Review Article

Prostatitis: current perspective on diagnosis and management

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Abstract

Prostatitis is a common and important urological problem which affects men of all ages. It is a challenging condition to be diagnosed and treated. It is classified under four categories according to the National Institute of Health Classification (Category 1 - Acute bacterial prostatitis, Category 2- Chronic bacterial prostatitis, Category 3-Chronic prostatitis / chronic pelvic pain syndrome, Category 4 – Asymptomatic inflammatory prostatitis). The most common causative organism for both acute and chronic prostatitis is Escherichia coli. Investigation and treatment of prostatitis depend on the clinical presentation of the respective clinical category. Antimicrobials are the mainstay of treatment of acute bacterial prostatitis according to the culture and sensitivity pattern. Chronic bacterial prostatitis needs a long duration of treatment depending on clinical conditions and treatment response. Surgery is rarely indicated in bacterial prostatitis except for a prostatic abscess. Granulomatous prostatitis is an uncommon inflammatory condition with different management options for morphologically different entities. This review looks at each category's presentation, aetiology, diagnosis, treatment, and prognosis

Introduction

Prostatitis is an important universal health problem with limited population-based studies and clinical evidence [1]. This results in limitations in clinical evaluation and treatment options in prostatitis.

The prostate gland comprises a basal cell layer and an overlying columnar secretary cell layer. Surrounding stroma contains a mixture of smooth muscle and fibrous tissue involved in infectious, inflammatory, hyperplastic, and neoplastic disorders. The prostate is classified into different zones. Most cancers arise from the peripheral zone, and most benign prostatic hyperplasia (BPH) arises from the transitional and central zones. Prostate-specific antigen (PSA) is a serine protease and a marker of prostatic disease, and its level increase with age, infection, benign prostatic hyperplasia, and prostate cancer [2].

Prostatitis is a combination of four clinical categories as described in the National Institute of Health (NIH) classification; acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis/chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis [3]. Proper evaluation, categorisation and appropriate management of different clinical syndromes are essential to reduce morbidity and improve the quality of life in patients diagnosed with prostatitis.

This review investigated each NIH prostatitis category's presentation, aetiology, diagnosis, treatment, and prognosis.

Methods

Google Scholar and PubMed literature searches were carried out with the above-mentioned keywords, and only the full-text articles were included.

Epidemiology

The prevalence of prostatitis varies between 2% to 9.7%, confounded by different sampling methods and epidemiological variations [3], and population-based studies needed to precisely identify prevalence are scant. Population-based studies from Europe and Asia show that 3% -14% of men experienced prostatitis-like symptoms in their lifetime. The variation may be due to genetic differences, cultural factors, lifestyle, socioeconomic status, and exposure to various risk factors. The lifetime risk of prostatitis increases with age, and the risk of subsequent episodes and progression to chronic prostatitis is higher in patients who have had a previous episode of prostatitis. [1, 3]. Prostatitis is a common urological problem in older men but is seen in young and middle-aged as well [1].

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Acute bacterial prostatitis

Acute bacterial prostatitis (ABP) is a bacterial infection of the prostate gland caused by an organism that defends the prostate gland's natural immune system. It is rare, accounts for 2-5% of prostatitis cases [4], and occurs in young and older men [1, 5]. Acute bacterial prostatitis can be caused by an organism from the natural flora of bacterial species, inoculated directly following urological procedures like transrectal or transurethral prostate biopsy or urethral instrumentation like cystoscopy. Haematogenous spread and ascending infections are the other modes. The most common causative organism for acute bacterial prostatitis is Escherichia coli, accounting for 50%- 80% of cases [5,6,7,8]. Other gram-negative organisms such as Proteus, Klebsiella, Enterobacter, Serratia and Pseudomonas are often identified. Gram-positive organisms identified are Staphylococcus, Streptococcus and a few other organisms, including Chlamydia trachomatis and Neisseria gonorrhoeae are identified as well [5, 7, 8].

