HHS Public Access

Author manuscript

Female Pelvic Med Reconstr Surg. Author manuscript; available in PMC 2023 March 01.

Published in final edited form as:

Female Pelvic Med Reconstr Surg. 2022 March 01; 28(3): e115–e119. doi:10.1097/SPV.0000000000001166.

Prevalence of Overactive Bladder Symptoms Among Women with Interstitial Cystitis/Bladder Pain Syndrome

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Abstract

Importance: Symptoms of urinary frequency, urgency, and urinary leakage are characteristic of overactive bladder syndrome. However, frequency and urgency symptoms are also present in the majority of patients with interstitial cystitis/bladder pain syndrome (IC/BPS).

Objective: Our objective was to describe the urge incontinence among women with IC/BPS, which may indicate true overlap of OAB and IC/BPS.

Study Design: This is a prospective study of women with IC/BPS diagnosed clinically in the Veterans Affairs Health Care system. Patients completed the Overactive Bladder (OAB) and the Female Genitourinary Pain Index (F-GUPI) questionnaires. Questions from the OAB questionnaire were used to analyze symptoms of urinary urgency and urge incontinence, respectively. Pain symptoms, urinary symptoms, and impact on quality of life were assessed based on F-GUPI. Patient demographics, comorbidities, and symptoms were reviewed.

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Results: Within the cohort of 144 women with IC/BPS, 100 (69%) had urinary leakage associated with the strong desire to void, and more likely to have incontinence compared to healthy controls ($p<0.001$). The IC/BPS group also had higher total and pain scores on F-GUPI ($p<0.001$), but pain scores were not affected by the presence of incontinence ($p=0.478$).

Conclusions: The prevalence of OAB symptoms of urinary leakage is high among women with IC/BPS. This may explain the efficacy of OAB medication and third-line therapies in this population.

Keywords

Interstitial cystitis; overactive bladder; urinary urgency; urge urinary incontinence

Introduction:

Interstitial cystitis (IC), also known as bladder pain syndrome (BPS), is a condition characterized by an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.[1] In the United States about 3.3 to 7.9 million women suffer with IC/BPS.[2,3] There are multiple hypotheses surrounding the etiology and pathophysiology of IC/BPS, though the cause remains unknown. Frequently, diagnosis is delayed or women are being misdiagnosed with other conditions like overactive bladder (OAB), chronic pelvic pain, or endometriosis before a true diagnosis of IC/BPS is established due to the overlap between these conditions. [1,2,4–7]

Overactive bladder (OAB) is a condition described as urinary urgency, frequency, nocturia, with or without urinary incontinence, in the absence of urinary tract infection or other pathology.[8] The prevalence of OAB is 13% among women and increases with age.[9–16] According to the National Overactive BLadder Evaluation (NOBLE) Program, the proportion of women with OAB who have urgency urinary incontinence (also known as “OAB-wet”) is similar to the proportion who do not leak (“OAB-dry”).[14] Symptoms of urgency and frequency are present in both IC/BPS and OAB. In fact, 59.2 % of women with IC/BPS experience painful filling and painful urgency, together known as Rand Interstitial Cystitis Epidemiology (RICE) Survey criteria.[3,17] However, the degree of symptom overlap between IC/BPS and OAB has not been established to date.

The goal of this study was to describe the prevalence of OAB symptoms among women with IC/BPS. Our secondary goal was to describe and compare patient demographics and clinical characteristics between patients with and without incontinence in the setting of an IC/BPS diagnosis.

Methods:

After obtaining IRB approval from the Veterans Affair Health Care System, we used the Veterans Affairs Informatics and Computing Infrastructure (VINCI) to identify all patients in the VA system between 1999 and 2016 with an ICD-9 or ICD-10 diagnosis code for

IC/BPS (595.1/N30.10) (n = 9,503). We selected a random sample of 755 charts of female patients to perform a detailed chart review to assess the accuracy of the IC/BPS diagnosis.

Patients were considered to have a correct IC/BPS diagnosis if they had at least two visits complaining of bladder-centric pain in the absence of positive urine culture at least 6 weeks apart (n=651). If the patient did not meet this criterion, she was considered to be misdiagnosed with IC/BPS and were removed from the analysis. Then, patients that had a history of any of the following exclusionary criteria were excluded from the analysis (n=129): pelvic radiation or systemic chemotherapy, bladder cancer at any time point, metastatic cancer, prior cystectomy, dyspareunia, vaginismus, vulvodynia, vulvar vestibulitis, history of recurrent urinary tract infections, end stage renal disease, or history of infection with human immunodeficiency virus (HIV). This left us with 522 charts meeting inclusion and exclusion criteria. Among these charts we randomly selected 200 charts to participate in the study.

