Original Article

One Anastomosis Gastric Bypass Surgery: Consequences-Over Diabetic Parameters

Bariatric Surgery Series: Paper IV

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Abstract

Introduction: Excessive weight gain in individuals leads to various metabolic disorders, such as diabetes mellitus, contributing to a further increase in body mass index (BMI). Thus, the patient enters a vicious cycle that leads to irreversible health damage. Bariatric surgery has displayed positive outcomes of weight loss with the return of BMI towards normal, which may reduce blood glucose levels to near normal. The remission of diabetes mellitus may be attributed to the reduction in inflammation, improvement of insulin resistance, lowering of peptide YY, and overall improved metabolic state of the body. ***Methods:*** One fifty patients, both female and male, in the age group of 20-60 years with grade II and grade III obesity having mean BMI of 45.63±6.54 (male) and 41.81± 5.93kg/m^2 (female) were randomly selected for this study. Hemoglobin, Fasting Blood sugar (FBS), 2 hours postprandial blood sugar (PP2BS). Hemoglobin A1c (HbA1c) serum insulin was assessed at the visit, marked as a baseline, then again at the visit 3 months, and finally at the visit by the patient 6 months after bariatric surgery. ***Results:*** Hemoglobin level increased significantly from baseline at the 3rd-month post-surgery visit. FBS increased substantially from baseline at the 3rd-month post-surgery visit, which decreased considerably at the 6th-month visit following surgery. HbA1c showed a significant decrease in level from baseline following surgery. ***Conclusion:*** Improvement in BMI following bariatric surgery may have a positive impact on blood glucose levels in diabetic patients who may hope to see better management of their condition and may enjoy a better quality of life.

Keywords: Bariatric surgery, Obesity, inflammation, organ damage, weight loss, health benefit

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1. Introduction

1.a. Connotation Diabetes Mellitus in Human Health

Diabetes Mellitus (DM) is a metabolism disorder that develops in individuals having disturbed insulin action or secretion. Individuals may also suffer from disturbance of both insulin action and secretion [1]. A relative deficiency of insulin in this condition occurs due to dysfunction of β-cell of the pancreas and resistance to insulin [2]. This is the fastest-growing global public health concern. The percentage of people affected is expected to increase from 2000 (2.8%) to 4.4% by 2030. Therefore, the number of individuals suffering from diabetes mellitus would rise from 171,000,000 to 366,000,000 [3]. In 2021, there were approximately 541,000,000 prediabetic subjects and 6.7 million deaths (12.2% of all causes of death globally) due to diabetes mellitus in the 20-79 age group [2,4]. The condition has repercussions on individuals and the health care system. Complications of diabetes mellitus led to financial hurdles for the healthcare system [1,5]. Complications faced by the suffering subjects include ophthalmological, neurological, cardiovascular, and renal disorders. Thus, diabetes mellitus significantly impairs health-related quality of life (HRQoL) due to complications that may develop [5].

A strong link exists between type 2 diabetes mellitus (T2DM) and obesity and overweight, ethnicity, family history, and aging [2,4]. Obesity is a significant factor leading to T2DM, contributing to an increase in the epidemiology of type diabetes mellitus chiefly because of physical activity lack, maternal obesity, and unhealthy diet [4] . Obesity causes changes in the microenvironment, leading to insulin signaling impairment, deterioration of the function of β-cell, promotes epigenetic/genetic vulnerability and aggravates distortion of the axis of microbiome-gut-brain which lead to metabolic disorders like T2DM [2].

1.b. Implications Metabolic Health and Diabetes Mellitus

Diabetes Mellitus, in the long run, leads to complications that deteriorate the quality of life. Long-term hyperglycemia and superoxide production in diabetic patients leads to chronic complications [1,6-8]. Various pathways involved are inflammation, cytokine expression and action, advanced glycosylation end-product, hormones, protein kinase activation, hexosamine's raised activity, polyol pathway, and mediators of inflammation [9,10]. The inflammatory mediators cause the loss of insulin section by β-cell progressively along with resistance to insulin [11,12]. Obesity and overweight effectively act as an accelerator of this process [13].

