

Original Article

Factors Determining Diabetic Remission after Sleeve Gastrectomy: A Prospective Study

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Received : 01-03-2019
Revision : 08-07-2019
Accepted : 19-09-2019
Published : 10-02-2020

INTRODUCTION

The epidemic rise in obesity prevalence in the late 1970s fuelled the debate to classify it as a disease; and in 1985, obesity was officially classified as a disease. The World Health Organization has described obesity as one of the today's most neglected public health problems, affecting every region of the globe.^[1] The problem of obesity has been observed to have a rising trend in the entire Indian subcontinent.^[2] Obesity is calculated as body mass index (BMI), and persons with BMI >30 kg/m² are considered as obese. Morbid obesity (BMI >40 kg/m²) is the harbinger of many diseases that affect essentially every organ systems such as cardiovascular, respiratory,

metabolic, musculoskeletal, endocrinal, reproductive, dermatological, neurological, and many more.^[3]

There are both nonsurgical and surgical interventions available at our disposal aimed at countering this ever-increasing global epidemic. However, surgical procedures have now superseded nonsurgical measures such as pharmacotherapy, dietary, and behavioral modifications. In 1991, the National Institute of Health Consensus stated that bariatric surgery is the

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How to cite this article: Jindal R, Gupta M, Ahuja A, Nain PS, Sharma P, Aggarwal A. Factors determining diabetic remission after sleeve gastrectomy: A prospective study. *Niger J Surg* 2020;26:66-71.

ABSTRACT

Background: An exponential rise in the prevalence of obesity and the associated type 2 diabetes mellitus (T2DM) has led to an explosion in the field of bariatric surgery worldwide. It has been proposed that laparoscopic sleeve gastrectomy (LSG) not only results in excess weight loss (EWL) but also leads to excellent glycemic control. **Aims:** However, not every patient benefits from the bariatric surgery. Furthermore, bariatric surgery is currently indicated based on body mass index (BMI), but BMI solely does not predict diabetes remission after the surgery. We aimed to study the outcome of LSG on the diabetic status and the factors predicting the disease remission. **Subjects and Methods:** This prospective study was conducted on 104 obese patients having T2DM who underwent LSG. Following surgery, the clinical outcome on weight loss, BMI, and glycemic control was studied for 6 months. Various positive and negative predictors of diabetic remission after the surgery were also determined. Student's *t*-test and Chi-square tests were applied. **Results:** LSG resulted in significant weight loss ($P < 0.05$); the percentage of EWL was 60.75 ± 6.30 at 6 months. Furthermore, surgery resulted in 78.9% remission of diabetes with fasting blood glucose and glycated hemoglobin values at 6 months being 121.13 ± 15.25 mg/dl and $6.19\% \pm 0.31\%$, respectively. Younger and heavier patients, those with lesser disease severity and shorter duration had better chances of disease remission. Gender had no correlation with disease remission. **Conclusion:** LSG is a successful treatment option for T2DM and is more beneficial if offered, not as a last option, but to younger, obese patients with mild disease severity and shorter disease duration after the failure of medical treatment.

KEYWORDS: *Bariatric surgery, diabetes remission, laparoscopic sleeve gastrectomy, predictor, type 2 diabetes mellitus*

Access this article online	
Quick Response Code: 	Website: www.nigerianjsurg.com
	DOI: 10.4103/njs.NJS_9_19

most effective treatment for morbid obesity leading to excellent long-term sustained weight loss along with the reduction of comorbidities and recommended surgery for obesity at a BMI of 40 kg/m² or a BMI >35 kg/m² with any comorbid conditions.^[4]

Obesity and type 2 diabetes mellitus (T2DM), both highly prevalent diseases, are very closely related and pose a serious threat to the health of an individual. There is seen an improvement in the clinical status of patients as various comorbid conditions respond to bariatric procedures such as hypertension, DM, and dyslipidemia. There is strong evidence that bariatric surgeries can treat most of the associated T2DM in morbidly obese patients.^[5] The reduction of mortality by bariatric surgery is mostly attributed to the reduction in diabetes-related death.^[6]

The remission of diabetes has been found to be associated with a range of excess weight loss (EWL) after surgery.^[7] However, optimal outcomes for diabetes remission after bariatric surgery will occur if patients who are best suited to the surgery are selected, and those who are not likely to benefit much are spared the procedure. Factors, such as old age, a longer T2DM history, and the use of insulin, reflect a destroyed beta-cell mass. These were the negative predictors of disease remission in the previous studies concerning bariatric surgery on morbidly obese patients.^[5,8] Using this type of predictor, it is possible to select patients that are best suited for the surgery and exclude those who would give poor results.^[9]

With the increasing burden of obesity and a paralleled increase in bariatric procedures worldwide, it is crucial to study the clinical outcome of bariatric surgery such as diabetes remission. Furthermore, it is necessary to determine the factors that are associated with diabetes remission following bariatric surgery, so as to be able to choose patients that are most likely to benefit from bariatric surgery.

