Published in final edited form as:
Int Urogynecol J. 2014 December ; 25(12): 1639–1643. doi:10.1007/s00192-014-2420-z.

Symptom Persistence in a Community Cohort of Women with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS): 3, 6, 9, and 12 month follow up from the RICE Cohort

Anne M. Suskind[1], **Sandra H. Berry**[2], **Marika J. Suttorp**[2], **Marc N. Elliott**[2], and **J. Quentin Clemens**[1]

[1]University of Michigan Department of Urology, Ann Arbor, MI

[2]RAND Corporation, Santa Monica, CA

Abstract

Introduction and Hypothesis—The persistence of interstitial cystitis/bladder pain syndrome (IC/BPS) symptoms has been described in women seeking medical care. The purpose of this study was to determine whether symptoms persist among a population-based sample of women.

Methods—A probability sample of U.S. women was identified through a two-stage telephone screening process using the RICE high-sensitivity case definition. A randomly-selected subgroup (n=508) was enrolled in a longitudinal study and interviewed about their symptoms at baseline, 3, 6, 9, and 12 months. Bivariate and multivariate linear regression analyses determined predictors of persistence of symptoms over the four waves.

Results—A total of 436 women with a mean age of 47.5 years responding to all waves were included in the analysis. Forty-one percent met the RICE high sensitivity case definition at baseline and in all four waves; an additional 21% met the definition at baseline and in three waves. Women with a college degree (+12% vs. no college, p=0.02) and who were younger (−5% per decade of age, p<0.01) had higher chances of symptom persistence at each wave. Scoring one standard deviation higher on the continuity of symptoms and the O'Leary Sant Interstitial Cystitis Symptom index increased the chances of symptom persistence by 4% and 2 %, respectively (both p's<0.01).

Conclusions—The majority of women demonstrated symptom persistence across at least three of four waves over 12 months. These women tended to be younger, college-educated, and to have reported a history of greater continuity of symptoms and higher severity of symptoms at baseline.

Corresponding Author, J. Quentin Clemens, MD, MSCI, University of Michigan Medical Center, Ann Arbor, MI 48109, qclemens@med.umich.edu, (phone) 734-936-7030, (fax) 734-232-2400.

Financial disclaimer/conflict of interest: none

Author Participation:
Suskind: protocol/project development, manuscript writing/editing
Berry: protocol/project development, manuscript editing
Suttorp: data collection and management, data analysis, manuscript editing
Elliott: manuscript editing and interpretation of data
Clemens: protocol/project development, manuscript editing

Keywords

longitudinal; population; survey

Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by bladder pain, urinary urgency due to pain, and urinary frequency. The RAND Interstitial Cystitis Epidemiology (RICE) study previously developed two validated case definitions for IC/BPS (1) and estimated that up to 6.5% of women in the United States met these criteria. (2) Not only are IC/BPS symptoms prevalent, but they have also been shown to negatively impact health related quality of life, significantly affecting the lives of these women.(3–5)

The extent to which symptoms of IC/BPS persist over time, however, has only been evaluated in cohorts of women seen in urology practices. The Interstitial Cystitis Data Base Study Group looked at prevalent cases of IC/BPS and found no long-term changes in disease severity over a median follow up of 31 months.(6) Likewise, another study that looked at incident cases of IC/BPS found that it was uncommon for symptoms to disappear over a median follow up time of 33 months.(7) What remains unknown; however, is whether these findings would differ among a community-based sample of women with symptoms of IC/BPS, compared to a sample of women who have sought care for their symptoms in a urologist's office.

In order to address this issue, we designed a study using a randomly selected subgroup of women identified by the nationally representative RICE cohort who were evaluated longitudinally at 3, 6, 9, and 12 months after baseline. Findings from this study will help elucidate the natural history of IC/BPS and inform patients and physicians dealing with this condition.

