Effect of Laparoscopic Sleeve Gastrectomy (LSG) Surgery on Weight Reduction and Serum Visfatin, Ghrelin and Leptin Levels in Morbidly Obese Subjects

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Abstract

Aim: this study aimed to investigate how Laparoscopic sleeve gastrectomy (LSG) Surgery affect the weight reduction and level of serum adipokines (Visfatin , Ghrelin and Leptin) in Morbidly Obese Subjects because of the Conflicting results that obtained from previous studies regarding the changes of adipokines following sleeve operation and weight reduction. ***Method****:* 20 Iraqi severely obese patients (12 females and 8 males), Mean ±SD of aged are 34.45±9.47, and 40 healthy lean controls (24 females and 16 males) Mean ±SD of aged are 33.90±9.31were studied. Anthropometric parameters and biochemical parameters (insulin resistant IR) as well as visfatin, ghrelin and leptin were analyzed before and 6 weeks after the operation. ***Results****: after surgery* Anthropometric indices (BMI) decreased significantly. The reduction of visfatin and the elevation of ghrelin were statistically not significant, whereas leptin level decrease significantly and insulin resistant (IR) decrease not significantly. moreover, there is a significant positive correlation between the change of serum leptin and (BMI)and visfatin correlated positively with insulin resistant (HOMA-IR).

Conclusions: sleeve Gastrectomy resulted in significant decrease in the (BMI), decreased serum visfatin, insulin resistant and increased ghrelin levels statistically not significant, while significant decrease in leptin level. Further studies with different design are suggested to clarify these changes.

Keywords: *Visfatin. Ghrelin. Leptin. obesity. Morbidly Obese. sleeve gastrectomy (LSG). Weight Reduction. insulin resistant.*

Introduction

Obesity was considered .as a chronic, relapsing, progressive, disease process that require intervention [1] Excess body weight, a burgeoning problem worldwide, which is a major risk factor for cardiovascular disease, Diabetes mellitus affects more than .180 million people around the world, .and the number of patients is.anticipate to increase to 300 million by 2025 [2].

Bariatric surgery is the most effective treatment for morbidly obese patients [3]. It is associated with significant and sustained weight loss and is more effective than lifestyle or medical management in achieving glycemic control and reductions in morbidity and mortality from cardiovascular disease and even cancer [4].

Laparoscopic sleeve gastrectomy (LSG) is a restrictive procedure, although irreversible [5,6]. The SG has many advantages over other current operations. The SG is less technically demanding than other operations with minimal morbidity [7].

Adipose tissue acts as an endocrine organ and produces numerous bioactive factors such as adipokines that communicate with other organs and modulate a range of metabolic pathways, the dysfunction of adipose tissue as a causal factor is linked to obesity and its related disorders [8].

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Visfatin (known as pre-B-cell colony-enhancing factor - PBEF or nicotinamide phosphoribosyl transferase - NAMPT) which is insulin-mimicking adipocytokine constitutively secreted from visceral (VAT) and probably subcutaneous adipose tissue, as well as hepatocytes and it is thought to play a pivotal role in the pathogenesis of obesity and metabolic syndrome [9]. visfatin actions can be endocrine, paracrine, and autocrine as well. These autocrine effects of visfatin may play an important role in regulating insulin sensitivity in the liver [10]. concentrations of visfatin are increased by hyperglycaemia and lowered HDL-cholesterol level [11], also visfatin plays a pivotal role as regulator of cell energy balance [12].

Ghrelin discovered in 1999 as a 28-amino acid acylated peptide first identified as an endogenous ligand for the growth hormone secretagogue receptor (GHSR) [13]. Itis present along the whole gastrointestinal tract with decreasing concentrations from stomach to colon [14]. In addition to stimulating growth hormone (GH) release, ghrelin has been further implicated in the regulation of appetite, secretion of gastric acid, gut motility, and insulin secretion [15]. From a functional point of view, the ghrelin system has been found to be involved in the modulation of a multiplicity of patho-physiological functions such as hormonal secretions, memory and learning processes, food intake, body weight gain, insulin release, B-cell survival, adiposity, energy homeostasis as well as inflammatory processes and it is consider as a hunger hormone [16].

