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ORIGINAL CONTRIBUTIONS

Micronutrient Deficiencies in Morbidly Obese Women Prior to Bariatric Surgery

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Abstract
Background Although morbid obesity is related to excess of energy and macronutrient intake, it does not rule out the presence of micronutrient deficiencies. The aim of this study was to evaluate food intake and the prevalence of micronutrient deficiencies in a group of morbidly obese women seeking bariatric surgery.
Methods A total of 103 morbidly obese women were studied prior to bariatric surgery. Anthropometry and body composition (dual-energy X-ray absorptiometry, DEXA) were performed on all subjects. Energy and nutrient intake was determined by food frequency questionnaire. Blood tests to assess micronutrients status, including plasma iron, ferritin, transferrin, zinc, copper, calcium, phosphorus, hemoglobin, hematocrit, mean corpuscular volume (MCV), and hair zinc, were performed. Folic acid, vitamin B_{12}, vitamin D, and parathyroid hormone (PTH) were also assessed in 66 subjects.
Results Mean energy intake was 2801±970 kcal/day. Carbohydrate, protein, and lipid intake represented 55±9.1, 13.9±3.3, and 32.5±8.2 % of total energy intake, respectively. Iron, calcium, and vitamin D intake was below the recommended dietary allowance. The prevalence of nutritional deficiencies were as follows: plasma iron 12.6 %, ferritin 8.7 %, transferrin 14.6 %, plasma zinc 2.9 %, calcium 3.3 %, phosphorus 2.3 %, hemoglobin 7.7 %, hematocrit 13.6 %, MCV 6.8 %, and hair zinc 15.7 %. In the subsample, 10.6 % had a vitamin B_{12} deficiency, 71.7 % showed low concentrations of vitamin D, and 66 % had high PTH levels. No folic acid or copper deficiencies were detected.
Conclusions Despite high daily energy intake and adequate macronutrient distribution, morbidly obese Chilean women seeking bariatric surgery present with deficient intake of some micronutrients and a high prevalence of micronutrient deficiencies.

Keywords Morbid obesity · Bariatric surgery · Nutritional status · Micronutrient deficiency · Vitamin D

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Introduction

The increasing prevalence of obesity is a global public health problem. A report published by the World Health Organization noted that in 2014, more than 1.9 billion adults were overweight and 600 million were obese [1]. In Chile, excess weight affects 67 % of the population over the age of 15 years, and morbid obesity rates have doubled over the past 7 years [2]. Obesity is a pathology associated with increased risk of metabolic and cardiovascular morbimortality. Conservative medical treatment (diet and exercise) fails to reliably produce significant weight reduction over the long term in patients with obesity [3]. Bariatric surgery, on the other hand, has been demonstrated to be an effective treatment for weight reduction, reducing comorbidities and mortality in selected patients with morbid obesity [4, 5].

The most frequent medium- and long-term complications from these surgeries are micronutrient deficiencies, due to reduced intake (restrictive surgeries), reduced absorption (malabsorptive surgeries), or both (restrictive plus malabsorptive surgeries) [6–8]. However, recent studies have demonstrated that individuals with morbid obesity have nutritional deficiencies prior to undergoing surgery, especially for iron, calcium, folic acid, vitamin B_{12}, and 25-hydroxy vitamin D (25(OH)D) [9–13]. It is imperative to screen for nutritional deficiencies pre-operatively in these patients, in order to intervene in a timely manner and prevent more serious nutritional complications after surgery. In Chile, there are no data available regarding nutritional deficiencies in patients seeking bariatric surgery. The objective of this study was to evaluate dietary intake and nutritional status of various micronutrients in morbidly obese women prior to bariatric surgery.

Materials and Methods

We evaluated 103 obese women approximately 30 days before a scheduled Roux-en-Y gastric bypass (RYGB) or vertical sleeve gastrectomy (VSG). Exclusion criteria were as follows: obesity of endocrinological origin, pregnancy, renal disease, or use of medication that affects nutritional status (corticosteroids, bisphosphonates, etc.). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee for Human Investigation of the Faculty of Medicine of the University of Chile. Informed consent was obtained from all individual participants included in the study.

