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Novelty Study Of Cholecystokinin And Its Relationship To Some Biochemical Parameters Before And After Gastric Sleeve Surgery For Both Sexes

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ABSTRACT

The study focused on the hormone cholecystokinin (CCK) and its relationship to obesity before and after gastric sleeve surgery. Forty-five samples were collected from obese patients of both sexes before surgery and served as a control group. They were followed up after surgery (group 1 after three months, group 2 after six months, and group 3 after nine months). Levels of CCK, CCKAR1, gastrin, ghrelin, leptin, GLP-1, GLP-2, amylase, lipase, ALPH, glucose, uric acid, lipid levels, and BMI were measured. The results showed significant improvements in the levels of biochemical variables in the patients, particularly after nine months. CCK levels showed a significant increase in their concentration after surgery and an effective interaction with other variables, reinforcing its preventive and therapeutic role in maintaining long-term physical health after gastric sleeve surgery, preventing complications, and combating obesity.

Keywords: *Obesity; CCK, Ghrelin, Sleeve gastrectomy (SG), family history.*

INTRODUCTION

The World Health Organization has described obesity as the greatest current threat to human health [1]. Current medical treatment strategies (diet, behavioral modifications, and medications) aimed at achieving and maintaining clinically significant weight loss remain limited. Bariatric surgery is an effective treatment for morbid obesity [2,3,]. Obesity is a global health problem, primarily influenced by environmental factors and genetic variations. Due to food intake, satiety signals suppress hunger signals [4,5]. These signals originate in the gastrointestinal tract and pancreas and transmit information from the periphery to the brain (via vagal neurons). Eating palatable food leads to uncontrolled ingestion behavior due to a shift from homeostatic to hedonic regulatory mechanisms for food intake [1]. These changes occur primarily in obese individuals and, consequently, lead to dysregulation of anorexia-inducing hormones. It is expected that females will continue to have a higher incidence of obesity, given the higher percentage of body fat in women for biological reasons [6]. Fundamental sex differences include the distribution and mobilization of adipose tissue storage, different insulin sensitivity and lipoprotein profiles, and the effects of gonadal hormones [7]. Although overweight and obesity are considered a problem in high-income countries, they are currently on the rise in low- and middle-income countries due to global free trade, economic growth, and urbanization [8]. Recent evidence has also shown that gastrointestinal hormones also act in the mesolimbic pathways. Therefore, these hormones may play a role in controlling both hedonic and static appetite. Among these hormones is cholecystokinin, a hormone produced primarily by L cells in the duodenum and jejunum, which is associated with satiety [9].

The aim of the study was to evaluate the role of CCK before and after gastric sleeve surgery, its impact on biochemical variables, and its relationship to weight.

MATERIALS AND METHODS

Samples

The study group included 45 patients of both sexes suffering from morbid obesity and dyslipidemia who underwent bariatric surgery in the Bariatric Surgery Department (General Surgery Department) at Al-Zahrawi Hospital. They were randomly assigned to three groups for postoperative follow-up (group 1 after 3 months (No. 8), group 2 after 6 months (No. 19), and group 3 after 9 months (No. 19)). The average age of the patients in the study group ranged from 20 to 55 years. Patients with diabetes, heart disease, and thyroid disease were excluded.

Samples were collected after fasting (12-13 hours) for measurements each of cholecystokinin hormone, cholecystokinin A receptor 1 (CCKAR1), gastrin, ghrelin, leptin, glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2) was measured by ELISA using a specific test kit, amylase (AMYL), lipase (Lip), alkaline phosphatase (ALP) were assessed through enzymatic methods using the Fuji device,, glucose (GLU), uric acid (UA), lipid profiles were measured using a specific kit by UV/VIS Spectrophotometer. While Body Mass Index (BMI) was calculated using the following formula: BMI(Kg/m2) = weight (Kg) / length(m2).

Statistical Analysis

Finally, SPSS software version 27 was used to analyze the data. The independent samples Duncan's multiple range test. A P-value of less than 0.05 was considered statistically significant.

