MANSOURA JOURNAL OF CHEMISTRY
Official Journal of Faculty of Science, Mansoura University, Egypt
E-mail: scimag@mans.edu.eg ISSN: 2974-4938

Evaluation of some diabetic response after Laparoscopic Sleeve Gastrectomy in morbidly obese diabetic patients

Nada Basim Atshan[1], Manar Refaat Abd-Elkhaliq, Nabil A. El-hak[2], Ahmed S. Shehatta[2], Magdy M. Youssef[3]

Department of Chemistry, Faculty of Science, Mansoura University, Mansoura, Egypt

Received:6/3/2021
Accepted:21/3/2021

Abstract: Obesity (a person with a body mass index [BMI] ≥ 30 kg/m2) is a serious health issue in the whole world. It is connected with diabetes mellitus risk **(1).** ***Aim:*** The main aim of our education was to evaluate the efficacy of Laparoscopic Sleeve Gastrectomy (LSG) on the changes in proinsulin and C-peptide levels before and then surgery by 3 months. ***Methods:*** Seventy patients were enrolled in our prospective study 20 samples are control group and 50 morbidly obese diabetic patients who have Type 2 Diabetes Mellitus (T2DM) at Department of general surgery. Assessing the effect of Laparoscopic Sleeve Gastrectomy on morbid obese patients with T2DM. All patients were under strict monitoring to record the changes in weight loss and improvement of T2DM markers; Fasting Blood Glucose (FBG), HOMA-IR, HbA1c, C-peptide and Proinsulin/insulin ratio at follow-up post 3months operative. ***Results:*** There was a greatly notable variance in BMI between baseline and after Surgery. Also levels of C-peptie, Proinsulin and Proinsulin/insulin ratio were all significantly decreased compared to preoperative baseline levels (P<0.001). ***Conclusion:*** Laparoscopic Sleeve Gastrectomy is an actual operative procedure to achieve a remarkable weight loss and controller of type 2 diabetes mellitus linked with major decline in leptin, C-peptide heights, Proinsulin and Proinsulin/insulin ratio after Laparoscopic Sleeve Gastrectomy.

keywords: Obesity, Type 2 diabetes of mellitus and laparoscopic Sleeve gastrectomy

1.Introduction

The risk for type 2 diabetes is enlarged by obesity through induction of insulin resistance. Insulin resistance involves insulin-induced glucose uptake is lessened in the insulin-sensitive tissue **(2).** Obesity contributes to around 55% of type 2 DM patients **(3).**

Type 2 diabetes mellitus (T2DM) is a chronic endocrine disorder with increasing prevalence worldwide **(4).** With impaired glucose regulation or T2DM in adults, proinsulin and insulin ratio (PI/I ratio) are frequently elevated **(5).** Endogenous insulin secretion is assessed best by measurement of C-peptide in patients with diabetes since it is secreted in equimolar amounts with insulin **(6).**

The incidence of obesity is steadily rising, and if secular trends continue, by 2025 an estimated40% of the US population will be obese **(7).** So weight reduction is a key therapeutic goal in both the prevention and management of T2DM **(8).** Laparoscopic sleeve gastrectomy operations has rapidly gained popularity in recent years, which is performed for obesity and obesity-associated T2DM **(9).** Laparoscopic Sleeve Gastrectomy led to long-term maintenance of weight loss. and major improvement in obesity-related T2DM **(10and 11).**

Aim of this Work:-

In our study we aim to:

Explore if proinsulin and C-peptide levels are changed or preserved in obese patients (BMI > 40 kg/m2) pre and then Laparoscopic Sleeve Gastrectomy operation.

Evaluate pro-insulin and its ratio to insulin (PI/I) and C-peptide as a risk factor for DM and obesity after Laparoscopic Sleeve Gastrectomy operation.

Materials and objects:

Sample collections

This cohort study is performed on 70 samples: 20 samples out of 70 are control group and 50 unhealthily obese diabetic patients with type 2 DM who were admitted to general surgery department, Mansoura University Hospitals, Mansoura, Egypt. These patients were subjugated to laparoscopic sleeve gastrectomy.

Data assembly

Data were collected prospectively and inserted into a database. All patients were evaluated with routine laboratory teasted in the form of blood count, serum albumin, serum bilirubin, Alt and Ast enzymes.

