Evaluation of the Impact of Sleeve Gastrectomy on Type 2 DM in Morbidly Obese Patients

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ABSTRACT

Background: *There is evidence that obesity worsens the metabolic abnormalities associated with Type 2 DM including hyperinsulinemia, hyperglycemia, hypertension, and hyperlipidemia. Recent studies had showed that diabetes resolve or improve in patients undergoing bariatric surgery.* ***Aim:*** *to evaluate the effect of sleeve gastrectomy on control of blood sugar in type 2 DM through follow up of serum level of glycated hemoglobin (HbA1c) and fasting blood sugar changes with excess body weight loss.* ***Patients & methods:*** *A prospective observational study done between June 2012 and September 2014, at Ain Shams university hospitals, Cairo, Egypt. It included forty morbidly obese patients with type 2 DM. Laparoscopic sleeve gastrectomy was done for all patients. The patients were followed up for postoperative morbidity, weight loss and improvement or resolution of diabetes (using blood sugar & glycated hemoglobin measurement).* ***Results:*** *40 morbidly obese, type 2 DM patients were included in the study. 28 patients (70%) showed complete resolution of DM while 12 patients (30%) showed improvement. A statistically significant difference was seen between resolved and improved groups regarding the duration of DM (less than 5 years), type of DM medication (better with oral hypoglycemic agents), status of DM control (controlled) and distribution of obesity (central type).* ***Conclusion:*** *Laparoscopic sleeve gastrectomy achieves good short term results in control of type 2 DM. Findings indicated that preoperative glycemic control and duration of the disease and the type of T2DM therapy used are important predictors of remission of the disease for patients who underwent laparoscopic sleeve gastrectomy.*

Key words: *sleeve gastrectomy, type 2 DM, morbid obesity.*

INTRODUCTION

Obesity is increasing in epidemic proportions worldwide. Because obesity causes a variety of medical disorders, including hypertension and diabetes, it is feared that it will replace smoking as the most important reversible cause of reduced longevity[1]. It has been estimated that more than 70% of all individuals who have T2DM are overweight and that one third are obese. There is an evidence of intrinsic interrelationship in terms of genetics, environment and pathophysiology between obesity and T2DM, which has been termed "diabesity''[2]. Furthermore, there is evidence that obesity worsens the metabolic abnormalities often associated with T2DM including hyperinsulinemia, hyperglycemia, hypertension, and hyperlipidemia [3].

Several studies had shown that weight loss have a favorable effect on DM. Among British men aged 40 to 59 years who were followed for a mean period of 12 years, weight loss of more than 4% during the first 5 years of follow-up showed a 1-5-times reduced risk for developing T2DM compared with that in men who had stable weight[4]. Bariatric surgery is now thought to have significant impact on treatment of type 2 DM. In a recent meta-analysis, diabetes was completely resolved in 76.8% and resolved or improved in 86 % of patients who underwent bariatric surgery [5]. At the present time, a number of different surgical procedures are available for treatment of severely obese patients. These procedures create weight loss by two mechanisms of action; restriction and mal-absorption [6].

The laparoscopic sleeve gastrectomy is a restrictive intervention consisting of a vertical gastrectomy including the entire greater curvature of the stomach while leaving in place an approximately 100-ml gastric tube along the lesser curvature [7,8].

The aim of this study is to evaluate the effect of sleeve gastrectomy on control of blood sugar in type 2 DM through follow up of serum level of glycated hemoglobin (HbA1c) and fasting blood sugar changes with excess body weight loss.

PATIENTS & METHODS

The study was a prospective observational study done between June 2012 and September 2014, at Ain Shams university hospitals, Cairo, Egypt. The study included forty morbidly obese type 2 diabetic patients. Inclusion criteria included 1) Age between 18 and 65 years, 2) BMI ≥ 35, 3) Type II DM on medical treatment, 4) Have no contraindication for general anesthesia, 5) Absence of other endocrine disorders that can cause obesity as hypothyroidism, Cushing syndrome, polycystic ovarian syndrome, and hypothalamic disorders. The following patients were excluded from the study: 1) Type I DM patients, 2) Diet controlled diabetes (not receiving medications), 3) Patients with extensive upper abdominal adhesions (previous attacks of severe pancreatitis or upper abdominal surgeries), 4) Patients with severe gastroesophageal reflux disease. 5) Patients who had previous gastrectomy, previous gastric bypass, barrett's esophagus, achalasia and severe gastric atony.

