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Original Article

Socio-demographic Characteristics, Biochemical and Cytokine Levels in Bulimia Nervosa Candidates for Sleeve Gastrectomy

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Abstract

Background: Eating disorders (EDs) are widely known by abnormal eating behaviors associated with significant medical complications. Bulimia nervosa (BN) is an eating disorder characterized by uncontrolled episodes of overeating typically followed by some form of compensatory behaviors. We aimed to determine the relationships between socio-demographic characteristics, biochemical markers, and cytokine levels in BN candidates for laparoscopic sleeve gastrectomy (LSG).

Methods: A case-control study was designed among 76 BN participants of Iranian descent who were candidates for LSG based on defined criteria for Bulimia by Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). The healthy control subjects (n = 42) were selected at random from academic staff in the college. Moreover, levels of biochemical parameters and serum cytokines were measured in serum samples.

Results: Routine consumption of caffeine (odds ratio [OR] = 3.1, 95% CI: 1.23–6.41, $P = 0.013$), tobacco (OR = 1.8, 95% CI: 0.67–3.57, $P = 0.03$), and alcohol (OR = 3.6, 95% CI: 0.84–7.18, $P = 0.048$), and depression history (OR = 2.8, 95% CI: 0.76–5.79, P = 0.037) were substantially more common among patients with bulimia. Also, the serum levels of fasting blood sugar ($P < 0.001$), HbA1c (P = 0.04), cholesterol ($P = 0.03$), triglycerides ($P = 0.01$), blood urea nitrogen ($P = 0.03$), and pro-inflammatory cytokines including IL-1β, IL-6, and TNF-α were significantly higher in BN candidates for LSG ($P \leq 0.001$).

Conclusion: Our findings reveal that lifestyle-related risk factors and a depression history were both related with a significantly increased risk of BN among the candidates for LSG. Furthermore, there is a relationship between clinical characteristics as well as levels of various biochemical and cytokines parameters in serum of BN patients.

Keywords: Biological markers, Bulimia nervosa, Cytokines, Eating disorders, Gastrectomy

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Introduction

Eating disorders (EDs) such as anorexia nervosa (AN) and bulimia nervosa (BN) are psychiatric disorders that occur on a continuum with behaviors shared across syndromes that negatively affect cognitive, physiological, and social activities.[1] Over the last years, the incidence rate of ED behaviors has been on the rise. It is estimated that 20 million women and 10 million men in the United States have experienced an ED at some point in their lives.[2] One research-based questionnaire on ED that was administered among Iranian school girls estimated the prevalence of BN at 3.2%.[3] Another study on an Australian population reported a doubling of incidence over a decade, and the socio-demographic characteristics strayed from comprehensively young white upper-class females to an upward trend in males and those of lower financial status as well as those in older age groups.[1] ED affects nearly 1.6% of women and 0.8% of men each year in the developed countries although it appears to be lower in developing countries.[4] Although the main reason for EDs is not yet clear, there may be both biological and environmental factors that put some persons at higher risk of developing ED.[2]

Bulimia nervosa is a psychological ED and mental health condition described by consuming a large quantity of food in one sitting, followed by an attempt to avoid gaining

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weight by purging what was consumed.[5] BN has a series of sign and symptoms such as swollen salivary glands in the jaw and neck regions, sore and chronic inflammation in throat, worn tooth enamel, progressively decaying and sensitive tooth (mainly because of stomach acid), severe dehydration due to purging of fluids, electrolyte imbalance (such as calcium, potassium, sodium, and various minerals), acid reflux and other gastrointestinal disorder and intestinal distress as well as irritation.[5] Furthermore, BN is frequently connected to other mental illnesses such as anxiety and depression or alcohol/substance abuse.[6] Social habits have been suggested as significant factors in etiologic models of BN and are critical for both the development and maintenance of these symptoms.[6] Various studies have illustrated the impact of social habits in EDs.[6-8] Most studies have indicated that EDs are associated with personality disorders, perfectionism, obsessive compulsive traits, and impulsivity.[7,8] Nevertheless, the role of a series of social habits such as using probiotics, caffeine, tobacco, alcohol, as well as hypertension, diabetes, and going on various diets in BN disorder in obese patients is still unclear and contradictive.[7]

Various reports illustrate that some socio-demographic characteristics such as suicide attempts,[9] depressed mood, low self-esteem, irritability, and generalized anxiety,[5] or other factors including being a student, obesity, osteoporosis, etc.[6-10] are more frequent in patients with bulimia.

