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Glycemic changes after sleeve gastrectomy in type 2 diabetic morbidly obese patients

Tarek Osama Hegazy, Ahmed Abd El-Halem Ewis

ABSTRACT

Aims: Obesity is gradually turning into an epidemic condition throughout the world and has become a social psychological and economic burden of growing proportions. Bariatric surgery is known to be a highly effective and long lasting treatment for morbid obesity and many related conditions, including type 2 diabetes mellitus (T2DM) and the metabolic syndrome (MS). The aim of this study is to assess the short- and long-term effects of laparoscopic sleeve gastrectomy (LSG) on body weight and glucose homeostasis in morbidly obese diabetic patients. Methods: That study was conducted on 40 patients, for the evaluation of the short- and long-term effects (one-day, three-month, six-month, nine-month and twelve-month) of LSG on body weight and glucose homeostasis by measuring fasting blood glucose level, postprandial blood glucose (PPBG), glycated hemoglobin (HbA1C), insulin level in morbid obese T2DM subjects not adequately controlled with medical therapy. Results: Resolution incidence by all parameters (FBG, PPBG and HbA1C) was 13 patient (32.5%), 27 patients (67.5%), 32 patients (80%) and 32 patients (80%) at third-month, sixth-month, ninth-month and 12th-month postoperatively, respectively. Conclusion: In our study, the surgical procedure of laparoscopic sleeve gastrectomy resulted in marked weight loss and decrease in the body mass index which improved glucose homeostasis and remission of T2DM. Our study showed that the LSG is associated with a high rate of resolution of T2DM at 12-month after surgery in severely obese subjects with T2DM.

Keywords: Laparoscopic sleeve gastrectomy (LSG), Type 2 diabetes mellitus (T2DM), Morbid obese, Postprandial blood glucose (PPBG), Glycated hemoglobin (HbA1C), Insulin

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Tarek Osama Hegazy[1], Ahmed Abd El-Halem Ewis[2]
Affiliations: [1]MD, MRCS, Lecturer in Department of General Surgery, Faculty of Medicine, Cairo University, Egypt; [2]MSc Kasr El-Aini, Faculty of Medicine, Cairo University.
Corresponding Author: Tarek Osama Hegazy, 30, Anas Ben Malek st., el Mohandeseen, Giza, Egypt; Ph: 20 01222493066; Email: ticegy@yahoo.com

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INTRODUCTION

Obesity is an increasingly serious health problem globally and is strongly associated with several medical problems. Some of these problems are considered direct complications of long-standing obesity [1]. These problems include an increased risk of cardiovascular morbidity and mortality, hypertension, sleep apnea, and diabetes mellitus (DM). Among these and other associated co-morbidities, the strongest link is found between obesity and DM [2]. Approximately, 80% of individuals with type 2 DM are obese [3].

The risk of developing DM increases with the severity and duration of obesity and a central distribution of body fat [4]. Morbidly obese subjects, as compared with lean subjects, have an approximately 40 times greater risk of developing type 2 diabetes. The waist circumference, rather than the body mass index (BMI), is the best predictor of type 2 diabetes. This is probably because waist circumference correlates better with intrabdominal fat [5]. Also, insulin resistance with hyperinsulinemia is characteristic to obesity and is present before the onset of hyperglycemia. After the onset of obesity, the first demonstrable changes are impairment in glucose removal and increased insulin resistance [6]. Currently, bariatric surgery is the only interventional method proved to induce significant long-term weight reduction which can result in significant clinical improvement in DM after weight loss [7].

MATERIALS AND METHODS

This is a prospective study which was conducted on 40 diabetic patients randomly selected suffering from morbid obesity (BMI > 35 and a diabetic) at Kasr El-Aini Hospital Faculty of Medicine from July 2011 to May 2013.

Patients were managed by laparoscopic sleeve gastrectomy to assess the short-and long-term effects of the procedure on glucose homeostasis.

Inclusion criteria included that the patient is only diagnosed as diabetic if HbA1c ≥ 6.5%, FBG ≥126 mg/dL and 2h-PPBG ≥ 200 mg/dL and has a BMI of >35, failed at other weight loss measures (diet or medical treatment) and psychologically stable.

