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Painful bladder symptoms related to somatic syndromes in a convenience sample of community women with overactive bladder symptoms

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Abstract

Purpose—Herein we aim to investigate the relationship between painful bladder filling and urinary urgency with somatic and chronic pain symptoms in women with overactive bladder (OAB) without an interstitial cystitis/bladder pain syndrome (IC/BPS) diagnosis.

Materials and Methods—Women meeting OAB criteria based on symptoms were recruited through the community (n=183, 83.9%) or Urology clinic (n=35, 16.1%) to complete validated questionnaires assessing urinary symptoms, somatic symptoms, and pain syndromes. Participants were categorized into 3 groups, (1) Neither (2) Either or (3) Both, based on their report of painful urinary urgency and/or painful bladder filling. Multivariable regression analyses were performed to determine factors predictive of having either or both painful urgency and/or painful filling.

Results—Of 218 women with OAB, 46% (n=101) had neither painful bladder filling nor urinary urgency, 43% (n=94) had either, and 11% (n=23) had both. Controlling for age, women with either or both urologic pain symptoms were more likely to have irritable bowel syndrome, chronic pelvic pain, and temporomandibular disorder compared to women in the neither group. Additionally, these women had higher pain intensity and somatic symptoms scores than women with neither symptom.

Conclusions—The majority of women with OAB, without a diagnosis of IC/BPS, reported either painful urgency, painful filling, or both. Experiencing painful urgency and/or filling was associated with increased somatic symptom burden and pain intensity. These findings support the hypothesis that OAB and IC/BPS diagnoses may represent a continuum of bladder hypersensitivity.

Keywords

overactive bladder; functional somatic disorders; bladder pain syndrome; interstitial cystitis

Introduction

Overactive bladder (OAB) is defined by the International Continence Society as “urinary urgency, with or without urgency incontinence, usually with frequency or nocturia”¹. Although pain symptoms are not considered a part of the OAB syndrome, prior data has demonstrated overlap between the OAB and Interstitial cystitis/Bladder pain syndrome (IC/BPS) symptoms experienced by patients. The Interstitial Cystitis multicenter database reported that 48% of IC/BPS patients experienced urgency, 40% urinary frequency 15 voids per day, and 20% had nocturia 4 times per night². Other studies support minimal differences in urinary frequency and urgency between patients with OAB and IC/BPS with 33% and 45% of patients with OAB experiencing pain with bladder filling³ and pain, pressure, or discomfort associated with the urge to urinate⁴, respectively.

The underlying pathophysiology of both OAB and IC/BPS remains unclear and despite clinical overlap, a common pathophysiologic association has not been definitively established. Central sensitization, characterized by neuronal plasticity and spinal hypersensitivity to afferent input, is implicated in the pain phenotype of several chronic pain and somatic conditions, collectively termed central sensitization syndromes (CSS)⁵. It has been suggested that OAB and IC/BPS overlap with CSS clinically. The prevalence of migraine, fibromyalgia, and chronic fatigue, was found to be higher in women with OAB than those without⁶ and somatic symptom burden correlated with OAB severity⁷. Furthermore, Lai and colleagues⁸ established that the symptoms of painful bladder filling and painful urgency were associated with more severe urologic symptoms and a higher somatic symptom burden in a population of men and women with urologic chronic pelvic pain syndromes. These findings suggest that chronic pain conditions alter the experience of OAB symptoms, or alternatively that OAB, IC/BPS, and CSS have common underlying pathophysiologic mechanisms affecting afferent sensory nerves.

The aim of this study was to investigate the relationship between painful filling and painful urgency with OAB severity, somatic symptoms, and CSS in women with OAB without a self-reported diagnosis of IC/BPS. We hypothesized that women with OAB and painful bladder symptoms would have a greater somatic symptom burden compared to women with OAB without associated pain symptoms.