Among the biochemical changes evaluated in patients with bulimia, metabolic defects such as abnormalities in protein homeostasis, glucose, lipid, and enzymes are relatively common.[11,12] Several studies have shown that increased serum levels of biochemical parameters are significantly related to BN.[13,14] Also, some studies have shown that cytokines play a critical role in ED, and pro-inflammatory cytokine levels such as IL-6, TNF-α, and IL-1β had an upward trend in patients with bulimia.[15,16]

In this study, we aimed to examine and compare the associations between socio-demographic characteristics, biochemical parameters, and cytokine levels in BN candidates for laparoscopic sleeve gastrectomy (LSG).

Materials and Methods

Participants

This case-control study was carried out on participants who visited the Tehran laparoscopic surgery group, Erfan Niayesh hospital, Tehran, Iran during the period from July 2018 to May 2019. The sample size was calculated using online software (www.dssresearch.com).

The target group (76 BN of Iranian descent) were selected from among 4138 individuals with obesity who were candidates for bariatric surgery (LSG). The inclusion criteria were: (1) full criteria diagnosis of BN (DSM-IV criteria); (2) age (older than 18 years); 3) body mass index (BMI = kg/m^2, higher than 35); (4) no evidence of organic brain syndrome or terminal illness and (5) informed consent. Moreover, the exclusion criteria were: (1) recent illnesses (i.e. within the two weeks preceding enrolment); (2) hepatitis due to viral or other causes; (3) illiteracy; (4) cognitive impairment; (5) comorbidity with schizophrenia; (6) suicide ideation and (7) psychoactive substance abuse. Also, healthy control subjects (n = 42) were selected at random from academic staff in the college, and subjects with a current or past ED were excluded from the control group. The control subjects were individually matched to the subjects with BN for three variables of age, sex, and BMI.

Measures and Variables

Interview-Based Diagnostic and Statistical Manual of Mental Disorders (DSM)

An interview process was conducted for all candidates for LSG by a psychiatrist in the surgery department. Seventy-six patients with obesity were administered the ED module of the Structured Clinical Interview, based on defined criteria for Bulimia by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-IV) for diagnosis of current or past BN symptoms.[17] This self-report questionnaire was derived from the Structured Clinical Interview for DSM-III-R (SCID)[18] and used to collect information related to DSM-IV criteria.

Questionnaire-Based Multidimensional Personality Questionnaire (MPQ)

The questionnaire was administered to participants in paper-and-pencil format. The Multidimensional Personality Questionnaire (MPQ) is a self-report questionnaire with several strengths in investigating the association between personality and obesity (Tellegen A. Brief manual for the multidimensional personality questionnaire. Unpublished manuscript, University of Minnesota, Minneapolis. 1982:1031-10). This questionnaire has 11 social habit scales: consuming probiotics (i.e. probiotic yogurt), caffeine, tobacco, and alcohol, as well as gender, hypertension, diabetes, going on various diets (vegetarianism, sarcophagy and raw food diet), age, weight and BMI. The MPQ was designed to minimize overlap among the scales and ensure fidelity, combined with a breadth of social habits for good bandwidth. Responses were rated from 1 (always) to 6 (never). The scores for each item differ from one another. The total score is the sum of all items ranging from 0 to 120. A score more than 30 was considered as indicator of ED. Moreover, the entire study population were subjected to weight and height measurement in order to calculate their BMI.

Measuring the Severity of Depression-Based Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) was used to evaluate

the severity of depressive symptoms in candidates.[19] The BDI is a 21-item self-report measure of depressive symptoms, extensively used to measure psychometric properties. It has several supporting points including internal consistency coefficients of more than 0.80.