Assessment of the diabetic condition was done by measurement of, C-peptide, postprandial blood glucose (PBG), blood pressure, fasting blood sugar (FBS), HbA1c, insulin levels and blood lipid levels, including low-density lipoprotein, triglyceride, cholesterol and high-density.

The Quantitative Determination of Circulating C-Peptide Concentrations in Human Serum

Using enzyme immunoassay (TEST KIT, Cat:10802) for the Quantitative Determination of Circulating C-Peptide Concentrations in human serum**..** The procedure was completed as described in the pamphlet. The sensitivity (detection limit) was established by determining the variability of the 0 ng/mL serum calibrator and using the 2SD (95% certainty) statistic to calculate the minimum.

Human Leptin ELISA

Leptin was detected an all seventy samples using Human leptin (leptin) ELISA Kit , SinoGeneClon Biotech Co., ltd Cat No: SG-10057 for the quantitative determination of human leptin concentration. Organize all reagents, samples, blank and working standards as described in instructior. Read absorbance at 450nm after pipette Stop Solution within 15min.

All routine laboratory data -AS Lipid profile, liver enzymes, FBS- was quantitatively determined spectrophotometry using Hitashi instrument. Complete blood count (CBC) parameters ah Hb, RBCs and WBCs were detrmined using.

ELISA for the Quantitative Measurement of Human Insulin Levels in blood

Using Enzyme Linked ImmunoSorbent Assay (TEST KIT. Cat: KT-886) for the Quantitative Measurement of Human Insulin Levels in blood. . This test kit is proposed for use in the quantitative determination of human Insulin in plasma or serum. Organize all samples and substances as described in instructior. The mentioned normal high cut-off for Insulin concentration by using this ELISA is 65 mIU/L with an valu level of 15 mIU/L (normal range 2.76 – 62.1 mIU/L, SD 16 mIU/L).

Enzyme-linked Immunosorbent Assay Kit For Proinsulin (PI)

The kit is a good inhibition enzyme immunoassay practice for the in vitro quantitative measurement of proinsulin in human serum, plasma, tissue homogenates, cell lysates, cell culture supernates and other biological solutions. Cat: CEA379Hu. The procedure was completed as described in the pamphlet. The minimum measurable dose of proinsulin is naturally less than 5.25pg/mL. The sensitivity of this test, or Lower Limit of Detection (LLD) was definite as the lowest protein focus that could be discerned from zero. It was formed by subtracting two standard deviations to the mean visual density rate of twenty zero standard replicates and calculating the corresponding concentration.

Statistical analysis

Data take out for this analysis involved pre and postoperative blood glucose, BMI, HbA1c, body weight, blood lipid, serum proinsulin and C- peptide level.A reduction in BMI is an indication for weight loss. Blood lipid included LDL, triglycerides, HDL and cholesterol. Student's t-test or ANOVA and chi-square (X2) test are used for comparisons of means for variable categories. $P<0.05$ was reflected to show a statistically significant alteration. SPSS statistical software (SPSS 22.0 for Microsoft Windows, SPSS Inc.) is used for all statistical analyses.

Results and Discussion:

Examination of BMI in the cases group Pre – and post- Laparoscopic Sleeve Gastrectomy.

The result in **Table 1.** showed that The mean BMI decreased from 49 ± 7.55 kg/m2 before operation to 43.07 ± 5.73 kg/m2 at the 3 month follow‑up examinations(Fig. 2).There was very high significant difference between cases group (preoperative) and cases group (postoperative); P < 0.001.

Table (1): Analysis of BMI in the cases group before and after Laparoscopic Sleeve Gastrectomy.

Parametr	Groups		Testof significance	P
	Pre-LSG (N=50) (Mean + SD)	Post-LSG (N=50) (Mean +SD)		
BMI (Kg/m^2)	49 ± 7.55	43.07± 5.73	t= 17.449	<0.001 *

Glycemic profile in the serum of cases group Pre – and post- Laparoscopic Sleeve Gastrectomy

The changes in fasting blood glucose (FBG), HOMA-IR, Proinsulin and Proinsulin/insulin ratio compared to the rate before working levels were highly remarkable reduction (P<0.001), while the insulin ranks decreased but not significantly (P=0.019).

