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ORIGINAL CONTRIBUTIONS

Long-Term Changes in Leptin, Chemerin, and Ghrelin Levels Following Roux-en-Y Gastric Bypass and Laparoscopic Sleeve Gastrectomy

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Abstract

Aim Published reports showed conflicting results regarding the sustained alterations in leptin, chemerin, and ghrelin concenratios after metabolic surgery. Therefore, we performed the present work to contrast the alterations in leptin, chemerin, and ghrelin levels one year after Roux-en-Y gastric bypass (RYGB) versus laparoscopic sleeve gastrectomy (LSG).

Methods The present research is a prospective, comparative one that followed 100 cases for whom RYGB or LSG was done. We assessed the serum values of adiposity-associated mediators, including adipokcytokines (leptin and active chemerin) and gastrointestinal hormones (total ghrelin). The primary outcome in the present study was the alterations in leptin, chemerin, and ghrelin values at 12 months after RYGB and LSG.

Results The serum leptin level decreased significantly in the LSG group with a mean change of − 170.8 ± 29.4 ng/mL ($p < 0.001$). Similarly, the serum leptin concentration decreased significantly in the RYGB group, with a mean change of − 165.42 ± 53.4 ($p < 0.001$). In addition, the mean reduction in baseline chemerin levels 12 months after the operation was considerable in the LSG cohort (− 23.24 ± 9.5 ng/mL) and RYGB group (− 22.12 ± 15.9 ng/mL). The ghrelin values demonstrated a notable reduction in the LSG cohort (− 0.083 ± 0.11 pg/mL) and RYGB group (− 0.068 ± 0.097 pg/mL). However, the changes in the three hormones were not substantially different between both groups ($p > 0.05$).

Conclusion Both RYGB and LSG result in a considerable, comparable decrease in the postoperative serum concentrations of leptin, chemerin, and ghrelin.

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Keywords Bariatric operations · Adipokines · Leptin · Ghrelin · Chemerin

Introduction

The epidemic of obesity has grown exponentially over the past few decades with reported prevalence of 37.7% among the United States (US) adults according to 2013–2014 National Health and Nutrition Examination Surveys (NHANES) [1, 2]. A similar proportion was reported by 2014 World Health Organization (WHO) estimates for the global prevalence of obesity [3]. Morbid or grade III obesity is assigned as a body mass index (BMI) above 40 m/kg^2 and characterized by a dramatic increase in the risks of comorbidities such as diabetes, cardiovascular (CV) diseases, obesity-hypoventilation syndrome (OHS), and cancers [4, 5]. Moreover, morbid obesity was linked to an elevated hazard of psychic disorders such as depression and anxiety [6]. Although diet, lifestyle modifications, and pharmacologic therapy are common options for the treatment of adiposity, the current evidence shows that these interventions fail to exhibit long-term weight reduction in morbidly fatty cases [7–9].

Presently, bariatric operations are considered the gold standard strategy for treatment of marked adiposity; the operation leads to dramatic and sustained weight loss, improvement in the quality of life, and reduction in the risks of obesity-related disorders [10]. Recent reports showed that almost 469,000 bariatric operations were performed all over the world in 2013, with 193,000 performed operations in the US alone [11]. Four widespread kinds of bariatric operations are performed worldwide, which are Roux-en-Y gastric bypass (RYGB), laparoscopic sleeve gastrectomy (LSG), gastric banding, and duodenal switch [10]. The first two types jointly constitute more than 80% of the metabolic surgeries done worldwide all over the world [12].

On the other hand, the increase in fat mass in adiposity is linked to significant hormonal alterations; it is now recognized that adipose tissue has a physiological endocrine function which is disturbed in obese patients [13, 14]. Adipokines, which are secreted by adipose tissue, are key regulators of food intake, lipid metabolism, insulin sensitivity, and glucose homeostasis [15]. A cumulative body of evidence has shown that dysfunction in adipokine pathways is a major contributor to the metabolic abnormalities seen in obesity [16]. Moreover, adipocytes secrete pro-inflammatory cytokines (referred to as "adipocytokines") which have a substantial role in the pathogenesis of insulin resistance and systemic inflammation [15]. Leptin is a major adipokine with potent anorexic and anti-diabetic roles. Past reports have shown that leptin modulates immune responses, stimulates the secretion of pro-inflammatory cytokines, and increases the risk of cardiovascular diseases in obese patients [17, 18]. Similarly, elevated levels of chemerin, a potent chemoattractant adipokine, were linked to insulin resistance and high blood pressure [19].

