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Epidemiology of prostatitis

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Abstract

Background—Prostatitis describes a combination of infectious diseases (acute and chronic bacterial prostatitis), chronic pelvic pain syndrome, and asymptomatic inflammation.

Materials and methods—We employed evidence-based methods to review the epidemiology of prostatitis syndromes.

Results—The prevalence of prostatitis symptoms could be compared in five studies surveying 10 617 men. Overall, 873 participants met various criteria for prostatitis, representing an overall rate of 8.2%, with prevalence ranging from 2.2 to 9.7%. A history of sexually transmitted diseases was associated with an increased risk for prostatitis symptoms. Men reporting a history of prostatitis symptoms had a substantially increased rate of benign prostatic hyperplasia, lower urinary tract symptoms and prostate cancer. In one study, the incidence of physician-diagnosed prostatitis was 4.9 cases per 1000 person-years. Two studies suggest that about one-third of men reporting prostatitis symptoms had resolution after 1 year. Patients with previous episodes and more severe symptoms are at higher risk for chronic pelvic pain.

Discussion—The prevalence of prostatitis symptoms is high, comparable to rates of ischamic heart disease and diabetes. Clinical evaluation appears necessary to verify that prostatitis is responsible for patients' symptoms. Prostatitis symptoms may increase a man's risk for benign prostate hypertrophy, lower urinary tract symptoms and prostate cancer. We need to define natural history and consequences of prostatitis, develop better algorithms for diagnosis and treatment, and develop strategies for prevention.

A resurgence of interest in prostatitis has occurred during the last decade. This has been accompanied by a new level of understanding of the epidemiology, morbidity and economic impact of these conditions. Much progress dates from the recognition that infection and inflammation are important in certain prostatitis syndromes. Despite limited information on the causes of other prostatitis syndromes, these conditions can be defined and important treatment studies have been initiated. This article employs evidence-based methods to review the epidemiology of prostatitis syndromes, examines the clinical implications of these data, and outlines areas for future research.

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1. Introduction

1.1. Current classification of prostatitis syndromes

Prostatitis describes a combination of infectious diseases (acute and chronic bacterial prostatitis), a chronic pelvic pain syndrome and asymptomatic inflammation. The National Institutes of Health classification has been accepted internationally and includes four syndromes (Table 1) [1].

Category I, acute bacterial prostatitis, is characterised by an acute bacterial urinary tract infection.

Category II, chronic bacterial prostatitis, is a persistent bacterial infection of the prostate leading to recurrent urinary tract infections caused by the same bacterial strain.

Category III, chronic prostatitis/chronic pelvic pain syndrome, is characterised by chronic pelvic pain symptoms in the absence of urinary tract infection. The symptoms include characteristic urogenital pain, voiding and sexual dysfunction that substantially reduce patients' quality of life. There are two subtypes.

- **a.** Inflammatory chronic prostatitis/chronic pelvic pain syndrome is associated with leukocytes in the expressed prostatic fluid, post-prostate massage urine or seminal fluid.
- **b.** Non-inflammatory chronic prostatitis/chronic pelvic pain syndrome with no evidence of urogenital inflammation.

Category IV, asymptomatic inflammatory prostatitis, occurs in patients who have no symptoms but who have documented inflammation in prostatic tissue or in their seminal fluid. For example, the most common prostatic inflammation ('prostatitis' as diagnosed by pathologists) represents the most common benign condition found in men who have biopsies to evaluate possible prostate cancer.

1.2. Identification of studies for systematic analysis

Papers published in peer-reviewed journals were included in this review. Papers in non-peer-reviewed supplements were excluded. An exhaustive list was obtained through the major databases (e.g., Medline, Embase, Cochrane Library and Science Citation Index). Search terms included: prostatitis, pelvic pain, inflammation, epidemiology and survey. We also reviewed tables of contents of the major urology journals and other relevant journals, for the previous 3 months, to take into account possible delay in indexing papers in the databases. These approaches identified more than 4000 references. After reviewing the titles and abstracts, 86 articles were identified for detailed review.

1.3. Inclusion criteria for epidemiological studies

For inclusion in this analysis, studies were required to meet criteria that have been outlined for epidemiological studies of prostatitis (Table 2) [2]. Three criteria were required: 1. Included studies were population-based rather than case series or referral patients from tertiary care institutions. 2. A clear case and standardised definition was required, ideally a reasonable relationship to patients seen in routine clinical practice. 3. Publication in the peer-reviewed literature was required.

