

Endometriosis and Interstitial Cystitis/Bladder Pain Syndrome: A Systematic Review of Prevalence, Urinary Symptoms, and Overlapping Pelvic Pain Syndromes

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ABSTRACT

Background: Endometriosis (10–15% of reproductive-aged women) and Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS; 2.3–6.5%) frequently coexist (15.5–78.3%) in women with chronic pelvic pain, yet overlapping symptoms often delay diagnosis and result in treatment failure.

Objective: This systematic review synthesizes evidence on the association between endometriosis and IC/BPS, focusing on prevalence, urinary symptoms, and overlapping pelvic pain syndromes.

Methods: A comprehensive literature search was conducted across PubMed, Embase, and the Cochrane Library (last five years) following PRISMA guidelines. Studies reporting original data on urinary symptoms or IC/BPS in endometriosis patients were included. Five studies (575 participants) were assessed using JBI critical appraisal tools.

Results: Urinary symptoms (dysuria) prevalence ranged from 22% (adolescents) to 50% (adults). Painful bladder syndrome was associated with poor sleep in 94% of affected women ($p < 0.01$). Deep infiltrating endometriosis showed significantly higher dysuria/dyschezia rates ($p < 0.001$), correlating with #ENZIAN compartments ($p < 0.05$). Overlapping visceral pain syndromes affected 74.2% of women with CPP. Symptoms improved with conservative therapy ($p < 0.001$) and anti-inflammatory approaches.

Conclusions: Endometriosis and IC/BPS frequently coexist, with a 3.74-fold increased risk of IC/BPS. Shared central sensitization and cross-organ mechanisms warrant multidisciplinary care. Routine IC/BPS screening in endometriosis patients with persistent pain is essential.

Keywords: Endometriosis; Interstitial Cystitis; Bladder Pain Syndrome; Chronic Pelvic Pain; Urinary Symptoms; Dysuria

INTRODUCTION

Chronic pelvic pain (CPP) is a debilitating condition affecting 6% to 25% of women worldwide and is associated with poor quality of life, reduced work efficiency, and substantial healthcare costs ^[1-3]. CPP accounts for nearly 10% of gynecology consultations, 12% of hysterectomies, and more than 40% of diagnostic laparoscopies ^[4,5]. The World Health Organization has defined CPP as a "neglected reproductive health morbidity" due to inadequate healthcare prioritization and resource allocation ^[6].

Endometriosis is a benign, estrogen-dependent gynecological disorder characterized by endometrial-like tissue outside the uterine cavity, causing persistent inflammation ^[1]. This condition affects approximately 10% to 15% of women of reproductive age and is one of the leading causes of CPP ^[1,2]. Common symptoms include dysmenorrhea, dyspareunia, abdominal pain, dyschezia, dysuria, and urinary frequency ^[3]. Endometriosis has been found in 52.4% to 61.5% of women undergoing evaluation for CPP ^[4]. The disease extent is described using the Revised American Society for Reproductive Medicine (rASRM) score and the #Enzian classification, with the latter better suited for deep infiltrating endometriosis ^[5,6].

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by urinary urgency, frequency, nocturia, and suprapubic or pelvic pain without identifiable infection or pathology ^[7]. IC/BPS is more common in women, with prevalence rates estimated between 2.3% and 6.5% in the United States, and women account for 80% to 90% of affected patients ^[7,8]. Diagnosis relies on a structured exclusion process incorporating medical history, physical examination, validated questionnaires such as the O'Leary-Sant score, and cystoscopy to exclude other causes and identify characteristic bladder findings ^[7,8].

A growing body of evidence suggests that endometriosis and IC/BPS frequently coexist in women with CPP, yet overlapping symptoms and non-standardized diagnostic pathways often delay recognition of dual pathology ^[1,4]. The coexistence of endometriosis and IC/BPS ranges from 15.5% to 78.3%, which is considerably higher than the prevalence of IC/BPS in the general population ^[7].

The pathophysiological mechanisms underlying this comorbidity involve peripheral and central sensitization, inflammation, aberrant innervation, immune dysregulation, and hormonally influenced processes ^[4,5]. Cross-organ sensitization, whereby inflammatory processes in one pelvic organ sensitize adjacent structures through shared neural pathways, has emerged as a leading explanatory framework ^[6].

Preclinical research has demonstrated that bladder cross-sensitization in endometriosis occurs in association with hyperexpression of transient receptor potential

ankyrin 1 (TRPA1) at both dorsal root ganglia and bladder mucosa ^[6,8]. Repeated retrograde menstruation intensifies central sensitization driven by neuroinflammation, creating a chronic inflammatory stimulus leading to persistent pain ^[5].

The clinical implications of this comorbidity are substantial ^[1,4]. The presence of coexisting IC/BPS in patients with endometriosis may explain why some patients continue to experience pelvic pain despite successful surgical or medical management of endometriotic lesions ^[1,7].

A recent international consensus committee identified endometriosis/adenomyosis as one of five main comorbid disorders associated with IC/BPS, alongside genito-pelvic pain disorder, overactive pelvic floor muscles, hormone-associated changes, and vulvodynia ^[8]. The identification of a non-bladder-centric phenotype suggests these patients may require different therapeutic approaches than those with isolated IC/BPS ^[7].