Table 1: NIH Prostatitis Classification System

Category		Types
I		Acute bacterial prostatitis
II		Chronic bacterial prostatitis
III		Chronic prostatitis/Chronic Pelvic Pain Syndrome
	A	Inflammatory
	B	Non inflammatory
IV		Asymptomatic inflammatory prostatitis

(Nickel JC et al, 1999)

Patients with acute bacterial prostatitis often present with sudden onset systemic illness with features like fever and malaise. Lower urinary tract storage symptoms, voiding symptoms and symptoms of urinary tract infection may also be present with or without associated pelvic pain. Often patients have a preceding history of urethral instrumentation [5,8].

The clinical picture varies from abdominal distension due to acute urinary retention to features of sexually transmitted disease. There could be associated suprapubic pain and tenderness. Digital rectal examination (DRE) often reveals an enlarged tender prostate suggestive of acute inflammation. However, prostate massage during DRE should be avoided as it may worsen patients' condition [5,8]. All patients suspected of acute bacterial prostatitis should undergo a full blood count, urine full report and urine culture. Rarely prostate abscess develops as a complication of acute bacterial prostatitis and could be a presenting feature.[4].

A study has shown that 6% of patients develop prostatic abscesses during follow-up after acute bacterial prostatitis. Imaging studies such as ultrasound scan (USS) kidney, ureter, bladder with or without trans-rectal probe and contrast-enhanced computed tomography (CECT) support the diagnosis in patients who are suspected of having prostatic abscess; especially when the duration of symptoms is prolonged or continuous voiding symptoms are present. Figure 1 demonstrates the hypoechoic collection of prostatic abscesses seen in transrectal USS. A prostatic abscess needs surgical drainage when it fails to respond to antibiotic therapy [5, 7, 9,10].

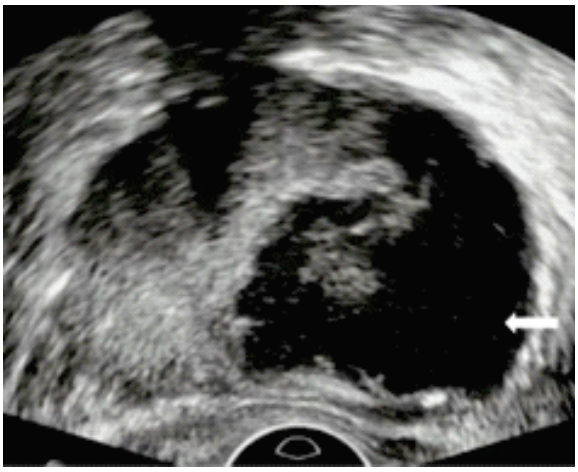

Figure 1 Trans rectal USS shows prostatic abscess.

Antimicrobials are the mainstay of treatment of acute bacterial prostatitis. The selection of appropriate antimicrobial agents depends on the degree of penetration of antibiotics into the infected prostate tissue and the transport mechanism. Non-protein bound and low molecular weight antibiotic molecules enter the prostate tissue through the opening between capillary endothelial cells. The penetration of antimicrobial agents is enhanced by; small molecular size, low protein binding, low degree of ionisation, high lipid solubility, high dissociation constant and high concentration gradient [6,11]. Table 2 depicts the antibiotics with good penetration into prostatic tissue. As bacterial acute prostatitis can be a serious infection, empirical treatment of high doses of parenteral antibiotics is required. According to the recommendations, broad-spectrum penicillin derivatives, fluoroquinolones or third generation cephalosporins are the preferred options.