Our study aimed at determining the status of T2DM following laparoscopic sleeve gastrectomy (LSG) and also, the factors that predetermine the remission of diabetes after surgery.

SUBJECTS AND METHODS

This prospective study was conducted between July 2013 and October 2017 on 104 obese patients who underwent LSG, and these patients were followed up for 6 months postoperatively. Approval was obtained from the institutional ethics committee. All the patients with BMI >35 kg/m² having T2DM were included in the study. Patients with a history of bariatric surgery,

those who suffering from terminal illness such as advanced-stage cancer or end-stage cardiac/renal disease and patients with psychiatric illness and active substance abuse were excluded from the study.

After obtaining written informed consent, particulars of the patient were duly noted, and a detailed history including symptoms, coexisting comorbid conditions, personal habits such as smoking or alcohol consumption, and treatment history was taken. The patient's history with respect to DM included type, duration, insulin dose and frequency, and dose of oral hypoglycemic agents (OHA). All patients underwent a comprehensive multidisciplinary bariatric evaluation by a dedicated bariatric team which included a bariatric surgeon, dietician, endocrinologist, gastroenterologist, psychiatrist, chest physician, anesthesiologist, and the cardiologist. The various sociodemographic characteristics and clinical parameters noted were age, gender, height, weight, fasting blood sugar (FBS) levels, and glycated hemoglobin (HbA1c) values. BMI was calculated from weight and height of the patient using the formula: BMI = weight/(height)².

After a detailed preanesthetic checkup and a written informed consent, patients were taken up for LSG. LSG was chosen as the procedure of choice here, given the fact that it has the least complication rate along with the easiness and shorter duration of surgery. The patients underwent a standard LSG using 2–12 mm ports, 1–5 mm ports, and a Nathanson liver retractor. Starting at a point on the greater curvature, 4–8 cm from the pylorus, 75%–80% of the greater curvature was excised using laparoscopic staplers leaving a narrow stomach tube. Postoperatively, patients were encouraged early ambulation, preferably on the same day of the surgery. Patients were started on liquid diet orally the next day of surgery after ruling out any leak on oral gastrografin study done on postoperative day 1.

Postoperatively, trends of the following parameters were studied at various intervals till 6 months: weight, BMI, FBS levels, HbA1c levels, and dose of insulin/OHAs.

Diagnostic, resolution, and improvement criteria for type 2 diabetes mellitus

Definition of diabetes: Treatment with OHA or insulin or HbA1C >6.5%.^[10]

Resolution criteria: HbA1c <6.5% without drug therapy.

Improvement criteria: Decrease in medication or HbA1c decrease >1% with no change in medication.

Depending on diabetes status in the postoperative period, patients were categorized into remission and nonremission groups.

Statistical analysis

Data analysis was done using SPSS software (IBM SPSS statistics for windows, version 20.0 Armonk, NY: IBM Corp). Student’s *t*-test and Chi-square tests were applied.

RESULTS

Of 104 patients, 62 (60%) patients were male and rest 42 (40%) were female. The mean age of patients was 47.02 ± 3.59 years. Mean weight, height, and BMI were 129.1 ± 10.2 kg, 1.60 ± 0.07 m, and 50.38 ± 4.95 kg/m², respectively. Mean FBS and HbA1c levels were 184.77 ± 17.7 mg/dl and $9.26\% \pm 0.92\%$, respectively. The mean duration of T2DM was 5.56 ± 3.27 years [Table 1].

Clinical outcome

A significant difference was noticed between the preoperative and postoperative values of mean weight

and mean BMI at 3 months and 6 months after the surgery [Table 2]. Reduction in the mean weight from a preoperative value of 129.1 ± 10.2 kg to postoperative value of 105.85 ± 10.30 kg at 3 months and 85.72 ± 9.65 kg at 6 months was found to be statistically significant. Furthermore, the values of mean BMI decreased significantly to 44.35 ± 4.56 kg/m² at 3 months and 36.58 ± 3.82 kg/m² at 6 months from a preoperative value of 50.38 ± 4.95 kg/m². LSG resulted in significant weight loss ($P < 0.05$); the percentage of EWL was 60.75 ± 6.30 at 6 months. This signifies the role of LSG as bariatric surgery.

Subsequent to surgery, fall in HbA1C and FBS levels were significant both at 3 months ($P < 0.0001$) and 6 months ($P < 0.0001$) postoperatively [Table 2]. HbA1C values decreased from a preoperative value of $9.26\% \pm 0.92\%$ to $7.26\% \pm 0.57\%$ and $6.19\% \pm 0.31\%$ at 3 and 6 months, respectively. A significant decline in the FBS levels at 3 months (150.80 ± 14.35 mg/dl) and at 6 months (121.13 ± 15.25 mg/dl) was also seen from a value of 184.77 ± 17.7 mg/dl prior to surgery. This signifies that LSG surgery resulted in the resolution of diabetes at 6 months after surgery.