Ghrelin is a gastrointestinal (GI) peptide that induces orexigenic states and positive energy balance; obese patients were found to have lower postprandial suppression of ghrelin than the normal population [20, 21]. Thus, excessive production of ghrelin has been implicated in the pathophysiology of obesity [22]. To date, published reports showed conflicting results regarding the sustained alterations in leptin, chemerin, and ghrelin levels after metabolic surgery. In addition, little research compared the changes in those adipokines and hormones following LSG. Therefore, we performed this study to compare the alterations in leptin, chemerin, and ghrelin concentrations 12 months after RYGB and LSG.

Materials and Methods

The current manuscript was prepared in concordance with the recommendations of STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) [23]. The study's protocol was confirmed and recorded by the university ethical committee. Written informed consents were taken from all patients before the study's enrollment.

Study Design and Patients

The present work is a prospective, comparative work that followed 100 obese patients who underwent RYGB or LSG. Adult patients patients with BMI > 40kg/m^2 or > 35 kg/m^2 with metabolic disorders in whom different non-surgical interventions did not succeed to attain acceptable and clinically beneficial weight reduction were included. We excluded patients with endocrinal causes for obesity, high-risk profile for anesthesia, psychosocial disorders, unsuitable social environment, previous metabolic surgery, acute illness, acute or chronic inflammatory conditions, malignancy, and/or any substantial problem after operation. Pregnant or lactating ladies at screening or operation were also precluded.

Cases were allocated for RYGB or LSG after a multidisciplinary group evaluation, comprising surgeons, internists, psychiatrists, and dietitians.

Surgical Techniques

In the LSG group, under general anesthesia, pneumoperitoneum was engendered with CO_2 and kept at a pressure of 15 mmHg. The prime portion of the fundus and the gastric body, beginning 5 cm proximal to the pylorus until the angle of His, were cut out along a bougie of 36 Fr placed at the lesser

curvature. The volume for the gastric pouch after the LSG ranged from 100 to 120 ml.

The surgical strategy of gastric bypass consisted of creating a restrictive portion by making a small gastric pouch and affixing a malabsorptive element, the bypass of the gastric remnant, duodenum, and proximal small intestine. The rate of malabsorption depended on the extent of the Roux limb, in our patients, between 120 and 150 cm. Our adopted approach of the typical laparoscopic proximal gastric bypass comprised of a small gastric pouch of 25 ml.

Data Collection

Studied subjects were submitted to detailed history taking and clinical evaluation before surgery. The anthropometric assessment comprised measurements of weight, BMI, waist, and hip circumferences. In addition, the preoperative evaluation included blood glucose profile and lipid profile. Blood samples were collected following an overnight fast. The antecubital vein was used to obtain the blood sample in an EDTA 10 mL Vacutainer tube. Within 1 h of sampling, the plasma was isolated by centrifugation at 1500×*g* for 15 min employing a refrigerated centrifuge. Lab investigations comprised fasting blood sugar, glycated hemoglobin HbA1c, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides, which were performed employing a standard automated analyzer and assessed following overnight fasting.

We measured the serum values of adiposty-associated molecules, comprising adipocytokines (leptin and active chemerin) and GI hormones (total ghrelin). Concentrations of leptin (Biovendor, Modrice, Czech Republic), chemerin (R&D Systems, Minneapolis, USA) and ghrelin (Linco Research, MO, USA) were assessed in duplicate employing enzyme-linked immunosorbent assays guided by the manufacturer's directives. Leptin assessment sensitivity was 0.2 ng/mL, and inter-assay and intra-assay coefficients of variation were less than 7.6 and 4.4%. Chemerin assessment sensitivity was 25 pg/mL, and inter-assay and intra-assay coefficients of variation were less than 5.2 and 4.1%. Ghrelin assessment sensitivity was 30 pg/mL, and inter-assay and intra-assay coefficients of variation were less than 7.8 and 1.9%. Adipokine-circulating levels were assessed at two time points: at the baseline and one year post-operative.

