OriginalResearchArticle

EffectsofLiraglutideonWeightReduction&MetabolicParametersinPatientslivingwithObesityWithandWithoutType2 DiabetesMellitusatFujairah Hospital

Abstrac

Background:

Obesityhasbecomeaglobalepidemicandisakeycontributortonumerousadverseconditions,includingType2DiabetesMellitus,cardiovascular disease, and strokes. Liraglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, has been found to be useful in promotingweightlossindiabeticsandpoly-cystic ovary syndromepatients.

Methods:

This study aimed to evaluate the response of patients with and without type 2 diabetes Mellitus who received a Liraglutide 3mg injection interms of weight reduction and improvement of metabolic parameters in the United Arab Emirates population. This study was conducted inFujairah Hospital, UAE, with 200 participants aged 18 years and above, including patients with and without type 2 diabetes Mellitus. The primaryobjective was to assess the reduction of Body Mass Index and changes in metabolic parameters. Secondary objectives included evaluating theeffectofweightreductiononfertilityforfemaleswithPCOSandthepotentialimprovementofpsychologicalwell-beingandqualityoflife.

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 12months, respectively. Males experienced a greater rate of weight reduction than females, while diabetic patients had a lower percentage ofweight loss than non-diabetic patients. Additionally, patients with PCOS were able to conceive regularly after reducing 10% of their body weightafter using Liraglutide, while the remaining 15 patients who were married but unable to conceive saw an improvement in their menstrual cycleandhirsutism.

Conclusion:

Comment [1]: This is not a decrease but an increase from the preceeding weight. Is this increase significant? Considering your defination of clinically significant weight loss in your introduction.

Comment [2]: What do you mean by conceive regularly

Comment [3]: Before making such sweeping statements , were all other cofounders eliminated or considered?

The results demonstrated that Liraglutide is an effective treatment for weight reduction and metabolic parameter improvement in the UAEpopulation. In addition, the study identified a correlation between weight reduction and improvements in psychological health, quality of life,andfertilityinfemaleswithPCOS.

Keywords:type2diabetes,bodymassindex(BMI),Polycysticovariansyndrome(PCOS).

INTRODUCTION

Obesity has become a global epidemic that affects diverse societies across both developed and developing countries. It is a key contributor tonumerous adverse conditions that include, but are not limited to, Type 2 Diabetes Mellitus, cardiovascular disease, and strokes (1). The first lineoftherapyforobesityislifestylemodificationinordertoachievesignificantweightloss.Clinically-relevantweightlossisdefinedasalossofmorethan 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 ofphysical exercise per week (2). The obesity treatment guidelines advocate for the use of pharmacological therapy in adults with refractoryobesity, where patients have a BMI ≥ 30 kg/m2, despite attempting lifestyle modification (3). Pharmacological therapy is also advocated forpatients with a BMI ≥ 27 kg/m2 and at least one comorbid condition, such as hypertension, dyslipidemia, insulin resistance, or type 2 diabetesmellitus (4). It is essential to counsel the patients about the importance of lifestyle changes alongside medical therapy in order to improveoutcomes.

Liraglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist that has been successfully used in the treatment of type 2 diabetes mellitus foryears. Weight loss has been described as an additional benefit to liraglutide therapy (5).In addition, Liraglutide has been found to be useful inblood pressure reduction as well as the modulation of metabolic parameters (6). To date, few meta-analyses have been conducted regardingLiraglutide'ssafetyandefficacyinindividualswithoutdiabetes.

Comment [4]: Clarify: Is liraglutide a weight reducing drug or what?

The UAE is among the top 40 countries worldwide for prevalence of obesity (7). At Fujairah hospital, we conducted a follow up study on peopleliving with obesity. Liraglutide 3 mg is one of the few medications licensed by the FDA for use in weight management and the health authority intheUAEmadeLiraglutide3mgavailableforuseinmanagingobesity.

Since many pharmacological agents show different effects in different regions, we conducted this study on patients in Fujairah, UAE, looking intotheeffectofLiraglutideonweightreductionandimprovingmetabolicparameters.

PATIENTSANDMETHODS

Aimofstudy

To evaluate the responses of patients, with and without type 2 diabetes Mellitus, who received liraglutide 3 mg injection, in terms of weightreductionandimprovementofmetabolicparameters.

Primaryobjective

To assess the reduction of BMI and changes in metabolic parameters. This includes lipid profiles, HbA1C in diabetics, and liver function tests. Theparameterswererecordedfromthedayliraglutidedruganddietwerestartedandcontinuedfor12monthsoftherapy.

Secondaryobjectives

To evaluate the effects of weight reduction on fertility for females with PCOS. In addition, to evaluate the benefits of weight reduction in theimprovementofpsychologicalwell-beingandofqualityoflife.

Study design

All aspects of the study, including consent forms, were Institutional Review Boards (IRB) approved prior to implementation. Fully informedconsentwasacquiredfromallparticipantsanditwasensuredthattheywerecompliantwithallstudyrequirements.

Aftergettinginformedconsent,patientdemographicsand comorbidities (diabetes mellitus) were recorded. BMI and HbA1C values weredocumented at intervals of 0, 3, 6, 9, and 12 months, whereas other laboratory investigations including a lipid profile, Hb, and vitamin D wererecordedatintervalsof0,6,and12months.WealsomeasuredAST,ALT,andALPvaluesat0,3,and6months.

An excel sheet was used to collect data for the measurable parameters and a questionnaire was filled out for non-measurable parameters likeimprovementinfunctionalcapacity,cognitivefunction,andinfertilityforfemaleswithPCOS.

Comment [5]: What tool was used to assess these functions? Be more specific and explicit

Studypopulation

The study was conducted in Fujairah Hospital, United Arab Emirates. We included 200 patients, all of whom were above the age of 18 years old.This included patients with and without type 2 diabetes mellitus who were started on Liraglutide 3 mg injections for weight management,includingthosewhoreceivedothermodalitiesforweightmanagement(bariatricsurgeryprocedures)butdevelopedweightregain.The

participants were willing to participate in the study, including regular follow-up visits to the obesity clinic for 12 months. Patients who stoppedtakingthedrugbefore6months,tookthedrugforlessthan6months,ordidnotattendregularfollow-upswereexcludedfromthestudy.

Comment [6]: The inclusion and exclusion criteria needs to be more specific? Eg How did you select those with PCOS and infertility? Did you exclude those on other fertility drugs?