Despite growing recognition of this association, significant gaps remain in the literature ^[1,4]. Heterogeneity in study designs, populations, diagnostic criteria, and assessment methods has resulted in wide variations in reported prevalence estimates ^[7]. The absence of standardized diagnostic protocols and lack of adequately powered prospective cohort studies limit understanding of the natural history of this comorbidity ^[1,8].

Delayed recognition of dual pathology may result in unsuccessful medical and surgical therapies and prolonged patient suffering ^[1,4].

The present systematic review aims to synthesize available evidence on the association between endometriosis and IC/BPS, with a specific focus on prevalence estimates, urinary symptoms, and overlapping pelvic pain syndromes, to inform clinical practice and guide future research.

METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines ^[9]. The review protocol was not prospectively registered, but the methodology followed established standards for systematic reviews of observational studies examining the association between endometriosis and interstitial cystitis/bladder pain syndrome. The research question was formulated using the PICO framework: Population (women with endometriosis), Intervention/Exposure (presence of endometriosis), Comparison (women without endometriosis or with other forms of endometriosis), and Outcomes (prevalence of urinary symptoms, diagnosis of IC/BPS, and overlapping pelvic pain syndromes).

Search Strategy

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, Embase, and the Cochrane Library, for studies published over the past five years. The search strategy utilized a combination of Medical Subject Headings (MeSH) terms and keywords related to endometriosis and IC/BPS. The search terms included: "endometriosis," "interstitial cystitis," "bladder pain syndrome," "painful bladder syndrome," "chronic pelvic pain," "urinary symptoms," "dysuria," "overlapping pain syndromes," "pelvic pain," "lower urinary tract symptoms," and "IC/BPS." Boolean operators (AND, OR) were used to combine search terms effectively. The search was limited to articles published in English and studies involving human subjects. Additionally, reference lists of included studies and relevant review articles were manually screened to identify any additional eligible studies that may have been missed by the electronic database search.

The complete electronic search strategies for PubMed, Embase, and the Cochrane Library, including Boolean operators, MeSH terms, filters, and the date of the final search, are provided in Supplementary Appendix 1 to facilitate reproducibility.

Inclusion and Exclusion Criteria

Studies were considered eligible for inclusion if they met the following criteria: (1) original research studies with original patient data (excluding review articles, protocols, editorials, and case reports); (2) included women with endometriosis diagnosed by surgical visualization, histological verification, or imaging criteria; (3) reported data on urinary symptoms (including dysuria, frequency, urgency, or painful bladder symptoms) or formal diagnosis of interstitial cystitis/bladder pain syndrome; (4) provided quantitative data on the prevalence of urinary symptoms or overlapping pelvic pain syndromes; and (5) were published in English within the last five years. Studies were excluded if they: (1) were review articles, systematic reviews, narrative reviews, protocols, case reports, or expert opinions without original patient data; (2) did not report specific data on urinary symptoms or IC/BPS; (3) focused exclusively on pelvic floor myofascial pain, migraine, nutritional status, or psychological aspects without addressing bladder symptoms; (4); or (5) lacked sufficient data extraction information. Interventional studies were eligible only if they reported baseline urinary symptoms or IC/BPS-related data relevant to the review objectives. Studies reporting only post-intervention outcomes without baseline data were excluded.

Study Selection and Data Extraction

The study selection process followed the PRISMA flow diagram guidelines. All identified records were imported into Rayyan, a web-based systematic review management software, for efficient screening and collaboration. Two

reviewers independently screened the titles and abstracts of all retrieved records to identify potentially eligible studies. Any discrepancies between reviewers were resolved through discussion and consensus, with a third reviewer consulted when agreement could not be reached. Full-text articles of potentially eligible studies were then retrieved and assessed against the inclusion criteria. Data extraction was performed independently by two reviewers using a standardized data extraction form developed specifically for this review. The extracted data included: study characteristics (author, year, country, study design), sample size, participant demographics (age, type of endometriosis), urinary symptoms assessed, diagnostic criteria for IC/BPS (if applicable), prevalence rates, statistical measures (p-values, odds ratios, confidence intervals), and key findings relevant to the association between endometriosis and IC/BPS.

Quality Assessment and Risk of Bias

The methodological quality and risk of bias of the included studies were assessed using appropriate critical appraisal tools from the Joanna Briggs Institute (JBI)^[10], selected based on the specific design of each study. For the cross-sectional study, the JBI Checklist for Analytical Cross-Sectional Studies was applied, evaluating criteria such as clear definition of inclusion criteria, detailed description of study subjects and setting, valid measurement of exposure and outcomes, identification and management of confounding factors, and appropriate statistical analysis. For the cohort study, the JBI Checklist for Cohort Studies was used, assessing comparability of groups, measurement of exposure and outcomes, adequacy of follow-up, and identification of confounding factors. The quasi-experimental study was assessed using the JBI Checklist for Quasi-Experimental Studies, evaluating criteria such as clear cause-and-effect relationships, comparability of groups, reliable outcome measurement, and appropriate statistical analysis. The case series was assessed using the JBI Checklist for Case Series, evaluating clear inclusion criteria, valid measurement of conditions, and completeness of reporting. The case-control study was assessed using the JBI Checklist for Case-Control Studies, evaluating appropriate case definition, representative case selection, appropriate control selection, comparability between groups, and valid measurement of exposure. Each study was assigned an overall risk of bias rating of "low," "moderate," or "high" based on the number and severity of methodological limitations identified.

