



# B1 Vitamin Deficiency After Bariatric Surgery, Prevalence, and Symptoms: a Systematic Review and Meta-analysis

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## Abstract

B1 deficiency is a very prevalent complication of bariatric surgery. This study reviews prevalence and symptoms of B1 vitamin deficiency after bariatric surgery. PubMed, Scopus, and Web of Science published were searched up to 10 Feb 2022, with the following keywords: Roux-en-Y gastric bypass, one anastomosis gastric bypass, Omega bypass, Mini bypass, Bariatric surgery OR Bariatric surgery, metabolic surgery, Weight loss surgery, Classic gastric bypass, Loop gastric bypass, Gastric Bypass, thiamine OR thiamin, beriberi, B1. A total of 11 studies examining 1494 patients were included in this meta-analysis. Twenty-seven percent of patients who underwent bariatric surgeries experience vitamin B1 deficiency. Thiamine supplements should be prescribed for the patients for the rest of their lives, and also standard post-surgery follow-ups are necessary in terms of monitoring dietary factors.

**Keywords** Bariatric surgery · Weight loss surgery · Metabolic surgery · B1 deficiency · Thiamin deficiency

## Introduction

Vitamin B1, also known as thiamine, is an essential micro-nutrient which is not produced in human body; hence, it should be provided via dietary routes. This vitamin is a member of vitamins B family (1). This group of vitamins is water-soluble and has major role in muscle contractility

and metabolism of pyruvate. The later issue is essential for several chemical reactions in the human body including nerve signal conduction, nerve membrane maintenance, and production of myelin and different neurotransmitters (1–5). Thiamin itself is largely involved in pathways that also create energy in cells and therefore its deficiency will cause oxidative stress, which lead to cell death and contribute to further symptoms and comorbidities (5–10). Beriberi is the disease of B1 deficiency and comprises a group of symptoms including polyneuritis, cardiovascular symptoms, and the neuropsychiatric Wernicke-Korsakoff syndrome (2, 11).

In recent decades, obesity has grown to become a major health issue and bariatric surgical procedures, as

### Key Points

- B1 deficiency is a very prevalent complication of bariatric surgery.
- B1 deficiency is relatively high among patients underwent bariatric surgery.
- Prescribing vitamin supplements and diet monitoring after bariatric surgery is essential.

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an optimal treatment, have also become more frequent. According to the IFSO global registry data, in 2019, bariatric surgeries exceeded 833,670 cases (12, 13). A major post-operative concern of such surgeries is late malnourishment which requires close follow-up and treatment with dietary supplementation. Since thiamin is a water-soluble vitamin, it cannot be stored in the body in large quantities or for long durations and regular dietary intake is paramount in maintaining adequate thiamin levels. In adults, the recommended daily intake (RDI) for men and women is 1.2 and 1.1 mg/day, respectively; in pregnant women, the RDI increases to 1.4 mg/dl (14). Depending on the source, thiamin uptake occurs through active absorption in nutritional doses and passive diffusion in pharmacological doses. The hydrolysis of the thiamin by phosphatase is essential for its absorption by the small intestine especially in the duodenum and proximal jejunum (15). Subsequently, phosphorylated thiamin is stored in the heart, kidney, liver, and brain tissues and has a limited half-life of 14–18 days (15–17). Several studies have documented high rates (15.5–29%) of thiamin deficiency in obese bariatric surgery candidates. The often vague presentation of thiamin deficiency mostly goes unnoticed, especially in individuals with a history of alcohol use disorder (15).

It was already established that Roux-en-Y gastric bypass, Billroth II partial gastrectomy, or total gastrectomy have been associated with risk of developing thiamin deficiency (18). Although more than a few clinical practice guidelines suggest the routine clinical assessment of micronutrients, as well as recommending regular mineral and vitamin supplementation following bariatric surgery, these recommendations are not set in firm evidence (19, 20). In addition, such supplementation and monitoring, which is often costly, may unnecessarily complicate clinical care. Therefore, a deeper and more comprehensive understanding of thiamine deficiency, its prevalence and supplementation, and its place following bariatric surgery is necessary. In this review, we aimed to measure the prevalence and symptoms of thiamin deficiency after bariatric procedures.

## Methods

This systematic review and meta-analysis was conducted according to latest version of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16] and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [15]. We investigated the entire English language scientific literature on thiamin deficiency after bariatric surgeries.

