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DIABETES AND OBESITY (M DALAMAGA AND F MAGKOS, SECTION EDITORS)

# Nutritional Deficiencies Before and After Bariatric Surgery: Prevention and Treatment

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## Abstract

*Purpose of Review* Bariatric surgery has the unique ability to drive substantial and sustainable weight loss in people living with obesity. Non-reversibility of these surgical techniques provides lifelong benefits but entails the need for continuous medical follow-up. The purpose of the current paper is to review and summarize current data on nutritional deficiencies in patients before and after bariatric surgery.

*Recent Findings* The cornerstone of preventing the emergence of disorders related to nutritional deficiencies is preoperative screening and correct supplementation since they may be exacerbated postoperatively. Following guidelines in conjunction to a lifelong personalized medical approach is of high importance.

*Summary* Bariatric surgery is a well-studied successful and durable means of weight loss that may lead to nutritional deficiencies. There is, thus, a medical need for careful monitoring and treatment of micro- and macronutrient deficiencies by an experienced multidisciplinary team.

**Keywords** Bariatric surgery · Micronutrients · Macronutrients · Nutritional deficiencies

## Abbreviations

| | |
|---|---|
| BS | Bariatric surgery |
| RYGB | Roux-en-Y gastric bypass |
| SG | Sleeve gastrectomy |
| BPD | Biliopancreatic diversion |
| BPD/DS | Biliopancreatic diversion with duodenal switch |
| BMI | Body mass index |

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## Introduction

Obesity is a chronic disease posing significant risks to patients through its multiple accompanying dysmetabolic sequelae and the ongoing, low-grade, inflammatory background [1]. While data concerning conservative therapy and new medications targeting obesity are constantly emerging, the treatment of obesity remains a difficult and often unsuccessful task due to oftentimes observed unsatisfactory percentage weight loss as well as potential weight regain, mainly attributed to adaptive alterations in endogenous mechanisms regulating energy intake [2]. On the other hand, bariatric surgery produces sustained beneficial effects on weight loss due to the robust changes of postprandial gut peptide responses observed postoperatively [3].

Although abundance in food is common in most developed countries and subsequent macronutrient deficiency is rare, the lower intake of healthy, high-quality calories contained in fresh fruits, vegetables, etc. leads to potential micronutrient deficiencies [4, 5]. Consumption of energy dense foods does not always indicate nutrient adequacy and various studies have shown that a great proportion of patients living with obesity present with nutritional deficiencies, with most indicating a prevalence of over 50% [5–7].

The risk of micronutrient malnutrition and the subsequent nutritional deficiencies found in patients scheduled to undergo bariatric surgery (BS) may be the result of poor diet quality, i.e., high-energy density, foods poor in micronutrients, erroneous dieting schemes, weight loss advised before surgery, and a result of medication side effects. Additionally, patients with obesity experience defective storage and bioavailability of specific nutrients and commonly have decreased sun exposure (mainly affecting vitamin D). Moreover, the subclinical inflammatory environment characterizing obesity increases hepcidin synthesis, ultimately decreasing iron absorption [4, 8]. Other mechanisms include small intestinal bacterial overgrowth that may end up consuming thiamine, B12 and fat-soluble vitamins [6, 9]. In order to correctly elucidate all mechanisms involved, the insufficiency of information concerning dietary intake, physical activity, and supplementation prior to BS should be addressed.

Postoperatively, nutritional deficiencies are dependent on the type and technique of the surgery imposing alterations in digestion and absorption as well as on postsurgical complications such as nausea and vomiting, food intolerance, reformed eating behavior, gut bacterial overgrowth, and low compliance to dietary and supplement recommendations [4, 6]. Most commonly, micronutrient deficiencies are usually present after BS, in contrast to macronutrient imbalances that are less commonly evident [10]. There is a strong recommendation for micro and/or macronutrient supplementation following BS [11]. Special attention should be given to BS patients that become pregnant in order to prevent any macro- and micronutrient deficiencies [12] and thus a careful evaluation and surveillance is of high importance, including laboratory screening every trimester depending on the surgical procedure (i.e., iron, folate, vitamin B12, vitamin D, calcium, fat-soluble vitamins, zinc, and copper) [13].

