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ORIGINAL CONTRIBUTIONS

Prevalence of Micronutrient Deficiencies Prior to Bariatric Surgery: Tehran Obesity Treatment Study (TOTS)

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Abstract
Background Micronutrient deficiencies are major concerns after bariatric surgery, although these conditions often go undiagnosed pre-surgery.
Objective To assess pre-surgery micronutrient status of an Iranian population of morbidly obese candidates of bariatric surgery in a cross-sectional study.
Methods A cross-sectional analysis of 2008 candidates for bariatric surgery, aged 15–65 years, with either body mass index (BMI) ≥ 40 kg/m^2 or 30 < BMI < 35 kg/m^2 with a medical comorbidity was conducted. In order to determine the micronutrient status of participants, blood samples were collected to assess serum concentrations of vitamins (B12 and D), minerals (copper, calcium, phosphate, and zinc), and iron profiles (total iron binding capacity, iron concentration, ferritin, and iron saturation), according to standard protocol.
Results The mean age and BMI of patients (79.3% female) were 37.8 years and 44.8 kg/m^2, respectively. Deficiencies were found for 25(OH) D (53.6%), vitamin B12 (34.4%), serum iron (10.2%), and low levels of hemoglobin (16.6%). The prevalence of other deficiencies were all below 10%. Body mass index had a negative correlation with iron, calcium, vitamin B12, and 25(OH) D and was positively correlated with copper.
Conclusion Micronutrient deficiencies, including vitamin D, vitamin B12, and iron, are commonly found among morbidly obese subjects who are potential candidates of bariatric surgery.

Keywords Bariatric surgery · Metabolic surgery · Micronutrient deficiency · Prevalence

Introduction

Obesity is a complex metabolic disorder and associated with related comorbidities such as cardiovascular disease, type 2 diabetes, dyslipidemia, and high blood pressure [1]. The increasing prevalence and severity of obesity most likely resulted from complex interactions of dietary intake, physical activity, genes, and environment [2] and today poses a public health crisis in both the developed and developing countries [3, 4]. Based on national studies, a noticeable increase in obesity prevalence (12.6 to 25.9%) from 2005 to 2014 has been reported among Iranians simultaneously with the rise documented in worldwide prevalence of this condition [5].

However, conventional medical treatments and lifestyle modifications seldom yield satisfactory long-term results in obese individuals [6] and bariatric surgery is the leading standard management of choice for durable weight loss [7]. Micronutrient deficiencies are major concerns after bariatric surgery [8], although these often remain undiagnosed pre-surgery [9–13]. Evidence shows micronutrient deficiencies such as iron, vitamin B_6, vitamin B_{12}, vitamin C, vitamin E, and 25-hydroxy vitamin D [25(OH) D] among obese individuals worldwide [14, 15]. These studies were carried out in populations that differed in

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ethnicity, environment, and dietary habits, factors which may have influenced the associations between specific micronutrient deficiencies and obesity. To the best of our knowledge, this is the first study exploring micronutrients status in a large group of morbidly obese patients, candidates for bariatric surgery, in a cross-sectional study in an Iranian population.

Methods

Subjects

This cross-sectional study was conducted to investigate pre-surgery micronutrient profiles of morbidly obese people in the framework of the Tehran Obesity Treatment Study (TOTS), an ongoing, single-institution, and prospective study initiated in March 2013. A detailed study protocol for TOTS is available elsewhere [16]. Briefly, after providing written informed consent, the patients enroll to undergo a bariatric procedure based on an individualized clinical decision plan. Participants aged 15–65 years old, with either BMI ≥ 40 kg/m^2 without coexisting medical problems or BMI ≥ 35 kg/m^2 and one or more severe obesity-related comorbidities, patients with BMI of 30–34.9 kg/m^2 with diabetes or metabolic syndrome may also be offered bariatric procedure [17]. Those who took multivitamin and minerals or had a positive history for minor thalassemia were excluded.