## Search Strategy

A comprehensive and systematic literature search was performed in PubMed and Scopus for articles published by February 10, 2022, including the following keywords “Roux-en Y gastric bypass,” “Omega bypass,” “mini bypass,” “One anastomosis gastric bypass,” “Bariatric surgery,” “Weight loss surgery,” “metabolic surgery,” “Gastric bypass,” “Loop gastric bypass,” “thiamin,” “thiamin deficiency,” or a combination of them in the title or abstract. The details on search query of each data source are provided in supplementary material. Inclusion criteria were including studies about all obesity or bariatric surgery assessing thiamin deficiency done as original or case series studies. Exclusion criteria were considered as animal studies and case reports.

## Data Extraction

After determining the included studies, the following variables and parameters were extracted: first author’s name, year of publication, sample size, study design, age, number of patients with thiamin deficiency, body mass index (BMI) before surgery and at the time of thiamin deficiency and its interval, supplementation, symptoms. Two independent investigators extract the articles independently. Any disagreements observed between the two reviewers were corrected by a third reviewer independent from the other two. We used the Newcastle Ottawa Scale (NOS) for qualitative assessment of the included studies [15].

## Statistical Analysis

The analysis was performed using STATA version 17. The main measure of the effect/effect size was prevalence (ratio of cases to the total population). We used the metaprop command for this purpose and if there is any zero incidence among the included studies Freeman-Tukey double arcsine transformation to stabilize the variances.

We evaluate the heterogeneity between studies with the I<sup>2</sup> index. I<sup>2</sup> values of 0% indicate no heterogeneity, 25% low, 25 to 50% moderate, and 50% high heterogeneity. Publication bias was analyzed the egger test and presented funnel plot. Averages of quantitative variables were only reported according to the articles and we just in the meta-analysis process weighted each study by *N* (sample size). For descriptive purposes, table and figure were used. In case of any publication bias, we used the trim fill method to overcome the possible effect of publication bias on the pooled estimate of thiamin deficiency.