In addition to the required criteria, at least one other desirable criterion was necessary for inclusion. 4. It is desirable to incorporate a validated survey instrument such as the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) [3]. To facilitate evaluation of varied populations, the NIH-CPSI has been translated and validated for use in

English [3], Spanish [4], Japanese [5], Chinese [6], Malay [6], German [7], Korean [8], Finnish [9], Italian [10], French [11], and Estonian [12]. However, a population-based study found low agreement between physician-diagnosed prostatitis and the NIH-CPSI pain measures, suggesting that the index, by itself, may have limited ability to determine the presence or absence of prostatitis [13]. Therefore, use of the NIH-CPSI was considered desirable, but was not required for inclusion. 5. A standardised strategy for surveying the population should be used to assure that participants are likely to represent the overall population. The optimal strategy should incorporate a mechanism to verify that cases identified in the survey actually met the case definition, such as a detailed chart review or, ideally, a standardised clinical examination. 6. The population should be large enough to provide reasonable statistical power for the desired comparisons.

2. Results

2.1. Limitations of the available literature

Although the studies described below met the inclusion criteria, most had important limitations. Few studies included adequate microbiological evaluation. Most did not include chart reviews or physical examination to assure that subjects did not have the exclusion criteria for chronic prostatitis (listed in Table 1, footnote 2). Most studies relied exclusively on symptom questionnaires, or portions of validated symptom assessment instruments. Such surveys are easy to administer, but they were not designed for diagnosis. Other urological conditions may present with symptoms that overlap the symptoms of prostatitis.

2.2. Prevalence of prostatitis symptoms

We identified ten studies that met the inclusion criteria. Of these ten studies: seven were from North America [14–19], two were from Asia [20,21], and one was from Europe [22].

2.3. Prevalence of prostatitis in studies that permitted comparison of various populations (Table 3)

The prevalence of prostatitis symptoms could be compared in five studies that surveyed varied ambulatory populations [14,15,17,20,21]. These populations included a total of 10 617 men. Overall, 873 participants met various criteria for symptoms of prostatitis, representing an overall rate of 8.2%. In these studies the prevalence of prostatitis symptoms ranged from 2.2% [17] to 9.7% [15], with a median rate of 8.7%.

Roberts and associates determined the occurrence of a physician-assigned diagnosis of prostatitis using a self-administered, validated questionnaire as part of the Olmsted County Study of Urinary Symptoms and Health Status Among Men study [14]. Their population included 2115 randomly selected 40–79-year-old men from Minnesota. Medical records were then reviewed for a physician-assigned diagnosis of prostatitis. Overall, the rate of a physician-assigned diagnosis of prostatitis was 9%. Participants with a previous prostatitis diagnosis had a much higher cumulative probability of subsequent prostatitis episodes (20%, 38% and 50% among men 40, 60 and 80 years old, respectively). These findings suggest that the prevalence of a physician-assigned diagnosis of prostatitis is high, comparable to rates of ischemic heart disease and diabetes. Participants suffering an initial episode of prostatitis were more likely to suffer from further episodes than other participants.

In a subsequent study, this group determined the prevalence of prostatitis-like symptoms in a community-based cohort of older men [17]. Their self-administered questionnaires included questions similar to the NIH-CPSI to evaluate a randomly selected sample of 40–79-year-old white men from Olmsted County, Minnesota. Subjects were participants in a longitudinal study of lower urinary tract symptoms. Of 1541 men, 182 (12%) had at least one urogenital pain

symptom, including 34 men (2.2%) with prostatitis-like symptoms. Participants reporting prostatitis-like symptoms had higher pain scores (mean 6.7 versus 0.5), urinary symptoms (mean 3.5 versus 2.1) and quality of life impact (mean 3.7 versus 1.9) compared to men who did not report prostatitis-like symptoms (all P <0.001). Pain frequency (odds ratio (OR) 39.2, 95% confidence interval (CI) 18.8–81.9) and intensity (OR 21.5, CI 8.7–52.9) were associated more strongly with prostatitis-like symptoms than with the urinary symptom score (OR 2.8, CI 1.4–5.6) or the quality of life impact score (OR 4.5, CI 1.9–10.7).

Nickel and associates employed questions similar to the NIH-CPSI pain domain to determine the prevalence of prostatitis-like symptoms in 20–74-year-old men from Eastern Canada [15]. Of 868 participants, 84 (9.7%) had chronic prostatitis-like symptoms (mean NIH-CPSI pain score 9.1 ± 0.3). Prostatitis-like symptoms occurred in 11.5% of men younger than 50 years old and in 8.5% of men ≥50 years old. Overall, 57 men (6.6%) had prostatitis-like symptoms and an NIH-CPSI pain score ≥8 (moderate-to-severe). Of participants with prostatitis-like symptoms, 60% sought medical evaluation.

