects of the study as well as consent forms were Institutional Review Boards (IRB) approved prior to implementation. Full informed consent was taken from all participants, while ensuring that they are compliant with all study requirements.

2.4 Inclusion Criteria

Adults above the age of 18 years, living with obesity, having or not having type2 diabetes mellitus who received Liraglutide injection 3 mg for weight management for a period of time range between 6 months and up to 12 months and who had regular follow up visits in obesity clinic.

2.5 Exclusion Criteria

- Adult above the age of 18 years of age who are living with obesity and received other modalities for weight management (bariatric surgery procedures or other medications for weight management)
- Adult patients living with obesity who received liraglutide for less than 6 months.
- Adults patients above the age of 18 years of age who received liraglutide for a period of 6 months up to 12 months but did not have regular follow up in obesity clinic.

After getting an informed consent, patient demographics, along with comorbidities (diabetes mellitus) were recorded. BMI and HbA1C values were documented at intervals of 0, 3, 6, 9 and 12 months, whereas other laboratory investigations including lipid profile, Hb and vitamin D were recorded at intervals of 0,6 and 12 months. We also measured AST, ALT and ALP values at 0,3, and 6 months.

An excel sheet was used to collect the data for the measurable parameters and questionnaire was filled for non-measurable parameters like improvement in functional capacity, cognitive function and infertility for female with PCOS.

- All patients included in the study received Liraglutide 3 mg for weight management.
- Starting dose as per protocol will be 0.6 mg subcutaneous injection for week one, followed by 1.2 mg for week 2, 1.8 mg for week 3, 2.4 mg for week 4, and 3 mg for week 5 (maximum dose).
- The minimum duration for the treatment is 6 months.
- The maximum duration is 12 months.

Clinically meaningful weight loss is defined as 5-10% weight loss, because this is the range in which many adverse health outcomes related to obesity – like diabetes, hypertension, dyslipidaemia and others – improve. Patients were evaluated at week 16 from starting date with a target of 5% weight loss at least.

2.6 Study Population

The study was conducted in Fujairah Hospital, Emirates Health Services, United Arab Emirates. We included 200 patients, all of whom were above the age of 18 years old. This included patients with or without type 2 diabetes mellitus, who started on Liraglutide 3 mg injection for weight management, including those who received other modalities for weight management (bariatric surgery procedures) and developed weight regain. The participants were willing to participate in the study with regular follow-up visits in the obesity clinic for 12 months. Patients who stopped taking the drug before 6 months, took the drug for less than 6 months or who did not attend regular follow-ups were excluded from the study.

2.7 Recruitment Methods

Subjects were identified through existing patient records for follow-up treatment in the obesity clinic at Fujairah hospital. All patients who met the inclusion criteria were recruited and informed about the retrospective nature of the study. Their weight, side effects, adherence to the drug, and improvement in general well-being were monitored. The difference in response to the drug in weight reduction between the individuals in the study was evaluated, as well as other factors that might have contributed to this difference in response, like psychological distress, adherence to physical activities, and dietary advice. Those who agreed to participate in the study were asked to fill out a questionnaire about the compliance and side effects of the drug during the first 6-12 months of treatment. We accessed their medical records to get the information illustrated in the Excel data sheet.

2.8 Statistical Analysis

2.8.1 Definition

The percentage of weight loss at 3 months was calculated by dividing the difference between the weight after 3 months and the baseline weight, by the baseline weight and multiplied by 100. The percentage of weight loss at 6 months and 12 months were similarly calculated, however, the difference between the weight after 6 months and the baseline weight, and the difference between the weight after 12 months and the baseline weight, were respectively used instead.

The study included patients that have been documented on hospital records as having Type 2 diabetes mellitus. The condition is characterized by chronic hyperglycemia due to acquired peripheral insulin resistance. According to the American Diabetes Association (ADA) American Diabetes, Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33(Suppl 1): S62–69., Diabetes Mellitus is diagnosed when a patient is found to have a fasting plasma glucose of ≥ 126 mg/dL (7.0 mmol/L), plasma glucose after 2-h oral glucose tolerance test (OGTT) ≥ 200 mg/dL (11.1 mmol/L), HbA1c ≥ 6.5% (48 mmol/mol), or a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

Statistical Methodology: Continuous variables were expressed as mean & medians and interquartile ranges (IQRs) or simple ranges, as appropriate. Categorical variables will be summarized as counts and percentages. Because the cohort of patients in our study was not derived from random selection, all statistics are deemed to be descriptive only All calculations will be performed by using SPSS version 23 statistical software. The data was analyzed by ANOVA statistical analysis. Chi-square was used to analyze the group difference. A p-value of < 0.05 was considered significant.