Dietary Intake Evaluation Dietary intake was individually assessed by an experienced clinical dietitian using a food frequency questionnaire (FFQ), and all participants were asked about the use of vitamin or mineral supplements [14–16]. Questionnaire results were analyzed with the Food Processor II software (ESHA Research, Salem, OR, USA) to calculate energy and nutrient intake, which uses a nutritional database for North American and Chilean foods [17]. These results were then used to analyze adequacy of nutrient intake according to standards published by the Food and Nutritional Board of the Institute of Medicine in association with Health Canada [18].

Anthropometry and Body Composition We measured body weight and height using a digital Seca scale (Vogel & Halke GmbH & Co, Germany) with a precision of 100 g. Patients were assessed wearing light clothing and no shoes. Results were used to calculate body mass index [BMI=weight (kg)/height (m)^2)]. Body composition was evaluated using dual-energy X-ray absorptiometry, DEXA (Lunar DPX-L, Madison, WI, USA), in slow scan mode. Results were used to calculate whole-body fat mass (FM).

Analytical Parameters Prior to surgery were evaluated the following parameters (cutoff points used to define a nutritional deficiency in parentheses): serum iron (<50 μg/dL), hemoglobin (<12 g/dL), hematocrit (<37 %), mean corpuscular volume (<80 fL), transferrin saturation (<16 %), serum ferritin (<12 μg/dL), plasma zinc (<70 μg/dL), hair zinc (<100 μg/g), plasma copper (<70 μg/dL), and plasma albumin (<3.5 g/dL). In a subgroup of patients, we also measured plasma folic acid (<1.5 ng/mL), vitamin B_{12} (<200 pg/mL), 25(OH)D (20–29 ng/mL insufficiency, <20 ng/mL deficiency), plasma calcium (<8.5 mg/dL), plasma phosphorus (<2.5 mg/dL), and parathyroid hormone (≥65 pg/mL) [10, 11, 19–22].

Hematologic and Biochemical Evaluation Hemoglobin (Hb) and mean corpuscular volume (MCV) were measured using a coulter cell counter (CELL-DYN 1700; Abbott Diagnostics, Abbott Park, IL, USA). Serum iron, total iron binding capacity (TIBC), and transferrin saturation (%TS) were assessed using the Fischer and Price method [23]. Serum ferritin (SF) was measured using the method recommended by the International Anemia Consultative Group (INACG) [24]. Plasma albumin, calcium, and phosphorus were measured using colorimetric and enzymatic methods.

Assessment of Vitamin, Mineral, and Parathyroid Hormone Levels Zinc and copper were measured using the method detailed by Smith et al. [25] and Ruz et al. [26] with a PerkinElmer AAnalyst 100 atomic absorption spectrometer (PerkinElmer Corp. Waltham, MA, USA). To measure hair zinc, a sample was collected from the area proximal to the occipital scalp, washed with non-ionic detergent, dried, digested with a mixture of HNO_3-H_2O_2, diluted with deionized water, and analyzed using atomic absorption spectrophotometry. Plasma folic acid, vitamin B_{12}, and 25(OH)D were measured using radioimmunoassay, and parathyroid hormone (PTH) was measured using immunoradiometric assay.

Statistical Methods The Kolmogorov-Smirnov test was used to assess whether the data were normally distributed. Results were expressed as mean±standard deviation (SD) for normally distributed variables. SPSS version 15.0 was used for data analysis.

Results

We evaluated 103 women seeking bariatric surgery. Average age was 36±9.6 years, BMI 43.1±5.3 kg/m^2, and fat mass 46.4 ±4.8 %. Type 2 diabetes mellitus, hypertension, dyslipidemia, and metrorrhagia were present in 11.6, 28.1, 45.6, and 1.9 %, respectively. No patient presented osteopenia or osteoporosis. Only one patient was receiving vitamin supplements because of metrorrhagia. Table 1 summarizes the group characteristics.

Estimated energy, macronutrient, and micronutrient intakes are shown in Tables 2 and 3, respectively. Average daily energy intake was 2801±970 kcal/day. Seven patients reported energy intakes of over 4000 kcal/day, including one patient who reported an intake of over 7000 kcal/day, while one patient reported an energy intake of less than 1000 kcal/day (data not shown).

The distribution of macronutrient intake was within the recommended range. Average dietary fiber intake was 23 g/day, below the adequate intake (AI) level. As shown in Table 3, iron, calcium, and vitamin D intake was below the recommended daily allowance (RDA), while zinc, copper, folic acid, vitamin B_{12}, and phosphorus intake was in the recommended range.