Recruitmentmethods

Subjects were identified through existing patient records for follow-up treatment in the obesity clinic at Fujairah hospital. All patients who metthe 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 inthestudywasevaluated,aswellasotherfactorsthatmighthavecontributedtothisdifferenceinresponse,likepsychologicaldistress,adherencetophysicalactivities,anddietary advice. Those who agreed to participate in the study were asked to fill out a questionnaire about thecompliance and side effects of the drug during the first 6-12 months of treatment. We accessed their medical records to get the informationillustratedintheExceldatasheet.

Comment [7]: Tis is confusing? Was this a retrospective or a prospective study? You caan not do a case control retrospective study, how and when did you use your selection criteria? How did you take the samples, if it was retrospective.

Comment [8]: These are modifiers, how did you eliminate or accommodate them?

Statistical

AnalysisDefinition

The percentage of weight loss at 3 months was calculated by dividing the difference between the weight after 3 months and the baseline weight,divided by the baseline weight and multiplied by 100. The percentage of weight loss at 6 and 12 months were similarly calculated. However, thedifference between the weight after 6 months and the baseline weight, and the difference between the weight after 12 months and the baselineweight,wereusedrespectivelyinstead.

Comment [9]: This does not agree with the results statement in your abstract

Thestudyincludedpatientsthathavebeendocumentedonhospitalrecordsashaving Type2diabetesmellitus.Theconditionischaracterizedbychronic hyperglycemia due to acquired peripheral insulin resistance. According to the American Diabetes Association (ADA), Diabetes Mellitus isdiagnosed 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 tolerancetest (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). The data wasanalyzedbyANOVAstatisticalanalysis.

Comment [10]: Reference

Results

BaselineCharacteristics

A total of 200 patients complying with the inclusion criteria were included in the study. 73% of the population were females (n=156) with a meanweight of 97.16 kg, compared to 27% (n=44) males with a mean weight of 113.82 kg (Table 1 and Table 2). Arab nationals constituted 99% of thestudy (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 diabetesmellitus with a mean Hba1c of 5.83 before starting the liraglutide treatment. 43 patients (21.5 %) had previously undergone bariatric surgery. 23femalepatients(14.7%)hadPCOS,15ofwhichweremarriedandunabletoconceive

In accordance with our inclusion criteria, all 200 patients underwent a minimum of 6 months of follow-ups. Of those, 54 patients (27%) werefollowedupwithforbetween6to12monthsand146patients(73%)werefollowedupformorethan1year.

Lifestyle modifications are necessary to manage excess weight and obesity in adults. Such changes were recommended to all patients from thestart of liraglutide treatment and were restated with each follow-up visit. Of the sample size, 109 patients (54.5 %) were compliant with dietarychanges,and95patients(47.5%)werecompliantwithregularphysicalactivity.5patientsdiscontinuedthedrugduetomajorsideeffects,mainlysev ere nausea and vomiting. A minority of patients (n=28, 14%) continued to take the drug despite experiencing such symptoms. Few patients(n<10)didnotadheretotreatmentduetosocialreasonsandfailuretoachievethedesiredweight.

WeightChanges

In terms of anthropometric measurements, weight, BMI, and percentage loss of excess weight were assessed. The mean baseline weight was100.98kg, which had significantly dropped to 97.54 kg, 96.00 kg, and 96.37 kg at 3, 6, and 12 months respectively (Table 3). This change wasstatisticallysignificant(P<0.001)ateachpointintime.ThemeanBMIbaselinewascalculatedtobe38.44kg/m2,whichdroppedto37.33kg/m2, 36.72 kg/m2, and 36.74 kg/m2 at 3, 6, and 12 months respectively (Table 3-3). 15 patients reported a lack of response to liraglutide in reducingtheir weight after the initial response during the first 6 months. This is known as the weight loss plateau, which can be explained by the body'sphysiological response. This response could either be due to a physiological adaptation to energy expenditure or the lack of adherence to weightlossinterventions,includinglifestylemodificationaswellasmedicationadherence,after6months9,10.

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

Inapatientwithdiabetes,thepercentageofweightlosswas3.7%at3months,incomparisonto4.2%weightlossinthenon-diabeticgroup.At6monthsthepercentageofweightlossincreasedto6.4%inthediabeticgroupincomparisonto8.5%inthenon-diabeticgroup.At12monthsthe

Comment [11]: Pls clarify, why some were followed up for 6/12 and others 1 year

Comment [12]: How did you accommodate all these setbacks?

Comment [13]: If the weight loss was only in first 6/12 why did you include the 12month? Is 9,10 a reference? Bracket and ref 8 are missing

diabeticgrouphadlost11.9% of their weight, while the non-diabetic group had lost 9.5%. This could be due to other modalities of treatmentthatcontributedtoweightlossinthediabeticgroup.

46 patients in the non-bariatric group had lost 5% of their body weight at 3 months (response to treatment group), while 13 patients in the samegrouphadlost10%oftheirweightat3months(superresponsegroup).Whencombinedwithdietandexerciseinareal-worldsetting,liraglutide 3.0mgdemonstratedsignificantweightloss.

Out of a total of 200 patients, 43 patients (21.5%) underwent bariatric surgery and received liraglutide for the management of post-bariatricweight regain. Tables show the average weight loss at 3, 6, and 12 months in bariatric patients and non-bariatric patients, respectively. Uponanalysis,wenoticedthatthemeanweightlossat3monthswashigherinpatientswhohadpreviousbariatricsurgeryby0.6kg.However,atthe6and 12 month follow-ups, the mean weight loss was higher in patients who had not undergone previous bariatric surgery (Figure 2). Therefore,we conclude that over a long period of time, liraglutide had a better effect on patients who had not undergone bariatric surgery before. Despitethe difference in weight loss between the two groups (bariatric vs. non-bariatric), we found that post-bariatric surgery patients with insufficientweight loss or excessive weight regain who use liraglutide 3.0 mg were able to achieve statistically significant weight loss, regardless of the typeofbariatricsurgerytheyhadundergone.

Post-bariatric surgery patients taking liraglutide 3.0 mg continued to lose weight at 1 year, although to less of an extent than those in thenon-bariatric group, and have a similar side effect profile to what is observed in patients without bariatric surgery, with the exception beingpotentially more severe adverse events reported. These results are promising as current methods for weight management in post-bariatricsurgicalpatientsarelimitedandcarrygreaterriskstothepatients.