RESULT

The results in Table (1) showed the level of clinical variables for patients before and after gastric sleeve surgery for both sexes.

Clinical Variables	Patients Before Gastric Sleeve Surgery Mean ± SD	Patients After Gastric Sleeve Surgery (3 month) Mean ± SD	Patients After Gastric Sleeve Surgery (6 month) Mean ± SD	Patients After Gastric Sleeve Surgery (9 month) Mean ± SD	p-value
CCK pg/ml	25.7 ± 5.2	28.6 ± 4.8	30.1 ± 7.1	31.3 ± 5.8	0.001***
CCKAR1 pg/ml	162.0 ± 4.6	167.4 ± 8.1	177.8 ± 8.6	216.1 ±27.2	<0.001***
Gastrin pg/ml	27.7 ± 1.19	37.3 ± 0.96	39.26 ± 1.8	41.1 ± 2.2	<0.001***
Ghrelin pg/ml	421.3± 7.2	392.1 ± 8.5	378±9.7	349.4±6.3	<0.001***
Leptin pg/ml	368.8 ± 2.8	371.1 ± 3.3	426.43 ± 19.2	435.5 ± 28.84	0.003***
GLP-1 pg/ml	31.9 ± 4.8	36.7±4.7	38.7±4.4	40.4±4.6	<0.001***
GLP-2 pg/ml	282.1±15.1	291.9 ± 9.2	306.4±29.1	322.4±23.7	0.04*
AMYL U/L	58.6±4.3	62.7.3±2.8	68.3±3.5	70.3±2.7	0.07(n.s)
Lip mg/dl	29.9±1.1	32.2±7.7	32.6±1.5	29.6±1.9	0.6(n.s)
ALPH U/L	18.0±1.1	19.5±6.6	18.5±1.2	16.5±1.5	0.9(n.s)
GLU mg/dL	132.2±5.9	84.1±2.0	79.9±2.2	73.0±4.7	<0.001***
UA mg/dL	6.4±1.2	5.0±1.5	5.1±0.9	4.6±1.6	<0.001***
CHO mg/dL	240.7 ± 8.3	159.1±11.7	161.4±8.7	161.0±6.9	<0.001***
TG mg/dL	169.4±9.0	90.6± 5.8	83.5±8.5	81.5±5.8	<0.001***
HDL-C mg/dL	32.3±1.2	44.0±8.0	49.8±8.1	52.4±3.5	<0.001***
LDL-C mg/dL	160.3±7.2	92.9±8.44	87.42±7.8	80.1±8.2	<0.001***
VLDL-C mg/dL	32.5±1.9	24.1±5.1	20.3±1.4	19.0±2.1	<0.001***
ABI	6.9±0.3	3.8±0.4	3.5±0.2	3.2±0.3	<0.001***
BMI	45.4±7.4	32.7±6.2	32.0±3.4	29.7±4.5	<0.001***

Table (1): Level of clinical variables for patients before and after gastric sleeve surgery for both sexes

The results in Table (2) showed the level of clinical variables for female patients before and after gastric sleeve surgery.

Table (2): Level of clinical variables for female patients before and after gastric sleeve surgery.