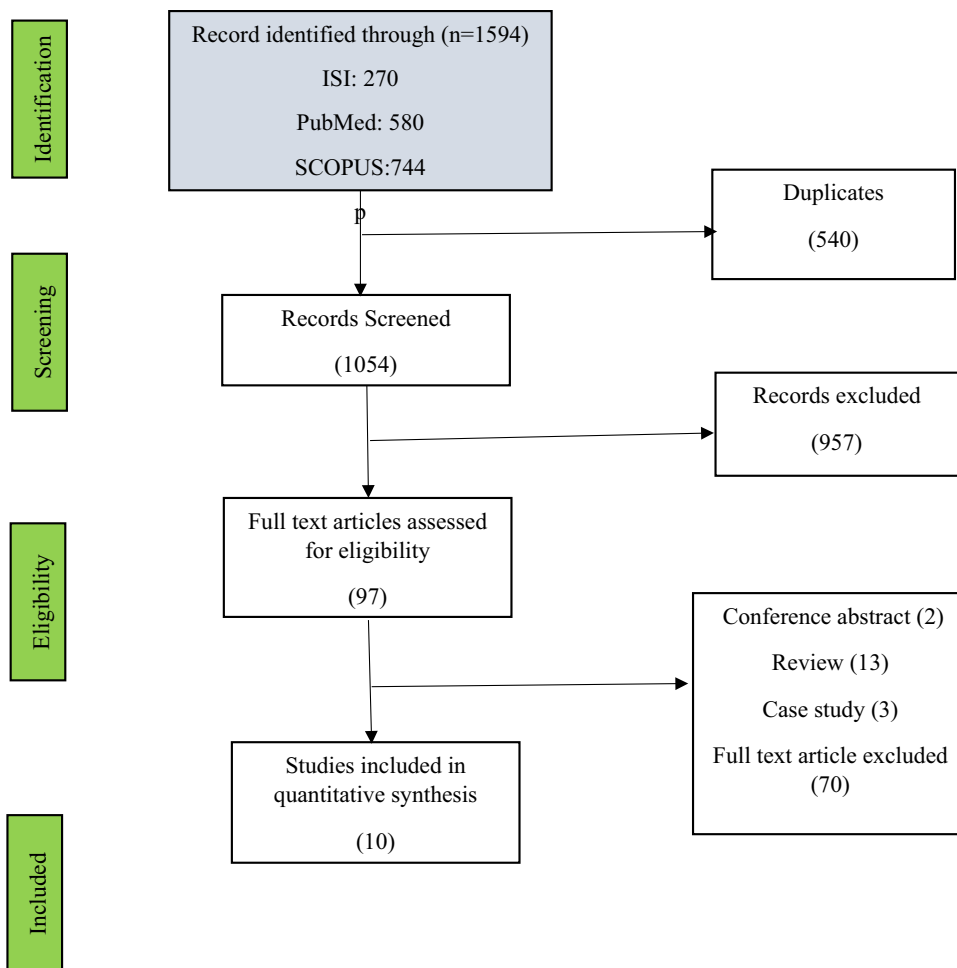
## Results

A total of 10 studies examining 2443 patients were included in this study (Fig. 1). Study characteristics of the patients included in the meta-analysis are presented in Tables 1 and 2. The mean age of the patients was  $38.17 \pm 8.02$  years. The mean interval between time of bariatric surgery and vitamin B1 deficiency was 16.41 months. Mean BMI before surgery and at the time of vitamin B1 deficiency was  $47.18 \pm 11.61 \text{ kg/m}^2$  and  $30.7 \pm 5.2 \text{ kg/m}^2$ , respectively (Table 1). The clinical symptoms, treatment, outcome, and important notes of the reported studies are shown in Table 2.

## Prevalence of Vitamin B1 Deficiency

Pooled estimation of a meta-analysis showed a prevalence of 22%, i.e., 22 out of every 100 bariatric surgeries experienced vitamin B1 deficiency at total study ( $I^2:97.04, p < 0.001$ ) (Fig. 2). The subgroup analysis and pooled estimation of a meta-analysis of prevalence of B1 deficiency for Roux-en-Y gastric bypass and sleeve gastrectomy reported a prevalence of 25% and 14% respectively (Fig. 3).

**Fig. 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses



The results of the analysis showed that bias publication has an influence on the creation of negative results, which is shown as asymmetry in the funnel plot. Meanwhile, evidence of publication bias was detected using Egger’s test (Egger’s test  $t = 3.16, P = 0.013, 95\% \text{ CI}: 0.79, 5.06$ ) (Fig. 4). Since we found substantial publication bias, we used the trim and fill method to address the effect of censored study on our pooled estimate. According to our analysis, it seems that four studies were censored due to publication bias and after pooling their effect on overall estimate, it showed that with considering unpublished papers, the pooled effect would decrease to 8%.

## Discussion

### Summary of Evidence

Thiamin is an essential factor for human biology and health. Thiamin insufficiency is estimated to be a rare in general population with proper diet (32). Nonetheless, it is a common dietary abnormality among the bariatric surgery candidates (17). The mechanism is related to inadequate

**Table 1** Quantitative characteristics of the included studies in the systematic review

Author	Year	Study design	Sample size	Age	Pre-op_BMI	Bariatric procedure	BMI with deficiency	Vitamin B1 deficiency (number)	Duration intervention (month)
Stephen G. Boyce (21)	2015	Retrospective	299	47.5 ± 11.4	50.5 ± 30.8	RYGB	NR	5	≥ 12
shilen v lakhani (22)	2008	Retrospective	80	46	53	RYGB	NR	39	≥ 12
Nath A (23)	2021	Retrospective	33	70 ± 3.4	35 ± 6.3	RYGB and SG	NR	20	≥ 12
Smelt HJM (24)	2020	Retrospective	970	46 ± 10	43 ± 5	SG	NR	65	≥ 12
Tang, L (25)	2018	Retrospective	105	39 ± 5.25	46.4 ± 7.3	SG	NR	27	≥ 12
Rossi (26)	2012	Cross-sectional	44	45.4 ± 9.5	50.2 ± 16.2	RYGB	28.9	25	≥ 12
Gadgil MD (27)	2014	Retrospective	456	30.7 ± 4.6	NR	Different bariatric procedure	NR	0	≥ 12
Guan B (28)	2018	Retrospective	269	31.67 ± 10.46	43.73 ± 11.03	RYGB and SG	NR	5	≥ 12
Hazart J (29)	2017	Retrospective	48	31.0 ± 5.8	47.6 ± 6.0	SG, GB, AGB	30.5 ± 7.4	20	≥ 12
Heusschen L (30)	2018	Randomized controlled trial	139	38.2 ± 12.4	47.6 ± 9.0	SG	NR	9	≥ 12

*RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *AGB* adjustable gastric banding, *GB* gastric bypass

vitamin repletion along with persistent, intractable vomiting. Deficiency can occur despite oral supplementation if emesis is present because it prevents effective absorption. There is special vulnerability in the early phase after weight loss surgery, when dietary intake is intentionally restricted to liquid and pureed consistency. Other known etiologies of thiamin deficiency are poor intake like diets high in polished rice, processed grains, alcoholism, parenteral nutrition lack of thiamin, and increased loss in diarrhea, increased thiamin utilization in pregnancy, lactation, hyperthyroidism, and medications like diuretics (16). In addition after BS, it is well known than low compliance of patients to use vitamin supplementations is a common cause of vitamin deficiency (33). Whatever the cause, bariatric surgery patients with persistent vomiting or extraordinarily rapid weight loss are at risk of thiamine deficiency (34). The normal thiamin concentration in EDTA-blood is about 20–100 µg/l and diagnosis of thiamin deficiency in all researches is serumic level below 20 µg/l (35).

The present meta-analysis was conducted to investigate the prevalence of thiamin deficiency following bariatric surgery. Based on our finding, the overall incidence of thiamin deficiency following bariatric surgeries is considerable. The pooled measure was about 27% which is close to the prevalence of thiamin deficiency among the patients the super obese patients (17). It should be taken into consideration that the prevalence of B1 deficiency prior to surgery was

not reported by majority of the included study; therefore, it is a bit hard to make direct causality association between bariatric procedures and B1 deficiency. In addition, vitamin deficiencies that exist before surgery in patients may get worse after surgery. Therefore, vitamin levels should be evaluated before surgery and if there is deficiency, it must be treated before the operation.

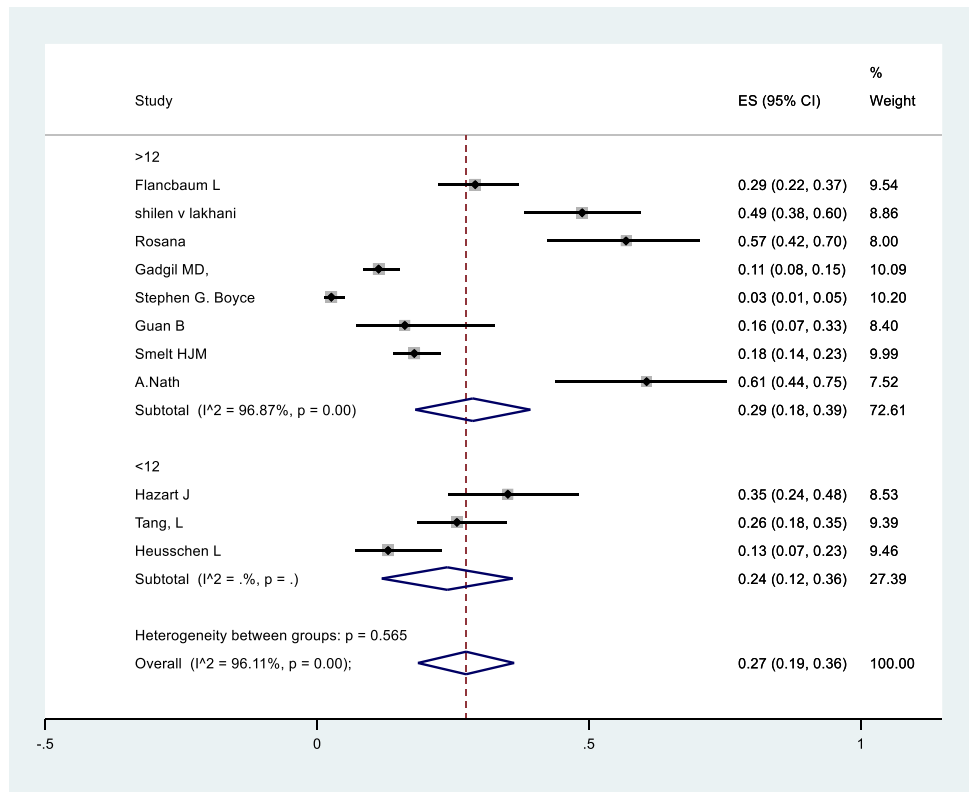
Moreover, thiamine deficiency has been observed in 15–29% of bariatric candidates (36). This indicates a considerable prevalence of thiamine deficiency in this population. Besides and in line with our results, thiamine deficiency can be counted as a major postoperative complication after bariatric surgeries; thus, it is recommended all the candidates should be screened for thiamine deficiency before the surgery and also receive thiamin supplementation after surgery (19, 20). According to the latest the American Society for Metabolic and Bariatric Surgery guideline on micronutrient screening and supplementation of the bariatric candidates, it is suggested to administer 12 mg of thiamin once a day or a 50 mg of thiamin in form of B-complex supplement or multivitamin once or twice a day to keep the thiamin blood level within normal range and prevent deficiency (20).