MetabolicParameters

ThebaselineHBA1cindiabeticpatientswas7.00,whichdroppedto6.83atthe12monthfollow-up,whichisrepresentedinTable4.ThelevelsofLDL in diabetic patients were not significantly affected, as demonstrated. Also, the improvement in ALT and ALP for liver function was significant.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 ALPfrombaseline.

OtherParameters

Of the 23 female patients who had PCOS, we noted an improvement in their general well-being and cognitive function after starting Liraglutidetreatment. The percentage of weight loss for patients with PCOS was 4.5 % of their weight at 3 months, which increased to 8.35 % at 6 months,andreach24%at12months.Asaresult,5patientswereabletoconceivenormallyafterlosing10%oftheirbodyweight,while2patients

Comment [14]: How were they selected and stratified? How many were in each arm? How were they paired?

Comment [15]: How many strata did you do? This is not clear? You need to clarify this in your methodology, how did you arrive at the number? What was the sampling technique used?

Comment [16]: Reference, are you presenting results or discussing?

Comment [17]: How? explain

succeeded in getting pregnant with IVF. 15 of the remaining group were married and failed to conceive, but their menstrual cycle and hirsutismimproved.

Overall, we noted that Liraglutide was well tolerated in our study group. Mild nausea was dominant at the beginning of the treatment as well asgastrointestinal side effects with one patient reporting severe bloating. One patient with a known history of allergy developed a skin rash andstoppedthetreatment.Treatmentwithliraglutideincombinationwithmetforminandlifestyleinterventionresultedinasignificantweightlossinover weightandobesewomenwithPCOS,indicatingthatliraglutidemaybeaneffectivealternativeforweightlossinthisgroupofpatients

Functional disabilities like breathing difficulties and snoring in a patient with obstructive sleep apnea, along with knee, joint, and back pain,improvedforthosewhoachieved10%weightloss.

Discussion

The current study indicates that Liraglutide use is an effective approach to weight loss in persons who are obese, diabetic, or have PCOS. Ourtreatment strategy resulted in a statistically significant decline in weight, BMI, and percentage of extra weight over a 12-month period.In ourstudy, anthropometric measurements were taken to determine weight, BMI, and excess weight loss (%). The average weight at the start of thetrial 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. Ateach time point, weight loss was statistically significant, with a p-value of less than 0.001. This study's findings are corroborated by another studyin which statistically significant decreases in BMI and weight parameters were achieved with the use of liraglutide compared to the use of aplacebo. These changes were detected through the end of 52 weeks, but not at 26 weeks. Similarly, our findings agree in part with those of priorstudies in the Chinese population (8), in which people with a higher initial BMI experienced substantial weight loss after 24 weeks of treatmentwithLiraglutide,andinaNorthernEastItaliancohort(9),whereweightlosswaslinkedtobaselinebodyweight.

Additionally,thisstudy'sresultsareconsistentwithpreviousresearch,whichdemonstratedtheinfluenceofgenderontheefficacyofLiraglutidein managing weight (10).In our study, both male and female patients lost weight, though the percentage of male patients who lost weight wasslightly higher.This contradicts previous research in which the female gender predominated; this may be owing to women's greater exposure toLiraglutide.

Inourstudy,wealsonoticedstatisticallysignificantchangesintheweightlossofdiabeticpatients.Thisfindingwasreplicatedbyatrialinwhichatotalof69individualsreportedareductioninbodyweightoneyearafterbeginningliraglutidemedication,while58patients(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 ± 4.8kg/m2 and the reduction in body weight was statistically significant and sustained over 4% at the 2-year mark after starting liraglutide. However,inourstudy,thisdecreaseinweightwaslessthanexperiencedbythenon-diabetics.

Comment [18]: What do you mean by well tolerated, you earlier said some people stopped due to side effects

Comment [19]: Were they diabetic ?

Comment [20]: reference

Comment [21]: reference

Comment [22]: Why 2 years? I thought the study was for 1 year

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. Thisresultisconsistentwiththreepreviousresearchstudies.Accordingtothem,sixmonthsoftreatmentwithliraglutideresultedinasignificantdropin 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 liverfunction. 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 frombaseline. This finding aligns with previous research, showing significant improvements in total cholesterol and triglycerides when compared toactivecomparators(15).

Furthermore, our data suggest that Liraglutide treatment can lead to improvement in general well-being and cognitive function for femalepatients with PCOS. Additionally, it 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 were noted in our study. The treatment also had a positive effect on the fertility of patients, as resultsdemonstrated 5 patients conceived normally and 2 patients conceived through IVF after losing 10% of their body weight.This is similar toanother study in which a 6-month controlled trial evaluated the effectiveness of daily liraglutide 1.8 mg on weight loss in 19 women with obesityand Polycystic Ovary Syndrome (PCOS) and 17 control subjects of similar age and weight. Both groups experienced a weight loss of 3-4% as aresultofliraglutidetreatment(16).However,thisresearchdidnotassessthecognitivefunctionofthesewomen.Ourstudyisthefirsttoevaluateweight loss along with cognitive function in patients with PCOS. Our study also reported some side effects, such as nausea and vomiting, that ledtosomepatientsdiscontinuingthetreatment.

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 amix of genders and patients with different comorbidities such as type 2 diabetes and PCOS. The study also had a relatively long follow-up periodof at least 6 months, allowing for the assessment of weight reduction over an extended time. In addition to liraglutide, the research includeddietaryandexerciseinterventions,offeringamorecomprehensiveperspectiveofthedrug'seffectivenessinconjunctionwithlifestyleimproveme nts.

The major limitation of this study was that the group included was not representative of the general population, as all patients were Arabnationals and the majority were Emirati. In addition, the trial lacked a control group, which would have permitted a comparison of the efficacy ofliraglutidewithothertreatmentsoraplacebo.Sinceonlyonepatientstoppedtakingthedrugbecauseofseverenauseaandvomiting,moredatashould have been collected on these adverse effects.Moreover, the data on pregnancy rates is limited. The study was also retrospectivelydesigned across the year 2021-2022, which may introduce bias in the data collection. However, it is one of the few trials done in the UAE with atotal of 200 patients to evaluate the effect of liraglutide on weight, BMI, and its adverse effects. In addition, we evaluated other metabolicparameters,includingeffectsonHbA1candLDL.

