

Original Article



The Impact of Obesity Surgery on Serum Uric Acid in People With Severe Obesity: A Retrospective Study

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ABSTRACT

Studies indicate an association between hyperuricemia (HUA) and metabolic syndrome risk factors. On the other hand, obesity is a major modifiable and independent risk factor for HUA and gout. However, evidence concerning the effects of bariatric surgery on serum uric acid levels is limited and not completely clarified. This retrospective study was carried out with 41 patients who underwent sleeve gastrectomy (n = 26) and Roux-en-Y gastric bypass (n = 15) from September 2019 to October 2021. Anthropometric, clinical, and biochemical data, including uric acid blood urea nitrogen and creatinine fasting blood sugar (FBS), serum triglyceride (TG), and serum cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), were measured preoperatively and postoperative 3, 6 and 12 months. From baseline to 6 and 12 months, bariatric surgery resulted in a significant decrease in serum uric acid of patients with severe obesity (p < 0.001). The decreases in serum FBS, TG, and cholesterol of patients were significant during 6 and 12 months of follow-up (p < 0.05). However, the HDL increase of patients was not statistically significant in 6 and 12 months (p > 0.05). Besides, although patients' serum level of LDL decreased significantly during the 6 months of follow-up (p = 0.007), it was not significant after 12 months (p = 0.092). Bariatric surgery significantly reduces serum uric acid levels. Therefore, it may be an effective supplementary therapy for lowering serum uric acid concentrations in morbidly obese patients.

Keywords: Bariatric surgery; Obesity; Uric acid; Weight loss

INTRODUCTION

Uric acid is the product of purine metabolism and is produced through the enzymatic degradation of hypoxanthine and xanthine. It is mainly synthesized in the liver and excreted through the kidneys and gut [1-3]. However, a high percentage of uric acid (90%) is generally re-absorbed and returned to the bloodstream. The serum uric acid concentration is unstable and is affected by genetic and environmental factors. When these factors are disrupted, hyperuricemia (HUA) may be resulted [4].

HUA has been identified as serum uric acid concentration above 420 or 340 $\mu\text{mol/L}$ in men and women, respectively [5]. HUA is a precondition for depositing monosodium urate crystals, which is gout's primary cause and is related to metabolic syndrome, insulin

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Haghighat N; Data curation: Vafa L; Formal analysis: Kamran H; Funding acquisition: Amini M; Investigation: Hosseini SV; Methodology: Haghighat N; Project administration: Hosseini SV; Resources: Amini M; Software: Kamran H; Supervision: Amini M; Validation: Mohammadi Z; Visualization: Aghakhani L; Writing - original draft: Aghakhani L; Writing - review & editing: Haghighat N.

resistance, renal disease, dyslipidemia, type 2 diabetes, liver failure, and cardiac disease [6-9]. The prevalence of HUA has rapidly risen among the general population [10]. As a result, HUA prevention and control have become a serious public health concern.

Evidence indicates an association between HUA and metabolic syndrome risk factors, such as diabetes, high blood pressure, dyslipidemia, insulin resistance, and obesity [11]. Obesity is a major modifiable and independent risk factor for HUA and gout [7,11]. In previous studies, HUA has been associated with body mass index (BMI), waist circumference, and the waist-height ratio [12].

Several studies have found that weight loss reduces serum urate levels and causes fewer cases of gouty arthritis [13,14]. Based on a recent update of American College of Rheumatology guidelines, weight loss is recommended for obese or overweight patients with gout [7,15].

Bariatric surgery reduces caloric intake by altering the anatomy of the gastrointestinal tract, and it is the most efficient way to help people lose weight, especially for people with morbid obesity [16]. Moreover, a significant weight reduction in morbidly obese patients is associated with a substantial decrease in metabolic risks [17].

Although previous studies have shown a substantial relationship between HUA and weight changes, evidence concerning the effects of bariatric surgery on serum uric acid levels is limited and not completely clarified. Therefore, the current study was conducted to evaluate the serum uric acid concentration in obese subjects before and after bariatric surgery.

