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Evaluation of Systemic Levels of Pro- and Anti-Inflammatory Cytokines TNF- α , CRP, and IL-10 in Bariatric Surgery Patients Before and After Surgery

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Abstract

The effect of obesity on the onset and spread of inflammatory pathways is tremendous. Gastric bypass surgery has continued to be a very effective measure to reduce morbid obesity. The main aim of this study was to determine the level of circulating tumour necrosis factor C -alpha (TNF- α) and C-reactive protein (CRP), and interleukin-10 (IL-10) in the morbidly obese patients before and after surgery. Twenty-two participants were the cohort which was followed over a period of twelve months. The plasma levels of TNF- α , CRP, and IL-10, and body mass index, lipid profiles were measured; all parameters showed a steady decrease during the period of observation. One month after surgery, IL-10 levels significantly increased to 968.8 ± 171.8 pg/mL, while TNF- α levels significantly decreased to 158.8 ± 38.18 pg/mL. CRP levels were 1.36 ± 0.88 mg/dL post-surgery. Overall, it can be concluded that the study yielded statistically significant decreases in patient BMI, with significant changes in biochemical parameters with positive results in cytokines.

Keywords: Bariatric Surgery patients, C-Reactive Protein, Immunomodulatory nutrients, Interleukin-10, and Tumor Necrosis Factor Alpha.

تقييم المستويات الجهازية للسيتوكينات المحفزة والمثبطة للالتهابات TNF- α و CRP و IL-10
لدى مرضى جراحة السمنة قبل وبعد الجراحة

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الخلاصة

يُعد تأثير السمنة على بدء وانتشار المسارات الالتهابية بالغ الأهمية. ولا تزال جراحة تحويل مسار الامعاء إجراءً فعالاً للغاية للحد من السمنة المفرطة. هدفت هذه الدراسة إلى تحديد مستوى عامل نخر الورم ألفا ($\text{TNF-}\alpha$) والبروتين المتفاعل C- (CRP) والإنترلوكين-10 (IL-10) في الدم لدى مرضى السمنة المفرطة قبل الجراحة وبعدها. شملت الدراسة 22 مشاركاً تمت متابعتهم على مدار 12 شهراً. تم قياس مستويات $\text{TNF-}\alpha$ و CRP و IL-10 في البلازما، بالإضافة إلى مؤشر كتلة الجسم ومستويات الدهون؛ وأظهرت جميع المؤشرات انخفاضاً مطرداً خلال فترة المتابعة. بعد شهر من الجراحة، ارتفعت مستويات IL-10 بشكل ملحوظ إلى 968.8 ± 171.8 بيكوغرام/مل، بينما انخفضت مستويات $\text{TNF-}\alpha$ بشكل ملحوظ إلى 158.8 ± 38.18 بيكوغرام/مل. بلغت مستويات البروتين C التفاعلي (CRP) 1.36 ± 0.88 ملغم/ديسيلتر بعد الجراحة. وبشكل عام، يمكن استنتاج أن الدراسة أسفرت عن انخفاضات ذات دلالة إحصائية في مؤشر كتلة الجسم للمرضى، مع تغيرات ملحوظة في المؤشرات البيوكيميائية، ونتائج إيجابية في السيتوكينات.

1. Introduction

Obesity is explained as the surplus build up of fat tissue that is caused by a continued positive energy balance. Its pathogenesis is complex, as it is a mix of environmental and genetic factors. The factual evidence has reported that plus to overeating of calories and genetic predisposition, a sedentary lifestyle is the leading cause of obesity [1-3]. Obesity epidemic is a significant health problem to the Indian population and similar tendencies are evident all over the world. This has increased the incidence of Type 2 diabetes mellitus, dyslipidaemia and hypertension and hence morbidity and mortality related to the metabolic conditions [2]. Recently research has linked these comorbidities to a systemic inflammatory state commonly found in obese patients [3]. Therefore, bariatric surgery is being explore as a therapeutic option to determine its effects on the decrease in serum levels of pro-inflammatory cytokines such as $\text{TNF-}\alpha$ and the increase in anti-inflammatory factors such as IL-10, in patients with morbid obesity [4, 5]. Nutrition cannot be neglected to regulate the caloric intake and mitigate the nutritional shortages; the modern studies confirm that nutrition plays a crucial role in the management of perioperative period. However, the high rates of deficiencies and comorbidities related to obesity (that arise before the surgery) place the patients in a group of individuals with increased risks. This increased susceptibility is largely explained by the fact that there is a loss of a section of the gastrointestinal tract which is an anatomical change that initiates an observable reduction in immune competence [6].

