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REVIEW

The Prevalence of Small Intestinal Bacterial Overgrowth After Roux-en-Y Gastric Bypass (RYGB): a Systematic Review and Meta-analysis

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Abstract

We reviewed the literature on the prevalence of small intestinal bacterial overgrowth (SIBO) after Roux-en-Y gastric bypass (RYGB). Eight studies examining 893 patients were included. The mean age of the patients was 48.11 ± 4.89 years. The mean BMI before surgery and at the time of SIBO diagnosis was 44.57 ± 2.89 kg/m^2 and 31.53 ± 2.29 kg/m^2, respectively. Moreover, the results showed a 29% and 53% prevalence of SIBO at < 3-year and > 3-year follow-up after RYGB, respectively. Symptoms included abdominal pain, diarrhea, bloating, nausea, vomiting, constipation, soft stool, frequent defecation, flatulence, rumpling, dumping syndrome, and irritable bowel syndrome. SIBO is prevalent after RYGB; digestive symptoms should prompt the consideration of SIBO as a potential etiology. Antibiotic therapy has proven to be therapeutic.

Keywords Small intestinal bacterial overgrowth · Bacterial overgrowth · Prevalence · Hydrogen breath test · Bariatric surgery · Metabolic surgery · Roux-en-Y gastric bypass · Sleeve gastrectomy · Adjustable gastric band · Biliopancreatic diversion with duodenal switch

Introduction

Obesity is a worldwide public health concern on the rise and is a multifactorial disease that has strongly been linked to metabolic syndromes and cancer. Despite the complexity of this disease, bariatric surgery (BS) has proven to be an effective treatment of obesity and related comorbidities. Different bariatric surgeries have been proposed and fall into three categories: first, hypo-absorptive procedures (Roux-en-Y gastric bypass and one anastomosis gastric bypass); second, malabsorptive procedures (biliopancreatic diversion with duodenal switch, single anastomosis duodenal-ileal bypass with sleeve, etc.); and third, restrictive procedures (sleeve gastrectomy and adjustable gastric band) [1–3].

Hypo-absorptive and malabsorptive bariatric procedures modify the normal anatomy of the digestive tract, may induce intestinal stasis, and promote the development of small intestinal bacterial overgrowth (SIBO) [1, 2]. Restrictive procedures, on the other hand, consist of reducing the stomach size from the greater curvature, wherefore less gastric acid is released; furthermore, a higher likeliness of acid suppression therapy after these procedures may lead to hypochlorhydria, which has been shown to slightly increase the risk for SIBO [4, 5].

SIBO is a heterogeneous pathology defined as an excess of bacteria in the small intestine leading to digestive symptoms such as abdominal pain, nausea, bloating, and diarrhea [4, 6]. SIBO and intestinal microbiota have been associated with various disease conditions, namely, diabetes, hypertension, and obesity. The association between SIBO and obesity has not been quantified. To date, there is no reliable data on

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Key points • SIBO is prevalent in bariatric patients before and after RYGB.
• Digestive symptoms such as diarrhea, nausea, and bloating may be potential etiology for SIBO after RYGB.
• Antibiotic treatments have proven to be therapeutic for SIBO in bariatric patients following RYGB.

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the prevalence of SIBO in the general population or at-risk population groups [4, 7–11].

Data on the prevalence of SIBO after BS are scattered in the literature; meanwhile, complaints of abdominal symptoms have commonly been reported in some patients after BS, especially RYGB. There is limited data exploring the role of SIBO in this increase in digestive symptoms, yet SIBO by itself might be a contributing factor, increasing vitamin deficiencies and affecting weight loss after BS [2, 12–15]. To the best of our knowledge, no study has evaluated available evidence on the prevalence of SIBO after RYGB; therefore, this study is the first.

We aimed to investigate the English language scientific literature on the prevalence of SIBO after RYGB in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.