The manner in which nutrient deficiencies may arise postoperatively is evident if one considers the areas of the intestine responsible for micro- and macronutrient absorption and the portion of the gut bypassed or removed in each bariatric procedure (Fig. 1). In Roux-en-Y gastric bypass (RYGB) a 15–30-mL proximal gastric pouch is created and the jejunum is transected 50–75 cm beyond the ligament of Treitz. The gastric pouch is subsequently anastomosed to the distal intestinal segment while the proximal intestinal segment is anastomosed to the jejunum. The redirection of the ingested nutrients into the roux limb of the jejunum and the bypassing of the duodenum and proximal jejunum result in decreased total energy intake owing to restriction, malabsorption, and, most importantly, altered gut-brain axis physiology [3, 5, 14]. In sleeve gastrectomy (SG), the stomach volume is reduced to approximately 20% while the pylorus is preserved, leading to accelerated gastric emptying and early exposure of the small intestinal mucosa to ingested nutrients, and thus both restriction and neurohormonal changes seem to be the key players to its efficacy [5, 14]. Biliopancreatic diversion (BPD) and BPD with duodenal switch (BPD/DS) impose a greater risk of nutritional deficiencies associated to the increased length of bypassed small intestine [13].

As one can easily understand, avoiding postoperative micro- and macronutrient deficiencies commences preoperatively by supplementing appropriately after routinely testing for the aforementioned. Adverse clinical outcomes including anemia, metabolic bone, and neurological disorders may be seen if adequate supplementation is not provided [6].

## Studies Assessing Nutritional Deficiencies Preoperatively

Multiple studies have evaluated the prevalence of micronutrient deficiencies preoperatively in patients referred for BS. Most observe lower than baseline levels of vitamin D, folate, B12, and iron, although differences in age, sex, ethnicity, geographical and seasonal factors, previous supplementation, and cutoffs for deficiency definition could explain discrepancies among studies. Prevalences in people intended for BS of iron deficiency and low hemoglobin levels, folate deficiency, and vitamin B12 vary significantly between studies (0 to 47%, 0 to 63%, and 0 to 23%, respectively) [15].

A hundred patients—among which 60% were female—with morbid obesity [mean body mass index (BMI) of $42.3 \pm 4.7$ kg/m$^2$] and non-alcoholic fatty liver disease (NAFLD) were evaluated prior to BS with respect to their nutritional status. This study showed a low prevalence in preoperative nutritional deficiencies in iron, ferritin, folic acid, thiamine, vitamin B12, vitamin D, and hemoglobin levels (6, 1, 1, 6, 0, 22, and 6%, respectively). As far as the intake of specific nutrients was concerned, iron, calcium, folic acid, vitamin B12, and thiamine intakes were below the Dietary Reference Intake recommendations for 46, 48, 58, 14, and 34% of the study population respectively, while no significant differences were found between genders for all micronutrients [7]. Although patients were advised to take a multivitamin 2–3 weeks prior to BS, only 15% of them followed this recommendation. Only 10% of women and 18.3% of men did not present any nutritional deficiency preoperatively [7, 10].

In another study, at least one micronutrient deficiency was present in 85.5% of patients pre-BS (mean BMI of $42.8 \pm 6.6$ kg/m$^2$) and 50% of them showed $\geq 2$ micronutrient deficiencies, with vitamin D deficiency being the most prevalent (74.5%). Other measured micronutrients were found highly deficient as well, including folate (33.5%), iron (32%), calcium (13%), and vitamin B12 (10%). Albumin was also found to be deficient in 5.5% of patients [6]. Moreover, increased CRP values in these patients were strongly found