Collection of Blood and Isolation of Serum

Blood samples were aseptically collected via cubital vein puncture from all subjects for serum (9 mL serum collection tubes) and whole blood (3 mL tubes with EDTA K_3) and immediately transferred to medical laboratory in an icebox. Serum collection tubes were centrifuged (4000 x g for 10 minutes) and serum was aspirated, aliquoted, and stored until use.

Measurement of Blood HbA1c

Glycated hemoglobin (HbA1c) was measured on whole blood samples with an immunoturbidimetric method using commercially available kit supplied by Pars Azmoon Co., Tehran, Iran.

Analysis of Biochemical Parameters

Levels of various clinical biochemistry parameters including aspartate aminotransferase (SGOT), fasting blood sugar (FBS), triglycerides (Tg), cholesterol (Chol), low-density lipoprotein (LDL), high-density lipoprotein (HDL), creatinine (Cr), blood urea nitrogen (BUN), alanine aminotransferase (SGPT), and alkaline phosphatase (ALP) were assessed using a fully automated biochemistry analyzer (COBAS MIRA® Plus). Each specimen was analyzed in triplicate and the median for each test was calculated.

Cytokine Measurements

Serum cytokines were measured using specific sandwich ELISA kits (Abcam, Cambridge, UK) for inflammatory cytokines (IL-6, IL-1β, and TNF-α) and anti-inflammatory cytokines (IL-4, IL-10, IL-13, and TGF-β) in duplicate. All ELISA results were quantified using a microplate reader (AccuReader, M965 Series, Metertech, Taipei, Taiwan). The minimum detectable dose of the IL-1β, TGF-β, IL-10, IL-6, TNF-α, IL-13 and IL-4 assays were 6.5, 0.03, 1, 2, 8, 0.15, and 0.7 pg/mL respectively.

Statistical Analysis

At the time of study design and before the process of collecting data, different types of confounders including measured (age, sex, etc) and unmeasured but measurable (smoking, alcohol, BMI, disease severity, etc) factors were predictable in this study. There are various methods to decrease confounding variables including randomization, restriction, and matching. So, in order to eliminate or control the effects of confounders and isolate the relationship of interest, we used the proper statistical tools (binary logistic regression model). In this way, all potential confounders were entered into the model and then non-significant variables were excluded using the backward method. This means that all the reported odds ratios (ORs) are adjusted for other variables (including confounders). Data were analyzed using Stata v.14 software. Additionally, pairwise correlations were evaluated using Phi coefficients. A *P* value less than 0.05 was considered as statistically significant.

Results

Study Population

Of the 4138 individuals with obesity who were candidates for weight loss surgery (LSG), 76 participants (1.83%) were diagnosed with BN by a psychiatrist in our surgery group. The socio-demographic characteristics of 76 BN candidates for weight loss surgery are shown in Table 1. The incidence of BN was highest in participants in the age group of 30–44 years (50%) while the age group 45–64 years had the lowest incidence of BN (18.42%). In addition, the rate of BN in females (60–78.95%) was higher than males (16–21.05%). The mean ± SD of BMI, weight and age were 41.4 ± 4.33 kg/m^2, 116.16 ± 15.49 kg and 34.80 ± 10.93 years, respectively for BN candidates for LSG. Because the control subjects were individually matched to the subjects with BN for age, sex and BMI, the distribution of these characteristics is similar in the two groups. Also, there were no significant differences in the presenting BMI, weight, and age. We have additionally shown that the older ages had the lowest prevalence of bulimia.

Table 1. Socio-demographic Characteristics of 76 Patients with Bulimia, Candidates for Weight Loss Surgery

Characteristics	n = 76
Age groups	
18–29	24
30–44	38
45–64	14
Gender	
Male	16
Female	60
Education	
0–12 years	43
+12 years	33
Marital status	
Single	24
Married	50
Others	2
Geographical area	
Rural	6
Urban	70
Employment	
Working	62
Homemaker	7
Retired	7

Characteristics of the participants, distribution of risk factors, and comorbidity in the two subject groups are presented in Table 2. Significant differences were evident between the participants with BN and the control subjects. In comparison with the healthy subjects, the BN subjects consumed significantly more caffeine (OR = 3.1, 95% CI: 1.23–6.41, $P = 0.013$), tobacco (OR = 1.8, 95% CI: 0.67–3.57, $P = 0.03$), and alcohol (OR = 3.6, 95% CI: 0.84–7.18, $P = 0.048$), or had a depression history (OR = 2.8, 95% CI: 0.76–5.79, $P = 0.037$) (Table 2). On the other hand, items such as consuming probiotics, blood pressure, diabetes, and going on various diets were not associated with bulimia in patients with obesity. Approximately more than half of all BN candidates for weight loss surgery (n = 44, 57.9%) were diagnosed with at least one comorbidity, while other BN participants (n = 32, 42.1%) did not have any comorbidity.