Materials and Methods

Clinical Cohort

As part of the RAND Interstitial Cystitis Epidemiology (RICE) study, a national telephone survey of 146,231 U.S. households was conducted to identify adult women with IC/BPS symptoms. Women were classified using the two RICE IC/BPS case definitions (one high sensitivity definition and one high specificity definition), using methods previously described.(1, 2) The high sensitivity definition (81% sensitivity, 54% specificity) includes the following two criteria: (1) pain, pressure, or discomfort in the pelvic area and (2) daytime urinary frequency 10+ or urgency due to pain, pressure, or discomfort, not due to fear of wetting. The high specificity definition (48% sensitivity, 83% specificity) includes the previous 2 criteria of the high sensitivity definition and adds the following additional criteria: (3) symptoms did not resolve after treatment with antibiotics and (4) no treatment with hormone injection therapy for endometriosis. The following exclusion criteria are applied to both definitions: bladder cancer, urethral diverticulum, spinal cord injury, stroke, Parkinson's disease, multiple sclerosis, spina bifida, cyclophosphamide treatment, radiation

treatment to pelvic area, tuberculosis affecting the bladder, uterine cancer, ovarian cancer, genital herpes, and pregnancy.(2) A randomly selected subgroup of these women who met both case definitions at baseline (n=508) were asked to participate in a longitudinal study. These women were interviewed about their symptoms at baseline, 3, 6, 9, and 12 months by a trained interviewer from the RAND Telephone Survey Center. This study was approved by the RAND Human Subjects Protection Committee (FWA00003425).

Telephone interviews consisted of questions pertaining to the subject's demographic information and symptoms. Symptom severity was assessed by 0–10 pelvic pain scales, the O'Leary-Sant Interstitial Cystitis Symptom Index (ICSI),(8) and the impact was assessed using the RICE Bladder Symptom Impact Scale (BSI).(9) The BSI is a 6-item scale developed by the RICE study to examine the effects of psychosocial and treatment interventions on quality of life in women with IC/BPS. For each instrument, a higher score indicates greater symptom severity. Women were also asked about the duration and persistence of their symptoms at each interview. Past continuity of symptoms was assessed at baseline with the following question: "Between the first time in your life that you ever remember having symptoms of pain, pressure, discomfort, frequency, or urgency that lasted for 3 or more months and now, how much of the time have you had symptoms like these": *All of the time*, *most of the time*, *about half of the time*, *some of the time*, or *rarely/never*? Information on the use of IC/BPS-specific treatments included any of the following Amitriptyline, pentosan polysulfate, hydroxyzine, dimethyl sulfoxide (DMSO), or bladder instillations, and information on the use of self-care for treating IC/BPS symptoms included relaxation techniques, support groups, and religious activities.

Statistical Analysis

Descriptive statistics were calculated for demographic information and symptom characteristics. This information was weighted based on methods previously described to account for sample design and non-response at baseline.(2) Women who had data for all four waves of the longitudinal analysis (86%, n=436), were more likely to be married and older, compared to those who did not have data for all waves. Further weighting was performed based on such patterns of non-response to follow-up for our subsample of 436 women.

Bivariate linear regression predicted the number of waves that the RICE IC/BPS high sensitivity definition was met. This outcome ranged from 0 (only met the definition at baseline) to 4 (met the definition at baseline and in all 4 subsequent waves). Only women who responded to all four follow-up waves were included in the analysis. Multivariate linear regression was performed for the same outcome, adjusting for all covariates. Results for continuous predictors were presented as standardized coefficients. All coefficients were divided by four (the number of study waves) to enable interpretation of data as the proportion of follow up waves with persistence of IC/BPS symptoms. Initial models included non-urologic conditions (reported diagnoses of chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia) as predictors; however, these were found to have no individual or combined effects and were removed from the final model.

Results

Baseline demographic and IC/BPS symptom characteristics of participants appear in Table 1. Overall, this study population had a mean age of 47.5 years, 79% were white, and 73% had at least some college education. Subjects had a mean duration of symptoms lasting 15.5 years, and 9.8% and 11.0% received care for their bladder symptoms from either an obstetrician/gynecologist or a urologist, respectively. Over 29% reported seeking no carefor their bladder symptoms, 11% had a diagnosis of IC/BPS, 8% received IC-specific treatments, and 46.4% reported using self-care for treatment of their bladder symptoms. The mean Bladder Symptom Index score was 1.8 (standard deviation 1.8) and the mean O'Leary-Sant Interstitial Cystitis Symptom Index was 10.5 (standard deviation 3.5) at baseline. The percentage of women who met the RICE IC/BPS high sensitivity case definition at baseline and at additional study waves is shown in Table 2. Notably, 41% met this case definition in all four subsequent waves, and an additional 21% in three of four subsequent waves, together accounting for over half of the study population. Only 8% of the study population met the case definition at no waves after baseline. The most common reason for not continuing to meet the case definition across waves was no longer reporting pain or pressure in the last 3 months, followed by not reporting urgency due to pain, pressure, or discomfort.

