International Journal of Medicine
ISSN (P): 1468-3814; ISSN (e): 2667-7008

https://www.theinternationalmedicine.com

Volume: 6(1) 2024

Original Research

INTERSTITIAL CYSTITIS / BLADDER PAIN SYNDROME: A COMPREHENSIVE REVIEW

Dr. Abhinav.B[1], Dr. Nithesh Jain[2], Dr. Nitish R Jayaharan[3]
[1] *M.Ch Urology, DrNB (Urology), Junior Consultant, Apollo Hospital, Chennai.*
[2] *M.Ch Urology, Senior Consultant and Clinical Lead, Department of Urology Apollo Hospital, Chennai.*
[3] *MBBS, Junior Resident, Department of Urology Apollo Hospital, Chennai.*

Received: 19 Aug 2024 / Accepted: 25 Oct 2024

Abstract
Bladder Pain Syndrome (BPS), previously known as interstitial cystitis, is a chronic condition characterized by pelvic pain associated with lower urinary tract symptoms in the absence of identifiable pathology. It represents a significant diagnostic and therapeutic challenge due to its multifactorial etiology and heterogeneous clinical presentation. Epidemiological estimates vary widely, reflecting differences in diagnostic criteria and underrecognition of the condition. The pathophysiology involves urothelial dysfunction, neurogenic inflammation, and central sensitization. Diagnosis is primarily clinical and requires exclusion of other urological, gynecological, and neurological conditions. Management follows a stepwise, multimodal approach beginning with conservative strategies and progressing to pharmacological, intravesical, neuromodulatory, and surgical interventions in refractory cases. Early diagnosis and individualized treatment significantly improve patient outcomes and quality of life.

Keywords: *Bladder pain syndrome, interstitial cystitis, chronic pelvic pain, Hunner lesions, neuromodulation.*

Introduction

Bladder Pain Syndrome (BPS) is a chronic and often debilitating disorder with reported prevalence ranging from 1.8 to 51 per 10,000 individuals worldwide, largely depending on the diagnostic criteria employed [15]. Historically referred to as interstitial cystitis, the condition is now defined based on symptomatology rather than histopathological findings, reflecting its complex and multifactorial nature. BPS imposes a substantial burden on patients, not only in terms of physical discomfort but also psychological distress, and has been recognized as a significant public health issue [1]. The diversity in clinical presentation and the absence of a single definitive diagnostic test contribute to delays in diagnosis and variability in management strategies. Despite the availability of multiple treatment modalities, outcomes remain inconsistent, making it challenging for clinicians to adopt a standardized approach [4].

Epidemiology:

BPS predominantly affects women, with a female-to-male ratio estimated at approximately 5:1 [15]. The prevalence is highly variable, ranging between 2% and 6% globally, largely due to differences in diagnostic definitions and study populations [1]. Underdiagnosis remains a significant concern, as symptoms often overlap with other common urological conditions such as urinary tract infections and overactive bladder syndrome. This overlap frequently leads to misdiagnosis and delays in appropriate management [8].

Etiopathogenesis:

The pathophysiology of BPS is complex and involves multiple interrelated mechanisms. One of the primary factors is urothelial dysfunction, where disruption of the glycosaminoglycan (GAG) layer increases bladder permeability, allowing urinary solutes to penetrate and irritate underlying tissues, thereby triggering inflammation [7]. Neurogenic inflammation also plays a central role, with increased activity of sensory afferent pathways and mast cell activation contributing to chronic pain and hypersensitivity [14]. In addition, autoimmune mechanisms have been implicated, as evidenced by associations with systemic inflammatory conditions, suggesting an immune-mediated component in certain patient subsets [14]. Central sensitization further amplifies the condition, wherein alterations in central nervous system pain processing pathways lead to heightened perception of pain even in response to minimal stimuli [14].

