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CLINICAL ARTICLE

Gynecology

High prevalence of small intestinal bacterial overgrowth and intestinal methanogen overgrowth in endometriosis patients: A case–control study

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Abstract

Objective: The purpose of this study is to raise awareness of small intestinal bacterial overgrowth (SIBO) and intestinal methanogen overgrowth (IMO) prevalence among patients with endometriosis to improve global recommendations in the standard of care for endometriosis.

Methods: This case–control study included a cohort of 1027 women who underwent the lactulose breath test (LBT) during their healthcare check-up to diagnose SIBO and/or IMO from November 2021 to June 2023. One hundred and forty-eight endometriosis patients were selected based on magnetic resonance imaging or a histological assessment. Each were matched with an equal number of women without endometriosis based on the exact age.

Results: SIBO/IMO prevalence was significantly higher among women with endometriosis, with up to 136 out of 148 who tested positive, 91.9% (95% confidence interval [CI] 86.3–95.7%) against 123 in the control group, 83.1% [76.1–88.8%], $P=0.0223$. Women with endometriosis showed a significantly higher incidence of altered transit than those without (85.8 vs. 71%, $P=0.0019$) and an increased prevalence of constipation (67.8 vs. 44.7%, $P=0.0017$) and dizziness (44.8 vs. 28.7%, $P=0.0245$). Overall, methane overgrowth accounted for up to 63.2% in women with endometriosis who tested positive for methane overgrowth. SIBO H2 was associated with a higher risk of developing diarrhea ($P=0.0027$), whereas those positive for IMO were at a higher risk of developing acid reflux ($P=0.0132$).

Conclusion: Abnormal digestive overgrowth should be assessed in all endometriosis cases, as this approach could offer a new therapeutic strategy.

KEYWORDS

bowel endometriosis, breath tracker, endometriosis, intestinal methanogen overgrowth (IMO), lactulose breath test, small intestinal bacterial overgrowth (SIBO)

1 | INTRODUCTION

Endometriosis is a chronic "estrogen-dependent inflammatory disease" characterized by the growth of endometrial tissue outside the uterine cavity. It is the most common cause of chronic pelvic pain and infertility in reproductive age women and is classified into four stages depending on the extent of the implants, their location (restricted to eutopic [intrauterine] endometrium or ectopic endometriotic tissue), and the presence and severity of cysts and adhesions. While symptoms such as dysmenorrhea, pelvic pain with intercourse, and fertility problems primarily affect the gynecological ecosystem, endometrial tissue might also grow in the surrounding tissues, resulting in a wider range of symptoms, including bowel movements or urination disorders.[1] Approximately 3.8%–37.0% of women with endometriosis have bowel endometriosis, also referred to as an endo belly.[2,3]

Bowel lesions in women with endometriosis are usually localized in the distal colon, often involving the sigmoid, rectum, and small bowel, eventually causing digestive dysfunction, symptoms, and/or stenosis in severe cases.[4–6]

Owing to inflammation and the presence of endometrial tissues or lesions in the abdominal cavity, women with bowel endometriosis often present with a distended or bloated abdomen (feeling of fullness and swelling in the abdominal area), bowel-related symptoms such as diarrhea, constipation, dyschezia, and, in rare cases, bowel obstruction. The exact cause of bowel endometriosis is not fully understood; however, hormonal imbalances, inflammation, and digestive dysfunction are believed to contribute to its development of this condition.[7,8] Gut microbiome dysbiosis can lead to functional gastrointestinal disorders such as irritable bowel syndrome (IBS) and functional dyspepsia (FD).[9] Studies have reported that bacterial overload in the gut, a type of microbiome dysbiosis, can manifest in the development of small intestinal bacterial overgrowth (SIBO) and intestinal methanogen overgrowth (IMO). Thus, SIBO/IMO and bowel endometriosis might have overlapping gastrointestinal symptoms such as constipation, diarrhea, fullness, bloating, flatulence, abdominal pain, discomfort, and weight loss. SIBO/IMO might occur simultaneously with other gastrointestinal disorders and with relatively nonspecific symptoms. Therefore, determining the influence of SIBO/IMO on the patient's symptomatology is often difficult, especially when it is diagnosed concurrently with pre-existing pathologies or health conditions.[10,11]