Analytical Measurements

Blood samples were taken from all participants as part of pre-surgery assessment to determine the micronutrient status and assess serum concentrations of vitamins (B_{12} and D), minerals (calcium, phosphorus, copper, and zinc), hemoglobin, hematocrit, and iron profiles (total iron binding capacity (TIBC), iron concentration, and ferritin). Serum vitamins B_{12} and D were measured using chemiluminescent enzyme immunoassay and enzyme immunoassay methods, respectively. Calcium and phosphorus were measured by methyl thymol blue colorimetry and UV-endpoint phosphomolybdate method, respectively. Copper and zinc were measured by colorimetric method of 3-5 di-bromo-2-paridylase and 5 bromo-2-paridylase, respectively. Serum hemoglobin and ferritin levels were measured using the cyan methemoglobin method and human ferritin enzyme immunoassay test, respectively. Serum iron and TIBC concentration was assessed using the spectrophotometric and colorimetric methods. The reference values are summarized in Table 1.

Fasting plasma glucose (FPG), serum triglycerides (TGs), total cholesterol (TC) by the enzymatic colorimetric method, and high-density lipoprotein-cholesterol (HDL-C) after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid were determined, each by using relevant kits. Using the Friedewald formula, low-density lipoprotein-cholesterol (LDL-C) was calculated from serum TC, TG, and HDL-C concentrations and expressed in mg/dl.

Table 1 Reference values

	Male	Female
Hemoglobin (g/dl)	14–17.5	12.3–15.3
Hematocrit (%)	41.5–50.4	35.9–44.6
Total iron binding capacity (μg/dl)	230–440	230–440
Ferritin (ng/ml)	15–200	12–150
Iron (μg/dl)	40–170	37–165
Copper (μg/dl)	70–140	80–155
Zinc (μg/dl)	50–150	50–150
Calcium (mg/dl)	8.5–10.5	8.5–10.5
Phosphate (mg/dl)	2.6–4.5	2.6–4.5
Vitamin B_{12} (pmol/l)	160–950	160–950
25 (OH) vitamin D (ng/ml)	≥ 20	≥ 20

Deficiencies were defined based on the amounts below the low limit of normal values

Comorbidity Measurements

Baseline data collected by the research team includes demographic data and physical examination. Patients are then referred for several assessments including cardiac and respiratory, gastrointestinal (endoscopy and abdominal ultrasound), and endocrine assessments for diagnosis comorbidities including *Helicobacter pylori*, hiatal hernia, peptic ulcer, gastroesophageal reflux disease (GERD), gallstone, fatty liver, enlarged liver size, cardiac angina, asthma, obstructive sleep apnea, and coronary heart disease (CHD). Other comorbidities such as arthritis and discopathy were based on patient self-report [16].

Other Measurements

All patients underwent routine history and physical examinations and baseline data including demographics (sex, age) and anthropometric indices (weight, height, and BMI) were obtained and documented.

Definitions

High cholesterol, high TGs, high LDL-C, and low HDL-C were defined as current therapy for a definite diagnosis of dyslipidemia or TC ≥ 200 mg/dl, TGs ≥ 150 mg/dl, LDL-C ≥ 130 mg/dl, and HDL < 40 mg/dl, respectively [18]. High blood pressure was defined as the SBP ≥ 140 or DBP $\geq$ 90 mmHg, or taking antihypertensive medication [19]. Diabetes was defined as fasting plasma glucose ≥ 126 mg/dl or current therapy for a definite diagnosis of diabetes and IFG was defined as FPG between 100 and 126 mg/dl [20].

Statistical Analysis

Continuous variables are reported as mean ± SD or median (25–75 interquartile range) and categorical variables as percentages. To test the difference of qualitative and quantitative variables between genders, Chi-square and independent *t* test or Mann-Whitney were used, respectively. Associations between quantitative variables with normal distribution and age or BMI were assessed by Pearson's correlation. Quantitative variables with skewed normal distribution were assessed by Spearman correlation coefficient. We set $\alpha = 0.05$ and $\beta = 0.20$ for all analyses and used two-sided tests. IBM SPPS v.22 (IBM corp., Chicago, USA) was used for all analyses.