Address for Correspondence Dr. Abhinav. B, M.Ch Urology, DrNB (Urology) Email: abhinavbalaji15@gmail.com.

DOI: 10.61336/im/24-1-20

Materials and Methods

This review is based on a comprehensive narrative synthesis of the literature. Relevant studies were identified through systematic searches of MEDLINE, Scopus, and CINAHL databases, focusing on clinical trials, systematic reviews, and guideline-based evidence pertaining to the diagnosis and management of BPS.

CLINICAL PRESENTATION

According to the International Continence Society, BPS is defined as persistent or recurrent chronic pelvic pain perceived to be related to the urinary bladder, accompanied by at least one additional urinary symptom such as urgency or frequency [8]. Patients typically present with urinary frequency that may range from 8 to as many as 50 voids per day, along with urgency that is primarily driven by the need to relieve pain rather than to prevent incontinence. Nocturia is also a common complaint. Unlike other lower urinary tract disorders, urinary incontinence is usually absent in BPS [8]. The natural history of the disease suggests a gradual worsening of symptoms over a period of three to five years, followed by a plateau phase, with late deterioration being relatively uncommon [8]. The psychological burden is significant, with a high prevalence of anxiety and depression reported among affected individuals [14].

Clinical Evaluation:

A thorough clinical evaluation is essential in patients suspected of having BPS. Physical examination should include assessment of the abdomen, external genitalia, and pelvic structures. In women, a bimanual pelvic examination is important to evaluate for pelvic floor tenderness, muscle tone, and trigger points, which may indicate a myofascial component to the pain. In men, a digital rectal examination should be performed to assess the prostate and pelvic floor. A focused neurological examination is also recommended to exclude underlying neurological disorders that may mimic or contribute to symptoms.

Diagnosis:

The diagnosis of BPS is primarily clinical and is based on the exclusion of other conditions that may present with similar symptoms. Initial investigations typically include urinalysis and urine culture to rule out infection, along with imaging studies when clinically indicated. Cystoscopy may be performed to exclude malignancy and to identify characteristic findings associated with BPS. Hunner lesions, which appear as localized inflammatory lesions with a central pale scar surrounded by erythematous mucosa, are observed in a minority of patients and define a distinct phenotype of the disease [9,11]. Glomerulations, once considered diagnostic, are now recognized as non-specific findings and are no longer required for diagnosis [10]. Hydrodistension during cystoscopy may provide additional information regarding bladder capacity and mucosal changes.

DIFFERENTIAL DIAGNOSIS:

Given the nonspecific nature of symptoms, it is essential to exclude other potential causes. Urological conditions such as urinary tract infections, bladder malignancy, and urolithiasis must be ruled out. In women, gynecological conditions including endometriosis and pelvic inflammatory disease should be considered. Gastrointestinal disorders such as inflammatory bowel disease and diverticular disease may present with overlapping symptoms. Neurological conditions, particularly multiple sclerosis, should also be considered in appropriate clinical contexts. In men, chronic prostatitis and bladder outlet obstruction represent important differential diagnoses.

MANAGEMENT:

The management of BPS is based on a stepwise and individualized approach, with the primary goal of symptom control rather than cure. Conservative management forms the cornerstone of initial therapy and includes lifestyle modifications such as avoidance of dietary irritants including caffeine, alcohol, and spicy foods, as well as smoking cessation. Stress management and behavioral therapies, including cognitive behavioral therapy, play an important role given the strong association with psychological comorbidities. Pelvic floor physiotherapy is particularly beneficial in patients with identified muscle tenderness or dysfunction.

Pharmacological therapy is introduced when conservative measures are insufficient. Analgesics such as nonsteroidal anti-inflammatory drugs and paracetamol are commonly used for pain control. Tricyclic antidepressants, particularly amitriptyline, are frequently prescribed due to their dual effect on pain modulation and urinary symptoms. Cimetidine, a histamine H2 receptor antagonist, has also shown benefit in some patients by modulating inflammatory pathways [7].