Obesity has become a serious worrying epidemic especially affecting the younger generations. In addition to the widespread impact on the overall health, obesity in these cohorts has been empirically linked with the dysregulation of blood pressure, hyperlipidemia, and hyperinsulinemia, thus increasing the risk of developing such conditions as type 2 diabetes mellitus and coronary artery disease. Some bariatric surgical procedures address these metabolic effects by eliminating the gastric portion responsible for producing ghrelin, a hormone that regulates hunger and metabolism. By lowering ghrelin levels, these surgeries can help mitigate some of the metabolic consequences of obesity. The areas with the highest rate of overweight and obesity are urban, compared to rural areas. This high incidence of overweight and obesity has led to the main causes of death in India being associated with cardiovascular problems and DM2, accounting for 17.9 million deaths annually and representing 31% of all global fatalities [7].

Obesity, incredibly visceral or central obesity, is the result of a combination of environmental, nutritional and social factors such as high-calorie, low-fibre diets, sedentary lifestyle and low awareness of this problem, leading to a lethal combination of obesity and insulin resistance, which generates devastating metabolic and biochemical alterations in

different organs and systems of the human body [8]. Adipose tissue has an extremely important implication, mainly due to its endocrine functions in inducing the synthesis of signalling proteins known as adipokines [9-11] (e.g: leptin and adiponectin), and various inflammatory factors such as Tumor Necrosis Factor α (TNF- α), Interleukins (IL) 1 β , IL-6, IL-18, tissue plasminogen activator inhibitor, as well as C-Reactive Protein (CRP) [12]. Various studies have strongly suggested that these factors could generate a pro-inflammatory and prothrombotic state in obese patients [13-14].

TNF- α has been detected 5 to 10 times higher in obese subjects and animals when compared to controls [15-18]. In *in vivo* studies, the expression of TNF- α has been associated with catabolic states that cause a wasting syndrome called cachexia [19-21]

In animal models [21-22], low serum levels of this cytokine are related to an exaggerated immune response to the antigen with excessive inflammation and tissue damage. In humans, low IL-10 levels are associated with the severity of various types of diseases. The action of IL-10 is to attenuate the inflammatory process induced by TNF- α , IL-6 and IL-1. Low levels of IL-10 have recently been associated with metabolic syndrome and DM2 [21-24]. There are various approaches to achieve weight reduction in patients with morbid obesity ($>40 \text{ kg/m}^2$) [25]. These include dietary and pharmacological strategies [26]. However, when other approaches fail, surgical strategies such as bariatric surgery exist. For over 40 years, bariatric surgery has proved to be a successful method, continuously refined through extensive experience and research. It carries a low risk of complications and helps patients maintain weight loss for a longer duration. The procedure typically requires a shorter hospital stay of 2–3 days compared to 5–8 days and is less invasive when performed laparoscopically. The benefits in these patients are due to the significant weight loss that affects capillary glycemia levels, insulin resistance, inflammatory cytokines and increased anti-inflammatory cytokines. However, certain mechanisms are not fully understood. The indications for subjecting a patient to bariatric surgery are Body Mass Index (BMI) $>40 \text{ Kg/m}^2$ or BMI $>35 \text{ Kg/m}^2$ associated with medical complications such as DM2 and metabolic complications related to obesity, dyslipidaemias, etc. [27]. Adequate nutrition is essential in modulating this immunity. Some foods have protective functions for our body and can increase the response of our defence system [28]. Foods that are sources of polyunsaturated fatty acids such as omega-3, vitamins such as A, C, D and E, minerals such as zinc and iron, proteins, probiotic microorganisms and prebiotic fibres can strengthen immunity [29]. With the above discussion, the question raised is: Does gastric bypass surgery reduce inflammatory cytokine levels and increase anti-inflammatory cytokine levels in morbidly obese patients?

The present study aimed to evaluate the effects of immunomodulatory nutrients and the serum levels of TNF- α , CRP, and IL-10 in patients with morbid obesity before undergoing gastric bypass surgery, as well as at 1, 2, 6, and 12 months postoperatively, at NRI Medical College, Mangalagiri, Andhra Pradesh, India.

2. Methodology

This is an exploratory, qualitative, cross-sectional, population-based, and descriptive research. Data were obtained through an online questionnaire with nutritional questions about the patient's and bariatric surgery's particularities, about the intake of immunomodulatory nutrients and identification data such as age, sex and anthropometric data such as current weight, pre-surgical weight, and pre-surgical and current BMI calculated through information obtained by the questionnaire [30].

Patients who attended the obesity clinic at NRI Medical College, Mangalagiri, Andhra Pradesh, India, were included in the study. Post-surgical assessments were conducted at the first, second, sixth, and twelfth months. At each appointment, the following measurements

and tests were performed: BMI, waist circumference, blood chemistry, complete blood count, postprandial glucose, glycosylated haemoglobin A1c, lipid profile, and levels of TNF- α , CRP, and IL-10. Variables studied in the current observational study are serum levels of pro-inflammatory factors TNF- α , CRP, and anti-inflammatory IL-10 as Dependent Variables, and the Independent Variable are gastric bypass surgery in morbidly obese patients.