Table 4 summarizes the nutritional status variables and prevalence of the micronutrient and albumin deficiencies identified, as well as the average plasma PTH and number of subjects with elevated PTH levels (secondary hyperparathyroidism).

Only 33 % of the sample had no nutritional deficiencies, while 33 % had a deficiency for one nutritional variable and 33.9 % had two or more deficiencies (Fig. 1).

The prevalence of anemia, low ferritin levels, and low serum iron was 7.7, 8.7, and 12.6 %, respectively. Low concentrations of other nutritional indicators of iron status varied from 6.8 % for MCV to 14.6 % for %TS. The prevalence of deficiency of the rest of nutritional parameters studied are shown in Table 4. No deficiencies for copper, folic acid, or albumin were detected in any of the patients evaluated.

Discussion

Bariatric surgery is the most effective treatment for significant long-term weight reduction and improvement in comorbidities and quality of life of severe and morbid obese subjects [27]. However, such procedure carries the risk of complications, such as deficiencies for micronutrients, even when supplements are used [13, 28–32]. Moreover, obese patient often present with micronutrient deficiencies before to bariatric surgery [9–13, 33–40].

There is limited information available regarding dietary intake by obese patients prior to bariatric surgery. In our study, average energy intake was 2801±970 kcal/day, approximately 700 calories more than reported in a Spanish population [11]. However, macronutrient caloric distribution was within the recommended range. It is noteworthy that compared with the Spanish group, our subjects showed a lesser intake of monounsaturated fats (32.9 vs. 50.4 g/day) and greater

Table 1 Demographic and body composition characteristics of 103 morbidly obese women studied

Variable	Mean±SD
Age (years)	36.0±9.6
BMI (kg/m^2)	43.1±5.3
Preoperative body weight (kg)	110.2±16.0
Excess of weight (kg)	52.7±14.0
% Fat mass by DEXA[a]	46.4±4.8
T-score BMD total body[a]	1.36±0.75
T-score BMD pelvis[a]	1.55±0.97
T-score BMD spine[a]	2.47±1.10

SD standard deviation, *BMI* body mass index, *BMD* bone mineral density, *DEXA* dual-energy X-ray absorptiometry

[a] *n*=100; three subjects could not be evaluated

Table 2 Energy and macronutrient intake of morbidly obese women determined by using a food frequency questionnaire (*n*=103)

Nutrient		Mean±SD
Energy:	kcal/day	2801±970
Carbohydrate:	g/day	386.4±144.7
	%TCV	55.0±91.0
Protein:	g/day	93.5±28.6
	%TCV	13.9±3.3
Fats:	g/day	101.8±49.7
	%TCV	32.5±8.2
Saturated fat:	g/day	29.4±16.8
	%TCV	9.3±3.0
Monounsaturated fat:	g/day	32.9±16.0
	%TCV	10.6±3.7
Polyunsaturated fat:	g/day	31.1±20.1
	%TCV	9.9±3.7
Cholesterol:	mg/day	289.7±186.6
Fiber:	g/day	23.0±12.1

SD standard deviation, *TCV* total caloric value

Table 3 Micronutrient intake and adequacy determined by using a food frequency questionnaire (n=103)

Nutrient	Mean±SD	RDA	Adequacy (%)
Iron (mg/day)	13.8±6.2	18	76.6
Zinc (mg/day)	11.6±4.4	8	145.0
Copper (mg/day)	1.7±0.6	0.9	188.0
Folic acid (μg/day)	699.0±397.0	400	174.7
Vitamin B_{12} (μg/day)	5.1±5.6	2.4	212.5
Calcium (mg/day)	815.9±372.1	1000	81.6
Phosphorus (mg/day)	1338.5±443.8	700	191.2
Vitamin D (IU/day)	127.7±108.2	600	21.3

SD standard deviation, *RDA* recommended dietary allowance

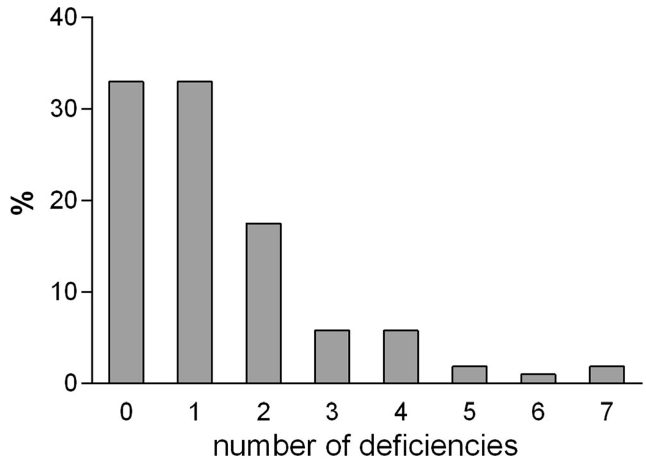

Fig. 1 Percentage of micronutrient deficiencies in morbidly obese women prior to bariatric surgery