Intravesical therapies are widely used and aim to restore the integrity of the GAG layer. Agents such as hyaluronic acid, chondroitin sulfate, heparin, lidocaine, pentosan polysulfate, and dimethyl sulfoxide are commonly employed, although no single agent has demonstrated clear superiority [7]. In patients who fail to respond to these treatments, intradetrusor injection of botulinum toxin A may be considered. While effective in reducing pain and urinary symptoms, this intervention carries a risk of urinary retention and requires appropriate patient counseling [6].

Neuromodulation techniques represent another therapeutic option, particularly in refractory cases. Noninvasive approaches such as transcutaneous electrical nerve stimulation can be administered at home, while more invasive options including percutaneous tibial nerve stimulation and sacral nerve stimulation may be considered in selected patients. Although success rates can be promising, the evidence supporting these modalities remains limited [5].

For patients with severe, refractory disease, immunosuppressive therapy with cyclosporine A may be considered. Surgical intervention is reserved as a last resort for those with debilitating symptoms unresponsive to all other treatments. Procedures such as urinary diversion, with or without cystectomy, may provide symptom relief but are associated with significant morbidity and require thorough preoperative counseling regarding risks and long-term implications [4].

Management of Hunner Lesions:

In patients with Hunner lesions, targeted therapy can lead to significant symptom improvement. Endoscopic interventions such as transurethral resection or fulguration of the lesions are commonly performed. Intralesional injection of corticosteroids, such as triamcinolone, provides localized anti-inflammatory effects and may offer additional benefit without the systemic side effects associated with oral steroids [11].

Treatments Not Recommended:

Certain therapies are no longer recommended in contemporary practice due to lack of efficacy and potential adverse effects. These include intravesical Bacillus Calmette-Guérin and prolonged antibiotic therapy, both of which have failed to demonstrate consistent clinical benefit and may contribute to complications such as antimicrobial resistance [7].

Conclusion

Bladder Pain Syndrome is a complex and heterogeneous condition that requires a multidisciplinary and individualized approach to management. Early recognition and a structured, stepwise treatment strategy can significantly improve patient outcomes and quality of life. While most patients achieve partial symptom relief, complete resolution remains uncommon, highlighting the need for continued research into more effective therapies.

References

1. Clemens JQ, Calhoun EA, Litwin MS, Walker-Corkery E, Markossian T, Kusek JW, McNaughton-Collins M; Urologic Pelvic Pain Collaborative Research Network. A survey of primary care physician practices in the diagnosis and management of women with interstitial