3. RESULTS

3.1 Baseline Characteristics

A total of 200 patients complying with the inclusion criteria were included in the study. 73% of the studied population were females (n=156) with a mean weight of 97.16 kg, compared to

27% (n=44) males with a mean weight of 113.82 kg (Table 1). The Arab nationals constituted 99% of the study (n=198), 93% being Emirati nationals (n- 186) and 1% (n=2) non-Arabs. A total of 39 (19.5%) patients were diagnosed with type 2 diabetes mellitus with a mean Hba1c of 5.83 before starting the liraglutide treatment. 43 patients (21.5 %) underwent previous bariatric surgery. 23 female patients (14.7 %) had PCOS, out of which 15 patients were married and unable to conceive.

In accordance with our inclusion criteria, all 200 patients underwent a minimum of 6 months follow up. Of those, 54 patients (27%) were followed up between 6 to 12 months and 146 patients (73%) followed up for more than 1 year.

Lifestyle modifications are necessary to manage overweight and obesity in adults.Such changes were recommended to all patients from the start of liraglutide treatment, and were reinstated with each follow up visit. Of the sample size, 109 patients (54.5 %) were compliant with dietary changes, and 95 patients (47.5%) were compliant with regular physical activity. 5 patients discontinued the drug due to major side effects, mainly severe nausea and vomiting. A minority of patients (n=28, 14%) continued to take the drug despite experiencing such symptoms. Few patients (n<10) did not adhere to treatment due to social reasons and failure to achieve desired weight.

3.2 Weight Changes

In terms of anthropometric measurements, weight, BMI and percentage loss of excess weight were assessed. The mean baseline weight was 100.98kg which had significantly dropped to 97.54 kg, 96.00 kg and 96.37 kg at 3 months, 6 months and 12 months respectively (Table 2 & Fig 1). This change was statistically significant P<0.001 at each point in time. The mean BMI baseline was calculated to be 38.44 kg/m2, which dropped to 37.33 kg/m2, 36.72 kg/m2, and 36.74 kg/m2 at 3 months,6 months and 12 months respectively (Table 3c). 15 patients reported lack of response to liraglutide in reducing their weight after initial response during the first 6 months. This is known as the weight loss plateau, which can be explained by the physiological response of the body. This response could either be due to the physiological adaptation to energy expenditure, or due to the lack of adherence to weight loss interventions, including lifestyle modification as well as medication adherence, after 6 months 9,10.

The male patients had on average a higher weight at baseline than females, as well as in each of the follow ups (3-month, 6 month and 12 months). Upon further analysis, we found that there were no statistically significant differences between genders in terms of BMI at baseline, 3 months, 6 months and 12 months (Table 3). However, the percentages of weight loss in males at 3 months, 6 months and 12 months were higher than the percentages of weight loss in females.

In patients with diabetes the percentage of weight loss was 3.7% at 3 months, in comparison to 4.2 % weight loss in non-diabetic group, at 6 months the percentage of weight loss increased to be 6.45 in diabetic group in comparison to 8.5% in non-diabetic group. And at 12 months' diabetic group lost 11.9% of their weight, while non-diabetic group lost 9.5%, the reason could be due to other modalities of treatment for diabetic group that contributed to their weight loss (Table 3).

46 patients in non-bariatric group lost 5% of their body weight at 3 months (response to treatment group), while 13 patients in the same group lost 10% of their weight at 3 months (super response group). When combined with diet and exercise in real-world setting, liraglutide 3.0 mg demonist red significant weight loss (Fig. 2).

Out of a total of 200 patients, 43 patients (21.5%) underwent bariatric surgery in the past and received liraglutide for management of post bariatric weight regain. (Fig. 2) Showed the average weight lost at 3 months, 6 months and 12 months in bariatric patients and non-bariatric patients, respectively. Upon analysis, we noticed that the mean weight loss at 3 months was higher by 0.6 kg in patients who had a previous bariatric surgery. However, at the 6 months and 12 months follow up, the mean weight loss was higher in patients who have not undergone previous bariatric surgery (Fig. 2). Therefore, we conclude that over a long period of time liraglutide had a better effect on patients who haven't undergone bariatric surgery before. Despite the difference in achieving weight loss between the two groups (bariatric Vs. non-bariatric), we found that post-bariatric surgery patients with insufficient weight loss or excessive weight regain who use liraglutide 3.0 mg were able to achieve astatically significant weight loss, regardless of the type of bariatric surgery procedure they had undergone.

Post-bariatric surgery patients taking liraglutide 3.0 mg continue to lose weight at 1 year (despite with less extent than non-bariatric group) and have a similar side effect profile as what is observed in patients without bariatric surgery, with the exception being potentially more severe adverse events reported in 2 cases. These results are promising as current methods for weight management in post-bariatric surgical patients are limited, and have greater risks to the patients.