Exclusion criteria included mental incompetence that prevents the patient from understanding the procedure, inability or unwillingness of the patient to change lifestyle postoperatively, drug and alcohol or other substance addiction, psychological instability and antagonistic family or unsupportive home environment.

All patients were subjected to the following preoperative workup after receiving a written consent according to ethical committee in Kasr El-Aini Hospital Faculty of Medicine:

1. Full clinical assessment including history taking and through examination, assessing BMI and waist circumference.
2. Laboratory investigations assessing patients fitness for the procedure including: liver functions, kidney functions, coagulation profile and complete blood count.
3. Chest X-ray and pulmonary function tests.
4. Hormonal assay to exclude underlying endocrine disorders, including and serum cortisol and thyroid functions.
5. Laboratory tests to assess glucose homeostasis including: fasting and two hours post prandial blood glucose, glycated hemoglobin and insulin level.

All operative procedures were performed laparoscopically. The first step consists of opening the gastrocolic ligament attached to the stomach, usually starting 10–12 cm from the pylorus towards the lower pole of the spleen. Then the gastric greater curvature is freed up to the cardioesophageal junction close to stomach. Meticulous dissection is performed at the angle of His with full mobilization of the gastric fundus. The mobilization of the stomach continues dissecting the greater gastric curve toward the antrum up to 5–7 cm from the pylorus. At this time a 36-Fr orogastric tube is inserted direct towards the pylorus, proximal to the lesser curvature of the stomach. Then, the stomach is resected with linear staplers parallel to orogastric tube along the lesser curve starting 5–7 cm far from pylorus. The orogastic bougie is replaced by a nasogastric tube that is positioned in the distal stomach to perform a methylene blue.

All patients were assessed postoperatively for the following:

1. Early and late postoperative complications.
2. Effect of the procedure on BMI and EWL (estimated weight loss after 3, 6, 9 and 12 months).
3. Effect of the procedure on glucose homeostasis by measuring, blood glucose level, glycated hemoglobin, insulin level after 1 day, 3, 6, 9 and 12 months.

All collected questionnaires were revised for completeness and consistency. Pre-coded data was entered on the computer using “Microsoft Excel (2010)”. Data was then transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed.

Data was summarized using mean and standard deviation or median and percentiles for quantitative variables and frequency and percentage for qualitative variables. Relative percentage change was calculated to get the actual change in each time measure. Relative percentage change = [(Post measure – Pre measure)] x 100.

Comparison between groups were done using independent sample t-test for quantitative variables. Repeated measures ANOVA test was conducted to compare different measures at different time situation with post hoc Bonferroni test for pair wise comparisons and assessment of step P value between the corresponding row measurement and the previous row measurement. Post hoc category represents letter or color labeling to summarize the pairwise comparisons between different measurements so that any two measurements having different letter or color label are statistically different at P value of 0.05. Pearson correlation coefficient (r) was calculated to test the association between quantitative variables.

RESULTS

Patient's characteristics

Patient Age: The mean age of the studied group was (38.8+7.0) years (range 25–50 years)

Patient gender: thirty-one (77.5%) patients were women and nine (22.5%) were men.

Patient BMI: The BMI of patients (Figure 1) were (35.0–39.9) = 1(2.5%), (40.0–44.9) = 9 (22.5%), (45.0–49.9)

= 13 (32.5%), (50.0–54.9) = 16(40%) and (55.0–59.9) = 1(2.5%).

Significant declining in fasting blood glucose levels was observed at 1 day postoperative (172.5.4+29 mg/dL) (P<0.001). Compared to the basal value (209+36.6 mg/dL) independent from the weight loss, but a significant declining occurred at third month (125.6+16.7) (P<0.001) and sixth month (111.7+20.9) (P = 0.004) was associated with a significant declining in BMI at third month (39.2+2.6 kg/m^2) (P<0.001) and sixth month (34.9+2.3 kg/m^2) (P<0.001) compared with the basal value (48.4+3.5 kg/m^2).

A non-significant declining in FBG occurred at nine month (105+18.3 mg/dL) (P = 0.25) and 12th months (102.9+21 mg/dL) (P = 1.0) despite a significant declining in BMI at nine months (32+2.3 kg/m^2) (P < 0.001) and 12 month (30.2+2.3 kg/m^2) (P < 0.001) as given in Table 1 and graphically it is shown in Figure 2.