Leptin is an adipose-derived hormone secreted by white adipose tissue, Given its role in the maintenance of energy homeostasis and body weight [17]. Leptin expression and circulating levels show circadian fluctuations, and also change with nutritional state [18]. leptin controls feeding by regulating multiple orexigenic neuropeptides and it is consider as a satiety hormone [19].

The aim of this study was to evaluate the role of sleeve gastrectomy in weight reduction and changes in circulating visfatin , ghrelin and leptin levels in morbidly obese subjects.

Material and Methods

The study was performed in 20 Iraqi morbidly obese subjects (12 females and 8 males) aged range (20-51 years), blood sample were collected before and 6 weeks after bariatric surgery. and in 40 healthy, non-obese subjects (24 females and 16 males) aged range (21-53 years). These patients received bariatric surgery after failure of other weight loss strategies Subjects with the following conditions were excluded from the study: Patients who had an acute illness,acute or chronic inflammatory or infective diseases, end-stage malignant disease, menopausal women ,women receiving contraceptive treatment ,any prostatic diseases (male) All participants gave their informed consent, and the study was reviewed and approved by the Ethics and Research Committee. The type of this study is intervention (prospective) study.

Laboratory measurements

Blood samples were collected after a 12-h fast .The serum was separated and frozen at −20◦C until analysis. Fasting plasma glucose was measured using Abbott ARCHITECT plus c4000 device. The serum insulin level was assayed using an immune radiometric method (Demeditec /Germany). The insulin sensitivity was determined using the Homeostasis Model Assessment Index of insulin resistance (HOMA-IR) according to the following formula: HOMA-IR = fasting insulin (μU/ml) × fasting glucose concentration (mmol/l) / 22.5 [20]. The serum concentrations of visfatin, ghrelin and leptin were determined by commercially available ELISA kits (Shanghai Biological/China, Demeditec /Germany).

Statistical Analysis

The statistical analysis was done with SPSS (Statistical Packages for Social Sciences- version 25). Differences between morbidly obese (MO)and controls were calculated using Student's t-test for independent samples. Differences between preoperative and postoperative data were tested by paired t-test (Student's t-test). Statistical significance was considered whenever the P value was equal or less than 0.05.

Results

Twenty Iraqi morbidly obese patients, 12 women and 8 men, participated in the study. Their mean age was 34.45 ± 9.47 years and their mean BMI at baseline 43.04 ± 5.2kg/m2, and 40 Iraqi healthy non-obese subjects 24 women and 16 male their mean age 33.90 ± 9.31years and their mean BMI at baseline 22.29 ± 2.01kg/m 2, after

six weeks of surgery a significant reduction in the BMI was observed 37.34±4.61 (P-value =0.0001). Concerning the circulating levels of the adipo/cytokines in the morbidly obese compared with controls this study shows that in MO visfatin and leptin were significantly higher, whereas ghrelin tended to be lower in MO compared with controls as shown in Figure 1,2,3.After six weeks of the **(LSG)** this study shows a reduction that statistically not significant in serum level of visfatin and in insulin resistant (HOMA-IR), elevation was statistically not significant in serum ghrelin level and a significant reduction was in serum level of leptin .Baseline levels of visfatin correlated positively with insulin resistant (HOMA-IR)(r=0.496 , P=0.026) as shown in Figure4 , also the study shows a strong positive significant correlation between (BMI) and serum Leptin post operatively (r=0.712, P=0.0001) as shown in Figure 5. The clinical and biochemical variables of the controls, patients before and after bariatric surgery are summarized in table1.