Material and Methods

This review was conducted in accordance with the guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA) 2015 statement [16]. All stages of literature search, study selection, data extraction, and quality assessment were performed independently by two authors. Any disagreement was resolved by discussion and consensus with a third reviewer (HA). This systematic review and meta-analysis was registered in the Prospective Register of Systematic Reviews (PROSPERO) with the registration ID: CRD42023463028 (available at https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=463028).

Literature Search

A systematic search was performed using an electronic search in PubMed, Google Scholar, and the Cochrane Library. The appropriate key terms and free text field search were performed for "small intestinal bacteria overgrowth," "bacteria overgrowth," "SIBO," "Bariatric surgery," "metabolic surgery," "Roux-en-Y gastric bypass," "gastric bypass," "Sleeve gastrectomy," and "biliopancreatic diversion with duodenal switch." The search included all study designs, with further studies not captured by the search identified via bibliographic cross-referencing. Titles and abstracts were screened independently for full-text review by the two investigators.

Inclusion Criteria

Included studies were limited to adults (18 years) who met the international criteria for bariatric surgery [17], and who underwent a primary Roux-en-Y gastric bypass (RYGB). The initial scope of this review was to investigate the prevalence of SIBO after all types of bariatric and metabolic procedures; given the scarcity of reports of this condition following different procedures but more abundant after RYGB, only studies reporting SIBO after RYGB were included in this systematic review and meta-analysis. Prospective and retrospective observational studies, randomized clinical trials, and non-comparative clinical studies were included. The date ranges from July 2000 and the last search was performed in August 2023.

Exclusion Criteria

Only studies published in English were included in this systematic review and meta-analysis. Abstracts, conference articles, opinion pieces, editorial letters, single case reports, reviews, and meta-analyses were excluded from the final review. Nonhuman studies were not included. Those without appropriate data published related to this study's primary and secondary outcomes were also excluded.

Data Extraction

Data on the included studies (author's name, year of publication, sample size, study design, age, BMI before bariatric surgery and at the time of SIBO diagnosis, number of patients with SIBO, follow-up time, and the results of each study) were recorded. To ensure accuracy, the data extraction process was independently performed by the two investigators and was reviewed by the senior investigator.

Statistical Analysis

Data analysis was performed using the Stata/SE 18.0 software version. The main measure of the effect/effect size was prevalence (ratio of cases to the total population). Cochrane's test (Q-test) showing significant heterogeneity in the meta-analysis and I^2 showing the amount of heterogeneity, ranging from 0 to 100%, were used to assess the heterogeneity among studies. Random-effects meta-analysis was performed to estimate the main index, which was the pooled prevalence at the 95% confidence interval. Forest plots were used to show the pooled prevalence of SIBO at < 3-year and > 3-year follow-ups. Small study publication bias effects were assessed using funnel plot visual inspection and Egger's test. Averages of quantitative variables were reported according to studies and were each weighted by sample size (N). A statistician was consulted for the statistical analysis and results were independently reviewed by the senior investigator to ensure validity.

Results

A total of 173 studies were retrieved by the initial literature search. An additional two studies were located through a manual search of the bibliography cross-referencing. After screening the study's titles and abstracts, 47 studies qualified for further analysis. Thirty studies were duplicates, and five studies were in other languages than English, therefore removed. Eight studies met the final inclusion criteria. The included studies were retrospective/prospective cohorts, matched cohorts, prospective randomized double-blinded, and observational randomized analytical cross-sectional studies. Moreover, in one study, the follow-up time was not determined; therefore, the data of this study was included in the descriptive analysis but not in the meta-analysis (Fig. 1; Table 1) [18].

Descriptive Characteristics

A total of 893 patients were included in this review and meta-analysis. The mean age of the patients was 48.11 ± 4.89 years. The mean BMI before surgery and at the time of SIBO diagnosis was 44.57 ± 2.89 kg/m^2 and 31.53 ± 2.29 kg/m^2, respectively. The characteristics of the patients included in this review are shown in Table 1.