To date, endometriosis remains largely an underdiagnosed condition owing to a lack of knowledge and global guidelines for clinicians. Ongoing inflammation, adherence, digestive motility alterations, gut microbiota dysbiosis, and psychopathological comorbidities such as anxiety and depression are frequently associated with endometriosis.[5,7,12–15] All these are known risk factors for SIBO or IMO, suggesting that microbial overgrowth could be a condition worth considering in the management of endometriosis.[16] There are currently no clear epidemiological data that can evaluate the true prevalence of SIBO/IMO in human populations, but numerous studies have shown a high prevalence of overgrowth concomitant with one or several diseases.[17–19] Accordingly, SIBO/IMO appears to be a direct or indirect consequence of a myriad of diseases that affect our physiology, eventually leading to aberrant overgrowth.[20–23]

To date, the association between endometriosis and SIBO/IMO remains poorly understood, as little to no literature exists regarding the prevalence of these microbial overgrowths in women with this gynecological condition. In this study, we examined a cohort of women diagnosed with endometriosis who underwent a breath test (BT) during their medical care for diagnosis of SIBO/IMO, which could be contributing to their symptoms, and analyzed whether it directly or indirectly affected their endometriosis status. This article aims to raise awareness of SIBO/IMO prevalence among patients with endometriosis to improve global recommendations in the standard of care for endometriosis and to propose alternative therapies in the management of its symptoms.

2 | PATIENTS AND METHODS

This case–control study included a cohort of 1027 women from November 2021 to June 2023 who came to the laboratory (Alphabio-Biogroup, Marseille, France) to investigate unexplained digestive symptoms. All participants underwent hydrogen/methane lactulose or glucose BT (LBT or GBT, respectively) during their healthcare check-up for diagnosis of SIBO/IMO. Among the 1027 women identified, a search for women diagnosed with endometriosis was performed at first in the self-report questionnaire and validated afterward when medical records could confirm the diagnosis with either magnetic resonance imaging (MRI) or a histological assessment following coelioscopic surgery. Eventually, a total of 149 (14.5%) women with endometriosis were included. Among those women, MRI exam and histological assessment revealed an endometriosis status classified stage 1 for 33.6%, stage 2 for 21.5%, stage 3 for 9.4%, and stage 4 for 35.5%. These patients with endometriosis were age-matched with the remaining 878 patients without endometriosis in a 1:1 ratio: matching was performed using a greedy algorithm based on perfect age-matching.[24] Overall, two groups of 148 patients (296 patients overall) were considered for future analyses (one patient with endometriosis was not matched with patients without endometriosis) (Figure 1). Being a real-life cohort, the women studied sometimes reported having one or more pathologies already diagnosed with or without endometriosis. Hence, to limit the impact of pathologies other than endometriosis, distinct subgroups were compared to better assess the correlation between SIBO/IMO and endometriosis.

Most SIBO/IMO tests were performed using lactulose (98%, $n = 290$). These tests were performed in a French laboratory with the Breath Tracker SC (Quintron Instrument Company, Inc. New Berlin, WI) during the study period (FDA Registered # 2124914; ISO 13485 Certified, MDSAP 671378 FM 671377).[25] H2 and CH4 measures were interpreted as previously described by Plauzolles et al.[26] using the North American Consensus as a reference.[27] Patients with and without endometriosis were compared based on the BT results and

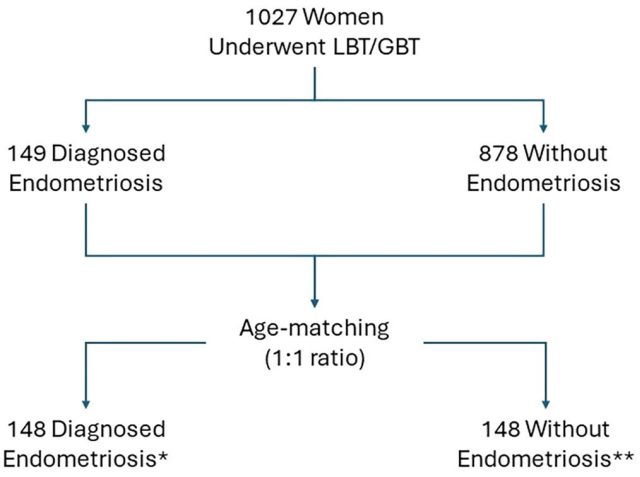

FIGURE 1 Study flowchart. †LBT/GBT: Lactulose breath test/glucose breath test. *One patient with endometriosis was not age-matched to a non-endometriosis patient. **730 patients with endometriosis were not age-matched to endometriosis patients.

clinical information collected through a self-report questionnaire. The questionnaire was provided on the day the patient was tested, and collected information regarding patient characteristics, including age, weight, height, and medical history, as well as current symptoms, including digestive, and extradigestive symptoms (Table 1).