Clinically meaningful weight loss is defined as 5-10% weight loss, because this is the range in which many adverse health outcomes related to obesity – like diabetes, hypertension, dyslipidaemia and others – improve.

62% of individuals in the SCALE obesity trial lost greater than 5% total body weight on liraglutide, while 6% of patients in the SCALE obesity trial for liraglutide lost greater than 20%.

3.3 Secondary Outcome

Metabolic parameters: Mean weight loss and proportion of patients losing at least 5% or 10% body weight were significantly lower with 1.8 mg dose of liraglutide dose than 3.0 mg, but comparison between the two doses were not controlled for multiplicity. BMI, systolic blood pressure, HbA1c, FPG, postprandial glucose increment; levels were significantly lower with liraglutide 3.0 mg than placebo ($p < 0.001$). Also the proportion of patients achieving the target HbA1c (below 7.0%) was significantly greater with liraglutide 3.0 mg, the baseline HBA1c in diabetic patients was 7.00 %, which dropped to 6.83 % at the 12-month follow-up Similar to previous SCALE Diabetes trial (Table 3a). The levels of LDL in diabetic patients were not significantly affected, as demonstrated.

Liver blood tests was performed, it is true that many cases of NAFLD are identified through abnormal serum alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT) levels. In clinical practice, abdominal ultrasound scan is the most commonly used method to diagnose fatty liver and magnetic resonance imaging for the quantification of hepatic steatosis, we could perform abdominal ultrasound for patients living with obesity during initial assessment. We noted the improvement in ALT and ALP for liver function was significant for those who lost 10% or more of their body weight.

There is a very strong relationship between weight and total and LDL cholesterol. A relatively weaker relationship in HDL - this is probably related to this being an acute weight loss study rather than looking at long-term. And an equally strong relationship for LDL and total cholesterol with triglycerides. So - validating weight loss as an intervention to reduce hyperlipidemi, and this is probably working through actually intervening on non-alcoholic fatty liver disease and excess VLDL production driven by excess carbohydrate and fat in the diet. In our study the reduction of LDL-c from baseline was 0.14 at 6 months, while ALT reduction was 1.19% at 6 months, and there was a 2.7% reduction in ALP from baseline (Table 3a to 3h).

Other parameters: Women with PCOS who have obesity who lose weight - even just 5% of body weight - can actually have substantial improvements in their clinical and biochemical features. it may be harder for a woman with PCOS to lose weight due to several contributing factors genetics factors, psychological factors - depression and anxiety may be inhibiting women with PCOS in her ability to lose weight, effects of sleep, insulin resistance itself be an impediment as well? and the differences in metabolic rate, which are contributing to possible difficulties in losing weight for women with PCOS.

Of the 23 female patients who had PCOS, we noted an improvement in their general well-being and signs of hyperandrogenism (hirsutism, acne) after starting Liraglutide treatment. The percentage of weight loss for patients with PCOS at 3 months was 4.5 % of their weight, increased to 8.35 % at 6 month and reach 24% at 12 months. As a result, 5 patients were able to conceive normally after they lost 10% body weight, while 2 patients succeeded to get pregnant with IVF. For the remaining 15 of them who were married and failed to conceive, their menstrual cycle and hirsutism improved.

Safety outcomes: Overall, liraglutide 3.0 mg is a well-tolerated long-term weight loss agent. The most common AEs (prevalence greater than 5%) are nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, dyspepsia, fatigue, dizziness, abdominal pain, and increased lipase. Gastrointestinal intolerability is common and in clinical trials was noted to be the most common reason for drug discontinuation in patients with adverse events. pancreatitis, acute gallbladder disease, serious hypoglycemia, heart

rate increase, hypersensitivity reactions and suicidal behavior. Also, it is marketed with a black box warning about the risk of medullary thyroid carcinoma as it has been shown to cause thyroid C-cell tumors in rats and mice; however, with the evidence to date including over 6000 patients, no increased risk for MTC has been observed in humans. Nevertheless, liraglutide is contraindicated in patients with a personal or family history of MTC or MEN. Liraglutide is also contraindicated in pregnancy and is not recommended in nursing mothers, patients taking insulin or other GLP-1 agonists.

Overall, we noted that Liraglutide was well tolerated in our study group**.** Mild nausea was dominant at the beginning of the treatment as well as gastrointestinal side effects with one patient reporting severe bloating. One patient with a known history of allergy developed a skin rash and stopped the treatment. Treatment with liraglutide in combination with metformin and lifestyle intervention resulted in a significant weight loss in overweight and obese women with PCOS, indicating that liraglutide may be an effective alternative for weight loss in this group of patients.