Results

We recruited a sample size of 2008 morbidly obese patients, all of whom were eligible for undergoing bariatric surgery. Pre-surgery characteristics of patients are listed in Table 2. Mean age and BMI of participants (79.3% female) were 37.8 ± 11.3 years and 44.8 ± 6.4 kg/m^2, respectively. Mean BMI of males was higher than females (45.5 ± 6.6 vs 44.6 ± 6.3, $P = 0.008$). Compared to men, women were significantly older, had lower TGs and SBP, and higher HDL-C; they also had lower prevalence of hypertension, high LDL-C, high TGs, and higher rate of low HDL-C in comparison to men ($P < 0.05$), whereas there were no significant differences in any of the other factors according to gender classification.

The mean concentrations of all micronutrients were within the normal range in both genders. Overall, the most prevalent of micronutrient deficiencies were found for 25(OH) D, vitamin B_{12}, hemoglobin, and serum iron in 53.6, 34.4, 16.6, and 10.2% of patients, respectively. The prevalence of other deficiencies were all below 10%. Prevalence of low hemoglobin, ferritin, serum iron and copper were higher in females compared to males, except for 25(OH) D deficiency, which was higher in males (Table 3).

Table 4 reports pre-surgery comorbidity status of patients according to sex. The most prevalent comorbidities with > 20% prevalence, were fatty liver, *Helicobacter pylori*, gallstone disease, GERD, and hiatal hernia; gallstone, arthritis, and discopathy were more prevalent among females compared to males ($P < 0.05$), whereas GERD, cardiac angina, and sleep apnea were more prevalent among males ($P < 0.05$).

Table 5 shows the correlations of micronutrients with patient age and BMI. Age was negatively correlated with hemoglobin ($r = -0.081$, $P = 0.001$) and positively correlated with 25(OH) D ($r = 0.211$, $P < 0.001$). Body mass index was negatively correlated with iron ($r = -0.091$, $P < 0.001$), calcium ($r = -0.065$, $P = 0.009$), vitamin B_{12} ($r = -0.127$, $P < 0.001$), and 25(OH) D ($r = -0.072$, $P = 0.005$) and positively correlated with copper ($r = 0.091$, $P = 0.001$).

As shown in Table 6, the prevalence of low hematocrit and ferritin were higher among patients aged > 35 years, compared to those aged ≤ 35 years; however, 25(OH) D deficiency was more prevalent in younger-aged individuals. Compared to patients with BMI > 45 kg/m^2, those with BMI ≤ 45 had higher frequencies of vitamin B_{12} deficiency ($P < 0.001$).

Table 2 Participant characteristics

Characteristic	Total ($n = 2008$)	Female ($n = 1593$)	Male ($n = 415$)	p value
Age (years)	37.8 ± 11.3	38.4 ± 11.5	35.4 ± 10.3	< 0.001
Body mass index (kg/m^2)	44.8 ± 6.4	44.6 ± 6.3	45.5 ± 6.6	0.008
LDL-cholesterol (mg/dl)	110.6 ± 33.0	110.3 ± 32.3	112.1 ± 35.9	0.415
High LDL-cholesterol (%)	452 (27)	349 (25.8)	103 (32.5)	0.015
Total cholesterol (mg/dl)	189.2 ± 39.1	189.1 ± 38.2	189.7 ± 42.7	0.817
High total cholesterol (%)	613 (37)	493 (36.8)	120 (37.7)	0.768
Triglycerides (mg/dl)	142 (103–191)	138 (101–187)	152 (114–212)	< 0.001
High triglycerides (%)	733 (44.2)	565 (42.3)	168 (52.3)	0.001
HDL-cholesterol (mg/dl)	47.9 ± 11.5	48.9 ± 11.5	43.9 ± 10.7	< 0.001
Low HDL-cholesterol (%)	915 (54.7)	782 (57.8)	133 (41.4)	< 0.001
Systolic blood pressure (mmHg)	122.5 ± 13.87	121.9 ± 13.8	125.1 ± 13.8	< 0.001
Diastolic blood pressure (mmHg)	78.8 ± 19.8	78.5 ± 21.3	80.2 ± 11.1	0.149
Hypertension (%)	591 (33.3)	447 (31.4)	144 (40.8)	0.001
Fasting plasma glucose (mg/dl)	109.0 ± 37.6	109.3 ± 38.2	107.8 ± 34.7	0.524
Diabetes (%)	431 (24.4)	355 (24.9)	76 (22.1)	0.274
Impaired fasting glucose (%)	437 (24.7)	343 (24.1)	94 (27.3)	0.209