In obesity, there is an accumulation of more than white adipose tissue, which brings about changes in the microenvironment. The characteristics of the obesity-induced altered microenvironment include hypoxia, fibrosis, inflammation, mitochondrial function dysregulation, and adipokine secretion [14,15]. These changes lead to insulin signal impairment, insulin resistance, reduced transport of glucose mediated by insulin, and increased dysfunction of β-cell [Figure 1][2, 16]. With the increase in adipocyte size, the cell's responsiveness to insulin decreases due to oxidative stress and stretching of the adipocyte surface [17].

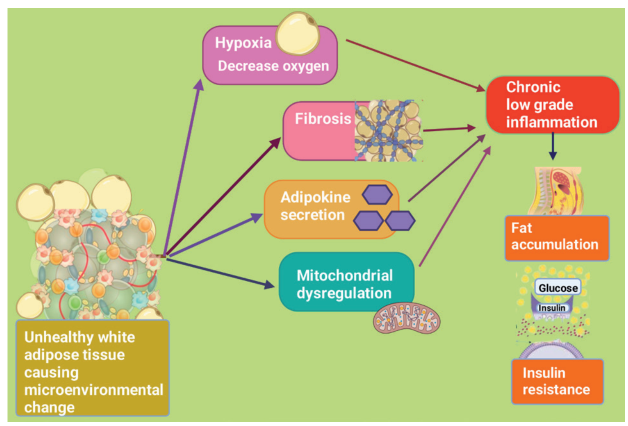


Figure 1 illustrates the changes in the microenvironment that take place in obesity, which eventually lead to insulin resistance and a decrease in β-cell of the pancreas. This figure has been drawn with the premium version of BioRender (https://biorender.com/ accessed on 26 July 2023) with license number QA25Y524R4. Image credit: Rahnuma Ahmad

Accumulation of white adipose tissue increases the volume of skeletal muscle, liver, and other organs with increased formation of diacylglycerol and activation of protein kinase C epsilon form in the liver and skeletal muscle. This causes reduced glucose uptake in muscle and disruption of glycogen synthesis activation by insulin, increasing blood glucose level [18]. Adipose tissue expansion within the liver promotes steatosis, aggravates apoptosis, and dysfunction of cells, which is induced by lipotoxicity [a usual disorder in which unoxidized long-chain fatty acids (i.e., triacylglycerol)] are stored in the body's adipose tissue) and result in resistance to insulin [19]. Adipokines and cytokines that are released by obesity-induced systemic inflammation suppress the action of insulin, which eventually causes increased transcription of enzymes for gluconeogenesis through activating of ceramide production pathway, Jun N-terminal kinase (JNK) and nuclear factor κB (NF-κB) [2].

1.c. Consequence Bariatric Surgery in Controlling Diabetes Mellitus

Bariatric surgery is of therapeutic benefit in patients with both diabetes mellitus and obesity. The surgery not only contributes to loss of weight but also to islet cell function recovery by causing reversal of disorders of metabolism and returning peptide YY and glucagon-like-peptide 1 (GLP-1) level to normal [20]. GLP-1 can cause stimulation of regeneration of β-cell, leading to protection against recurring diabetes [21] [Figure 2].

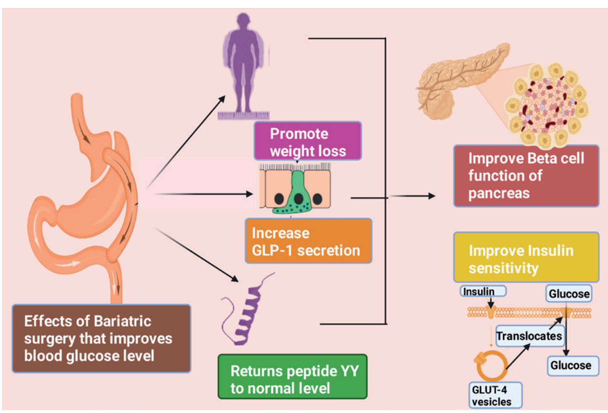


Figure 2: Demonstrates alterations that occur following bariatric surgery that help improve blood sugar levels in patients. GLP-1: Glucagon-like peptide 1. This figure has been drawn with the premium version of BioRender (https://biorender.com/ accessed on 26 July 2023) with license number NI25YLFMMZ. Image credit: Rahnuma Ahmad