2.1 Characteristics of Patients

The sample selected for convenience and included all patients who visited the obesity clinic at the NRI Medical College, Mangalagiri, Andhra Pradesh, India, from March 2022 to December 2022 were included, with a total of 22 patients.

The study included patients with morbid obesity or grade 3 obesity, along with other comorbidities, consisting of 22 participants, 17 men and 5 women. The average age of the participants was 42 years, ranging from 19 to 58. The current study excludes patients who did not sign the consent form for participation, pregnant or lactating individuals, those whose bariatric surgery was cancelled due to comorbidities or elevated surgical risk, and patients who died during the protocol implementation were excluded from the current study.

Once the patient was selected to participate in the protocol, a clinical record is made, which includes a complete clinical history. Anthropometric evaluation, preoperative laboratory tests, Complete blood count, Liver function tests, Coagulation times, Hb1Ac, Serum levels of TNF- α , CRP and IL-10, Blood chemistry, and other clinical profiles were tested before and after surgery at 1-, 2-, 6- and 12-months period.

To obtain the samples, 10 mL of blood was taken from a peripheral vein from each patient after 8-12 hours of fasting. Serum was obtained from each sample and analysed in the laboratory using conventional methods on automated equipment with radioimmunoassay techniques.

The levels of IL-10, TNF- α and CRP, in each sample, were determined using sandwich ELISA kits from PathScan Chemiluminescent (Cell Signal, Boston, MA, USA).

2.2 Assessment of the consumption of immunomodulatory nutrients

The consumption of immune-modulating nutrients was assessed through a digital questionnaire with questions about nutritional particularities adopted after bariatric surgery, type of surgical procedure, whether the patient had ever taken supplements with any immune-modulating nutrients, and signs and symptoms of some nutritional deficiencies.

A survey was designed based on work of Amaral E Melo GR et al. (2020) [31], incorporating questions about individuals' dietary habits and nutritional status. It was modified to include online questions focused on immune modulation. The questionnaires were scored based on the signs and symptoms in the body and served as screening for possible hypermeabilities. They are scored from 0 to 3 points, where 0 - symptom/rarely present; 1 - mild/occasional symptom; 2 - moderate/frequent symptom; 3 - severe/very frequent symptom, and interpreted according to the classification in Table 1.

Table 1: Interpretation for classification of Intestinal Hypermeability

Questions
Pre-surgical weight
What surgical technique was used?
How many Liters or glasses of water do you usually drink per day?
Dark green leafy vegetables (kale, taro, mustard, watercress, chard...)
Tubers (manioc, potato, yam...)
Orange fruits and vegetables (pumpkin, mango, carrot, papaya...)
Eggs
Corn, sunflower, and soybean oil
Olive oil
Oilseeds (nuts, cashews, almonds)
Milk
Milk products (cheese, butter, yogurt...)
Citrus fruits (e.g.: orange, passion fruit, acerola, kiwi, lemon...)
Do you consume any of the following items?
Do you have difficulty seeing in low-light environments, dry skin, or dry eyes?
Do you have problems with poor wound healing, hair loss, and weak nails? Do you have weak bones or muscle pain?
Do you have skin spots, inflammation and frequent bleeding gums?
Do you have frequent inflammation or infections?
Do you have dizziness, irritation, fatigue, shortness of breath and loss of appetite?
Do you have regular bowel movements?
Did you feel any improvement in your immunity after surgery?

2.3 Anthropometric Data Collection and Classification

Anthropometric information was collected using a digital questionnaire, which obtained data such as pre-surgical weight, current weight, height, and pre-surgical and current BMI. These were calculated from the information acquired and classified according to the cutoff points presented in Table 2.

Table 2: Cut-off point for BMI classification for adults [32]

BMI (kg/m ²)	Classification	Grade Obesity/Class	Risk of disease
< 18.5	Skinny or Low Weight	0	Normal or high
18.5 – 24.9	Normal or eutrophic	0	Normal
25 – 29.9	Overweight or pre-obese	0	Little elevated
30 – 34.9	Obesity	I	High
35 – 39.9	Obesity	II	Very High
> 40	Obesity	III	Serious

2.4 Data collection and analysis of results

The data were presented in absolute and relative frequency; this information refers to issues related to the modulation of immunity through nutrients, patient characteristics and intestinal hypermobility. Personal and anthropometric data were collected using mean and standard deviation with the help of Microsoft Office Excel 2019 software and SPSS software.

3. Results

Table 3 or Figure 1 displays the mean $\pm$ SD of CRP levels. The first column represents the CRP values before surgery (4.88 ± 1.85). The second column shows the CRP levels one month post-surgery (1.36 ± 0.88), indicating a significant decrease from baseline. Subsequent measurements at two months (1.03 ± 0.73), six months (0.97 ± 0.65), and twelve months (0.78 ± 0.31) demonstrate that the lowered CRP levels were maintained over the follow-up period.