Preoperative workup

All patients were subjected to complete clinical assessment including full history taking (with emphasis on feeding history and if the patient is sweet eater or not, duration of obesity, history of previous trials of weight loss whether surgical or non-surgical) together with medical history for comorbidities especially DM (type, onset, course, duration, current medications, controlled or not), hypertension, cardiac and respiratory problems, family history of obesity, previous DVT and past surgical history. Complete physical examination including weight and height measurement and calculation of BMI, assessment of type of obesity (android or peripheral), abdominal examination for (scar of previous surgery, hernial orifices and organomegaly) and cardiac and pulmonary evaluation was also done. Medical consultation for proper control of blood sugar was done. Investigations included Laboratory investigations: complete blood picture, Blood sugar (fasting and 2 hours postprandial), liver function tests, renal function test, coagulation profile, serum calcium, HbA1c, lipid profile, thyroid function tests and other investigations as chest X-ray, ECG, Abdominal u/s, pulmonary function test and Echocardiography for patients above 40 or cardiac history. Upper gastrointestinal endoscopy was done for all patients. Low molecular weight heparin (Enoxaparin 40 mg subcutaneous) was given 12 hours prior to surgery. Prophylactic antibiotic was given with induction of anaesthesia (cefotaxime 2gm i.v.).

The operation was done by the standard laparoscopic technique via Verress needle placed in the left subcostal region at the mid-clavicular line. A five-port technique was employed. Dissection begin with opening of the greater omentum using Ligasure along the greater curvature of the stomach 6 cm proximal to the pylorus and continued cephalad to the gastro-esophageal junction and the left crus. Passage of a 36 French bougie through the esophagus and the stomach and into the pylorus aligned along the lesser curvature was done. Gastric transection is completed using sequential firings of the Endo-GIA. After completing the transection, the entire staple line is inspected carefully to make sure that the staples are well formed. The transected stomach was removed through by enlarging the supra-umbilical port site incision.

After completion of the gastric transection the integrity of the staple line is tested by methylene blue injected into the stomach.