As the preoperative mean FBG was 112.36 ± 16.70 and the postoperative mean was 101.14 ± 8.54, the preoperative mean HOMA-IR 2.1 ± 1.43 and the postoperative 1.44 ± 0.81, the preoperative mean Proinsulin 66.23 + 40.1 and the postoperative 29.56 + 9.33 , and the preoperative mean Proinsulin/insulin ratio 9.35 and the postoperative 6.2

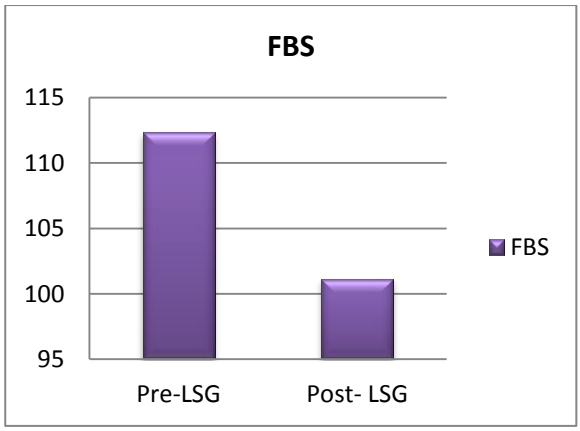

Figure (1): Mean serum level of FBS in pre- and post- Laparoscopic Sleeve Gastrectomy. Student's t test was used for the examination of the difference between each two groups. P< 0.05 was significant.

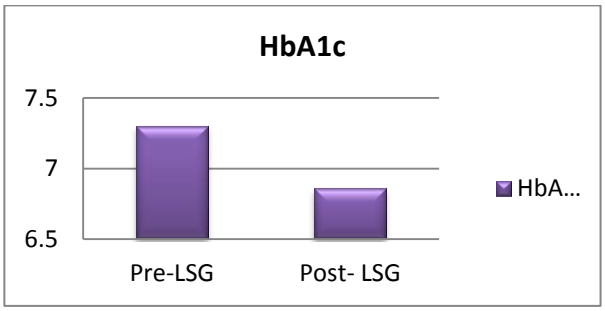

Figure (2): HbA1c changes after operation.

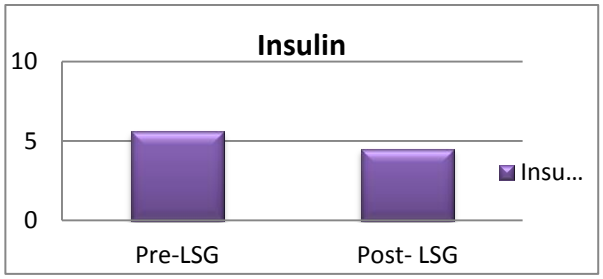

Figure (3): Mean serum level of Insulin in pre- and post- Laparoscopic Sleeve Gastrectomy. Student's t test was used for the examination of the difference between each two groups. P< 0.05 was significant.

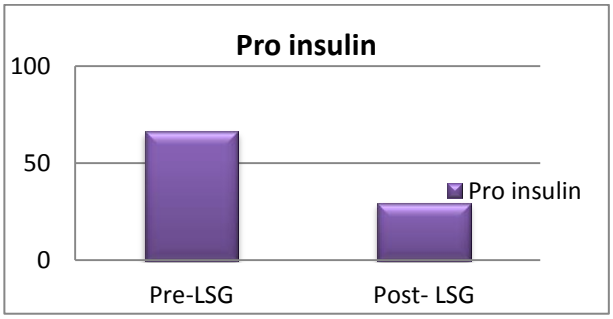

Figure (4): Mean serum level of proinsulin in pre- and post- Laparoscopic Sleeve Gastrectomy. Student's t test was used for the examination of the difference between each two groups. P< 0.05 was significant.

P<0.001

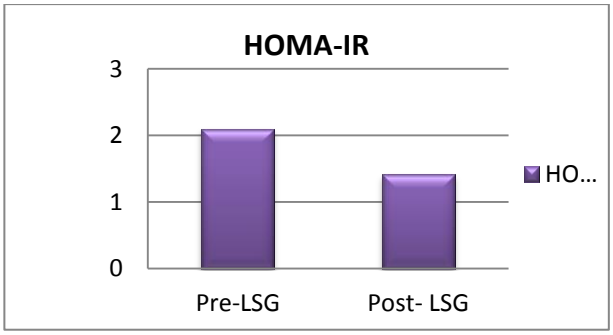

Figure (5): Serum HOMA-IR changes in patients before and after Laparoscopic Sleeve Gastrectomy.

