Symptoms of Interstitial Cystitis, Painful Bladder Syndrome and Similar Diseases in Women: A Systematic Review

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Purpose: In women symptoms of interstitial cystitis are difficult to distinguish from those of painful bladder syndrome and they appear to overlap with those of urinary tract infection, chronic urethral syndrome, overactive bladder, vulvodynia and endometriosis. This has led to difficulties in formulating a case definition for interstitial cystitis, and complications in the treatment and evaluation of its impact on the lives of women. We performed a systematic literature review to determine how best to distinguish interstitial cystitis from related conditions.

Materials and Methods: We performed comprehensive literature searches using the terms diagnosis, and each of interstitial cystitis, painful bladder syndrome, urinary tract infection, overactive bladder, chronic urethral syndrome, vulvodynia and endometriosis.

Results: Of 2,680 screened titles 604 articles were read in full. The most commonly reported interstitial cystitis symptoms were bladder/pelvic pain, urgency, frequency and nocturia. Interstitial cystitis and painful bladder syndrome share the same cluster of symptoms. Chronic urethral syndrome is an outdated term. Self-reports regarding symptoms and effective antibiotic use can distinguish recurrent urinary tract infections from interstitial cystitis in some but not all women. Urine cultures may also be necessary. Pain distinguishes interstitial cystitis from overactive bladder and vulvar pain may distinguish vulvodynia from interstitial cystitis. Dysmenorrhea distinguishes endometriosis from interstitial cystitis, although many women have endometriosis plus interstitial cystitis.

Conclusions: In terms of symptoms interstitial cystitis and painful bladder syndrome may be the same entity. Recurrent urinary tract infections may be distinguished from interstitial cystitis and painful bladder syndrome via a combination of self-report and urine culture information. Interstitial cystitis and painful bladder syndrome may be distinguished from overactive bladder, vulvodynia and endometriosis, although identifying interstitial cystitis and painful bladder syndrome in women with more than 1 of these diseases may be difficult.

Key Words: bladder; cystitis, interstitial; pain; symptoms; female

Prior literature indicates a general lack of a consensus on the case definition of IC in women.[1–3] Difficulties with advancing a case definition, especially for epidemiological research, arose due to the overlap in symptoms between IC and other conditions. Toward the development of a case definition for use in epidemiological research in women we performed a systematic literature review to 1) determine the differences and similarities in reports by women of the symptoms of 3 seemingly related conditions, including IC, PBS and CUS, and 2) determine how best to distinguish IC based on patient reports of symptoms of diseases with similar symptoms, including UTI, OAB, vulvodynia and endometriosis.

MATERIALS AND METHODS

To determine appropriate search terms for IC and related conditions we consulted experts in IC, urology, gynecology and pelvic pain who served as consultants for the current study (see Appendix). Based on their input we performed systematic literature searches of the PubMed® database from 1950 to the present using the word diagnosis and synonyms (diagnostic criteria, case definition and terminology) and the name of each disease (IC, PBS, CUS, UTI, OAB, vulvodynia and endometriosis). Our consultants also suggested supplementing these searches with a search on pelvic floor dysfunction and 1 on incontinence. We did not search and review identifiable conditions with symptoms similar to those of IC that are already accepted as NIDDK exclusionary criteria for IC, eg bladder cancer, bladder stones, exposure to cyclophosphamide or pelvic radiation.[2]

Two types of articles were sought, including 1) systematically developed diagnostic criteria and 2) empirically based reports of the symptom prevalence of each disease in women. Because the initial search for endometriosis and diagnosis yielded 7,514 articles, we refined it before screening, using additional key words suggested by our study consultants, ie endometriosis plus frequency, urgency or bladder.

Two coders selected potentially relevant articles based on an independent title screening. Abstracts of these articles were reviewed and independently coded as relevant or irrelevant and relevant articles were obtained and read in full. The coders independently abstracted the prevalence rates of various symptoms and discrepancies were resolved through

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TABLE 1. *Literature search and results*

Search Terms	No. Titles Screened	No. Articles Read
Diagnosis AND:		
Interstitial cystitis	804	333
Painful bladder disorder/syndrome	326	16
Vulvodynia	103	77
Pelvic floor dysfunction	96	19
Overactive bladder	199	57
Urethral syndrome	126	66
Urinary tract infection, chronic or persistent, not recurrent, asymptomatic or complicated	339	11
Incontinence (not stress)	70	11
Endometriosis AND:		
Bladder	303	—
Urinary frequency	4	—
Urinary urgency	4	—
Combined terms	306	14
Totals	2,680	604

Searches were de-duplicated and titles from the search using the key word, endometriosis, only were not screened.

collaboration. Studies typically described only a subset of symptoms of interest. Any abstracted studies that included 100 patients or greater and had systematic inclusion criteria, ie consistently used the same criteria to define the disease sample, were used to compare symptoms. However, we included smaller studies when necessary if other information on the topic was not available. When several articles appeared to describe results based on the same data set, we included only the article that reported the largest number of patients.