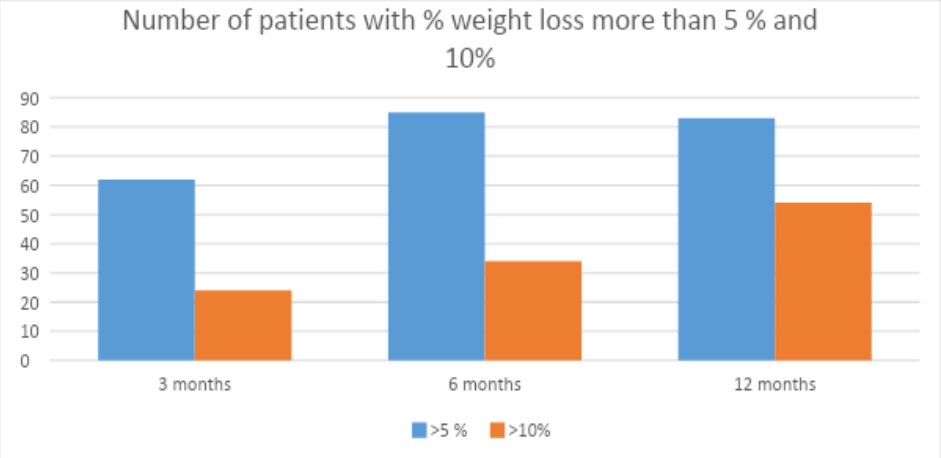

Fig. 1. Number of patients with % weight loss more than 5% and 10%

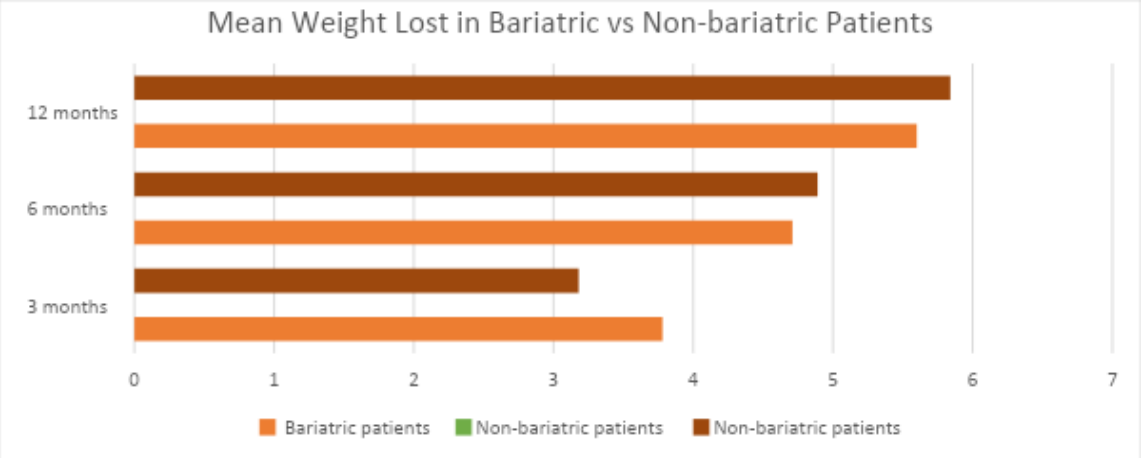

Fig. 2. Mean weight lost in Bariatric vs. Non – bariatric patients

Table 1. Baseline characteristics for all subjects in the study

Character	Gender		DM	
	Female	Male	DM	Non-DM
Number of Patients	156	44	39	161
Total Number	200		200	

Primary outcome results for the study: Change in body weight (Kg)

Table 2a. Changes in obesity measures after starting Liraglutide (changes in BMI):

		BM1 (0) BEFORE STARTING THE DRUG	BMI-1 (3 MONTH)	BMI (6 MONTH)	BMI (9 MONTH)	BMI (12 MONTH)
N	Valid	200	200	200	190	165
Mean		38.44	37.35	36.73	36.39	36.73
Median		37.00	36.00	35.00	35.00	36.00
Minimum		25	25	23	5	22
Maximum		58	58	59	59	59

Table 2b. Average Weight and Average BMI in diabetic and non-diabetic patients

Parameter	Average Weight (kg/m2)		Average BMI (kg/m2)	
Time Interval	**Diabetic**	**Non-Diabetic**	**Diabetic**	**Non-Diabetic**
0 months	100.7093168	101.4487179	38.16189441	39.59794872
3 months	97.2584472	98.72051282	38.16189441	38.99205128
6 months	95.57509317	97.76923077	38.30025641	38.30025641
12 months	95.84485075	98.246875	36.15781955	39.184375