Next, 100 healthy control women younger than 90 years old were selected using VINCI from a list of patients who did not have an ICD-9 or ICD-10 diagnosis of IC/BPS or other conditions which might be confused with IC/BPS (pelvic radiation or systemic chemotherapy, bladder cancer, metastatic cancer, prior cystectomy, dyspareunia, vaginismus, vulvodynia, vulvar vestibulitis, history of recurrent urinary tract infections, end stage renal disease, or history of HIV).

Interest letters and consent forms were mailed to patients with IC/BPS and healthy controls. Then, study personnel followed up via phone and those women who consented to participate were mailed questionnaires (IC/BPS n = 177, healthy controls n = 62). Healthy control subjects were only allowed to be enrolled if they consented to providing a urine sample. All consented participants were then sent questionnaires: Overactive Bladder Questionnaire (OABq) and Female Genitourinary Pain Index (F-GUPI).

The OABq was used to analyze the prevalence and severity of OAB symptoms (urinary urgency, urinary leakage, urinary incontinence). The OABq contains 33 items evaluating symptom bother and health related quality of life. Question four (“accidental loss of small amount of urine”) and question eight (“urine loss associated with strong desire to urinate”) were used to identify subjects with urinary leakage and urinary urgency, respectively. Available responses to these two questions ranged from “not at all” to “a very great deal.” Urinary incontinence was defined as any urinary leakage.

The Female Genitourinary Pain Index (F-GUPI) is a statistically validated bladder pain survey that contains nine questions and assesses three subscales: pain symptoms, urinary symptoms, and impact on quality of life.[18]

Patients who did not complete or had missing data on OABq and F-GUPI questionnaires were excluded from the analysis.

Using ICD-9 and ICD-10 codes (Table 1) we identified comorbidities common in IC/BPS population including history of depression, history of alcohol abuse, history of post-traumatic stress disorder (PTSD), and history of irritable bowel syndrome (IBS) among

IC/BPS cohort and healthy controls.[19] We compared demographics and OAB symptoms between the two groups. The IC/BPS patients were then compared based on the presence or absence of urinary incontinence to assess the impact of incontinence on IC/PBS.

We summarized categorical data with frequencies and percentages and continuous data were summarized using the median. We examined differences between groups using Kruskal-Wallis tests for continuous variables and Chi-squared tests for categorical variables. Statistical significance was defined as $p<0.05$. All analyses were performed using SAS 8.4.

Results:

After receiving questionnaires from the consented participants and excluding those with missing data we had 201 charts for review: 144 women in the IC/BPS cohort and 57 healthy controls. IC/BPS patients were predominantly White (101; 71%) and non-Hispanic (127; 93%) (Table 2). Among the IC/BPS cohort, 52% (75) had a history of depression, 52% (75) PTSD, 32% (46) IBS, and 8% (11) a history of alcohol abuse. A history of depression ($p=0.030$) and IBS ($p=0.021$) were statistically more prevalent among women with IC/BPS than HC. There were no other statistically significant differences in demographic features between healthy controls and women with IC/BPS (all $p>0.05$). We found that 81% (116 women) in the IC/BPS group had urinary leakage based on the OAB-q, with 40 patients having “a little bit” and 20 having “a very great deal” of leakage. A strong desire to void associated with urinary leakage was present among 69% (100) of women with IC/BPS.

Among healthy controls the prevalence of urinary leakage was 46% (26), and urinary loss associated with a strong desire to void was present in 30% (17). When compared, the IC/BPS cohort had a significantly higher prevalence of urinary leakage and associated strong desire to void than the healthy control cohort ($p<0.001$, Table 2). 81% (116 women) of the IC/BPS group experienced incontinence, compared with 46% (26 women) in the HC group ($p<0.001$.) The IC/BPS cohort had higher total scores and pain subscale scores on F-GUPI compared to HC ($p<0.001$).

There was no statistically significant difference in demographics and comorbidities between women in the IC/PBS group with and without incontinence. Although total F-GUPI scores were higher for women with incontinence, F-GUPI pain subscale scores were not statistically different between women with IC/BPS with and without urinary leakage (Table 3).