Groups having different letter or color code are significantly different at p value of 0.05.

The postprandial blood glucose levels had a significant declining at one day postoperative (240.3+30.9) mg/dL (P<0.001) compared to the baseline (280.7+45.4) mg/dL independent from the weight loss. At (3,6,9) months after surgery a significant declining in PPBG (P<0.001) occurred but it was associated with significant reduction of BMI. After 12 months a significant reduction of BMI occurred (P<0.001) with non-significant decline in the PPBG level given in Table 2 and graphically it is shown in Figure 3.

Groups having different letter or color code are significantly different at p value of 0.05.

The mean of HbA1C reached (7+0.8)%, (6.3+0.7)% and (6+0.7)% at (3,6,9) months respectively showing a significant declining (P < 0.001), but non-significant declining occurred at 12 month (P = 0.16) with a significant reduction of BMI by time (3, 6, 9, 12) months as given in Table 3 and Figure 4.

Groups having different letter or color code are significantly different at p value of 0.05.

Serum insulin levels showed a sharp and significant reduction at postoperative one day (13.5+2.2 uU/mL) (P < 0.001) and 3 months (4.4+1.8 uU/mL) (P < 0.001), but a non significant changes occurred at 6 months (5.3+1.5 uU/mL) (P = 0.51), 9 months (5.2+1.3 uU/mL) (P = 1) and 12 months (4.8+1 uU/mL) (P = 0.85), as given in Table 4 and graphically it is shown in Figure 5.

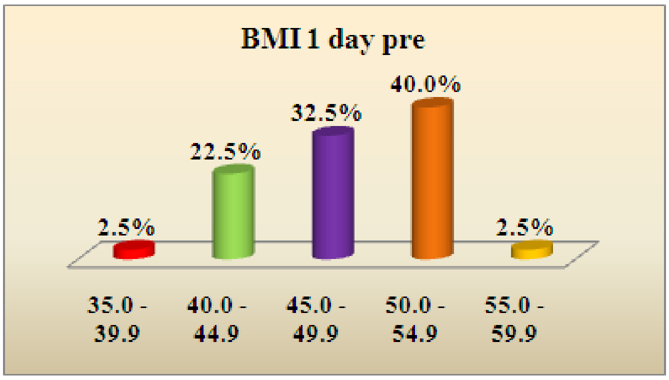

Figure 1: Body mass index of patients preoperatively. Showing distribution of patients 1(2.5%),9(22.5%),13(32.5%),16(40%) and 1(2.5)% according to BMI ranges.

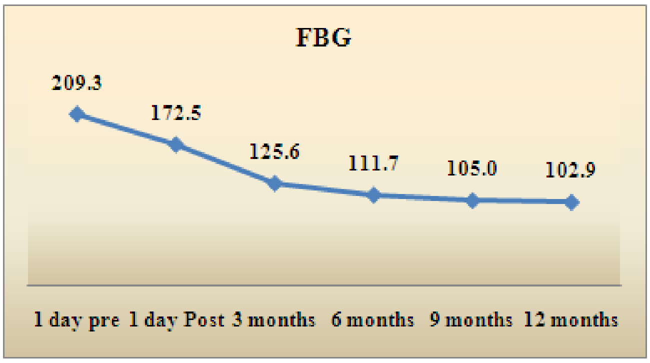

Figure 2: Improvement of fasting blood Glucose (FBG) by time after sleeve gastrectomy.

Table 1: Improvement of fasting blood Glucose (FBG) by time after sleeve gastrectomy.

FBG	Mean ± SD	Step P value	Post hoc category	Global P Value
1 day pre	209.3 ± 36.6	.....	A	< 0.001
1 day Post	172.5 ± 29	<0.001	B	HS
3 months	125.6 ± 16.7	<0.001	C	
6 months	111.7 ± 20.9	0.004	D	
9 months	105.0 ± 18.3	0.25	D	
12 months	102.9 ± 21.0	1.0	D	

Groups having different letter or different color code are significantly different at p value of 0.05

Table 2: Improvement of postprandial blood glucose (PPBG) by time after sleeve gastrectomy.