Table 2c. Percentage of weight loss in diabetic and non-diabetic patients

	Percentage weight loss (%)		Number of diabetic patients with weight loss of		Number of non-diabetic patients with weight loss of	
Time Interval	**Diabetic**	**Non-Diabetic**	**>5%**	**>10%**	**>5%**	**>10%**
3 months	3.79	4.29	15	7	46	10
6 months	6.43	8.59	21	9	63	21
12 months	11.95	9.59	20	11	62	34

Table 2d. Significance between DM & Non -DM and BMI reduction at 6 months

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
DM	39	2.2564	.67738	.10847	2.0368	2.4760	1.00	3.00
NO DM	161	2.0745	.61799	.04870	1.9783	2.1707	1.00	3.00
Total	200	2.1100	.63238	.04472	2.0218	2.1982	1.00	3.00

Table 2e. Significance between DM and BMI reduction at 6 months

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.039	1	1.039	2.618	.107
Within Groups	78.541	198	.397		
Total	79.580	199			

Table 2f. Assumptions for Statistical Tests

Independent Samples Test		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Body weight variability	Equal variances assumed	1.393	.239	1.316	198	.190	.18602	.14135	-.09272	.46476
	Equal variances not assumed			1.284	56.206	.205	.18602	.14490	-.10424	.47627

Table 2g. Results of Statistical analysis

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
BM1 (0) BEFORE	DM	39	39.62	7.188	1.151	37.29	41.95	28	57
START THE	NO DM	161	38.15	6.090	.480	37.20	39.10	25	58
DRUG	Total	200	38.44	6.327	.447	37.55	39.32	25	58
BMI-1 (3 MONTH)	DM	39	38.95	7.688	1.231	36.46	41.44	25	58
	NO DM	161	36.96	6.026	.475	36.02	37.89	25	58
	Total	200	37.35	6.412	.453	36.45	38.24	25	58
BMI (6 MONTH)	DM	39	38.26	7.903	1.266	35.69	40.82	25	58
	NO DM	161	36.36	6.163	.486	35.40	37.32	23	59
	Total	200	36.73	6.560	.464	35.82	37.64	23	59
BMI (9 MONTH)	DM	37	38.41	8.315	1.367	35.63	41.18	25	59
	NO DM	153	35.91	6.791	.549	34.82	36.99	5	58
	Total	190	36.39	7.159	.519	35.37	37.42	5	59
BMI (12 MONTH)	DM	32	39.16	8.520	1.506	36.08	42.23	25	59
	NO DM	133	36.15	6.536	.567	35.03	37.27	22	58
	Total	165	36.73	7.037	.548	35.65	37.82	22	59

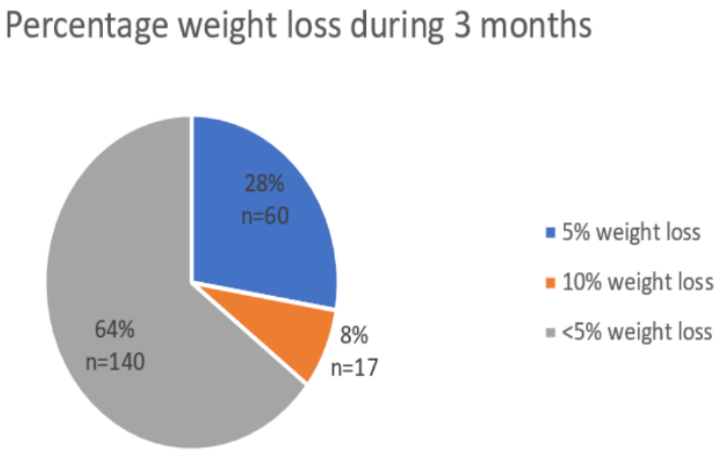

Fig. 3. Percentage weight loss during 3 months

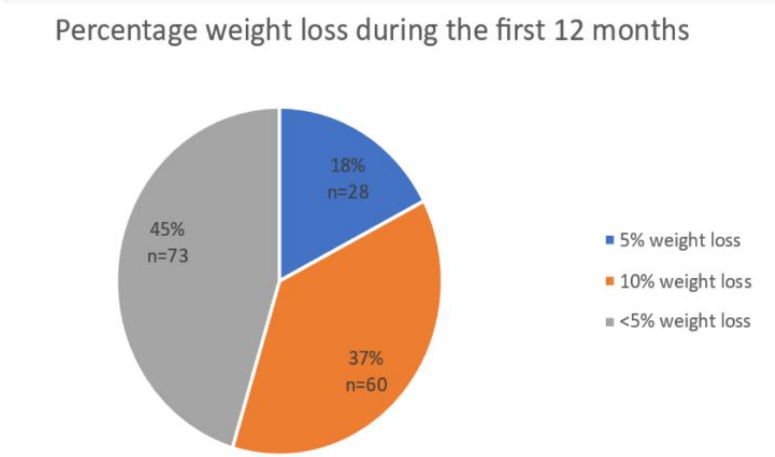

Fig. 4. Percentage weight loss during 12 months

Improvement in metabolic parameters for patients with type 2 diabetes mellitus:

Table 3a. changes in metabolic parameters for patients with Type-2 Diabetes Mellitus during the course of treatment

Parameter	Baseline	Follow-up	Difference
HBA1C	5.828	5.65	0.141
LDL	3.18	3.22	0.214
ALT	33.81	34.25	1.195
ALP	71.67	69.37	2.74

Table 3b. Changes in HBA1C during the course of treatment for patients with Type2 DM

		HBA1C (0) before starting liraglutide	HBA1C at 3 months	HBA1C at 6 months	HBA1C at (9) month	HBA1C at 12 months
N	Valid	200	200	200	192	166
Mean		5.85	5.73	5.71	5.74	5.81
Median		6.00	6.00	6.00	6.00	6.00
Variance		1.073	.831	.862	1.081	1.066
Minimum		4	3	4	4	4
Maximum		12	10	10	12	12

Table 3c. Significance of HBA1c reduction for DM after 6 months

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Recoded_HBA1C	Equal variances assumed	273.304	.000	4.770	198	.000	.40054	.08398	.23494	.56615
	Equal variances not assumed			6.345	93.586	.000	.40054	.06312	.27520	.52588

Table 3d. Changes in LDL-patients' patient with Type2 DM during the treatment course:

		LDL –C BEFORE STARTING LIRAGLUTIDE	LDL –C AT 6 MONTHS	LDL -C AT 12 MONTHS
N	Valid	200	199	198
Mean		2.96	3.15	3.19
Median		3.00	3.00	3.00
Minimum		1	1	1
Maximum		6	50	48

Table 3e. Significance of LDL- C change for patients with DM after 12 months

	DM	N	Mean	Std. Deviation	Std. Error Mean
LDL-C AT 12 MONTHS FROM STARTING LIRAGLUTIDE	**DM**	39	3.92	7.296	1.168
	NO DM	159	3.01	1.936	.154

Table 3f. LDL--C at 12 months from starting Liraglutide 3.0 mg for weight management

Independent Samples Test										
		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
LDL (2) AT 12 MONTH FROM STARTING LIRAGLUTIDE	Equal variances assumed	6.421	.012	1.395	196	.165	.910	.653	-.377	2.198
	Equal variances not assumed			.773	39.321	.444	.910	1.178	-1.472	3.293

Table 3g. Significance of ALT reduction for DM patients after 6 months

ALT at 6 months					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	1598.288	1	1598.288	1.146	.286
Within Groups	276236.307	198	1395.133		
Total	277834.595	199			

Table 3h. Significance of ALP changes for the DM group after 6 months

Independent Samples Test										
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
ALP at 6 months	Equal variances assumed	2.910	.090	1.330	197	.185	5.634	4.235	-2.717	13.986
	Equal variances not assumed			1.138	49.603	.260	5.634	4.949	-4.308	15.577