Clinical Variables	Patients Before Gastric Sleeve Surgery Mean ± SD	Patients After Gastric Sleeve Surgery (3 month) Mean ± SD	Patients After Gastric Sleeve Surgery (6 month) Mean ± SD	Patients After Gastric Sleeve Surgery (9 month) Mean ± SD	p-value
CCK pg/ml	26.3 ± 4.4	29.2± 5.3	29.5 ± 6.5	32.4±5.6	0.005***
CCKAR1 pg/ml	167.5±5.2	174.4±11.7	184.0±20.9	236.0±18.2	<0.001***
Gastrin pg/ml	28.8±1.5	34.3±1.4	38.12±1.7	42.3±3.2	<0.001***
Ghrelin pg/ml	399.5±10.9	379.1±10.2	359.4±11.4	344.3±5.8	<0.001***
Leptin pg/ml	377.5±14.1	418.4±26.8	432.6±32.2	531.3±54.6	0.009***
GLP-1 pg/ml	33.38±4.7	37.7±2.5	39.7±5.1	41.2±4.7	0.001***
GLP-2 pg/ml	256.2 ±12.9	287.1±16.2	312.2± 12.3	313.3±27.4	0.05*
AMYL U/L	55.3±8.7	59.0±4.3	60.4±4.6	68.4±4.8	0.09(n.s.)
Lip mg/dl	28.7±6.6	27.0±1.4	31.2±7.2	30.9±8.2	0.3(n.s.)
ALPH U/L	18.5±1.4	29.0±2.3	19.2±1.5	14.8±1.6	0.1(n.s.)
GLU mg/dL	135.2±8.5	85.3±11.9	84.7±2.3	71.5±10.5	<0.001***
UA mg/dL	6.1±1.2	4.8±1.1	4.2±1.5	3.9±1.2	0.001***
CHO mg/dL	239.4±12.0	170.0± 13.1	164.0±9.5	159.5±7.2	<0.001***
TG mg/dL	174.5±11.8	92.4±6.5	83.5±9.1	74.3±5.9	<0.001***
HDL-C mg/dL	33.2±1.5	52.5±5.5	52.2±3.1	57.6±3.7	<0.001***
LDL-C mg/dL	158.3±10.9	100.8±12.2	83.7±10.8	75.6±9.9	<0.001***
VLDL-C mg/dL	33.6±2.6	20.9±1.6	16.7±3.6	14.8±3.2	<0.001***
ABI	6.5±2.4	3.5±1.5	3.3±1.0	3.2±0.8	<0.001***
BMI	45.8±1.5	34.6±0.95	29.2±0.7	28.2±1.6	<0.001***

While the results in Table (3) showed the level of clinical variables for male patients before and after gastric sleeve surgery.

Table (3) showed the level of clinical variables for male patients before and after gastric sleeve surgery.

Clinical Variables	Patients Before Gastric Sleeve Surgery Mean ± SD	Patients After Gastric Sleeve Surgery (3 month) Mean ± SD	Patients After Gastric Sleeve Surgery (6 month) Mean ± SD	Patients After Gastric Sleeve Surgery (9 month) Mean ± SD	p-value
CCK pg/ml	24.7±1.5	29.8±4.3	27.6±1.2	31.4±3.1	0.008***
CCKAR1 pg/ml	151.7±8.6	164.7±5.1	182.7±12.8	196.1±24.5	0.001***
Gastrin pg/ml	26.1±1.8	37.26±0.96	38.7±1.4	41.1±3.8	<0.001***
Ghrelin pg/ml	421.3±8.6	376.5±12.2	377.6±23.2	358.7±14.4	0.005***
Leptin pg/ml	354.2±12.1	371.0±2.3	437.9±28.2	442.63±32.5	0.02*
GLP-1 pg/ml	29.6±4.0	37.7±2.6	40.4±0.8	42.3±1.5	<0.001***
GLP-2 pg/ml	273.7±12.7	278.7±28.2	312.9±13.2	345.2±51.6	0.03*
AMYL U/L	62.3±3.1	68.0±5.5	66.3±3.7	63.4±6.2	0.5(n.s.)
Lip mg/dl	32.0±1.6	37.5±7.5	32.5±2.3	30.6±6.9	0.9(n.s.)
ALPH U/L	17.1±1.6	17.5±2.0	18.1±1.1	17.1±1.1	0.4(n.s.)
GLU mg/dL	127.0±7.1	102.1±5.8	86.7±1.8	72.8±3.3	<0.001***
UA mg/dL	6.8±1.2	6.1±1.3	5.6±1.4	5.2±0.9	0.01**
CHO mg/dL	242.9±32.0	195.1±10.2	158.2±17.0	157.1±11.8	<0.001***
TG mg/dL	160.9±13.8	88.5±10.6	75.0±10.7	67.0±9.8	0.001***
HDL-C mg/dL	31.0±1.9	35.5±1.5	46.4±3.4	53.0±4.3	<0.001***
LDL-C mg/dL	163.0±8.9	92.5±11.6	90.2±14.9	85.0±12.4	<0.001***
VLDL-C mg/dL	30.3±2.7	31.5±1.2	19.3±2.5	15.0±2.1	0.003***
ABI	7.5±1.8	4.2±0.2	3.7±1.3	3.0±0.67	<0.001***
BMI	44.6±1.4	30.5±2.2	29.4±1.6	26.7±2.2	<0.001***