MATERIALS AND METHODS

Study design and participants

In this retrospective study, medical records of patients who underwent sleeve gastrectomy (SG) and Roux-en-Y gastric bypass at the Ghadir Mother and Child Hospital, run under Shiraz University of Medical Sciences, between September 2019 to October 2021 were gathered. Adult patients aged 18–65 years with severe obesity which was defined as BMI > 40 kg/m² or > 35 kg/m² with at least one associated obesity-related comorbidity, and who had a follow-up of at least 6 months were included. However, patients with incomplete medical records, under 18 years of age, or lost in follow-up before the 6-month follow-up after the operation were excluded. Moreover, patients with a history of smoking, alcohol use, psychiatric problems, gout, thyroid-related diseases and cancer were excluded. Patients were divided into 2 groups based on follow-up duration. One group was those with 3 and 6 months follow-up and the other group was those patients in the first group who were not lost to follow-up with 3, 6 and 12-month follow-ups. All the surgery procedures were performed by the same surgeon. Informed consent was provided from patients. The researchers adhered to the Declaration of Helsinki, and the study protocol was approved by the Shiraz University of Medical Sciences Ethics Committee (IR.SUMS.REC.1401.476).

Data collection

Patients' data were extracted from the patients' medical records. For baseline information, patients were visited, and demographic data, including age and sex, type of surgery, history of past medical diseases, and anthropometric measurements, such as weight, BMI, waist, and hip circumferences, were entered into a checklist by a nutritionist. Besides, preoperative

serum laboratory parameters of patients, including uric acid, creatinine, blood urea nitrogen (BUN), fasting blood sugar (FBS), triglyceride (TG), cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL), were recorded. Patients were followed 3, 6, and 12 months following the operation, and the same laboratory tests and anthropometric information were recorded in the postoperative visits by the same nutritionist.

Statistical analysis

The statistical analysis was performed with SPSS software (released 2019, IBM SPSS Statistics for Windows, version 26.0; IBM Corp., Armonk, NY, USA). The information was presented by number and percentage (%) or mean \pm standard deviation. Besides, repeated measure analysis was used for data interpretation, and a p value lower than 0.05 was considered statistically significant.

RESULTS

Forty-one patients with a mean age of 43.6 ± 6.8 years were included, of which 32 (78.0%) were female. Besides, 26 (63.4%) patients underwent SG while 15 patients (36.6%) underwent gastric bypass. The comorbidities and baseline anthropometric measures of the patients are demonstrated in **Table 1**.

Table 2 shows the weight outcomes of the patients at 3, 6, and 12 months after the operation. Although no patients were lost to follow-up during the 6-month follow-up concerning weight outcomes, 16 patients were lost in the 12-month follow-up. As shown, all anthropometric measures, including weight, BMI, and hip and waist circumferences of the patients, were decreased significantly during the 6 and 12-month follow-ups (all $p < 0.001$).

Analysis using repeated measure revealed serum uric acid of patients decreased significantly during the 6-month follow-up ($p < 0.001$). Regarding the 12-month follow-up, 16 patients were lost to follow-up; however, the decrease remained significant ($p < 0.001$). As shown in **Figure 1**, uric acid of patients had a constantly decreasing trend during the 3 and 12 months of follow-up.

Table 1. Baseline information

Variables	Data (n = 41)
Age (yr)	43.6 \pm 6.8
Female	32 (78.0)
Surgery	
Gastric bypass	15 (36.6)
Sleeve gastrectomy	26 (63.4)
Weight measures	
Weight (kg)	113.1 \pm 21.0
BMI (kg/m ²)	43.1 \pm 5.9
Hip circumference (cm)	133.0 \pm 12.2
Waist circumference (cm)	126.1 \pm 13.8
Comorbidities	
Hypothyroidism	4 (9.8)
Diabetes mellitus	5 (12.2)
Hyperlipidemia	4 (9.8)
Cardiovascular disease	0 (0.0)
Hypertension	6 (14.6)

Values are presented as number (%) or mean \pm standard deviation.