All values are presented as mean±SD or *n* (%) except for triglycerides, which is presented as median (25-75 IQR)

Table 3 Pre-operative micronutrient status of patients

	Total ($n = 2008$)	Male ($n = 415$)	Female ($n = 1593$)	*P*-value
Hemoglobin (g/dl)				
Mean ± SD	13.7 ± 1.6	15.4 ± 1.4	13.3 ± 1.3	<0.001
Deficiency (%)	286 (16.6)	41 (12.5)	245 (17.6)	0.025
Hematocrit (%)				
Mean ± SD	42.0 ± 14.0	46.2 ± 3.9	41.0 ± 15.3	<0.001
Deficiency (%)	146 (8.5)	27 (8.3)	119 (8.6)	0.860
Total iron binding capacity (μg/dl)				
Mean ± SD	355 ± 55	350 ± 53	356 ± 55	0.128
Deficiency (%)	9 (0.8)	3 (1.4)	6 (0.7)	0.328
Ferritin (ng/ml)				
Median (25-75 IQR)	52.0 (28.0-99.0)	160.5 (93.3-267.2)	41.6 (24.0-74.8)	<0.001
Deficiency (%)	77 (7.7)	1 (0.5)	76 (9.5)	<0.001
Iron (μg/dl)				
Mean ± SD	74.2 ± 35.5	92.6 ± 36.4	69.9 ± 33.8	<0.001
Deficiency (%)	152 (10.2)	10 (3.5)	142 (11.7)	<0.001
Copper (μg/dl)				
Mean ± SD	119.9 ± 30.4	112.6 ± 23.5	121.6 ± 31.6	<0.001
Deficiency (%)	66 (4.9)	6 (2.3)	60 (5.5)	0.030
Zinc (μg/dl)				
Mean ± SD	88.3 ± 20.3	93.3 ± 19.6	87.1 ± 20.3	<0.001
Deficiency (%)	38 (2.5)	6 (2)	32 (2.6)	0.559
Calcium (mg/dl)				
Mean ± SD	9.40 ± 0.50	9.50 ± 0.57	9.37 ± 0.48	<0.001
Deficiency (%)	22 (1.4)	2 (0.7)	20 (1.5)	0.407
Phosphate (mg/dl)				
Mean ± SD	3.75 ± 0.64	3.82 ± 0.66	3.73 ± 0.63	0.034
Deficiency (%)	17 (1.1)	5 (1.7)	12 (1)	0.342
Vitamin B_{12} (pmol/l)				
Median (25-75 IQR)	241 (100-360)	248 (105-347)	237 (98-367)	0.844
Deficiency (%)	504 (34.4)	93 (32.6)	411 (34.8)	0.483
25 (OH) vitamin D (ng/ml)				
Median (25-75 IQR)	18.0 (10.0-30.0)	16.6 (9.6-25.0)	18.0 (10.0-31.0)	0.049
Deficiency (%)	822 (53.6)	174 (59.2)	648 (52.3)	0.033

Discussion

To the best of our knowledge, this is the first study exploring micronutrient status in a large population of morbidly obese patients in Iran. In this study, we assessed the baseline micronutrient status of patients who were candidates for bariatric surgery and showed a high prevalence of micronutrient deficiencies. The most prevalent micronutrient deficiencies were 25(OH) D, vitamin B12, hemoglobin, and serum iron. The prevalence of other deficiencies were all below 10%.