RESULTS

Table 1 shows the literature searches. The titles of select articles were circulated among our consultants, who suggested additional relevant reports. Article bibliographies were also used to identify additional reports. Of the 2,680 titles screened 604 were obtained and read in full.

IC

Although Skene first used the term interstitial cystitis in 1887,[4] widely acceptable diagnostic criteria for IC were not developed until a small group of urologists was convened by the NIDDK 100 years later.[2] These preliminary criteria, which were modified at a 1988 meeting,[3] required mucosal ulcers, as first identified by Hunner.[5] Pain on bladder filling that was relieved by emptying as well as suprapubic, pelvic, urethral, vaginal or perineal pain and/or glomerulations (epithelial hemorrhages elicited by bladder hydrodistention) were deemed positive factors for IC, of which 2 were required for diagnosis. Urgency was not included in the consensus criteria at the meeting because it was assumed that virtually all patients would present with urgency.

Pain was a prominent part of the case definition discussion at the 1987 NIDDK meeting.[2] Gillenwater et al introduced IC by referring to "painful bladder disease."[2] Holm-Bentzen presented extensive data on "the painful bladder syndrome."[2] Held et al surveyed 127 board certified urologists about their experiences with patients with IC and pain was ranked as the single most common criterion for diagnosing IC, while "pain on filling and relieved by emptying" was ranked fourth and nonpain symptoms were ranked lower, including urgency as seventh, nocturia as seventeenth and waking frequency as nineteenth.[6]

Symptom prevalence. Of the abstracted studies reporting prevalence rates of IC symptoms we identified 6 studies with 100 patients or greater, of whom almost all were female.[6–11] Two studies were excluded because inclusion criteria were unclear.[12,13] In the 6 abstracted studies 63% to 92% of patients reported pain (table 2). Four studies were useful for understanding the locations and character of pain in patients with IC.[8,11,14,15] Pain in the bladder, urethra and vagina was most commonly reported and most patients reported the character of pain as pressure, aching or burning (table 3). Two studies described activities that relieved or increased pain.[6,8] Urination decreased pain in 57% to 73% of patients. For pain exacerbation 61% of patients reported stress, 50% reported sexual intercourse and 49% reported constrictive clothing.[8] Certain foods and drinks were reported to exacerbate IC pain in 1 study, including acidic beverages in 54% of patients, coffee in 51% and spicy foods in 46%.[8]

In addition to pain, symptoms of urgency, frequency and nocturia were commonly reported (table 2). Other types of urinary and pain symptoms have been observed to a lesser extent. Held et al reported that 47% of patients with IC said that they had difficulty starting urine flow and 51% reported difficulty emptying the bladder.[6] Dyspareunia was reported by about half of patients with IC (table 2).[6,8,11] Although 2 articles mentioned incontinence symptoms in women with IC,[14,16] it is not considered part of the diagnosis.[17]

The literature search also revealed 3 symptom indexes developed for IC clinical trials.[18–20] These indexes have been successfully used to assess symptom severity and response to therapy. However, to our knowledge no question-

TABLE 2. *Reports of symptoms by disease*

Condition	% Pts (No. studies) Pain	Urgency	Frequency	Nocturia	Dyspareunia	Incontinence
IC	63–92 (6)[6–11]	84–98 (5)[6–9,11]	80–92 (5)[6–9,11]	61–89 (5)[6,7,9–11]	45–57 (3)[6,8,11]	26 (1)[6]
PBS	95 (1)[22]	69 (1)[22]	97 (1)[22]	97 (1)[22]	Not reported	Not reported
OAB	Not reported	Recruiting criterion (5)[33–37]	Recruiting criterion (3),[35–37] 85 (1)[34]	Not reported	Not reported	55–74 (5)[33–37]
Vulvodynia	57–91 Vulvar (2)[45,63]	46 (1)[63]	45 (1)[63]	Not reported	71–81 (2)[45,63]	Not reported
Endometriosis	80–90 Dysmenorrhea (2),[51,52] 62 CPP (1)[52]	Not reported	Not reported	Not reported	43–62 (2)[51,52]	Not reported

Only symptoms reported in the referenced studies are included and each symptom was defined differently in the articles summarized.