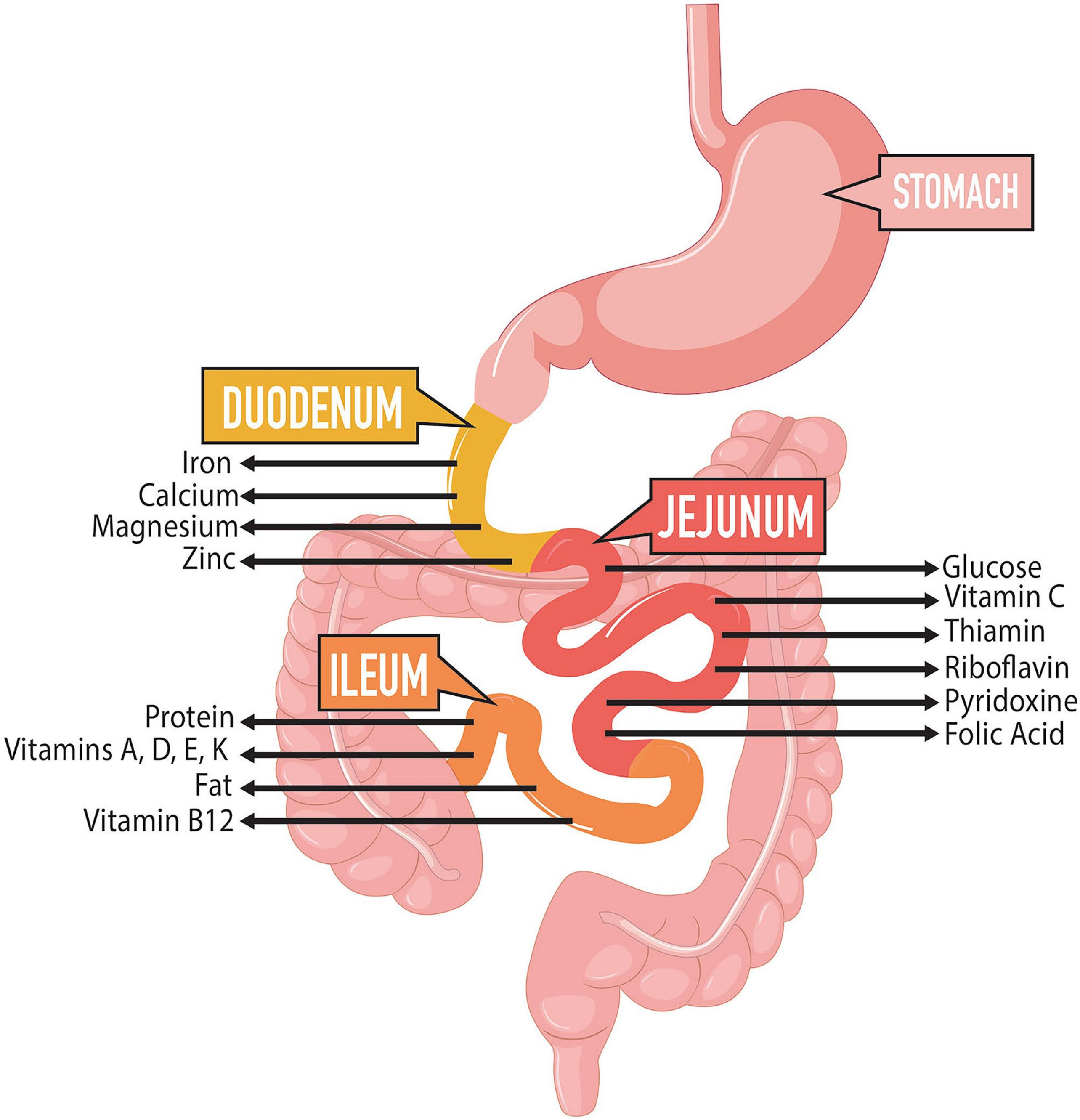


**Fig. 1** Sites of micro- and macronutrient absorption in the gastrointestinal tract

to be associated with vitamin B12 and folate deficiencies as well as with the presence of multiple micronutrient deficiencies [6].

In a study of Chilean women (103 patients) with morbid obesity seeking BS, although macronutrient consumption measured via a food questionnaire was adequate, the prevalence of nutritional deficiencies was also high: iron in 12.6%, ferritin in 8.7%, transferrin in 14.6%, zinc in 2.9%, calcium in 3.3%, and phosphorus in 2.3% of patients. Additionally, 10.6% had a vitamin B12 deficiency, 71.7% showed low concentrations of vitamin D, and 66% had high PTH levels. Folic acid and copper levels were not deficient [16].

In another study evaluating 115 women referred for BS, deficiencies were found in 6.1% of the subjects for albumin, 21.7% for prealbumin, and 5.2% for ferritin. No deficiencies were apparent for vitamins A, E, or K, except for 71.3% who had a moderate deficiency of vitamin D (< 30 ng/mL) and 26.1% who had severe deficiency (< 15 ng/mL). Deficiencies were found in 9.5% for vitamin B12, 25.2% for folic acid, 67.8% for copper, and 73.9% for zinc [17].

Wolf et al. evaluated micronutrient status in 43 BS candidates with morbid obesity (BMI: 52.6 ± 10.5 kg/m$^2$) and underlined multiple micronutrients deficiencies, i.e., vitamin D in 84%, β-carotene in all, and ascorbic acid in one-third of the patients. Correlations between serum/plasma concentrations and nutritional intake (estimated via a 3-day food record) and associations between low concentrations and inadequate intake were not found [18].