Figure 2 A - TURP in prostatic abscess. B - Trans rectal drainage of prostatic abscessAs Escherichia coli (E coli) is the commonest causative organism, the selection of empirical antimicrobial agents should be focused on eradicating the above. Culture and antibiotic sensitivity patterns then further guide the treatment. Parenteral antibiotics can be changed to oral once the fever and acute illness are settled. Less severe cases could be treated with oral fluoroquinolones with a minimum duration of 10 days. Acute urinary retention could be treated with suprapubic, intermittent, or indwelling.

catheterisation, however, suprapubic catheterisation is the recommended option [8]. In the absence of the need for drainage of prostatic abscess, surgery should be avoided in bacterial prostatitis [5, 12]. Fig 2 shows transrectal drainage of the prostatic abscess. Trans-urethral resection of prostate (TURP) in such patients reduces the duration of antibiotic therapy and improves voiding symptoms [10]

Chronic bacterial prostatitis

Chronic bacterial prostatitis occurs in 2%-5% of all prostatitis cases [4]. It is defined by identifying an organism in prostatic secretion culture in a patient with symptoms, such as perineal, loin or suprapubic pain associated with recurrent episodes of urinary tract infection. This may or may not be associated with obstructive or voiding symptoms. Typically, the patients are asymptomatic between episodes [7]. Recurrent urinary tract infections occur in 25%-43% of patients with chronic bacterial prostatitis [4]. Patients generally present with insidious onset of progressive symptoms over months. The nonspecific nature of symptoms makes the diagnosis difficult in routine clinical settings [13]. Patients diagnosed with acute bacterial prostatitis have a 10% risk of developing chronic bacterial prostatitis in future, and 10% of such patients develop chronic pelvic pain syndrome [7].

The organism implicated in the aetiology of chronic bacterial prostatitis is E Coli, which accounts for 80% of such cases. Other organisms implicated are gram-negative species of Enterococcus and Pseudomonas [4, 7].

Table 2: Antibiotics with good penetration into prostatic tissue

Antibiotics
Fluoroquinolone
Trimethoprim – sulfamethoxazole
Clindamycin
Doxycycline
Azithromycin
Cephalosporins
Carbapenems
Piperacillin
Other aminoglycosides

Wagenlehner FM et al, 2013

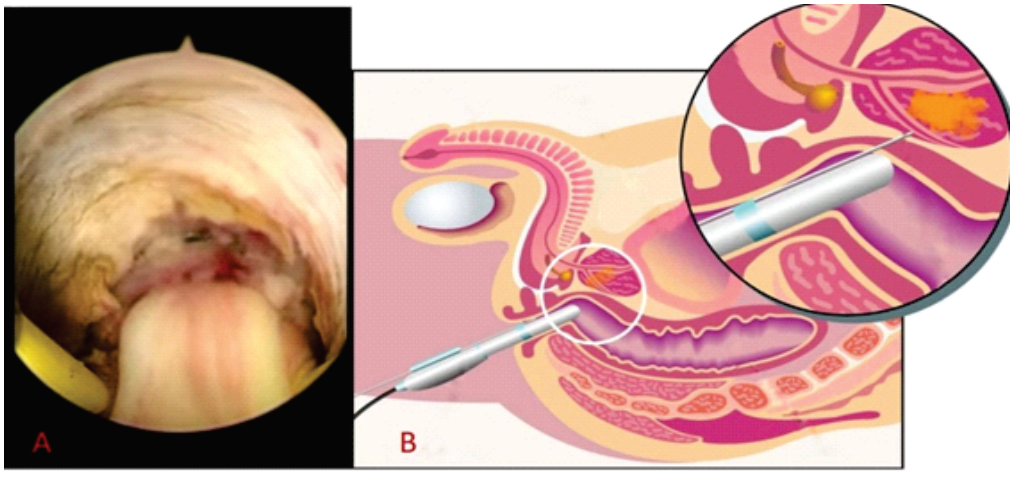

Figure 2 A - TURP in prostatic abscess. **B -** Trans rectal drainage of prostatic abscess