First, a comparative study between the two groups of patients was performed to identify the prevalence of SIBO and/or IMO in patients with and without endometriosis among the included 296 patients (mean age 38.5 years, standard deviation [SD] 11.1) (Table 1). Second, SIBO types were correlated with the prevalence of symptoms in both groups to characterize the presence of these overgrowths among women with endometriosis.

2.1 | Statistical analyses

Data are reported as mean (SD) or frequency (%) according to their type. χ^2-tests, Fisher's exact test, or the Cochran Mantel Haenszel test were used to compare qualitative data, and Student's *t*-test or Wilcoxon test was used to compare quantitative data according to the type.

First, SIBO/IMO rates in patients with and without endometriosis were compared. Second, the SIBO/IMO groups were compared for presence of H_2, CH_4, or mixed H_2/CH_4- in the breath. Multivariate logistic regression was used to distinguish the effects of the groups. Only variables with $P<0.05$ on univariate analysis were included in THE multivariate model. *P*-values were adjusted using the Bonferroni method to account for multiple comparisons. Statistical significance was set at $\alpha<0.05$, unless otherwise indicated. Statistical outcomes, including *P*-values, odds ratios (OR), and confidence intervals (95% CIs), were reported in the appropriate contexts. The statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3 | RESULTS

3.1 | Characteristics of patients

A total of 148 women with endometriosis were age matched with 148 women without endometriosis. Each patient underwent at least one BT in the laboratory during the study period. Among the 148 women with endometriosis, 136 (91.9%, [95% CI 86.3–95.7%]) were diagnosed with SIBO H_2 and/or IMO, compared to 123 (83.1%, [95% CI 76.1–88.8%]) among the 148 without endometriosis. Thus, the prevalence of SIBO/IMO was significantly higher in the patients with endometriosis ($P=0.022$) (Figure 2). Being a real-life cohort, the women studied sometimes reported having one or more pathologies already diagnosed in addition to endometriosis. Hence, to eliminate the effects of coexisting pathologies, a subgroup analysis was performed to examine SIBO/IMO prevalence among women with endometriosis only ($n=88$) compared to women without endometriosis and any other diagnosed condition or pathology ($n=94$). The comparison showed an even greater prevalence of SIBO/IMO in women with endometriosis than in women without endometriosis or any other coexisting pathology: 83/88 (94.3% [95% CI 87.2–98.1%]) vs. 75/94 (79.8% [95% CI 70.3–87.4%]), $P=0.004$.

The recorded symptoms significantly differed between the two groups. Regarding digestive symptoms, women with endometriosis showed a significantly higher prevalence of altered transit than women without endometriosis: 127 (85.8%) vs. 105 (71.0%), ($P=0.002$) (Table 1). Hence, constipation (88 [59.9%] vs. 73 [49.3%], $P=0.069$) and diarrhea (82 [55.8%] vs. 67 [45.3%] $P=0.071$) was observed to be more prevalent in women with endometriosis but did not reach statistical significance. Regarding extradigestive symptoms, a higher prevalence of headache (82 [55.8%] vs. 64 [43.2%], $P=0.031$), fatigue (131 [89.1%] vs. 118 [79.7%], $P=0.026$) and dizziness (69 [46.9%] vs. 51 [34.5%], $P=0.029$) was reported in patients with endometriosis. Multivariate analysis confirmed altered transit as an independent factor in patients with endometriosis: OR 2.30 (95% CI 1.26–4.21), $P=0.007$.

In the subgroup analysis, as previously described, altered transit was significantly higher in women with endometriosis (76 [86.4%] vs. 65 [69.1%], $P=0.006$), and symptoms such as constipation (59 [67.8%] vs. 42 [44.7%], $P=0.002$) and dizziness (39 [44.8%] vs. 27 [28.7%], $P=0.025$) were reported to have a significantly higher prevalence in women with endometriosis (Table 2). Multivariate analysis confirmed dizziness in patients with endometriosis: OR 2.04 (95% CI 1.06–3.95), $P=0.034$.