consumption of polyunsaturated fats (31.1 vs. 10.1 g/day), which may be attributable to the fact that the typical Mediterranean diet is rich in sources of monounsaturated fats such as olives, versus the commonly consumed Chilean diet which is typically rich is vegetable oils such as sunflower and soybean.

Average dietary fiber intake was 23 g/day, close to the 25 g/day recommended for increased satiety, improved gastrointestinal transit, and to help regulate plasma glucose and cholesterol levels. Although underreporting intake is a common problem when relying on dietary questionnaires in obese population, only one subject reported a caloric intake below 1000 kcal/day.

Our patients had an average iron intake (13.8±6.2 mg/day) below the RDA of 18 mg/day and similar to data reported by Moizé et al. (12.8 mg/day) [11]. It is interesting that the average of iron intake in our group is superior to that reported by Pizarro et al. in Chilean non-obese female population in similar range of age from Santiago city (6.6±2.4 mg/day) [41].

Morbidly obese individuals commonly show dietary patterns characteristic of western developed nations, with a high intake of sugar, saturated fat, and carbonated beverages, resulting in an unbalanced diet lacking in micronutrients [10, 34, 35]. The low rates of adequate calcium and vitamin D consumption may be attributable to poor intake of dairy products, fatty fish, and multivitamin supplements; furthermore,

Table 4 Nutritional indicators and prevalence of nutritional deficiencies

Micronutrient (units)	*n*	Cutoff for deficiency	Mean±SD	Subjects with deficit (%)
Plasma iron (μg/dL)	103	50	80.2±30.8	13 (12.6 %)
Hemoglobin (g/dL)	103	12	13.5±1.0	8 (7.7 %)
Hematocrit (%)	103	37	40.1±3.2	14 (13.6 %)
MCV (fL)	103	80	85.7±4.9	7 (6.8 %)
Transferrin saturation (%)	103	16	23.9±9.2	15 (14.6 %)
Ferritin (μg/L)	103	12	40.3±22.5	9 (8.7 %)
Plasma zinc (μg/dL)	103	70	87.5±10.3	3 (2.9 %)
Hair zinc (μg/g)	102	100	153.4±72.7	16 (15.7 %)
Plasma copper (μg/dL)	103	70	119.7±32.7	0 (0 %)
Folic acid (ng/mL)	66	1.5	11.6±2.4	0 (0 %)
Vitamin B_{12} (pg/mL)	66	200	537.2±316.8	7 (10.6 %)
Calcium (mg/dL)	90	8.5	9.0±0.5	12 (13.3 %)
Phosphorus (mg/dL)	86	2.5	3.6±0.6	2 (2.3 %)
Vitamin D (ng/mL)	39	20–29[a]	24.6±12.8	10 (25.6 %)
		<20[b]		18 (46.1 %)
Albumin (g/dL)	95	3.5	4.1±0.3	0 (0 %)
PTH (pg/mL)	39	65	87.9±45.8	26 (66.6 %)[c]

SD standard deviation, *MCV* mean corpuscular volume, *PTH* parathyroid hormone

[a] Vitamin D insufficiency

[b] Vitamin D deficiency

[c] Subjects with elevated PTH levels

obese people often follow heterodox and unbalanced diets in pursuit of rapid weight loss, which may also contribute to micronutrient deficiency, despite a high caloric intake [42, 43].

Data regarding nutritional indicators for obese patients seeking bariatric surgery are scarce; however, some authors have noted low pre-surgical plasma concentrations of iron, hemoglobin, ferritin, zinc, folic acid, vitamin B_{12}, 25(OH)D, calcium, among others. (Table 5) [9–13, 33–40].