PPBG	Mean ± SD	Step P value	Post hoc category	P Value
1 day pre	280.7 ± 45.4	.....	A	< 0.001
1 day Post	240.3 ± 30.9	<0.001	B	HS
3 months	172.7 ± 37.4	<0.001	C	
6 months	144.5 ± 30.7	<0.001	D	
9 months	133.0 ± 32.0	0.02	E	
12 months	128.5 ± 36.4	1.0	E	

Groups having different letter or color code are significantly different at p value of 0.05

Table 3: Improvement of glycated hemoglobin (HbA1C) by time after sleeve gastrectomy.

HbA1C "H"	Mean ± SD	Step P value	Post hoc category	P Value
1 day pre	10.3 ± 0.9	.....	A	< 0.001
1 day Post	9.1 ± 0.9	<0.001	B	HS
3 months	7.0 ± 0.8	<0.001	C	
6 months	6.3 ± 0.7	<0.001	D	
9 months	6.0 ± 0.7	0.001	E	
12 months	5.8 ± 0.6	0.16	E	

Groups having different letter or different color code are significantly different at p value of 0.05.

Table 4: Improvement of insulin level by time after sleeve gastrectomy.

Insulin	Mean ± SD	Step P value	Post hoc category	P Value
1 day pre	24.7 ± 5.2	.....	A	< 0.001
1 day Post	13.5 ± 2.2	<0.001	B	HS
3 months	4.4 ± 1.8	<0.001	C	
6 months	5.3 ± 1.5	0.51	C	
9 months	5.2 ± 1.3	1.0	C	
12 months	4.8 ± 1.0	0.85	C	

Groups having different letter or different color code are significantly different at p value of 0.05.

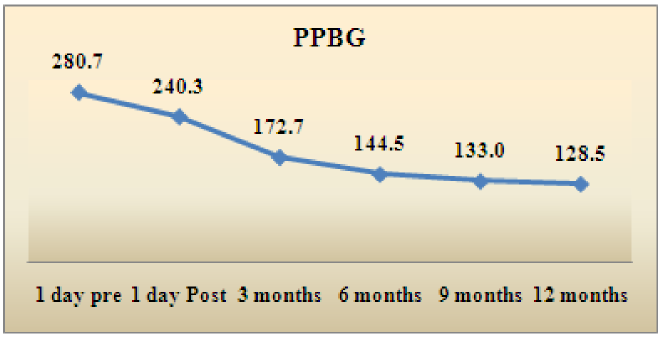

Figure 3: Improvement of postprandial blood glucose (PPBG) by time after sleeve Gastrectomy.

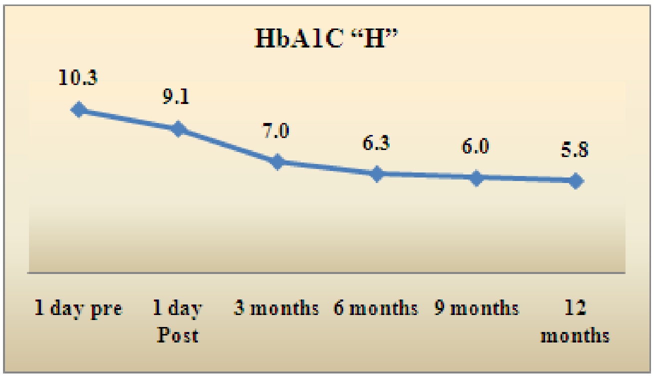

Figure 4: Improvement of glycated haemoglobin(HbA1C) by time after sleeve gastrectomy.

Groups having different letter or color code are significantly different at p value of 0.05.

A postoperative improvement of BMI occurred with a significant declining (weight loss) at third month, sixth month, ninth months and 12th month (P<0.001) as given in Table 5 and Figure 6.

Groups having different letter or color code are significantly different at p value of 0.05.

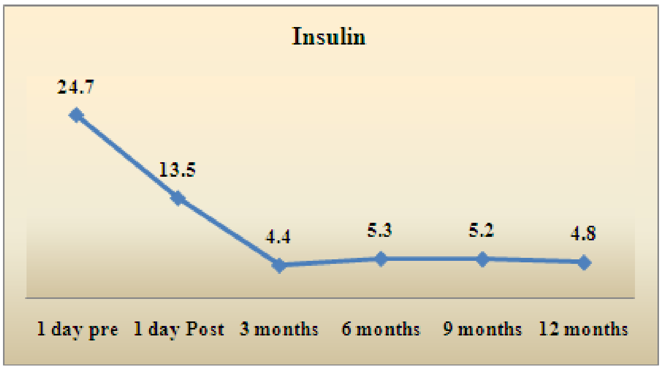

Figure 5: Improvement of insulin level by time after sleeve gastrectomy.