3.2 | SIBO types in endometriosis

Regardless of the endometriosis status, SIBO H_2/CH_4 is the most prevalent SIBO type in our cohort (128; 49.4%), followed by SIBO H_2 (90; 34.8%), and SIBO CH_4 also referred to as IMO (41; 15.8%). Methane overgrowth, including IMO only ($n=17/136$) and SIBO H_2/CH_4 ($n=69/136$), was highly prevalent in women with endometriosis,

TABLE 1 Breath test, demographic, and symptoms data according to endometriosis diagnosis.

Characteristics	Overall breath tests (*N* = 296)	Univariate analysis			Multivariate analysis	
		Breath tests in patients without endometriosis (*N* = 148)	Breath tests in patients with endometriosis (*N* = 148)	*P* (Endometriosis vs. others)	Odds ratio (95% CI)	*P*
Age (years)—Mean (SD)	38.5 (11.1)	38.5 (11.1)	38.4 (11.1)	1.000	-	-
BMI (kg/m^2)—Mean (SD)	22.8 (4.6)	22.9 (5.1)	22.6 (4.1)	0.933	-	-
Sugar intake—*N* (%)				1.000		
Glucose	6 (2.0%)	3 (2.0%)	3 (2.0%)		-	-
Lactulose	290 (98.0%)	145 (98.0%)	145 (98.0%)			
Transit type—*N* (%)				0.002		
Normal	64 (21.6%)	43 (29.1%)	21 (14.2%)		1.00	-
Altered	232 (78.4%)	105 (71.0%)	127 (85.8%)		2.30 (1.26–4.21)	0.007
Digestive symptoms—*N* (%)						
Bloating	248 (84.1%)	124 (83.8%)	124 (83.8%)	1.000	-	-
Gas	249 (84.4%)	124 (83.8%)	125 (85.0%)	0.767	-	-
Constipation	161 (54.6%)	73 (49.3%)	88 (59.9%)	0.069	-	-
Diarrhea	149 (50.5%)	67 (45.3%)	82 (55.8%)	0.071	-	-
Nausea	121 (41.0%)	56 (37.8%)	65 (44.2%)	0.265	-	-
Overflow	197 (66.8%)	102 (68.9%)	95 (64.6%)	0.434	-	-
Abdominal pain	219 (74.2%)	106 (71.6%)	113 (76.9%)	0.303	-	-
Acid reflux	132 (44.8%)	65 (43.9%)	67 (45.6%)	0.774	-	-
Irregular transit	146 (49.7%)	73 (49.3%)	73 (50.0% of 146)	0.908	-	-
Food intolerance	122 (41.4%)	57 (38.5%)	65 (44.2% of 147)	0.320	-	-
Other type of symptoms—*N* (%)						
Headache	146 (49.5%)	64 (43.2%)	82 (55.8%)	0.031	1.29 (0.78–2.14)	0.322
Fatigue	249 (84.4%)	118 (79.7%)	131 (89.1%)	0.026	1.59 (0.78–3.23)	0.202
Mental fog	153 (51.9%)	74 (50.0%)	79 (53.7%)	0.520	-	-
Anxiety	150 (50.9%)	77 (52.0%)	73 (49.7%)	0.684	-	-
Dizziness	120 (40.7%)	51 (34.5%)	69 (46.9%)	0.029	1.24 (0.73–2.10)-	0.420
Articular pain	126 (42.7%)	56 (37.8%)	70 (47.6%)	0.090	-	-
Skin problems	115 (39.0%)	61 (41.2%)	54 (36.7%)	0.430	-	-
Other symptoms	47 (15.9%)	26 (17.6%)	21 (14.3%)	0.441		-
SIBO type—*N* (%)				0.054		
CH4	41 (13.9%)	24 (16.2%)	17 (11.5%)		-	-
H2+	90 (30.4%)	40 (27.0%)	50 (33.8%)			
DUAL (CH4/H2+)	128 (43.2%)	59 (39.9%)	69 (46.6%)			
Negative	37 (12.5%)	25 (16.7%)	12 (8.1%)			
Patients without pathology—*N* (%)	182 (61.5%)	94 (63.5%)	88 (59.5%)	0.474	-	-

Abbreviations: BMI, body mass index; SD, standard deviation; SIBO, small intestinal bacterial overgrowth.

