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Original article

High prevalence of irritable bowel syndrome in women with chronic pelvic pain and discerning features relevant to deep endometriosis

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ABSTRACT

Objective: Endometriosis is a chronic inflammatory condition associated with chronic pelvic pain (CPP), dysmenorrhea and bowel-related symptoms. Significant overlap exists between endometriosis and other benign abdominal pathologies, including irritable bowel syndrome (IBS). We aimed to identify the prevalence of IBS-related symptoms in a group of women undergoing either diagnostic or therapeutic surgical interventions for CPP.

Materials and methods: This ethically approved (IRAS 294803) prospective case-control study was undertaken between 8th November 2021 and 22nd February 2023. Premenopausal women presenting to the Liverpool Women's Hospital for surgical investigation and management of CPP completed an electronic questionnaire containing questions pertinent to the Rome IV diagnostic criteria for IBS and the validated British Society for Gynaecological Endoscopy (BSGE) endometriosis and pelvic pain questionnaire. Patients were grouped according to surgical findings: control (no endometriosis) (n = 49), superficial endometriosis (SE) (n = 21), or deep endometriosis (DE) (n = 19).

Results: Sixty-six (74.2%) women included in this study had a concurrent diagnosis of IBS. The prevalence of IBS was significantly higher in patients without surgical evidence of endometriosis (83.7% vs. 62.5%, p = 0.02). When considering endometriosis subtypes, patients with DE were less likely to meet the diagnostic criteria for IBS than those with SE and no endometriosis (57.9% vs. 66.7% vs. 83.7%, p = 0.062).

Conclusion: Patients presenting with CPP, regardless of the underlying diagnosis of endometriosis, have a high prevalence of concomitant IBS. Clinicians should discuss bowel symptoms with all CPP patients and consider commencing concurrent IBS treatments as appropriate to improve patient symptoms.

Introduction

Endometriosis is a complex, enigmatic condition that causes significant physical, psychological, and economic burdens for many women [1–3]. Endometriosis is characterised by endometrial-like tissue outside the uterine cavity. Under the influence of altered hormonal, vascular, and immune environments, ectopic endometrial tissue proliferates and infiltrates into surrounding structures [4,5]. Symptoms of endometriosis are extensive and include chronic pelvic pain (CPP), infertility, dyspareunia, dysmenorrhea, and gastrointestinal symptoms such as constipation, diarrhoea and dyschezia [6]. These symptoms can be cyclical, increasing in intensity during the menstrual period [7], and can affect the quality of life and mental health of women suffering from the condition [8,9].

Endometriosis can be surgically categorised into two subtypes based on the depth of invasion into host tissue: superficial endometriosis (SE) and deep endometriosis (DE) [10,11], with DE being the most severe form of the disease [12]. DE often involves the bowel, with associated bowel-related symptoms, and may respond poorly to medical and other nonsurgical treatments [13]. Surgical management of DE is challenging,

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with an increased risk of complications due to endometriotic lesions invading vital organs such as the bowel and bladder; thus, DE often requires collaborative input from allied specialists, including colorectal surgeons and urologists.

Despite the well-documented symptoms of endometriosis, none are specific enough to provide a definitive diagnosis or differentiate between subtypes. Consequently, laparoscopic visualisation of the pelvis remains the definitive diagnostic approach for women who do not respond to, or are not suitable for, medical therapy and who proceed to surgical management. This approach is associated with high healthcare resource utilisation, significant patient risk, and extended recovery times. The development of a noninvasive, definitive diagnostic test for endometriosis is a top priority from the patient's perspective, and it may help in offering appropriate surgical intervention early, with the involvement of specialised specialists, such as colorectal surgeons, in cases of bowel-involving endometriosis [14].

Many women with endometriosis have other coexisting conditions, such as irritable bowel syndrome (IBS). IBS is a functional bowel disorder characterised by abdominal pain and alterations in bowel habits [15]. At present, there is no reliable diagnostic test for IBS. Instead, a diagnosis is generated by evaluating symptoms using the Rome IV criteria (Textbox 2: Irritable Bowel Syndrome Subtype - Rome IV Diagnostic Criteria & Textbox 1: Irritable Bowel Syndrome - Rome IV Diagnostic Criteria) [16]. The considerable overlap between the symptomatology of endometriosis and IBS further complicates diagnostic uncertainty [17,18]. However, the management of endometriosis and IBS is substantially different. Endometriosis treatment traditionally centres around hormonal therapy and surgical excision of the disease [26], whereas IBS is primarily managed by a combination of patient education, pharmacological agents for managing diarrhoea or constipation, and dietary alterations [19,20]. The overlap of symptoms and the necessity for an invasive test to diagnose endometriosis definitively contribute to a significant delay between the initial symptoms and specialist review. This delay is particularly relevant for patients with DE involving the bowel. Early referral to specialist care benefits these patients, as they are more likely to respond positively to specialised treatments [21].