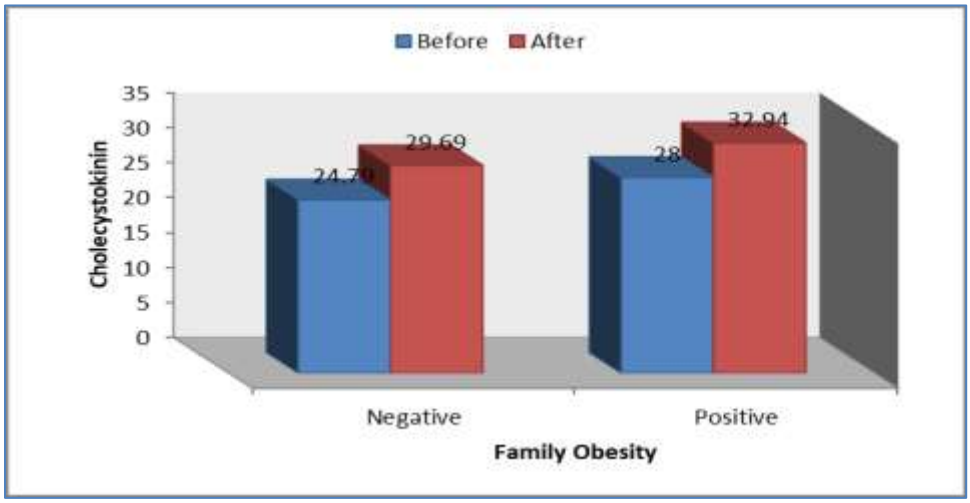

Figure (1): Concentration of CCK according to the family history before and after Gastric Sleeve Surgery

DISSECTION

The results in Table (1), showed a significant increase in CCK, CCKAR1, gastrin, leptin, GLP-1, GLP-2, and AMYL levels in obese patients in all three groups after gastric sleeve surgery compared to the same patients

before surgery. This is because after gastric sleeve surgery, the stomach volume is significantly reduced, leading to faster gastric emptying and increased delivery of nutrients, particularly fats and proteins, to the small intestine. This rapid nutrient transport stimulates the remaining I cells, leading to increased CCK secretion [10]. The elevated CCKAR1 levels after surgery may also indicate adaptive receptor responses to elevated CCK levels, enhancing the body's ability to effectively regulate digestion and satiety. CCK receptors (CCKRs) regulate various physiological functions, including digestion, satiety, emotional regulation, pain perception, and memory [11]. The results show a significant increase in gastrin levels after gastric sleeve surgery. This increase in gastrin may reflect physiological changes in gastric acid secretion and gastrointestinal function, as well as an adaptation to the anatomical changes resulting from surgery. Gastrin, produced by G cells in the abdominal cavity, acts as a major stimulator of gastric acid secretion [12]. Consistent with our findings, a recent study conducted in 2024 sought to determine the role of gastrin in improving glutamic acid (GLU) metabolism [13]. Elevated GLP-1 levels indicate improved GLU regulation and enhanced insulin secretion after gastric sleeve surgery [14]. The study hypothesized that elevated plasma GLP-1 levels, induced by GLU administration, were responsible for the elevated insulin secretion rates and subsequent hypoglycemia observed in our lean human cohort after gastric sleeve surgery. Additionally, GLP-1 levels were positively correlated with measures of obesity, insulin resistance, blood pressure, and inflammatory markers, suggesting that elevated GLP-1 may serve as a compensatory response to obesity-related metabolic disturbances [15]. In pancreatic beta cells, GLP1 is a potent inhibitor of glucagon secretion (which is also strictly glutamic acid-dependent), possibly resulting from a direct effect on pancreatic alpha cells [16]. Results also indicated elevated GLP-2 levels in patients after gastrectomy, particularly in the first months following surgery. They attributed this increase to increased nutrient delivery to the small intestine as a result of accelerated gastric emptying and changes in gut hormone signaling [17]. In the same table, an increase in leptin levels was observed after surgery. This change reflects alterations in adipose tissue signaling, likely due to changes in body fat composition following massive weight loss, consistent with leptin's role in regulating energy balance [18]. However, bariatric surgery has been shown to restore leptin signaling in obese individuals, with significant improvements compared to non-obese controls. Interestingly, improved leptin signaling after bariatric surgery has been associated with improved cognitive function, suggesting that restoring leptin signaling may contribute to the cognitive improvements observed in patients following the procedure [19].