ClinicalImplications

Comment [23]: Reference

Comment [24]: How

Comment [25]: How did you assess that

Comment [26]: Conflicting statement. You said the one with rashes stopped

Comment [27]: Is this a limitation?

Comment [28]: Is this alimitation?

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

Comment [29]: These statements are presumptious

Conclusion

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

Disclosure: Theauthorsreportnoconflictofinterestinthisstudy

RESULTS:

Table1:Baselinecharacteristicsforallsubjectsinthestudy:

Baselinecharacter	TotalNumberofpatients=-200
Male	44
Female	156

UAENational	186

Age26-60years	97
Diabetic	39
Non-Diabetic	161

Table2: Durationoftreatment(month):

Durationoftreatment(Months)	TotalNumberofPatients
3-6	200
7-9	193
10-12	167
Morethan12	146

Comment [30]: This table is confusing,

Table2-2:Baselinecharacteristicsforallsubjects:Gender:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	Male	44	5.9	22.0	22.0
	Female	156	20.9	78.0	100.0
	Total	200	26.8	100.0	

Table2-3:Baselinecharacteristicsforallsubjects:Nationality:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	UAE	186	24.9	93.0	93.0
	Arab	12	1.6	6.0	99.0
	Non-Arab	2	.3	1.0	100.0
	Total	200	26.8	100.0	

Table2-4:PatientwithType2Diabetes:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	DMN	39	5.2	19.5	19.5
	ODM	161	21.6	80.5	100.0
	Total	200	26.8	100.0	

Comment [31]: You need to make new tables, not just copy and paste from SPSS, Most of the tables are fragmented and repeated

Table2-5:PatientswithPCOS

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	HAS PCOS	23	3.1	11.5	11.5
	NO PCOS	177	23.7	88.5	100.0
	Total	200	26.8	100.0	

Tabe2-6:thepatienthadbariatricsurgeryinthepastandwastreatedwithLiraglutide3.0mgforweightregain:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	HADSURGERY	43	5.8	21.5	21.5
	NOSURGERY	157	21.0	78.5	100.0
	Total	200	26.8	100.0	

Primaryoutcomeresultsforthestudy:Changein

bodyweight(kg):

Table3-1:Meanofweightlossduringthecourseoftreatment:

TimeInterval	MeanofweightlossduringthecourseoftreatmentwithLiraglutide3.0mgforweightmanagement
Mean of weight at 0 months	100.98
Mean of weight at 3 months	97.54
Mean of weight at 6 months	96.00
Mean of weight at 12 months	96.37

Table3-2:PercentageofweightlossinobesityafterstartingLiraglutide3mgbygender:

n=200	Percentageloss (%)	3months	6months	12months
Weight(Kg)	Female	2.932	4.541	5.237
	Male	3.996	5.177	6.663

BMI(Kg/m2)	Female	2.361	4.165	5.278
	Male	4.192	5.233	6.376

Table3-3:ChangesinobesitymeasuresafterstartingLiraglutide(changesinbodyweight):

	AGE /YEAR	WEIGHT 0 (BASELINE)	WEIGHT1(AT3MONTH)	WEIGHT2(AT6 MONTH)	WEIGHT3(AT12MONTH)
N Valid	200	200	200	200	166
Mean	38.04	100.87	97.57	96.03	96.30
Median	38.00	98.50	94.00	93.00	94.50
Minimum	18	65	64	64	61
Maximum	77	164	158	156	156

Table3-4:ChangesinobesitymeasuresafterstartingLiraglutide(changesinBMI):

	BM1 (0) BEFORESTARTING THEDRUG	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

Table3-5:percentageandnumberof patients'weight loss:

Timeinterval	Number of non-bariatric patients with weight loss of	
	>5%	>10%
3 months	46	13
6 months	65	23
12 months	65	38

Table3-6:Meanweightlostinpost-bariatricweightregainpatients:

Timeinterval	Meanofweightloss(kgs)
Meanofweightlostat3months	3.78

Comment [32]: Tis does not agree with your write up, how come the wt loss at 12months was more than 6/12 here?