Materials and Methods

Following Institutional Review Board approval, adult women with OAB were recruited through the clinic (n=35, 16.1%) or through the community (n=183, 83.9%) via electronic advertisement to participate in this questionnaire-based study. Inclusion criteria included women 18 or older with OAB symptoms based on a score 4 on the OAB-V3 awareness tool, a three-item screening tool⁹. Women were excluded if they reported neurologic diagnoses (i.e. multiple sclerosis, spinal cord injury, or stroke) or a history of pelvic radiation, bladder cancer, or bowel diversion. Questionnaires assessed demographics, urinary tract symptoms, and pain conditions.

Validated questionnaires specific to the lower urinary tract included the 8-item Overactive Bladder Questionnaire symptom scale (OABq-SS)¹⁰ and the 13-item Overactive Bladder Questionnaire Health Related Quality of Life (OABq-HRQL) scale¹¹. Both the OABq-SS and OABq-HRQL were transformed to a 100-point score with a higher score on the OABq-SS indicating more severe symptoms, while a lower score on the OABq-HRQL indicated a greater negative effect on health-related quality of life related to OAB. A difference of 10 points for these transformed scores is considered clinically meaningful. Urgency urinary incontinence (UUI) was defined by a response of at least “somewhat” to urine loss associated with a strong urge to urinate from the OABq.

The Somatic Symptom Scale (SSS)¹² measures somatic symptom burden through assessment of gastrointestinal, pain, fatigue, and cardiopulmonary symptoms over the preceding 7 days. The Patient-Reported Outcomes Measurement Information System (PROMIS) Pain intensity is a NIH sponsored instrument including three items that evaluates pain intensity at its worse, average, and current on a scale of 1 (none) to 5 (very severe)¹³. Scoring is done using the PROMIS Assessment Center Scoring Service available online. The final score is represented as a T-score with standard error standardized to the United States general population and a T-score >50 represents a worse pain intensity than average.

Patients were asked to self-report (“if you ever had or ever have had the following medical conditions”) a diagnosis of CSS, specifically low back pain, restless leg syndrome, temporomandibular joint (TMJ) disorder, neck pain, chronic fatigue syndrome, endometriosis, chemical sensitivity, vulvodynia, and IC/BPS. Chronic pelvic pain was defined as: “Pelvic pain, either constantly or off and on, for 3 months or more. By pelvic pain I mean pain below the belly button or in the female organs.”¹⁴ The diagnosis of irritable bowel syndrome (IBS) was based on Rome III criteria¹⁵. The diagnosis of migraine was based on a validated self-administered questionnaire and included a positive response to having migraines or tension headaches in addition to one of the following associated symptoms: 1) activity limited by migraine in last 3 months, 2) nausea, or 3) photophobia¹⁶. The diagnosis of fibromyalgia was based on American College of Rheumatology guidelines using minimum cut-offs for wide pain index and somatic symptom score¹⁷.

For the primary analysis, we examined a population of women with OAB without a self-reported diagnosis of IC/BPS (community recruited women) or a clinical diagnosis of IC/BPS (women recruited from clinic). The final study cohort of 218 women were categorized into three groups based on the presence of painful urgency and/or painful filling: (1) Neither symptom (2) Either symptom and (3) Both symptoms in a similar classification scheme published by Lai et al⁸. The RAND Interstitial Cystitis Epidemiology questionnaire was used to assess painful urgency and painful filling¹⁸. Painful urgency was reported as pain, pressure, or discomfort associated with the urge to urinate and painful filling was defined as a “Yes” response to “In the past week, have you experienced pain or discomfort as your bladder fills?” Responses to validated questionnaires were compared between the three groups. Secondly, to ensure that the population of women with OAB without a self-reported diagnosis of IC/BPS, but endorsing both painful urinary urgency and painful bladder filling symptoms, was different from those women self-reporting an IC/BPS diagnosis, comparisons were also done between those two groups.