T2DM subjects have raised fat in the liver and pancreas compared to normoglycemic BMI-matched individuals [22]. Multiple studies reported a reduction in fat content in the liver following bariatric surgery with the improvement of sensitivity of hepatic cells to insulin, resulting in fasting blood glucose level improvement 7 days following the surgery [23-29]. However, content of fat reduction in the pancreas following surgery takes more extended time, which may be up to 8 weeks, to return to non-diabetic level [23,30]. Such a study suggests the effect of fat accumulation in the liver and pancreas on T2DM-type pathogenesis, and a reduction in such adiposity can improve T2DM [21].

Remission of T2DM may occur within the initial eight weeks following surgery; while it has been suggested in another study, it was observed that resistance to insulin improvement requires a longer time and is partly due to weight loss [30]. This study was therefore carried out to monitor the changes in blood glucose levels following bariatric surgery, which would further contribute to the existing knowledge in this field of study.

2. Objectives of the Study

The study is taken with the objective of the consequences of BMI change over the Diabetic parameters in patients opting for OAGB/MGB surgery.

3. Materials and Methods

3.a. Study Details

Study Type: Longitudinal observational study.

Study Period: This study was conducted from January 2021 to January 2022

Sampling Type: Universal sampling was done with the patient's consent, and patients were informed about the possible benefits, side effects, and risks associated with the surgical interventions.

Study Subject: The subjects of this research were recruited from Asian Bariatrics Hospital, SG Highways, Ahmedabad, Gujarat, India

Methods of Enrollment and Randomization: Patients were enrolled between February 2021 and July 2021, and a 6-month follow-up was completed by January 2022.

Project Details: This is the fourth paper of the principal author of the Bariatric Surgery project. The earlier Paper 1, 2, and 3 were published in the Bangladesh Journal of Medical Science (https://www.banglajol.info/index.php/BJMS/article/view/66965; https://banglajol.info/index.php/BJMS/article/view/68669; https://banglajol.info/index.php/BJMS/article/view/68665) [31-33].

3b. Sample Size Calculation Asian Bariatrics Plus Hospital is a wide-ranging and sizeable center of obesity and metabolic surgery in India, where approximately 20-25 patients are operated on each month. Thus, to meet the required sample size of 120-150, subjects will be enrolled for 6 months and followed up for another 6 months post-bariatric surgery.

Sample Size Estimation with Single Group Mean: N = (Zα/2)2 s2 / d2

Zα/2 = standard deviation for the two-tailed alternative hypothesis at a significance level.

S = the standard deviation obtained from the previous study or pilot.

D = the estimate's accuracy or how close to the true mean.

Zα/2=3.29; s=6; d=1.5.

The calculated sample size would be 130. If the allowance of 10% for missing, losses to follow-up, and withdrawals are assumed, then the corrected sample will be 143 subjects. The corrected sample size thus obtained is 130/ (1.0-0.10) approximately equal to 130/0.9 = 145; for 20% allowances, the corrected sample size will be 156. So, the estimated sample size preferred for this study would be 130-156 (Reference: https://pubmed.ncbi.nlm.nih.gov/29346210/) [34].

Inclusion Criteria: The age range included was between 20–50 years, belonging to both genders, with a mean BMI of 45.63±6.54 (male) and 41.81±5.93kg/m^2 (female). Exclusion criteria: Any previous weight loss surgery history, severe cardio-respiratory disease, cancer, oral steroid treatment, and psychiatric medications, as per the recommendations indicated for bariatric surgery [Figure 3].