Vitamin D deficiency is a prevalent public health concern worldwide. Many investigators report low serum 25(OH) D levels in both people with obesity and those seeking weight loss surgery [9–11, 21–23]. People with obesity have 35 and 24% higher frequency of vitamin D deficiency in comparison to normal weight and overweight individuals, respectively [21]. Different definitions for determination of vitamin D deficiency leads to reported wide range of vitamin D deficiency (22–100%) in non-Middle Eastern morbidly obese populations [10, 11, 20, 24, 25]; however, based on serum 25(OH) D levels < 20 ng/ml, as used in our study, studies report a wide range of vitamin D deficiency of about 22–80% [20, 26] in morbid obese pre-operative populations, and we showed that 53% of our participants were vitamin D deficient (Table 7).

The exact mechanism by which obesity leads to low circulating 25(OH) D levels remains unknown; however, obesity-associated vitamin D insufficiency is most likely due to decreased bioavailability of vitamin D from cutaneous and dietary sources because of its deposition in body fat compartments [35]. Comparison of vitamin D deficiency in other

Table 4 Pre-operative comorbidity status of patients

	Total (n = 2008)	Male (n = 415)	Female (n = 1593)	*P*-value
Helicobacter pylori	635 (31.6)	121 (29.2)	514 (32.3)	0.236
Hiatal hernia	506 (25.2)	97 (23.4)	409 (25.7)	0.374
Peptic ulcer	207 (10.3)	52 (12.5)	155 (9.7)	0.095
Gastroesophageal reflux disease	584 (29.1)	158 (38.1)	426 (26.7)	<0.001
Gallstone	588 (29.3)	98 (23.6)	490 (30.8)	0.004
Fatty liver				<0.001
I	493 (24.6)	53 (12.8)	440 (27.6)	
II	674 (33.6)	149 (35.9)	525 (33)	
III	349 (17.4)	123 (29.6)	226 (14.2)	
Cardiac angina	11 (0.5)	5 (1.2)	6 (0.4)	0.057
Asthma	57 (2.8)	8 (1.9)	49 (3.1)	0.210
Sleep apnea	56 (2.8)	19 (4.6)	37 (2.3)	0.013
Arthritis	202 (10.1)	17 (4.1)	185 (11.6)	<0.001
Discopathy	282 (14)	45 (10.8)	237 (14.9)	0.035
Coronary heart disease	102 (5.1)	27 (6.5)	75 (4.7)	0.137

All values are presented as n (%)

regions is difficult due to marked regional and seasonal variations [36]. Insufficient dietary supplies of vitamin D in countries where foodstuffs are not supplemented, leads to generally low dietary intakes of vitamin D, one possible explanation of which is that severe obesity carries a high risk of nutritional deficiencies even in young patients, who often present with abnormal eating behavior patterns [37]. Although in our study, participants ≤ 35 years old were more vitamin D deficient, the Krzizek et al. study, which was the only study that investigated the association of vitamins deficiency in pre-surgery morbid obese between various age groups, showed no difference in vitamin D deficiency among various age groups [16]. Previous studies indicated that adults compared to older people had higher risk of vitamin D deficiency especially in cold seasons [17], which may be related to higher requirements in adults, and lower exposure to sun light; elderly people most likely to consume vitamin D supplements and their serum vitamin D levels are more related to supplement consumption, so that they are less affected by vitamin D deficiency, compared to adults.