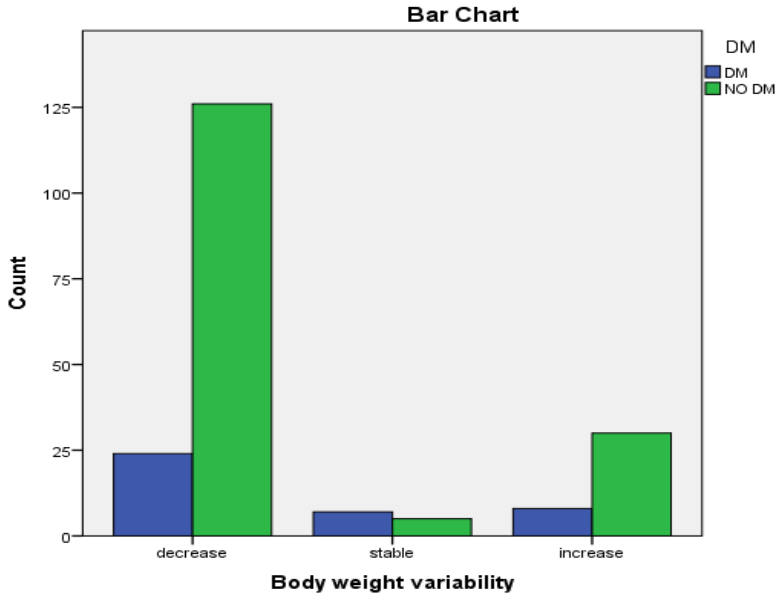

Chart 1. Weight changes during treatment period

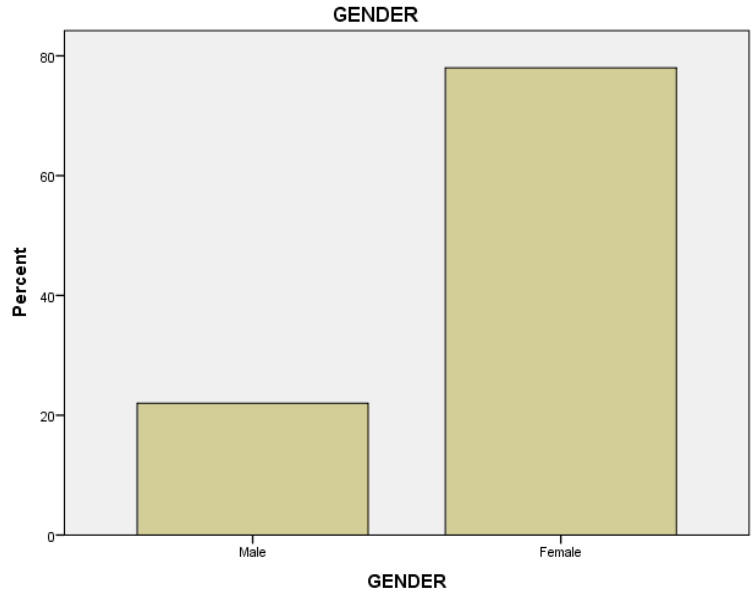

Chart 2. Gender

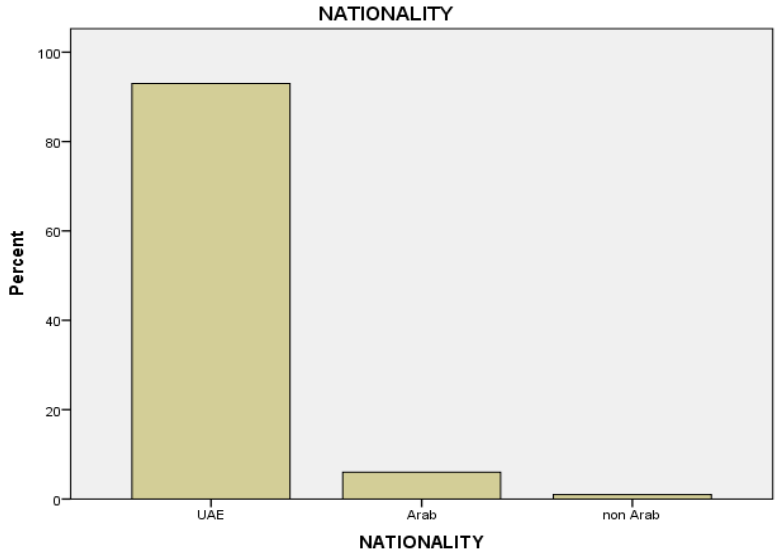

Chart 3. Nationality

Functional disabilities in our study, like breathing difficulties (using standardized questionnaires, middle-aged subjects with obesity, we found that over 80% reported shortness of breath after climbing two flights of stairs compared to those symptoms only being present in 16% of similarly aged non-obese controls)which improved when they lost weight, also snoring in a patient with obstructive sleep apnea, along with knee, joint, and back pain, showed similar results and improvement for those who achieved 10% weight loss.

We evaluated patients' compliance to the drug, dietary advice and physical activity during each visit of follow-up, it showed good compliance to lifestyle changes result in better result of weight loss.

4. DISCUSSION

The current study indicates that Liraglutide use is an effective approach to weight loss in persons who are living with obesity, diabetic, or have PCOS. Our treatment strategy resulted in a

statistically significant decline in weight, BMI, and percentage of extra weight over a 12-month period. In our study, anthropometric measurements were taken to determine the weight, BMI, and excess weight loss (%). The average weight at the start of the trial was 100.98 kg. This was reduced to 97.54 kg after three months, 96.00 kg after six months, and 96.37 kg at the end of the 12-month trial. At each time point, weight loss was statistically significant, with a p-value of less than 0.001. This study's findings are corroborated by another study in which statistically significant decreases in BMI and weight parameters were achieved with the use of liraglutide compared to the use of a placebo. These changes were detected through the end of 52 weeks, but not at 26 weeks. Similarly, our findings agree in part with those of prior studies in the Chinese population [8], in which people with a higher initial BMI experienced substantial weight loss after 24 weeks of treatment with Liraglutide, and in a Northern East Italian cohort [9], where weight loss was linked to baseline body weight.