Diagnosis of chronic bacterial prostatitis

The gold standard test for diagnosing chronic bacterial prostatitis is the four-glass test (Fig 3) described by Meares and Stamey. This focuses and identifies the infective focus along the lower urinary tract and prostate. Four samples are tested; first voided, mid-stream, expressed prostatic secretion, and post-prostate massage urine. [7, 13]. Considering the patient's inconvenience, discomfort and cost, the four-glass test is hardly used in clinical practice. A simple and easy two-glass test includes a clean catch urine sample before an examination and another sample of prostatic secretion during or first voided sample following a prostatic examination. A routine urine culture cannot be used alone to diagnose chronic bacterial prostatitis. When considering seminal fluid culture, a negative culture cannot rule out bacterial prostatitis. However, positive seminal fluid culture in a patient with high clinical suspicion of chronic prostatitis confirms the diagnosis and warrants antibiotic treatment [13].

Treatment

Chronic bacterial prostatitis is difficult to treat and needs a long duration of treatment with a fluoroquinolone for at least 3-4 weeks. Depending on the response and clinical condition, this may need to be extended further. In the presence of fluoroquinolone resistance, prolonged treatment of 2 -3 months of trimethoprim or cotrimoxazole is advised [8]. Other than antibiotic treatment, anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) can be used in chronic bacterial prostatitis to reduce symptoms and inflammation. Despite the long duration of antibiotic therapy, a 25%-50% recurrence rate can be seen [7]. Alpha-blockers (Tamsulosin) reduce symptoms as well as recurrences [12]. A combination of alpha-blockers and antibiotics has been reported to have an increased cure rate than antibiotics alone [8, 12]. Some treatment-resistant patients managed with an intra-prostatic injection of antibiotics and radical transurethral prostate resection have resulted only in modest outcomes [4]. Generally, surgery should be avoided in chronic prostatitis, except in the case of prostatic abscess [7,12]

Chronic abacterial prostatitis (chronic pelvic pain syndrome)

Chronic abacterial prostatitis (CAP) is described as genitourinary pain without pathogenic bacteria detected by standard microbiological methodology. It is further categorised as inflammatory and non-inflammatory, depending on the presence or absence of white cells in expressed prostatic secretion, ejaculation, post-prostate massage urine, or prostate biopsy [14]. Despite the inadequate understanding of the relevance of white blood cells in a specimen, lack of standardisation of investigation techniques, lack of cut-off value for elevated white blood cells, and lack of understanding regarding the microorganisms that are detected in the specimen in the above-mentioned diagnostic investigation, NIH classification system is still effective and useful in both clinical and in research settings [15].

CAP affects approximately 10%-15% of men of all ages and is more common in 36-50 years [16]. The main symptoms are genitourinary pain and associated voiding and sexual dysfunction. However, pain may be absent in patients who have already been diagnosed with chronic prostatitis, and obstructive or voiding symptoms may predominate at the time of presentation. The NIH Chronic prostatitis symptom Index (NIH – CPSI) is a commonly used questionnaire for assessing symptom severity in patients with chronic prostatitis [15].

The cause of chronic prostatitis remains unclear and may be associated with bacterial pathogens; Viruses and fungi have also been rarely implicated [14]. Non-infectious causes such as inflammation, intra prostatic urinary reflux, hormonal imbalance, pelvic floor tension myalgia and psychological disturbances are considered as well. Patients who are predisposed to chronic prostatitis develop symptoms after being exposed to above mentioned possible risk factors [14,17]. The diagnosis of CAP is difficult in a clinical setting due to unclear aetiological factors and absence of standard diagnostic tools. Therefore, proper clinical evaluation of the patient is important to exclude other diseases that cause urinary tract symptoms. Urinary obstruction and urinary retention warrant thorough evaluation before a diagnosis of chronic prostatitis is considered. Prostatic calcification is common in patients with CPPS, which is associated with the level of inflammation, positive bacterial culture and duration of symptoms [18]. Fig 5.0 shows the prostatic calcification in TRUS.