Overall risk of bias was determined according to the proportion of JBI checklist items fulfilled. Studies meeting $\geq 80\%$ of applicable criteria were classified as low risk, 50–79% as moderate risk, and $< 50\%$ as high risk.

Data Synthesis and Analysis

Due to the heterogeneity in study designs, populations, and outcome measures, a narrative synthesis approach

was adopted rather than meta-analysis. The findings from the included studies were summarized descriptively, with emphasis on the prevalence of urinary symptoms, diagnostic rates of IC/BPS, and evidence of overlapping pain syndromes in endometriosis patients. Quantitative data were extracted as reported in each study, including percentages, p-values, and odds ratios where available. The findings were organized into thematic categories based on the type of evidence provided: direct evidence of IC/BPS diagnosis, urinary symptoms (dysuria), and overlapping pelvic pain syndromes. The results were presented in structured data extraction tables to facilitate comparison across studies.

RESULTS

PRISMA flow diagram illustrates the systematic screening process for study inclusion. A total of 931 records were identified from database searches, of which 341 duplicates were removed, leaving 590 records for screening. Following title and abstract screening, 298 records were excluded, and 292 reports were sought for retrieval, with 49 unavailable. Of the 243 full-text reports assessed for eligibility, 238 were excluded due to wrong outcomes (n=112), wrong population (n=79), or being abstracts only (n=47). Ultimately, 5 studies met the inclusion criteria and were included in the systematic review.