In a study of 58 BS candidates, among which 77.6% were female (median BMI was 46.3 kg/m$^2$), a high percentage was found deficient in both vitamin D (92.9%) and serum iron concentration (36.2%). Moreover, vitamin D and vitamin A levels were negatively correlated with age while vitamin D was also negatively correlated with BMI [19].

In a more recent study in 247 Chinese patients (mean BMI 38.01 ± 7.11 kg/m$^2$) also investigated preoperatively for BS, a prevalence of preoperative nutritional deficiencies was 76.9% for 25 (OH) vitamin D, 19.84% for globulin, 11.7% for albumin, 11.0% for sodium, 8.3% for folic acid, 10.5% (male) and 6.3% (female) for chloride, 4.1% for calcium, and 3.1% (male) and 0.7% (female) for ferritin. 11.9% of subjects were found with elevated PTH as well. Both albumin and 25 (OH) vitamin D deficiencies were more common in patients with BMI ≥ 47.5 kg/m$^2$, while a higher waist circumference (WC) (≥ 130 cm) was associated with a higher rate of albumin deficiency [20].

## Studies Assessing Nutritional Deficiencies Pre- and Postoperatively

van Rutte et al. compared 407 patients preoperatively and 1 year postoperatively. Preoperatively, anemia was present in 5%, low ferritin in 5%, vitamin B6 in 24%, and low folic acid in 24% of patients. Consistent with other studies, low level of vitamin D was present in 81% of patients. Interestingly, vitamin A had excessive levels in 72% of patients. Despite supplementation, 1 year postoperatively, anemia prevalence increased slightly in 6%, low ferritin levels in 8% of patients, low vitamin B12 in 11.5%, low thiamine in 9%, while folate deficiency and D hypovitaminosis decreased (although still found in 12.5% and 36% respectively) [21].

Ben-Porat et al. aimed to identify risk factors for postoperative deficiencies studying patients pre and 1 year postoperatively. Before BS, 15% had anemia, while deficiencies in iron, folate, and B12 were 47%, 32%, and 13%, respectively. Women were more deficient in iron (56% vs 26% in men). Pre-BS, deficiency in vitamin D and elevated parathyroid hormone were 99% and 41%, respectively. One year post BS, the deficiencies in hemoglobin and vitamin B12 worsened to 20% and 17% respectively while deficiencies in iron, folate, vitamin D, and PTH improved (28%, 21%, 94%, and 10%, respectively). It is worth noting that deficiencies of hemoglobin, folate, and B12 before surgery were predictors for deficiencies 1 year after surgery [22].

Taking into consideration the multiple and consistent results of studies confirming the pre-BS nutritional deficiencies and the subsequent further deterioration if unproperly investigated and subsequently supplemented, a routine screening evaluation of nutritional status is recommended. Supplementation of identified deficiencies should be advised pre-BS taken that micronutrient deficiencies can be a predictor of deficiencies postoperatively [22]. Most identified micronutrient deficiencies would not give ground for postponement of BS [10]. Whether preoperative weight loss may contribute to micronutrient deficiencies has not been clarified, yet it could be a possible cause.

## Nutritional Deficiencies: Prevention and Treatment

According to the Practice Guidelines for the Perioperative Nutrition, Metabolic, and Nonsurgical Support of Patients Undergoing Bariatric Procedures – 2019 Update commissioned by the American Association of Clinical Endocrinologists, the Obesity Society, American Society of Metabolic and Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists Boards of Directors as well as according to the British Obesity and Metabolic Surgery Society Guidelines on perioperative and postoperative biochemical monitoring and micronutrient replacement for patients undergoing bariatric surgery—2020 update, routine evaluation and thereafter monitoring in specific time points is of high importance in order to prevent or treat potential nutritional disorders that accompany BS [13, 15].

Patients with, or at risk for, micronutrient deficiencies in the early (< 5 days) post-procedure period should be offered supplementation with two adult multivitamin-multimineral formulations (containing among others thiamine, iron, zinc, copper, and selenium and folic acid) preferably in chewable form for at least the first 3–6 months [9, 13, 15].

Both calcium and vitamin D should be regularly assessed, in order to reduce osteoporosis and fracture risk, known to be increased in patients undergoing BS [23]. Elemental calcium supplementation of 1200 to 1500 mg/day in SG and RYGB and 1800 to 2400 mg/day in BPD with duodenal switch in both diet and as citrated supplement in divided doses is recommended [9, 13]. Iron and calcium supplements should be given with 1–2 h distance. Pre- and annual postoperative assessment for vitamin D levels is advised and depending on the levels at least 2000 to 3000 IU of vitamin D supplementation daily should be prescribed in order to accomplish 25-OH vit D levels well over 30 ng/mL. Larger doses may be necessary and caution should be implemented in order to prevent secondary hyperparathyroidism [13].

