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The Impact of Sleeve Gastrectomy on Inflammatory Markers and Immune Response: A Study of Cytokine Changes, Weight Loss, and Insulin Resistance

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Abstract **Objectives:** This study aim to assess how individuals who had gastric bypass surgery or sleeve gastrectomy changed in terms of their blood cytokine levels. Methods: A total of 40 patients who are having bariatric surgery and have a BMI greater than 35. Gastrectomy patients were divided into three groups: those who had the procedure before to surgery, those who had it three months after, and those who had it six months after. Demographic information, weight, BMI, blood sugar, CRP levels, and cytokine levels of IL-1β, IFN-α, IFN-γ, α, MCP-1, IL-23, and IL-33 at the time of hospitalisation and six months after surgery. **Results:** Preoperative interleukin-1 beta (IL-1β) levels in patients were significantly elevated compared to concentrations measured at 3 months (1.39±0.82 mg/dL) and 6 months (0.74±0.13 mg/dL) post-surgery (2.64±0.9 mg/dL, P<0.001). Furthermore, a statistically significant difference was observed between the two postoperative groups (3-month vs. 6-month follow-up, P<0.001). Similarly, preoperative concentrations of interleukin-12 (IL-12) and interleukin-23 (IL-23) were markedly higher than levels detected at both 3 and 6 months post-surgery. A significant disparity in IL-12 and IL-23 levels was also noted between the 3-month and 6-month postoperative cohorts (P<0.001). The current findings indicate a considerable rise in IL-33, IFN-α, and IFN-γ in patients before to surgery as compared to both groups after surgery. However, no statistically significant difference was observed between the two postoperative groups (3-month vs. 6-month follow-up) (P<0.05). Moreover, human monocyte chemoattractant protein-1 (MCP-1) showed no significant difference across all groups. **Conclusion:** The current study shown that weight reduction after bariatric surgery also results in a regression in inflammation, which may be linked to the inflammasome.

Key Words Gastric bypass, obesity, sleeve gastrectomy, cytokine

INTRODUCTION

A low-grade systemic inflammatory factor is associated with obesity. Although sleeve gastrectomy (SG) may result in considerable weight reduction, the post-operative alterations and inflammatory cytokines have not been thoroughly examined in many studies. Excessive bodily fat buildup brought on by a positive energy balance is known as obesity. Tumour necrosis factor and several interleukins are among the inflammatory mediators released by the adipose tissues (AT). Obesity causes an overexpression of these cytokines [1].

Bariatric surgery is the most successful weight loss technique (BS). The first stage, however, is lifestyle modification, which has some noteworthy outcomes [2]. Globally and within Iraq, sleeve gastrectomy is the most commonly performed bariatric surgical procedure. About 80% of the stomach is removed during a sleeve gastrectomy and replaced with a tubular stomach, which limits food intake and causes weight reduction [3]. Changes to the anatomy of the gastrointestinal tract are not a part of lifestyle intervention therapies, nor are they invasive. While is not associated with long-term risks, it results in significantly less weight reduction compared to the two most common bariatric surgeries: Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG) [2]. These techniques remain the primary surgical interventions for obesity treatment. Studies have shown that bariatric surgery may enhance neurocognitive performance in obese people in

addition to promoting weight reduction. However, the exact mechanism by which bariatric surgery enhances neurocognitive performance is yet unknown [4].

For adults and adolescents with morbid obesity, bariatric surgery is becoming more widely recognised as an effective therapeutic option. In the early postbariatric phase, nutritional deficiencies may develop or worsen, hormonal balance may shift (particularly following sleeve gastrectomy), the proinflammatory cytokine profile may change, and the gut microbiome and permeability may undergo significant changes, all of which may lead to an immunomodulatory imbalance [5]. These modifications may favour a proinflammatory metabolic profile by altering brain barrier permeability, causing gut dysbiosis, and inducing encephalomyelitic T cell activation. Such alterations may result in myelopathy, especially multiple sclerosis, in those who are genetically predisposed or who have other risk factors. Key Takeaway [5,6]: Although postbariatric myelopathy is uncommon, it should be taken into account in bariatric patients who have pertinent postoperative symptoms. An activation of inflammatory signalling pathways and an increase in cytokine production may result from the structural disturbance of neuronal and hormonal processes linked to bariatric surgeries [6].