Treatment and Symptoms

RYGB was used for the treatment of obesity and related comorbidities in all patients included in this review. Digestive symptoms reported during the follow-up period included abdominal pain, diarrhea, bloating, nausea, vomiting, constipation, soft stool, frequent defecation, flatulence, rumpling, dumping syndrome, irritable bowel syndrome, hair loss, scleroderma, and diabetes (Table 2).

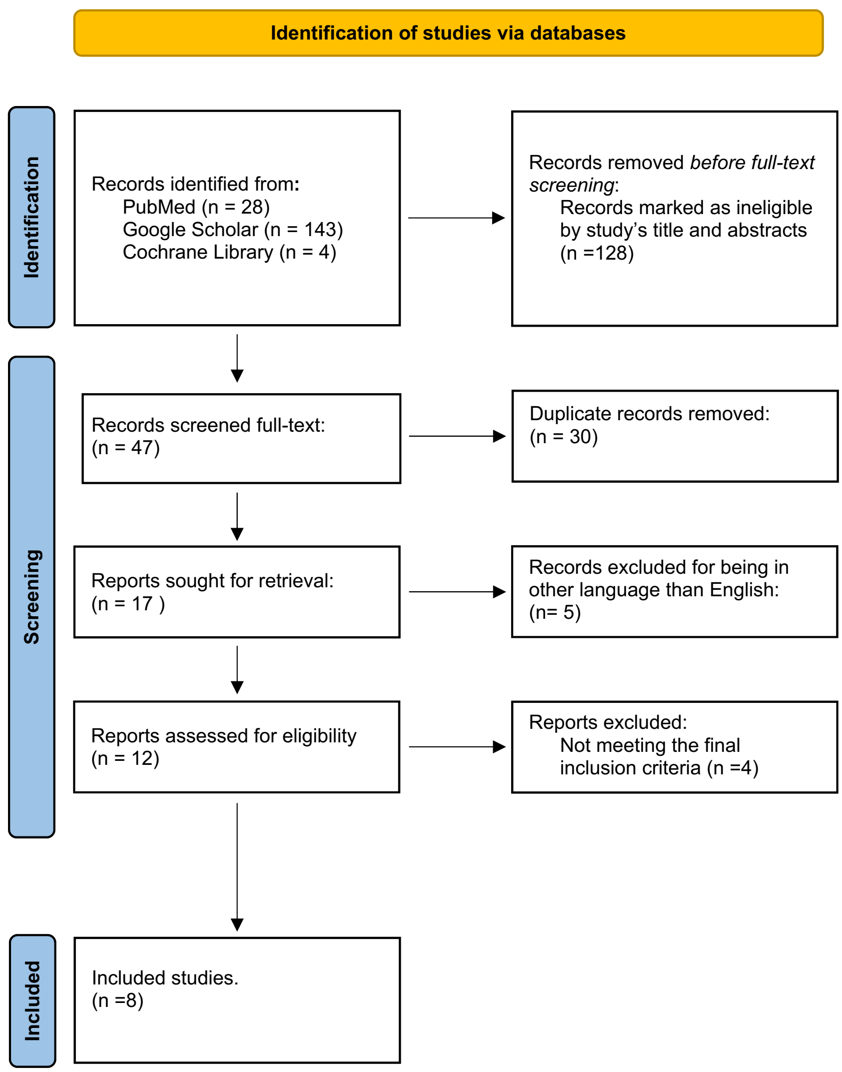

Fig. 1 PRISMA flowchart of literature search and data extraction and selection (*n* represents the number of articles included)

Prevalence of SIBO at < 3-Year Follow-up

Pooled estimation of meta-analysis of prevalence from three studies reported a prevalence of 29%; i.e., suggesting that 29 out of every 100 RYGB surgeries experience SIBO at < 3-year follow-up. The heterogeneity index is $I^2 = 94.45\%$ (Fig. 2).