Symptoms associated with both IBS and endometriosis substantially affect women's physical, financial, and psychological well-being. A 2022 study estimated the direct cost of IBS-related ill health to an individual patient to be £556.65 (standard deviation (sd) £1023.92) and the direct healthcare system cost to be between £1.3 and £2 billion in the UK [22,23]. Similarly, the estimated yearly healthcare-associated cost for endometriosis is € 9,579 (95% confidence interval (CI) €8,559 8,559-€ €10,599) per patient [24]. Previous research has typically explored the relationship between IBS and endometriosis as a single entity rather than its distinct subtypes. Therefore, the association between IBS and DE is poorly understood.

This study aimed to identify the prevalence of IBS-related symptoms in a group of women undergoing either diagnostic or therapeutic surgical interventions for CPP. We hypothesised that there may be significant differences in IBS symptomatology between women with DE and women with either SE or no endometriosis. We used a comprehensive questionnaire that included the Rome IV criteria, and patients were allocated to groups (SE, DE, or CPP without endometriosis) based on surgical findings. Our findings are thus expected to provide a deeper understanding of the relationship between endometriosis and IBS, facilitating early diagnosis and the expedited initiation of the most appropriate form of treatment.

Methods

Patient and public involvement

A James Lind Alliance (JLA) priority-setting partnership (PSP) expressed concerns over the delay in treatment experienced by patients with endometriosis. The PSP also highlights the impact of patients' symptoms, including bowel-related symptoms, on their overall quality of life [25].

When consulted via a patient focus group, patients at the Liverpool Women's Hospital further confirmed the importance of the above priorities to our local population of women. Considering these priorities, we designed our research project to improve the diagnosis of endometriosis and further investigate the relationships among CPP, endometriosis, and bowel symptoms.

Study population

Women attending the Liverpool Women's Hospital who were undergoing laparoscopy and had a history of CPP were invited to participate in the "Biospecimens for the Evaluation of Endometriosis-Associated Pain" (BEEAP) study, an ethically approved and university-sponsored case-control study (IRAS ID 294803).

Our inclusion criteria were patients assigned female at birth, over 18 years of age, who were able to speak and read English and were undergoing laparoscopy for the diagnosis or treatment of CPP. CPP is defined in accordance with the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline No. 41, which describes CPP as “intermittent or constant pain in the lower abdomen or pelvis of a woman, lasting for at least six months, not occurring exclusively with menstruation or intercourse, and not associated with pregnancy” [26]. Patient recruitment occurred at the Liverpool Women's Hospital between 8th November 2021 and 22nd February 2023.

After providing informed consent, patients completed a questionnaire modified from the British Society of Gynaecological Endoscopy (BSGE) questionnaire to assess endometriosis-associated symptoms and the Rome IV diagnostic questionnaire for IBS. The BSGE questionnaire uses a 0–10-point Likert scale to record specific symptoms, including pain, dyspareunia, and bowel and bladder symptoms. Other medical and surgical history, including previous endometriosis excisional surgery, drug history, hormonal contraceptive use and general health-related outcomes, were recorded. The questionnaires were completed electronically using Microsoft Forms on patients' electronic devices. A paper version of the same questionnaire was provided for patients who were unable to access it electronically.

Experienced endometriosis specialist surgeons performed laparoscopy to determine the presence or absence of endometriosis. Peritoneal biopsies were obtained for histological confirmation. The presence of endometrium-like glands or stroma was considered indicative of active endometriosis. In contrast, findings limited to fibrosis were interpreted as burnt-out disease without active endometriosis. In cases of discordance between surgical findings and histology, the patient was excluded from the final analysis.

The revised American Society for Reproductive Medicine (rARSM) guidelines were used to assign a disease severity stage, with stage I/II considered superficial and stage III/IV considered deep [21].

Patients were allocated into three groups according to disease status identified during surgery in conjunction with histological analysis of lesions: control group (CPP without macroscopic evidence of endometriosis), SE group and DE group.

The Rome IV criteria (Textbox 1 and Textbox 2) were used to diagnose IBS and its subtypes according to patients' questionnaire responses.

Textbox 1: Irritable Bowel Syndrome - Rome IV Diagnostic Criteria

Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with two or more of the following criteria:

1 Related to defecation
2 Associated with a change in the frequency of stool

3 Associated with a change in the form (appearance) of stool

(These criteria should be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.)
;1;

Textbox 2: Irritable Bowel Syndrome Subtype - Rome IV Diagnostic Criteria

- IBS with Constipation (IBS-C)
  - >25% of their bowel movements associated with BSFS 1 or 2,
- IBS with Diarrhoea (IBS-D)
  - >25% of their bowel movements associated with BSFS 6 or 7
- IBS with a mixed subtype of alternating constipation and diarrhoea (IBS-M)
  - >25% of their bowel movements associated with BSFS 1 or 2 and >25% of their bowel movements associated with BSFS 6 or 7.
- Undefined IBS (IBS-U)
  - Insufficient abnormality of stool consistency to meet criteria for IBS-C, D or M