Proinsulin / insulin ratio in the cases group pre- and post- Laparoscopic Sleeve Gastrectomy

The Proinsulin points were highly notably decreased at follow-up post 3months operative (P<0.001), while the insulin levels decreased but not significantly (P=0.019).

The Proinsulin / insulin ratio levels were highly notably decreased at follow-up post 3months operative (P<0.001).

Table (2): Proinsulin / insulin ratio in the cases group pre- and post- Laparoscopic Sleeve Gastrectomy

	Cases Groups		Testofsignificance	P
	Pre- LSG(N=50)(Median)	PostLSG(N=50)(Median)		
Insulin (mIU/L)	5.6	4.5	z= - 2.366	0.019*
Proinsulin (mIU/L)	64	29.3	z= - 6.301	< 0.001*
Proinsulin/insulin ratio	9.35	6.2	z= 3.354	< 0.001*

Analysis of obesity related hormones and biomarkers in the cases group pre – and post- Laparoscopic Sleeve Gastrectomy.

Levels of hormones related to obesity and biomarkers were repeated three months after Laparoscopic Sleeve Gastrectomy to identify changes associated with weight loss. At follow-up, the fasting levels of C-peptie and leptin were all significantly decreased in comparison to preoperative levels (P<0.001).

After Laparoscopic Sleeve Gastrectomy induced weight loss, patients had significantly lower levels of leptin 174.74 + 151.62 compairing to preoperative 498.64 + 485.04, also C-peptie level was decreased following surgery with a significant difference between preoperative cases 5.03 + 2.9 and postoperative cases 2.36 + 1.55

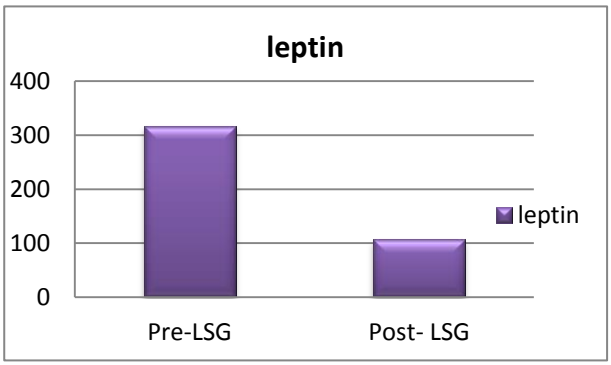

Figure (6): Leptin changes pre- and post- Laparoscopic Sleeve Gastrectomy

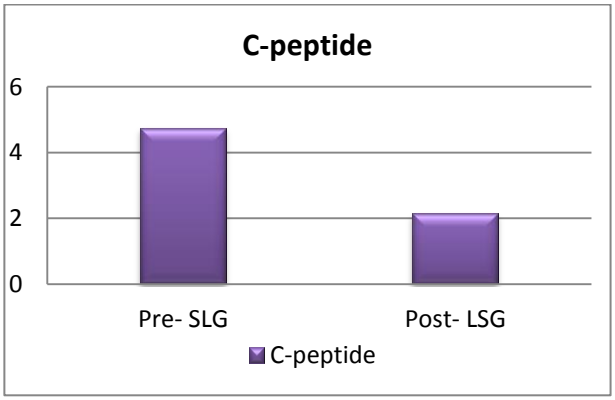

Figure (7): C- peptide changes pre- and post- Laparoscopic Sleeve Gastrectomy.

Analysis of lipid profile in the cases group pre – and post- Laparoscopic Sleeve Gastrectomy

A highly significant reduction in blood cholesterol and triglycerides levels at follow-up examinations three months post-operation (P<0.001).

HDL levels increased following surgery with a greatly major difference

(P<0.001) between preoperative cases (34.06 ± 6.42) and postoperative cases (39.95 ± 10.35), while a highly significant reduction in LDL levels at 3 months (P<0.001) following surgery **(Table 3).**

Table (3): analysis of lipid profile in the cases group pre – and post- Laparoscopic Sleeve Gastrectomy

	Groups		Test of significance	P
	Pre-LSG(N=50)(Mean +SD)	Post-LSG(N=50)(Mean + SD)		
Cholesterol (mg/dl)	201.32 ± 40.27	136.46 ± 36.47	t= - 5.727	< 0.001*
TGs (mg/dl)	169.90±41.09	105.3± 39.5	t= - 5.727	< 0.001*
HDL (mg/dl)	34.06 ± 6.42	39.95 ± 10.35	t= - 5.727	< 0.001*
LDL (mg/dl)	125.63 ± 39.96	83.87 ± 29.05	t= - 5.727	< 0.001*