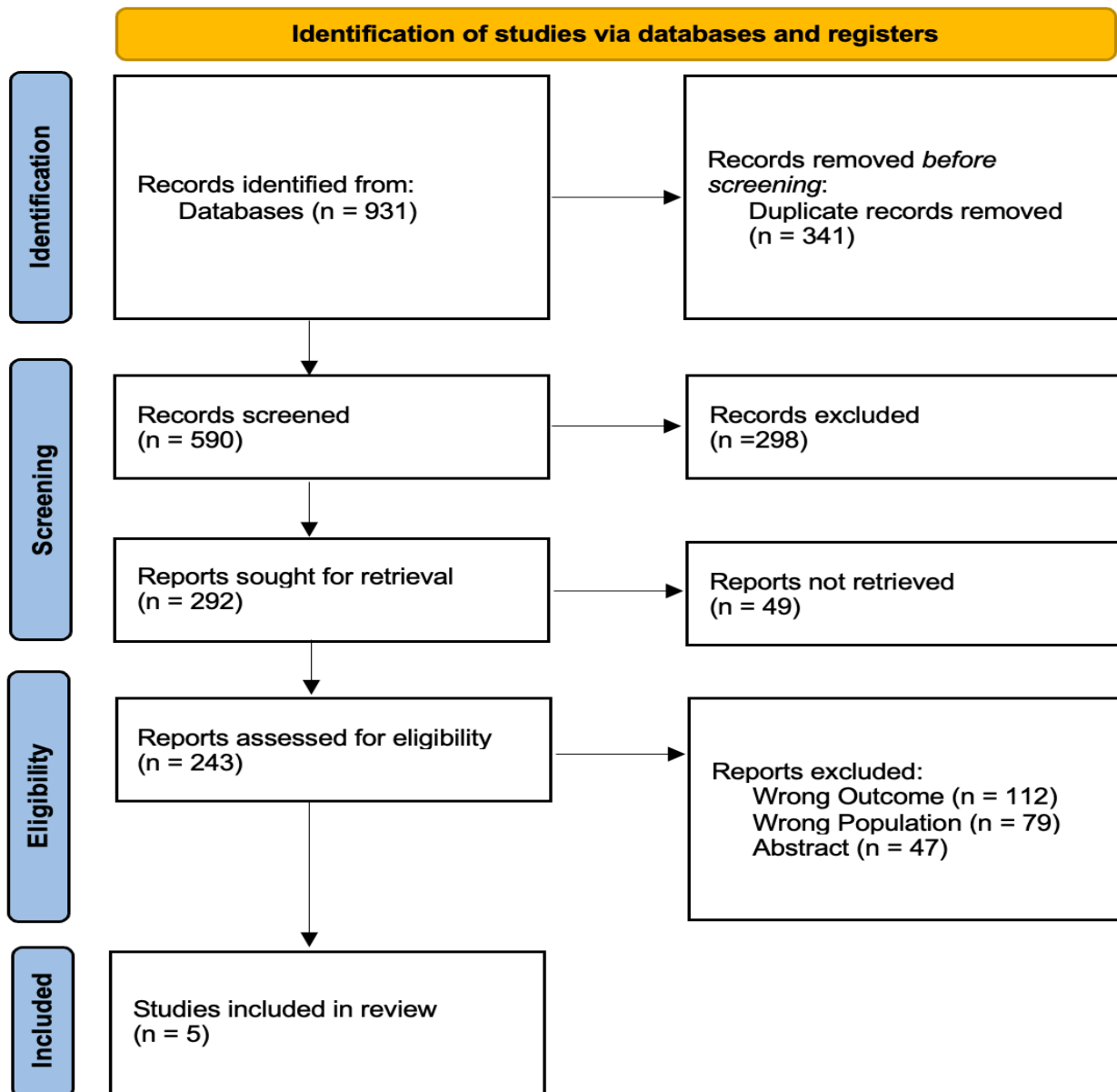


Figure 1: PRISMA Flow Diagram of Study Selection Process

Table 1 summarizes the key characteristics and demographic data of the five included original studies. The studies originate from various geographic settings, with one conducted in Chisinau, Moldova ^[12] and another in Liverpool, United Kingdom ^[15]; the remaining three studies did not specify their country of origin ^[11, 13, 14]. The study designs vary considerably, comprising one cross-sectional study ^[11], one cohort study ^[12], one interventional comparative study ^[13], one prospective longitudinal study ^[14], and one prospective case-control study ^[15].

The sample sizes ranged from 32 adolescent girls in the smallest study ^[14] to 190 reproductive-aged patients in the largest cohort ^[12], with a total of 575 participants across all five studies. The sample populations were exclusively female, reflecting the nature of endometriosis research and associated pelvic pain syndromes.

Notably, the adolescent population studied by **Khashchenko et al.** ^[14] represents a unique focus on younger patients, while the remaining studies focused on adult women of reproductive age. Baseline characteristics varied, with some studies assessing patients with deep endometriosis specifically ^[11, 12], others including various forms of endometriosis ^[13, 15], and one focusing exclusively on adolescent girls with genital endometriosis ^[14]. The study by **Powell et al.** ^[15] included a control group of women without endometriosis who presented with chronic pelvic pain, providing valuable comparative data.

All studies utilized validated assessment tools for pain evaluation, including the Visual Analog Scale (VAS) ^[12, 13, 14], the Biberoglu and Behrman scale ^[12], the Pittsburgh Sleep Quality Index (PSQI) ^[11], the O'Leary-Sant Interstitial Cystitis Symptoms and Problem Index ^[11], and the Rome IV diagnostic criteria for irritable bowel syndrome ^[15].

The interventional study by Huliieva and Chayka ^[13] evaluated treatment outcomes using enzyme therapy combined with hormonal treatment, providing therapeutic context for the management of chronic pelvic pain and associated urinary symptoms in endometriosis patients.

Table 2 presents the key outcomes, variables, and main numerical findings from each included study. The cross-sectional study by de Souza *et al.* ^[11] assessed the impact of painful bladder syndrome (PBS) on sleep

quality in women with deep endometriosis, finding that 94% of patients with PBS were poor sleepers, and that PBS increased sleep disturbances by nearly fivefold ($p < 0.01$), confirming PBS as a significant comorbidity that independently affects sleep quality beyond pain alone ^[11].

The cohort study by Ivanova and Codreanu ^[12] demonstrated that patients with deep infiltrating endometriosis (DIE) had significantly higher pain intensity scores ($p < 0.01$) and a broader spectrum of symptoms, with dysuria and dyschezia being significantly more prevalent ($p < 0.001$), and these urinary symptoms correlated with specific #ENZIAN classification compartments ($p < 0.05$), highlighting the importance of assessing bladder symptoms in endometriosis patients ^[12].

The interventional comparative study by Huliieva and **Chayka** ^[13] provided quantitative evidence of the prevalence of urinary symptoms, reporting dysuria in 9.5% of the treatment group versus 50.0% in the control group ($p < 0.001$), demonstrating that bladder symptoms are common in endometriosis patients and respond to treatment ^[13].

The prospective longitudinal study by **Khashchenko et al.** ^[14] found that 22% of adolescent girls with endometriosis reported dysuria at baseline, with significant improvement after one year of conservative therapy ($p < 0.001$), indicating that urinary symptoms manifest early in the disease course and are amenable to treatment ^[14].

Finally, the case-control study by **Powell et al.** ^[15] investigated overlapping visceral pain syndromes, finding that 74.2% of all women with chronic pelvic pain had concurrent irritable bowel syndrome (IBS), with higher prevalence in those without surgical evidence of endometriosis (83.7% vs. 62.5%, $p = 0.02$), supporting the hypothesis that overlapping pelvic pain syndromes, including IC/BPS, are frequently underdiagnosed in this patient population ^[15].

Overall, the included studies had acceptable methodological quality, with the main limitations being small sample sizes in some studies ^[14], lack of blinding in interventional designs ^[13], and incomplete reporting of confounder adjustment ^[12], which should be considered when interpreting the findings of this systematic review as illustrated in table 3.