;1;

Data synthesis and statistical analysis

The results reported here follow the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for case-control studies [27]. Statistical analysis was undertaken using Stata 18 (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC.). The outcomes are presented as frequencies and their corresponding percentages. Nonnormally distributed data, determined using the Kolmogorov-Smirnov Test, is presented as medians and interquartile ranges, and normally distributed data are presented as means and standard deviations. A comparison of cohorts of nonparametric data was undertaken using the chi-square test, and parametric data were analysed using ANOVA, Student's t-test, and the Mann–Whitney U test. A p-value of <0.05 was considered to indicate statistical significance. All the graphs were generated using OriginPro (OriginPro 2021b 9.8.5.212) or Stata 18.

Results

Patient characteristics

Eighty-nine patients with a mean age of 33.9 ± 6.9 years were included in the analysis. Detailed study characteristics are provided in Tables 1 and 2.

Forty-nine (55.1%) patients had CPP with no evidence of endometriosis at the time of diagnostic laparoscopy (control cohort), and 40 (44.9%) were found to have visible endometriosis. Twenty-three patients (23.6%) had evidence of SE (SE cohort), and 19 (21.3%) patients had DE (DE cohort) (Fig. 1).

A significant difference in the age of the cohorts was noted; patients with endometriosis were younger, with a mean age of 32.1 ± 6.9 years compared to 35.4 ± 6.8 years in those without endometriosis ($p = 0.02$). Otherwise, the cohorts were broadly comparable, with no significant differences in characteristics, including BMI, smoking status, alcohol consumption, previous history of pelvic inflammatory disease (PID), prior history of endometriosis, nulliparity, previous history of IBS, pregnancy status, patients currently attempting to conceive and fertility treatment (defined as any medical or surgical interventions, and assisted reproductive technologies). (Tables 1 and 2).

IBS

In total, 66 (74.2%) patients satisfied the Rome IV criteria for a diagnosis of IBS, including 25 (62.5%) patients with endometriosis and 41 (83.7%) patients without endometriosis (odds ratio (OR) 3.08, 95% CI 1.03–9.56, $p = 0.02$). Therefore, patients who did not have a surgical diagnosis of endometriosis were significantly more likely to have a diagnosis of IBS. When the endometriosis phenotypes were compared, 14 out of 21 (66.7%) patients with SE had IBS, whereas 11 out of 19 (57.9%) patients with DE had IBS (p = 0.06) (Fig. 2).

Table 1
Study Characteristics Table (Two-group comparison).

	No Endometriosis	Endometriosis	Total	*p*-value
N (%)	49 (55.1%)	40 (44.9%)	89 (100.0%)	
Age - Mean (SD)	32.306 (6.615)	35.900 (6.736)	33.921 (6.871)	0.013
rASRM Stage				
Stage I	0 (0.0%)	10 (25.0%)	10 (11.2%)	<0.001
Stage II	0 (0.0%)	11 (27.5%)	11 (12.4%)	
Stage III	0 (0.0%)	10 (25.0%)	10 (11.2%)	
Stage IV	0 (0.0%)	9 (22.5%)	9 (10.1%)	
BMI - Mean (SD)	26.471 (5.798)	29.132 (6.117)	27.667 (6.057)	0.039
BMI Category				
Underweight	1 (2.0%)	3 (7.5%)	4 (4.5%)	0.463
Normal Weight	16 (32.7%)	15 (37.5%)	31 (34.8%)	
Overweight	17 (34.7%)	14 (35.0%)	31 (34.8%)	
Obese	15 (30.6%)	8 (20.0%)	23 (25.8%)	
Smoking Status				
Current Smoker	7 (14.3%)	7 (17.5%)	14 (15.7%)	0.860
Never Smoked	38 (77.6%)	29 (72.5%)	67 (75.3%)	
Ex-Smoker	4 (8.2%)	4 (10.0%)	8 (9.0%)	
Current Alcohol Use				
Yes	18 (36.7%)	16 (40.0%)	34 (38.2%)	0.752
No	31 (63.3%)	24 (60.0%)	55 (61.8%)	
Previous History of Irritable Bowel Syndrome				
Yes	15 (30.6%)	15 (37.5%)	30 (33.7%)	0.494
No	34 (69.4%)	25 (62.5%)	59 (66.3%)	
Previous History of Pelvic Inflammatory Disease				
Yes	4 (8.2%)	3 (7.5%)	7 (7.9%)	0.908
No	45 (91.8%)	37 (92.5%)	82 (92.1%)	
Previous History of Endometriosis?				
Yes	24 (49.0%)	22 (55.0%)	46 (51.7%)	0.572
No	25 (51.0%)	18 (45.0%)	43 (48.3%)	
Nulliparity				
Yes	25 (51.0%)	11 (27.5%)	36 (40.4%)	0.025
No	24 (49.0%)	29 (72.5%)	53 (59.6%)	
Hormonal Therapy				
Yes	23 (46.9%)	13 (32.5%)	36 (40.4%)	0.167
No	26 (53.1%)	27 (67.5%)	53 (59.6%)	
Previous Fertility Treatment				
Yes	7 (14.3%)	5 (12.5%)	12 (13.5%)	0.806
No	42 (85.7%)	35 (87.5%)	77 (86.5%)	