Statistical analysis

All continuous variables were determined to be normally distributed with minimal skewness and mean $\pm$ standard deviation is reported. Comparisons of continuous variables were performed using one way analysis of variance to analyze differences between groups. Categorical variables were analyzed using Chi-squared testing. The primary exposure was the group category of neither, either, or both. The primary outcomes were analyzed with multivariable logistic and linear regression modeling adjusting for age. Analysis was performed using the SPSS statistical software (IBM SPSS Statistics for Windows, version 24.0; IBM, Armonk, NY).

Results

Demographic data for the 218 respondents with OAB based on symptoms, without a diagnosis of IC/BPS, meeting inclusion and exclusion criteria are presented in Table 1. Overall, the average age was 45.3 ± 14.6 with 83% (n=181) identifying as non-Hispanic white and 63.7% (n=139) having at least a college degree. There were no differences in age, race/ethnicity, or level of education between the three groups.

In this cohort, 88 (40.4%) women reported painful urgency only, 6 (2.8%) painful filling only, and 23 (10.5%) both, while 101 (46.3%) reported neither symptom. The most common co-morbid somatic syndrome in this population was lower back pain in 90 (41.3%) women followed by migraine in 82 (37.6%) (Table 2). The overall mean PROMIS pain intensity score was 43.6 ± 8.7 (range 30.7–71.8). The incidence of UII in this population was over 50%, and no relationship with painful bladder symptoms was identified.

An increase in OAB symptoms scores (Figure 1A), pain intensity (Figure 1C) and somatic symptom burden (Figure 1D) and a decrease in OAB related quality of life scores (Figure 1B) from neither>either>both was seen.

Logistic regression analyses adjusted for age, established that the diagnosis of IBS, chronic pelvic pain, or TMJ disorder were associated with an increased likelihood of having either or both painful filling and/or painful urgency compared to neither symptom (Table 3).

Additionally, women with both symptoms were 5.2 times (95% CI 1.7, 16.1) more likely to have neck pain than women with only one symptom. There was no difference in the odds of having IBS, chronic pelvic pain, TMJ disorder, or chronic fatigue syndrome in women who had both symptoms versus women with either symptom (data not shown).

To confirm that our selected cohort of women with OAB without a self-reported diagnosis of IC/BPS was different from an IC/BPS population of women, we compared those women without IC/BPS who reported both pain symptoms to those women self-reporting IC/BPS (Table 4).

Discussion

In this population of women with OAB without a diagnosis of IC/BPS, the majority (54%) reported symptoms of either painful urgency or painful filling or both. Having certain CSS,

specifically IBS, chronic pelvic pain, or TMJ disorder was predictive of having painful bladder symptoms. Women with painful bladder symptoms were three times more likely to have IBS and 13 times more likely to have chronic fatigue syndrome. These findings are analogous to those of Lai et al⁸ where women with IC/BPS, diagnosed by self-report of pain, pressure, or discomfort localized to the bladder or pelvic region that was associated with lower urinary tract symptoms. In his study, women with IC/BPS had a higher likelihood of having IBS or chronic fatigue syndrome across the gradient of neither>either>both. Our study has confirmed an ordinal effect on somatic symptom burden in a population of women with OAB.

The PROMIS pain intensity scores also progressively increased from the neither to either to both groups. This may reflect that women with painful filling and/or painful urgency have systemic hypersensitivity or dysregulated afferent sensory function, such as that seen with central sensitization. Central sensitization is thought to result from repeated painful stimuli, which induces functional changes in secondary spinal afferent nerves, causing afferent hypersensitivity¹⁹. Temporal summation, which is an indicator of central sensitization, is measured by an increase in pain perception to a series of stimuli delivered a constant intensity and frequency, such as heat. A group of women undergoing third-line therapy for OAB demonstrated higher pain intensity scores and greater temporal summation compared to controls²⁰. On sub-analysis, women with self-reported IC/BPS exhibited the greatest degree of temporal summation, although it was not statistically significantly higher than the OAB group. Whether the associations between urgency perceptions and global pain intensity represent a manifestation of widespread changes to pain sensitivity or whether the painful urgency symptoms contribute mechanistically to a more widespread afferent dysfunction remains to be determined.