Total iron at a quantity of 18 to 60 mg daily via multivitamin-multimineral regimens and additional supplements as well as vitamin B12 orally if absorbed or parenterally (sublingualy, subcutaneously, or intramuscularly) if inadequately absorbed are advised [13].

Vitamin A is among the micronutrients that should be measured especially in the first year following RYGB or BPD without/with duodenal switch while vitamins E and K should be investigated in patients that present with associated symptoms such as hepatopathy, neuromuscular impairment, and coagulopathy. Vitamin K levels should be monitored by measuring serum vitamin K1 and protein induced by vitamin K absence or antagonism (PIVKA-II), although this may be not readily available in all laboratories [15]. If patients present with an indication for vitamin A supplementation, the usual dose includes 5000–10,000 IU daily for SG, RYGB and 10,000 IU daily for BPD/DS [13]. Vitamin A deficiency symptoms include deterioration in night vision, dry eyes, fatigue, and hyperkeratosis [15].

Iron and ferritin levels are included in the postoperative evaluation of patients, especially in those with anemia. Monitoring should be performed in all patients within the first 3 months and following the first trimester every 3 to 6 months until 1 year postoperatively, and then annually. Treatment of low levels includes formulations providing up to 150–200 mg of elemental iron daily [13] while intravenous iron infusion may be suggested to patients with oral iron intolerance or refractory deficiency. Larger doses may be appropriate for women of reproductive age. Vitamin C supplementation to increase iron absorption may be considered [13]. Iron deficiency anemia is frequently asymptomatic [8], yet clinical/laboratory features of iron deficiency may include microcytic anemia, fatigue, difficulty in concentrating, glossitis, hair loss, and nail dystrophy (koilonychia). Factors implicated in iron deficiency after BS include decreased intake, reduced secretion of hydrochloric acid, and reduction in the absorptive surface area imposed on a pre-BS predisposition for iron deficiency (low baseline ferritin levels) frequently found in people living with obesity [24, 25].

Vitamin B12 monitoring should be performed in all patients pre and at least annually or earlier postoperatively, since vitamin B12 deficiency can emerge several years after BS, presenting with megaloblastic anemia and neuropathy among other manifestations [15]. Additionally, one should consider measuring serum methylmalonic acid, with or without homocysteine, in symptomatic and asymptomatic patients with a history of B12 deficiency or preexisting neuropathy. Oral supplementation of 350–1000 mcg daily or more is recommended to maintain normal vitamin B12 levels or parenteral B12 if normal levels cannot be maintained [13]. Caution should be exercised regarding several medications that exacerbate B12 deficiency like metformin, colchicine, and proton-pump inhibitors as well as in patients with high-dose folic acid requirements (> 1000 mcg/day). Folic acid supplementation before B12 correction may unmask a B12 deficiency state [13]. Folic acid is usually supplemented in a dosage of 400–800 mcg daily contained in the aforementioned multivitamin-multimineral regimen or in larger doses in suspected deficiencies [13, 15]. Nonetheless, in refractory anemias, other causes should be sought such as copper, selenium, and zinc levels.

Selenium should be screened if patients present with relevant symptoms such as persistent anemia, chronic diarrhea, cardiomyopathy, or metabolic bone disease or with high suspicion of deficiency [13, 15]. Zinc on the other hand is usually included in the daily multivitamin-multimineral regimen at a dose of 8–22 mg/day depending on BS type. Symptoms of zinc insufficiency include chronic diarrhea, poor wound healing, hair loss, pica, dysgeusia, or unexplained hypogonadism or erectile dysfunction in male patients. Serum copper and ceruloplasmin levels may be evaluated in patients with RYGB or BPD without/with duodenal switch at least annually and special care should be given to patients with symptoms such as anemia, neutropenia, thrombocytopenia, neuromuscular abnormalities, or impaired wound healing [13, 15]. Supplementation with 2 mg daily is included in the multivitamin-multimineral preparation while intravenous copper is reserved for severe deficiency. Of note, zinc supplementation can cause copper deficiency [13, 15].