Serum Levels of Biochemical and Cytokine Parameters in Patients with Bulimia Nervosa

The cytokine and biochemical parameters in serum of BN candidates for LSG and control group are shown in Table 3. In comparison to the control subjects, the serum levels of FBS ($P < 0.001$), HbA1c ($P = 0.04$), cholesterol ($P = 0.03$), triglycerides ($P = 0.01$), and BUN ($P = 0.03$) were significantly higher in BN candidates for LSG, whereas the serum levels of SGOT, HDL, LDL, Cr, SGPT, and ALP were not significantly different ($P > 0.05$). Additionally, the concentration of pro-inflammatory cytokines including IL-6, TNF-α, and IL-1β showed an upward trend in the serum of BN candidates for LSG ($P < 0.001$) while it was decreasing for anti-inflammatory cytokines such as IL-4 ($P > 0.05$), IL-10 ($P = 0.04$), IL-13 ($P = 0.03$), and TGF-β ($P > 0.05$). Moreover, seven of the BN patients had previously been diagnosed as having abnormal cholesterol levels. These patients were taking Atorvastatin oral tablet at the time of the study. Four participants had a past history of gastric bypass surgery and 9 had controlled type 2 diabetes (T2D) treated with metformin prior to the current study.

Pairwise Statistical Associations

Table 4 illustrates the associations between biochemical parameters and clinical characteristics of 76 BN candidates

Table 2. Characteristics of the Participants, Distribution of Risk Factors, and Comorbidity in the Two Subject Groups

Characteristics	BN Subjects (n = 76)		Healthy Control Subjects (n = 42)		*P* Value	Odds Ratio	95% CI
	No.	%	No.	%			
Gender							
Male	16	21.05	11	26.2	0.525	1.2	0.31–1.91
Female	60	78.95	31	73.8			
Probiotics							
Consumer	17	22.36	6	14.3	0.263	2.1	0.64–4.96
Non- consumer	59	77.63	36	85.7			
Caffeine							
Consumer	38	50.00	10	23.8	0.013*	3.1	1.23–6.41
Non- consumer	38	50.00	32	76.2			
Tobacco							
Current smoker	27	35.53	7	16.66	0.030*	1.8	0.67–3.57
Never smoked	49	64.47	35	83.33			
Alcohol							
Drinker	19	25.00	4	9.53	0.048*	3.6	0.84–7.18
Non-drinker	57	75.00	38	90.47			
Diet							
Vegetarianism	3	3.94	8	19.04	0.853	1.9	0.13–5.26
Raw eating diet	3	3.94	2	4.77	0.853	1.9	0.13–5.26
Sarcophagy	70	92.10	32	76.2	0.577	1.1	0.28–2.81
Diabetes							
Diabetic	14	18.42	5	11.9	0.693	1.1	0.32–2.11
Non- diabetic	62	81.58	37	88.1			
Blood pressure							
Hypertension	8	10.53	4	9.53	0.819	1.2	0.26–2.85
Normal	68	89.47	38	90.47			
Depression							
Positive	22	28.94	2	4.77	0.037*	2.8	0.76–5.79
Negative	54	71.05	40	95.23			

*The significance of the exposure (likelihood ratio statistic, $\chi 2$) and odds ratios with their significance levels and 95% confidence intervals (CI) are given for each parameter.