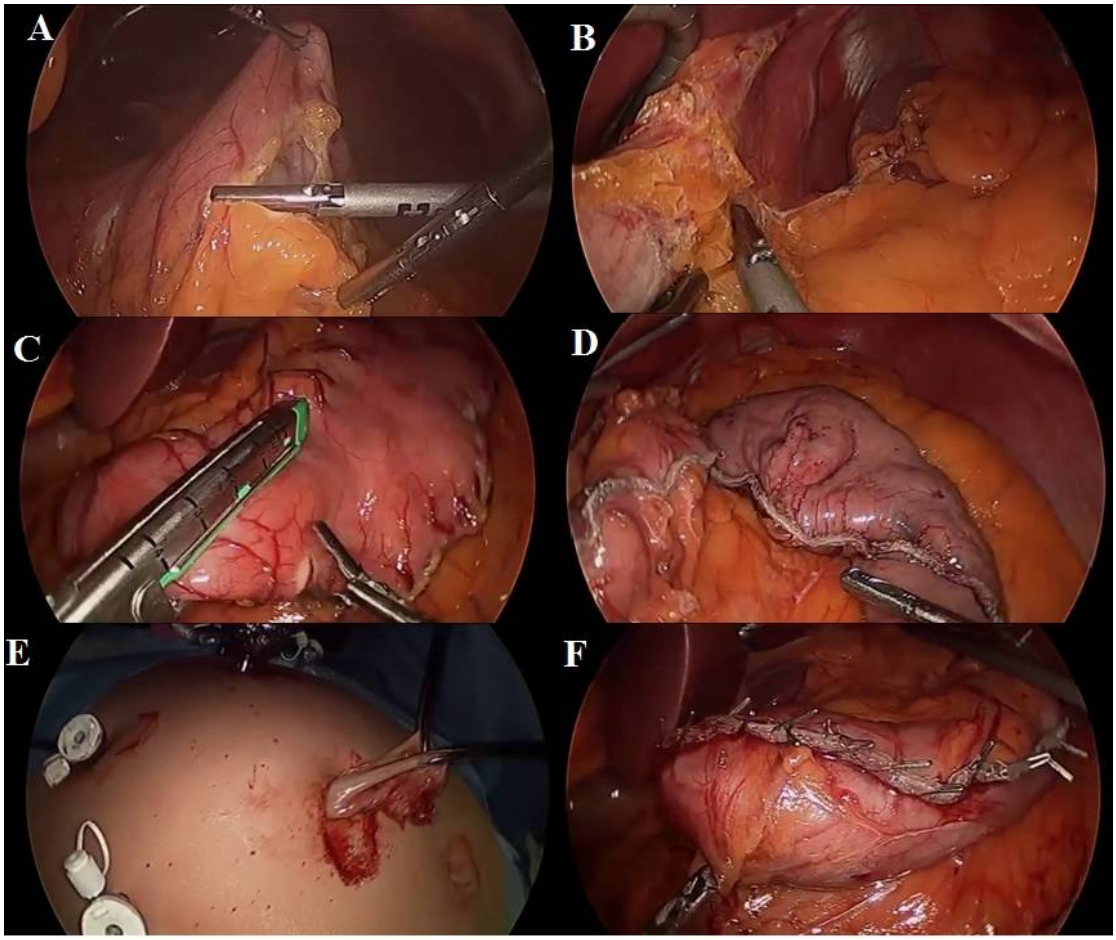

Fig. 1: Different steps of LSG: **A:** Opening of greater omentum using ultrasonic dissector, **B:** Left crus is completely freed of any attachment. **C:** Endo-GIA stapler is applied across the antrum. **D:** After completion of gastric transection. **E:** Stomach retrieval through port site incision. **F:** Gastric pouch distended with methylene blue to test for leak (clips were applied to stomach edge for better hemostasis).

Postoperative care

Close observation for vitals (ICU admission if indicated) was done. Continuation on insulin sliding scale with RBS measurement every 6 hours was done along with chest physiotherapy, early mobilization and low molecular weight heparin administration until full mobilization. Close monitoring for evidence of leak (fever, tachycardia, and severe abdominal pain) was done. Gastrografin study was done on second postoperative day as a routine to rule out leak before starting oral intake. Patients were discharged after full ambulation and proper oral fluid intake. Medical consultation was done before discharge for postoperative regimen for blood sugar control and for planning for regular follow up visits with medical team.

Feeding protocol was explained to the patients. The recommended feeding protocol was divided into 4 stages as follows: *Stage 1*: Liquid diets for 2 weeks. *Stage 2*: Pureed diet for 2 weeks. *Stage 3*: Semisolid diet for 4 weeks. *Stage 4*: Regular diet (avoid high calorie diet like sweets).

Follow up of cases

Follow up visits in outpatient department were done at 1 week postoperative, then 1, 3, 6 and 12 months. Detection of any postoperative complications was done. Measurement of body weight, excess weight loss and BMI was done with each visit together with measurement of

HbA1c and RBG at 3, 6 and 12 months and follow up of changes in dose or discontinuation of anti-diabetic medications. On the postoperative evaluation, DM was considered resolved in patients with a fasting blood glucose level < 126 mg/dl and HbA1c level below 6.5% in absence of any hypoglycemic medication (In accordance with the International Diabetes Federation and American College of Endocrinology recommendations for target of diabetes control [9]). DM was considered improved if a reduction in the HbA1c and/or FBS had occurred but still above the reference level estimated for resolution. DM was considered unchanged if no resolution or improvement criteria were identified. The patients were divided into groups according to the final outcome and patients' characteristics were compared in these groups to determine the patient characteristics that might have a significant impact on the final effect of sleeve gastrectomy on DM.

Statistical Analysis:

Relevant preoperative, operative and postoperative data were collected, tabulated and statistically analyzed. Categorical variables were compared with the X2 test and continuous variables were compared with the paired t-test. P value <0.05 was considered statistically significant.

RESULTS

The study included 40 morbidly obese patients, type 2 DM on medical treatment. The group age ranged between 19-55 years with a mean ± SD of 34.88 ± 9.53 years. The group BMI ranged between (36.1-55.7 kg/m²) with a mean ± SD of 44.86 ± 5.83 kg/m². The group excess weight ranged between (28.4-87.6 kg) with a mean ± SD of 52.35 ± 17.14 kg. Of the 40 patients, 28 (70%) were women and 12 (30%) were men. 11 patients (27.5%) had central obesity, 3 patients (7.5%) had peripheral obesity and 26 patients (65%) had both. The characteristics of the study group regarding different aspects of diabetes are shown in table (1).

Table (1): Characteristics of the study group regarding different aspects of diabetes.