Study's Outcomes

The primary aim in the present study was the alterations in leptin, chemerin, and ghrelin concentrations 12 months after RYGB and LSG. The secondary aims included the association between the alterations in adipokine-concentrations levels and type of bariatric surgery, and the correlation analysis between the alterations in adipokine-concentrations and clinical/laboratory variables.

Statistical Analysis

Data entry, processing, and statistical analysis were done employing SPSS version 22.0. We used frequency tables with percentages for the presentation of the categorical variables; the numerical data were expressed as mean (± standard deviation) or median (interquartile range [IQR]) according to the normality of the data which was assessed using the Shapiro-Wilk Test. Tests of significance (Student's *t* test, or Mann-Whitney's test) were used for quantitative data according to the normality of the data, and chi-square was employed for qualitative data. The correlation coefficient was calculated to measure the correlation between different quantitative data. A p value of lower than 0.05 was counted as statistically significant.

Results

The current work comprised 100 grown-up cases with morbid adiposity who underwent either RYGB ($N = 50$ patients) or LSG ($N = 50$ patients). The mean age of the included subjects was 41.8 ± 8.6 and 42.5 ± 8.8 years old in LSG and RYGB, respectively. There were no considerable variations between both cohorts regarding initial weight ($p = 0.46$), BMI ($p = 0.62$), waist circumference ($p = 0.51$), and hip circumference ($p = 0.37$). The percentage of elevated blood pressure was comparable between both cohorts (46% versus 48%, $p = 0.99$). There were no significant variations between the LSG and RYGB cohorts regarding HbA1c ($p = 0.71$) and fasting blood sugar ($p = 0.41$) as well; 46% of the patients in LSG had diabetes compared with 34% in RYGB cohort ($p = 0.31$). Besides, the lipid profile parameters were comparable between both groups, with a little higher percentage of dyslipidemia in the LSG group that did not attain the threshold of statistical significance (42% versus 36%; $p = 0.68$). The prevalence of gastroesophageal reflux disease (GERD) was 26% in the LSG cohort and 32% in the RYGB cohort ($p = 0.65$). Table 1 shows the preoperative characteristics of the included patients.

Postoperatively, both techniques were effective in reducing weight, BMI, hip and waist circumference, blood glucose parameters, blood pressure, and lipid profile parameters ($p < 0.001$). There were no substantial variations in the anthropometric measurements between both cohorts ($p > 0.05$). The percentage of hypertension decreased notably to reach 14% in the LSG cohort and 16% in the RYGB cohort, with no significant difference between both groups ($p > 0.98$). Five (10%) patients had diabetes at the end of follow-up in the LSG cohort compared with 6% in the RYGB cohort ($p = 0.71$). The prevalence of postoperative dyslipidemia was comparable between the LSG and RYGB groups (14% versus 12%, respectively; $p = 0.99$). Similar findings were noted regarding the prevalence of postoperative GERD and obstructive sleep apnea (Table 2).

Table 1 The baseline characteristics of study participants

	LSG (n = 50)	Roux-en-Y (n = 50)	p value
Age (years), mean ± SD	41.8 ± 8.6	42.5 ± 8.8	0.68
Height (cm), mean ± SD	169.4 ± 6.4	167.54 ± 7.3	0.17
Weight (kg), mean ± SD	126.9 ± 10.6	124.32 ± 10.2	0.46
BMI (kg/m^2), mean ± SD	44.2 ± 3.3	43.79 ± 3.4	0.62
Waist circumference (kg), mean ± SD	128.6 ± 6.1	127.9 ± 5.2	0.51
Hip Circumference (kg/m^2), mean ± SD	116.6 ± 4.3	117.36 ± 3.6	0.37
SBP (mmHg), mean ± SD	149.1 ± 17.4	153.1 ± 11.4	0.72
DBP (mmHg), mean ± SD	90.94 ± 16.6	89.2 ± 14.6	0.91
Hypertension, no. (%)	23 (46%)	24 (48%)	0.99
FBG (mg/dL), mean ± SD	152.4 ± 45.2	160.1 ± 47.9	0.41
HbA1c (%), mean ± SD	7.26 ± 1.3	7.17 ± 1.2	0.71
DM, no. (%)	23 (46%)	17 (34%)	0.31
Cholesterol (mg/dL), mean ± SD	221.2 ± 43	216.36 ± 38.4	0.55
Triglyceride (mg/dL), mean ± SD	202.7 ± 31.3	199.62 ± 32.9	0.63
HDL (mg/dL), mean ± SD	54.5 ± 5.3	55.1 ± 6.7	0.41
LDL (mg/dL), mean ± SD	158.1 ± 41	147.86 ± 33.1	0.17
Dyslipidemia, no. (%)	21 (42%)	18 (36%)	0.68
GERD, no. (%)	13 (26%)	16 (32%)	0.65