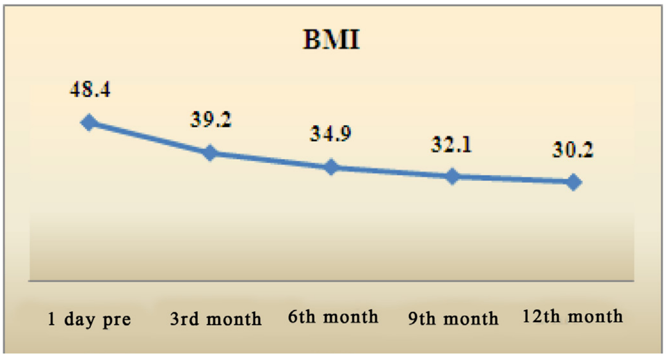

Figure 6: Improvement of BMI by time after sleeve gastrectomy.

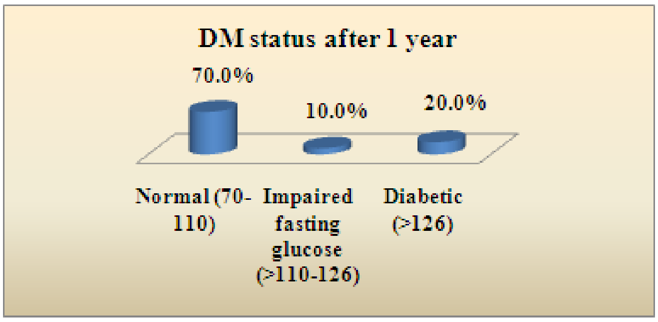

Figure 7: DM status assessed by measuring FBG after 12 months post sleeve gastrectomy.

The FBG after 12 months reached to normal level (70-110) mg/dL in 28 patients (70%), impaired fasting glucose (>110-126) mg/dL in 4 patients (10%) and diabetic (>126) mg/dL in 8 patients (20%) (Table 6). graphically it is shown in Figure 7.

The resolution incidence by FBG occurred in 23 patients (57.5%), 29 patients (72.5%), 32 patients (80%) and 32 patients (80%) at third month, sixth month, ninth month and 12th months postoperatively, respectively (Table 7).

Table 5: Improvement of BMI by time after sleeve gastrectomy.

BMI	Mean ± SD	Step P value	Post hoc category	P Value
1 day pre	48.4 ± 3.5	......	A	< 0.001
3 months	39.2 ± 2.6	<0.001	B	HS
6 months	34.9 ± 2.3	<0.001	C	
9 months	32.1 ± 2.3	<0.001	D	
12 months	30.2 ± 2.3	<0.001	E	

Groups having different letter or different color code are significantly different at p value of 0.05

Table 6: DM status assessed by measuring FBG after 12 months post sleeve gastrectomy

	Frequency	Percentage
FBG after 12 months		
Normal (70–110)	28	70%
Impaired fasting glucose (>110–126)	4	10%
Diabetic (>126)	8	20%

Table 7: Resolution incidence by FBG (< 126 mg/dL)

	Resolved		Not resolved	
Time	N	%	N	%
1 day post	0	0.0	40	100.0
3 months	23	57.5	17	42.5
6 months	29	72.5	11	27.5
9 months	32	80	8	20
12 months	32	80	8	20

DISCUSSION

The level of obesity have been increased rapidly especially in the past 50 years, in the United Kingdom between 1980 and 1997, levels of overweight in men increased from 39–52% and in women from 32–53% and obesity in the same period increased three fold from 6–17% in men and from 8–20% in women [8]. Also in United Sates nearly two-thirds of adults are overweight (BMI > 25 kg/m^2), nearly one-third are considered obese (BM1 > 30 kg/m^2) and 4.7% one extremely obese (BMI > 40 kg/m^2) [9].