Discussion

The prevalence of OAB symptoms among IC/BPS symptoms is not well established. This can be explained by the fact that IC/BPS diagnosis in itself is challenging. In prior studies, about 46% of women had received alternative diagnoses for the same symptoms prior to being diagnosed with IC/BPS,[4] at the same time some women are being misdiagnosed with IC/BPS while having other similar urinary conditions, like OAB.[19]

Clinically we tend to differentiate between IC/BPS and OAB by the motivation to void: fear of leakage (OAB) versus discomfort and pain with filling (IC/BPS). The high prevalence

of urinary incontinence among IC/BPS patients demonstrated in our study suggests that the traditional differentiation based on fear of leakage might not be applicable to every patient. In our study we found that many women have both.

We should consider the high prevalence of OAB symptoms among women with IC/BPS when making treatment choices. Currently the stepwise approach to IC/BPS treatment[1] begins with stress management and coping techniques, proceeding with second-line options: physical therapy, multimodal pain management, oral agents (antihistamines, tricyclic antidepressants), and intravesical installations. Third-line therapy includes bladder hydrodistension and fulguration of Hunner's lesions, when present. The next step is a trial of intravesical injection of botulinum toxin A or sacral neurostimulation, both of which overlap with third-line treatment for OAB refractory to medical therapy.[20] Our study may help explain why OAB therapies are often effective in patients with IC/BPS. For example, intravesical injection of botulinum toxin demonstrated 63% improvement in pain among IC/BPS patients versus 15% in the placebo group,[21] similarly to 60% versus 22% in the trial by Pinto et al.,[22] and 72% overall improvement with botulinum toxin vs 25% with placebo by Akiyama et al.[23] Smith et al. found a decrease in daytime frequency and nocturia by 44% and 45% respectively ($p<0.01$).[24] In the same way, neuromodulation resulted in significant improvement in symptoms among IC/BPS patients.[25,26] It is reasonable to incorporate a trial of OAB treatment modalities into the therapy for IC before moving to more invasive options.

As expected, pain scores on the GUPI subscale were higher for women in the IC/BPS cohort than health controls ($p<0.001$). However, GUPI pain subscale scores were not statistically different between women with IC/BPS with and without incontinence. This finding supports the proposal in the Multi-Disciplinary Approach to the Study of Pelvic Pain (MAPP) network that pain symptoms and urinary symptoms should be assessed separately, as pain, not urinary symptoms, were shown to have an adverse impact on quality of life in patients with IC/PBS.[27] It may be that a large proportion of patients with IC/BPS also have OAB. Similarly, Griffith et al. demonstrated that symptoms of depression among MAPP study subjects were linked to pain symptoms, but not to urinary symptoms.[28] Distinguishing one group of symptoms from another provides a better opportunity to maximize success with symptom-specific treatment options.

The present study has several limitations. First, our data comes from a VA cohort, which may not represent the population at large, as US veterans might have had different stressors and health risks. Second, all patients in our databases have the same insurance payor status, which potentially did not allow us to control for socioeconomic status. Next, we were limited by our definition of IC/BPS and the availability of hand-abstracted data. Patients were considered to have a correct IC/BPS diagnosis if they had two visits complaining of bladder-centric pain in the absence of positive urine culture at least 6 weeks apart. Patients who were lost to follow up or those who were diagnosed with a UTI instead of IC/BPS flare might have been missed. These limitations are mitigated by the fact that the VA cohort represents a large, heterogeneous, population-based dataset. We applied a novel methodology where the scope of a large population-based dataset was combined with individual chart review, which is known to reduce the challenges associated with studying IC/BPS.[29]

Conclusion

Overall, the prevalence of urinary leakage associated with the strong desire to void is high (69%) among women with IC/BPS. This may explain the efficacy of OAB therapies in this population. Further studies of the effect of OAB-targeted treatment on urinary symptoms among women with IC/BPS are needed.

Disclosures and source of Funding:

This publication was supported by the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $5.5 million with 100 percent funded by CDC/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by CDC/HHS, or the U.S. Government. This work was funded by a grant (5U01DP006079) from the Centers for Disease Control and Prevention.

The remaining authors reported no disclosures.

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Table 1:

ICD-9/ICD -10 Diagnosis Codes Used for Analysis.