Prevalence of SIBO at > 3-Year Follow-up

Pooled estimation of meta-analysis of prevalence from four studies reported a prevalence of 53%; i.e., indicating that 53 out of every 100 RYGB surgeries experience SIBO at > 3-year follow-up. The heterogeneity index is $I^2 = 98.89\%$ (Fig. 3).

Publication Bias

The results of the analysis showed that there was no significant influence on the creation of negative results. Since there were few studies, it was not easy to judge the symmetry of the funnel plot. Meanwhile, no evidence of publication bias was detected using Egger's test (Egger's test $t = 1.85$, $P = 0.12$, 95% CI − 11.31 to − 6.11) (Fig. 4).

Discussion

An association between SIBO and obesity has been reported with conflicting results. A previous study investigating the prevalence of SIBO in patients with obesity using the hydrogen

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

Author	Year	Study design	*N*	Age (years)	Pre-op BMI (mean ± SD, kg/m^2)	Post-op BMI (mean ± SD, kg/m^2)	< 3-year SIBO, *N*	> 3-year SIBO, *N*
Shah et al. [37]	2013	Prospective	151	50	42.8	-	-	9
Andalib et al. [24]	2015	retrospective	63	49	-	35 ± 10	-	51
Sabate et al. [2]	2017	Prospective	65	39.6 ± 11.7	45.7 ± 6.3	-	26	-
Jirapinyo et al. [26]	2019	Retrospective	151	54 ± 11	48.1 ± 9.4	32.6 ± 7.8	-	69
Wagner et al. [29]	2020	Prospective, randomized double-blinded	73	43.3 ± 10.5	42.8	-	4	-
Mouillot et al. [6]	2020	Retrospective cohort	63	48.5 ± 36	-	28.1 ± 4.7	-	63
Dolan et al. [18]	2020	Matched cohort	271	54.6 ± 08	-	30.6 ± 1.0	199 (follow-up time not specified)	
Novljan et al. [23]	2022	Observational randomized analytical cross-sectional	56	49.54 ± 9.99	-	30.98 ± 6.55	24	-

Table 2 Treatment and symptoms reported in studies

Author	Surgery types	Mean interval time of diagnosis in months (ranges) from the time of surgery	Symptoms
Shah et al. [37]	RYGB	57	Constipation
Andalib et al. [24]	RYGB	65 (6–228)	-
Sabate et al. [2]	RYGB, AGB	19.45 (9.2–36)	Diarrhea, constipation, abdominal pain, rumbling, dumping syndrome, vomiting/regurgitation
Jirapinyo et al. [26]	RYGB	96	Abdominal pain, bloating, constipation, diarrhea, gas/flatulence
Wagner et al. [29]	RYGB	3	Abdominal pain, soft stools, nausea
Mouillot et al. [6]	RYGB, SG, OAGB	40	Diarrhea, abdominal pain, bloating
Dolan et al. [18]	RYGB	-	Nausea, vomiting, bloating, diarrhea
Novljan et al. [23]	RYGB, OAGB	26.98 (2–108)	Frequent defecation, scleroderma, irritable bowel syndrome, diabetes

RYGB, Roux-en-Y gastric bypass; *AGB*, adjustable gastric band; *SG*, sleeve gastrectomy; *OAGB*, one anastomosis gastric bypass