Discussion

Fifty morbidly obese diabetic cases with Type 2 Diabetes Mellitus (T2DM) involved in our study. Their mean age was 37.60± 9.56 years and their mean BMI at baseline 37.60± 9.56 kg/m2, and 20 samples are control group their mean age 41.30± 6.16 years and their mean BMI at baseline 41.30± 6.16 kg/m 2, after surgery a high significant reduction in the BMI was observed from 49 ± 7.55 kg/m2 preoperatively to 43.07 ± 5.73 kg/m2 ($P < 0.001$).

Laparoscopic Sleeve Gastrectomy is a bariatric surgery which is safe and effective in weight loss **(12).** The present work shows a remarkable reduction in the BMI of patients after surgery ($P < 0.001$), this result agrees with previous findings reported by **(13)** who find a significant decrease in the BMI of patients before 53.8±8 (range, 40–75 kg/m2) and after 47.34±4.4 (range, 37–56.7 kg/m2) one year of operation with a p value less than 0.0001.

Studies have shown rapid improvements of HOMA-IR and plasma glucose suggesting that Laparoscopic Sleeve Gastrectomy might be more than a simple gastric restriction **(14).** Levels of Fasting blood glucose (FBG) as well. Insulin resistance (stated as the HOMA IR) decreased pointedly 7 days and 1 month later surgery; this was reported by **(15)**. This is similar to our results, as in our study the changes in fasting blood glucose (FBG) and HOMA-IR as opposed to the mean preoperative stages were highly noteworthy reduction ($P<0.001$). Also **(14)** found that a significant decrease of IR during the first 3 months following bariatric surgery and **(16)** demonstrated that, mean FBG rate was 105.40±31.42 mg/dL in the preoperative period, it lessened statistically significantly to 92.96±17.69 mg/dL at postoperative 12th month ($p<0.0001$).

An elevated proinsulin and its ratio to insulin (PI/I ratio) reflects impairment of glucose regulation or T2DM in adults **(5).** Our result which revealed that the Proinsulin and Proinsulin / insulin ratio levels were highly significantly decreased at follow‑up examinations ($P<0.001$), while the insulin levels decreased but not significantly ($P=0.019$).

leptin lowers appetite as a circulating signal, so obese individuals generally exhibit a higher circulating concentration of leptin than normal **(17).** Our data indicated that Levels of the obesity related hormones and biomarkers were repeated 3 months after Laparoscopic Sleeve Gastrectomy to recognize changes associated with weight loss. At follow-up, the fasting levels of leptin was remarkably decreased compared to preoperative baseline levels ($P<0.001$).This result is consistent with previous findings which reported by **(18)** concluded that, there is a remarkable reduction in the serum leptin level of patients after Laparoscopic Sleeve Gastrectomy surgery from their base line.

patients with T2D have higher levels of C-peptide before operation than postoperative **(19).** In this result at follow-up, C-peptie was notably decreased in comparison to preoperative baseline levels ($P<0.001$).

Our work showed that the level of blood cholesterol and triglycerides were highly significant decreased after surgery ($P<0.001$), HDL levels increased following surgery with a highly noteworthy change ($P<0.001$) between preoperative cases (34.06 ± 6.42) and postoperative cases (39.95 ± 10.35), while the LDL points were highly notably lessened at 3 months ($P<0.001$) following surgery. This result agrees with findings reported by **(20)** explain that Patients receiving Laparoscopic Sleeve Gastrectomy, a significant increases in HDL from 48.4 to 54.5 mg/dl ($p < 0.01$) and decreases in triglycerides from 141.7 to 109.3 mg/dl ($p < 0.01$).