Insulin resistance is brought on by inflammation linked to fat. Thus, there may be a reciprocal relationship between the effects of inflammation and metabolic alterations. The first line of treatment for obesity is often lifestyle change via food and exercise [7]. However, weight rebound is typical and the decrease in weight loss is usually minor. Proinflammatory cytokines play a critical role in regulating vascular reactivity, thrombosis, angiogenesis, insulin resistance, sympathetic nerve activity, and inflammatory processes. There are studies comparing the levels of certain blood cytokines before and after bariatric surgery, but there are few studies that look at both cytokines and the number of patients [8].

Obesity-related metabolic dysfunction is exacerbated by persistent low-grade inflammation and altered cytokine levels [9]. Not enough research has been done on the degree of cytokine alterations and how they affect metabolic gains after bariatric surgery.

MATERIALS AND METHODS

Study Design and Participants

Between October 2023 and October 2024, a cross-sectional research was carried out in the private medical clinic in AL-Harthia, Baghdad. Patients undergoing bariatric surgery (either vertical sleeve gastrectomy [VSG] or Roux-en-Y gastric bypass [RYGB]) were recruited from a private medical clinic. Eligibility criteria included obesity defined as a body mass index (BMI) >40 kg/m^2 or a BMI >35 kg/m^2 accompanied by one or more obesity-related comorbidities. Individuals who have undergone prior weight reduction surgery were not included. lean individuals without a history of diabetes or cardiovascular disease (BMI ≤26 kg/m^2). This cross-sectional investigation comprised 40 pairings that were matched by age, sex, and ethnicity. Participation in a prospective cohort trial was open to all patients having bariatric surgery. Forty of these patients attended follow-up appointments at three and six months.

Laboratory Measurements

Weight (in kilogrammes) divided by height (in square meters) was used to compute BMI. Venous blood samples were collected in the morning following an overnight fast. Samples were centrifuged at 3200 g for 7 minutes to separate serum, after which aliquots were stored at -80°C for subsequent analysis. Fasting glucose levels were measured, and serum insulin concentrations were quantified using a commercial ELISA kit (Millipore Human Insulin; Billerica, MA). The homeostasis model assessment of insulin resistance (HOMA-IR) was used to calculate insulin resistance (28).

A commercial ELISA kit (Jiancheng, Nanjing, China) was used to quantify cytokines linked to insulin resistance (IFN-α, IFN-γ), inflammasome activation (IL-1β), inflammation resolution (IL-12, IL-33), and Th17 cell-mediated responses (MCP-1, IL-23), following the manufacturer's protocol. Using immunoturbidimetry, serum CRP was measured at 570 nm using a Roche Cobas Mira chemical analyser (Germany, Roche Cobas 8000).

Statistical Analysis

Continuous variables, presented as mean±standard error of the mean (SEM) with ranges, were confirmed to follow a normal distribution. Categorical variables are expressed as proportions (percentages). To normalize cytokine concentrations, a logarithmic transformation was applied. Comparisons of biochemical and demographic characteristics between lean and obese groups were performed using Student's t-test for normally distributed data. All analyses were conducted using Stata Statistical Software version 11.0 (StataCorp LP, College Station, TX). A two-tailed P -value <0.05 was considered statistically significant.

Ethical Considerations

All participants were informed about the nature and purpose of the study and gave written consent before enrollment. Their personal data were kept confidential, and coded identifiers were used in place of names to protect privacy. Participation was entirely voluntary, and patients were free to withdraw at any time without affecting their medical care. Ethical approval was obtained from the appropriate institutional review board, ensuring that all procedures followed standard ethical guidelines.

RESULTS

Participant Characteristics

The present study enrolled 40 patients with gastrectomy. Patients with gastrectomy were categorized into 3 groups,

those who are patients before surgery, after 3 month of surgery and after 6 months of surgery. Table 1 displays the demographic details of gastrectomy patients [1]. The average age of gastrectomy patients was 48.20±8.15 years old. Overall, there were 19 (47.5%) females and 21 (52.5%) males.