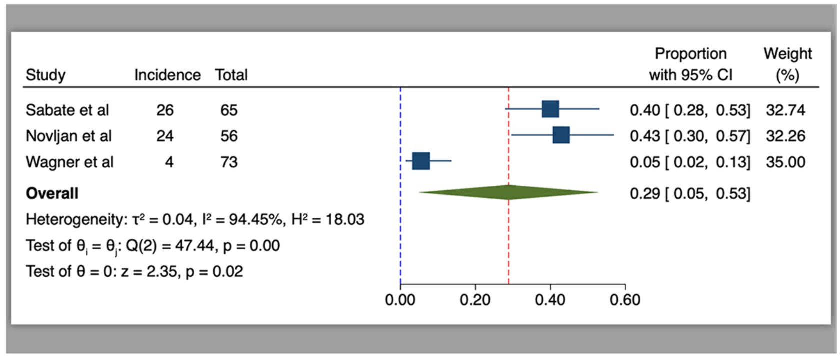

Fig. 2 Forest plot showing the prevalence of SIBO at < 3 years follow-up

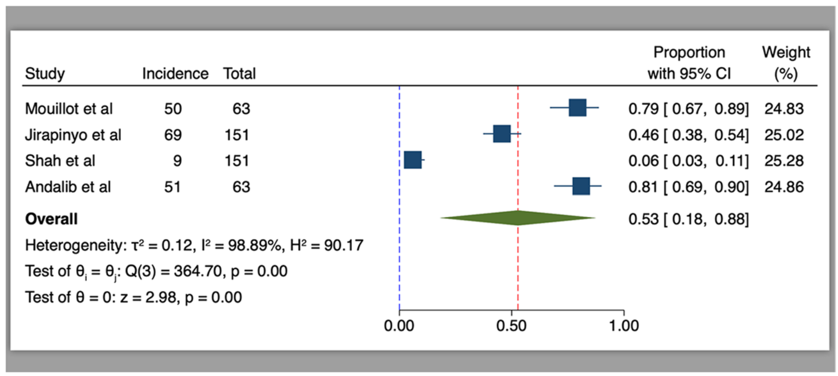

Fig. 3 Forest plot showing the prevalence of SIBO at > 3 years follow-up

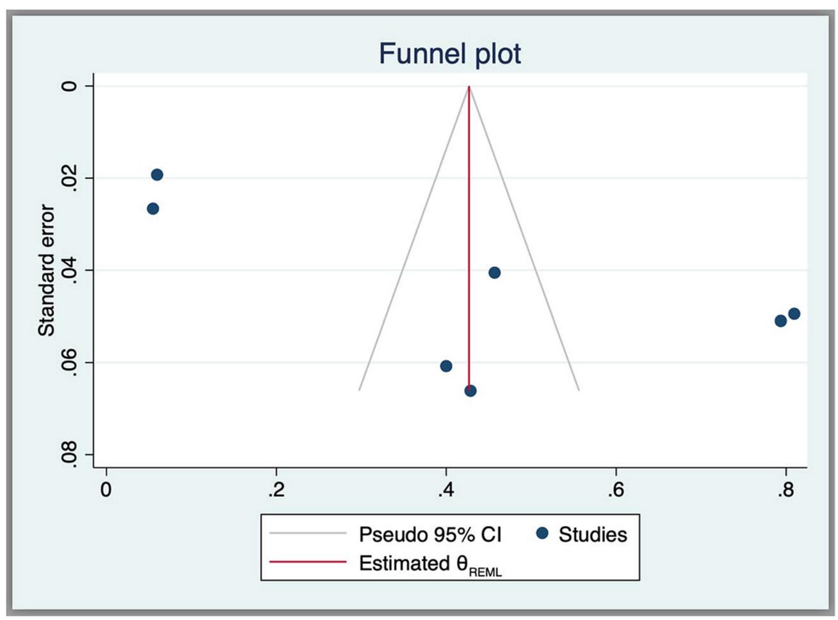

Fig. 4 Bias publication assessment in the funnel plot

breath test found 89% of SIBO in their studied population [4, 5, 19]. A link between SIBO and high BMI, body fat, and pro-inflammatory cytokines has been shown in subjects with obesity before BS, although this could secondarily be due to small intestinal motility disorders [2, 7, 20, 21]. To a certain extent, these reports beg the question of the implication of preoperative SIBO in patients with obesity on its occurrence after BS.