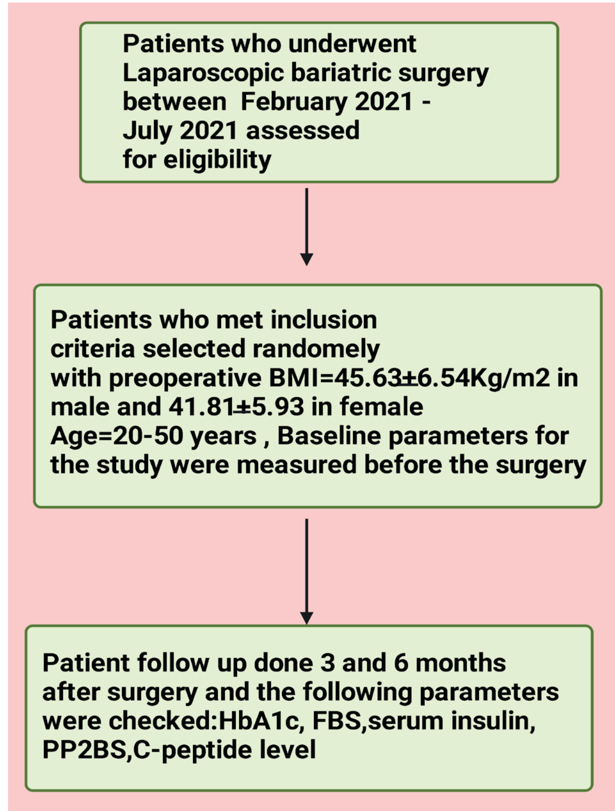


Figure 3: Depicts the schematic diagram of the study method of this research. BMI: Body mass index; FBS: Fasting blood sugar; PP2BS: 2 hours postprandial blood sugar. This figure has been drawn with the premium version of BioRender (https://biorender.com/ accessed on 26 July 2023) with license number XG25YUQ1AP . Image credit: Rahnuma Ahmad

3c. Anthropometric Evaluation

Weight, height, and BMI were used for anthropometric evaluation. The patients were weighed on a Bioelectrical Impedance Machine In Body 770, and BSM 170 in body measuring scale was used for height measurements.

3d. Surgical Intervention

A laparoscopic technique was used for the surgery. A 5 mm Endopath instrument at Palmer's point was used to create the pneumoperitoneum and the remaining 3 ports –11 mm supra-umbilical port, 12mm right of right Rectus muscle port, and 5 mm port on right hypochondrium was created. Gastroesophageal junction dissection was done by retracting the fundus and dividing the peritoneum overlying the GE junction using a Goldfinger instrument. Further, the greater omentum was divided vertically to the upper line of the transverse colon and later divided transversely. DJ flexure was identified, and a loop of a small bowel was traced to 150 cm. The loop was then pulled up in ante colic fashion and anchored to the greater curvature opposite the incisura. Dissection for the gastric pouch was started by creating a window in the lesser curve near the incisura. Subsequent stapler firing made the required stomach pouch of around 100ml. 36 Fr Gastric Calibration Tube was used. Alimentary and biliopancreatic limb measurements were 150 cm.

3e. Nutritional Intervention

The diabetic profile of the subjects was examined at the baseline visit, and the same tests were repeated at 3 months and 6 months after surgery. The dietary recommendation was a low-calorie diet with lesser simple carbohydrates and a high-protein diet of 800-1000 kcal/ 0.8 g per kg IBW). The diet progressed in texture over 1 month, and later, the diet was revised as per the weight loss observed over time. A balanced diet consisting of all food groups was included.

All patients in the postoperative period received commercially available mineral and vitamin supplements, per American Society of Metabolic & Bariatric Surgery (ASMBS) guidelines, 2018, after a week of surgery. At follow-up, the patients were asked about supplement compliance, dietary concerns, and complaints after surgery like gastric reflux, constipation, diarrhea, nausea, vomiting, etc.

3f. Biochemical Assays

Various biochemical tests were done to see the diabetes parameters like FBS, PP2BS, Serum Insulin level, C-peptide level, and HbA1C.

3g. Statistical Method

In our analysis, we used descriptive statistics to summarize our collected data. We calculated the mean and standard deviation for continuous variables, such as biomarker measurements, to measure central tendency and dispersion, respectively. Categorical variables were summarized using percentages to indicate the proportion of each category within the sample.

To examine the changes in biomarkers before and after follow-up, we conducted a paired sample t-test. This statistical test allowed us to compare the means of the biomarkers within the same individuals and assess the mean difference between pre-operative and post-operative measurements.