Much of the improvement of diabetes has been related to the excess weight loss after surgery. However, some effects appear to be independent from weight loss occurring prior to it. Although early reports concentrated on the clinical effects of the improvement of diabetes, recent works have focused on glycemic control and measurements of insulin resistance [10].

Regarding LSG, recent studies have shown that this procedure is associated with a marked reduction of ghrelin secretion which is produced by the gastric fundus involved in meal time hunger regulation and it is also known to exert several diabetogenic effects (increase in growth hormone, cortisol, and epinephrine). Therefore, its suppression could contribute to improved homeostasis [11].

Several studies done on effect of LSG on amelioration of T2DM, one study in 2010 showed that after LSG a sharp and significant reduction of serum glucose and insulin concentration and HOMA IR values was observed at fifth day postoperatively in comparison with the preoperative finding (P=0.027, P<0.01, and P<0.01, respectively). Moreover, in seven of these patients, serum glucose and insulin concentration and HOMA IR values were already significantly lower than the preoperative ones at the third postoperative day. In obese patients, at the 15th postoperative day, both serum glucose and insulin concentration and HOMA IR remained significantly lower than the preoperative value (P=0.01, P<0.01, and P<0.01). By contrast, at this time the BMI was not significantly changed in comparison with the preoperative values (EWL 14.7%). At 30th and 60th days postoperative, serum glucose and insulin concentration and HOMA IR values remained substantially unchanged in spite of a significant weight loss (EWL 23.6% and 32.2%), respectively as given in Table 8 [12].

In 2009 a study showed that the fasting glucose levels had changed significantly from baseline to 2 and 6 months, decreasing from (158.93±19.65 mg/dL) at baseline to (139.83±12.03 mg/dL) and (128.32±7.03 mg), respectively and these results indicate that LSG is effective in improving or resolving T2DM in morbidly obese patients [13].

This improvement or resolution of diabetes was contributed to a significant declining in the BMI from (46.12±10.86 kg/m^2) at the baseline to (38.27±6.59 kg/m^2) and (35.78±4.11 kg/m^2) at 2nd–6th month, respectively as given in Table 9 [13].

Another study in 2011, showed that the fasting blood glucose after LSG significantly decreased from the baseline ((131±42 mg/dL) to (87±19 mg/dL) at third month and remained within the normal range at 9th–15th month the fasting plasma insulin declined significantly by 68–87% following the intervention (P<0.001). As a consequence HOMAIR dramatically decreased by 86% (P<0.008) three months after surgery and remained stable there after (91%, P<0.04). Mean HbA1C reached 5.9±0.6% at third month and remained unchanged at (9th–15th) month (5.8±0.7) (<0.03) compared to the basal value (7.5±1.9%). The declining in the FBG, insulin and HbA1C was associated with significant decreasing in BMI from baseline (48±8 kg/m^2) at third months and (34±6 kg/m^2) (P<0.001) as given in Table 10 [14].

The results of these three studies are comparable to our study as an improvement of fasting blood glucose (FBG) occurred by time postoperatively, the FBG levels were improved with significant declining at one day (P<0.001), third month (P<0.001) and sixth month (P<0.004) but non-significant declining at ninth month (P<0.25) and 12th month (P=1.0).

The postoperative serum insulin levels improved due to decreased insulin resistance with a significant declining at one day (P<0.001) and third month (P<0.001) but non-significant at sixth month (P<0.91), ninth month (P=1.0) and 12th month (P=0.85).

Table 8: Anthropometric and metabolic modifications in SG group.

	Before SG	3 days P.O. (7 patients)	5 days P.O	15 days P.O	30 days P.O	60 days P.O
BMI (kg)	44.76±7.2	-	-	43.3±7.7	40.1±7.8	31.52±6.8
Excess weight loss (%)	-	-	-	14.7±7.7	23.6±3.1	32.2±1.8
Serum FBG (mg/dL)	166±22.1	104.5±8.2	114.8±4	118.7±27.2	111±24.4	113±20.6
Serum insulin (mg/L)	41.8±13.2	12.6±3.2	14.8±7.9	26.3±13.6	20.4±10.9	29.8±20.6
HOMA IR	17.1±9.4	3.2±7.9	4.3±3.4	7.5±4.0	5.4±2.8	5.1±2.3

Table 9: %EWL, BMI, HbA1C, FBG at baseline, 2, 6 months postoperatively.