IBS phenotypes

Among the 66 patients diagnosed with IBS based on the Rome IV criteria, 14 (21.2%) had a constipation subtype (IBS-C), nine (13.6%) had diarrhoea (IBS-D), 13 (19.7%) had mixed (IBS-M), and 30 (45.5%) had undefined (IBS-U) disease. No significant difference in subgroup composition was noted by either two-group (control versus endometriosis, $p = 0.25$) or three-group comparisons (control versus SE versus DE, $p = 0.392$) (Fig. 3).

Previous diagnosis of IBS

Thirty (33.7%) of the 89 respondents had a preexisting diagnosis of IBS (Table 1 and Table 2). Interestingly, 23 (76.6%) patients with a prior diagnosis of IBS were found to meet the Rome IV criteria, thereby reconfirming their diagnosis of IBS based on their responses to our questionnaire. In contrast, 43 out of 59 (72.9%) patients without a history of IBS met the Rome IV criteria based on their responses to our

Table 2
Study Characteristics Table (Three-group comparison).

	Control	Superficial Endometriosis	Deep Endometriosis	Total	*p*-value
N (%)	49 (55.1%)	21 (23.6%)	19 (21.3%)	89 (100.0%)	
Age - Mean (SD)	32.306 (6.615)	35.905 (6.131)	35.895 (7.520)	33.921 (6.871)	0.047
rASRM Stage					
Stage I	0 (0.0%)	10 (47.6%)	0 (0.0%)	10 (11.2%)	<0.001
Stage II	0 (0.0%)	11 (52.4%)	0 (0.0%)	11 (12.4%)	
Stage III	0 (0.0%)	0 (0.0%)	10 (52.6%)	10 (11.2%)	
Stage IV	0 (0.0%)	0 (0.0%)	9 (47.4%)	9 (10.1%)	
BMI - Mean (SD)	26.471 (5.798)	29.515 (6.803)	28.709 (5.412)	27.667 (6.057)	0.109
BMI Category					
Underweight	1 (2.0%)	1 (4.8%)	2 (10.5%)	4 (4.5%)	0.714
Normal Weight	16 (32.7%)	9 (42.9%)	6 (31.6%)	31 (34.8%)	
Overweight	17 (34.7%)	7 (33.3%)	7 (36.8%)	31 (34.8%)	
Obese	15 (30.6%)	4 (19.0%)	4 (21.1%)	23 (25.8%)	
Smoking Status					
Current Smoker	7 (14.3%)	2 (9.5%)	5 (26.3%)	14 (15.7%)	0.641
Never Smoked	38 (77.6%)	17 (81.0%)	12 (63.2%)	67 (75.3%)	
Ex-Smoker	4 (8.2%)	2 (9.5%)	2 (10.5%)	8 (9.0%)	
Current Alcohol Use					
Yes	18 (36.7%)	11 (52.4%)	5 (26.3%)	34 (38.2%)	0.226
No	31 (63.3%)	10 (47.6%)	14 (73.7%)	55 (61.8%)	
Previous History of Irritable Bowel Syndrome					
Yes	15 (30.6%)	11 (52.4%)	4 (21.1%)	30 (33.7%)	0.089
No	34 (69.4%)	10 (47.6%)	15 (78.9%)	59 (66.3%)	
Previous History of Pelvic Inflammatory Disease					
Yes	4 (8.2%)	1 (4.8%)	2 (10.5%)	7 (7.9%)	0.790
No	45 (91.8%)	20 (95.2%)	17 (89.5%)	82 (92.1%)	
Previous History of Endometriosis?					
Yes	24 (49.0%)	17 (81.0%)	5 (26.3%)	46 (51.7%)	0.002
No	25 (51.0%)	4 (19.0%)	14 (73.7%)	43 (48.3%)	
Nulliparity					
Yes	25 (51.0%)	6 (28.6%)	5 (26.3%)	36 (40.4%)	0.079
No	24 (49.0%)	15 (71.4%)	14 (73.7%)	53 (59.6%)	
Hormonal Therapy					
Yes	23 (46.9%)	9 (42.9%)	4 (21.1%)	36 (40.4%)	0.144
No	26 (53.1%)	12 (57.1%)	15 (78.9%)	53 (59.6%)	
Fertility Treatment?					
Yes	7 (14.3%)	2 (9.5%)	3 (15.8%)	12 (13.5%)	0.820
No	42 (85.7%)	19 (90.5%)	16 (84.2%)	77 (86.5%)	