The prevalence of SIBO was investigated by Sabate et al. in 378 patients with obesity before undergoing BS; the authors of the study reported 55 (15.4%) patients who tested positive after the hydrogen breath test from the overall studied population. After surgery in the RYGB group, 26 out of 65 (40%) patients were found with SIBO at a median postoperative follow-up of 9.2 months [2]. Kaniel et al.

recorded 0% of SIBO preoperatively, at the median follow-up of 6 months; 37.0% of patients presented with SIBO after OAGB, indicating an independent implication of BS on the occurrence of SIBO [22].

An association between RYGB and a higher incidence of SIBO has been demonstrated [18, 23]; Sabate et al. found a higher incidence of SIBO associated with RYGB than in patients who underwent the AGB, where no difference was noted between pre- and postoperative occurrence of SIBO [2]; moreover, in a study conducted by Mouillot et al., the incidence of SIBO was compared after three different bariatric procedures (RYGB, OAGB, SG). In their study, the incidence of SIBO did not significantly differ in terms of the type of BS that the patients underwent [6]. Based on the current literature on the prevalence of SIBO, most studies are concerned with subjects after RYGB due to the modification of the digestive tract after this procedure which may predispose them to SIBO. The effect of other BS on the incidence of SIBO has not been explored (Table 2), yet they have been shown to potentially play a role in the occurrence of SIBO [6, 18].

SIBO is a heterogenous pathology that may lead to digestive symptoms, and few studies have reported a higher incidence of SIBO in patients presenting with digestive symptoms [6, 18, 24]. Although RYGB has been shown to improve gastroesophageal symptoms, digestive symptoms have commonly been reported after this procedure. A study analyzing the gastrointestinal quality of life index (GIQLI) in 86 patients after BS found that patients' quality of life in terms of digestive symptoms worsened following RYGB [25]. In all included studies in this review, the presence of digestive symptoms was consistent with SIBO after RYGB but was nonspecific requiring a breath test or aspiration of intestinal fluid to confirm the diagnosis of bacterial overgrowth. The lack of specificity of digestive symptoms could be in part due to a high opiate use that may contribute to symptoms like nausea, diarrhea, and delayed oral-cecal transit time (OCTT) after RYGB [18]. However, it may be reasonable to recommend a routine workup for SIBO in patients with a history of RYGB, in the context of abdominal symptoms [22].

The golden standard method for the diagnosis of SIBO has been through the quantitative bacterial culture derived from jejunal or duodenal aspiration fluid, with a total growth of $> 10^5$ colony-forming units/mL of intestinal fluids for at least 48 h considered positive for SIBO. Due to the difficulties in obtaining cultures, various breath tests including glucose H_2, and lactulose breath tests have been suggested [11]. According to the 2017 North American consensus, the glucose breath test is a useful, inexpensive, safe, and noninvasive diagnostic test for SIBO [6, 26]. The glucose and lactulose breath tests were the common methods used for the diagnosis of SIBO in all included studies; however, breath testing methods can be problematic after RYGB given the rapid transit through the small bowel of glucose or lactulose, reaching the colon and initiating fermentation by colonic bacteria, leading to an early rise in breath hydrogen that might be falsely attributed to bacteria in the small intestine [18, 27]. Moreover, glucose dosage for the breath test differed in studies ranging from 25 to 75 g of glucose. The protocol by Gasbarrini et al. suggested offering 50 g of glucose for the diagnosis of SIBO after RYGB [11]; a further recommendation was to reduce the amount of glucose offered to avoid the development of dumping syndrome. Although such a difference in glucose dosage could influence the sensitivity of the test, it would not compromise its specificity [28–30].

The use of PPI has been associated with SIBO, and the risk of occurrence has particularly been found to be higher after PPI treatment for more than 12 months. A meta-analysis analyzing the effect of PPI treatment on the incidence of SIBO found that patients being treated with PPI were at a significantly higher risk for developing SIBO with an odds ratio of 2.289 (95%CI, 1.238–4.205) [6, 31]. In a previous study by Mouillot et al., bariatric patients treated with PPI were associated with a higher incidence of SIBO on an average follow-up of 40 months regardless of the type of BS [6]. Thereaux et al. showed that one out of four patients who underwent BS remained treated with PPI until 4 years, especially following restrictive bariatric procedures, suggesting that these patients might be at a high risk for developing SIBO [5]. The influence of PPI use in combination with restrictive bariatric procedures on the incidence of SIBO has not been demonstrated; more studies are needed to elucidate possible adverse effects of PPI use after restrictive BS in the context of SIBO.