Table 3. Cytokine and Biochemical Levels in serum of BN Candidates for LSG and Control Subjects

Parameters		Reference Value	BN Patients (n = 76)	Control Group (n = 42)	*P* Value	Trend
Biochemical	SGOT	0–42 IU/L	29.7 ± 6.9	25.2 ± 2.97	NS	↑
	FBS	70–100 mg/dL	176.2 ± 44.3	89.5 ± 8.9	<0.001	↑
	HbA1c	Non-diabetic <5.7 % (39 mmol/mol) 5.7 % ≤Prediabetic ≤ 6.4 % (46 mmol/mol) Diabetic ≥6.5 % (48 mmol/mol)	7.2 % ± 2.4	5.5 % ± 2.9	0.04	↑
	Chol	40–200 mg/dL	273.1 ± 42.8	178 ± 27.6	0.03	↑
	Tg	40–200 mg/dL	229.2 ± 83.1	139 ± 69.4	0.01	↑
	HDL	30–70 mg/dL	40.8 ± 9.8	38.7 ± 10.4	NS	↑
	LDL	40–130 mg/dL	89.5 ± 27.1	79.3 ± 13.7	NS	↑
	BUN	7–20 mg/dL	25.1 ± 5.5	11.8 ± 2.3	0.03	↑
	Cr	0.5–1.0 mg/dL	1.21 ± 0.39	0.75 ± 0.15	NS	↑
	SGPT	0-42 IU/L	29.6 ± 10.4	24.4 ± 2.71	NS	↑
	ALP	Female: 64-36 IU/L Male: 80-306 IU/L	167.9 ± 36.9 170.2 ± 38.3	115.6 ± 16.9 109.1 ± 15.3	NS	↑
Cytokine	IL-1β	pg/mL*	374.3 ± 20.7	285.2 ± 28.9	<0.001	↑
	IL-6	pg/mL*	193.4 ± 18.3	149.7 ± 21.3	<0.001	↑
	TNF-α	pg/mL*	507.8 ± 30.3	257.1 ± 23.2	<0.001	↑
	IL-4	pg/mL*	4.48 ± 1.1	6.17 ± 2.7	NS	↓
	IL-10	pg/mL*	48.3 ± 4.7	68.4 ± 7.7	0.04	↓
	IL-13	pg/mL*	5.3 ±1.4	10.6 ±2.5	0.03	↓
	TGF-β	ng/mL*	0.1 ± 0.01	1.9 ± 0.2	NS	↓

NS, not significant; SGOT, serum glutamate-oxaloacetate transaminase; FBS, fasting blood sugar; HbA1c, Hemoglobin A1c; Chol, Cholesterol; Tg, Triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen; Cr, creatinine; SGPT, serum glutamic-pyruvic transaminase; ALP, alkaline phosphatase; IL, Interleukin; TNF, tumor necrosis factor; TGF, transforming growth factor.
*Normal levels of cytokines are different in each individual. Data are expressed as mean ± SD.

Table 4. Pairwise Statistical Associations Between Biochemical Parameters and Clinical Characteristics (for 76 BN candidates for LSG)

Parameter	SGOT	FBS	HbA1c	Chol	Tg	HDL	Cr	BUN	LDL	SGPT	ALP	Hypertension	Diabetes
FBS	NS	—	—	—	—	—	—	—	—	—	—	—	—
HbA1c	NS	*P*<0.001	—	—	—	—	—	—	—	—	—	—	—
Chol	NS	NS	NS	—	—	—	—	—	—	—	—	—	—
Tg	NS	NS	NS	*P*<0.001	—	—	—	—	—	—	—	—	—
HDL	NS	NS	NS	*P*<0.001	*P*<0.001	—	—	—	—	—	—	—	—
Cr	NS	NS	NS	NS	NS	NS	—	—	—	—	—	—	—
BUN	NS	NS	NS	NS	NS	NS	*P*<0.01	—	—	—	—	—	—
LDL	NS	NS	NS	*P*<0.01	*P*<0.01	*P*<0.01	NS	NS	—	—	—	—	—
SGPT	*P*<0.001	NS	NS	NS	NS	NS	NS	NS	NS	—	—	—	—
ALP	*P* = 0.017	NS	NS	NS	NS	NS	NS	NS	NS	*P* = 0.025	—	—	—
Hypertension	NS	NS	NS	*P*<0.001	*P*<0.001	NS	NS	NS	NS	NS	NS	—	—
Diabetes	NS	*P*<0.001	*P*<0.001	NS	NS	NS	*P*<0.01	*P* = 0.01	NS	NS	NS	*P* = 0.037	—
Depression	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