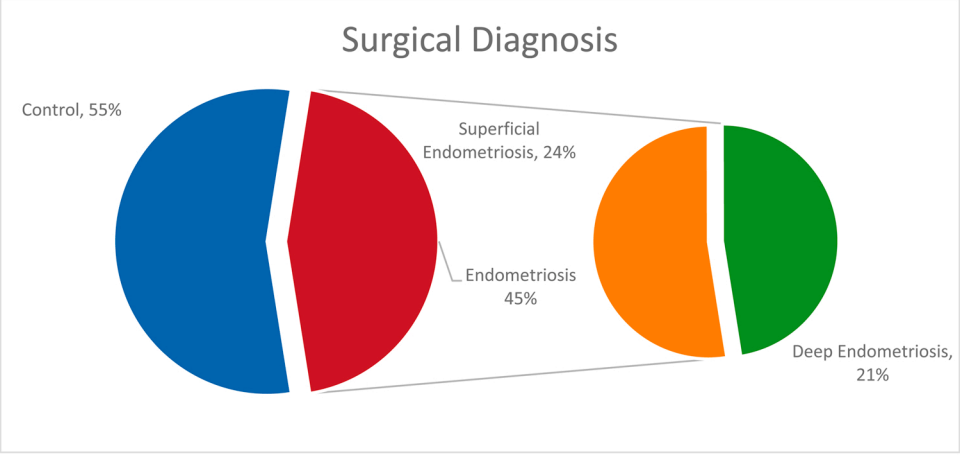

Fig. 1. Pie chart representing the proportion of patients by surgical diagnosis.

questionnaire.

Pelvic inflammatory disease (PID) and IBS prevalence

Seven patients had a previous history of PID. Notably, all seven (100%) patients had a concurrent diagnosis of IBS based on Rome IV criteria, whereas 59 out of 82 (72.0%) of those who did not have a preexisting diagnosis of PID ($p = 0.104$).

Impact of hormonal contraception on the prevalence of IBS

After excluding 13 patients who were either pregnant or trying to conceive, we found that only 35 out of 76 (46.1%) patients used any form of hormonal contraception. Compared with control and SE patients, patients with DE were least likely to use contraception (4 out of 8 (22.2%) vs. 23 out of 41 (56.1%) vs. 8 out of 17 (47.1%), $p = 0.055$).

Thirty-two out of 41 (76.3%) women who were not on hormonal treatment for CPP received a diagnosis of IBS, whereas 26 out of 35

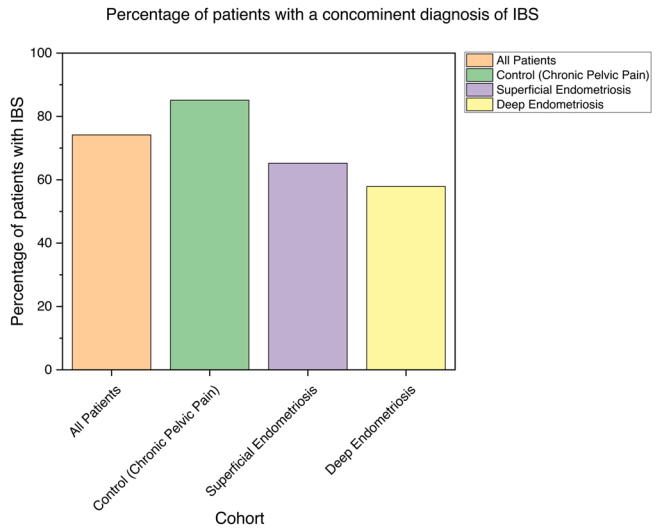

Fig. 2. Bar chart comparing the percentage of patients with a concurrent diagnosis of IBS according to endometriosis subtype at three different IBS diagnostic cutoffs.

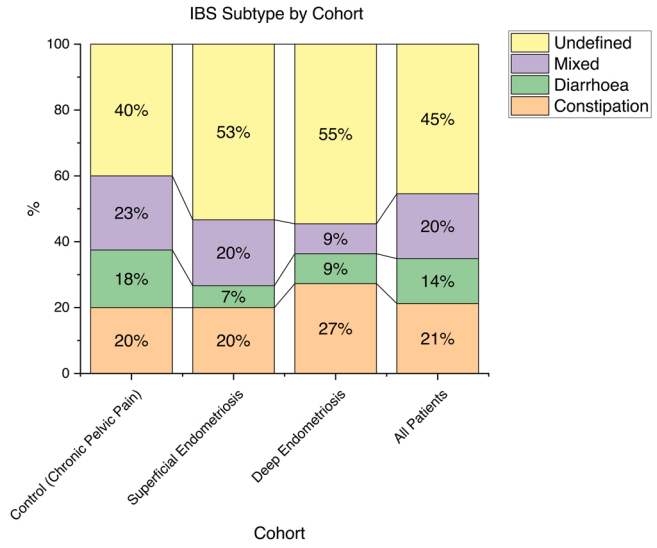

Fig. 3. Stacked bar chart comparing the proportion of patients with IBS subtype according to endometriosis subtype.