In our study, we measured various nutritional indicators and found that the prevalence of anemia was 7.7 %, iron deficiency as reduced plasma iron 12.6 %, and low ferritin of 8.7 %. Interestingly, the iron deficiency and anemia rates found in our study are considerably lower than those reported by studies carried out in other countries [10, 11, 13, 33, 37, 40]. Low plasma iron concentrations found in our study are consistent with the low iron intake reported in the FFQ, as well as with the fact that the patients were mainly young women in reproductive age. According to the First National Health Survey carried out in Chile in 2003 (ENS-2003), average hemoglobin level for young women was 13.7 g/dL, and the prevalence of anemia among women living in Santiago was 4.0 % [44]. Therefore, our data suggest that while the average hemoglobin levels in our patients were similar to those reported by the ENS-2003 (13.5 vs. 13.7 g/dL), the rate of anemia among our patients was nearly double that of women non-obese in the same age group and geographic location in Chile.

In terms of zinc, low plasma and hair concentrations were detected in about 3 and 15 % of our patients, respectively. These values differ considerably from those reported by other authors [11, 12, 35, 36, 38, 39] (Table 5). Such differences may be attributable to poor dietary habits in the general population, socioeconomic factors, gastrointestinal pathologies, and/or the use of different cutoff points for defining nutritional deficiency.

In addition to a poorly balanced diet lacking in vitamins and minerals, other factors, such as alcohol consumption, chronic subclinical inflammation, and obesity itself, are associated with deficiencies of many micronutrients [45]. Differences between the prevalence of zinc deficiency in plasma versus hair may be due to the fact each of the various methods to evaluate the nutritional status of zinc is susceptible to issues that affect the validity of the findings, and hair zinc may be a less sensitive indicator [46, 47].

The subgroup studied showed 10.6 % of vitamin B_{12} deficiency. It is important to note that adequate vitamin B_{12} stores in the human body can maintain stable plasma levels of this vitamin for long periods of time; therefore, a plasma vitamin B_{12} deficiency suggests low intake over a prolonged period of foods such as fish, shellfish, meat, dairy products, and multivitamins or, at a lower rate, malabsorption of vitamin B_{12} due to intrinsic factor deficiency. In terms of vitamin D status, measured as plasma 25(OH)D, 71.7 % of the patients

Table 5 Prevalence (%) of altered hematologic variables and nutritional deficiencies compared to other studies

	Present study	van Rutte et al. [37]	Papamargaritis et al. [38]	Gobato et al. [39]	Ewang-Emukowhate et al. [40]	Damms-Machado et al. [13]	Moize et al. [11]	de Luis et al. [12]	Schweiger et al. [10]	Ernst [36]	Toh et al. [9]	Flancbaum [33]
Gender	F	F–M	F–M	F–M	F–M	F–M	F–M	F	F–M	F	F–M	F
Plasma iron	12.6	38	NM	2.7	49	29	26.3	NM	35.1	NM	15.7	42
Hemoglobin	7.7	5	NM	NM	0	NM	22.2	2.6	18.4	5.9	5	19.1
MCV	6.8	5.5	NM	NM	4	NM	NM	NM	18.6	NM	NM	NM
Ferritin	8.7	7	NM	2.77	NM	NM	10.3	5.2	23.9	9.1	1.1	9.9
Plasma zinc	2.9	0	6.7	55.5	NM	NM	32	73.9	NM	26.1	NM	NM
Plasma copper	0	NM	2.3	0	NM	NM	NM	67.8	NM	0	NM	NM
Folic acid	0	24	NM	0	18	5.5	3.8	25.2	24.3	3	0	NM
Vitamin B_{12}	10.6	11.5	NM	NM	25	9.3	2.2	9.5	3.6	19.4	1.8	0
Calcium	13.3	0.5	NM	13.8	NM	0	4.8	NM	0.9	NM	0	3.5
Phosphorus	2.3	14	NM	NM	NM	NM	NM	NM	2	6.9	0	NM
Vitamin D insufficiency	25.6	NA	NM	NM	67.5	NA	26.3	48.7	NM	66.1	NA	NA
Vitamin D deficiency	46.1	81	NM	NM	24	83	67.7	43.5	NM	24.2	57.1	68
Low Albumin	0	0	NM	0	NM	NM	1	6.1	0	25	0.9	1
Hyperparathyroidism	66.6	28.5	NM	NM	NM	NM	41	22.6	39	37	25	NM

MCV mean corpuscular volume, *NM* not measured, *NA* not available, *F* female, *M* male

Table 6 Prevalence (%) of altered hematologic variables and nutritional deficiencies compared to Chilean healthy childbearing age women