Regarding amylase (AMYL) levels, amylase levels were slightly increased. This is primarily responsible for carbohydrate digestion, and its levels can reflect pancreatic activity. The observed stable levels indicate that pancreatic function is largely preserved after sleeve gastrectomy [20]. The slight increase in lipase levels observed after sleeve gastrectomy (SG) may be attributed to postoperative dietary changes, particularly in fat intake, and potential metabolic adaptations. This finding is consistent with research by Ohira et al., 2021 [21], which found that lipase levels remained stable or increased slightly after sleeve gastrectomy. The observed decrease in cholesterol and LDL cholesterol levels is consistent with existing research demonstrating that sleeve gastrectomy effectively reduces atherogenic lipid levels [22], and is likely due to changes in bile acid metabolism and improved insulin sensitivity [23]. The significant increase in HDL-C levels observed in this study is also consistent with recent research findings. Sleeve gastrectomy improves HDL-C function by enhancing reverse cholesterol transport [24]. Weight loss after bariatric surgery is closely associated with a significant decrease in triglycerides and an increase in HDL cholesterol in morbidly obese patients. Surgery reduces hepatic lipid synthesis and improves peripheral lipid clearance (Garai et al., 2021). According to Wang et al., 2025, patients showed a significant decrease in cholesterol [25].

The results in Table (2) showed a significant and progressive increase in CCK levels in women after gastric sleeve surgery at different postoperative intervals: 3 months, 6 months, and 9 months, with a p=0.005. The increase in serum CCK levels after gastric sleeve surgery in women is the result of increased stimulation of the cells that produce it in the distal part of the small intestine or changes in the number of these cells in the duodenal mucosa [26]. The results in Table (2) showed a significant and progressive increase in the level of