Bivariate and multivariate linear models predicting the persistence of IC/BPS symptoms are shown in Table 3. Having a college degree was the largest predictor of symptom persistence in the multivariate model, where subjects with a degree demonstrated a 12% higher chance of symptom persistence compared to those without a degree($p<0.02$). Younger age at baseline was also a significant predictor of persistence of symptoms in the multivariate model, with a 5% lower chance of persistence per wave per decade of age ($p<0.01$). For example, a woman age 35 would have a 10% higher chance of symptom persistence over each wave compared to a woman 20 years (2 decades) older at age 55. Finally, scoring one standard deviation higher on continuity of symptoms and on the O'Leary Sant Interstitial Cystitis Symptom Index corresponded to a 4% ($p<0.01$) and 2% ($p<0.01$) higher chance of persistence of symptoms at each wave, respectively. Degree of pelvic pain at baseline did not significantly independently predict persistence of IC/BPS symptoms in the multivariate model ($p=0.28$).

Discussion

Almost half (41%) of the subjects met the RICE IC/BPS high sensitivity definition in all waves of the study and an additional 21% met the definition in three of four follow-up waves, indicating a high amount of persistence of symptoms over the 12 months following baseline assessment. We have previously demonstrated that IC/BPS symptoms are common(2) and bothersome(5) in U.S. women. The findings of the current study indicate that these symptoms persist upon serial investigations in a population based sample of women with symptoms of IC/BPS.

Other studies have evaluated longitudinal trends in IC/BPS in cohorts of women previously diagnosed with this symptom complex. The Interstitial Cystitis Data Base study group

evaluated 637 patients who were followed for a median of 31 months to find that symptoms fluctuated some over time but that there was no significant long-term change in overall disease severity on average.(6) Another study in a cohort of 312 women with a history of IC/BPS who were followed for a median time of 33 months found that 35% of women reported improvement in symptoms from baseline, but only 9% reported at least temporary symptom remission, suggesting that the severity of symptoms can change over time, but that the disappearance of symptoms was uncommon.(7) Our findings are significant in that they highlight a similar trend of symptom persistence among community-based women, indicating that a large number of women have persistent symptoms of IC/BPS but do not seek medical care from a urologist.

Our study provides new insight into which women are at greatest risk for symptom persistence. The most common reason for not continuing to meet the RICE high sensitivity case definition among study respondents who met the definition only at baseline (representing 8% of the sample) was no longer reporting pain or pressure in the last 3 months, followed by not reporting urgency due to pain, pressure, or discomfort.

This study is unique in that it identifies predictors of symptom persistence among a community based sample of women with symptoms of IC/BPS. Our findings that women with a history of continuity of symptoms and higher levels of symptom severity predict the persistence of IC/BPS symptoms over time seems intuitive and is not surprising although validation opens the potential for better prediction of which women are likely to have persistent symptoms.

Our finding that younger age is associated with symptom persistence is interesting and warrants further investigation. Others have shown that there is a bimodal age distribution at time of diagnosis of IC/BPS that peaks at approximately age 20 to 24 and again around age 50 to 64. Differences in symptomology between these two age distributions have also been demonstrated, where the younger cohort tends to have more dyspareunia, external genitalia pain, urinary urgency, and dysuria whereas the older cohort tends to have more nocturia and urinary incontinence.(10) Taken together, these findings imply that there may be a different pathophysiology responsible for IC/BPS symptoms in the younger versus older population of women and our findings could be interpreted within this context to imply that younger women may have a slightly different phenotype of IC/BPS that tends to be more persistent in nature over time. Our findings that having a college education predicts persistence of symptoms over 12 months is a little more difficult to interpret and may serve as a surrogate for other unidentified factors.An additional important finding of our study was that the majority of our subjects received no care (29.3%) or care from a family doctor or general internist (45.1%) for their IC/BPS symptoms, and only 11.0% and 9.8%received care from a urologist or an obstetrician/gynecologist, respectively. Taken together with our finding that the duration of symptoms lasted 15.5 years, on average, means that there is a significant population of women in the community who have been suffering from this condition for a long time without receiving specialty care. These findings imply that there is a lack of information regarding this condition and/or treatment and referral of this condition in the community and there is much room for improvement within the healthcare system to better serve this patient population.