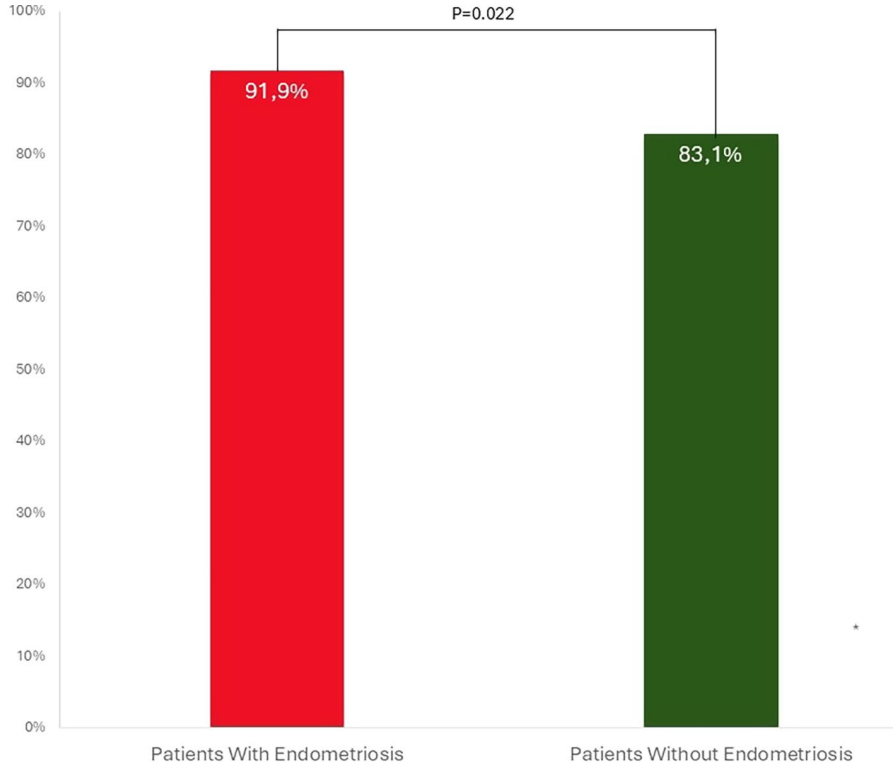

FIGURE 2 Prevalence of SIBO/IMO among women with and without endometriosis. Intestinal methanogen overgrowth (IMO); SIBO, small intestinal bacterial overgrowth.

accounting for up to 63.2% of women with endometriosis who were positive for overgrowth. Women with endometriosis who were positive for SIBO H_2, were at a higher risk of developing diarrhea ($P=0.003$), whereas those positive for IMO were at a higher risk of developing acid reflux ($P=0.013$) (Table S1). In this subgroup, similar correlations were observed between diarrhea and H_2 ($P=0.005$) and between acid reflux and CH_4 ($P=0.024$). However, eliminating the effects of coexisting pathologies revealed a significantly higher risk of nausea in women with endometriosis who were positive for IMO. When comparing CH_4 overgrowth (SIBO CH_4 and H_2/CH_4) with H_2 overgrowth only, there was a higher risk of diarrhea ($P=0.002$) and food intolerance ($P=0.041$) when endometriosis cases were diagnosed using SIBO H_2 only (Table S2). In the subgroup analysis, the correlation between diarrhea and H_2 remained significant ($P=0.002$) (Table S3).

4 | DISCUSSION

To the best of our knowledge, this is the first case–control study to report that 91.9% of women with endometriosis who self-report digestive symptoms present with a positive BT for SIBO, IMO, or both. Endometriosis-related digestive tract disease has been reported in approximately 50% of symptomatic patients with endometriosis, with bowel endometriosis accounting for 3.8% to 37% of cases.[2,28–30] In this cohort, >85% of endometriosis cases reported having an altered transit, with the majority presenting with additional digestive symptoms, such as bloating, gas, abdominal pain, nausea, constipation, and diarrhea. All of these are recognized bowel endometriosis symptoms that overlap with the clinical signs and symptoms of SIBO/IMO.