In our sample of obese patients, 34.4% had vitamin B12 deficiency, a prevalence higher than those previously reported worldwide (< 25%, Table 7). Such differences may be attributable to poor dietary habits in the general population and socioeconomic factors. Another explanation may be the high prevalence of GERD (26–38%) and *Helicobacter pylori* (29.2–32.3%) which are usually accompanied by use of proton pump inhibitors (PPI), drugs which reduce the absorption of B_{12} and leads to B_{12} deficiency [38, 39] and has previously led to 6–30% B_{12} deficiency in obese patients taking PPI [40]. Our result was even higher than an earlier study [41] performed in Tehran on 1252 patients with morbid obesity;

Table 5 Correlation coefficients of micronutrients abnormalities with patients' characteristics

	Age	*P*-value	Body mass index	*P*-value
Hemoglobin (g/dl)	−0.081	0.001	0.036	0.136
Hematocrit (%)	−0.012	0.608	−0.006	0.811
Total iron binding capacity (μg/dl)	0.027	0.378	0.026	0.397
Ferritin (ng/ml)	−0.049	0.123	0.030	0.345
Iron (μg/dl)	−0.009	0.736	−0.091	<0.001
Copper (μg/dl)	−0.042	0.124	0.091	0.001
Zinc (μg/dl)	−0.038	0.142	−0.021	0.413
Calcium (mg/dl)	−0.021	0.410	−0.065	0.009
Phosphate (mg/dl)	−0.013	0.613	0.017	0.492
Vitamin B_{12} (pmol/l)	0.036	0.172	−0.127	<0.001
25 (OH) vitamin D (ng/ml)	0.211	<0.001	−0.072	0.005

Table 6 Frequency of micronutrient deficiencies by age and body mass index categories

	Age (years)		p value	Body mass index (kg/m^2)		p value
	≤ 35	> 35		≤ 45	> 45	
Hemoglobin (g/dl)	114 (14.9)	170 (18.2)	0.068	151 (15.7)	134 (17.8)	0.237
Hematocrit (%)	54 (7.1)	91 (9.8)	0.047	80 (8.3)	65 (8.7)	0.787
TIBC (mcg/dl)	4 (0.8)	5 (0.9)	> 0.999	5 (0.9)	4 (0.8)	> 0.999
Ferritin (ng/ml)	19 (4.2)	57 (10.7)	< 0.001	43 (7.8)	34 (7.7)	0.925
Iron (mcg/dl)	61 (9.3)	90 (10.9)	0.326	79 (9.5)	73 (11.0)	0.351
Copper (μg/dl)	26 (4.3)	39 (5.3)	0.389	38 (5.2)	27 (4.4)	0.526
Zinc (μg/dl)	20 (2.9)	18 (2.2)	0.387	18 (2.2)	20 (2.9)	0.344
Calcium (mg/dl)	8 (1.1)	14 (1.6)	0.458	10 (1.1)	12 (1.7)	0.350
Phosphate (mg/dl)	10 (1.5)	7 (0.8)	0.225	12 (1.4)	5 (0.7)	0.211
Vitamin B_{12} (pmol/l)	228 (34.6)	270 (34.1)	0.853	236 (29.2)	268 (40.9)	< 0.001
25 (OH) vitamin D (ng/ml)	421 (61.0)	392 (47.3)	< 0.001	442 (52.2)	378 (55.3)	0.239

Arshad Et al. showed that 20.9% of patients with morbid obesity, randomly selected from among patients referred to an obesity clinic, had vitamin B12 values < 200 and reported that BMI was adversely associated with serum vitamin B12; although they used a higher cutoff (200 vs 150), our study had slightly higher results. Despite similarities between studies, the difference could be attributed to selected population (clinically referred patients vs bariatric surgery candidates).

Previous epidemiologic studies report that overweight individuals are at higher risk of iron deficiency than normal weight ones [33, 42]; potential explanations for this association include dilutional hypoferremia, poor quality or restricted diets, increased iron requirements, and/or impaired iron absorption in obese individuals due to increased circulation of hepcidin [43].

