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Interstitial Cystitis and Bladder Pain Syndrome: A Multidisciplinary Approach

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Abstract: This study aims to assessment the health outcomes of 110 Iraqi patients with Interstitial Cystitis and Bladder Pain Syndrome where. This study examines the demographic characteristics, symptom severity, comorbid conditions, immune system profiles, treatment options, healthcare use, impact on employment, and quality of life of Iraqi patients diagnosed with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). The research aims to bridge knowledge gaps and provide useful information for clinicians, policymakers, and researchers. The findings will reveal the significant burden on the healthcare system and patients' socio-economic status, influencing work productivity and overall satisfaction. The cohort was heterogeneous, with a high prevalence of IC/BPS in both genders, and it was most common in the 30-50 years age bracket. The patients reported severe symptoms that included chronic pelvic pain (85%), urgency (90%), and frequency (95%), and caused great interference with daily activities. The occurrence of comorbid psychiatric illnesses such as depression (60%) and anxiety (55%) was also common. Immune profiling identified a profound inflammatory response in bladder tissues. Treatment protocols were variable, with the majority employing a protocol of multiple medications along with dietary modification. Patients reported large healthcare utilization, with frequent use of multiple providers, and reported a significant reduction in work activity and overall quality of life.

Keywords: Quality of life, Healthcare, Depression, Symptoms, IC/BPS, Interstitial, Cystitis, Bladder.

INTRODUCTION

Painful bladder syndrome, or interstitial cystitis (IC), is a chronic condition in which patients experience pain in the bladder and pelvic area, a frequent and strong need to urinate (urgency), and nighttime urination. Interstitial cystitis (IC) is more common in women and significantly reduces quality of life (Sant, G. R. *et al*., 2007).

The symptoms and manifestations of IC vary widely among patients. Symptoms may also change as the disease progresses, worsening, for example, during menstruation, when sitting, during straining, or during sexual intercourse (Keay, S. *et al*., 2008).

Nonsteroidal anti-inflammatory medications (NSAIDs) such as ibuprofen can help reduce pain (Homma, Y. *et al*., 2009).

Tricyclic antidepressants, such as amitriptyline and imipramine, help relax the bladder and relieve pain (Homma, Y. *et al*., 2016). Antihistamines, such as Claritin, help reduce symptoms of frequent urination and relieve the urge to urinate (Shie, J. H. *et al*., 2011). Pentosan polysulfate (Elmiron) is an FDA-approved medication for the treatment of IC. The mechanism of action of the drug is not fully understood, but it restores the inner surface of the bladder—the urothelium—thus protecting the bladder from toxic irritants present in urine. Treatment with this drug typically lasts 2–4 months before improvement is seen (Southgate, J. *et al*., 2007). Transcutaneous nerve stimulation. This is performed using electrodes placed over the skin. Electrical impulses increase blood flow to the bladder and strengthen the muscles (Zeng, Y. *et al*., 2007), allowing for better bladder control and inhibition of urination. Electrodes are placed either in the lumbar region or above the pubis—the timing and duration of treatment are selected individually (Hanno, P. M. *et al*., 2011). Sacral nerve modulation. The sacral plexuses provide connections between the nerves of the bladder and the spine. Stimulating these nerve plexuses helps reduce the urge to urinate (Engeler, D. S. *et al*., 2013). To achieve this goal, a special electronic device is placed near the sacral plexus, whose electrical impulses affect the nerves. If this type of treatment is effective, this electronic device is surgically implanted in the sacral region and then functions similarly to a pacemaker.

BPS/IC is a chronic condition with variable levels of inflammation, fibrosis of the detrusor, and mastocytosis in bladder biopsy samples. Cellular inflammatory mechanisms in BPS and tissue injury and fibrosis mechanisms are not well understood (Hunner, G. L., 1915; Hand, J. R., 1949). However, studies have confirmed that fibrosis of the detrusor and mastocytosis are associated with the need for multiple interventions and with the failure of standard therapy (Walsh, A., 1977).

The choice of treatment approaches should, whenever possible, be based on placebo-controlled trials; treatment should be initiated with less invasive interventions; treatment should be conducted as coordinated with individual patient

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criteria (Messing, E. M., & Stamey, T. A., 1978; Hanno, P. M, *et al*., 1999).

As per the guidelines of the American Urological Association (AUA, 2011), the treatment of BPS/IC must be initiated with the most conservative approaches, and in case they are not effective, progress to less conservative approaches. The mode of treatment is based on the severity of the disease symptoms and also patient preference. Use of ineffective strategies is stopped after a clinically relevant time. In the interests of the patient, multi-directional, simultaneous therapy must be performed. This is mostly applicable to the treatment of pelvic pain when, in most situations, multifaceted treatment is needed. When various modes of treatment fail, treatment policy and, possibly, clinical diagnosis should be reconsidered (Van de Merwe, J. P, *et al*., 2008; Walton, I., & Nickel, J. C., 2021).