Vitamin deficiencies have been associated with SIBO, especially vitamin B_{12}, fat-soluble vitamins, and excessive folate levels [22, 27, 32]. The adverse nutritional deficiencies of SIBO can be multifactorial. In patients with SIBO, due to a competitive uptake of vitamin B_{12} by aerobes bacteria, vitamin B_{12} deficiency may occur as a result [33]. In the case of fat-soluble vitamins, bacteria overgrowth may lead to bacterial deconjugation of the bile salts which are reabsorbed in the jejunum rather than the ileum and cause fat malabsorption, thus deficiencies in fat-soluble vitamins [34, 35]. These deficiencies could also in part be associated with diminished food intake due to digestive symptoms after surgery [36]. Excessive folate may be explained by increased synthesis of folate by bacteria in the small bowel [37–39].

Antibiotic therapy has been shown to effectively treat and improve digestive symptoms in bariatric patients diagnosed with SIBO after surgery and in the general population; up to this date, there is no consensus on the choice, dosage, and duration of antibiotic therapy for SIBO; therefore, different therapies have been tested. In a previous study of bariatric patients who tested positive for SIBO following RYGB, 43 (59%) out of 73 patients reported symptom improvement after 3 months of antibiotic therapy; patients treated with oral gentamicin in combination with metronidazole therapy showed a therapeutic efficacy of 62% compared to those treated with sequential monotherapy with oral metronidazole with 42% in treating SIBO with no statistically significant difference in the therapeutic efficacy [6]. Similar findings were presented by Jirapinyo et al. whereby the antibiotic treatment showed symptom improvement in 78% of patients [27]. In the general population, antibiotic therapy has proven to be effective in the treatment of SIBO. A meta-analysis comparing the efficacy of different antibiotic therapies found that the monotherapy of rifaximin had a hydrogen breath test normalization rate of 49.5% and metronidazole with a normalization rate of 51.2% [40]. Malchior et al. found that 67% of patients treated with metronidazole for SIBO experienced symptom improvement, compared with 25% of those treated with carbosylane for 10 days [41]. However, in one study, a recurrence of digestive symptoms for SIBO was reported in 32.4% of patients at 9 months after successful antibiotic therapy; given the diversity of intestinal microbial species, broad-spectrum antibiotic therapy may be favored [42, 43].

Although this study was the first to report the most current prevalence of SIBO after RYGB, there were a few limitations worth mentioning. First, most reported outcomes were retrieved from prospective or retrospective studies, which might interfere with concluding reliable results and limit our understanding of the prevalence of SIBO after RYGB. Second, the small number of included studies with small sample sizes might have impacted the between-study heterogeneity and the final results. Third, the incidence of SIBO was not evaluated before BS in quite a lot of studies, as its known in patients with morbid obesity the prevalence of SIBO is higher than in healthy populations.

Conclusion

The prevalence of SIBO is significantly high following RYGB; digestive symptoms such as nausea, vomiting, and diarrhea which are common after this procedure should prompt the consideration of SIBO as a potential etiology. Antibiotic treatments, namely, metronidazole, gentamicin, and rifaximin, have proven to be therapeutic in bariatric patients following RYGB and in the general population; however, the choice and dosage of antibiotic medications are still not determined. Given the inherent limitations of the study's design and sample sizes, these results should be interpreted with care. Future large-sized RCTs are required to fully understand the prevalence of SIBO following RYGB, treatment, and the possible incidence of this condition after different types of BS.

Declarations

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

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

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