Diabetic status

Of 104 patients, diabetes was completely resolved in 82 patients (78.9%) at 6 months after surgery and in the remaining 22 patients (21.1%), diabetic status was improved, out of which 12 patients had the dose of insulin decreased, and ten patients were switched over to OHAs [Figure 1].

Predictor analysis for diabetes remission

Five preoperative factors were found to likely predict diabetes remission after LSG. These included age, BMI, HbA1c, FBS levels, and duration of T2DM. Table 3 shows their mean preoperative values in both the remission and nonremission groups and the difference in them being significant.

Results showed that younger patients and patients with higher BMI values had better remission rates of diabetes than their older and lower BMI counterparts. Other positive predictors of diabetes remission after

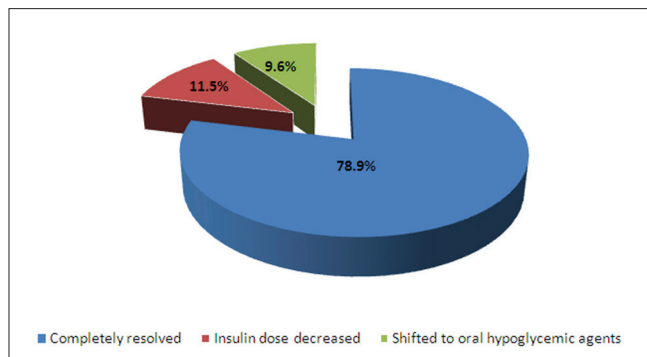


Figure 1: Diabetic status

Table 1: Patient’s preoperative characteristics

<i>n</i>	104
Male, <i>n</i> (%)	62 (60)
Females, <i>n</i> (%)	42 (40)
Mean age (years)	47.02 ± 3.59
Mean height (m ²)	1.60 ± 0.07
Mean weight (kg)	129.1 ± 10.2
Mean BMI (kg/m ²)	50.38 ± 4.95
Mean fasting glucose (mg/dl)	184.77 ± 17.7
Mean DM duration (years)	5.56 ± 3.27
Mean HbA1c (%)	9.26 ± 0.92

BMI: Body mass index, DM: Diabetes mellitus, HbA1c: Glycated hemoglobin

Table 2: Clinical outcomes

Clinical parameter	Mean			<i>P</i>	
	Preoperative	Postoperative at 3 months	Postoperative at 6 months	Preoperative versus 3 months	Preoperative versus 6 months
Weight (kg)	129.1 ± 10.2	105.85 ± 10.30	85.72 ± 9.65	<0.0001	<0.0001
BMI (kg/m ²)	50.38 ± 4.95	44.35 ± 4.56	36.58 ± 3.82	<0.0001	<0.0001
HbA1c (%)	9.26 ± 0.92	7.26 ± 0.57	6.19 ± 0.31	<0.0001	<0.0001
Fasting glucose levels (mg/dl)	184.77 ± 17.7	150.80 ± 14.35	121.13 ± 15.25	<0.0001	<0.0001

BMI: Body mass index, HbA1c: Glycated hemoglobin

Table 3: Predictor analysis of diabetes remission

Factor	Mean		P, χ^2
	Remission (n=82)	Nonremission (n=22)	
Age (years)	45.54±2.03	52.54±2.57	<0.0001
Gender			
Male	25	6	0.699, 0.149
Female	16	5	
Diabetes duration (years)	4.01±1.11	11.26±2.01	<0.0001
BMI (kg/m ²)	51.95±4.18	44.47±2.57	<0.0008
FBS (mg/dl)	179.94±16.62	202.73±6.47	<0.0005
HbA1c (%)	9.08±0.81	9.945±1.05	0.004

BMI: Body mass index, FBS: Fasting blood sugar,
HbA1c: Glycated hemoglobin

LSG included preoperative HbA1c, FBS levels, and the duration of DM. Patients with higher values of FBS and/or HbA1c had lesser chances of diabetes remission than those with lower values. Furthermore, the results showed that patients with a shorter history of diabetes received more benefits of the bariatric surgery in terms of resolution of the disease. However, no association was found between gender and postoperative outcome of diabetes remission after LSG.

DISCUSSION

Speculations do not exist regarding the emerging role of bariatric surgery in the treatment of DM. The most widely performed bariatric procedures are Roux-en-Y gastric bypass, adjustable gastric banding, biliopancreatic diversion (with or without duodenal switch), and sleeve gastrectomy.^[11] LSG, a bariatric procedure is being performed since 1999.^[12] Earlier LSG was performed for high-risk patients or as an adjunctive surgical procedure to biliopancreatic diversion in high-risk cases. Now, it is a preferred procedure for common morbid obesity even in low-risk patients due to its cost, safety, and effectiveness in weight reduction.