The first column presents the TNF- α levels before surgery. Post-surgery measurements were taken at one month, showing a significant reduction, which was sustained in the following months: two months, six months, and finally at twelve months (Figure 2).

Table 3 or Figure 3 presents the mean $\pm$ SD values of IL-10 levels in pre-surgical and post-surgical patients. The first column shows the IL-10 levels before surgery. The second column represents the levels one month after bypass surgery, significantly increasing to 968.8 ± 171.8 . The third column shows the IL-10 levels two months post-surgery, rising to 1046.3 ± 139.9 . The fourth and fifth columns display measurements at six months and twelve months post-surgery, with levels maintained throughout this period

Table 3 shows the evolution of morbidly obese patients who underwent bypass surgery. Pre-surgical and post-surgical follow-ups are at 1 month, 2 months, 6 months, and 12 months. The anthropometric variables BMI and waist circumference showed the following behaviour with significant improvement, which was expected. Still, it should be noted that these patients maintained BMI and circumference over 12 months and that they are related to the levels of CRP, TNF- α decreased and increased proportionally with the levels of IL-10 when compared with the anthropometric variables. Regarding glucose, postprandial glucose, triglycerides, total cholesterol, HDL and LDL, it revealed a significant decrease in the same way when TNF- α , CRP and IL-10 are re-evaluated, attributing that this weight loss through this method improves the metabolic situation and is sustained. There were variables such as systemic blood pressure and glycosylated haemoglobin, without showing significant changes.

Table 3: Comparison of patients' variables before and after surgery

	Pre-Surgery		Post-Surgery				
Parameters	Pre-Surgery	1-month	2-months	6-months	12-months	p-Value	
BMI (Kg/m²)	45.43±7.92	38.76±8.29	34.33±5.86	32.55±4.88	30.44±5.58	0.001	
BP SYST (mmHg)	122.5±13.99	117.25±12.55	113.62±9.22	108±19.69	119.4±24.48	0.015	
BP DIA (mmHg)	80±8.16	73.62±5.28	71.75±5.49	70.12±14.93	66.2±14.44	0.01	
C waist size (cm)	126.3±19.78	116.75±16.82	109.5±6.01	98.37±9.57	99.2±8.04	0.002	
Blood glucose (mg/dL)	96.6±9.44	88.25±9.09	88±7.38	86.37±4.77	85±4.74	0.023	
Postprandial glucose (PPG) (mg/dL)	94.1±15.92	87.5±16.69	78.5±7.46	73.25±12.65	62±10.83	0.014	
Triglycerides (mg/dL)	147.2±78.95	122.92±43.88	112.25±22.75	106±31.64	105±6.78	0.03	
Total cholesterol (mg/dL)	182±22.87	156.37±30.92	160.62±18.60	156.12±21.38	166.8±19.13	0.018	
HDL cholesterol (mg/dL)	40.7±8.51	35.13±11.08	42.5±14.48	50.25±18.07	67.2±40.07	0.04	
Glycosylated haemoglobin (HbA1c %)	4.63±0.77	4.64±1.01	4.40±1.22	5.19±1.08	5.40±0.29	0.034	
C-reactive protein (CRP) (mg/dL)	4.88±1.85	1.49±0.94	1.30±0.82	0.85±0.57	0.78±0.31	0.0007	
TNF-alpha Protein (pg/L)	303.7±66.59	158.8±38.18	119.16±14.59	116±22.15	120±13.45	0.0003	
Interleukin-10 (IL-10) (pg/L)	687.1±112.3	968.84±171.8	1046.3±139.9	1137.2±84.02	1097.5±99.6	0.0001	

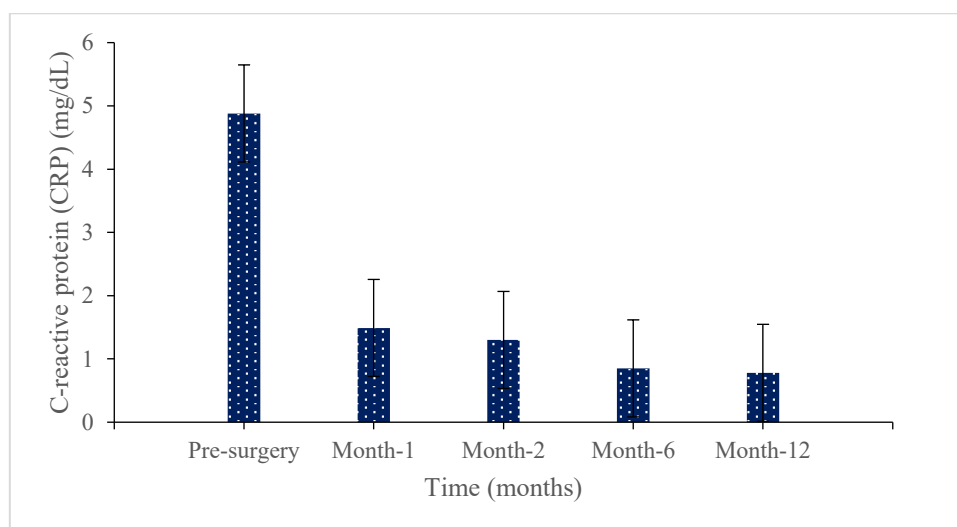


Figure 1: Significant decrease in CRP levels in patients undergoing bariatric surgery compared to baseline and follow-up up to twelve months.