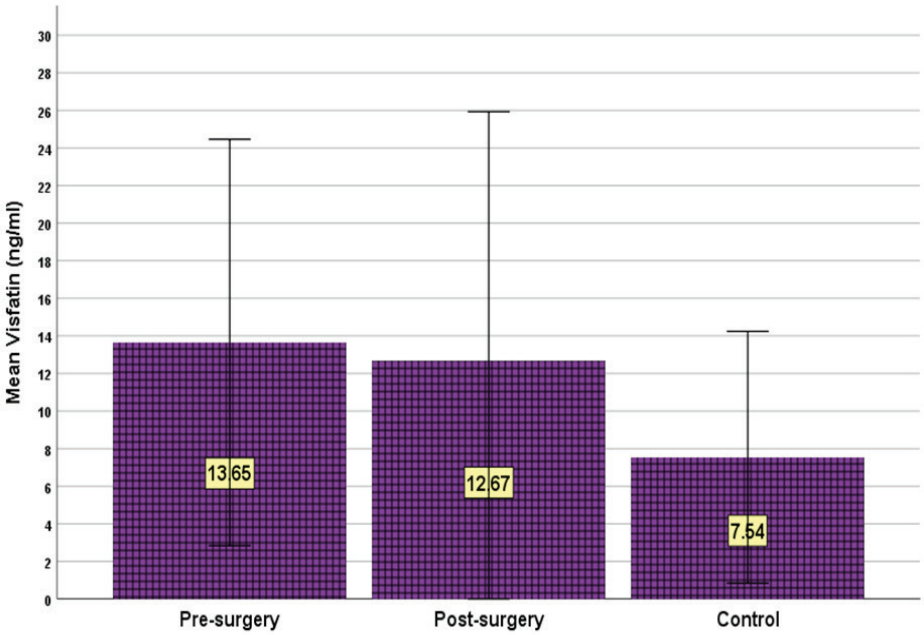

Figure 1. the Mean ±SD of serum visfatin for patients (pre, post-surgery) and controls

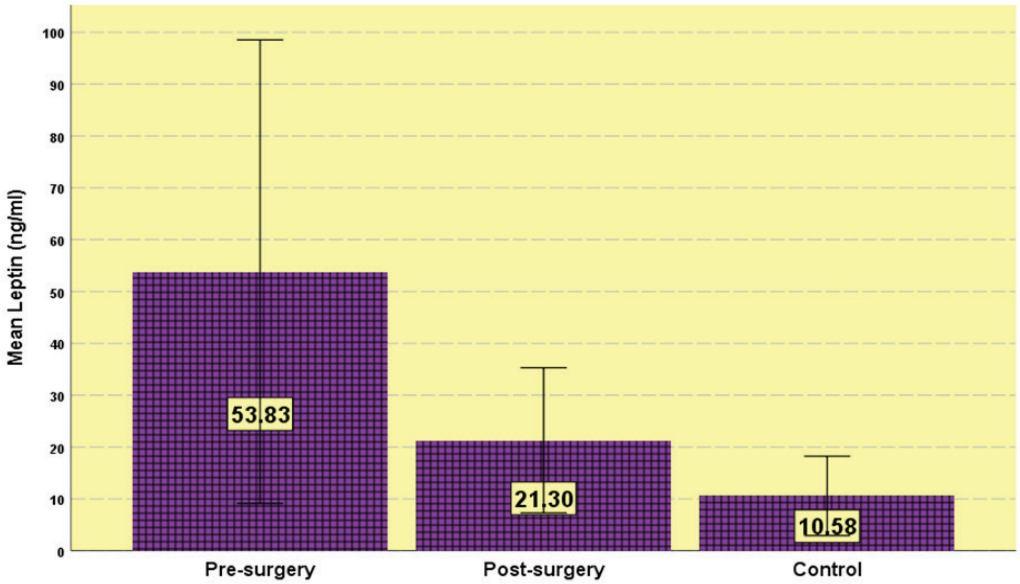

Figure 2. the Mean ±SD of serum leptin for patients (pre, post-surgery) and controls