On the other hand, the difference between the prevalence of B1 deficiency among the different types of bariatric procedures can be a sign of a possible association between type of bariatric procedure and risk of thiamin deficiency. According to the studies characteristics, the mean age consisted of

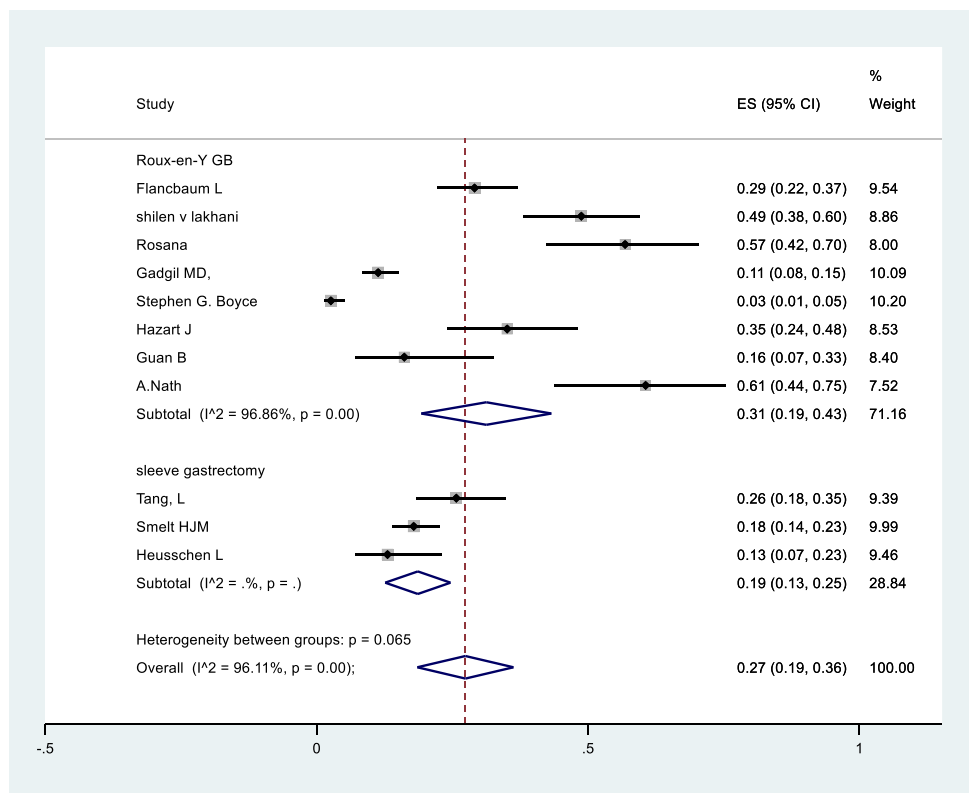
**Table 2** Clinical sign, treatment, outcome, and important notes of the reported studies