NS, not significant; FBS, fasting blood sugar; HbA1c, Hemoglobin A1c; Chol, Cholesterol; Tg, Triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BUN, blood urea nitrogen; Cr, creatinine; SGPT, serum glutamic-pyruvic transaminase; ALP, alkaline phosphatase.
P value < 0.05 was considered significant.

for LSG. We observed higher levels of cholesterol and triglyceride in BN candidates for LSG showing clinical signs of hypertension, as compared with their counterparts ($P < 0.001$). Diabetes was significantly associated with FBS ($P < 0.001$), HBA1c ($P < 0.001$), creatinine ($P < 0.01$), BUN ($P = 0.01$), and hypertension ($P = 0.037$). Also, when compared to other biochemical parameters, depression did not show any association in the subjects studied ($P > 0.05$).

Table 5 presents the relationships of cytokine levels and clinical characteristics in BN candidates for LSG. Cytokine levels, particularly inflammatory markers including IL-6, TNF-α, and IL-1β were elevated in patients with BN who had at least one comorbidity (diabetes, depression, and hypertension) ($P < 0.01$). However, our finding demonstrates that the serum levels of anti-inflammatory cytokines such as IL-4 and IL-10 were associated with a

Table 5. Correlation Coefficients and Significance Values between Cytokine Levels and Clinical Characteristics (Based on the 76 BN Candidates for LSG)

Parameter	IL-1β	IL-6	TNF-α	IL-4	IL-10	IL-13	TGF-β	Hypertension	Diabetes
IL-6	$P<0.001$	—	—	—	—	—	—	—	—
TNF-α	$P=0.017$	$P<0.001$	—	—	—	—	—	—	—
IL-4	NS	NS	NS	—	—	—	—	—	—
IL-10	NS	NS	NS	$P<0.01$	—	—	—	—	—
IL-13	NS	NS	NS	$P<0.01$	$P<0.001$	—	—	—	—
TGF-β	NS	NS	NS	$P<0.001$	$P<0.001$	$P<0.01$	—	—	—
Hypertension	$P<0.01$	$P<0.001$	$P<0.01$	NS	NS	NS	NS	—	—
Diabetes	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	$P<0.001$	NS	NS	$P=0.037$	—
Depression	$P<0.001$	$P<0.001$	$P<0.001$	NS	NS	NS	NS	NS	NS

NS, Not significant.
P value < 0.05 was considered significant.

decrease in patients with bulimia and diabetes ($P<0.001$). We also identified significant correlation between diabetes and hypertension in patients with bulimia ($P = 0.037$). On the other hand, no considerable relationships were found for TGF-β, hypertension, diabetes, and depression ($P>0.05$).

Discussion

In this study, we demonstrated the relationship between socio-demographic characteristics, biochemical markers, and pro-inflammatory as well as anti-inflammatory cytokine levels in BN candidates for LSG.

Among BN patients, females and those who routinely consumed caffeine, tobacco, and alcohol, or had a depression history were more likely to have bulimia. In accordance with these results, various studies have reported similar results regarding gender,[20] consuming caffeine, tobacco, and alcohol, or depression.[10] Martin et al showed that higher BMI and weight were significantly connected to occurrence of bulimia nervos.[6] Similar to our findings, several studies have shown that older ages had a lower prevalence of BN and were less likely to develop bulimia.[21,22]

According to our results, mean serum levels of FBS, cholesterol, and triglyceride were increased in BN candidates for LSG. In line with these findings, significantly elevated levels of FBS,[13,23] cholesterol,[11,13,23] and triglyceride[11,13] have been shown by various studies. Elevated levels of cholesterol and triglycerides are also a risk factor for hypertension and cardiovascular diseases.[11] In contrast, Monteleone et al reported no association between serum levels of FBS and bulimia conditions.[11] Also, some researchers believe that serum levels of triglyceride,[23] creatinine,[23] and ALP[24] do not change in patients with bulimia. Nevertheless, in our results, serum levels of ALP, creatinine, and BUN were higher than normal levels. In this study, we found no change in HDL levels which is in contrast with findings of another study.[13] Our findings show that serum level of HbA1c was increased. In this regard, Takii et al reported similar results for concentration of HbA1c in patients with bulimia and T2D compared with patients with bulimia.[25]