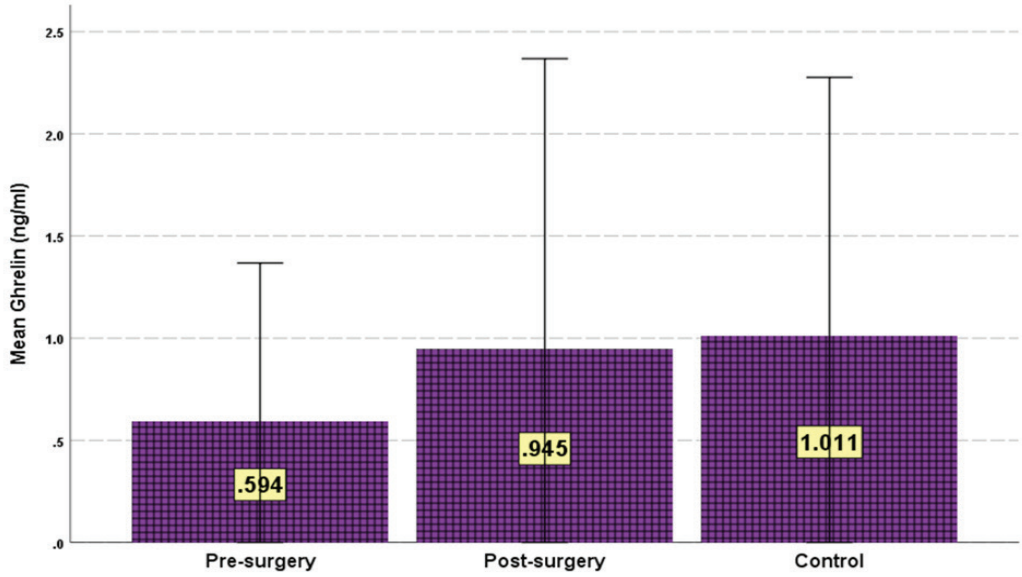

Figure 3. the Mean ±SD of serum ghrelin for patients (pre, post-surgery) and controls