Limitations of the study include a selection bias as women with more severe OAB symptoms may have been more likely to complete the questionnaires. Furthermore, the demographics of the study population (i.e. predominantly Caucasian and college-educated) may limit generalizability of the findings. Women with a diagnosis of IC/BPS were excluded from inclusion in the primary analysis, however it is possible that some of these women recruited from the community would qualify for this diagnosis if evaluated in a clinical setting. However, even in patients reporting both painful urgency and painful filling, the average PROMIS pain intensity score was below average, meaning less intense pain, than the general population, indicating a less severe population of women with pain. Additionally, a comparison of women with both pain symptoms without a diagnosis of IC/BPS to women with a diagnosis of IC/BPS showed no difference in OAB-ss. The absolute difference in pain intensity and somatic symptom scores was small, but statistically higher in women with a diagnosis of IC/BPS, establishing that the studied cohort of women with OAB and painful bladder symptoms was different from women endorsing an IC/BPS diagnosis. With the exception of the diagnoses of IBS, chronic pelvic pain, fibromyalgia, and migraines, which were based on diagnostic criteria, women were asked to self-report the other CSS diagnoses which may introduce a degree of response bias. Also, the frequency of some of the pain syndromes was low in this population, therefore potentially not allowing for detection of differences between the three groups.

Based on clinical overlap as well as data suggesting increased central sensitization, it seems that OAB and IC/BPS exist on a continuum of bladder sensitivity with urgency and frequency symptoms predominating on one end and pain symptoms on the other. Identifying the underlying etiology of this spectrum, as well as clinical and physiologic factors that predict where on the continuum a woman's pathology exists, may help to develop new and targeted treatment options. Further study in a fully characterized, clinically evaluated cohort of patients is necessary to confirm our hypothesis and findings.

Conclusions

In this cohort of women with OAB, without IC/BPS, a large percentage of women reported painful filling and/or painful urgency. We identified associations between these pain symptoms and chronic somatic syndromes, as well as increased pain intensity and somatic symptom burden. These findings may lead to further understanding of the underlying pathophysiology of OAB and IC/BPS and lead to the development of new therapies aimed at restoring afferent nerve function.

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Figure 1.
Relationship of OABq-SS (A), OABq-HRQL (B), pain intensity (C), and somatic symptom score (D) from neither > either > both in OAB population.

Table 1

Demographic and clinical data of participants

	Neither	Either	Both	p-value
No. of participants	101	94	23	
Age, mean (SD)	47.6 (14.5)	43.1 (15.2)	44.4 (11.5)	0.088
Race/ethnicity, no. (%)				0.099
Non-Hispanic white	78 (77.2)	80 (85.1)	23 (100)	
Non-Hispanic black	17 (16.8)	9 (9.6)	0 (0)	
Other	6 (5.9)	5 (5.3)	0 (0)	
Highest education, no. (%)				0.561
Less than high school	1 (1)	0 (0)	0 (0)	
High school graduate	11 (10.9)	8 (8.5)	0 (0)	
Some college or Associate's degree	24 (23.8)	28 (29.8)	7 (30.4)	
College graduate	37 (36.6)	40 (42.6)	9 (39.1)	
Graduate or professional degree	28 (27.7)	18 (19.1)	7 (30.4)	