Variable	Preoperatively	2 mo	6 mo
%EWL	0	28.20±2.11 (n=30)	35.41±2.23 (n=29)
BMI (kg/m²)	46.12±10.86 (n=30)	38.27±6.59 (n=30)	35.78±5.11 (n=29)
HbA1c (%)	6.36±0.82 (n=14)	6.02±0.57 (n=11)	5.92±0.33 (n=12)
Fasting blood glucose (mg/dL)	158.93±19.65 (n=30)	139.83±12.03 (n=30)	128.34±7.03 (n=30)

Table 10: Changes in body weight,arterial blood pressure,and main biochemical parameters following LSG.

	Baseline N=25	3 months N=25	Change %	P-value	9-15 months N=15	Change %	P-value
BMI (kg/m²)	48±8	39±8	19	0.001	34±6	30	0.001
FPG (mg/dL)	131±42	87±19	33	0.008	91±20	31	0.01
FPI (mU/L)	20±13	6.5±5	68	0.005	2.5±0.7	87	0.001
HbA1c (%)	7.5±1.9	5.9±0.6	21	0.03	5.8±0.7	23	0.03
HOMA-IR	6.4±3.9	0.7±0.35	86	0.008	0.54±0.2	91	0.04

FPG: fasting plasma glucose
FPI : fasting plasma insulin

The improvement in insulin sensitivity is primarily due to weight loss, reduction in inflammatory mediators, and decreased calorie intake although the contribution of weight independent mechanisms seems very likely, rapid improvement of glucose hoemostasis before substantial weight loss has occurred [15].

Also, our study showed that the postoperative levels of postprandial blood glucose (PPBG) showed an improvement with a significant declining at one day (P<0.01), third month (P<0.001), sixth month (P<0.001) and ninth month (P=0.02) but non-significant at 12th month (P=1.0). (By researching we did not find a published data about PPBG levels after SG for comparing with our results).

In our study, postoperative improvement of glycated hemoglobin (HbA1C) levels was observed with a significant declining at one day (P<0.001), third month (P<0.001), sixth month (P<0.001), ninth month (P<0.001) and non-significant at 12th month (P=0.16).

A study, in 2008, reported that SG is associated with a high resolution of T2DM at short-term (4 months after surgery), and this resolution rate was comparable to that after GBP (51.4% and 62%, respectively, P=0.0332) [16]. In another study reporting at 12th month T2DM had resolved, respectively, in 33 out of 39 (84.6%) and 44 out of 52 (84.6%) of the SG and GBP subjects (P=0.618) [17].

Rosenthal et al. [13] in 2009, showed that the resolution of T2DM was observed in 27% at second month and 63% at sixth month of follow-up .

In our study the resolution of T2DM was 32.5% at third month, 72.5% at sixth month, 80% at ninth month and 80% at 12th month without hypoglycemic medications.

CONCLUSION

In our study the surgical procedure of laparoscopic sleeve gastrectomy resulted in marked weight loss and decrease in the body mass index which improved glucose homeostasis and remission of type 2 diabetes mellitus. Our study showed that the laparoscopic sleeve gastrectomy is associated with a high rate of resolution of Type 2 diabetes mellitus at 12th month after surgery in severely obese subjects with Type 2 diabetes mellitus.

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Author Contributions

Tarek Osama Hegazy – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ahmed Abd El-Halem Ewis – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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ABOUT THE AUTHORS

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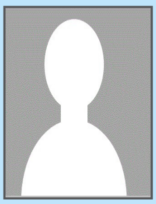
Tarek Osama Hegazy is lecturer in Department of Surgery, Kasr al-Aini School of Medicine, Cairo University, Cairo, Egypt. He earned undergraduate degree (MBBCH) from Kasr al-Aini School of Medicine and postgraduate degrees (MSc) and (MD) from Department of Surgery Kasr al-Aini School of Medicine, Cairo University, Cairo, Egypt and (MRCS) from Royal College of Surgery, London, England. He has published six research papers in national and international academic journals.



Ahmed Abdel Halem Ewis (MBBCH, MSc) is Specialist of General Surgery, and a faculty in Department of Surgery, Faculty of Medicine, Cairo University, Egypt. His field of interest includes researching management of comorbidities of morbid obesity.

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