Gut dysbiosis and abnormal overgrowth, such as SIBO and IMO, can affect physiology in many aspects of life, primarily involving digestive and extra-digestive symptoms. Interestingly, in this study, the prevalence of extradigestive symptoms such as headache (82 [55.8%] vs. 64 [43.2%], $P=0.031$), fatigue (131 [89.1%] vs. 118 [79.7%], $P=0.026$), and dizziness (69 [46.9%] vs. 51 [34.5%], $P=0.029$) was significantly higher in women with endometriosis who tested positive for SIBO and/or IMO than in those without endometriosis. Incidence of constipation (59 [67.8%] vs. 42 [44.7%], $P=0.002$) and dizziness (39 [44.8%] vs. 27 [28.7%], $P=0.025$) remained significantly higher in women with endometriosis, thus confirming the combined effect of coexisting SIBO/IMO and endometriosis on women's health. Interestingly, methane overgrowth was highly prevalent in women with endometriosis, accounting for up to 63.2% of women with endometriosis who tested positive for methane overgrowth. A comparison of the different SIBO types diagnosed in women with endometriosis revealed a correlation between diarrhea and H_2 ($P=0.002$) and between acid reflux and CH_4 ($P=0.024$).

The multifactorial nature of endometriosis and the overlap of symptoms with other pathologies can often delay diagnosis by

TABLE 2 Breath test, demographic, and symptoms data according to endometriosis diagnosis and excluding other pathology.

		Univariate analysis			Multivariate analysis	
Characteristics—excluding other pathology	**Overall breath tests (*N* = 182)**	**Breath tests in patients without endometriosis (*N* = 94)**	**Breath tests in patients with endometriosis (*N* = 88)**	***P***	**Odds ratio (95% CI)**	***P***
Age (years)—Mean (SD)	37.6 (11.2)	37.2 (11.2)	38.0 (11.2)	0.667	-	-
BMI (kg/m^2)—Mean (SD)	22.0 (3.9)	22.4 (4.7)	21.6 (2.8)	0.762	-	-
Sugar intake—*N* (%)				0.674		
Glucose	5 (2.8%)	2 (2.1%)	3 (3.4%)		-	-
Lactulose	177 (97.2%)	92 (97.9%)	85 (96.6%)			
Transit type—*N* (%)				0.006		
Normal	41 (22.5%)	29 (30.9%)	12 (13.6%)		1.00	-
Altered	141 (77.5%)	65 (69.1%)	76 (86.4%)		1.96 (0.85–4.55)	0.117
Digestive symptoms—*N* (%)						
Bloating	*N* = 181	84 (89.4%)	*N* = 87	0.674	-	-
Gas	160 (88.4%)	81 (86.2%)	76 (87.4%)	0.526	-	-
Constipation	153 (84.5%)	42 (44.7%)	72 (82.8%)	0.002	2.04 (1.06–3.95)	0.054
Diarrhea	101 (55.8%)	40 (42.6%)	59 (67.8%)	0.217	-	-
Nausea	85 (47.0%)	32 (34.0%)	45 (51.7%)	0.700	-	-
Overflow	64 (35.4%)	65 (69.2%)	32 (36.8%)	0.847	-	-
Abdominal pain	124 (68.5%)	66 (70.2%)	59 (67.8%)	0.393	-	-
Acid reflux	132 (72.9%)	33 (35.1%)	66 (75.9%)	0.238	-	-
Irregular transit	71 (39.2%)	47 (50.0%)	38 (43.7%)	0.938	-	-
Food intolerance	91 (50.3%)	35 (37.2%)	44 (50.6%)	0.377	-	-
	73 (40.3%)		38 (43.7%)			
Other type of symptoms—*N* (%)						
Headache	*N* = 181	37 (39.4%)	*N* = 87	0.130	-	-
Fatigue	81 (44.8%)	72 (76.6%)	44 (50.6%)	0.218	-	-
Mental fog	145 (80.1%)	42 (44.7%)	73 (83.9%)	0.861	-	-
Anxiety	82 (45.3%)	45 (47.9%)	40 (46.0%)	0.471	-	-
Dizziness	82 (45.3%)	27 (28.7%)	37 (42.5%)	0.025	2.04 (1.06–3.95)	0.034
Articular pain	66 (36.5%)	29 (30.9%)	39 (44.8%)	0.187	-	-
Skin problems	64 (35.4%)	40 (42.6%)	35 (40.2%)	0.077	-	-
Other symptoms	66 (36.5%)	13 (13.8%)	26 (30.0%)	0.814	-	-
	24 (13.3%)		11 (12.6%)			
SIBO type—*N* (%)				0.039		
CH_4	27 (14.8%)	13 (13.8%)	14 (15.9%)		1.00	-
H_2^+	49 (26.9%)	23 (24.5%)	26 (29.6%)		1.02 (0.37–2.77)	0.303
DUAL (CH_4/H_2^+)	82 (45.1%)	39 (41.5%)	43 (48.9%)		1.10 (0.44–2.78)	0.142
Negative	24 (13.2%)	19 (20.2%)	5 (5.7%)		0.30 (0.08–1.09)	0.023