Table 2. Weight outcomes in 6- and 12-month of follow-up

Variables	6-mon follow-up (n = 41)		p value	12-month follow-up (n = 25)		p value
Weight (kg)	Preoperative	113.1 ± 21.0	< 0.001	Preoperative	117.7 ± 21.0	< 0.001
	3 mon	92.3 ± 16.2		3 mon	94.3 ± 15.2	
	6 mon	82.8 ± 14.4		6 mon	85.1 ± 12.4	
				12 mon	77.7 ± 12.0	
BMI (kg/m ²)	Preoperative	43.1 ± 5.9	< 0.001	Preoperative	44.7 ± 5.7	< 0.001
	3 mon	35.2 ± 4.8		3 mon	36.0 ± 4.4	
	6 mon	31.1 ± 4.4		6 mon	31.9 ± 3.8	
				12 mon	29.1 ± 4.1	
Hip circumference (cm)	Preoperative	133.0 ± 12.2	< 0.001	Preoperative	136.3 ± 12.3	< 0.001
	3 mon	117.3 ± 10.3		3 mon	120.1 ± 9.9	
	6 mon	110.4 ± 10.3		6 mon	113.3 ± 9.5	
				12 mon	107.4 ± 9.7	
Waist circumference (cm)	Preoperative	126.1 ± 13.8	< 0.001	Preoperative	128.1 ± 12.3	< 0.001
	3 months	110.3 ± 11.3		3 mon	111.2 ± 9.8	
	6 mon	103.8 ± 10.6		6 mon	105.4 ± 9.9	
				12 mon	102.2 ± 9.0	

Values are presented as mean ± standard deviation. The p values refer to variation from preoperative to 3 months, 6 months and 12 months within groups (repeated measures analysis).

BMI, body mass index.

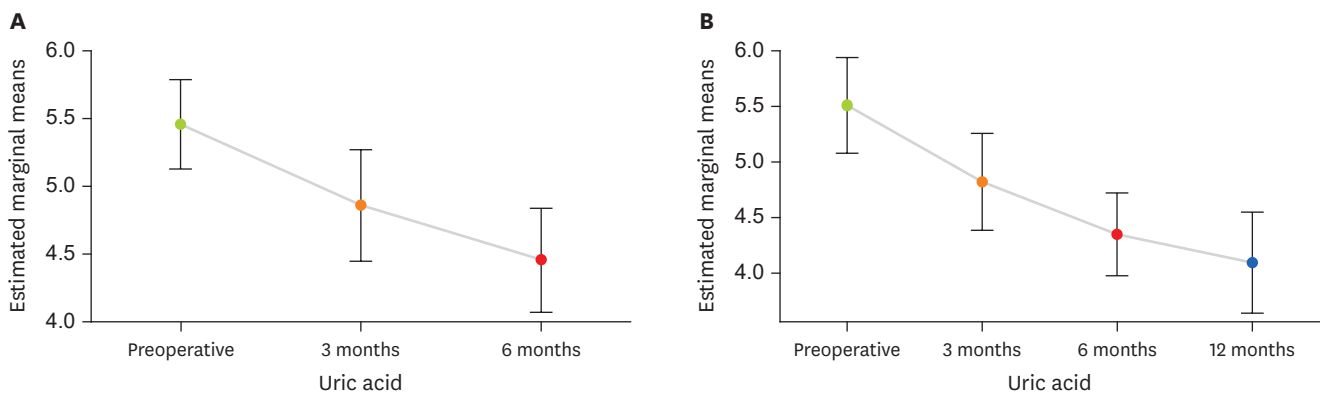


Figure 1. Uric acid changes over 6 months and 12 months of follow-up.

Changes in both BUN and creatinine of patients were not statistically significant during the 6 and 12-month follow-ups ($p > 0.05$). Of note, the mean serum creatinine of patients was 1.8 mg/dL preoperatively, decreased to a mean of 0.8 mg/dL after 3 months of surgery, and remained 0.8 mg/dL till the 12-month follow-up; although this decrease may be clinically significant, it did not reach a statistical significance.