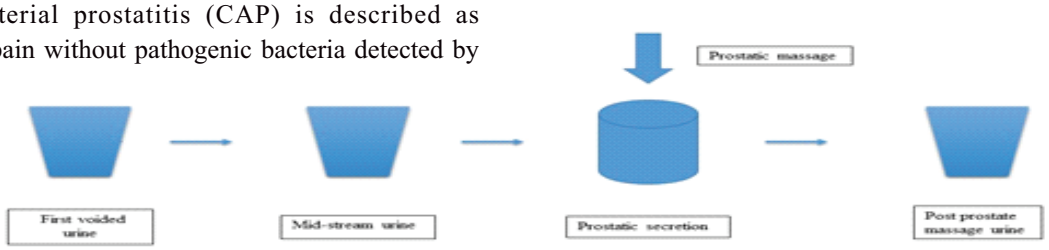

Figure 3.0 Meares and Stamey test

NIH-Chronic Prostatitis Symptom Index (NIH-CPSI)

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?

a. Area between rectum and testicles (perineum) ☐yes ☐No
b. Testicles ☐yes ☐No
c. Tip of the penis (not related to urination) ☐yes ☐No
d. Below your waist, in your pubic or bladder area ☐yes ☐No

2. In the last week, have you experienced:

a. pain or burning during urination ☐yes ☐No
b. Pain or discomfort during or after sexual climax (ejaculation)? ☐yes ☐No

3. How often have you had pain or discomfort in any of these areas over the last week?

☐ 0 Never
☐ 1 Rarely
☐ 2 Sometimes
☐ 3 Often
☐ 4 Usually
☐ 5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?

0 1 2 3 4 5 6 7 8 9 10
No pain pain as bad as you can imagine

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

☐ 0 Not at all
☐ 1 Less than 1 time in 5
☐ 2 Less than half the time
☐ 3 About half the time
☐ 4 More than half the time
☐ 5 Almost alway

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?

☐ 0 Not at all
☐ 1 Less than 1 time in 5
☐ 2 Less than half the time
☐ 3 About half the time
☐ 4 More than half the time
☐ 5 Almost always

Impact of Symptoms

7. How much have your symptoms kept you from doing the kinds of things you would usually do0, over the last week?

☐ 0 None
☐ 1 Only a little
☐ 2 Some
☐ 3 A lot

8. How much did you think about your symptoms, over the last Week?

☐ 0 None
☐ 1 Only a little
☐ 2 Some
☐ 3 A lot

Quality of Life

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

☐ 0 Delighted
☐ 1 Pleased
☐ 2 Mostly satisfied
☐ 3 Mixed (about equally satisfied and dissatisfied)
☐ 4 Mostly dissatisfied
☐ 5 Unhappy
☐ 6 Terrible

Scoring the NIH-Chronic Prostatitis Symptom Index Domains

Pain: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, and 4 = ...
Urinary Symptoms: Total of items 5 and 6= .....
Quality of Life Impact: Total of items 7, 8, and 9=.....

Figure 4 NIH-Chronic prostatitis symptoms index

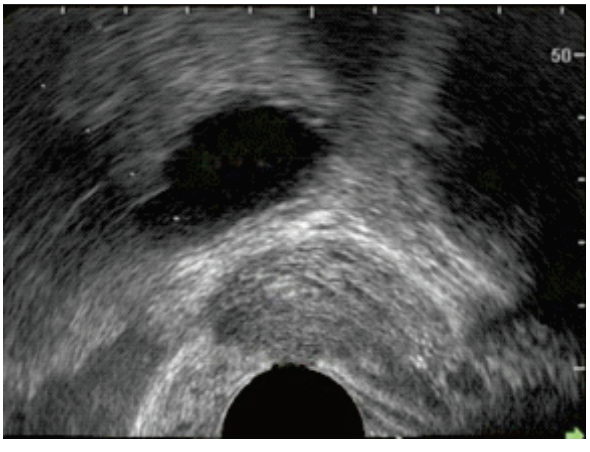

Figure 5.0 Prostatic calcification on TRUS

Treatment of chronic pelvic pain syndrome

Treatment with a combination of ciprofloxacin and doxazosin (an alpha blocker) for 30 days reduces symptoms and discomfort and increases the quality of life [19]. The chronic prostatitis collaboration research network recommends treatment, as shown in Table 3 [4].