(74.3%) were treated with hormones. The prevalence of IBS did not differ between the groups ($p = 0.701$).

Discussion

Main Findings

This study reports the previously unknown prevalence of IBS between subphenotypes of endometriosis. Although the coexistence of IBS symptoms with endometriosis is well known, the prevalence of endometriosis specific to subphenotypes has not been clarified. Our findings further highlight that symptoms of endometriosis significantly overlap with IBS symptoms.

A recent systematic review using the ROME IV reported the prevalence of IBS in women to be 12% [28]. Three recent systematic reviews collating prior studies reported a pooled prevalence of IBS in women with endometriosis of between 23.4% and 37%, with an overall OR of 2.39–3.26, compared with those without an endometriosis diagnosis [29,30,35].

Comparatively, our study demonstrated a substantially higher prevalence (62.5%) of IBS among women who had contemporaneous surgical confirmation of endometriosis. Furthermore, in contrast to previous publications, the women in our study, without evidence of endometriosis at the time of laparoscopic examination of the pelvis but who presented to gynaecologists with CPP and other typical symptoms associated with endometriosis, had an even higher prevalence (85.1%) of IBS, clearly above the population prevalence [31]. Our findings echo the results obtained by Maroun et al., who demonstrated that up to 90% of women with a diagnosis of endometriosis may have concurrent gastrointestinal symptoms [32].

The following reasons can explain the differences between previous systematic review findings and our study. Previous studies that reported a lower prevalence of IBS in women with endometriosis reported a historical diagnosis of endometriosis. In contrast, our study assessed IBS symptoms with a contemporaneous surgical diagnosis of the presence or absence of endometriosis. A significant number of the previous studies included in the systematic reviews also depended on the patient-declared diagnosis of endometriosis, which may or may not have been confirmed surgically. Furthermore, a prior diagnosis may not necessarily indicate the presence of current active endometriosis lesions, as confirmed by laparoscopy in our patient group. The diagnostic criteria used in the various studies may also influence the reported prevalence (Rome II, Rome III, Rome IV, and VAS-IBS). Finally, the effects of concurrent use of either IBS treatments or hormonal or pain-management treatments may also alter the IBS diagnosis and thus may explain the observed differences.

There is growing recognition of the pathophysiological overlap between IBS and endometriosis. Both conditions are characterised by a chronic inflammatory state, with elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and prostaglandins. These mediators can disrupt gastrointestinal motility and contribute to the abdominal pain, bloating, and altered bowel habits typical of IBS [33].

Visceral hypersensitivity is a hallmark of both disorders [34]. In endometriosis, the proliferation and disruption of nerve fibres within ectopic lesions, combined with central sensitisation, lead to an exaggerated perception of pain [35]. Similarly, patients with IBS exhibit impaired pain modulation and heightened visceral sensitivity [35], suggesting a shared neurogenic pathway that amplifies nociceptive signalling in both conditions.

Moreover, gut dysbiosis and small intestinal bacterial overgrowth (SIBO) are increasingly recognised in both IBS and endometriosis. These microbial imbalances may perpetuate inflammation and contribute to the production of pro-inflammatory cytokines, further exacerbating symptoms [35]. The frequent use of hormonal therapies in endometriosis management, particularly estrogen-based treatments, has also been implicated in altering gut microbiota composition. This hormonal influence may worsen dysbiosis and intensify gastrointestinal and pelvic pain, reinforcing the bidirectional relationship between the two conditions [36].

Prevalence of IBS in CPP and Endometriosis Phenotypes

Compared with women with endometriosis, patients with CPP without any evidence of endometriosis at the time of surgery had the highest prevalence of IBS (83.7% vs. 62.5%, $p = 0.02$). When considering the subphenotypes of endometriosis, we found that patients with DE, the most severe form of endometriosis, were the least likely to have a diagnosis of IBS compared with SE patients and control patients (57.9% vs 66.7% vs 83.7%, $p = 0.06$). The high prevalence of IBS in women without a diagnosis of endometriosis potentially represents a true underlying diagnosis of IBS, which may exacerbate their CPP and add to the burden of their symptoms.

Successful treatment of IBS symptoms may substantially improve

patients' CPP, increase their quality of life, and prevent unnecessary diagnostic surgery. Considering the high prevalence of IBS and the low risk associated with IBS-directed treatments, we can recommend early screening for IBS in women with CPP and initiating treatment as needed before considering invasive interventions.