*p value < 0.05 significant, **p value < 0.001 highly significant

LSG, laparoscopic sleeve gastrectomy; *BMI*, body mass index; *DM*, diabetes mellitus; *GERD*, gastroesophageal reflux disorder; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *FBG*, fasting blood glucose; *HbA1c*, glycated hemoglobin

Table 2 The changes in clinical and laboratory parameters 12 months after LSG and Roux-en-Y

Variables	LSG (n = 50)		p value	Roux-en-Y (n = 50)		p value	p value[#]
	Baseline	After 12 months		Baseline	After 12 months		
Weight (kg), mean ± SD	126.9 ± 10.6	101.62 ± 8.9	< 0.001**	124.32 ± 10.2	100.7 ± 8.6	< 0.001**	0.29
BMI (kg/m^2), mean ± SD	44.2 ± 3.3	35.36 ± 2.6	< 0.001**	43.79 ± 3.4	35.04 ± 2.3	< 0.001**	0.71
Waist circumference (kg), mean ± SD	128.6 ± 6.1	109.46 ± 6.8	< 0.001**	127.9 ± 5.2	109.34 ± 5.9	< 0.001**	0.92
Hip circumference (kg/m^2), mean ± SD	116.6 ± 4.3	102.16 ± 3.6	< 0.001**	117.36 ± 3.6	102.98 ± 2.9	< 0.001**	0.205
SBP (mmHg), mean ± SD	149.1 ± 17.4	126.46 ± 12.8	0.003*	153.1 ± 11.4	126.46 ± 12.8	< 0.001**	0.99
DBP (mmHg), mean ± SD	90.94 ± 16.6	79.02 ± 11.4	< 0.001**	89.2 ± 14.6	79.02 ± 11.4	< 0.001**	0.99
Hypertension, no. (%)	23 (46%)	7 (14%)	< 0.001**	24 (48%)	8 (16%)	< 0.001**	0.98
FBG (mg/dL), mean ± SD	152.4 ± 45.2	117.2 ± 27.8	< 0.001**	160.1 ± 47.9	115.72 ± 38.9	< 0.001	0.79
HbA1c (%) mean ± SD	7.26 ± 1.3	5.97 ± 0.6	< 0.001**	7.17 ± 1.2	6.1 ± 4.9	< 0.001**	0.368
DM, no. (%)	23 (46%)	5 (10%)	< 0.001**	17 (34%)	3 (6%)	< 0.001**	0.71
Cholesterol (mg/dL), mean ± SD	221.2 ± 43	173.38 ± 31.8	< 0.001**	216.36 ± 38.4	172.88 ± 31.9	< 0.001	0.93
Triglyceride (mg/dL), mean ± SD	202.7 ± 31.3	193.64 ± 33.5	< 0.001**	199.62 ± 32.9	189.54 ± 34.8	< 0.001**	0.55
HDL (mg/dL), mean ± SD	54.5 ± 5.3	61.8 ± 6.5	< 0.001**	55.1 ± 6.7	63.36 ± 7.2	< 0.001**	0.25
LDL (mg/dL), mean ± SD	158.1 ± 41	113.98 ± 37.1	< 0.001**	147.86 ± 33.1	104.58 ± 28.3	< 0.001**	0.15
Dyslipidemia, no. (%)	21 (42%)	7 (14%)	< 0.001**	18 (36%)	6 (12%)	< 0.001**	0.99
GERD, no. (%)	13 (26%)	4 (8%)	< 0.001**	16 (32%)	5 (10%)	< 0.001**	0.99
OSA, no. (%)	21 (42%)	7 (14%)	< 0.001**	23 (46%)	7 (14%)	< 0.001**	0.99

*p value < 0.05 significant, **p value < 0.001 highly significant

LSG, laparoscopic sleeve gastrectomy; *BMI*, body mass index; *DM*, diabetes mellitus; *GERD*, gastroesophageal reflux disorder; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *FBG*, fasting blood glucose; *HbA1c*: glycated hemoglobin; *OSA*, obstructive sleep apnea.