the CCKAR1 receptor hormone in women after gastric sleeve surgery at different postoperative intervals: 3 months, 6 months, and 9 months, with a $p<0.001$. The results demonstrate that gastric sleeve surgery leads to an increase in the number of CCKAR1 receptors (expression) in tissues. This means that the number of receptors in the vagus nerve, brain, or pancreas often does not remain constant after surgery, and gastric sleeve surgery may also affect the sensitivity of these receptors [27]. The results shown in the same table also showed a significant and gradual increase in gastrin levels in women after gastric sleeve surgery at different points after the procedure: 3 months, 6 months, and 9 months. At a p-value <0.001, gastric sleeve surgery may be associated with increased gastrin levels due to changes in the gastrointestinal tract after surgery, such as a reduction in stomach size or changes in the number of gastrin-producing G cells [28]. This study showed that gastrin levels are higher in women than in men. This may be due to a combination of physiological and hormonal factors associated with the female sex, particularly estrogen and progesterone, as these hormones can influence gastrin secretion and the response of gastric cells to it. Estrogen, in particular, may enhance the stimulation of parietal cells to secrete gastrin. After gastric sleeve surgery, a large portion of the stomach is removed, which may reduce the number of parietal cells that secrete hydrochloric acid. This decrease in acidity may lead to positive feedback that stimulates gastrin secretion, as gastrin is normally secreted in response to decreased gastric acidity [29]. The results in Table (2) also showed a significant gradual decrease in ghrelin levels in women after gastric sleeve surgery at different stages after the operation: 3 months, 6 months, and 9 months, at a p-value <0.001. This value indicates increased regional and neural sensitivity of feeding control systems (such as GHS-R receptors in the stomach/brain) in women, which may be due to the effect of estrogen and differences in fat distribution [30]. Table (2) also showed a significant gradual increase in leptin levels in women after gastric sleeve surgery at different points postoperatively: 3 months, 6 months, and 9 months ($p = 0.009$). This may be attributed to the higher percentage of body fat in women compared to men, as leptin is directly related to body fat percentage. It has been observed that women, even after gastric sleeve surgery, retain a higher fat mass than men, and even with weight loss, the amount of leptin secreted by adipose tissue remains higher [19]. The results in Table (2) also showed a significant and sequential increase in GLP-1 levels in women after gastric sleeve surgery at different points after the procedure: 3 months, 6 months, and 9 months, with a p-value of 0.001. This is because after gastric sleeve surgery, the speed of food passage from the stomach to the intestine increases, stimulating L cells located in the distal part of the intestine (ileum and colon) to secrete larger amounts of GLP-1 after eating. GLP-1 affects appetite centers in the brain (especially the hypothalamus) [31]. The results also showed a slight and gradual increase in GLP-2 levels in women after gastric sleeve surgery at different points after the procedure: 3 months, 6 months, and 9 months, with a p-value of 0.05. This increase is associated with improved satiety and reduced diarrhea and malabsorption. In this study, a slight difference in GLP-2 levels was observed in women after gastric sleeve surgery, which may indicate how the digestive system has adapted to the procedure, contributing to reduced adverse effects on the small intestine and supporting the rebalancing of digestive hormones. In contrast, women who underwent gastric sleeve surgery showed a gradual decrease in glutamic acid (GLU) levels over different postoperative periods (3, 6, and 9 months) with a probability of $p<0.001$. The improved glutamic acid tolerance after bariatric surgery is largely attributed to increased secretion of the incretin hormone GLP-1, which significantly enhances insulin secretion, as well as improved insulin sensitivity resulting from weight loss, particularly in women. The exact cause of postoperative weight loss has not yet been fully determined. However, strict calorie restriction immediately after surgery, coupled with positive hormonal changes, may contribute to effective weight loss, which is believed to be sustainable in the long term. This is partly related to the sustained increase in satiety-promoting hormones such as GLP-1 and gastrin, along with a decrease in hunger-stimulating hormones such as ghrelin [32]. The results in Table (2) also showed a significant, gradual decrease in uric acid levels in women after gastric sleeve surgery at different points postoperatively: 3 months, 6 months, and 9 months, with a p-value of 0.001. Our study contributes novel observations by distinguishing the rate of decline in serum uric acid levels after surgery. Bariatric surgery appears to be a promising

intervention for reducing serum uric acid levels and may help mitigate the long-term risk of gout in obese individuals. Therefore, we examined the effect of bariatric surgery on uric acid levels and sought to investigate the rate of decline in serum uric acid levels after surgery, as determined by sex-specific threshold levels. Bariatric surgery has been shown to effectively lower serum uric acid levels in obese individuals, particularly during the first nine months postoperatively, and this may be ably due to the fact that obese women often suffer from insulin resistance after gastric sleeve surgery, insulin metabolism improves, leading to a decrease in UA accumulation in the blood. In addition, increased renal excretion of UA may be possible. With weight loss, kidney function and its ability to eliminate waste products such as UA improve, as well as dietary changes after surgery. The diet after gastric sleeve surgery is low in purines (found in red meat and legumes), which helps reduce UA production.