A strength of this study is its prospective data collection at 3-month intervals from a probability sample of symptomatic women to assess self-reported symptom status. Nevertheless, this study should be evaluated with certain limitations in mind. First, as previously mentioned, subjects were selected for this study based on the RICE IC/BPS case definitions using population-based screening methods and not based on a physician's diagnosis. We believe that this is a strength of the study in that it more accurately assesses IC/BPS symptoms in the community at large, as opposed to those solely among patients who sought treatment for their symptoms, making our findings generalizable at a population level. Second, it is possible that small associations between baseline characteristics and symptom persistence went undetected and would have been statistically significant in a larger study.

In conclusion, a large majority of community based women with symptoms of IC/BPS demonstrated substantial persistence of symptoms over a period of 12 months. A college education, younger age, higher scores on past continuity of symptoms, and higher scores on the O'Leary Sant Interstitial Cystitis Symptom Index were all found to significantly increase the chance of persistence across each subsequent study wave. Such information adds value to the literature by demonstrating similar levels of symptom persistence of IC/BPS between symptomatic women in the community and women being seen in urology practices, further indicating women with IC/BPS may be underdiagnosed and undertreated in the community. Additionally, information from this study can help physicians to counsel their patients with IC/BPS regarding the likelihood that their symptoms will persist over time. Taken together, these finding add significant insights to care for patients with IC/BPS both at the level of the population and in the care of individual patients.

Acknowledgments

Funding: NIDDK U01DK070234-01 and Dr. Suskind's efforts were supported by NIH/NIDDK Grant T32 DK07782

List of Abbreviations

BSI	Bladder Symptom Impact Scale
DMSO	Dimethyl sulfoxide
IC/BPS	Interstitial cystitis/bladder pain syndrome
ICSI	Interstitial Cystitis Symptom Index
RAND	Research ANd Development
RICE	RAND Interstitial Cystitis Epidemiology

References

1. Berry SH, Bogart LM, Pham C, Liu K, Nyberg L, Stoto M, et al. Development, validation and testing of an epidemiological case definition of interstitial cystitis/painful bladder syndrome. The Journal of urology. 2010 May; 183(5):1848–1852. PubMed PMID: 20303099. Epub 2010/03/23. eng. [PubMed: 20303099]

2. Berry SH, Elliott MN, Suttorp M, Bogart LM, Stoto MA, Eggers P, et al. Prevalence of symptoms of bladder pain syndrome/interstitial cystitis among adult females in the United States. The Journal of urology. 2011 Aug; 186(2):540–544. PubMed PMID: 21683389. Epub 2011/06/21. eng. [PubMed: 21683389]

3. Nickel JC, Tripp DA, Pontari M, Moldwin R, Mayer R, Carr LK, et al. Psychosocial phenotyping in women with interstitial cystitis/painful bladder syndrome: a case control study. The Journal of urology. 2010 Jan; 183(1):167–172. PubMed PMID: 19913812. Epub 2009/11/17. eng. [PubMed: 19913812]

4. El Khoudary SR, Talbott EO, Bromberger JT, Chang CC, Songer TJ, Davis EL. Severity of interstitial cystitis symptoms and quality of life in female patients. J Womens Health (Larchmt). 2009 Sep; 18(9):1361–1368. PubMed PMID: 19743907. Epub 2009/09/12. eng. [PubMed: 19743907]

5. Suskind AM, Berry SH, Suttorp MJ, Elliott MN, Hays RD, Ewing BA, et al. Health-related quality of life in patients with interstitial cystitis/bladder pain syndrome and frequently associated comorbidities. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2012 Oct 7. PubMed PMID: 23054497. Epub 2012/10/12. Eng.

6. Propert KJ, Schaeffer AJ, Brensinger CM, Kusek JW, Nyberg LM, Landis JR. A prospective study of interstitial cystitis: results of longitudinal followup of the interstitial cystitis data base cohort. The Interstitial Cystitis Data Base Study Group. The Journal of urology. 2000 May; 163(5):1434–1439. PubMed PMID: 10751852. Epub 2001/02/07. eng. [PubMed: 10751852]

7. Warren JW, Greenberg P, Diggs C, Horne L, Langenberg P. A prospective early history of incident interstitial cystitis/painful bladder syndrome. The Journal of urology. 2010 Dec; 184(6):2333–2338. PubMed PMID: 20952011: Epub 2010/10/19. eng. [PubMed: 20952011]

8. O'Leary MP, Sant GR, Fowler FJ Jr, Whitmore KE, Spolarich-Kroll J. The interstitial cystitis symptom index and problem index. Urology. 1997 May; 49(5A Suppl):58–63. PubMed PMID: 9146003. Epub 1997/05/01. eng. [PubMed: 9146003]

9. Bogart LM, Suttorp MJ, Elliott MN, Clemens JQ, Berry SH. Validation of a quality-of-life scale for women with bladder pain syndrome/interstitial cystitis. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2012 Nov; 21(9):1665–1670. PubMed PMID: 22146841. Pubmed Central PMCID: 3406260. Epub 2011/12/08. eng.