[#] p value for the difference in clinical and laboratory parameters between studied groups at 12 months

In terms of the main outcomes of the current work, the serum leptin level declined considerably in the LSG cohort to reach 84.1 ± 21.3 ng/mL (mean change − 170.8 ± 29.4 ng/mL; $p < 0.001$). Similarly, the serum leptin concentrations decreased significantly in the RYGB group with a mean change of − 165.42 ± 53.4 ($p < 0.001$); the difference between both cohorts was not notably significant ($p = 0.53$). In addition, the mean reduction in baseline chemerin levels 12 months after the operation was significant in the LSG group (− 23.24 ± 9.5 ng/mL) and RYGB group (− 22.12 ± 15.9 ng/mL). However, the difference in serum chemerin levels between both groups was not significant at baseline ($p = 0.37$) and 12 months after the operation ($p = 0.32$). The ghrelin values demonstrated a notable reduction in the LSG cohort (− 0.083 ± 0.11 pg/mL) and RYGB cohort (− 0.068 ± 0.097 pg/mL), with no considerable variations between both cohorts ($p = 0.49$; Table 3).

The correlation analysis showed that there was statistically significant positive realationship between the mean change in serum chemerin levels with fasting blood sugar ($r = 0.255$; $p = 0.01$) and HbA1c ($r = 0.26$; $p = 0.001$). While the mean change in serum ghrelin levels correlated negatively with BMI ($r = -0.246$; $p = 0.014$), waist circumference ($r = -0.289$; $p = 0.042$), HbA1c ($r = -0.252$; $p = 0.011$); yet, it correlated positively with triglyceride levels ($r = -0.\ 0.288$; $p = 0.004$) (Table 4).

Discussion

The current body of evidence shows that adipose tissue has substantial endocrinal functions, including the release of adipokines and other cytokines, which are key players in the development of metabolic disorders in obesity. Although RYGB and LSG are effective procedures for reduction of weight and remission of adiposity-linked co-morbidities, published reports showed conflicting results regarding the effect of those techniques on the long-term alterations in adipocytokines and GI hormone levels. In the present study, both RYGB and LSG led to a substantial decline in serum leptin, chemerin, and ghrelin concentrations 12 months after the operation. However, such changes were comparable between the RYGB and LSG groups. The mean alterations in serum chemerin values were linked to alterations in blood glucose profile. The mean changes in ghrelin levels were correlated with changes in BMI, triglycerides, and HbA1c, but not free blood sugar.

Leptin is a polypeptide hormone secreted by adipose tissues in an amount that is proportional to body fat content [24]. Serum leptin plays a critical role in controlling body weight and energy balance by acting centrally in the hypothalamus. Through binding to its receptors in the brain and activation of the JAK-STAT signaling pathway, leptin induces anorexic status, high metabolic rate, and thermogenesis [25]. Therefore, high serum leptin level is frequently encountered after high food consumption in order to regulate body weight and energy expenditure. In obese individuals, it was observed that high leptin levels were not associated with anorexia or reduction in body fat mass, presumably due to endogenous leptin-resistance mechanisms mediated by defective leptin transport to the brain, impaired expression of leptin, the pro-inflammatory role of leptin, or rarely genetic mutations [26–28]. However, the leptin-resistance status appears to be limited to the metabolic functions of leptin sparing its other effects such as stimulation of pro-inflammatory cytokines, inflammatory vascular response, atherosclerosis, and thrombosis [29]. Therefore, high leptin levels in obese individuals can precipitate to increased risks of CV diseases [30] and cognitive dysfunction [31]. Our results showed that both

Table 3 The changes in leptin, chemerin, and ghrelin Levels following Roux-en-Y gastric bypass and LSG