Moreover, analysis using repeated measure showed that the decreases in serum FBS, TG, and serum cholesterol of patients were significant during 6 and 12 months of follow-up ($p < 0.05$). However, the HDL increase of patients was not statistically significant (p of 0.417 and 0.378 during 6 and 12-month follow-ups, respectively). Besides, although the patients' level of LDL decreased significantly during the 6 months of follow-up ($p = 0.007$), it was not significant after 12 months ($p = 0.092$) (**Table 3**).

Table 3. Changes in serum parameters over 6- and 12-month of follow-up

Variables	6-month follow-up		p value	12-month follow-up		p value
Uric acid (mg/dL)	(n = 41)		< 0.001	(n = 25)		< 0.001
	Preoperative	5.4 ± 1.0		Preoperative	5.5 ± 1.0	
	3 mon	4.8 ± 1.2		3 mon	4.8 ± 1.0	
	6 mon	4.4 ± 1.2		6 mon	4.3 ± 0.9	
			12 mon	4.0 ± 1.1		
BUN (mg/dL)	(n = 41)		0.925	(n = 26)		0.561
	Preoperative	11.8 ± 3.9		Preoperative	10.9 ± 3.9	
	3 mon	11.7 ± 4.1		3 mon	11.9 ± 4.6	
	6 mon	11.6 ± 3.8		6 mon	10.9 ± 3.7	
			12 mon	11.8 ± 3.4		
Creatinine (mg/dL)	(n = 41)		0.532	(n = 26)		0.095
	Preoperative	1.4 ± 2.2		Preoperative	1.8 ± 2.7	
	3 mon	1.0 ± 1.3		3 mon	0.8 ± 0.3	
	6 mon	1.0 ± 1.4		6 mon	0.8 ± 0.2	
			12 mon	0.8 ± 0.1		
Fasting blood sugar (mg/dL)	(n = 41)		0.003	(n = 26)		0.004
	Preoperative	111.2 ± 50.0		Preoperative	107.8 ± 42.9	
	3 mon	94.5 ± 32.3		3 mon	87.9 ± 10.2	
	6 mon	88.3 ± 20.9		6 mon	84.3 ± 19.1	
			12 mon	84.3 ± 17.5		
Serum triglyceride (mg/dL)	(n = 41)		< 0.001	(n = 26)		< 0.001
	Preoperative	157.6 ± 83.1		Preoperative	149.5 ± 46.6	
	3 mon	123.0 ± 48.2		3 mon	121.0 ± 33.2	
	6 mon	106.6 ± 26.8		6 mon	106.5 ± 28.2	
			12 mon	105.0 ± 37.2		
Serum cholesterol (mg/dL)	(n = 39)		0.001	(n = 21)		0.007
	Preoperative	185.8 ± 34.1		Preoperative	188.1 ± 39.0	
	3 mon	171.3 ± 28.7		3 mon	169.2 ± 31.9	
	6 mon	169.7 ± 33.4		6 mon	169.7 ± 37.8	
			12 mon	164.5 ± 32.2		
HDL (mg/dL)	(n = 39)		0.417	(n = 21)		0.378
	Preoperative	45.6 ± 9.3		Preoperative	42.9 ± 8.1	
	3 mon	48.0 ± 12.2		3 mon	44.9 ± 14.1	
	6 mon	46.2 ± 10.1		6 mon	43.5 ± 9.3	
			12 mon	47.1 ± 10.5		
LDL (mg/dL)	(n = 39)		0.007	(n = 21)		0.092
	Preoperative	106.6 ± 29.9		Preoperative	104.3 ± 29.3	
	3 mon	97.3 ± 23.7		3 mon	98.4 ± 25.6	
	6 mon	93.0 ± 28.0		6 mon	92.3 ± 29.4	
			12 mon	88.3 ± 30.1		

Values are presented as mean ± standard deviation. The p values refer to variation from preoperative to 3 months, 6 months and 12 months within groups (repeated measures analysis).