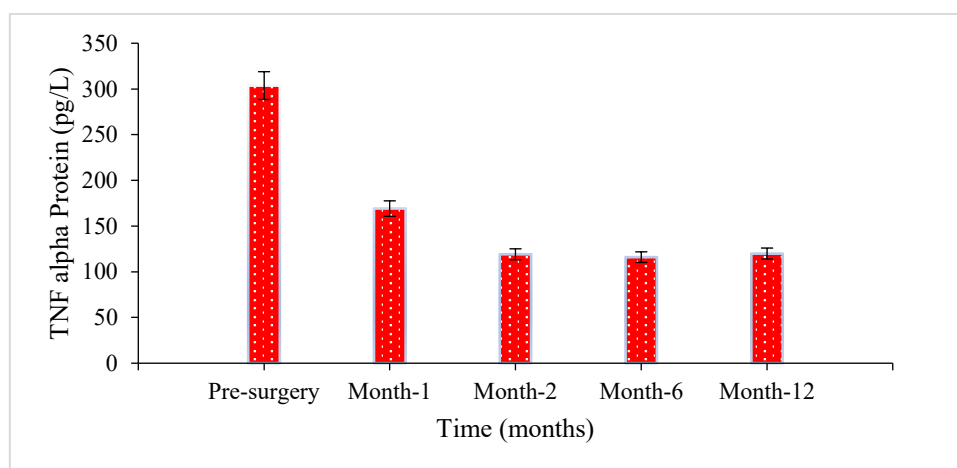


Figure 2: TNF- α levels before surgery and at 1, 2, 6, and 12 months

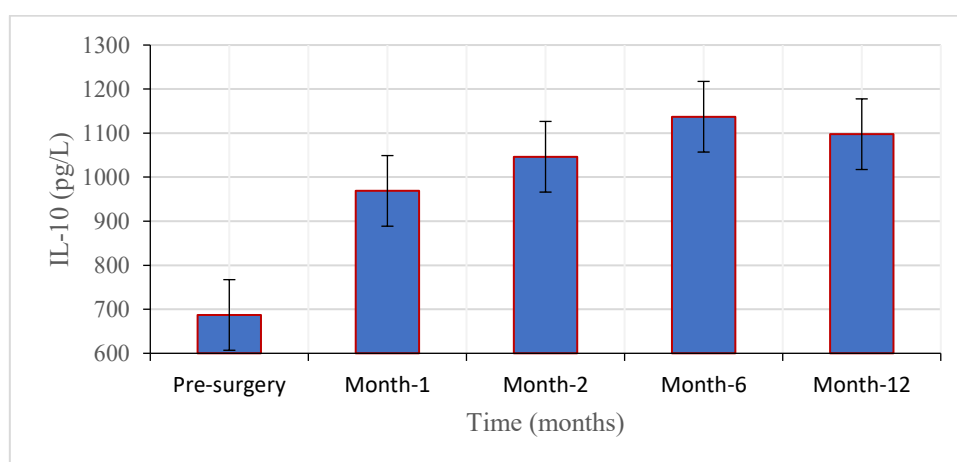


Figure 3: IL-10 levels before surgery and at 1, 2, 6, and 12 months show an increase from the preoperative value to 1 month, and are maintained over 12 months.

The substantial decrease in BMI and waist circumference from pre-surgery to subsequent time points (1 month, 2 months, etc.) suggests that the p-value for these parameters is significantly below 0.05. The results show that there is a significant and statistically significant improvement in the post-surgical procedure [33].

The level of CRP showed a sharp and sustained reduction that started at the baseline and continued during the 1-, 2-, 6-, and 12- months postoperative periods, with p-value less than 0.05, thus indicating a statistically significant attenuation. Similarly, post-surgery a significant decrease in the TNF- α concentration was observed with p-value below 0.05, which highlights the presence of a significant decrease in pro-inflammatory activity. On the other hand, the levels of IL-10 increased significantly during the post-operative time with a p-value less than 0.05, which reflects the significant increase in the intensity of anti-inflammatory effects during the time. Moreover, glycaemic control indicators such as the level of fasting glucose, post-prandial glucose, triglycerides, and lipid profile in general showed a significant improvement after treatment, which is a significant increase in the overall metabolic parameters [34]. In contrast, systemic blood pressure and glycosylated haemoglobin (HbA1c) exhibit only minor fluctuations, suggesting no significant change over the study period.