We observed an elevation in the production of pro-inflammatory cytokines including IL-6, TNF-α, and IL-1β in subjects with BN. In line with our results, Brambilla et al and Nagata et al found an increase in concentration of pro-inflammatory cytokines levels including IL-6, TNF-α, and IL-1β in patients with bulimia.[15,16] Increases in the amount of pro-inflammatory cytokines levels in serum may be due to low levels of physical activity and exercise in obese subjects that may be related to obesity, bulimia, insulin resistance, and diabetes.[26] Various reports from clinical and animal studies show that pro-inflammatory cytokines (IL-6 and TNF-α) play an important role in regulation of both mood and appetite.[27] However, previous studies provide highly variable data from which a strong conclusion cannot be drawn.[9,28] The findings have not proved that pro-inflammatory cytokines might be overproduced in specific parts of the brain and act in specific areas (without coherently raised serum levels and/or immune production), and it is not clear yet whether this is due to undernutrition or an underlying cause specific to BN.[9,27,29]

According to our results, the serum levels of anti-inflammatory cytokines such as IL-4, IL-10, IL-13, and TGF-β had a decreasing trend in patients with bulimia. A few reports have measured anti-inflammatory cytokines. Raymond et al reported that TGF-β is not different in patients with bulimia.[29] The literature suggests that cytokines such as IL-10 may also control energy balance[30,31]; consequently, a disturbance in this system may trigger inappropriate eating behavior, potentially presenting clinically as obesity and BN.

In this study, a significant relationship was illustrated between an increase in pro-inflammatory cytokines, T2D, depression, and high blood pressure. In accordance with these results, studies have addressed fundamental pathways by which cytokines may contribute to depression.[32,33] In addition, although the role of inflammation in the progression of diabetes is not approved yet, it is possible that inflammation is induced by diabetes.[34] Also, previous research suggests that patients with hypertension

have an altered profile of pro-and anti-inflammatory cytokines.[35] Since patients with bulimia mainly tend to eat alone and in secret, these changes may be involved in the pathophysiology of certain psychopathological characteristics of BN and cannot be clarified by the co-occurrence of other psychological problems.[6] In line with this, previous reports have supposed that a series of biochemical alterations might arise from non-fasting situation of participants[11,13] which can be considered as a notable limitation to this study.

Our study has several limitations. First, the small sample size was appropriate for analysis of the association between blood levels of biochemical factors, cytokines, and socio-demographic features and clinical characteristics in BN candidates for LSG, but needs to be repeated in larger samples. Second, the control group consisted mostly of academic staff in the college, which might have caused a bias in the analysis in this group. Third, our questionnaires, as well as data on height and weight, were based on information provided by the subjects and are thus susceptible to response biases. More research is required given the limitations of recent studies, particularly gender imbalances among the populations studied.

In conclusion, our findings suggest that there are some relationships between blood levels of biochemical parameters, cytokines, and socio-demographic characteristics and clinical characteristics in BN candidates for LSG. Additionally, lifestyle-related risk factors and depression history both increase the risk of BN; however, it is not clear which is the cause and which is the consequence. Therefore, additional community-based studies are needed in order to confirm the findings and provide evidence for emerging factors that may be associated with BN candidates for LSG. This would also contribute to our understanding of the etiology of BN.

Authors' Contribution

MT, TA and SDS designed the study; Data collection and data analysis were performed by JKK, FE and SB; SASS and MRYN wrote the first draft of the paper; ARS revised the paper and prepared the final draft; SB provided supervision throughout each stage of writing, which has been approved by all authors.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The project was conducted in agreement with the Declaration of Helsinki[36] and was approved by the Research Ethics Committee of the Pasteur Institute of Iran, Tehran (Approval ID: IR.PII.REC.1397.029). Informed written consent was acquired from all participants prior to their registration in this study.

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