	Present study n=103	Mujica-Coopman et al. [49] n=64	de la Maza et al. [50] n=30	González et al. [51] n=30	ENS-2003 [44] n=312	Hertrampf et al. [52] n=751
Hemoglobin	7.7		10		4	
Ferritin	8.7		30			
Plasma zinc	2.9	4.7				
Plasma copper	0	3.1	0			
Folic acid	0[a]		0			0
Vitamin B_{12}	10.6[a]		0			23.4
Vitamin D						
insufficiency	25.6[b]					
deficiency	46.1[b]		16.6	27		

[a] n=66

[b] n=39

evaluated showed insufficiency and deficiency. 25(OH)D deficiency in the obese population has been described in many studies, with a reported inverse correlation between BMI and 25(OH)D plasma concentration. The exact mechanism by which obesity leads to low circulating 25(OH)D levels remains unknown; a multifactorial mechanism has been proposed, with components including low vitamin D intake, lack of exposure to sunlight, reduced rates of cutaneous conversion, and sequestration of vitamin D in adipose tissue [48]. In our study, we found a very low vitamin D intake, with only 21.3 % reporting adequate intake. We did not measure solar exposure or cutaneous conversion of pro-vitamin D3. As described by other authors, low plasma 25(OH)D concentrations negatively affect intestinal absorption of calcium, manifesting as a secondary hyperparathyroidism in 66.6 % of the subgroup studied (PTH ≥65 pg/mL).

Our study and other similar reports demonstrate that micronutrient deficiency is prevalent among a population with morbid obesity and is perhaps more common than previously thought. Prevalence studies for micronutrient deficiencies in apparently healthy population in Chile are scarce. To our knowledge, in addition to the ENS-2003 data, there are only four published studies reporting prevalence of deficiency for micronutrients in healthy childbearing age women in Chile with varying results depending on the type of study, sample type, sample size, and cutoffs to define the deficits (Table 6) [44, 49–52].

Of the 103 patients in this study, 66 % showed a deficiency condition of at least one micronutrient. Our study suggests that despite high caloric intake, the diet in obese individuals may not be sufficiently balanced to meet minimum requirements for micronutrients. Furthermore, the bioavailability of the nutrients depends on various factors such as chemical form and geographical origin of the nutrient, food matrix, nutrient-nutrient interactions, interactions with other components of the diet, cooking and processing methods, and the physiological and/or pathological state of the individuals consuming such foods, among these: age, gender, nutritional status, gastrointestinal secretions, intestinal permeability, intestinal pathologies, surgical history, and concomitant diseases.

In addition to the relationship between morbid obesity and risk of micronutrient deficiencies discussed above, there is another dimension of this association worthy to be explored, that is the effects of micronutrient status on chronic diseases. Thus, current evidence provides only a partial explanation for the role of various micronutrient deficiencies implicated in the development of chronic diseases. For example, there are associations between 25(OH)D deficiency and risk of developing diabetes mellitus, cardiovascular disease, and some forms of cancer, such as colorectal cancer; vitamin B_6 deficiency and depressive symptoms, cardiovascular events; low vitamin C levels and general mortality, myocardial infarction, and biliary pathology; and zinc deficiency and chronic liver diseases [36]. These findings, taken together with the results of the present study, suggest that further research into the role of micronutrient deficiency in the pathophysiology of various comorbidities associated with obesity is warranted.

In conclusion, our study suggests that the prevalence of micronutrient deficiencies among obese women seeking bariatric surgery in Chile is high. This is of clinical and practical importance because these deficiencies are usually attributable solely to the bariatric surgery. Our study suggests that it is important to systematically screen these deficiencies and correct them before surgery to reduce the incidence of subnormal micronutrient status associated to the surgical procedure. The causes of micronutrient deficiencies pre- and post-bariatric surgery are multifactorial. It is imperative that the medical community continues to explore the role of these deficiencies in the pathophysiology of the diverse comorbidities associated with obesity.

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Conflicts of Interest The authors Andrés Sánchez, Pamela Rojas, Karen Basfi-fer, Attila Csendes, Jorge Inostroza, Juana Codoceo, and Alejandra Valencia declare that they have no conflict of interest. The authors Fernando Carrasco, Karin Papapietro, and Manuel Ruz disclose that they are co-authors of the Fund for Science and Technology (FONDECYT) grants 1040765 and 1080576 that funded the present study.

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