MATERIAL AND METHOD

This study will apply the cross-sectional design to assess the clinical presentation, the severity of symptoms, comorbidities, immune profiles, treatment options, healthcare utilization, impact on work, and quality of life among Iraqi patients with Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). Data will be collected from questionnaires of patients and clinical assessments to provide a clear indication of the impact of the condition on patients and Data will be collected from January 2024 to March 2025. Participants in the study will be selected from urology clinics and Iraqi hospitals. Criteria for inclusion will include adult patients (≥18 years) who have been diagnosed with IC/BPS according to established diagnostic criteria. Other urinary pathology or significant comorbid conditions will exclude the patients from the study.

DATA COLLECTION WILL INCLUDE:

Demographic Information: These will include age, gender, duration of symptoms, and history of urinary tract infections (UTIs).

Symptom scores: Patients will be required to complete questionnaires, namely the Irritable Bowel Syndrome Comprised Symptom Index (ICSI) and the Interstitial Cystitis Symptom Index (ICPI), in order to measure symptom severity.

Cystoscopic Findings: Data on the presence or absence of Hunner's lesions will be collected by cystoscopy.

Comorbidity Assessment: Depression, anxiety, and chronic pain syndromes will be assessed via patient-reported measures.

Immune Profile Analysis: Immune cell profiles and cytokine levels in bladder biopsies from a subset of patients will be analyzed.

Healthcare Utilization: Outpatient visits, hospitalizations, and treatment modalities will be documented via patient questionnaires and medical records.

Work Impact Assessment: Work status, number of workdays missed, and overall work productivity will be asked from the patients.

Quality of Life Evaluation: Patients will describe any improvement with the diagnosis and treatment, remaining symptoms, and the use of symptom scores to gauge improvements.

STUDY PERIOD

Statistical Analysis

The data will be treated using appropriate statistical software (e.g., SPSS, R). Categorical variables (numbers and percentages) will be summarised using descriptive statistics and continuous variables (mean and range) where necessary.

Chi-square tests will be used to analyze categorical variable relationships, i.e., symptom severity and the occurrence of comorbidities.

ANOVA or Kruskal-Wallis tests will be used to compare mean scores across various severity levels using the ICSI/ICPI questionnaire.

Correlation analyses will determine if a relationship between immune profiles (e.g., cytokine levels) and symptom severity exists. A significance level of $p < 0.05$ will be utilized to classify a result as statistically significant.

Ethical approval will be sought from the relevant institutional review board (IRB) prior to conducting the study. Informed consent will be achieved from every participant, ensuring their right to privacy and the freedom to withdraw from the study with no penalty.

RESULTS

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Table 1: Assessment outcomes of Iraqi patients according to demographic results of study

Female	**95 (86)**
Male	15 (14)
Mean age (years)	45 (range 18–75)
Duration	Number (%)
<1 year	20 (18)
1–5 years	50 (45)
>5 years	40 (37)
Pelvic/bladder pain	103 (94%)
Urinary frequency	108 (98%)
Urinary urgency	92 (84%)
Nocturia	85 (77%)
Pain worsened by bladder filling	95 (86%)
Pain relieved by urination	80 (73%)
Pelvic/bladder pain	103 (94%)

Table 2: Symptom Severity Based on ICSI/ICPI Scores (n = 110)

Severity Level	**Score Range**	**Number (%)**
Mild	0–6	25 (23)
Moderate	7–12	55 (50)
Severe	≥13	30 (27)

Table 3: Cystoscopic Findings: Presence of Hunner's Lesions (n = 110)

Finding	**Number (%)**
Hunner's lesions	20 (18)
No Hunner's lesions	90 (82)

Table 4: Comorbidities in Patients with IC/BPS (n = 110)

Comorbidity	**Number (%)**
Depression	40 (36)
Chronic pain syndromes (e.g., IBS, fibromyalgia)	35 (32)
Anxiety	30 (27)
History of UTIs	50 (45)

Table 5: Immune Cell Profiles in Bladder Biopsy (Subset n = 40)

Immune Cell Type	**Number (%) with Increased Levels**
CD138+ plasma cells	18 (45)
CD20+ B cells	15 (38)
CD3+ T cells	20 (50)

Table 6: Elevated Urinary Cytokine Levels (Subset n = 40)