Body Mass Index (BMI)

Body Mass Index (BMI) comparisons between patient groups were performed, and the findings are shown in table (2). Patients before surgery had a mean BMI of 43.17±6.01, those after three months of surgery had a mean of 34.88±5.42, and those after six months of surgery had a mean of 27.64±4.97. The difference between the mean levels of the two groups was highly significant (p = 0.001).

Table 3 summarizes the metabolic parameters (fasting blood glucose [FBS], insulin, and HOMA-IR) across patient groups. The mean fasting blood glucose levels were: Pre-surgery: 91.30±7.97 mg/dL, 3 months post-surgery: 79.72±3.02 mg/dL, and 6 months post-surgery: 78.25±1.32 mg/dL

Statistically significant differences (p<0.001) were observed when comparing pre-surgery levels to both post-surgery time points. However, no significant difference (P<0.05) was detected between the 3-month and 6-month postoperative groups.

The mean insulin levels across patient groups were: Pre-surgery: 12.47±1.32 mU/L, 3 months post-surgery: 6.36±0.79 mU/L, and 6 months post-surgery: 6.06±0.67 mU/L. Preoperative insulin levels were significantly higher than those observed at both postoperative time points (p<0.001).

However, there was no significant difference between the two groups of patients after surgery (those who had surgery three months later and those who had surgery six months later) (p<0.05). The current findings indicate that there is no significant difference between the groups based on HOMA-IR mean levels (p<0.05).

Figure 1 illustrates Serum high-sensitivity C-reactive protein (hs-CRP) concentrations in patients before surgery were significantly greater than in patients after 3 months of surgery, or patients after 6 months of surgery (0.76±0.11 mg/dl versus 0.31±0.07 mg/dL and 0.19±0.07 mg/dL, respectively, p<0.001). Also, there was significant difference between both group of patients after surgery (patients after 3 months of surgery and patients after 6 month of surgery), (p<0.05).

Table 4 and Figure 2 indicates that Interleukin-1 beta (IL-1β) concentrations were significantly elevated in preoperative patients compared to levels at 3 months (1.39±0.82 mg/dL) and 6 months (0.74±0.13 mg/dL) post-surgery (2.64±0.9 mg/dL, p<0.001). Notably, a statistically significant difference was also observed between the two postoperative groups (3-month vs. 6-month follow-up, p<0.001). Additionally, patients' pre-operative IL-12 and IL-23 concentrations were noticeably greater than those of patients three or six months post-operatively. A statistically significant difference in interleukin-12 (IL-12) and interleukin-23 (IL-23) levels was observed between the two postoperative groups (3-month vs. 6-month follow-up, p<0.001). The current findings indicate a considerable rise in IL-33, IFN-α, and IFN-γ in patients before to surgery as compared to both groups after surgery. However, no statistically significant difference was observed between the 3-month and 6-month postoperative groups (p<0.05). Moreover, human monocyte chemoattractant protein-1 (MCP-1) showed no significant difference across all groups.

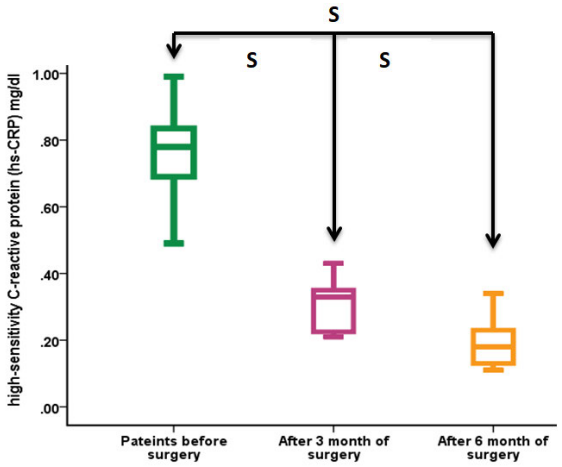

Figure 1: Serum high-sensitivity C-reactive protein level in patients before surgery, patients after 3 month of surgery and patients after 6 month of surgery, S: Statistically significant p<0.05

Table 1: Characteristics of patients with gastrectomy

Characteristic	patients with gastrectomy (n=40)
Age (years)	48.20±8.15
Gender	
Male	21 (52.5%)
Female	19 (47.5%)

Table 2: Distribution of BMI mean in patients' groups.