Time (pre- and post-operative follow-up) served as the primary predictor variable in our regression model, as we sought to understand how Anastomosis Gastric Bypass Surgery affected the biomarkers over time. To analyze the impact of time, we employed a repeated measure ANOVA, which accounted for repeated measurements within the same individuals (pre- and post-operative). Time was treated as a fixed effect, representing its overall effect on the biomarkers across all individuals. Additionally, we included the within-subject difference as a random effect to capture individual-specific variation in biomarker changes. Our regression model also incorporated other covariates such as age, sex, and comorbidities.

We considered p-values less than 0.05 to determine statistical significance. For our statistical analysis, we used STATA 15 (StataCorp, LP, College Station, Texas, USA), while GraphPad Prism 8.3.2 was employed to generate figures that visually represented the results of our analysis.

3h. Ethical Approval

This study was approved by the Institutional Review Board of Asian Bariatrics Hospital, SG Highways, Ahmedabad, Gujarat, India, with Reference number IECHR-AB/2021/15 dated 14/09/2021. All the study subjects verbally explained the study's intention, motive, and future scientific publication. Written informed consent was obtained before data collection commenced.

4. Results

This observational study involved the inclusion of 150 patients who were scheduled to undergo Anastomosis Gastric Bypass Surgery. The mean age of the patients was 41.7 years, with a standard deviation of 14.7 years (mean±SD: 41.7±14.7).

Among the study participants, 56 individuals (37.3%) were male, while 94 (62.7%) were female. This distribution highlights a higher representation of female patients in the study cohort.

Regarding comorbidities, hypertension was identified as the most prevalent condition among the enrolled patients, affecting 49.3% of them. This was followed by obstructive sleep apnea syndrome (OSAS) at 32.7% and a history of diabetes at 29.3%. Additional comorbidities, such as dyslipidemia and hypothyroidism, were present in 20.7% and 16.7% of the patients, respectively (Table 1).

Table 1: Demographic characteristics of the study participants

Factors	Observation
Age	41.7±14.7
Sex	
Male	56(37.3%)
Female	94(62.7%)
H/O Diabetes	44(29.3%)
H/O Hypertension	74(49.3%)
H/O OSAS	49(32.7%)
H/O Dyslipidemia	31(20.7%)
H/O Hypothyroidism	25(16.7%)

Data were presented as mean±Std or number with percent in the parenthesis.

Table 2: Difference in outcome biomarkers level before and after one Anastomosis Gastric Bypass Surgery.

	Baseline	Visit-1	p-value	Visit-2	p-value
Hb, (g/dl)	12.8±1.47	13.0±1.43	0.012	13.3±2.86	0.077
FBS, (mg/dl)	118.3±50.3	127.9±61.7	0.012	113.2±12.3	<0.001
HbA1c, (%)	6.98±1.74	5.92±0.99	<0.001	5.95±1.29	<0.001

Data was presented as mean±SD. A paired sample t-test was used to estimate the p-value, and the comparison was between baseline with visit-1 and visit-2.

The analysis revealed several significant findings. Hemoglobin levels increased significantly from baseline (12.8±1.47 g/dl) to Visit-1 (13.0±1.43 g/dl, p=0.012), but this increase was not statistically significant at Visit-2 (13.3±2.86 g/dl, p=0.077). Fasting blood sugar level significantly increased from baseline (118.3±50.3 mg/dl) to Visit-1 (127.9±61.7 mg/dl, p=0.012). However, at Visit-2, the levels decreased significantly (113.2±12.3 mg/dl, p<0.001) compared to baseline. HbA1c levels exhibited a significant decrease from baseline (6.98±1.74%) to Visit-1 (5.92±0.99%, p<0.001), and this reduction was sustained at Visit-2 (5.95±1.29%, p<0.001) (Table 2 and Figure 1).

After completing a single Anastomosis Gastric Bypass Surgery, the post-operative data was analyzed and compared with the pre-operative values for Hb, FBS, and HbA1c. The findings revealed that only HbA1c demonstrated a significant reduction at visit 1 by 1.16% (95% CI= -1.48, -0.84, p<0.001) and at visit 2 by -1.12% (95% CI=-1.52, -0.73, p<0.001).