Table 1: Study Characteristics and Demographic Data

Study (Author, Year [Ref])	Country / Setting	Study Design	Sample Size	Sample Description	Key Baseline Features / Demographics
de Souza <i>et al.</i> , 2023 ^[11]	NR	Cross-sectional study	140 women	Women with deep endometriosis (DE)	Assessed for CPP and Painful Bladder Syndrome (PBS) using the O'Leary-Sant Interstitial Cystitis Symptoms and Problem Index. Mean age NM.
Ivanova & Codreanu, 2025 ^[12]	Chisinau, Moldova	Cohort study	190 reproductive-aged patients	85 patients with Deep Infiltrating Endometriosis (DIE) vs. 105 with alternative endometriosis forms	Patients divided according to #ENZIAN classification. Pain measured using VAS and Biberoglu & Behrman (B&B) scales. Age range NM.
Huliieva & Chayka, 2026 ^[13]	NM	Interventional comparative study	124 patients	Patients with histologically confirmed endometriosis after surgical treatment	Main Group (n=74): hormonal therapy + enzyme therapy; Control Group (n=50): hormonal therapy only. Mean age NM.
Khashchenko <i>et al.</i> , 2022 ^[14]	NM	Prospective longitudinal study	32 girls	Adolescent girls (aged 14–17 years) with confirmed genital endometriosis	Assessed before and after 1 year of conservative therapy (NSAIDs + gestagens). Mean baseline pain intensity on menstruation: 8.3 ± 1.6 (V scale).
Powell <i>et al.</i> , 2026 ^[15]	Liverpool, UK	Prospective case-control study	89 women	Premenopausal women undergoing surgical investigation for CPP	Grouped by surgical findings: Control (no endometriosis, n=49), Superficial Endometriosis (SE, n=21), and Deep Endometriosis (DE, n=19). Mean age 41.8 ± 8.4 years (overall from original study population).

NR: not reported.

Table 2: Outcomes, Variables, and Key Findings

Study (Author, Year [Ref])	Key Variables Assessed	Main Numerical / Quantitative Findings	Qualitative Conclusions & Implications for IC/BPS Association
de Souza <i>et al.</i>, 2023 ^[11]	Impact of PBS on sleep quality (Pittsburgh Sleep Quality Index – PSQI); O'Leary-Sant Index for IC symptoms/problems.	• Only 13% of DE women had good sleep. • 94% of DE patients with PBS were poor sleepers. • PBS increased sleep disturbances by nearly fivefold ($p < 0.01$).	Adding PBS to CPP in women with DE is devastating for overall sleep quality. It impacts sleep dimensions unaffected by pain alone, confirming PBS as a significant comorbidity that warrants separate assessment and management.
Ivanova & Codreanu, 2025 ^[12]	Pain syndrome intensity (VAS and B&B scales); Presence of dysuria and dyschezia; Correlation with #ENZIAN compartments.	• Pain intensity (VAS and B&B) significantly higher in DIE group ($p < 0.01$). • Dysuria and dyschezia significantly more prevalent in DIE ($p < 0.001$). • Symptom profiles showed statistical correlation with specific #ENZIAN compartments ($p < 0.05$).	High-intensity pelvic pain combined with extragenital symptoms (including dysuria) is fundamental for clinical diagnosis of DIE. Urinary symptoms (dysuria) correlate with specific anatomical compartments, highlighting the need to assess bladder symptoms in endometriosis patients.
Huliieva & Chayka, 2026 ^[13]	Frequency of dysuria, dyschezia, pelvic pain, and dyspareunia after 1 month of treatment.	• Dysuria: 9.5% in main group vs. 50.0% in control group ($p < 0.001$). • Pelvic pain: 13.5% vs. 54.0% ($p < 0.001$). • Dyschezia: 10.8% vs. 28.0% ($p = 0.03$). • Dyspareunia: 12.0% vs. 46.0% ($p < 0.010$).	Enzyme therapy (streptokinase/streptodornase) significantly reduced clinical manifestations of CPP and associated urinary symptoms (dysuria). The study reported significantly lower dysuria rates in the intervention group than in the control group (9.5% vs. 50.0%, $p < 0.001$).
Khashchenko <i>et al.</i>, 2022 ^[14]	Dysuria, gastrointestinal symptoms, restriction of daily activity; Pain intensity (VAS).	• 22% of adolescents reported dysuria at baseline. • After 1 year of therapy: urinary disorders decreased significantly ($p < 0.001$). • Pain intensity on menstruation decreased from 8.3 ± 1.6 to significantly lower ($p < 0.001$).	Urinary symptoms (dysuria) are present in a notable percentage (22%) of adolescent endometriosis patients. These symptoms respond well to conservative management. Early recognition of urinary symptoms in young patients may help identify those at risk for developing IC/BPS later.
Powell <i>et al.</i>, 2026 ^[15]	Prevalence of Irritable Bowel Syndrome (IBS) using Rome IV diagnostic criteria; Endometriosis subtype correlation.	• 74.2% (66/89) of all women with CPP had concurrent IBS. • IBS prevalence: 83.7% in no endometriosis, 66.7% in SE, and 57.9% in DE ($p = 0.062$). • Significantly higher in patients without surgical evidence of endometriosis (83.7% vs. 62.5%, $p = 0.02$).	Patients with CPP have a high prevalence of overlapping visceral pain syndromes (IBS). This supports the hypothesis that IC/BPS (as a fellow visceral pain syndrome) is similarly underdiagnosed in these patients. Clinicians should actively screen for and treat overlapping syndromes, including bladder symptoms, to improve patient outcomes.