4. References

1. Golzarand M, Toolabi K and Farid R. (2017). The bariatric surgery and weight losing: a meta-analysis in the long- and very long-term effects of laparoscopic adjustable gastric banding, laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy on weight loss in adults. Surg Endosc; **31**: 4331-4345.
2. Ye J. (2013). Mechanisms of insulin resistance in obesity. Front Med; 7:14-24.
3. Centers for Disease Control and Prevention (CDC). (2004). Prevalence of overweight and obesity among adults with

diagnosed Diabetes United States, 1988-(1994) and 1999-2000". MMWR. Morbidity and Mortality Weekly Report; **53(45)**: 1066-1068.
4. Olokoba AB, Obateru OA and Olokoba LB. (2012). Type 2 diabetes mellitus: a review of current trends. *Oman Med J*; **27**: 269-273.
5. Berghes Cv , Brabant G, Biebermann H, Krude H and Wiegand S. (2011). Proinsulin and the Proinsulin/Insulin Ratio in Overweight and Obese Children and Adolescents: Relation to Clinical Parameters, Insulin Resistance, and Impaired Glucose Regulation. Pediatr Diabetes; **12**: 242-249.
6. Jones AG and Hattersley AT (2013). The clinical utility of C-peptide measurement in the care of patients with diabetes. Diabet Med; **30**: 803–817.
7. Kopelman PG. (2000). Obesity as a medical problem. Nature; **404**: 635-643.
8. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R and Matthews DR.(2015). Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care; **38**: 140-149.
9. Iannelli A, Dainese R, Piche T, Facchiano E and Gugenheim J. (2008). Laparoscopic sleeve gastrectomy for morbid obesity. *World J Gastroenterol*; **14**: 821-827.
10. Major P, Wysocki M, Pędziwiatr M, Małczak1 P, Pisarska1 M and Budzyński A. (2016). Laparoscopic sleeve gastrectomy for the treatment of diabetes mellitus type 2 patients-single center early experience. Gland Surg; **5**: 465-472.
11. Çetinkünar S, Erdem H, Aktimur R, Aziret M, Özdaş S, Yürekli B and Yetişir F. (2015). The effect of laparoscopic sleeve gastrectomy on morbid obesity and obesity-related comorbidities: a cohort study. Ulus Cerrahi Derg; **31**: 202-206.
12. Landau Z, Karplus G, Hanukoglu A, Abiri S, Levy A and Serour F. (2011). [Laparoscopic sleeve gastrectomy (LSG) in adolescents with morbid obesity]. Harefuah; 150: 765-768, 816, 815. Hebrew. PMID: 22111118.
13. Elbanna H, Ghnnam W, Negm A, Youssef T, Emile S, El Metwally T and Elalfy K. (2016). Impact of preoperative body mass index on the final outcome after laparoscopic sleeve gastrectomy for morbid obesity. Ulus Cerrahi Derg; **32**: 238-243.
14. Cătoi AF, Pârvu A, Mironiuc A, Galea RF, Mureşan A, Bidian C and Pop I. (2016). Effects of sleeve gastrectomy on insulin resistance. Clujul Med; **89**: 267-272.
15. Hady HR, Dadan J, Gołaszewski P and Safiejko K. (2012). Impact of laparoscopic sleeve gastrectomy on body mass index, ghrelin, insulin and lipid levels in 100 obese patients. Wideochir Inne Tech Maloinwazyjne; **7**: 251-259.
16. Batman B and Altun H. (2020) The Effects of Laparoscopic Sleeve Gastrectomy on Glucose Metabolism in Patients with a Body Mass Index below 35 kg/m². Sisli Etfal Hastan Tip Bul; **54**: 36-40.
17. Von Schnurbein J, Heni M, Moss A, Nagel SA, Machann J, Muehleder H, Debatin KM, Farooqi S and Wabitsch M. (2013). Rapid improvement of hepatic steatosis after initiation of leptin substitution in a leptin-deficient girl. Horm Res Paediatr; **79**: 310-317.
18. Varlık Erol , Cengiz Aydın and Levent Uğurlu. (2019). Changes in ghrelin, leptin and insulin levels after laparoscopic sleeve gastrectomy . *Ege Journal of Medicine*; **58**: 21-26.
19. Ramos-Leví AM, Matía P, Cabrerizo L, Barabash A, Torrejón MJ, Sánchez-Pernaute A, Torres AJ and Rubio MA. (2013). C-peptide levels predict type 2 diabetes remission after bariatric surgery. Nutr Hosp; **28**: 1599-15603.
20. Zhang F, Strain GW, Lei W, Dakin GF, Gagner M and Pomp A. (2011). Changes in Lipid Profiles in Morbidly Obese Patients After Laparoscopic Sleeve Gastrectomy (LSG). OBES SURG; **21**: 305-309.