Table 3. The effect of after one Anastomosis Gastric Bypass Surgery on biomarkers between follow-up and pre-operation.

	Hb		FBS		HbA1c	
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Time						
Pre-operation	Ref.		Ref.		Ref.	
FW-1	0.19(-0.10, 0.48)	0.190	-5.87(-20.1, 8.36)	0.419	-1.16(-1.48, -0.84)	<0.001
FW-2	0.15(-0.22, 0.51)	0.433	3.39(-14.3, 21.1)	0.707	-1.12(-1.52, -0.73)	<0.001

Repeated measure ANOVA was used to estimate the p-value.

5. Discussion

In this study, the hemoglobin level increased from baseline at visit 1 . Similar finding was observed in a study done by Montano-Pedroso *et al*., in which they reported a rise in hemoglobin concentration in blood seven days after bariatric surgery [35]. They suggested that the bone marrow is stimulated by erythropoietin, which increases bone marrow's ability to produce cells by many folds. This may cause hyperplasia of erythroid cells, which is observed by the 3rd to 5th day postoperatively [35]. The rise in the activity of bone marrow may occur in response to post-operative acute anemia due to blood loss during surgery. The rapid recovery of hemoglobin levels after surgical intervention shows no significant increase in hemoglobin levels in our study. Montano-Pedroso *et al*., reported that similar finding in their analysis [35].

In this study, the fasting blood glucose level increased at visit 1 postoperatively, which decreased on the 2nd visit after bariatric surgery. A similar finding was noted in several studies [37-39]. About 30-100% of the subjects who underwent bariatric surgery in these studies could sustain average fasting blood glucose levels within a few days following the surgery. It was suggested that the possible reason for the lowering of Fasting Blood Glucose level was due to the drop of the basal production rate of glucose by the liver rise in suppression of production of glucose by hepatic cells mediated by insulin provided that the patient consumes a low-calorie diet of about 1100 kcal/day following surgery. Also, a diet of about 800 kcal/day causes, within 4-10 days, a decrease in fasting blood glucose and concentration of insulin [40-44].

HbA1c decreased in this study, suggesting improved

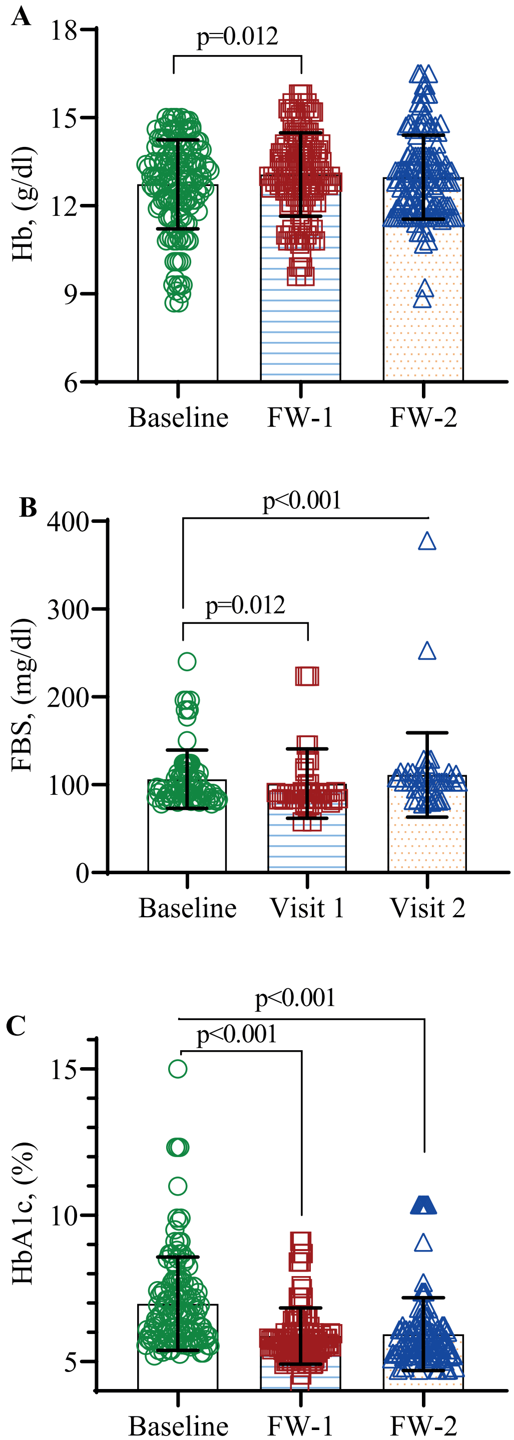
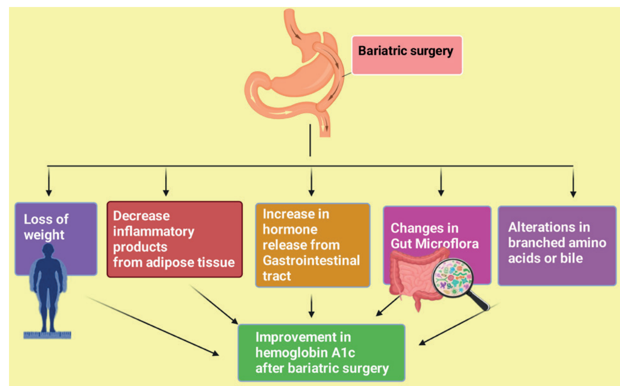