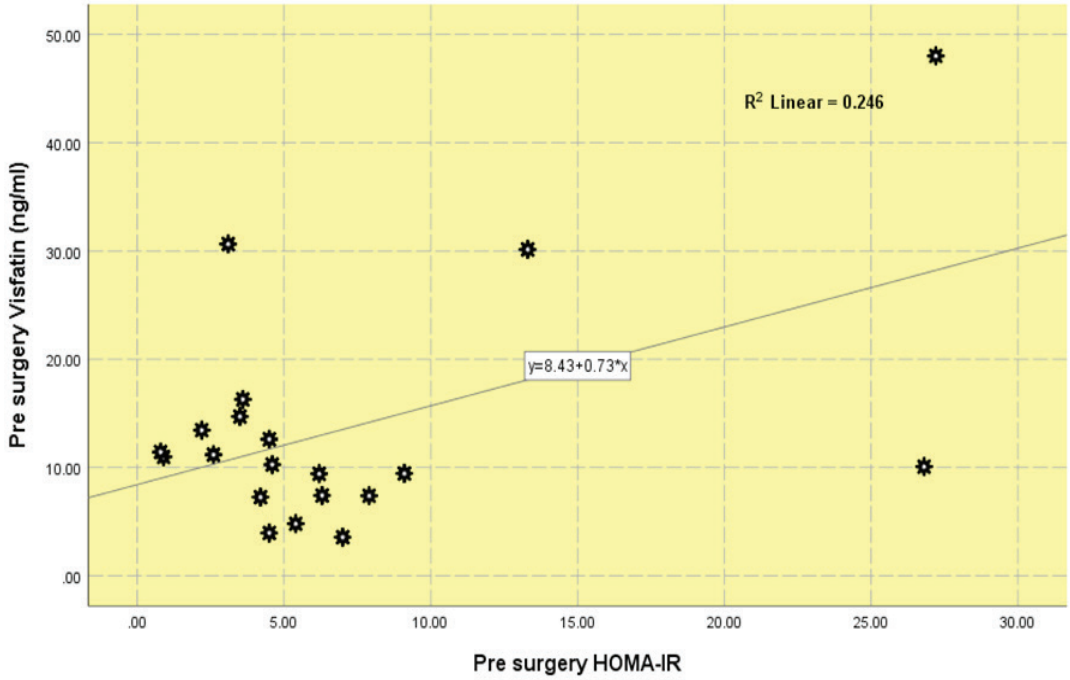

Figure 4. the linear correlation between pre-HOMA-IR and serum visfatin (ng/ml) among Pre-surgery morbid obese patients

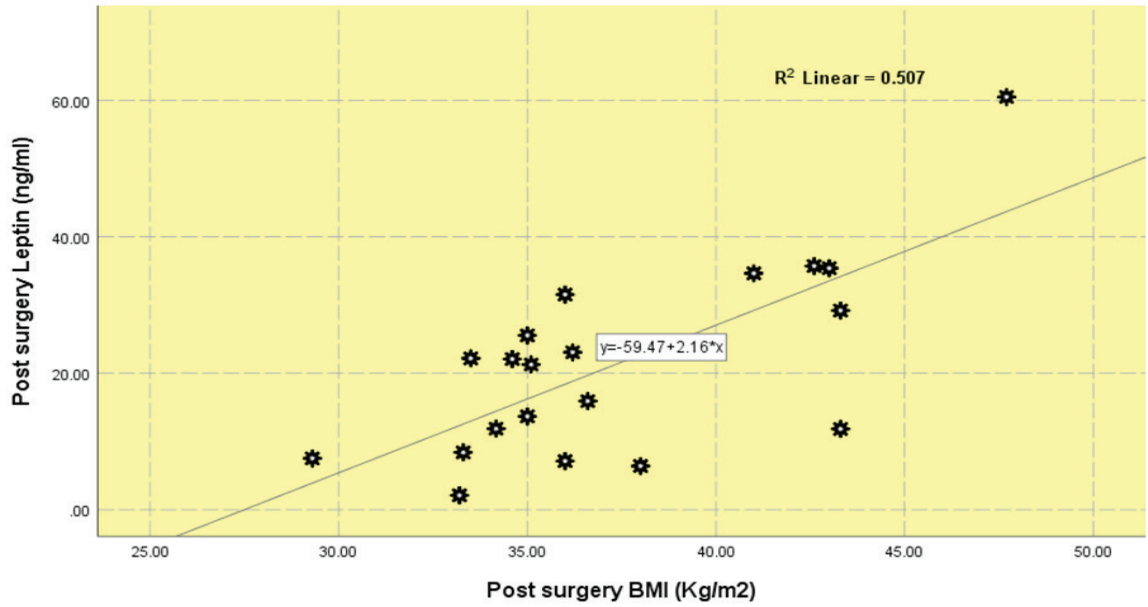

Figure 5. the linear correlation between post-BMI and serum leptin (ng/ml) among Post-surgery for morbid obese patients.

Table 1. the clinical and biochemical variables in healthy controls and morbidly obese subjects before and 6 weeks after Laparoscopic sleeve gastrectomy .