Author	Clinical sign and symptoms	Treatment	Final clinical outcome	Important notes
Boyce S (21)	Not declared	Not declared		
Lakhani S (22)	Not observed	Thiamin	Symptoms resolved	
Nath A (23)	Multiple sign and symptoms based on different subtypes were considered	Thiamin		Focusing on deficiencies of thiamin, vitamin B12, vitamin D, and iron in geriatric, bariatric patients could enforce treatments designed to prevent development of disabling deficiency syndromes
Smelt H (24)	Not declared	Thiamin	Vitamin deficiencies resolved	Sleeve gastrectomy patients benefit from the specialized multivitamin supplements
Tang, L (25)	Nausea, vomiting, ocular abnormalities, mental status changes, ataxia	Multivitamin	Thiamine deficiency resolved	Identify predictive demographic, postoperative, and behavioral factors so that appropriate measures can be taken to prevent thiamin deficiency in <i>vertical sleeve gastrectomy</i> patients
Rossi (26)	Not declared	Not declared	Evaluate the nutrient intake of women who had undergone RYGB surgery	The nutrient intake of women who had under-gone RYGB is very similar to that of non-operated women, with the exception of a reduced intake of iron, zinc and vitamins B1 and B12, which may be due to the difficulty of consuming meat and a balanced diet. The findings of this study emphasize the importance of appropriate nutritional intervention and the regular use of multivitamin and mineral supplements for these patients
Gadgil MD (27)	No declare	No declare	Micronutrient testing and deficiencies	Most laboratory testing occurred in less than half the women and was triggered by anemia. Increased testing may help identify nutrient deficiencies and prevent consequences for maternal and child health
Guan B (28)	No declare	No declare	Nutritional deficiencies	Nutritional deficiencies found before surgery indicated that should not attribute postoperative nutritional deficiencies to bariatric surgery only
Hazart J (29)	No declared	Multivitamin supplementation	Prevalence of maternal deficiencies in micronutrients	Prevalence of micronutritional deficiencies and small-for-gestational-age neonates is high in pregnant women following bariatric surgery. Specific nutritional programs should be recommended for these women
Heusschen L (30)	Not observed	Multivitamin supplement	Vitamin and mineral deficiencies	Optimized multivitamin supplement only affected serum levels of folic acid, PTH and vitamin B1, and anemia rates compared to a standard multivitamin supplement

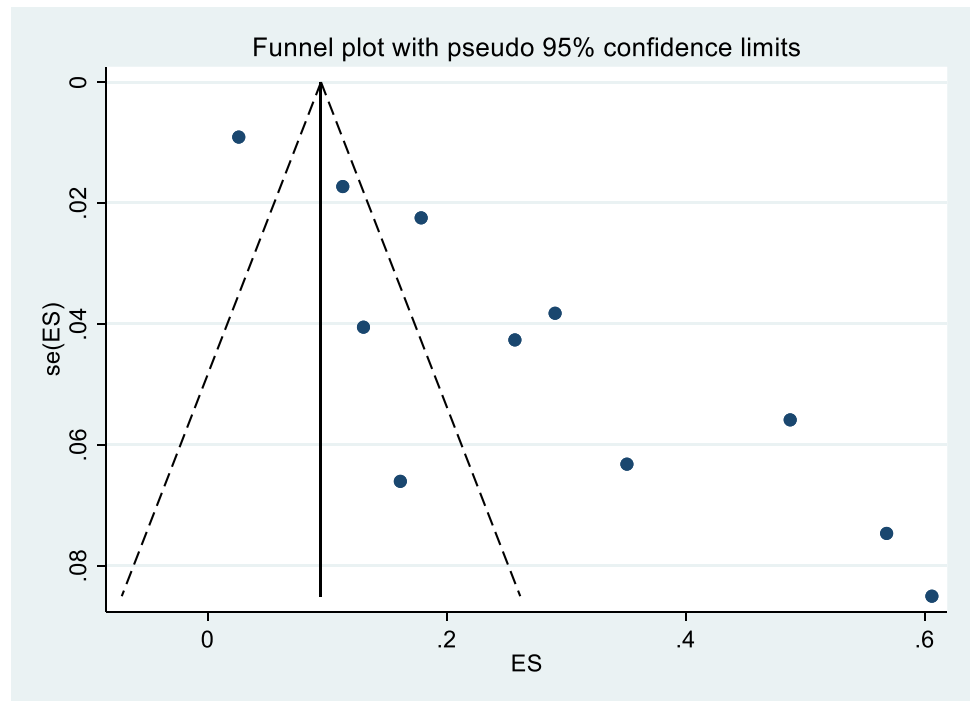
**Fig. 2** Forest plot the prevalence of vitamin B1 deficiency after bariatric surgery