Tan and associates conducted a cross-sectional study to determine the prevalence of prostatitis symptoms, lower urinary tract symptoms, and erectile dysfunction in Singapore [20]. Of 1087 21–70-year-old participants, 2.7% had, ‘pain or discomfort suggestive of prostatitis’, compared to >20% who had lower urinary tract symptoms. The average age of men with prostatitis-like symptoms was 43 years old. Participants with prostatitis-like symptoms had worse erectile function (P < 0.003) and a lower quality of life score (P < 0.001) than other participants.

Cheah and associates surveyed an ethnically and racially diverse population in Northern Malaysia [21]. They surveyed 1% of 20–50-year-old men in Penang, Malaysia. To assure that prostatitis was responsible for participants’ symptoms, urological evaluation was recommended for cases identified during the survey study. Of 3147 participants, 275 (8.7%) met the survey criteria for chronic prostatitis. The prevalence of prostatitis ranged from 8% among Chinese and Malays, to 12% among Indians, and 16% among other racial/ethnic groups (P <0.05). Of 87 subjects who met the survey definition, 63 (72%) met the NIH consensus criteria for chronic prostatitis/chronic pelvic pain syndrome after clinical evaluation.

2.4. Other epidemiological studies of prostatitis (Table 4)

Five additional studies met the inclusion criteria but were not directly comparable to those summarised above because of the different denominators or outcome measures employed by the investigators [16,22–24].

Using the National Ambulatory Medical Care Survey database, Collins and associates evaluated outpatient physician visits by men >18 years old in the US [16]. Randomly selected physicians completed forms summarising reasons for patient visits and physician diagnoses. Of 58 955 ambulatory visits, 5% had genitourinary symptoms. These data suggest that prostatitis was a diagnosis in 2 000 000 visits annually including 700 000 physician visits by men 18–50 years old and 900 000 physician visits by men >50 years old. Of visits for prostatitis, 47% were to primary care physicians and 46% were to urologists. Prostatitis was diagnosed in 1% of all primary care physician visits and in 8% of all visits to urologists. The rate of a prostatitis diagnosis was 13-fold greater for visits to urologists than for visits to primary care physicians. In this cohort, prostatitis was diagnosed more commonly among 36–65-year-old men than among 18–35-year-old men. Patients with prostatitis received antimicrobial therapy 45% of the time compared to 27% of the time for patients without genitourinary symptoms.

In a subsequent study, this group evaluated the prevalence and correlates of prostatitis symptoms among United States health professionals without prostate cancer [23]. Subjects provided demographic, clinical and lifestyle information; urological diagnoses; and described

lower urinary tract symptoms. Of the 31 681 participants, 16% had a self-reported history of prostatitis. Participants reporting a history of benign prostatic hyperplasia (BPH) had a 7.7-fold greater odds of a history of prostatitis, those with severe lower urinary tract symptoms had 2.8-fold greater odds of a history of prostatitis, and men with moderate lower urinary tract symptoms had a 1.8-fold greater odds of prostatitis. Other factors associated with a history of prostatitis included a history of sexually transmitted disease (OR 1.8), stress at home (OR 1.5) and stress at work (OR 1.2). The 2163 men with prostatitis alone were younger and had less severe urinary symptoms than the 4575 men with BPH alone.

Mehik and associates determined the prevalence of prostatitis symptoms among 2500 randomly selected men in the most Northern provinces of Finland (Oulu and Lapland) aged 20–59 [22]. The lifetime prevalence of prostatitis symptoms was 14.2%, with the risk for prostatitis increasing with age. Compared to men 20–39 years old, the risk of prostatitis was 1.7 times greater for men 40–49 years old, and 3.1 times greater for men 50–59 years old. The incidence of prostatitis was 37.8/10 000 person years. Of 261 men with symptoms of prostatitis, 27% suffered from prostatitis at least once a year, including 16% who had persistent symptoms. There was seasonal variation, with 63% of participants experiencing their worst symptoms during the winter. Divorced and single men had a lower risk of prostatitis than married men.

Clemens and associates used computer searches of the Kaiser Permanente Northwest (Portland, Oregon) database during a 2-year interval to identify 1223 men with new physician diagnoses of prostatitis [25]. Chart reviews were performed on a random subset to categorise cases using the NIH definitions. Of 303 incident cases reviewed, the distribution was 58 (19%) type I/II, 189 (62%) type III, 33 (11%) type IV and 23 (8%) other. The incidence of physician-diagnosed prostatitis was 4.9 cases per 1000 person-years, with type III prostatitis accounting for 3.3 cases per 1000 person-years. Primary care physicians made 78% of new prostatitis diagnoses.