Variable	Pre-surgery No=20	Post-surgery No=20	Control N0=40	p-value (pre x C)	p-value (pre x post)
BMI	43.04±5.2	37.34±4.61	22.29±2.01	0.0001*	0.0001*
HOMA-IR	7.19±7.37	4.70±5.95	1.51±0.59	0.0001*	0.083
Visfatin	13.65±10.81	12.67±13.26	7.54±6.70	0.009*	0.778
Ghrelin	0.594±0.774	0.945±1.422	1.011±1.265	0.182	0.082
Leptin	53.83±44.70	21.30±14.00	10.58±7.66	0.0001*	0.002#

***Significant difference between two independent means using Student-t-test at 0.05**

#Significant difference between two dependent means using Paired-t-test at 0.05

Discussion

The present study shows a significant reduction in the weight of patients after six weeks of surgery (P=0.0001), this result agrees with previous findings reported by (Hosseinzadeh-Attar, M. J. et al 2013) who find a significant decrease in the BMI of patients before and after six weeks of surgery [21]. In addition to the weight loss (Auguet, T. et al., 2013) showed that visfatin level is higher significantly in morbid obese patients when make comparison to lean control ($p < 0.001$) [22]. data of the present study confirm these findings. visfatin level decreases after surgery but statistically not significant, which agrees with a previous study done by (El Makromy, G. M. 2017) that showed Weight reduction

after (LSG) is associated with a significant decrease in circulating level of visfatin in MO patients. It is worth to mention that, the difference in the follow up duration (three months) is the reason for their decreasing appear significantly [23]. Obesity is considered as a low-grade inflammation, which is improved following weight loss, therefore, it is expected that weight reduction modulates secretion of adipokines from adipose tissue. Visfatin has been considered as a new pro-inflammatory adipokine [24]. Since the main site of visfatin secretion is VAT, it was suggested that its plasma concentration is correlated with visceral obesity. A decreased amount of VAT following weight loss would suggest a reduction in visfatin concentrations after bariatric surgery [25]. This study present a reduction in the level of serum ghrelin in morbid obese patients when compared to control, this results is in agreement with previous study done by (Lin, E. et al. 2004) who have revealed that lean controls had significantly higher plasma ghrelin levels when compared with morbidly obese humans [26]. Regarding the level of ghrelin after surgery, this study shows elevation but statistically not significant in the level of Ghrelin for patients after six weeks of surgery, this finding is agreed with previous study reported by (Terra, X et al. 2013) who demonstrated an increase in ghrelin levels, after bariatric surgery-induced weight loss (SLG)[27]. A possible explanation could be that in restrictive bariatric surgery, passage of food through the stomach, although to a lesser extent, is still taking place. Gr cells are not exhausted and react with an increased production of ghrelin, which could result in increased appetite in patients after gastric restriction [27]. A confounding issue in comparing studies is the patients' actual state of energy homeostasis, whether patients are in phases of weight loss or in phases of a steady state. In operated patients still experiencing an active weight loss, increased ghrelin concentrations were found [28]. The present result also agrees with (Purnell, J. Q. 2003) who concluded that, as body mass index (BMI) decrease the ghrelin level increase because they are correlated negatively [29]. Concerning leptin (Wroblewski, E. et al. 2016**)** who find that obese patients had higher leptin level than non-obese controls [30]. this finding agrees with the result of this study that shows a significant elevation in the level of serum Leptin for the morbid obese patients in compare to controls. Also This study demonstrated that there is a significant reduction in the level of serum leptin of patients after surgery from their base line. This result is consistent with previous findings which reported by (Varlık E.et al, 2019) concluded that, leptin level decrease significantly from its base line value after (SLG) [31]. About the correlation this study shows positive significant correlation between pre-HOMA-IR and serum Visfatin) , that explained by the following, hyperinsulinemia (IR), is the most common biochemical abnormality seen in obesity [32]. Obesity induces the release of visfatin from adipocytes, in order to overcome the (IR) the body increase the production of visfatin [33].

In conclusion Laparoscopic sleeve gastrectomy has successful weight reduction associated with decrease in circulating visfatin , increase ghrelin level , decrease in leptin level and get improvement in insulin resistant.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

Funding: Self-funding

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