10. Rais-Bahrami S, Friedlander JI, Herati AS, Sadek MA, Ruzimovsky M, Moldwin RM. Symptom profile variability of interstitial cystitis/painful bladder syndrome by age. BJU international. 2012 May; 109(9):1356–1359. PubMed PMID: 21883848. [PubMed: 21883848]

Table 1

Weighted subject demographics and symptom characteristics at baseline.

	N=436
Age in years, median (min, max); mean (SD)	47.6 (19, 87); 47.5 (14.1)
Race, %	
White	79.1
Hispanic	10.4
Black	7.0
Other	3.5
Education, %	
No college	27.3
Some college	41.2
College degree plus	31.5
Annual Household Income, %	
Under $35,000	29.0
$35, 000 to $60,000	25.2
Greater than $60,000	45.8
Married, %	61.1
Duration of pain symptoms in years, median (min, max); mean(SD)	10.9 (1, 63); 15.5 (15.3)
Type of doctor usually seen for bladder symptoms, %	
No care	29.3
Family doctor/general internist	45.1
OB/Gyn	9.8
Urologist	11.0
Nurse or other type of doctor	4.8
Diagnosis of IC/BPS	11.0
Received any IC-specific treatment, %	8.0
Uses any self-care for bladder symptoms, %	46.4
Severity of worst pain, pressure, or discomfort in the last 3 months (based on pelvic pain scale 0-10), median (min, max); mean (SD)	4.6 (0, 10); 5.3 (2.1)
Continuity of symptoms: between the first time you had symptoms (pain, pressure, discomfort, urinary symptoms) and now, how much time have you had symptoms?, %	
Rarely/never	6.2
Some of the time	44.1
About half of the time	19.8
Most of the time	18.2
All of the time	11.7
Bladder Symptom Index, median (min, max); mean (SD)	1.1 (0, 7); 1.8 (1.8)
O'Leary-Sant Interstitial Cystitis Symptom Index, median (min, max); mean (SD)	10.1 (1, 20); 10.5 (3.5)

Table 2

Weighted Percentage of Subjects who met the RICE IC/BPS high sensitivity case definition at baseline and at various numbers of waves during the study.

Number of waves	% (N=436)
Baseline only	7.8
Baseline + 1	11.8
Baseline + 2	18.2
Baseline + 3	21.1
Baseline + 4	41.1

Table 3

Bivariate and Multivariate linear regression models predicting the number of waves of symptom persistence of IC/BPS (0-4 waves). Data are presented as the proportion of follow up waves with persistence of IC/BPS symptoms.

	Bivariate Estimate	p-value	Multivariate Estimate	p-value
Age in decades	**−0.04**	**<0.01**	**−0.05**	**<0.01**
Non-Hispanic White race/ethnicity	0.01	0.81	0.03	0.53
Education				
No college	−0.09	0.08	**−0.12**	**0.02**
Some college	−0.01	0.82	−0.05	0.24
College degree plus	Ref		Ref	
Annual Household Income				
Under $35,000	0.00	0.94	0.03	0.60
$35, 000 to $60,000	−0.06	0.24	−0.04	0.42
Greater than $60,000	Ref		Ref	
Married	0.02	0.60	0.04	0.27
Diagnosis of IC/BPS	0.02	0.77	−0.04	0.44
Most of the time pelvic pain scale 0-10 over the last 3 months (per SD)	**0.02**	**0.02**	0.01	0.25
Continuity of symptoms at baseline (per SD)	**0.07**	**<0.01**	**0.04**	**<0.01**
Bladder Symptom Index at baseline (per SD)	0.03	<0.01	0.01	0.28
O'Leary-Sant Interstitial Cystitis Symptom Index at baseline (per SD)	**0.02**	**<0.01**	**0.02**	**<0.01**

Boldface coefficients and p-values indicate p<0.05