Patients' characteristics	**Mean ± SD (Range)**	
HbA1c(%)	7.65 ± 0.48 (6.7-9)	
FBS(mg/dl)	157.73 ± 10.16 (138-179)	
Patients' characteristics	**Percentage (%)**	**Number of patients (n)**
Preoperative DM medications	OHA 72.5% (n=29)	Insulin 27.5% (n=11)
Duration of DM	< 5 years 55% (n=22)	> 5 years 45% (n=18)
Family history of DM	Positive 62.5% (n=25)	Negative 37.5% (n=15)
Status of DM	*Controlled 70% (n=28)*	*Uncontrolled 30% (n=12)*

The mean operative time was 90 minutes (range 55-180), and all operations were performed laparoscopically except for two cases (5%) that were converted to open surgery, one because of uncontrolled bleeding from short gastric vessels and the second because of stapler failure. No mortality was recorded in the study. Average estimated blood loss was < 50 cc for all cases except for the two patients converted to open where first patient lost about 700 cc of blood and second patient lost 400 cc. No other intraoperative complications were encountered in the study.

Regarding the weight loss results, the mean BMI had decreased to 42.365 ± 5.829 kg/m² after 1 month, to 39.27 ± 5.48 after 3 months, to 36.06 ± 5.525 after 6 months and finally to 33.025 ± 4.584 after 12 months. The mean excess weight loss (EWL%) after 1 month was 13.22 ± 4.587 %, 28.99 ± 10.573 % after 3 months and was 46.31 ± 17.777 % and 60.835 ± 19.565 % after 6 and 12 months respectively (figure 2).

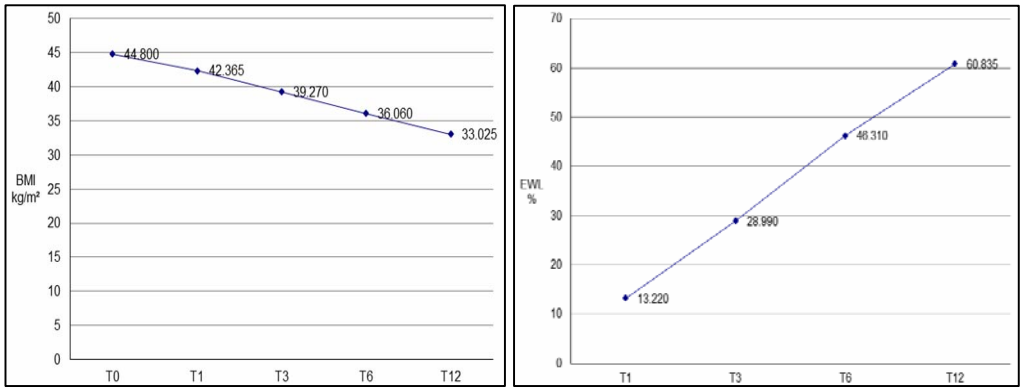

Fig. 2: Mean BMI & excess weight loss trends in the study.

Regarding Blood sugar and HbA1c trends, the mean FBS had decreased to 130.975 ± 10.027 mg/dl at 3 months and to 117.65 ± 10.027 mg/dl after 6 months and to 111.825 ± 14.775 mg/dl after 12 months. The mean HbA1c had decreased to 6.81 ± 0.416 % after 3 months and to 6.333 ± 0.403 % after 6 months and finally to 6.218 ± 0.518 after 12 months (figure 3).

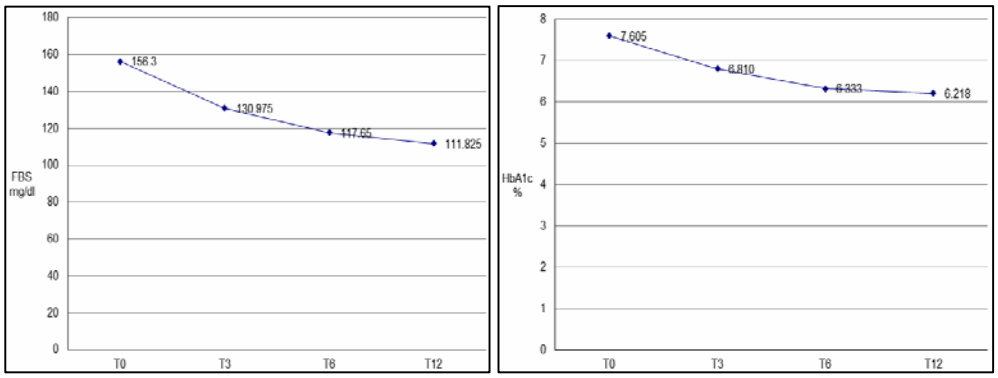

Fig. 3: Mean fasting blood sugar & HbA1c level trends in the study.