Figure 1: Difference in studied biomarkers after one Anastomosis Gastric Bypass Surgery. Paired sample t-test was applied to see the difference between baseline with follow-ups 1 & 2.

blood glucose levels following the surgery. A similar finding was reported by Liu *et al*., in 2022 [45]. They observed a median HbA1c decrease of 27.2% following bariatric surgery. They mentioned that loss of weight and restriction of calories may have a significant role in such outcomes. They also suggested that other causes, such as decreased inflammatory factors production from adipose tissue, raised release of hormones from the gastrointestinal tract, gut microflora changes, and alterations in the concentration of branched amino acids or bile within the circulation contribute to the improvement of HbA1c [45-47] [Figure 4].

Figure 4: Depicting the changes following Bariatric



surgery that led to improvement in HbA1c). This figure has been drawn with the premium version of BioRender (https://biorender.com/ accessed on 26 July 2023) with license number SI25Z58R94. Image credit: Rahnuma Ahmad.

6. Conclusion

Obesity has become a global public health concern. This chronic condition is paving the way for an astounding worldwide population suffering from several disorders, including T2DM. Bariatric surgery may be a more lasting solution for obesity, aiding weight loss and remission of chronic illnesses like T2DM, as observed in this research work. Weight loss and various other mechanisms promoted through bariatric surgery may lead to improved blood glucose levels in patients, which can be maintained through adopting a healthy lifestyle that includes a proper nutritious diet. The obese population who cannot lose weight through lifestyle modification and pharmacological intervention can, therefore, opt for bariatric surgery, which may also benefit those who suffer from high blood glucose levels and increased BMI immensely.

7. Recommendation

Close monitoring of blood sugar is needed for diabetic patients following bariatric surgery. Also, a proper nutritious diet is recommended for these patients. More such studies with a larger population may be carried out. The general population suffering from obesity needs to learn about the possible benefits of bariatric surgery since benefits include more than weight loss. With remission of T2DM, the patients would also become free from the threat of suffering from diabetic complications.

Consent for Publication

The author reviewed and approved the final version and has agreed to be accountable for all aspects of the work, including any accuracy or integrity issues.

Disclosure

The author declares that they do not have any financial involvement or affiliations with any organization, association, or entity directly or indirectly with the subject matter or materials presented in this editorial. This includes honoraria, expert testimony, employment, ownership of stocks or options, patents, or grants received or pending royalties.

Data Availability

The data is exclusively available from the principal author for research purposes only.

Authorship Contribution

All authors contributed significantly to the work, whether in the conception, design, utilization, collection, analysis, and interpretation of data or all these areas. They also participated in the paper's drafting, revision, or critical review, gave their final approval for the version that would be published, decided on the journal to which the article would be submitted, and made the responsible decision to be held accountable for all aspects of the work.

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