Relationship between pelvic inflammatory disease and irritable bowel syndrome

We noted an apparent greater prevalence of IBS in patients with a preexisting history of PID than in those without PID (100% vs 72.0%, $p = 0.10$). Our findings agree with those of a previous study of primary care patients, which revealed an increased risk of IBS diagnosis in patients with a prior history of PID (OR 6.4, 95% CI 5.6–7.4) [37].

PID is also associated with endometriosis. A large Taiwanese national cohort study revealed an association between endometriosis and prior PID, with a hazard ratio (HR) of 3.02 (95% CI 2.85–3.2) [38]. The underlying relationships among PID, IBS, and endometriosis remain unclear. A potential unifying aetiology is that PID creates a pro-inflammatory environment within the pelvis, leading to the proliferation and propagation of endometriotic lesions, as well as increased gut mucosal immune activation, dysbiosis, and visceral hypersensitivity, which are hallmarks of IBS.

Relationship between hormonal contraception use and irritable bowel syndrome

Worsening of IBS symptoms at the time of a woman's menstrual period and improvement in symptoms in women using oral contraception have been reported [39], suggesting a hormonal influence on IBS symptoms. Our study has not demonstrated any significant difference in the prevalence of IBS between women using hormonal contraception and women who do not, and a larger sample set with more detailed information, for example, if hormonal treatment results in amenorrhea, will help further the understanding of the relevance of hormonal therapy to IBS symptoms. Further research is necessary to evaluate the significance of this relationship.

Notably, only 46.1% of the patients included in this analysis who were not trying to conceive used hormonal contraception. Hormonal therapy is considered the first-line treatment for the management of suspected endometriosis and is deemed to be particularly effective in the treatment of superficial disease [40]. All patients, unless they have specific contraindications, such as a desire for pregnancy or patient dissent, should commence hormonal therapy. It is possible that a significant improvement in patient symptoms would have been achieved through hormonal treatment, and as such, the need for invasive surgery would have been reduced.

Irritable bowel syndrome and other benign pathologies

A high prevalence of IBS is described with other chronic pain conditions, e.g., in patients presenting with biliary colic symptoms [41]. Owing to symptom overlap, patients with IBS have increased rates of pelvic and abdominal surgery. Longstreth et al. reported an increased likelihood of cholecystectomy (OR 2.09, 95% CI 1.89–2.31, $p < 0.01$), appendicectomy (OR 1.45, 95% CI 1.33–1.56, $p < 0.01$), hysterectomy (OR 1.70, 95% CI 1.55–1.87, $p < 0.01$), and back surgery (OR 1.22, 95% CI 1.05–1.43, $p < 0.01$) in those with a diagnosis of IBS [42].

Up to 40% of patients will continue to suffer from symptoms following cholecystectomy [43], and 28.7% of patients will continue suffering from symptoms following endometriosis surgery [44]. All surgeries are associated with risks of morbidity and mortality. Furthermore, Misal et al., in a survey of 253 patients who underwent surgery for endometriosis or CPP, reported that 16.3% of patients regretted their decision to undergo surgery [45]. Screening and treating IBS early when managing patients with chronic pain conditions, such as CPP, is a low-risk approach with the potential for substantial patient benefit.

Finally, there is considerable symptom overlap between irritable bowel syndrome (IBS), pelvic pain, and inflammatory bowel disease (IBD). Neri et al. reported a high prevalence of endometriosis among patients with IBD [46]. Consequently, clinicians managing women with pelvic pain and gastrointestinal symptoms should remain vigilant for the possibility of IBD. Current guidance from the National Institute for Health and Care Excellence (NICE) recommends biochemical investigations, including full blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and antibody testing for coeliac disease, to identify patients with potential concomitant diagnoses [47].

Limitations

Our prospective case-control study included patients who presented to our tertiary referral hospital with CPP during the study period and who underwent invasive diagnostic or therapeutic surgery to manage CPP. Although ESHRE and BSGE guidance recommends initial medical therapy for the management of suspected endometriosis, our study does not include this population and therefore may not be fully generalisable to this subgroup of women. However, surgical laparoscopic visualisation of the pelvis remains the primary method for establishing a conclusive diagnosis and is the definitive diagnostic approach for women who do not respond to, or are unsuitable for, medical therapy and who proceed to surgical management [48].

The Rome IV criteria were used to diagnose IBS, and the questionnaire was completed on the day of surgery. This makes the diagnosis of both endometriosis and IBS robust and synchronous.

Our patient population included women with CPP with or without a diagnosis of endometriosis. We do not have a comparative group of women without CPP to ascertain the prevalence of IBS. In the future, obtaining information on the prevalence of IBS in patients undergoing benign pelvic surgery for reasons other than endometriosis, such as tubal ligation for sterilisation, salpingectomy, and ovarian cystectomy, may provide this information. Recent research has revealed a high prevalence of CPP and endometriosis in these populations, which requires an appropriate study design to account for.