BUN, blood urea nitrogen; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

DISCUSSION

HUA is caused by an imbalance between the consumption of exogenous purine and endogenous production and expulsion [17]. Since HUA is an essential indicator of many diseases [6-9], preventing and controlling serum uric acid levels has become a critical clinical solution [18]. Long-term treatment for HUA will be costly and risky. Therefore, reducing the incidence of HUA requires a better understanding of its risk factors and initiating prevention early [12].

In previous studies, a positive relationship has been found between serum uric acid levels and obesity risk. Several mechanisms may contribute to the interaction between HUA and obesity. The hepatic and peripheral lipogenesis can be accelerated by HUA leading to obesity, and obesity is also a contributing factor to higher levels of serum uric acid [7,19]. Further,

obesity may impair renal clearance of uric acid, which may explain its positive relationship with serum uric acid levels.

It is believed that treatment of obesity and decreasing BMI may significantly impact serum uric acid and renal urate excretion and play an essential role in regulating serum uric acid levels [20]. The process of losing weight is not easy for morbidly obese people, and despite their best efforts, many obese individuals are unable to alter their obesity status. As a result, they may enter a cyclical pattern of losing weight and gaining back, and the important thing to note is that metabolic disorders are closely associated with weight fluctuations in obesity conditions [11].

Bariatric surgery is the best alternative to losing weight in morbidly obese patients [21]. In this study, we found that serum uric acid levels of patients with severe obesity decreased significantly 6 and 12 months after the surgery. Similarly, multiple studies have shown that bariatric surgery effectively reduced serum uric acid levels in morbidly obese patients [18,22-24]. Sjöström et al. [25] found that, as compared to usual care, bariatric surgery also reduced uric acid levels in the long-term follow-up, 2 and 10 years after surgery of patients who underwent gastric surgery compared to the control group. Besides, in a meta-analysis study published in 2019, Yeo et al. [26] concluded that weight loss after bariatric surgery could reduce serum uric acid levels and decrease gout attacks.

For many years, benzbromarone and allopurinol were the main treatments for lowering urate levels. In some obese patients, these therapies did not seem practical at reducing serum uric acid [10]. Furthermore, patients with HUA or gout may require long-term medication for the rest of their lives, and medication adherence and side effects are significant concerns since gout and HUA are chronic diseases [18].

Evidence regarding an association between HUA and metabolic syndrome risk factors, such as high blood pressure, dyslipidemia, diabetes, insulin resistance, and obesity, is growing. [11]. Yuan et al. [27] conducted a meta-analysis and reported that each 1 mg/dL increase in the serum uric acid level could raise metabolic syndrome risk by 30%. Obesity is the most common cause of metabolic syndrome [28]. In this study, we found that after surgery, besides reducing weight and BMI, the other parameters related to the metabolic syndrome such as waist circumference, serum TG levels, cholesterol levels, and FBS, significantly improved. Also, Aguilar-Olivos et al. [29], in a review study, revealed that bariatric surgery has beneficial effects on weight, insulin resistance, alterations in glucose metabolism, and hypertension. Even though bariatric surgery is currently used exclusively for weight loss and not directly for HUA or metabolic syndrome-associated diseases, these conditions are prevalent in most morbidly obese people [28].

Some limitations of this study should be acknowledged. First, we did not evaluate the dietary intake or physical activity of patients. Therefore, the contribution of any changes in diet contaminant on serum uric acid could not be determined. Secondly, the relatively small sample size of our study is one of its limitations. Lastly, we did not consider the level of alcohol consumption and the number of cigarettes smoked by participants, which both may affect serum uric acid [20].

In conclusion, this retrospective study demonstrated that bariatric surgery could significantly reduce serum uric acid levels. Thus, bariatric surgery may be an effective supplementary

therapy for lowering serum uric acid concentrations in morbidly obese patients and reducing the risk of gout or other HUA-related diseases.

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