Daniels and associates conducted a cross-sectional analysis from a prospective cohort study of older men recruited from six clinical centres in the Boston area [24] Of 5821 men >65 years old, 1439 (25%) self-reported a history of prostatitis. Participants with a history of prostatitis were more likely to self-report a history of prostate cancer (26% versus 7%; $P < 0.0001$) and BPH (83% versus 38%; $P < 0.0001$) compared with men no history of prostatitis. Overall, a history of prostatitis was associated with an 8-fold increased risk for BPH (CI 6.8–9.5) and a 5.4-fold increased risk for a history of prostate cancer (CI 4.4–6.6).

3. Natural history of prostatitis symptoms

We identified only two studies that considered the natural history of prostatitis symptoms that met the inclusion criteria [26,27]. Both studies considered the outcome after the usual clinical treatment in North American populations.

Nickel and associates conducted a 1-year follow-up study of their cohort from Eastern Canada [26]. A questionnaire incorporating the NIH-CPSI pain and voiding domains was compared for 40 men who had reported prostatitis-like symptoms in their initial survey and 119 age-matched controls without prostatitis-like symptoms in the same survey. Fifteen men (38%) with prostatitis in the initial survey did not report similar symptoms 1 year later, while 25 men (63%) experienced persistent symptoms. Four men (3%) in the control group reported prostatitis-like symptoms in the follow-up survey. Thus, about one-third had resolution of prostatitis-like symptoms after 1 year (usually those with a shorter duration and less severe symptoms). The severity of symptoms of men with persistent, chronic prostatitis remained relatively unchanged over the year.

Turner and associates studied 286 men with physician-diagnosed prostatitis in a large health-maintenance organisation [27]. Telephone interviews were conducted at baseline, 3, 6 and 12-

month follow-up. On average, symptoms improved substantially during months 1–3, modestly from months 3–6, then remained unchanged. Better outcomes were noted for men whose initial visit was for a first lifetime episode compared with a recurrent episode. Patients with more severe symptoms were more likely to report symptoms 1 year later ($P = 0.0008$). They concluded that men who make physician visits for new prostatitis/pelvic pain episodes experience usually improve during the next 6 months. However, chronic, persistent or recurrent symptoms are common. Patients with previous episodes and more severe symptoms are at higher risk for chronic pelvic pain.

4. Discussion

The limited number of studies that met our evidence-based criteria were sufficient to support the conclusion that prostatitis is an important worldwide problem that merits additional investigation. The prevalence of prostatitis-like symptoms (defined variously) ranged from 2% to 9.7%, with a mean prevalence of 8.2%. Possible reasons for this almost five-fold variation in prevalence include differences: in study design, selection of populations for investigation, cultural factors, variations in practice patterns, genetic differences or exposure to undefined risk factors. Identification of the reasons underlying such epidemiological variation may identify factors that may be changed to decrease the risk, morbidity and consequences of chronic prostatitis syndromes.

Prostatitis-like symptoms result in a substantial number of physician visits. Sixty percent of participants with prostatitis-like symptoms sought medical help [15]. The odds of a prostatitis diagnosis were 13-fold greater during visits to urologists during visits to visits to primary care physicians. Patients with prostatitis received antimicrobials 45% of the time compared to 27% of the time for patients with no genitourinary symptoms [16]. Prostatitis was a diagnosis in 2 000 000 visits annually in the US, including 8% of all visits to urologists and 1% of all primary care physician visits [16]. Men with prostatitis symptoms appear to be at increased risk for persistent symptoms and for recurrent episodes. Participants with a previous prostatitis diagnosis had a substantially higher cumulative probability of subsequent episodes of prostatitis [14,27].

Symptom surveys alone may have limited ability to distinguish patients with prostatitis from patients with other urological disorders [13]. Clinical evaluation appears necessary to verify that prostatitis is indeed responsible for patients' symptoms [21]. Limited data also suggest that a history of prostatitis symptoms is more common in individuals with both BPH and prostate cancer. Men reporting a history of BPH had an 8-fold greater odds of a history of prostatitis [16]. Other factors associated with a history of prostatitis included lower urinary tract symptoms, a history of sexually transmitted disease and stress.