Clinical resolution or improvement in DM occurred in all patients evaluated by the study. 28 patients (70%) showed complete resolution in the form of HbA1c<6.5% and FBS<126 mg/dl without any diabetic medications. 12 patients (30%) showed improvement in HbA1c and FBS levels but still above the reference level which is 6.5% for HbA1c and 126 mg/dl for fasting blood sugar (figure 4).

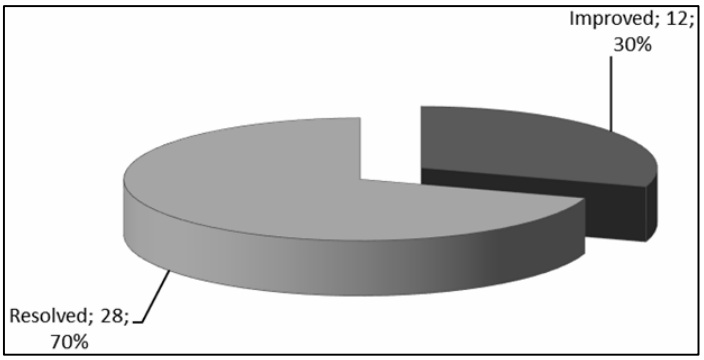

Fig. 4: Diabetes status after surgery (total population).

To find the predictors of outcome, the forty patients were divided into two groups regarding final outcome (resolved or improved). This outcome is compared between both groups in association with patient characteristics to identify predictors of outcome for complete resolution of type 2 DM. Univariate analysis revealed no statistically significant difference between both groups as regard gender, age, height, weight, BMI, excess weight, baseline FBS and baseline HbA1c level. On the other hand, univariate analysis revealed that there was a statistically significance between resolved and improved groups regarding the duration of DM (less than 5 years), type of DM medication (better with oral hypoglycemic agents), status of DM control (controlled) and distribution of obesity (central type) denoting that these parameters can be predictors for occurrence of full resolution of DM after sleeve gastrectomy (table 2).

Table (2): The result of multivariate analysis of different factors affecting the DM improvement outcome (NS: none significant, S: significant, HS: highly significant, OHA: oral hypoglycemic agent).

Outcome		**Improved**	**Resolved**	**Chi-square**		
		Number		**X^2**	**P-value**	**significance**
Gender	**Female**	7	21	1.08	0.299	NS
	Male	5	7			
Duration of D.M	**<5 years**	3	19	6.23	0.013	S
	>5 years	9	9			
D.M medication	**OHA**	7	22	1.66	0.0198	NS
	Insulin	5	6			
Diabetes control	**Controlled**	0	28	48.87	<0.001	HS
	Not	12	0			
Distribution of obesity	**Central**	0	11	9.62	0.008	HS
	Peripheral	1	2			
	Both	11	15			
		Improved	**Resolved**	**T-test**		
		Mean ±SD		**T**	**P-value**	**significance**
Age		37.917±9.346	31.857±9.717	1.83	0.076	NS
Weight (kg)		116.958±18.943	118.804±22.382	-0.25	0.804	NS
Height (m)		160.917±8.262	162.786±8.408	-0.65	0.521	NS
BMI (kg/m2)		45.058±5.027	44.689±6.640	0.17	0.864	NS
Excess weight (kg)		52.100±15.001	52.357±19.257	-0.04	0.967	NS
FBS (mg/dl)		161.333±8.948	154.143±11.398	1.94	0.060	NS
HbA1C (%)		7.783±0.486	7.529±0.499	1.49	0.144	NS

DISCUSSION

Sleeve gastrectomy (SG) recently, has been indicated as a definitive treatment in patients with BMI >35 kg/m2 or BMI>30 kg/m2 associated with co-morbidities, and it has been proposed for patients with moderate obesity BMI >35 kg/m2 and metabolic syndrome [10]. SG can be performed by an open laparotomy or by laparoscopy (LSG) [11]. Because of the relative technical ease of performance compared to other bariatric procedures, acceptable operative time, low complication rate and reports of average excess weight loss of 51-83% at 1 year with improvement in co-morbidities, many surgeons began to consider LSG as a primary single-stage restrictive procedure [10].