Additionally, this study's results are consistent with previous research (McGill, J.; Vlajnic, A.; Knutsen, P.; Recklein, C.; Rimler, M.; Fisher, S. Effect of gender on treatment outcomes in type 2 diabetes mellitus. Diabetes Res. Clin. Pr. 2013, 102, 167–174. [CrossRef], which demonstrated the influence of gender on the efficacy of Liraglutide in managing weight [10]. In our study, both male and female patients lost weight, though the percentage of male patients who lost weight was slightly higher. This contradicts previous research in which the female gender predominated; this may be owing to women's greater exposure to Liraglutide.

In our study, we also noticed statistically significant changes in the weight loss of diabetic patients. This finding was replicated by a trial in which a total of 69 individuals reported a reduction in body weight one year after beginning liraglutide medication, while 58 patients (67.4%) demonstrated an improvement in blood sugar control [11]. The patient's body mass index (BMI) decreased from 27.3 ± 5.4 kg/m2 to 25.9 ± 4.8 kg/m2 and the reduction in body weight was statistically significant and sustained over 4% at the 2-year mark after starting liraglutide. However, in our study, this decrease in weight was less than that experienced by non-diabetics.

In addition, we discovered that the HBA1c levels of diabetic patients reduced from 7.00 % at baseline to 6.83 % after 12 months of follow-ups. This result is consistent with three previous SCALE research trials. According to them, six months of treatment with liraglutide resulted in a significant drop in HbA1c values, ranging from 0.5% to 1.15 [12-14]. Similarly, in our research, there was a significant improvement in ALT and ALP for liver function. The reduction in LDL-c from baseline was 0.14 at 6 months, while the reduction in ALT was 1.19% at 6 months and 2.7% in ALP from baseline. This finding aligns with previous research, showing significant improvements in total cholesterol and triglycerides when compared to active comparators [15].

Furthermore, our data suggest that Liraglutide treatment can lead to improvement in general well-being for female patients with PCOS. Additionally, liraglutide 3.0 mg injection appears to be an effective weight loss therapy for PCOS patients, as a weight loss of 4.5% at 3 months, 8.35% at 6 months, and 24% at 12 months was noted in our study. The treatment also had a positive effect on the fertility of patients with PCOS, as results demonstrated 5 patients conceived normally and 2 patients conceived through IVF after losing 10% of their body weight [16].

4.1 Strength & Limitations

The strengths of this study include a relatively large sample size of 200 patients and the fact that the study population was diverse, including a mix of genders and patients with different comorbidities such as type 2 diabetes and PCOS. The study also had a relatively long follow-up period of at least 6 months, allowing for the assessment of weight reduction over an extended time. In addition to liraglutide, the research included dietary and exercise interventions, offering a more comprehensive perspective of the drug's effectiveness in conjunction with lifestyle improvements.

The major limitation of this study was that the group included was not representative of the general population, as all patients were Arab nationals and the majority were Emirati. In addition, the trial lacked a control group, which would have permitted a comparison of the efficacy of liraglutide with other treatments or a placebo. Since only one patient stopped taking the drug because of severe nausea and vomiting, more data should have been collected on these adverse effects. Moreover, the data on

pregnancy rates is limited. The study was prospectively designed across the year 2021-2022. However, it is one of the few trials done in the UAE with a total of 200 patients to evaluate the effect of liraglutide on weight, BMI, and its adverse effects. In addition, we evaluated other metabolic parameters, including effects on HbA1c and LDL for patients with type 2 diabetes mellitus.

4.2 Clinical Implications

The therapeutic implications of this study imply that the liraglutide 3 mg daily injection may be an effective weight management strategy for patients with or without type 2 diabetes mellitus in diabetics, the study revealed a significant decrease in BMI and improvements in metabolic indicators such as lipid profiling and HbA1c. In addition, weight loss improved the fertility of women with PCOS, as well as their psychological health and quality of life. These results imply that liraglutide may be a viable therapy choice for patients with type 2 diabetes in terms of weight management and metabolic control. Moreover, it appears to be beneficial for PCOS patients.

5. CONCLUSION

The study on the drug Liraglutide showed that it induced significant weight loss, as well as improvement in HbA1c levels when combined with lifestyle modification. The results of this study were as predicted and support the findings of previous SCALE trials, with non-substantial variations attributed to differing ethnicities within trial groups. As a result, we recommend the usage of liraglutide 3.0 mg injection as an integral part of weight loss management for patients living with obesity.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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