3.1 Assessment of the consumption of immunomodulatory nutrients

Table 4 shows modest to positive associations ($r = 0.55$ – 0.66) between the number of alternatives reported and the symptoms of nutritional shortage, implying that the probability of several deficiencies rises as symptoms do. For symptoms including skin lesions and bleeding gums, the strongest correlation (r) 0.66, CI: 0.36–0.85, indicated a possible relationship to vitamin C deficiency. Confidence intervals spanning all objects are limited and do not cross zero, supporting statistical dependability. These findings highlight the importance of monitoring these symptoms in clinical evaluations since they imply consistent correlations between reported symptoms and possible micronutrient shortages.

Table 4: Signs and symptoms of vitamins deficiency

Questions	I do not have	I only have 1 alternative	I have 2 alternatives	I have 3 alternatives	I have 4 alternatives	I have 5 alternatives	R-value	95% CI
Do you have difficulty seeing in low-light environments, dry skin or dry eyes?	54.5% (12)	27.3% (6)	13.6% (3)	9.1% (2)	-	-	0.62	[0.31 – 0.83]
Do you have problems with poor wound healing, hair loss and weak nails?	22.7% (5)	31.8% (7)	36.4% (8)	9.1% (2)	-	-	0.55	[0.22 – 0.79]
Do you have weak bones or muscle pain?	54.5% (12)	27.3% (6)	13.6% (3)	4.5% (1)	-	-	0.59	[0.27 – 0.81]
Do you have skin spots, inflammation and frequent bleeding gums?	72.7% (16)	22.7% (5)	4.5% (1)	0% (0)	-	-	0.66	[0.36 – 0.85]
Do you have dizziness, irritation, fatigue, shortness of breath and/or loss of appetite?	36.4% (8)	22.7% (5)	13.6% (3)	13.6% (3)	9.1% (2)	4.5% (1)	0.61	[0.30 – 0.83]

Table 5 shows the number of participants who use supplements from the listed items that may support immune system improvement. It shows that a small portion does not consume any of the items. The majority uses 2 or more supplements for assistance, where there was a relevant

number of combinations between omega 3, proteins, and probiotics, demonstrating that the most used supplement is multivitamins, both isolated 44.1% (n=10) and combined with other supplements 38.5% (n=8).

Table 5: Supplements used by individuals.

Supplements	% (n)
Poly-vitamins	44.1% (10)
Omega 3	4.5% (1)
Proteins	3.3% (1)
Prebiotic Fibers	0
Probiotics	4.5% (1)
No consumption of any items above	15% (3)
:A combination of more than 2 or more supplements	36.3% (8)

Table 6 shows the results of the intestinal permeability questionnaire, which can identify an imbalance of pathogenic and non-pathogenic microorganisms (called dysbiosis) that would be detrimental to the absorption of nutrients and, consequently, to the immune system. The results showed that most symptoms were absent or rare. However, in some questions, a good portion of the participants had complaints of diarrhea and/or constipation 59.5%, abdominal pain and distension 52.9%, frequent or chronic fatigue 48.4%, memory and mood changes 71.2% and food allergies 41.8%.

Table 6: Frequency of Intestinal Hypermobility Symptoms

Symptoms	Absent/Rare %	Mild/ Occasional %	Moderate/ frequent %	Severe/very common %
Diarrhea and/or constipation	40.5%	33.7%	17.0%	8.8%
Abdominal pain/bloating	47.1%	0.3%	13.7%	7.2%
Mucus or blood in stool	93.5%	4.6%	0.7%	1.3%
Joint pain/arthritis	65.7%	16.3%	1.0%	1.0%
Frequent/chronic fatigue	51.6%	33.7%	10.1%	4.6%
Food allergies	58.2%	25.8%	9.8%	6.2%
Nasal congestion	68.3%	19.3%	8.5%	3.9%
Asthma/airway allergies	82.4%	10.8%	5.6%	1.3%
Eczema/hives	83.3%	11.1%	3.9%	1.6%
Memory/mood changes	28.8%	38.9%	20.3%	12.1%
Acute/chronic inflammation	83.0%	12.1%	2.6%	2.3%
Use of anti-inflammatory drugs	75.8%	17.6%	3.9%	2.6%
History of antibiotic use	69.0%	22.5%	5.6%	2.9%
Alcohol consumption	74.5%	15.0%	5.6%	4.9%
Ulcerative colitis/Crohn's disease/Celiac disease	95.8%	2.9%	1.0%	0.3%