Table 3: Treatment option of chronic pelvic pain syndrome

1st line	fluoroquinolone / trimethoprim-sulfamethoxazole
2nd line	tamsulosin, alfuzosin, terazosin
3rd line	finasteride, pentosan polysulfate, phytotherapies
Other	biofeedback, pelvic floor training, thermal treatment

[Habermacher GM *et* al, 2006]

Asymptomatic inflammatory prostatitis

According to the NIH classification, asymptomatic inflammatory prostatitis is defined as the presence of inflammatory cells in prostatic secretion or prostatic tissue histological samples in the absence of symptoms of prostatitis. This is diagnosed incidentally when patients are evaluated for other diseases. It is the common underlying pathology in patients with a benign prostatic enlargement (BPE). An elevated level of PSA correlates with the degree of prostatic inflammation [20]. Asymptomatic prostatic inflammation causes morphological changes in the prostate tissue, resulting in symptomatic BPE. As patients are asymptomatic, treatment is not indicated, except in the following situations: patients with elevated PSA, patients on evaluation for infertility and patients with a confirmed diagnosis with prostate biopsy [21].

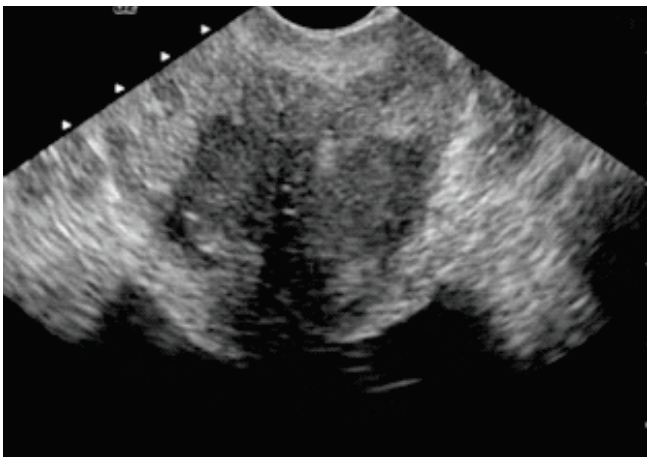

Figure 6.0 Contour deformity along the margin of prostate

Granulomatous prostatitis

Granulomatous prostatitis is an uncommon inflammatory condition with a group of morphologically different entities. It is classified as specific (SGP), nonspecific (NSGP), post-surgical and due to systemic granulomatous disease [22]. Digital rectal examination reveals hard fixed nodules in the case of granulomatous prostatitis [23]. Diagnosis of granulomatous prostatitis is based on histopathology, which shows epithelioid granulomas with or without inflammation. Inflammation may spread to peri prostatic tissue and results in the loss of normal anatomical landmarks (fig 6.0) [22]. Specific granulomatous prostatitis commonly occurs due to tuberculosis resulting from systemic genitourinary tuberculosis or BCG instillation given for bladder carcinoma [22]. NSGP is the commonest type and accounts for 60% of cases. NSGP are self-limiting, while SGP needs specific treatment [23].

Conclusion

Prostatitis is a common disease with a worldwide prevalence and a challenge to treat. According to the NIH classification system, it is categorised as acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis or chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis. Antibiotic treatment is the mainstay of management in prostatitis. Without proper diagnosis and treatment, it leads to morbidity and significant impairment of quality of life. CAP is a diagnosis of exclusion due to its unclear aetiology. Large randomised controlled trials are required in the future for a clear understanding and treatment of CAP. Due to the limited evidence of data on the Asian population, epidemiology-based studies are required in this field in future

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