The results in Table (2) indicate that gastric sleeve surgery (GS) has a significant and statistically significant effect on improving serum lipid levels in obese women. Significant decreases were observed in women, particularly 9 months after gastric sleeve surgery, in CHO, TG, LDL-C, VLDL-C, and BMI, along with a significant increase in HDL-C levels after surgery. All of these changes were statistically significant at $p<0.001$, respectively. Gastric sleeve surgery reduces stomach volume by 70-80%, leading to a rapid and automatic feeling of fullness. It also induces important hormonal changes that promote fat burning, such as a decrease in ghrelin (the hunger hormone) as a result of gastric sleeve surgery, and an improvement in satiety hormones, which reduces the desire to eat, after surgery, the body begins to rely on stored fat as an energy source due to the calorie deficit, this leads to lipolysis and a loss of fat mass. Most obese women suffer from insulin resistance syndrome. After gastric sleeve surgery, metabolism improves and the body begins to burn fat more efficiently [33]. Although many studies do not focus specifically on women, the reason for the post-surgical fat reduction in women is likely due to estrogen, which positively influences intestinal hormone sensitivity and fat metabolism. Furthermore, women experience a stronger response to satiety hormones after gastric sleeve surgery. A significant reduction in the atherosclerosis index has also been observed as a result of gastric sleeve surgery. It reduces blood vessel thickness, reduces inflammation, and improves endothelial function and clotting factors, effectively leading to a significant reduction in atherosclerosis indices in obese women.

The results in Table (3) showed a significant increase in CCK levels in men after gastric sleeve surgery at different time points: 3 months, 6 months, and 9 months ($p=0.008$). This may be due to changes in the way food passes through the small intestine and its speed of arrival after the operation, which leads to appetite suppression and stimulation of digestive enzyme secretion. A significant weight loss was also observed, particularly in visceral fat. The results of the same table also showed a significant sequential increase in CCKAR1 receptor levels in men after gastric sleeve surgery at different time points (3 months, 6 months, and 9 months) ($p=0.001$). When CCK is released from the small intestine after eating, especially fats and proteins, it binds to the CCKAR1 receptor, leading to a decrease in appetite. The CCKAR1 receptor is primarily expressed in the gallbladder, pancreas, and small intestine, suggesting that CCKAR1 signaling may be one of the ways to maintain energy balance in the digestive system. Gastric sleeve surgery in obese men can modify the CCKAR1 gene, positively affecting a potential mechanism by which the hypothalamic-pituitary-adrenal (HPA) network regulates energy balance. The gut-brain axis is a complex bidirectional communication network between the brain and the gastrointestinal tract, regulating the secretion of several gut hormones in response to food before absorption, maintaining energy balance. The results shown in Table (3) also showed a significant and sequential increase in gastrin levels in men after gastric sleeve surgery at different time points: 3 months, 6 months, and 9 months, with a p-value <0.001. Gastrin is secreted after an increase in gastric pH, leading to gastric acid secretion [34]. Sleeve gastrectomy (SG), a bariatric surgery in which 80% of the gastric globules are removed, poses a challenge to gastric pH stability and increases the liver's efficiency in eliminating harmful fats [35]. After gastric sleeve surgery, a large portion of the fundus of the stomach is surgically removed, significantly reducing the number of ghrelin-producing cells. The remaining ghrelin-producing tissue becomes unavailable for nutrition, resulting in decreased secretory capacity and impaired vagal