In our study the mean operative time was 90 minutes (range 55-180), and all operations were performed laparoscopically except for two cases that were converted to open (5%), one because of uncontrolled bleeding from short gastric vessels

and the second because of stapler failure. The average estimated blood loss was < 50 cc for all cases except for the two patients converted to open where first patient lost about 700 cc of blood and second patient lost 400 cc. No major intra or post complications or mortality were recorded in the study.

Gumbs and his colleagues reported the incidence of complications among 646 patients who underwent SG. Morbidities included leak (0.9%) , strictures (0.7%), postoperative bleeding (0.3 %) , pulmonary embolism (0.3%) , delayed gastric emptying (0.3%), intra-abdominal abscess (0.1%), wound infection (0.1%), splenic injury (0.1%) ,and trocar site hernia (0.1%). mortality (0.6%), conversion (0.1%) [12]. These data goes in agreement with our data and suggest the safety of SG as a bariatric procedure, except for conversion rate in our study (5%) which is relatively high compared with other studies but this could be attributed to the small sample size in our study.

In analysis of postoperative data and outcome, the BMI showed a decrease from a mean preoperative value 44.8 ± 6.139 to 33.025 ± 4.584 kg/m² after 1 year with average excess weight loss of 60.835 ± 19.565 % at the end of the 12 months postoperative follow up period. Other published studies of outcomes after SG had reported a mean excess weight loss of 63% after 12 months [12], which is similar to our results. This can be attributed to the fact that LSG is less complex and easy to master operation, so most series report generally similar short term results.

Regarding the control of DM during the follow up period, the overall DM resolution or improvement was 100%, with 70% of patients showing complete resolution and 30% of patients showing improvement within one year. Study of changes in blood sugar during follow up period, showed that there was a drop of fasting blood sugar (FBS) from a mean baseline value of 156.3±11.12 mg/dl to 111.825±14.775 mg/dl at 1 year with a decrease of HbA1c from a baseline value of 7.605 ± 0.503 % to 6.218±0.518 at 1 year. A systematic review of the existing evidence has suggested that LSG for morbid obesity results in resolution or improvement of type II DM in most patients with results generally similar to ours. Although approximately two thirds of the patients experienced complete DM resolution, the remaining one third of patients had significant improvement [13].

To identify the predictors for complete resolution of DM, the forty patients were divided into two groups regarding the final outcome (resolved or improved) and the groups were compared in association with patients' characteristics. The analysis had showed that for sleeve gastrectomy, the T2DM remission rate was higher for patients with a shorter duration of disease (<5 years), better preoperative glycemic control (controlled) and central distribution of obesity. In addition, patients with T2DM requiring insulin treatment were associated with lower rate of remission compared with those on oral hypoglycaemic agent therapy. The published data shows similar results to those of our study. A systematic review of the existing evidence had suggested that LSG for morbid obesity results in resolution or improvement of type II DM in most patients. Although approximately two thirds of the patients experienced complete DM resolution, the remaining one third of patients had significant improvement[14]. These observations are in agreement with previous reports and suggest that the remaining functional pancreatic β cell mass is an important predictor factor for T2DM after surgery and should be considered preoperatively[15]. Also, Schauer and his colleagues found that after laparoscopic Roux-en-Y gastric bypass, patients with a shorter duration of disease had better outcomes. They also reported that patients with less severe disease can be expected to have a better resolution rate, suggesting the importance of early surgical intervention. Patients with DM for <5 years had better improvement and resolution rates. Early surgical intervention in patients with DM has been suggested by different studies [16].

The results of this study suggest that LSG can be considered as a standard treatment for DM in morbidly obese patients who are appropriate surgical candidates.

In Conclusion LSG had an overall DM resolution or improvement of 100%, with (70%) showing complete resolution and (30%) of patients showing improvement after one year. Findings indicate that the clinical features of T2DM (preoperative glycemic control, duration of the disease and the type of T2DM therapy used) are important predictors of remission of the disease for patients who underwent LSG. Remission rate was higher for patients with a shorter duration of disease (<5 years) and with

better preoperative glycemic control (controlled) and patients with central distribution of obesity. Cases with T2DM requiring insulin were associated with lower rate of remission compared with cases on oral hypoglycemic agent therapy.

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