Study groups		Mean ±SD	p-value
Groups	Before surgery	43.17±6.01[A]	<0.001[HS]
	After 3 months of surgery	34.88±5.42[B]	
	After 6 months of surgery	27.64±4.97[C]	
Different latter denote to the significant differences at p< 0.05			

SD: Standard deviation; †: One way ANOVA; HS: Highly-significant at p<0.001

Table 3: Metabolic factors (FBS, Insulin, and HOMA-IR) in patients groups

Groups	FBS (mg/dl)	Insulin (mU/L)	HOMA-IR
Before surgery	91.30±7.97[A]	12.47±1.32[A]	1.22±0.37[A]
	78.0-112.0	7.80-15.50	0.81-3.40
After 3 months of surgery	79.72± 3.02[B]	6.36±0.79[B]	1.15±0.31[A]
	73.0-87.0	4.50-7.50	0.02-1.56
After 6 months of surgery	78.25±1.32[B]	6.06±0.67[B]	1.12±0.27[A]
	70.0-82.0	4.70-7.30	0.08-1.41
p-value	0.001**	0.001**	0.332
Different latters denote to the significant differences at p<0.05			

SD: Standard deviation; †: One way ANOVA; **: Significant at p<0.05

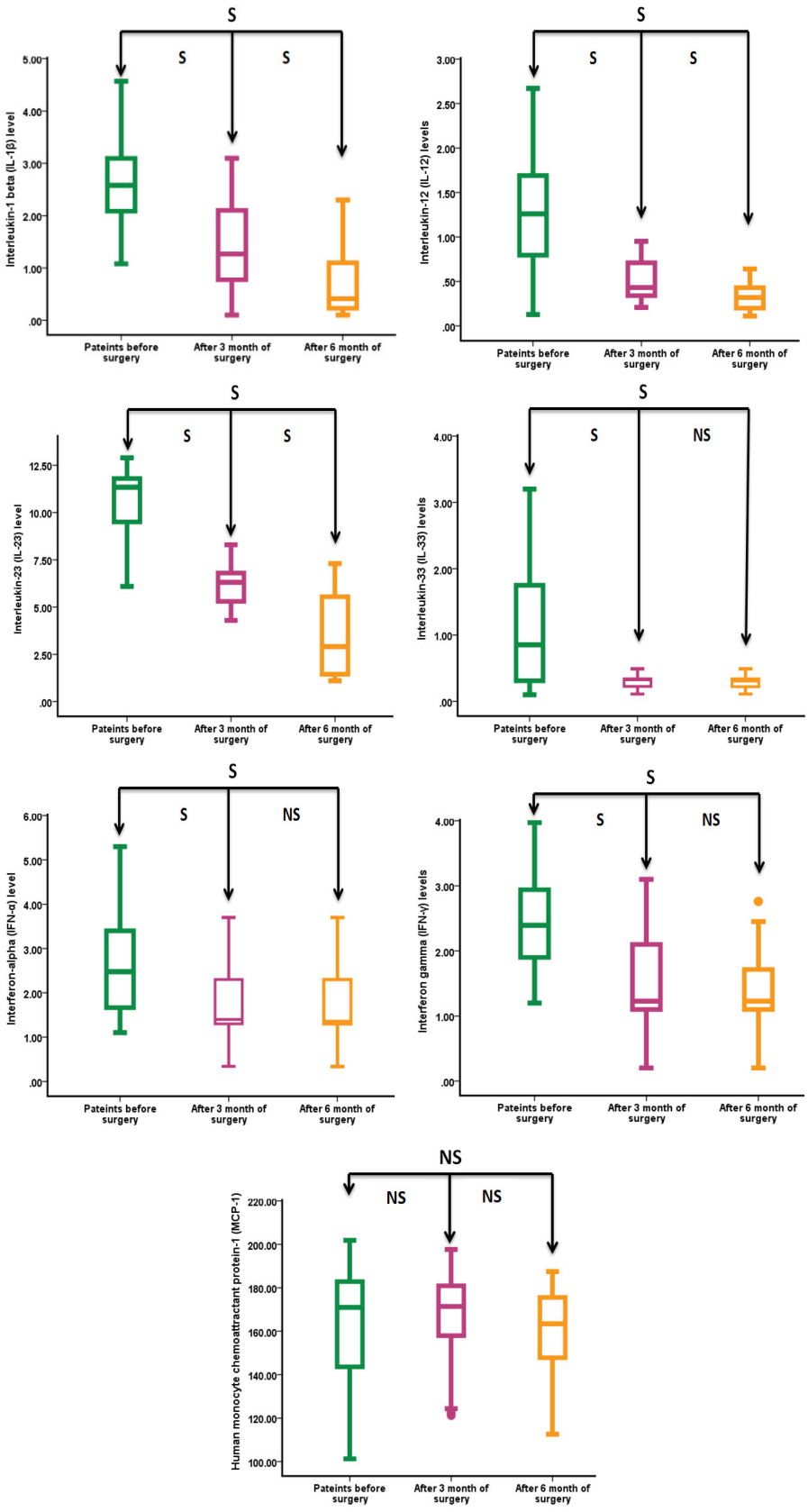

Figure 2(A,B,C,D, E and D): Serum level of immunological parameters (IL-1B, IL-12 IL-23, IL-33 IFN-α, IFN-γ and Anti-dsDNA) in patients before surgery, patients after 3 month of surgery and patients after 6 month of surgery. NS: Not statistically significant, S: Statistically significant p<0.05

Table 4: Measurements of Immunological parametersin patientsgroups