Diagnosis	**ICD-9/ICD-10 codes**
Interstitial cystitis/bladder pain syndrome (IC/BPS)	595.1/N30.10
Alcohol abuse	305.0-305.03/ F10.10, F10.120, F10.121, F10.129, F10.14, F10.150, F10.151, F10.159, F10.180-F10.182, F10.188, F10.19-F10.21, F10.220, F10.221, F10.229-F10.232, F10.239, F10.24, F10.250, F10.251, F10.259, F10.26, F10.27, F10.280-F10.282, F10.288, F10.29, F10.920, F10.921, F10.929, F10.94, F10.950, F10.951, F10.959, F10.96, F10.97, F10.980-F10.982, F10.988, F10.99
Depression	296.3-296.36/ F33.0, F33.1, F33.2, F33.3, F33.40-F33.42, F33.8, F33.9
Post-traumatic stress disorder (PTSD)	309.81/ F43.10, F43.11, F43.12, F43.9
Irritable bowel syndrome (IBS)	564.1/ K58.0, K58.1, K58.2, K58.8, K58.9

Table 2:

Patient characteristics by IC/BPS status in the VA population

	Diagnosed with IC (N=144)	Healthy Control (N=57)	p value
Age at time of consent			0.073[1]
Median	52.0	50.0	
Q1, Q3	43.5, 60.0	38.0, 58.0	
Race			0.477[2]
Missing	2	0	
Black	38 (27%)	16 (28%)	
White	101 (71%)	38 (67%)	
Other*	3 (2%)	3 (5%)	
Ethnicity			0.646[2]
Missing	7	2	
Hispanic	10 (7%)	3 (5%)	
Not Hispanic	127 (93%)	52 (95%)	
History of depression			0.030[2]
No	69 (48%)	37 (65%)	
Yes	75 (52%)	20 (35%)	
History of alcohol abuse			0.789[2]
No	133 (92%)	52 (91%)	
Yes	11 (8%)	5 (9%)	
PTSD			0.085[2]
No	69 (48%)	35 (61%)	
Yes	75 (52%)	22 (39%)	
IBS			0.021[2]
No	98 (68%)	48 (84%)	
Yes	46 (32%)	9 (16%)	
Urinary leakage [Accidental loss of small amount of urine (OAB-q)]			<0.001[2]
Not at all	28 (19%)	31 (54%)	
A little bit	40 (28%)	15 (26%)	
Somewhat	20 (14%)	4 (7%)	
Quite a bit	24 (17%)	3 (5%)	
A great deal	12 (8%)	3 (5%)	
A very great deal	20 (14%)	1 (2%)	
Incontinence			<0.001[2]
No	28 (19%)	31 (54%)	
Yes	116 (81%)	26 (46%)	
Urinary urgency [Urine loss associated with a strong desire to urinate (OAB-q)]			<0.001[2]

	Diagnosed with IC (N=144)	Healthy Control (N=57)	p value
Not at all	44 (31%)	40 (70%)	
A little bit	33 (23%)	6 (11%)	
Somewhat	17 (12%)	5 (9%)	
Quite a bit	12 (8%)	4 (7%)	
A great deal	15 (10%)	2 (4%)	
A very great deal	23 (16%)	0 (0%)	
Total F-GUPI score			<0.001[1]
Median	27.0	3.0	
Q1, Q3	18.0, 34.0	1.0, 12.0	
F-GUPI pain subscale			<0.001[1]
Median	12.0	0.0	
Q1, Q3	8.0, 16.0	0.0, 4.0	

[1] Wilcoxon

[2] Chi-Square

Abbreviations: F-GUPI: Female -Genitourinary Pain Index; IBS: irritable bowel syndrome; IC/BPS: interstitial cystitis/bladder pain syndrome; OAB: overactive bladder; PTSD: post-traumatic stress disorder

[*] Other Group includes Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and multiracial.

Table 3:

Patient characteristics for IC/BPS cohort stratified by accidental loss of urine (OABq) in the VA population

	No incontinence (N=28)	Incontinence (N=116)	p value
Age at time of consent			0.486[1]
Median	52.0	52.0	
Q1, Q3	43.0, 54.5	44.0, 61.0	
History of depression			0.806[2]
No	14 (50%)	55 (47%)	
Yes	14 (50%)	61 (53%)	
History of alcohol abuse			0.912[2]
No	26 (93%)	107 (92%)	
Yes	2 (7%)	9 (8%)	
PTSD			0.131[2]
No	17 (61%)	52 (45%)	
Yes	11 (39%)	64 (55%)	
IBS			0.380[2]
No	21 (75%)	77 (66%)	
Yes	7 (25%)	39 (34%)	
Total F-GUPI score			0.034[1]
Median	24.0	28.0	
Q1, Q3	17.5, 27.5	18.0, 35.0	
F-GUPI pain subscale			0.517[1]
Median	11.5	12.0	
Q1, Q3	9.0, 14.0	8.0, 17.0	

[1]Wilcoxon

[2]Chi-Square

Abbreviations: F-GUPI: Female -Genitourinary Pain Index; IBS: irritable bowel syndrome; IC/BPS: interstitial cystitis/bladder pain syndrome; OAB: overactive bladder; PTSD: post-traumatic stress disorder