Meanofweightlostat6months	4.71
Meanofweightlostat12months	5.60

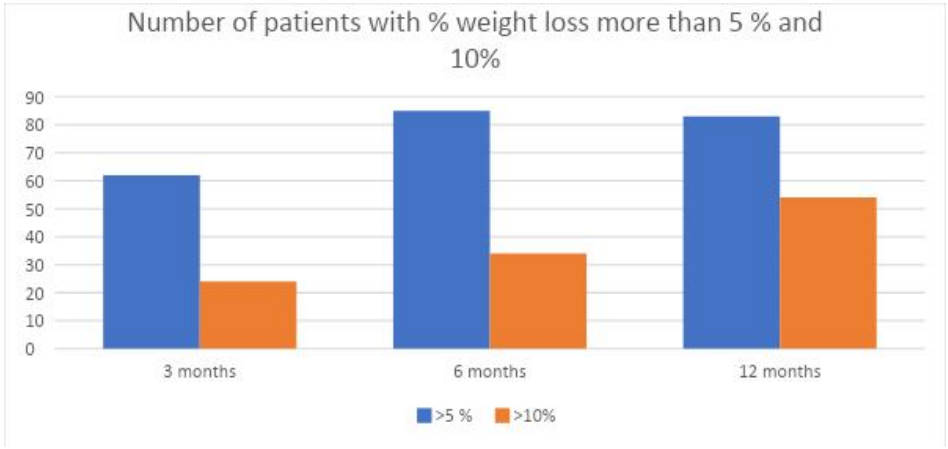


Figure:1BargraphshowingWeightlosescinario

Figure:2MeanweightlossinBariatricvsNon-Bariatricpatients

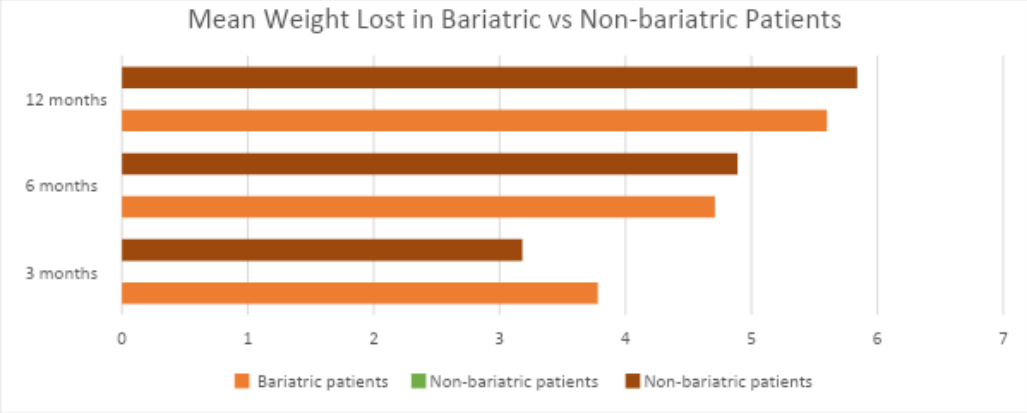


Figure:2MeanweightlossinBariatricvsNon-

BariatricpatientsTable:Timeintervalfordiabetic

TimeInterval	AverageWeight(kg/m2)	
andnondiabeticpatients	**Diabetic**	**Non-Diabetic**
0months	100.7093168	101.4487179
3months	97.2584472	98.72051282
6months	95.57509317	97.76923077
12months	95.84485075	98.246875

	Percentageweightloss(%)	
TimeInterval	Diabetic	Non-Diabetic
3months	3.79	4.29
6months	6.43	8.59
12months	11.95	9.59

	Numberofdiabeticpatientswithweightlossof	
Timeinterval	>5%	>10%
3months	15	7
6months	21	9
12months	20	11

	Numberofnon-diabeticpatientswithweightlossof	
Timeinterval	>5%	>10%
3months	46	10
6months	63	21
12months	62	34

	AverageBMI(kg/m2)	
TimeInterval	Diabetic	Non-Diabetic
0months	38.16189441	39.59794872
3months	38.16189441	38.99205128
6months	38.30025641	38.30025641
12months	36.15781955	39.184375

TimeInterval	AverageBMI(kg/m2)inFemales	
	PCOS	NoPCOS
0months	36.79	38.67
3months	35.38	37.59
6months	34.09	37.07
9months	33.59	36.78
12months	32.99	37.21

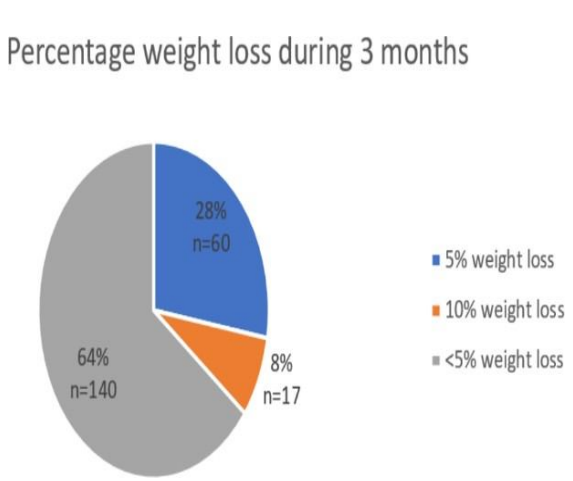
TimeInterval	AverageWeightinFemales(Kgs)	
	PCOS	NoPCOS
0months	95.11	101.6
3months	90.71	98.43
6months	87.62	97.10
12months	87.15	97.44

TimeInterval	Percentageweightloss(%)	
	PCOS	NoPCOS
3months	4.59	4.58
6months	8.35	8.35
12months	24.52	5.88

Timeinterval	NumberoffemalepatientshavingPCOSwithweightlossof	
	>5%	>10%
3months	11	2
6months	12	7
12months	12	6

Comment [33]: You need to be specific ? Your write up said 5%, not more rhan 5, also the 10% not > 10

Timeinterval	Numberoffemalepatientshavingno PCOSwithweightloss of	
	>5%	>10%
3months	50	15
6months	72	23
12months	70	39



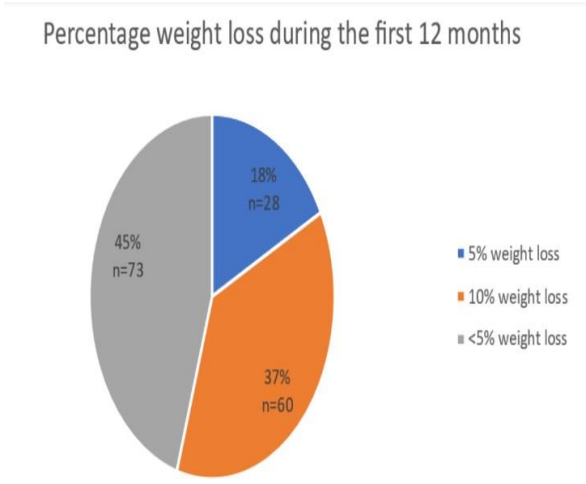


Figure2Percentageweightlossduring3months ***Figure3Percentageweightlossduringfirst12months***

Comment [34]: Repeatations, you cant have table and diagrams with the same information

Table3-7:BodyweightvariabilitybetweenDiabeticandNon-diabeticpatientsduringthecourseoftreatmentwithLiraglutide3.0mg:

		DM		Total
		DM	NO DM	
Body weight variability	decrease	24	126	150
	stable	7	5	12
	increase	8	30	38
		39	161	200

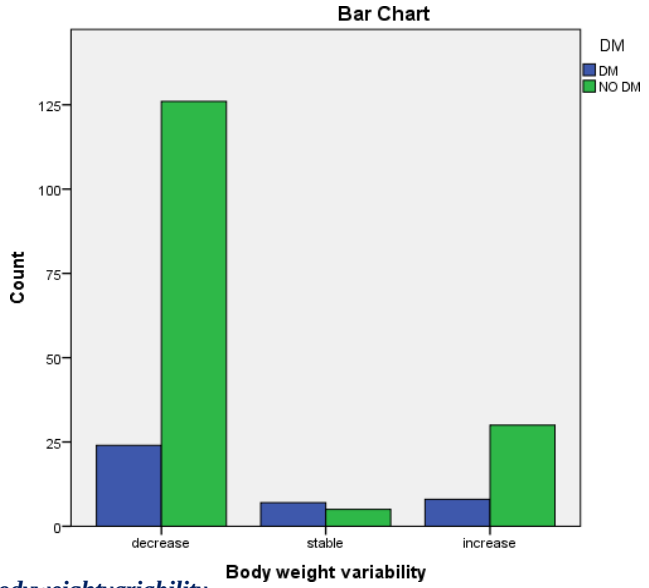


Chart:1Bodyweightvariability

IMPROVEMENTINMETABOLICPARAMETERS

Table4-1:changesinmetabolicparametersduringthecourseoftreatment:

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

Table4-2:ChangesinHBA1Cduringthecourseoftreatmentforpatientswith Type2DM

		HBA1C(0) beforestartingliraglutide	HBA1C at3months	HBA1C at6months	HBA1C at(9)month	HBA1C at12months
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

Table4-3:SignificancebetweenDMandHBA1cafter6months

IndependentSamplesTest

		Levene'sTestforEqualityof Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig.(2-tailed)	Mean Difference	Std. ErrorDifference	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

Recoded_HBA1C

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	below or equal	85	11.4	42.5	42.5
	5above 5	115	15.4	57.5	100.0
	Total	200	26.8	100.0	

Table4-4:ChangesinLDL-CforapatientwithType2DMduringthetreatmentcourse:

		LDL–C BEFORESTARTINGLIRAGLUTIDE	LDL–C AT6MONTHS	LDL-C AT12MONTHS
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

Table4-5:ChangesinLDL-patients'patientwithType2DM during the treatment course:

		LDL – CBEFORESTARTING LIRAGLUTIDE	LDL–C AT6MONTHS	LDL-C AT12MONTHS
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 4-6:Significance between DM andLDLafter12 months:

	DM	N	Mean	Std. Deviation	Std. Error Mean
LDLAT12MONTHSFROMSTARTINGLIRAGLUTIDE	DM	39	3.92	7.296	1.168
	NO DM	159	3.01	1.936	.154

Table4-7:LDL--cat12monthsfromstartingLiraglutide3.0mgforweightmanagement:

IndependentSamplesTest

	Levene'sTestfor Equality ofVariances	t-test for Equality of Means

Comment [35]: All these tables are conflicting with your statements in the text. These table shows that all your patients are diabetic?

Comment [36]: This does not show significance, what test did you use?

		F	Sig.	t	df	Sig.(2-tailed)	MeanDifference	Std. ErrorDifference	95% Confidence Interval of the Difference	
									Lower	Upper
variancesLDL(2)AT12MONTHFROMSTARTINGLIRAGLUTIDE	Equal 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

Table4-8:averageLDL-CreductioninpatientswithPCOS:

TimeInterval	AverageLDLinFemales(mg/dl)	
	PCOS	**NoPCOS**
0months	3.10	3.10
6months	5.15	5.15
12months	2.94	2.94

Bodyweight variability betweenDiabetic and Non-diabeticpatients during the courseof treatment withLiraglutide 3.0 mg:

Table4—9:BodyweightvariabilitybetweenDiabeticandNon-diabeticpatientsduringthecourseoftreatmentwithLiraglutide3.0mg:

		DM		Total
		DM	NO DM	
Body weight variability	decrease	24	126	150
	stable	7	5	12
	increase	8	30	38
		39	161	200

Table4-10:ChangesinALTduringthetreatmentcourse:

		ALT before starting Liraglutide 3.0 mg	ALT at 3 months	ALT at 6 months
N	Valid	200	200	200
	Missing	546	546	546
Mean		33.80	32.75	34.21
Median		27.00	28.00	27.00
Minimum		4	2	3
Maximum		134	166	467

Table4—11:SignificancebetweenDMandALTafter6months

ALTat6months

	Sum ofSquares	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			

Table4-12: SignificanceofALPchangesintheDMgroupafter6months

IndependentSamplesTest

		Levene'sTestforEqualityof Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig.(2-tailed)	MeanDifference	Std. ErrorDifference	95% Confidence Interval of the Difference	
									Lower	Upper
ALPat 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

Table4-13:SignificancebetweenDMandBMIreductionat6months:

	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

Table4-14SignificancebetweenDMandBMIreductionat6months:

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

IndependentSamplesTest		Levene'sTestforEquality ofVariances		t-test for Equality of Means						
		F	Sig.	t	df	Sig.(2-tailed)	MeanDifference	Std. ErrorDifference	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:4—16 **Descriptive**

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
BM1(0)BEFORESTARTINGTHE DRUG	DM	39	39.62	7.188	1.151	37.29	41.95	28	57
	NO DM	161	38.15	6.090	.480	37.20	39.10	25	58
	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

Table5-1:COMPLIANCETODIETMGDURINGTHECOURSEOFTREATMENT:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	COMPLIANTTODIET	109	14.6	54.5	54.5
	NOCOMPLAINTTODIET	91	12.2	45.5	100.0
	Total	200	26.8	100.0	

Table5-2:COMPLIANCETOPHYSICALACTIVITYDURINGTHE COURSE OFTREATMENT:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	COMPLIANTWITHPHYSICAL ACTIVITY	95	12.7	47.5	47.5
	NO COMPLIANCE	105	14.1	52.5	100.0

	Total	200	26.8	100.0	

Table5—3:COMPLIANCETOMEDICALTREATMENTWITHLIRAGLUTIDE3.0MG:

		Frequency	Percent	ValidPercent	Cumulative Percent
valid	COMPLIANT WITH MEDICAL TREATMENT	142	19.0	71.7	71.7
	NO COMPLIANT	56	7.5	28.3	100.0
	Total	198	26.5	100.0	

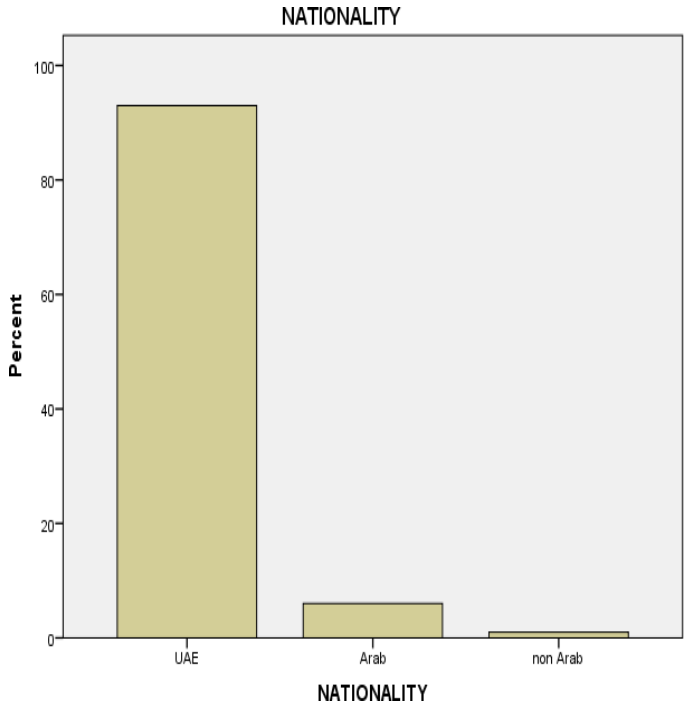
Table5—4:MajoradverseeffectsofLiraglutide3.0mg:

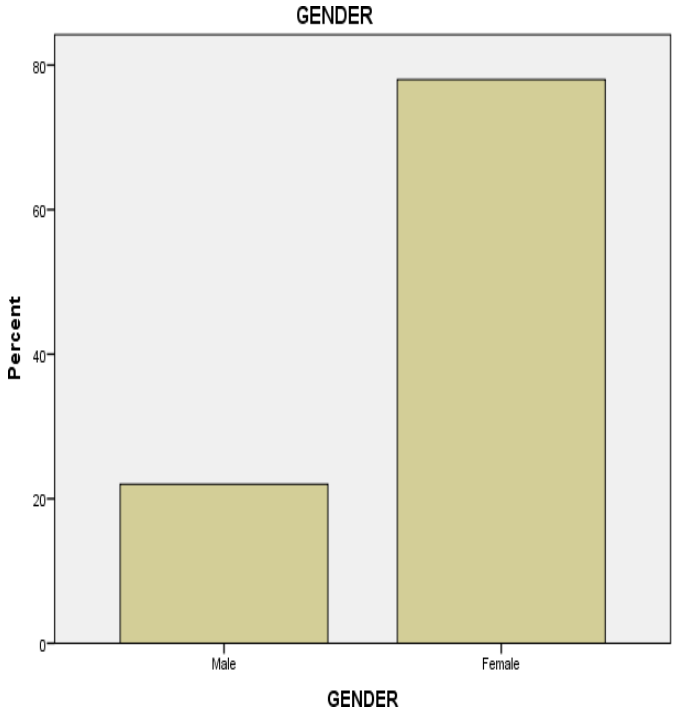
Sideeffects	Number of patients
Nausea	150
Abdominal pain and bloating	100
Menstrual irregularities	3
Constipation	100
Headache	75
Anxiety	3

Skin allergy	2

Table5—6:Majoradverseeffectsreportedduringthe treatmentcourse:

		Frequency	Percent	ValidPercent	Cumulative Percent
Valid	REPORT SIDE EFFECT	28	3.8	14.0	14.0
	NO SIDE EFFECT	172	23.1	86.0	100.0
	Total	200	26.8	100.0	





graphshowinggendervariability

Chart:2,3.Bar

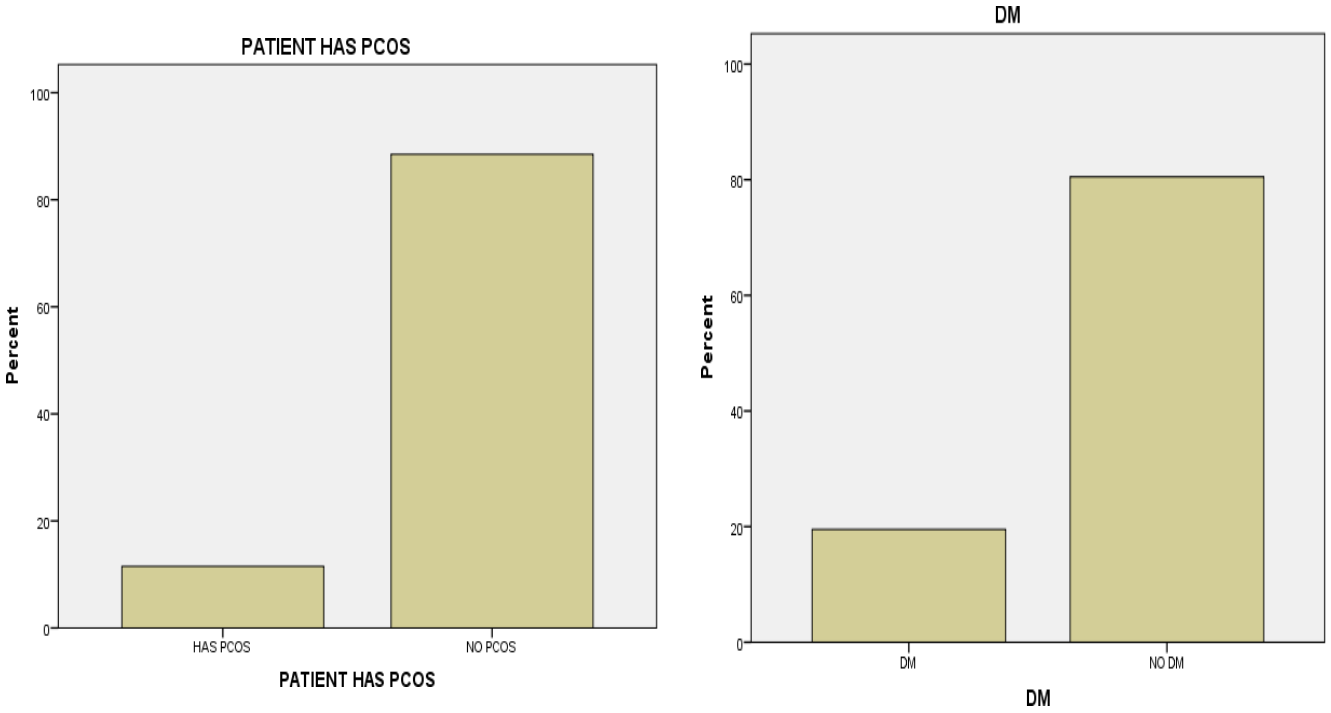
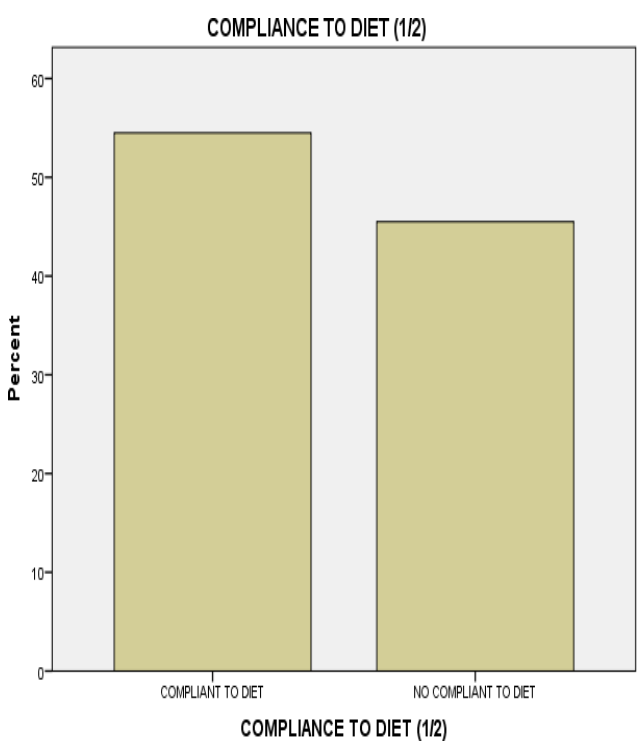