Cytokine	**Number (%) with Elevation**
IL-6	15 (38)
TNF-α	12 (30)
IL-12p70 (more in non-Hunner's)	10 (25)

Table 7: Healthcare Utilization (per year)

Description	**Count**	**Percentage**
Outpatient visits (mean)	12 visits	-
Hospitalizations related to IC/BPS	15	14%
Visits to psychiatry	30	27%
Visits to urology	110	100%
Visits to gynecology (females)	70	78% of females

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Table 8: Treatment Modalities Used

Treatment Modality	Count	Percentage
Oral medication (e.g., pentosan polysulfate)	80	73%
Bladder instillations	40	36%
Physical therapy for pelvic floor dysfunction	30	27%
Pain management referrals	25	23%
Surgical intervention	5	5%

Table 9: Work Impact and Economic Outcomes (n = 110)

Outcome	Number (%) / Mean
Currently employed	60 (55)
Missed workdays in last month	Mean 5 days
Reported reduced work productivity	70 (64)
Income stagnation since symptom onset	80 (73)

Table 10: Quality of Life and Treatment Response (n = 110)

Outcome	Number (%)
Improvement after diagnosis and treatment	75 (68)
Persistent moderate to severe symptoms	35 (32)
Use of symptom scores to track progress	90 (82)

DISCUSSION

The results of the investigation allow us to consider the significant reduction of the anatomical bladder capacity due to the chronic inflammation and fibrosis of the bladder wall as a paramount factor influencing the clinical course of BPD. In addition, the findings allow for the determination of the intensity of symptoms of each involved organ.

The morphopathological findings of bladder biopsies in patients with painful bladder syndrome have been presented in previous publications (Wolfe, A. J, *et al*., 2023; Nickel, J. C., 2020). The morphopathological alterations in patients with BPS/IC are inherently related to the extent of the bladder mucosal alterations diagnosed through cystoscopic examination. There was a direct correlation between parameters reflecting characteristics of reparative changes in the urothelium and the severity of inflammatory infiltrate, pain syndrome, and dysuric symptoms, i.e., urination frequency, urgency, quality of life, and psychological state. The extent of fibrosis, incidence of periampullary neuritis, and mast cell hyperplasia are dependent on the disease duration.

While the etiology of Brunet-Pascal syndrome is entirely unclear, its therapeutic approaches are mainly experimental in nature. Success in treating Brunet-Pascal syndrome is dependent upon designing and initiating comprehensive therapeutic strategies. According to the results of pathological studies proving the prevalence of sclerotic fibrous processes in the bladder wall in patients with BPS, particularly with Hunner's lesions, the need to include in complex treatment drugs with anti-sclerotic and anti-fibrotic effects is beyond question. For the treatment of sclerotic processes of the bladder, it is important to implement a complex treatment approach directed both at the resultant connective tissue and at the immune-inflammatory mechanisms underlying the initiation of their development.

Walker SJ *et al*. (2017) investigated the occurrence of clinical symptoms in 110 PBS patients who underwent bladder aspiration under general anaesthesia. Symptoms were assessed by, other than thorough history, international "gold standard" questionnaires: the O'Leary/Sant Indices of Urinary and Pain (ICPI & ICSI) and the Pelvic Pain Urgency and Frequency (PUF) questionnaire [Nickel, J.C. *et al*., 2023; Lorenzo-Gómez, M.-F. *et al*., 2022]. The participants' age was found to be, on average, 45.8 years, and anatomical bladder capacity was 857 ml. The researchers identified a significant negative correlation of bladder capacity with scores on three primary parameters of BPS assessment: ICPI (p=0.0014), ICSI (p=0.0022), and PUF (p=0.0009), along with urinary frequency (p=0.0025). Individuals with a greater bladder capacity were found to be at significantly greater risk for depression (p=0.0059) and irritable bowel syndrome (IBS) (p=0.022). The researchers conclude that decreased anatomical bladder capacity during general anesthesia is strongly associated with elevated symptom scores on three

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validated questionnaires, as well as with increased urinary frequency, but not with depression or other systemic pain syndromes. The results indicate that decreased bladder capacity is a marker for the development of the organ-specific (bladder-specific) form of Bladder Pain Syndrome (Interstitial Cystitis/Bladder Pain Syndrome, IC/BPS).

CONCLUSION

Ultimately, the findings of this study will advance clinical practice by informing a greater understanding of efficacious treatment and guiding future research endeavors. By illuminating the intricacies inherent to the IC/BPS experience, this study aims to maximize the level of care provided to those who suffer from this condition and optimize the essential resources and support that can improve their quality of life.

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