These epidemiological studies provide an important foundation for a research agenda. Future studies should be population-based. The case definition should be clear and should have a reasonable relationship to clinical practice. Medical record review and ideally clinical evaluation should verify that chronic prostatitis is responsible for subjects' symptoms. It is also important to limit confounding issues, including treatment bias, selection bias and referral bias. These issues can pose particular problems for studies limited to tertiary care patients from referral centres. We need to define natural history and consequences of prostatitis. Most importantly, we need to develop better algorithms for diagnosis and treatment of prostatitis syndromes and to determine strategies for primary prevention.

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Table 1

Classification of prostatitis syndromes[1]

Category	Name	Characteristics
I	Acute bacterial prostatitis	Acute bacterial infection Acute urinary tract infection
II	Chronic bacterial prostatitis	Persistent bacterial infection Recurrent urinary tract infections
III	Chronic prostatitis/chronic pelvic pain syndrome	Characteristic pelvic pains, urinary complaints and sexual dysfunction Absence of other urological disorders[2]
Subtype a	Inflammatory subtype	Leukocytes in the expressed prostatic fluid, post-prostate massage fluid or seminal fluid
Subtype b	Non-inflammatory subtype	No inflammation in the expressed prostatic fluid, post-prostate massage fluid or seminal fluid
IV	Asymptomatic inflammatory	Asymptomatic patients with inflammatory infiltrates in prostate tissue or seminal fluid specimens evaluated for other indications [3]

[1] After reference [1]

[2] Patients with potentially significant urological causes are excluded from the chronic prostatitis/chronic pelvic pain category. These exclusion criteria include: duration less than 3 months, presence of lower genitourinary tract cancer (i.e., transitional cell carcinoma, carcinoma in situ, or prostate cancer), active urolithiasis, active urogenital tract infection (i.e., bacteriuria, genital herpes, genitourinary tuberculosis), gastrointestinal disorders (i.e., fissure in ano, inflammatory bowel disease, fistula), radiation of chemical cystitis, acute urethritis, acute epididymitis, acute orchitis, functionally significant urethral stricture disease, or neurological disorder affecting the bladder.

[3] Asymptomatic patients may be diagnosed while undergoing evaluation for suspicion of prostate cancer (e.g., elevated PSA or prostate nodule) or have seminal inflammation noted during evaluation of infertility.

Table 2

Criteria for inclusion of epidemiological studies[1]

Characteristic	Desirable	Undesirable
1. Subjects[2]	Population-based	Tertiary-care
2. Case-definition[2]	Clear and standardized	Patient recall or standard of care
3. Peer-reviewed[2]	Published	Meeting only or published non-reviewed supplement
4. Survey instrument[3]	NIH-CPSI[4], with evaluation for exclusion criteria	None
5. Survey-strategy[3]	Standardized and representative Clinical verification to exclude inappropriate cases	Retrospective record review No clinical evaluation
6. Population size[3]	Sufficient to provide statistical power	Small, providing low statistical power

[1] Modified from reference [2]with the additional requirement that studies be published in the peer-reviewed literature.

[2] Characteristics 1, 2, and 3 were required for inclusion in this review.

[3] In addition, each study had to have at least one other desirable characteristic (4, 5, or 6).

[4] Use of the NIH-CPSI was considered a desirable study characteristic, but this was not required for inclusion in this systematic review.

Table 3

Epidemiological studies evaluating the prevalence of prostatitis symptoms

Author, Year, Country, Reference	Population	Number, Age range (years)	Prevalence of prostatitis-like symptoms
Roberts, 1998, USA [14]	Minnesota	2115 men 40–79	9%
Nickel, 2001, Canada [15]	Patients of family practitioners	868 men 20–74	9.7%
Tan, 2002, Singapore [20]	Cross-sectional study	1087 men 21–70	2.7%
Roberts, 2002, USA [17]	Random community dwelling men, Minnesota	1541 men 40–79	16% GU pain 2.2% prostatitis
Cheah, 2003, Malaysia [21]	Random sample	3147 men 20–50	8.7%

Table 4

Other epidemiological studies of prostatitis symptoms

Author, Year, Country Reference	Population	Number, Age range(years)	Prevalence of prostatitis-like symptoms
Collins, 1998, USA [16]	National Ambulatory Medical Care Survey	58 955 visits >18	5% overall Urology: 8% Primary care: 1%
Mehik, 2000, Finland [22]	Randomly selected	1832 men 20–59	Lifetime prevalence (incidence) 14.2%
Collins, 2002, USA [23]	Health care professionals without prostate cancer	31 681 men	Self-reported history: 16%
Clemens, 2005, USA [26]	Managed care population, Oregon	181 949 person-years	Incidence: 4.9 cases/1000 person-years
Daniels, 2005, USA [25]	Community-dwelling older men, Boston area	5821 >65	25% self-reported