Chart:4,5BargraphshowingPCOSandDM



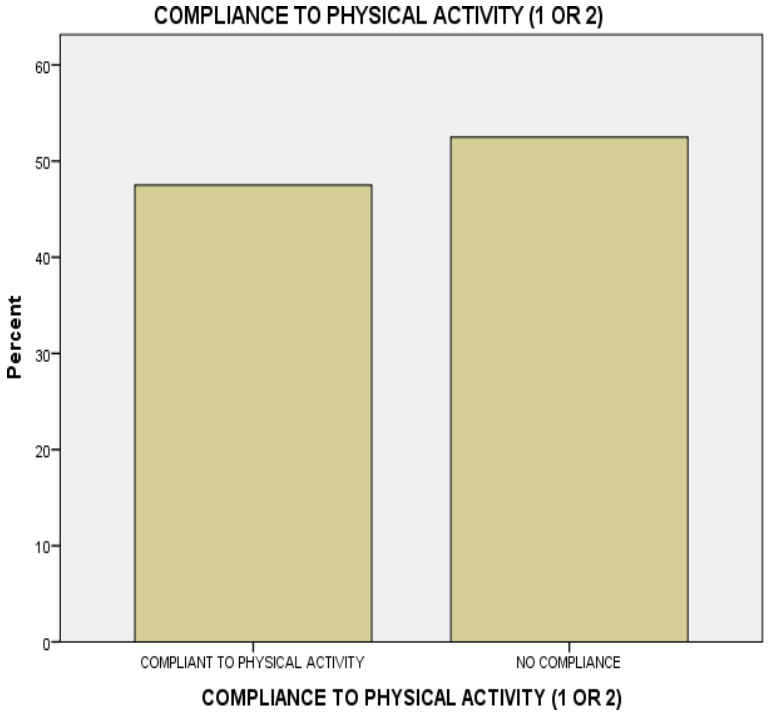
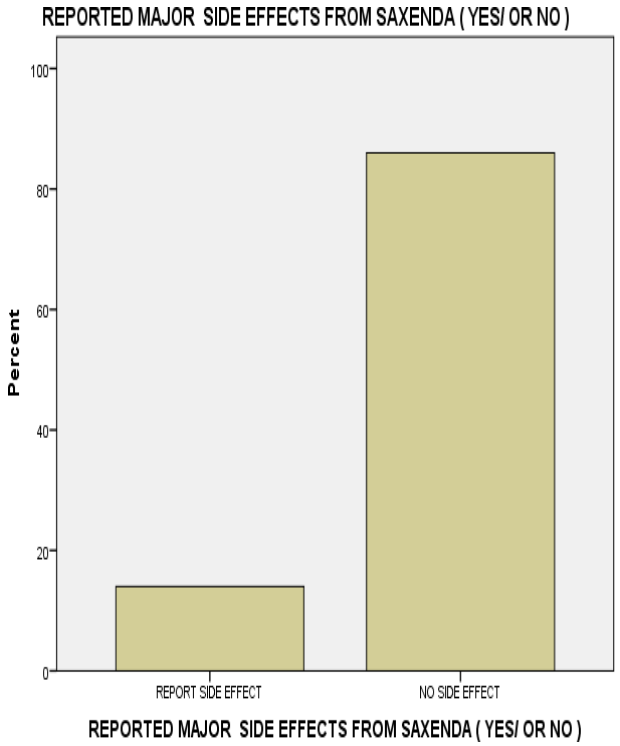


Chart:6,7Compliencetodietandphysical activity



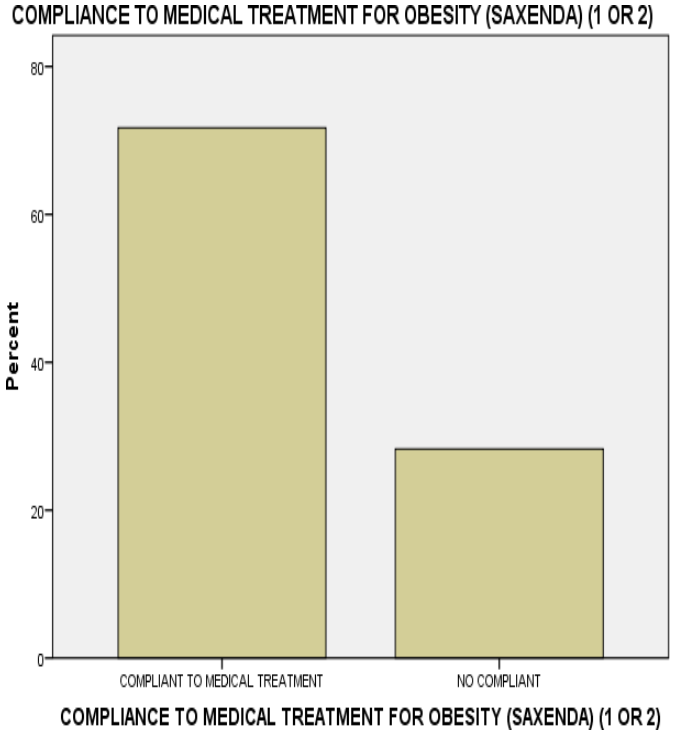


Chart8,9:Sideeffectfromsaxenda

Chart:10 Bariatric surveyreport

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