**Fig. 3** Forest plot the prevalence of vitamin B1 deficiency based on type of bariatric surgery



**Fig. 4** Bias publication assessment in the funnel plot



a wide range of 25 to 70 years. The study of Nath et al. (23) showed different characteristics in comparison to other studies in which the mean age was about 70 years and the mean of BMI was about 35 kg/m<sup>2</sup>. Other studied showed similar baseline characteristics. The pooled prevalence of thiamin deficiency in studies with Roux-en-Y surgery was about 12% higher than the prevalence in sleeve surgery. Comparing their 95% CIs, we can conclude that the mention difference is statistically significant. One possible explanation for this difference would be the fact that in RYGB procedure, the key sections of the small bowel which responsible for the absorption of the B1 are bypassed; therefore, the risk of B1 deficiency is expected to be high among the RYGB candidates. Thiamine deficiency can occur within 8 to 15 weeks after MBS or even shorter in susceptible patients (37–39). Duration wise, the pooled prevalence of thiamin deficiency was about 3% higher in more than 12 months of follow-up; however, this different may not be statistically significant comparing their 95% CI. Other than the quantitative results, the qualitative systematic showed some important information. The early stages of thiamine deficiency may present with anorexia, indigestion, constipation, malaise, heaviness, and weakness of the legs, tender calf muscles, numbness in the legs, and an increased pulse rate (40). Syndromes caused by frank thiamine deficiency, including beriberi, Wernicke's encephalopathy (WE), and Korsakoff syndrome, commonly present with a classic triad of symptoms including ocular abnormalities, gait ataxia, and mental status changes. It is important to note that all three components of the triad may not be present at time of diagnosis; hence, providers should

not rely on all three components presenting at one time in order to make a definitive diagnosis (41).

From clinical presentation perspective, the most prevalent clinical signs and symptoms were nausea, vomiting, and anemia. In five studies, nausea and vomiting were reported as the initial symptoms of the thiamin deficiency (22, 24, 25, 29, 31).

The European Federation of Neurological Societies recommends postoperative monitoring of the thiamine levels of patients for at least 6 months and, where necessary, performing parenteral thiamine supplementation (42). A 100-mg oral thiamine supplementation twice a day is the standard treatment for thiamine deficiency. Patients with symptoms of Wernicke's encephalopathy or acute psychosis need to be kept under medical surveillance in the hospital. These patients should receive at least 250 mg/day thiamine intramuscularly or intravenously for 3–5 days (42–44). If thiamine deficiency after bariatric surgery cannot be treated with oral thiamine supplementation, it is associated with excessive bacterial growth in the small intestine. Antibiotic treatment is needed to overcome this deficiency, which is called bariatric beriberi.

Deficiencies of other vitamins such as vitamin D and minerals were also reported among the included studies (27, 31). This implies that despite of beneficiary effect of bariatric procedures regarding the weight loss, and also improvement of particular comorbidities including diabetes and hypertension, these procedures put candidates in poor nutritional state; hence, nutritional support in patients who underwent bariatric surgery is of vital essence (31). However, the number of clinical trials in this respect is limited.

## Limitations

The most important limitation of this study was variation in the effect sizes of the studies. Egger's test shows a significant publication bias and in line with that, the funnel plot showed asymmetry for the study effects. This may be due to their different baseline characteristics and lower sample sizes. However, the reasons of different prevalence should be investigated in future. Furthermore, we did not consider confounding factors such as chronic alcoholism and preoperative serum level of thiamine. Also, we did not include case reports studies in this systematic review which were reported Wernicke's encephalopathy and other rare manifestation of severe thiamine deficiency.

## Conclusion

The overall pooled prevalence of thiamin deficiency was 22% and it was 11% higher in Roux-en-Y surgery in comparison to sleeve gastrectomy. Therefore, its diagnosis is easily delayed or missed by community healthcare providers or providers not familiar with the bariatric surgery patient. Thiamine deficiency in the bariatric surgery patient is a complication that can present quickly and cause serious side effects if left unreported or misdiagnosed. Bariatric experts are likely familiar with the presentation and treatment of this deficiency; however, sharing this knowledge and educating community providers who also treat bariatric patients are essential to avoiding the potentially permanent and devastating results of undiagnosed thiamine deficiency. Baseline conditions may affect this prevalence in different populations. The risk factors of thiamin deficiency and the effect of nutritional support and treatment in such patients should be investigated in future. Currently, multidisciplinary approach in managing obese patients is necessary.

## Declarations

**Ethics Approval** For this type of study, formal consent is not required.

**Informed Consent Statement** N/A

**Conflict of Interest** The authors declare no competing interests.

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