Last but not least thiamine (vitamin B1) may be screened and is additionally supplemented in a dosage of at least 12 mg daily, preferably 50–100 mg daily from a B-complex formulation or a multivitamin-multimineral supplement. Patients with severe thiamine deficiency should be treated with intravenous regimens and one should be vigilant to recognize and treat this serious disorder promptly, especially in patients with predisposing factors such as female gender, African Americans, and patients that present with symptoms of the gastrointestinal tract, heart failure, prolonged vomiting, parenteral nutrition, alcohol abuse, neuropathy or encephalopathy, or small intestinal bacterial overgrowth [13]. Of note, clinicians in care of patients that have undergone BS should be familiar with the clinical manifestations of thiamine deficiency, i.e., cerebral Beri Beri and Wernicke's encephalopathy (ataxia, confusion, and coma), dry Beri Beri (neuropathy and neuritis), or wet Beri Beri (cardiac insufficiency with tachycardia and respiratory symptoms) [15]. Recommended vitamin and minerals supplementation is presented in Table 1.

On the other hand, BS can be also complicated with macronutrient deficiencies. Specifically, out of the three macronutrients, protein malnutrition is commonest particularly in patients undergoing RYGB as well as BPD/DS,

**Table 1** Recommended postoperative vitamin and mineral supplementation

| | Dosage | Comments |
|---|---|---|
| Elemental iron | 150–200 mg/day | • Vitamin C supplementation may be added to increase iron absorption<br>• Intravenous iron infusion may be considered in refractory deficiency |
| Vitamin B12 | 350–1000 µg/day | • Via disintegrating tablets, sublingual, liquid, or intranasal route<br>• Intramuscular supplementation may be considered |
| Folic acid | 400–800 mcg/day | • Higher doses may be needed depending on BS procedure and in women of childbearing age |
| Zinc | 8–22 mg/day | • Higher doses may be needed depending on BS procedure |
| Calcium | 1200–1500 mg/day | • Higher doses may be needed depending on BS procedure |
| Vitamin D3 | 2000–3000 IU/day | • Higher doses may be needed depending on BS procedure<br>• Dosage should be titrated to therapeutic 25-OH-VitD levels |
| Copper | 2 mg/day | • Higher doses may be needed depending on BS procedure<br>• Intravenous infusion may be considered in severe deficiency |
| Thiamine | 50–1000 mg/day | • Higher doses may be needed depending on BS procedure<br>• Intravenous infusion may be considered in severe deficiency |
| Vitamin A | 5000–10000 IU/day | • Higher doses may be needed depending on BS procedure |
| Vitamin E | 15 mg/day | • Higher doses may be needed depending on BS procedure |
| Vitamin K | 90–120 mcg | • Higher doses may be needed depending on BS procedure |

Dosage supplementation varies depending on BS procedure and level of deficiency (13,15)

owing to their malabsorptive properties, manifesting with serum albumin levels below 3.5 mg/dL, usually apparent in the first postoperative months. Causes include malabsorption as well as limited food tolerance for protein-rich foods [9]. Clinicians should have a high level of suspicion when patients present with relevant symptoms such as peripheral edema and excess loss of fat-free mass. The dietary protein intake after BS is 60–80 g/day or 1.1–1.5 g/kg of ideal body weight [9, 13]. Increased intake may be needed depending on the BS procedure and the patient's need [13], without underestimating the importance of high-quality protein. Severe protein malnutrition may lead to secondary kwashiorkor syndrome characterized by hepatosteatosis, exocrine pancreatic insufficiency, edema, and multiple skin disorders [26]. These rare severe clinical entities may require parenteral tube feeding.

## Conclusion

Bariatric surgery causes substantial and sustainable weight loss. The cornerstone of preventing the emergence of disorders related to nutritional deficiencies is preoperative screening and correct supplementation since they may be exacerbated postoperatively. Following guidelines in conjunction to a personalized medical approach in a lifelong manner is of high importance. Non-reversibility of these surgical techniques provides durable benefits but entails the need for continuous medical follow-up. Clinicians providing care for patients that have undergone BS should have a high level of suspicion for laboratory indications and clinical symptoms related to nutritional deficiencies. Aggressive evaluation and treatment are warranted for all patients that present with clinical manifestations.

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**Author Contribution** GA conceived and designed the review. GA, SKK, MD, and AK performed the literature review. All authors were involved in the preparation and revision of the manuscript.

## Compliance with Ethical Standards

**Ethics Approval and Consent to Participate** No ethics approval was necessary since it is a review manuscript.

**Conflict of Interest** The authors declare no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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