Table 3: Risk of Bias Assessment

Study (Author, Year [Ref])	Study Design	Assessment Tool	Risk of Bias Summary
de Souza <i>et al.</i> , 2023 ^[11]	Cross-sectional	JBIChecklist for Analytical Cross-Sectional Studies	Low risk. Clear inclusion criteria, validated exposure/outcome measures (PSQI, O'Leary-Sant), appropriate statistics. Limitation: no response rate reported.
Ivanova & Codreanu, 2025 ^[12]	Cohort	JBIChecklist for Cohort Studies	Moderate risk. Clearly defined groups and reliable pain measures (VAS, B&B). Limitation: no information on confounder identification/ adjustment strategies.
Huliieva & Chayka, 2026 ^[13]	Interventional Comparative	JBIChecklist for Quasi-Experimental Studies	Moderate risk. No randomization or blinding, but groups comparable at baseline; reliable outcome measures and clear statistical reporting ($p < 0.001$).
Khashchenko <i>et al.</i> , 2022 ^[14]	Prospective Longitudinal	JBIChecklist for Case Series	Moderate risk. Small sample size ($n=32$) and lack of control group; however, prospective design and use of validated pain scales strengthen quality.
Powell <i>et al.</i> , 2026 ^[15]	Case-Control	JBIChecklist for Case-Control Studies	Low risk. Clear case/control definitions; appropriate control selection from same population; valid measures (Rome IV criteria); adequate statistical analysis.

DISCUSSION

Our study, comprising a total of 575 participants, revealed consistently high rates of urinary symptoms and overlapping pain syndromes among women with endometriosis, supporting the concept that these conditions frequently coexist and share common pathophysiological mechanisms. The cross-sectional study by de Souza *et al.* ^[11] demonstrated that 94% of women with deep endometriosis and painful bladder syndrome were poor sleepers, with PBS increasing sleep disturbances by nearly fivefold ($p < 0.01$) ^[11]. This finding underscores the substantial clinical burden of bladder symptoms in endometriosis patients and highlights the need for routine screening for IC/BPS in this population. Similarly, the cohort study by Ivanova and Codreanu ^[12] found that dysuria and dyschezia were significantly more prevalent in patients with deep infiltrating endometriosis compared to those with other forms of endometriosis ($p < 0.001$), with these urinary symptoms correlating with specific #ENZIAN classification compartments ($p < 0.05$) ^[12]. These results align with previous research demonstrating that deep endometriosis frequently involves the urinary tract and produces bladder-related symptoms that may be mistaken for primary bladder pathology.

The prospective longitudinal study by Khashchenko *et al.* ^[14] further corroborated these findings, reporting that 22% of adolescent girls with endometriosis experienced dysuria at baseline, with significant improvement after one year of conservative therapy ($p < 0.001$) ^[14], indicating that urinary symptoms manifest early in the disease course and are amenable to treatment.

The prevalence of urinary symptoms observed in our included studies is consistent with the broader literature on endometriosis and IC/BPS comorbidity. A recent systematic review and meta-analysis by Inzoli *et al.* ^[16] evaluated the coexistence of endometriosis and IC/PBS in women with chronic pelvic pain, finding a prevalence range of 15.5% to 78.3%, which is substantially higher than the prevalence of IC/PBS in the general population (estimated at 2.7% to 6.5%). This wide range reflects the considerable heterogeneity in study designs, diagnostic criteria, and patient populations, yet consistently demonstrates that the coexistence of these conditions is far more common than previously recognized. The authors of that meta-analysis emphasized that in cases of endometriosis unresponsive to treatment, other causes of chronic pelvic pain such as IC/PBS must be ruled out ^[16].

Our findings corroborate this recommendation, as the interventional study by Huliieva and Chayka ^[13] demonstrated that dysuria was present in 50% of the control group receiving hormonal therapy alone, compared to only 9.5% in the group receiving combined

hormonal and enzyme therapy ($p < 0.001$) ^[13], indicating that bladder symptoms are prevalent even in treated endometriosis populations and may persist despite adequate gynecological management. Furthermore, the interventional study showed significant reductions in pelvic pain (from 54% to 13.5%, $p < 0.001$), dyspareunia (from 46% to 12%, $p < 0.010$), and dyschezia (from 28% to 10.8%, $p = 0.03$) ^[13], providing comprehensive evidence of the clinical overlap between endometriosis and lower urinary tract symptoms.