Abbreviations: BMI, body mass index; SD, standard deviation; SIBO, small intestinal bacterial overgrowth.

6 to 8 years, or sometimes over a decade, depending on the country.[31–34] Thus, prior to being diagnosed with endometriosis, patients are often diagnosed and/or misdiagnosed with other conditions or pathologies that share similar clinical manifestations, including IBS, inflammatory bowel diseases, and food intolerance. Interestingly, as IBS is frequently diagnosed concomitantly with endometriosis, it is important to note that some patients with IBS treated for SIBO/IMO no longer fit the Rome criteria for IBS when targeted SIBO/IMO therapy is successful.[35,36] This implies that the diagnosis and treatment of digestive overgrowth could open the path to a more personalized treatment approach for women with endometriosis, thus suggesting a need for updating the current clinical guidelines for the management of endometriosis.

Finally, given the prevalence of SIBO/IMO in women with endometriosis, regardless of disease severity, endometriosis might have a greater effect on the digestive tract and general health than previously reported. SIBO/IMO testing for the management of endometriosis can identify additional treatment targets with a larger range of therapeutic strategies.

To evaluate whether one of the two coexisting conditions might have more influence on the presence and severity of the different signs and symptoms reported by the patient in this study, it would have been interesting to compare women with endometriosis and SIBO/IMO with women with endometriosis without SIBO/IMO. However, given the high prevalence of SIBO/IMO in endometriosis patients, the two groups did not have equal sizes, with the group of endometriosis patients without SIBO/IMO being too small ($n=12$ and $n=5$ in the subgroup) to reach any conclusion or trend regarding the pathophysiology of SIBO/IMO in these women. A post-hoc power analysis, calculated at 75%, highlights a minor limitation in our study's design. Although close to the standard threshold (i.e. 80%), this result indicates that future studies with larger sample sizes might provide further clarity on the associations observed. Particular attention must be paid to the retrospective nature of the study, which might induce a selection bias. Another limitation of our study is the absence of a healthy control group, which might have resulted in an underestimation of the tendencies observed in our analysis, as our control group was represented by women investigating existing symptoms. Looking at the literature, Shah et al. show a prevalence of SIBO among a healthy population estimated at 20.9% ($n=693/3320$).[9] The low prevalence in the healthy human population in comparison to our group of patients with symptoms and/or patient with endometriosis show that SIBO/IMO develops when our health or digestive function might be compromised. Hence SIBO/IMO are not specific to a specific pathology but might present more or less incidence in patients depending on the nature of the pathology and its implications on our digestive system and functioning. In the future, further studies with larger cohorts would allow the evaluation of the true effects that SIBO/IMO might have on endometriosis pathophysiology, as will some longitudinal studies examining patients before and after SIBO/IMO treatment and eradication.

Meanwhile, SIBO/IMO is increasingly being investigated by clinicians and is being included in clinical recommendations for disease management; however, the guidelines for endometriosis management still need to be updated.[27,37]

Considering that both SIBO/IMO and endometriosis can be asymptomatic and might evolve into symptomatic conditions that could affect the patient's health and quality of life, testing for SIBO/IMO in women with endometriosis without digestive symptoms could also constitute a preventive medical approach and contribute to preventing the worsening of their disease and general health.

AUTHOR CONTRIBUTIONS

Conception: PH, JPE, AP; Planning: PH, AP; Carrying Out: AP, NC, JB, ANB, BG, FR; Analyzing: AP, GP; Writing: PH, JPE, GP, AP.

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CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

All fully anonymized individual participant data that underlie the results reported in this article will be made available.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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