cystitis/painful bladder syndrome. Urology. 2010 Aug;76(2):323-8. doi: 10.1016/j.urology.2009.12.047. Epub 2010 Mar 19. PMID: 20303575; PMCID: PMC2892204.
2. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, Hewitt DJ, Jadad AR, Katz NP, Kramer LD, Manning DC, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robinson JP, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Witter J. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. Pain. 2003 Dec;106(3):337-345. doi: 10.1016/j.pain.2003.08.001. PMID: 14659516.
3. Kamel MH, Gardner R, Tourchi A, Tart K, Raheem O, Houston B, Bissada N, Davis R. Pyocystis: a systematic review. Int Urol Nephrol. 2017 Jun;49(6):917-926. doi: 10.1007/s11255-017-1562-6. Epub 2017 Mar 7. PMID: 28265966.
4. Osman NI, Bratt DG, Downey AP, Esperto F, Inman RD, Chapple CR. A Systematic Review of Surgical interventions for the Treatment of Bladder Pain Syndrome/Interstitial Cystitis. Eur Urol Focus. 2021 Jul;7(4):877-885. doi: 10.1016/j.euf.2020.02.014. Epub 2020 Mar 1. PMID: 32127327.
5. Sharma N, Rekha K, Srinivasan JK. Efficacy of transcutaneous electrical nerve stimulation in the treatment of chronic pelvic pain. J Midlife Health. 2017 Jan-Mar;8(1):36-39. doi: 10.4103/jmh.JMH_60_16. PMID: 28458478; PMCID: PMC5367222.
6. Kuo HC, Jiang YH, Tsai YC, Kuo YC. Intravesical botulinum toxin-A injections reduce bladder pain of interstitial cystitis/bladder pain syndrome refractory to conventional treatment - A prospective, multicenter, randomized, double-blind, placebo-controlled clinical trial. Neurourol Urodyn. 2016 Jun;35(5):609-14. doi: 10.1002/nau.22760. Epub 2015 Apr 24. PMID: 25914337.
7. Jones P, Hjelle KM, Mohn J, Guðbrandsdottir G, Roth I, Chaudhry AA, Bergesen AK, Beisland C. Current Status of Intravesical Therapies for Bladder Pain Syndrome (BPS): A Narrative Review of Emerging Evidence. Urology. 2021 Oct;156:e48-e57. doi: 10.1016/j.urology.2021.05.042. Epub 2021 Jun 9. PMID: 34118230.
8. Kim SH, Kim TB, Kim SW, Oh SJ. Urodynamic findings of the painful bladder syndrome/interstitial cystitis: a comparison with idiopathic overactive bladder. J Urol. 2009 Jun;181(6):2550-4. doi: 10.1016/j.juro.2009.01.106. Epub 2009 Apr 16. PMID: 19375103.
9. Messing E, Pauk D, Schaeffer A, Nieweglowski M, Nyberg LM Jr, Landis JR, Cook YL, Simon LJ. Associations among cystoscopic findings and symptoms and physical examination findings in women enrolled in the Interstitial Cystitis Data Base (ICDB) Study. Urology. 1997 May;49(5A Suppl):81-5. doi: 10.1016/s0090-4295(99)80336-7. PMID: 9146006.
10. Wennevik GE, Meijlink JM, Hanno P, Nordling J. The Role of Glomerulations in Bladder Pain Syndrome: A Review. J Urol. 2016 Jan;195(1):19-25. doi: 10.1016/j.juro.2015.06.112. Epub 2015 Aug 28. PMID: 26318984.
11. Whitmore KE, Fall M, Sengiku A, Tomoe H, Logadottir Y, Kim YH. Hunner lesion versus non-Hunner lesion interstitial cystitis/bladder pain syndrome. Int J Urol. 2019 Jun;26 Suppl 1:26-34. doi: 10.1111/iju.13971. PMID: 31144757.
12. Whitmore KE, Fall M, Sengiku A, Tomoe H, Logadottir Y, Kim YH. Hunner lesion versus non-Hunner lesion interstitial cystitis/bladder pain syndrome. Int J Urol. 2019 Jun;26 Suppl 1:26-34. doi: 10.1111/iju.13971. PMID: 31144757.
13. Turner-Warwick R, Whiteside CG, Worth PH, Milroy EJ, Bates CP. A urodynamic view of the clinical problems associated with bladder neck dysfunction and its treatment by endoscopic incision and trans-trigonal posterior prostatectomy. Br J Urol. 1973 Feb;45(1):44-59. PMID: 4690150.
14. McKernan LC, Walsh CG, Reynolds WS, Crofford LJ, Dmochowski RR, Williams DA. Psychosocial co-morbidities in Interstitial Cystitis/Bladder Pain syndrome (IC/BPS): A systematic review. Neurourol Urodyn. 2018 Mar;37(3):926-941. doi: 10.1002/nau.23421. Epub 2017 Oct 9. PMID: 28990698; PMCID: PMC6040587.
15. Curhan GC, Speizer FE, Hunter DJ, Curhan SG, Stampfer MJ. Epidemiology of interstitial cystitis: a population based study. J Urol. 1999 Feb;161(2):549-52. PMID: 9915446.