The association between endometriosis and IC/BPS is further supported by population-based epidemiological evidence. A nationwide population study by Wu *et al.* ^[17] examined the risk of bladder pain syndrome/interstitial cystitis among women with endometriosis in Taiwan, following 9,191 subjects with endometriosis and 27,573 controls over a three-year period. The incidence of BPS/IC during follow-up was 0.2% in the endometriosis group versus 0.05% in the control group, with a hazard ratio of 4.43 (95% CI: 2.13-9.23) for developing BPS/IC over the three-year period. After adjusting for comorbidities, the hazard ratio remained significant at 3.74 (95% CI: 1.76-7.94, $p < 0.001$) ^[17]. Current observational evidence suggests that endometriosis is associated with an increased likelihood of IC/BPS; however, a causal relationship cannot be inferred from the available studies. Our included case-control study by Powell *et al.* ^[15] adds another dimension to this understanding, demonstrating that 74.2% of all women with chronic pelvic pain had concurrent irritable bowel syndrome, with the highest prevalence (83.7%) observed in women without surgical evidence of endometriosis ^[15]. While this study focused on IBS rather than IC/BPS, it highlights the broader phenomenon of overlapping visceral pain syndromes in chronic pelvic pain patients, these findings demonstrate the high prevalence of overlapping visceral pain syndromes in women with chronic pelvic pain; however, because this study evaluated IBS rather than IC/BPS, it should be interpreted as indirect rather than direct evidence for the association between endometriosis and IC/BPS. The authors noted that patients with deep endometriosis were less likely to meet IBS diagnostic criteria than those with superficial endometriosis and no endometriosis (57.9% vs. 66.7% vs. 83.7%, $p = 0.062$) ^[15], suggesting that deep infiltrative disease may present with more pronounced gynecological symptoms that overshadow bowel manifestations, yet the overall burden of overlapping syndromes remains substantial.

The pathophysiological mechanisms underlying the association between endometriosis and IC/BPS are increasingly understood through the framework of central sensitization and cross-sensitization of pelvic organs. A systematic review by Lepka *et al.* ^[18] found that central sensitization prevalence in the endometriosis population

ranges from 11.3% to 58.2%, rising to 74.8% in specialized tertiary referral centers. Furthermore, every one-point increase in preoperative Central Sensitization Inventory (CSI) score raised the risk of persistent pain after surgery (OR 1.02, $p = 0.02$)^[18], suggesting that central sensitization is a key predictor of surgical outcomes.

These findings are consistent with the conceptual framework proposed by **Bautrant**^[19], who identified a uterine pain and hypercontractile syndrome (UPHS) that shares pathophysiological features with bladder pain syndrome and irritable bowel syndrome. The author argued that severe primary dysmenorrhea corresponds to a nociplastic pain state within the framework of central sensitization, paving the way for a better understanding of visceral pain syndromes that frequently co-occur in this population^[19].

Similarly, a review by the International Association for the Study of Pain described endometriosis-associated pain as a product of peripheral sensitization, central sensitization, and cross-sensitization, with comorbid pain syndromes sharing overlapping pathophysiological mechanisms. This mechanistic understanding explains why patients with endometriosis often present with multiple overlapping pain conditions, including IC/BPS, and why treatment must address both peripheral lesions and central pain processing. The role of central sensitization in the persistence of pain despite adequate surgical treatment for endometriosis is particularly relevant, as up to 40% of patients experience persistent pelvic pain after lesion excision, suggesting that central mechanisms play a dominant role in a significant subset of patients.

The diagnostic challenges inherent in distinguishing between endometriosis and IC/BPS are well documented in the literature. A clinical opinion published in the International Urogynecology Journal^[20] noted that endometriosis and IC/BPS frequently coexist in women with chronic pelvic pain, yet overlapping symptoms and non-standardized diagnostic pathways often delay recognition of dual pathology. The authors proposed that a structured surgical approach combining laparoscopy and diagnostic cystoscopy may improve identification and clinical characterization of this overlap^[20]. This recommendation is particularly relevant given that our included studies demonstrate that bladder symptoms (dysuria) are present in 22% of adolescent endometriosis patients^[14] and up to 50% of adult patients in certain populations^[13].

The prospective longitudinal study by **Khashchenko et al.**^[14] showed that urinary disorders improved significantly after one year of conservative therapy with naproxen and dienogest ($p < 0.001$), with reductions in restriction of daily activities ($p < 0.001$), gastrointestinal symptoms ($p < 0.001$), and the need for mandatory pain medication ($p < 0.001$)^[14]. This suggests

that early recognition and treatment of bladder symptoms may improve outcomes, particularly in adolescent populations where early intervention may prevent the development of chronic pelvic pain syndromes. However, the persistence of symptoms in some patients despite treatment^[13] indicates that a subset of patients may have primary IC/BPS rather than secondary bladder irritation from endometriosis, underscoring the need for comprehensive urological evaluation. The study by **Huliieva and Chayka**^[13] demonstrated that enzyme therapy (streptokinase and streptodornase) combined with hormonal treatment significantly reduced dysuria compared to hormonal therapy alone, suggesting that addressing inflammatory and fibrotic components may be beneficial in managing bladder symptoms in endometriosis patients^[13].

Our findings have important clinical implications for the management of women with endometriosis and chronic pelvic pain. The high prevalence of urinary symptoms and overlapping pain syndromes observed in our included studies suggests that routine screening for IC/BPS should be integrated into the standard evaluation of endometriosis patients, particularly those with refractory pain or persistent bladder symptoms despite adequate gynecological treatment.