Variables		LSG ($n = 50$)	Roux-en-Y ($n = 50$)	p value
Leptin (ng /ml), mean ± SD	Baseline	254.96 ± 41.6	248.64 ± 54.1	0.51
	After 12 months	84.1 ± 21.3	83.22 ± 31.4	0.87
Mean change± SD		− 170.8 ± 29.4	− 165.42 ± 53.4	0.53
p value		< 0.001**	< 0.001**	
Chemerin (ng/ml), mean ± SD	Baseline	88.48 ± 8.1	90.08 ± 9.7	0.37
	After 12 months	65.24 ± 12.3	67.96 ± 14.9	0.32
Mean change ± SD		− 23.24 ± 9.5	− 22.12 ± 15.9	0.67
p value		< 0.001**	< 0.001**	
Ghrelin (pg/ml), mean ± SD	Baseline	1.11 ± 0.14	1.1 ± 0.14	0.84
	After 12 months	1.02 ± 0.14	1.03 ± 0.11	0.72
Mean change ± SD		− 0.083 ± 0.11	− 0.068 ± 0.097	0.49
p value		< 0.001**	< 0.001**	

*p value < 0.05 significant, **p value < 0.001 highly significant

LSG, laparoscopic sleeve gastrectomy

Table 4 The correlation analysis between the changes in adipokine-circulating levels and clinical/laboratory variables at 12 months postoperatively

Variables	Leptin (ng/ml),		Chemerin (ng/ml),		Ghrelin (pg/ml)	
	r	*p* value	*r*	*p* value	*r*	*p* value
Age (years)	− 0.117	0.45	− 0.053	0.714	0.172	0.23
Height (cm)	0.015	0.92	0.08	0.581	− 0.120	0.41
Weight (kg)	0.043	0.76	0.094	0.516	− 0.069	0.63
BMI (kg/m^2)	0.042	0.77	− 0.115	0.428	− 0.246	0.014*
Waist circumference (kg)	0.237	0.098	0.261	0.68	− 0.289	0.042*
Hip circumference (kg/m^2)	− 0.032	0.82	0.083	0.57	0.043	0.76
SBP (mmHg)	0.157	0.28	0.222	0.121	0.007	0.96
DBP (mmHg)	0.019	0.89	− 0.172	0.234	0.007	0.76
FBG (mg/dL)	− 0.204	0.55	0.255	0.01*	0.097	0.51
HbA1c (%)	− 0.221	0.12	0.261	0.001**	− 0.252	0.011*
Cholesterol (mg/dL)	− 0.007	0.97	− 0.057	0.69	0.019	0.89
Triglyceride (mg/dL)	− 0.217	0.13	− 0.080	0.58	0.288	0.004*
HDL (mg/dL)	− 0.001	0.99	0.138	0.34	− 0.046	0.75
LDL (mg/dL)	− 0.061	0.67	0.011	0.94	0.188	0.19

*p value < 0.05 significant, **p value < 0.001 highly significant

BMI, body mass index; *DM*, diabetes mellitus; *GERD*, gastroesophageal reflux disorder; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *FBG*, fasting blood glucose; *HbA1c*, glycated hemoglobin

RYGB and LSG led to a significant reduction in serum leptin level 1 year after the operations. However, the changes in serum leptin level did not correlate significantly with the improvement in BMI, lipid profile, or blood glucose profile. In concordance with our findings, Geloneze et al. [32] reported a considerable decline in serum leptin levels during a 1-year follow-up of patients who underwent RYGB. Similarly, Kalinowski et al. [33] reported a considerable decrease in serum leptin concentrations 1 year after RYGB and LSG, with no significant difference between both techniques. Another two reports had comparable, significant reduction in serum leptin levels after either RYGB or LSG [34, 35]. Such a positive effect of RYGB and LSG in serum leptin level can be attributed to postoperative improvement in the endogenous leptin-resistance status associated with obesity, as well as the improvement of glucose homeostasis.