Parameters	Before surgery (n = 40)	After 3 months of surgery (n = 40)	After 6 months of surgery (n = 40)	p-value
IL-1B (pg/mL)	2.64±0.9[A]	1.39±0.82[B]	0.74±0.13[C]	< 0.001**
IL-12 (pg/mL)	1.23± 0.33[A]	0.51±0.12[B]	0.31±0.11[C]	0.001*
IL-23 (pg/mL)	10.50±1.9[A]	6.01±1.03[B]	3.62±0.91[C]	0.001*
IL-33 (pg/mL)	1.07±0.32[A]	0.31±0.08[B]	0.29±0.07[B]	0.015*
IFN-α(pg/mL)	2.56±0.66[A]	1.73±0.51[B]	1.71±0.53[B]	0.021*
IFN-γ (pg/mL)	2.41±0.43[A]	1.37±0.27[B]	1.28±0.27[B]	0.027*
MCP-1 (pg/mL)	163.5±17.3[A]	164.3±21.5[A]	158.4±18.7[A]	0.493
Different latters denote to the significant differences at p<0.05				

Test= one way ANOVA; †= *: Significant at p<0.05

Table 5: Correlation between Immunological parameters in patients groups

	Immunological parameters													
	IL-1B		IL-12		IL-23		IL-33		IFN-α		IFN-γ		MCP-1	
Parameters	R	P	r	P	R	P	R	p	R	P	r	P	r	p
IL-1B	1													
IL-12	0.555	0.001*	1											
IL-23	0.630	0.001*	0.640	0.001*	1									
IL-33	0.420	0.001*	0.486	0.001*	0.406	0.001*	1							
IFN-α	0.331	0.001*	0.326	0.001*	0.322	0.001*	0.262	0.004*	1					
IFN-γ	0.460	0.001*	0.502	0.001*	0.556	0.001*	0.323	0.001*	0.233	0.010*	1			
MCP-1	0.082	0.374	0.088	0.339	0.059	0.525	0.050	0.587	0.111	0.226	0.144	0.117	1	