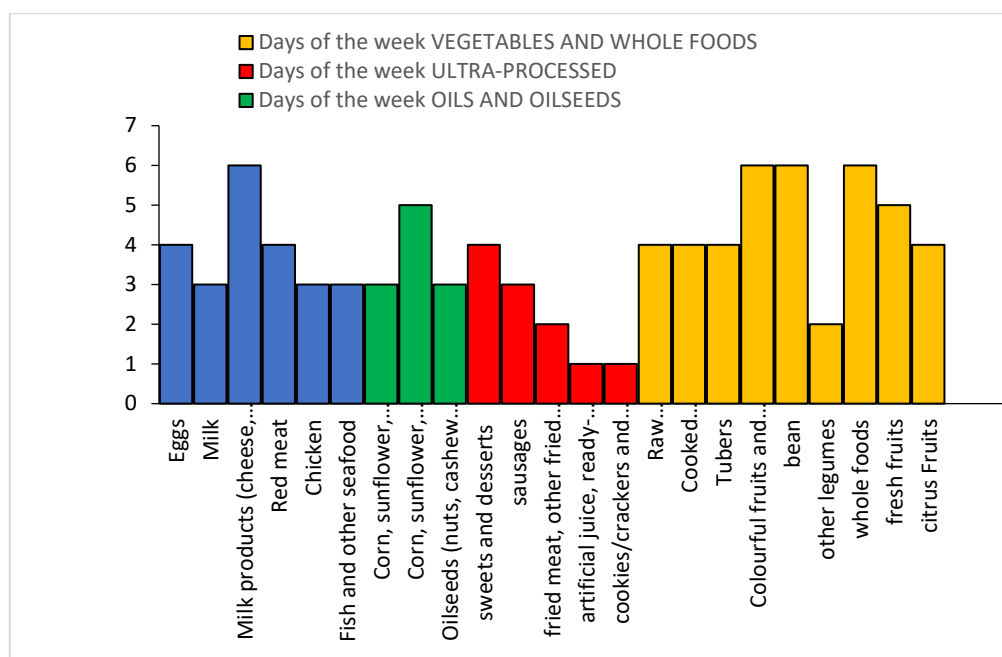


Figure 4: Average number of days of food consumption.

Figure 4 illustrates the following key observations, visually representing the data and trends related to the study.

- The average consumption of milk, dairy products, eggs, and meat, where the average consumption of milk, chicken, and fish was 3 days, eggs and red meat 4 days, and dairy products 6 days per week.
- The average weekly consumption of oils and oilseeds, where corn, sunflower, soybean and oilseed were consumed 3 days a week and olive oil 5 days a week.
- The average weekly consumption of vegetables and whole foods, where raw vegetables or legumes, cooked vegetables or legumes, tubers and citrus fruits had an average consumption of 4 days, orange vegetables, beans and whole foods 6 days, fresh fruits 5 days and other legumes only 2 days a week.
- The average weekly consumption of ultra-processed foods, where sweets and desserts had the highest consumption of 4 days and then sausages consumed on 3 days, fried meat, other fried foods, barbecue or barbecue 2 days a week, artificial juice, ready-made meals/fast food and soft drinks 1 day, cookies/crackers and jarred snacks 0 days of consumption per week.

4. Discussion

This study frames the strong impact of bariatric surgical surgery on the systemic inflammatory milieu that is evident in the patients with morbid obesity. One of the most significant findings is that pro-inflammatory cytokines, including tumor necrosis factor alpha (TNF- α) and C-reactive protein (CRP), are significantly attenuated, at the same time as the anti-inflammatory cytokine interleukin -10 (IL -10) is significantly increased [21], which is evident as early as one month after the operation and continues to be observed over a twelve-month period. Taken together, such results suggest that the Roux-en-Y gastric bypass provides a significant decrease in the persistent, low grade inflammatory condition of obesity [22].

The proinflammatory cytokine tumor necrosis factor-alpha (TNF- α) which is mainly produced by the adipose tissue in individuals with obesity is a critical determinant of the pathogenesis of insulin resistance and systemic inflammation. High levels of TNF- α worsen metabolic imbalances, dysfunctional endothelial processes and increase the risk of cardiovascular disease [22-23]. In this study, TNF- α levels were significantly reduced following surgery, aligning with decreased BMI and improved metabolic markers. Similarly, CRP, an acute-

phase reactant elevated in inflammatory states and a known predictor of cardiovascular events, declined progressively at each follow-up interval. This sustained reduction indicates a lowering of systemic inflammation and a favorable shift in metabolic risk profile.

The information previously discussed suggests that TNF- α could be a mediator of insulin resistance and that its secretion could also be related to obesity and increased visceral fat deposition [22, 34]. The information on obesity and insulin resistance has increased over the last 20 years. It is worth mentioning that various authors such as Spiegelman and Hotamisligil have been involved in this topic, publishing several studies describing the close relationship between the immune system through low-grade inflammation, obesity and insulin resistance [15]. This low-grade inflammation is the initiator and maintains these alterations for several years, affecting all organs and systems (adipose tissue). Therefore, it is important to explain that in patients who lose weight, levels of biochemical markers such as glucose, lipids, glycosylated haemoglobin, BMI, and systemic blood pressure improve. Additionally, this study also observed that bariatric surgery not only reduces markers of metabolic alteration but also lowers inflammatory factors and increases anti-inflammatory factors, suggesting that the procedure is effective in reversing the low-grade inflammatory state in patients with morbid obesity. The current study observed this balance between the decrease in inflammatory factors (CRP and TNF- α) and the increase in IL-10 in our study group.