Chemerin is an important component of the immune system and adipokine that is secreted by white fat tissue. Chemerin has a major contribution in body weight hemostasis and energy balance through regulation of adipogenesis and insulin sensitivity [36]. As adipose tissues expand and chronic low-grade inflammation develops in obese individuals, the level of serum chemerin elevates markedly [37]; previous reports have shown that elevated levels of chemerin were associated with many obesity-related metabolic and inflammatory disorders such as insulin resistance, CV diseases, metabolic syndrome, and Chron's disease [36, 38]. Moreover, it was found that serum chemerin levels correlated positively with BMI, triglyceride levels, and blood glucose, which reflects its importance as a proxy for the metabolic state in obese patients [19]. However, little research investigated the impact of bariatric operations and massive weight reduction on serum chemerin concentrations. In this work, we found that the serum chemerin decreased significantly 1 year after the operation, with no significant differences in this reduction between the two employed techniques. The mean alterations in serum chemerin values were linked to the alterations in blood glucose profile and BMI. In line with our findings, Terra et al. [34], reported significant, comparable decrease in serum chemerin levels after RYGB and LSG. The change in serum chemerin was correlated with body weight and blood glucose level; thus, the authors postulated that the improvement in serum chemerin might have occurred secondarily to the improvement in glucose hemostasis and body weight [34]. Other studies demonstrated significant decreases in serum chemerin levels after bariatric surgery [39, 40].

The GI hormone, ghrelin, is the only gut hormone that induces appetite, initiates feeding, and increases energy intake [41]. The serum level of ghrelin increases during prolonged fasting, and it is suppressed by food intake [42]. Thus, diet-based weight loss strategies are associated with elevated serum ghrelin levels, which may obstacle sustained and effective weight loss [43]. As an efficacious strategy for massive weight reduction, bariatric surgery can result in a notable reduction in fasting serum ghrelin concentrations. In the present study, we demonstrated a substantial decrease in fasting serum ghrelin 1 year after RYGB and LSG. The changes in serum ghrelin were significantly correlated with BMI, blood glucose profile, and triglyceride level. In line with our findings, Cummings et al. [44] reported a significant reduction in 24-hour profile of

ghrelin after RYGB. Other prospective studies reported a reduction in serum ghrelin levels after LSG [45] and RYGB [46, 47]. The reduction of serum ghrelin level after LSG is expected as the procedure involves the removal of stomach fundus, the main site for the secretion of ghrelin [48]. However, the published literature appears inconsistent regarding the effect of RYGB on serum ghrelin levels. For example, Santiago-Fernández et al. [49] reported a significant increase in serum ghrelin after RYGB and a significant reduction in its level after LSG. Kalinowski et al. [33] and Stoeckli et al. [50] also showed similar findings. Other reports showed no changes in ghrelin levels after RYGB [51, 52]. Such heterogeneity in the published literature was postulated to arise from evaluating the patients at different time points; it was reported that the ghrelin hemostasis differs according to the metabolic state of the patients, whether they are in weight loss phase or steady phase [53, 54].

Among the drawbacks of the present work is the absence of a control group (because of ethical issues). And so, each patient was considered as his/her own control (pre and post-operative). In Besides, more future neatly destined extensive work is needed for comparative efficacy regarding these results and try to compensate for the possible lifestyle confounders.

In conclusion, RYGB and LSG led to significant sustained reductions in the serum adipokine values (leptin and chemerin) and GI hormone (ghrelin), with no specific impact of the type of surgery on the extent of these reductions. Our study also showed that the changes in serum chemerin and ghrelin were initimately linked to the changes in blood sugar profile and triglyceride concentrations. Such findings may reflect that the improvements in these hormones may result from the improvement in insulin sensitivity and body weight after metabolic surgery. Nevertheless, future research is still warranted to elaborate the mechanistic approaches of such notable changes in these molecules and how they affect the clinical outcomes.

Novelty of the Study

To our knowledge, there are no much data in the literature addressing the effect of Roux-en-Y and LSG on leptin, chemerin, and ghrelin in addition to associated metabolic changes in one single study. The present study seems to be at least one of the first studies to address that issue. In addition, among the strengths of this study are the large number of studied patients with quite long-term follow-up period. This point may make our study fairly unique as it is often difficult to get patients back after 1 year for follow-up.

In addition, new insight into the role of these studied adipocytokines makes them interesting goals for novel therapeutic strategies in chronic inflammatory conditions relating to obesity, and concomitant metabolic co-morbidities. Thence, the current work adds to the existing concention on the impact of bariatric surgery on systemic adipokines.

Compliance with Ethical Standards

Informed consents were obtained from all patients included in the study

Conflict of Interest The authors declare that they have no conflict of interest.

Ethics Approval This study was approved by the institutional review board/clinical medical research ethics committee.

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