r: Pearson correlation

Tables 5 displayed the relationships between the immunological parameters (IL-1B, IL-12, IL-23, IL-33, IFN-α, IFN-γ, and MCP-1) in the patient groups. The present findings demonstrate statistically significant positive correlations between multiple cytokine pairs: IL-1β strongly correlated with IL-12 (r = 0.555, P = 0.001), IL-23 (r = 0.630, P = 0.001), IL-33 (r = 0.420, P = 0.001), IFN-α (r = 0.331, P = 0.001), and IFN-γ (r = 0.460, P = 0.001). IL-12 also showed significant associations with IL-23 (r = 0.640, P = 0.001), IL-33 (r = 0.486, P = 0.001), IFN-α (r = 0.326, P = 0.001), and IFN-γ (r = 0.502, P = 0.001), while IL-23 correlated with IL-33 (r = 0.406, P = 0.001), IFN-α (r = 0.322, P = 0.001), and IFN-γ (r = 0.556, P = 0.001). Additionally, IL-33 correlated with IFN-α (r = 0.262, P = 0.004) and IFN-γ (r = 0.323, P = 0.001), and a weaker but significant correlation was observed between IFN-α and IFN-γ (r = 0.233, P = 0.010). All correlations achieved statistical significance (P ≤ 0.01), with the strongest associations observed between IL-1β and IL-23, as well as IL-12 and IL-23.

DISCUSSION

An estimated one-third of individuals worldwide suffer from obesity, which is a serious public health issue [10]. Obesity significantly elevates the risk of metabolic syndrome, type 2 diabetes, hyperlipidemia, cardiovascular disease, and certain cancers [11]. This heightened risk is linked to a state of chronic low-grade inflammation termed the “inflammome” which involves elevated systemic cytokine production and immune cell infiltration into adipose tissue [12].

According to our research, SG was successful in improving BMI and achieving significant weight reduction, even in the short term. Bariatric surgery is recognized as the most effective and durable long-term intervention for severe obesity and has emerged as a viable treatment option for type 2 diabetes in adults [13]. A widely utilized method for assessing pancreatic β-cell function and insulin resistance is the homeostatic model assessment of insulin resistance (HOMA-IR), which relies on fasting glucose and C-peptide levels. The relationship between fasting blood glucose and insulin reflects the balance between hepatic glucose production and insulin secretion, a dynamic process regulated by a feedback loop between the liver and pancreatic β-cells [14].

Laparoscopic sleeve gastrectomy (LSG), the most widely performed bariatric surgery, involves resecting ~80% of the stomach along the greater curvature, leaving a 100-150 mL gastric pouch. Approximately 75% of LSG patients achieve complete or improved diabetic remission, with average weight loss of 40-60% of excess body weight and a BMI reduction of 8-10 kg/m². While its precise antidiabetic mechanism remains unclear, proposed pathways include mechanical restriction of caloric intake, hormonal changes (e.g., increased adiponectin/leptin, reduced TNF-α/IL-6) enhancing insulin sensitivity and β-cell function, altered bile acid signaling suppressing hepatic glucose production, accelerated incretin (GLP-1) secretion improving insulin release, and reduced ghrelin levels suppressing appetite. These combined effects synergistically improve glycemic control, underscoring LSG’s efficacy in diabetes management [15].

Previous studies have shown that obesity alters adipokines and inflammatory cytokines. Obesity elevates

circulating levels of interleukins (e.g., IL-1β, IL-1Ra, IL-6, IL-8, IL-10) and cytokines (e.g., TNF-α, soluble TNF receptor 2 [sTNFR2], plasminogen activator inhibitor 1), which drive chronic inflammation and insulin resistance (16-20). Key proinflammatory cytokines, including C-reactive protein, IL-6, and TNF-α, are significantly reduced within 6 months following bariatric surgery, correlating with improved metabolic outcomes [21,22].

Secretory molecules called cytokines may react to a variety of bodily changes at various levels, produce distinct response mechanisms to the same stimulus, and many of their roles are still unclear. While the impact of obesity on cytokine profiles remains inconsistently interpreted across studies, our findings suggest that bariatric surgery-induced weight loss may reverse chronic inflammation. Notably, greater weight reduction was associated with more pronounced anti-inflammatory effects [23].

CONCLUSION

In Conclusion the current research showed that weight reduction after bariatric surgery also results in a regression in inflammation, which may be linked to the inflammasome.

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