The most conspicuous outcome of LSG is the reduction in body weight. Weight loss is the most important factor that determines whether a procedure succeeds as bariatric surgery or not. Our study shows a significant reduction of both mean weight and BMI postoperatively, which ascertain the relevance of LSG as a bariatric procedure. Similar results were also seen in studies by Gluck *et al.*,^[13] and Boza *et al.*^[3] A reduction of BMI by 5% corresponds to a 33% reduction of T2DM.^[14] In addition to a significant reduction in FBS levels, a significant reduction in HbA1c values was also seen, both at 3 months' and 6 months' postoperatively. The diabetic cure rate at 6 months was 78.9%, whereas improvement in the diabetic status was seen in all the

104 patients. This validates LSG as a treatment option for diabetes. These results are consistent with a study by Abbatini *et al.*,^[15] who observed a diabetic remission rate of 80.9% after LSG. Furthermore, 100% diabetes resolution rate was seen in a study by Omana *et al.* after LSG in patients with diabetes.^[16] Many other authors also noted a significant reduction in HbA1c and FBS values after LSG.^[8,17,18]

Weight loss after LSG is attributed to reduced size and decreased distensibility of the stomach. Furthermore, LSG leads to accelerated gastric emptying, which may alter the regulatory neurohormonal mechanisms such as GLP-1 hormone production from the distal gut and thus contributing to weight loss and better glucose metabolism. LSG patients experience early satiety and less hunger drive due to decreased levels of ghrelin, a hunger stimulatory hormone produced by P/D1 cells in the fundus of stomach and epsilon cells in pancreas.^[19] Alteration in the composition of gut microbiota after bariatric surgery may also play a role in the diabetic remission and weight loss.^[20]

Predictor analysis done in our study showed that age, BMI, duration of T2DM, HbA1c, and FBS levels to be positive predictors of diabetic remission after LSG, whereas gender had no correlation with remission. In a recent study, Dixon *et al.* revealed glycemic response after bariatric surgery to be associated with BMI, disease duration, fasting C-peptide levels, and degree of weight loss.^[21] The age was found to be a significant predictor of diabetes remission in a study on the Asian population.^[6] Like in our study, other studies also confirm higher remission rates with younger age.^[22,23] Remission rates of DM dropped by 12% on addition of 12 years of age in a study by Hamza *et al.*,^[24] the rationale being higher beta-cell reserve in younger patients. However, Hamza *et al.* also showed female gender to be a positive predictor of diabetes remission; this was not the case in our study. Jurowich *et al.* also concluded that the gender was a negative predictor of disease remission.^[25]

We also noticed in our study, that patients with lower BMI had lower remission rates than those with higher BMI. Similar findings were observed for the 1st time by Lee *et al.*^[26] Higher BMI is usually associated with greater weight loss and hence, the higher remission rates. However, controversy exists, where Mingrone *et al.* found remission and BMI to be inversely related.^[27] Robert *et al.* found that super morbid obesity (BMI > 50) to be a negative predictor of DM remission.^[28] This may be explained by the fact that higher BMI means severe insulin resistance and/or a greater destroyed beta-cell mass.

Higher FBS and HbA1c values indicate severe disease status and thus, a higher insulin resistance state along with a lower beta-cell functional reserve. This decreases the likelihood of disease remission, as was found in our study. This is in accordance with many authors who report higher remission rates with lower HbA1c values.^[8,29,30]

Like us, many authors also supported in their studies that the duration of T2DM is an important predictor of disease remission.^[5,8,31] The most important finding in a study by Lee *et al.* included T2DM duration to be the most important predictor of diabetes remission.^[6] In a recent study, the remission rate dropped down to 13% if disease duration was >5 years.^[31] Shorter disease duration means a greater preserved beta-cell mass and therefore better the chances of disease remission after LSG.

CONCLUSION

In addition to sustained and efficacious weight loss, LSG shows promising results as a treatment option for T2DM. More favorable outcomes are seen in younger patients, patients with higher BMI, lower HbA1c, and relatively shorter duration of diabetes. Therefore, LSG should be offered early in the course of DM, particularly in morbidly obese patients when the disease is not so severe so that remission from diabetes could be achieved. Long-term remission and not just cure of the disease should be the desired goal.

However, ours is an observational study with a small sample size which surely does lack a control group. Unlike ours, a longer follow-up period may reveal some information regarding sustained and long-term effects of bariatric surgery. Nonetheless, RCTs comparing outcomes of various bariatric surgeries may add further insight into the patient.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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