Table 2

Clinical data of participants

	Neither	Either	Both	p-value
No. of participants	101	94	23	
Central sensitivity syndromes, no. (%)				
Low back pain	32 (31.7)	36 (38.3)	10 (43.5)	0.356
Migraine	37 (36.6)	26 (27.7)	7 (30.4)	0.408
IBS	12 (13.0)	25 (29.4)	7 (30.4)	0.012
Pelvic pain	5 (5.4)	15 (17.6)	5 (21.7)	0.011
Restless leg syndrome	14 (13.9)	9 (9.6)	0 (0)	0.145
TMJ disorder	3 (3.2)	13 (15.3)	3 (21.7)	0.018
Neck pain	7 (7.6)	8 (9.4)	6 (26.1)	0.012
Fibromyalgia	7 (7.6)	5 (5.3)	1 (4.3)	0.858
Endometriosis	6 (5.9)	3 (3.2)	1 (4.3)	0.663
Chemical sensitivity	3 (3.0)	1 (1.1)	1 (4.3)	0.516
Chronic fatigue syndrome	1 (1.0)	4 (4.2)	3 (21.7)	0.016
Vulvodynia	0 (0)	1 (1.1)	0 (0)	0.516
Urgency urinary incontinence	53 (52.5)	48 (51.1)	12 (52.2)	0.980
OAB-ss, mean (SD)	39.1 (22.4)	41.6 (23.4)	46.3 (21.3)	0.364
OAB-HRQL, mean (SD)	72.0 (23.5)	66.7 (25.1)	61.1 (25.1)	0.099
PROMIS pain intensity score, mean (SD)	40.9 (8.4)	43.5 (8.3)	47.3 (6.3)	0.002
Somatic symptom score-8, mean (SD)	7.2 (5.4)	8.6 (4.9)	10.1 (5.2)	0.032

Table 3

Regression analyses adjusting for age

	Either [*]		Both [*]	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Central sensitivity syndromes				
Low back pain	1.5	0.8, 2.6	2.0	0.8, 5.1
Migraine	0.6	0.3, 1.1	1.1	0.4, 2.6
IBS	3.0	1.4, 6.1[†]	3.5	1.2, 9.8[†]
Pelvic pain	3.3	1.2, 9.0[†]	4.5	1.2, 16.3[†]
Restless leg syndrome	0.8	0.3, 1.9	0.3	0.04, 2.5
TMJ disorder	6.7	1.9, 23.9[†]	9.1	2.0, 41.4[†]
Neck pain	1.1	0.4, 2.9	5.9	1.9, 18.0[†]
Fibromyalgia	0.8	0.2, 2.5	2.1	0.5, 8.9
Endometriosis	0.7	0.2, 2.9	1.1	0.1, 10.8
Chemical sensitivity	0.4	0.04, 4.2	1.9	0.2, 20.4
Chronic fatigue syndrome	4.1	0.8, 21.1	13.0	2.1, 79.9[†]
Urge urinary incontinence	1.1	0.6, 2.0	1.1	0.4, 2.8
	β coefficient		β coefficient	
OABq-SS	3.8	-2.5, 10.2	8.2	-2.0, 18.4
OABq-HRQL	-6.6	-13.4, 0.31	-11.8	-22.8, -0.8[‡]
PROMIS Pain intensity	2.96	0.63, 5.28[‡]	6.5	2.76, 10.28[‡]
Somatic symptom score	1.55	0.07, 3.03[‡]	2.97	0.58, 5.36[‡]

* Neither was the reference category

[†] Statistically significant logistic regression result

[‡] Statistically significant linear regression result

Table 4

Analysis of women with OAB and both pain symptoms compared to women with a diagnosis of IC/BPS

	OAB with Both	IC/BPS	p-value
No. of participants	23	23	
OAB-ss, mean (SD)	46.3 (21.3)	59.7 (28.7)	0.077
OAB-HRQL, mean (SD)	61.1 (25.1)	37.4 (31.9)	0.007
PROMIS pain intensity score, mean (SD)	47.3 (6.3)	51.9 (7.4)	0.028
Somatic symptom score-8, mean (SD)	10.1 (5.2)	15.7 (7.2)	0.005