function, which impairs the neuronal signals stimulating secretion. This anatomical and functional change results in a significant decrease in circulating ghrelin levels after surgery, particularly after nine months, as shown in Table (3) at p=0.005. The results in Table (3) also showed a gradual increase in serum leptin levels in males at different times after gastric sleeve surgery: 3 months, 6 months, and 9 months, at p=0.02. Emerging evidence suggests that this increase may reflect improved leptin sensitivity or compensatory hormonal adaptations aimed at restoring energy balance. Bariatric surgery may elevate leptin receptors or reduce leptin resistance in the hypothalamus, allowing increased leptin to exert stronger effects on anorexia [36]. Furthermore, the observed sex-specific response in this study may be attributable to differences related to sex, fat distribution, or postoperative hormonal and metabolic adaptations, as men exhibit a different pattern of response to satiety hormones after surgery due to differences in fat distribution, metabolic activity, or testosterone. The results in Table (3) also showed a sequential increase in serum GLP1 and GLP2 levels in males after gastric sleeve surgery for the three groups (3 months, 6 months, and 9 months) at $p < 0.001$ and $p = 0.03$, respectively. GLP-1 and GLP-2 levels increase after gastric sleeve surgery due to significantly accelerated gastric emptying, which leads to rapid delivery of nutrients to the distal part of the small intestine, where the L cells responsible for secreting these hormones are concentrated [32]. Postoperative modification of gut hormones, especially GLP-1, which plays a crucial role in regulating appetite and GLU metabolism, contributes to improved insulin sensitivity and pancreatic insulin secretion [37]. As for the decrease in glucose levels in men after gastric sleeve surgery for the same time periods, as shown in Table (3) at a p-value <0.001, this is due to GLP-1 and its role in regulating blood sugar. It is secreted after eating, where it stimulates glucose-dependent insulin secretion from pancreatic beta cells and inhibits bits glucagon secretion (which raises blood sugar) [38]. Among the various metabolic changes associated with obesity, elevated serum uric acid levels have drawn particular attention, as shown in the same table, especially nine months after gastric sleeve surgery at p=0.01. Greater weight loss reduces purine production and increases renal uric acid excretion, leading to improved insulin resistance, as insulin resistance impedes renal insulin secretion. Reducing general inflammation in the body after weight loss also contributes to lower uric acid levels [39]. Men are often more prone to hyperuricemia due to their greater muscle mass and protein-rich diets, so gastric sleeve surgery significantly improves this condition [40]. As shown in Table (3), the majority of patients no longer required lipid-lowering medications within the first six to nine months after surgery, indicating the effectiveness of gastric sleeve surgery in improving dyslipidemia. This study documented that gastric sleeve surgery not only resulted in a traditional improvement in lipid profile but also produced positive changes in HDL-C function. Although gastric sleeve surgery causes significant weight loss, its metabolic benefits extend beyond weight loss. It reduces residual lipid (RC)—a dangerous type of fat associated with diabetes and inflammation—through changes in hormones, eating patterns, and bowel function. This reduction in visceral cholesterol may be an important predictor of heart disease risk beyond simply lowering LDL cholesterol [41,42].

Figure (1) illustrates that genetic factors play a role in obesity, and that the hormone CCK plays an important role in improving the health status of individuals who have undergone gastric sleeve surgery, especially those with a family history. From a genetic perspective, these genetic elements contribute to the regulation of body weight by modulating energy balance within the central nervous system. However, it is important to emphasize that genetic predisposition alone does not fully explain the difference in postoperative outcomes between the morbidly obese (FAO) and moderately obese (SO) groups [43]. These differences likely arise from a multifactorial interaction between genetic makeup and environmental influences. From an environmental perspective, patients who undergo gastrectomy (SG) often share similar lifestyles and dietary patterns with their family members [44].

CONCOLUTION

Cholecystokinin levels showed a significant increase in their concentration after surgery and an effective interaction with other variables, which reinforces their preventive and therapeutic role in maintaining long-term physical health after gastric sleeve surgery, preventing complications, and combating obesity, especially in individuals with a family history.

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Ethical Consideration
The study was authorized by our organization and the board of review of authors. It was conducted in accordance with institutional policy, all applicable national laws, and the principles of the Helsinki Declaration.

Conflict 0f Interests
The author confirm that this article content has no conflicts of interest.

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