Conversely, IL-10, known for its anti-inflammatory and immune-regulating functions, increased significantly postoperatively. IL-10 acts by inhibiting the synthesis of pro-inflammatory cytokines and promoting immune balance. Its elevation post-surgery suggests the restoration of immunological homeostasis, potentially offering long-term protection against metabolic and inflammatory disorders [21].

Among the signs and symptoms questioned, 47.1% of the participants had 1 or more symptoms of difficulty seeing in low-light environments, dry skin and dry eyes. This is due to a possible lack of vitamin A. The signs and symptoms present may indicate poor supplementation or low protein absorption that would hinder the absorption/assimilation of vitamin A. Regarding poor healing, hair loss and weak nails, there were 76.4% complaints of 1 or more alternatives; these signs indicate possible zinc deficiency. A study by Wang et al. (2023) [35] with 324 post-surgical participants showed a deficiency in 42.5% of participants, showing that the highest prevalence of deficiency was in biliopancreatic diversion procedures with duodenal switch (duodenal switch), while the present study obtained only 1 of the people undergoing DS.

Regarding omega-3, 18.5% of participants reported using supplementation. Omega-3 has well-documented benefits for immune and inflammatory responses by enriching immune cell membranes and promoting anti-inflammatory mediator production [36]. Protein supplementation was used by 31.7% of participants, a crucial measure given the common deficiency post-surgery due to reduced gastric volume and early satiety. Whey protein is particularly beneficial in preserving lean mass and modulating immunity through its immunoglobulin content and anti-inflammatory action [37–39].

The healthy microbiota is imperative to the effective functioning of the immune defence system. The effect of intestinal hyperpermeability is the enhancement of the generation of inflammatory cytokines, and a nutrient-enriched and balanced diet contributes to immune regulation and gut integrity maintenance [40–42].

The average intake of protein-rich foods including eggs and red meat was four times per week compared to six times of dairy products, which could be explained by the fact that the latter were more intolerable after surgery [4, 43–45]. The consumption of oil and nuts was three days / week; olive oil was taken five days. These food items contain unsaturated fatty

acids and bioactive compounds which mediate the anti-inflammatory mechanisms [46,47]. The emphasis on whole foods was made in accordance with dietary guidelines, which recommend satiety and glycemic control [48].

Although the frequency of consumption of ultra-processed foods included moderate frequency level, it remains an issue of concern. A reduced consumption of these products could be linked to postoperative intolerance and dumping syndrome. These foods lack the vital micronutrients which play a critical role in immune functionality as well as metabolic homeostasis [49,50].

Conclusions

Bariatric surgery showed an outcome on the reduction of systemic inflammation and metabolic health in patients with morbid obesity without a longer follow-up period of 12 months. The level of pro-inflammatory cytokines such as TNF- α and CRP reduced significantly, whereas the production of the anti-inflammatory cytokine IL-10 also increased significantly. The indication of immunological changes are time-dependent in accordance with quantifiable changes in body mass index, waist circumference, glycemic, and dyslipidemic indices. These results highlight the point that gastric bypass not only has an important effect of reducing weight but also has a modulatory effect on the proinflammatory milieu that is implicated with obesity-associated comorbidities. However, nutrition issues were also highlighted in the study. It reported the presence of clinical symptoms of vitamin A, zinc and iron deficiencies suggesting that they were either not eaten properly, or could have been poorly absorbed. It is important to mention that multivitamin preparations became the most commonly used supplements. Despite the available literature, there is still a poor adoption of protein and immunomodulatory supplements which include omega -3 fatty acids and probiotics. The continued postoperative nutritional monitoring is invaluable in maintaining clinical outcomes, enhancement of immune response, and prevention of micronutrient deficiencies. Overall, it can be concluded that bariatric surgery is a valuable treatment procedure that can be used on the way to reversing obesity-associated inflammation and improving the quality of life. To ensure that the palate re-education process is not complicated and in order to reduce the risk of the occurrence of nutrient deficiencies, the nutritional evaluation is to be conducted thoroughly after the operation. Clinical manifestations indicate that there is a deficiency of vitamin A, zinc, and iron, and the deficiency of vitamins C and D was reported less frequently. The prevailing supplementation was multivitamins and they were regularly used together with other agents according to the advice of experts. Protein intake was found to be suboptimal although it is necessary to have lean body mass. Use of immunomodulatory adjuncts which included probiotics, omega-3 fatty acids and prebiotic fibers was strongly limited which could be due to lack of awareness about the therapeutic effects.

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

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