The population-based study by **Namugosa et al.**^[21] found that among 533 patients with IC/BPS, 108 (20.3%) reported a history of endometriosis, and those with concurrent endometriosis were younger, had larger bladder capacity, and had a higher number of nonurological associated symptoms. Importantly, patients with concurrent endometriosis were more likely to report comorbidities such as chronic pelvic pain, chronic fatigue, fibromyalgia, migraines, and pelvic floor dysfunction, suggesting a non-bladder-centric (systemic pain disorder) phenotype^[21]. This phenotype-based approach to IC/BPS classification has been increasingly recognized as clinically valuable, as it enables more targeted therapeutic strategies. Furthermore, a systematic review by **Knox et al.**^[22] evaluated central sensitization in bladder pain syndrome, providing additional evidence for the role of central mechanisms in the persistence of bladder pain.

The recognition that endometriosis-associated IC/BPS may represent a distinct phenotype with systemic pain features has significant implications for treatment selection, suggesting that multimodal approaches addressing both peripheral and central pain mechanisms may be more effective than bladder-directed therapy alone.

The high rate of IBS in chronic pelvic pain patients (74.2%) reported by **Powell et al.**^[15] further emphasizes the need for comprehensive assessment of all pelvic organ systems rather than isolated gynecological evaluation, as patients frequently present with multiple overlapping pain conditions that require integrated multidisciplinary management.

The clinical relevance of our findings is further supported by the substantial impact of painful bladder syndrome on quality of life, as demonstrated by de Souza *et al.* ^[11], who reported that only 13% of women with deep endometriosis had good sleep quality, with PBS being a major contributor to sleep disturbances. The study showed that chronic pelvic pain worsened subjective sleep quality by more than threefold ($p = 0.019$), increased sleep disturbances by nearly sixfold ($p = 0.03$), and decreased sleep duration by practically sevenfold ($p = 0.019$), while PBS independently increased sleep disturbances by nearly fivefold ($p < 0.01$) ^[11]. These findings highlight the devastating effect of combined CPP and PBS on overall sleep quality, probably because PBS impacts some sleep dimensions unaffected by CPP and amplifies the problem in those already affected by pain. The authors concluded that the addition of PBS to CPP in women with deep endometriosis is devastating for overall sleep quality, emphasizing the need for comprehensive symptom management that addresses both gynecological and urological components ^[11].

This is particularly important given that poor sleep quality is associated with increased pain sensitivity, reduced quality of life, and worse treatment outcomes in chronic pain populations. The interventional study by Huliieva and Chayka ^[13] provides evidence that addressing inflammatory and fibrotic components through enzyme therapy may improve both gynecological and urinary symptoms, suggesting that anti-inflammatory strategies may be beneficial in managing the complex symptomatology of endometriosis-associated IC/BPS ^[13]. Additionally, the correlation between dysuria and specific #ENZIAN compartments reported by Ivanova and Codreanu ^[12] suggests that imaging and classification systems may help predict which endometriosis patients are at highest risk for bladder involvement, enabling more targeted screening and early intervention ^[12].

LIMITATIONS

This systematic review acknowledges several limitations: it includes only five studies, which limits the primary research available on endometriosis and IC/BPS. There is significant heterogeneity in study designs, affecting data pooling and evidence quality. Diagnostic criteria for IC/BPS varied, raising concerns about misclassification. Geographic generalizability is limited due to unspecified study origins and a predominance of European and Middle Eastern settings. Sample sizes varied widely, with some studies lacking robust methodologies like randomization and blinding, which could introduce biases. Additionally, many studies focused on urinary symptoms rather than formal IC/BPS diagnoses. The absence of standardized definitions for conditions complicates synthesis, and the exclusion of certain literature may have omitted valuable contextual

insights. Publication bias could not be formally assessed because only five studies were included and no meta-analysis was performed.

CONCLUSION

This systematic review suggests an association between endometriosis and interstitial cystitis/bladder pain syndrome (IC/BPS). However, the available evidence is limited by the inclusion of only five heterogeneous observational studies, precluding definitive conclusions regarding causality or the magnitude of the association. Shared pathophysiological mechanisms warrant a multidisciplinary management approach. Clinicians should be vigilant for IC/BPS in patients exhibiting urinary symptoms, as early urological referral may enhance diagnostic accuracy and treatment outcomes. The review also underscores the impact of painful bladder syndrome on quality of life, recommending comprehensive symptom assessment and potential combined anti-inflammatory therapies for managing bladder symptoms in these patients. Future research should focus on diagnostic algorithms and targeted therapeutic strategies to improve care integration for affected women.

DECLARATIONS

Ethics Approval and Consent to Participate

As this study is a systematic review of previously published literature, it did not involve the collection of primary data from human or animal subjects. Therefore, formal ethical approval and individual participant consent were not required. All included studies were conducted in accordance with the ethical standards of their respective institutional and/or national research committees.

Consent for Publication

Not applicable, as this manuscript does not contain any individual person's data in any form (e.g., individual details, images, or videos).

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All authors cooperated in drafting, writing, synthesis of the study and they reviewed and approved the final manuscript.

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