In the current study, we measured various iron indicators and found that based on serum iron concentration, 10.2% of our study population are iron deficient, while based on ferritin levels, 7.7% are deficient; these results are comparable with a previous report of iron deficiency in France, where Lefebvre et al. [11], in a cross-sectional study of 267 patients with obesity, reported overall ferritin and serum iron deficiency to be 5.7 and 17.3%, respectively, values lower than reports from the USA (36.2% based on serum iron) and Israel (38.8% based on serum iron in children) [10, 26].

Comparison of the results of these epidemiological studies is difficult because of differences in number of participants and age distribution of the study population.

We found that more females were iron deficient than males, based on hemoglobin, ferritin, and serum iron concentrations (17.6 vs 12.5%, 9.5 vs 0.5%, and 11.7 vs 3.5%, respectively), results in agreement with previous studies that reported female gender was a variable associated with a greater incidence of iron deficiency. Lower ferritin concentration in women patients could be due to menstruation, hormonal status, or even diverse food patterns compared to males [44]. In the present study, patients aged over 35 years had higher iron deficiency based on serum ferritin, in accordance with the findings of Krzizek et al., who reported lower ferritin levels in Australian patients, aged 34–45 years compared to younger

Table 7 Prevalence of altered hematologic variables and micronutrient deficiencies compared to the ranges lower and upper reported prevalence in other published studies

	Present study (%)	Range of reported deficiencies (%)
Hemoglobin	16.6	0.0–22.2 [9, 27]
Hematocrit	8.5	NM
Total iron binding capacity	0.8	22.4 [10]
Ferritin	7.7	1.0–23.9 [16, 28]
Plasma iron	10.2	2.7–49.0 [27, 29]
Plasma copper	4.9	0.0–67.8 [30, 31]
Plasma zinc	2.5	0.0–73.9 [31, 32]
Calcium	1.4	0.0–13.8 [29, 32]
Phosphate	1.1	0.0–21.6 [11, 33]
Vitamin B_{12}	34.4	0.0–25.0 [27, 34]
25 (OH) vitamin D (< 20 ng/ml)	53.6	22.0–80.0 [20, 34]

NM not measured

ones, a finding which could reflect longer standing menstruation irregularities in this age group [16].

We found a positive correlation between BMI and copper levels similar to previous studies; serum levels of copper were higher in obese compared to normal or underweight individuals, and drastically decreased after obtained to weight reduction following weight loss surgery [45–47]. Regarding to the positive correlation between leptin, the important and effective hormone on weight gain and obesity, and serum levels of copper [48], higher serum levels of copper in obese subjects, may be justified by increasing the levels of serum leptin following weight gain.

Among our study limitations, because of the cross-sectional design of the study, the cause-and-effect associations could not be evaluated. We were unable to account for confounding factors including socioeconomic status, diet, and physical activity, as data on these factors were not available. Laboratory tests were not performed in a single laboratory. Selecting our population from among candidates of bariatric surgery led to limited numbers of males, which may also be considered a limitation. Strengths of the present study however include an evaluation of large data set that allowed us to broaden the range of data currently available. Furthermore, this is the first large study conducted in a Middle Eastern population, assessing the micronutrient status in a morbidly obese population of candidates scheduled for bariatric surgery.

Our results showed that many people with obesity are deprived of multiple micronutrients, including vitamin D, iron, and vitamin B_{12}. From a clinical point of view, it seems reasonable to recommend that more attention be paid to assessment of both micronutrient and BMI status simultaneously. Any micronutrient deficiency should systematically be screened and compensated for by supplementation and dietary advice to prevent possible comorbidities.

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Compliance with Ethical Standards

Conflict of Interests The authors declare that they have no conflict of interest.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Human Rights/Ethical Approval The ethics committee of the Research Institute for Endocrine Sciences (RIES) of Shahid Beheshti University of Medical Sciences approved the study protocol.

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