Our cohort was recruited from a tertiary referral centre specialising in complex endometriosis. As such, the sample may not be representative of the broader population of women with endometriosis, especially those with milder disease or asymptomatic presentations. Additionally, while recruiting from a single geographic region ensures consistency in environmental exposures, it limits the generalisability of the findings.

The diagnosis of IBS was based on the Rome IV criteria [16]. Although these criteria are validated as a diagnostic tool, our approach did not incorporate additional investigations or clinical examinations typically performed during a comprehensive IBS assessment. Consequently, the diagnosis in this context may lack the robustness of one made by an expert clinician and should therefore be interpreted with caution.

Our study employs a prospective design, incorporating contemporaneous surgical assessment of the pelvis with symptom evaluation, and includes a well-characterised patient population with endometriosis subphenotypes to enhance the robustness of the findings and the overall reporting quality. Due to our stringent study design, the number of patients remains small. Accordingly, we were unable to perform subgroup

analysis based on demographic features, such as hormone use. The prevalence of IBS reported in this population needs to be confirmed in adequately powered future studies.

Recommendations

It is of substantial importance that primary care physicians, specialist gynaecologists, and women suffering from these symptoms are aware of concurrent IBS diagnosis in women with CPP. Research undertaken by Moore et al. demonstrated considerable improvement in bowel-related endometriosis symptoms following the commencement of a low-FODMAP diet [49]. Our data demonstrating the high prevalence of IBS in this cohort of patients further suggests that bowel-related symptoms are recorded for all patients presenting with CPP, and a diagnosis of IBS is considered by all clinicians managing them. Furthermore, early commencement of hormonal empirical treatment for endometriosis, pharmacological agents for symptomatic relief of bowel symptoms, and a FODMAP-based diet are recommended for women with CPP and bowel symptoms at initial presentation, aiming to reduce symptom burden and improve quality of life. Patients who do not respond to this initial management can be referred to secondary care for further investigations and management.

Conclusion

CPP is a common symptom that may or may not be associated with endometriosis. Substantial symptom overlap exists between women presenting with CPP, with a presumed diagnosis of endometriosis, and those with IBS. The incidence of IBS is substantially high in patients with CPP undergoing invasive surgical procedures. Clinicians should consider the high prevalence of IBS, actively seek a diagnosis and initiate concurrent treatment for IBS with hormonal treatment as the initial step in managing women with CPP suggestive of endometriosis. Improving patient and clinician awareness of IBS and increasing the prevalence of IBS in women with CPP will facilitate screening for IBS, which is a low-risk and low-cost intervention that may improve patients' quality of life and reduce the need for invasive, high-risk, and expensive surgical interventions. To develop more effective treatments, further research is needed to understand the underlying interactions between IBS and endometriosis, particularly in subphenotypes.

CRediT authorship contribution statement

SGP, JNRW, CSP and DKH conceptualised and developed this prospective study. Methodology, including study design and ethical application, was undertaken by SGP and JNRW under senior supervision from DKH. IA and DH contributed to patient identification and recruitment. SGP and JW extracted relevant data from questionnaires, and SGP conducted the statistical analysis. SGP, JW and DKH wrote the manuscript. All authors contributed to the interpretation of the data and presentation, as well as the review, critical revision, and approval of the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Simon G. Powell: Conceptualization; Methodology; Data curation; Formal analysis; Visualization; Writing – original draft; Writing – review & editing.

James N.R. Wyatt: Conceptualization; Methodology; Writing – review & editing.

Christopher Probert: Conceptualization; Writing – review & editing.

Dharani K. Hapanagama: Conceptualization; Methodology; Supervision; Writing – original draft; Writing – review & editing.

Ilyas Arshad: Investigation; Resources.

Shakil Ahmed: Investigation; Resources.

Christopher J. Hill: Data curation; Writing – original draft; Writing – review & editing.

Patient consent

We declare that informed consent, both written and verbal, was obtained from all the participants involved in this study.

Ethical approval

Southwest Research Ethics Committee, IRAS ID 294803, 03/09/2021.

Ethical approval and patient consent

The Southwest Research Ethics Committee (IRAS ID 294803) granted ethical approval, and the University of Liverpool acts as the sponsor (UoL001640). All patients recruited in this study provided written informed consent to participate.

Declaration of Generative AI and AI-assisted technologies in the writing process

While preparing this work, the author used Grammarly, a word processing software, for proofreading and grammatical improvement. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the publication's content.

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Data sharing statement

The datasets used and analysed during the current study are available from the corresponding author upon reasonable request.

Transparency statement

The lead author SGP affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities

The research findings will be disseminated through press releases, interviews with local and national media, social media posts on X, and academic conferences.

Provenance and peer review

Not commissioned; externally peer-reviewed.

Prior presentations

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Clinical trial registry number

Not applicable.

Data availability

No additional data are available.

Declaration of competing interest

All authors have completed the ICMJE uniform disclosure form, available at www.icmje.org/disclosure-of-interest/. No support from any organisation for the submitted work other than that described above; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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