

Prospective Observational Study on Improving the Utility of Clinical Phenotyping in Interstitial Cystitis/Painful Bladder Syndrome at Tertiary Care Unit

Yasir Iqbal Lone¹, Haamid Hassan Bhat², Shah Nawaz Hussain Siddiqi³, Nahid Khan⁴, Amir Iqbal Lone⁵ and Annam Qayoom^{6*}

¹Senior Resident, Department of Urology, Government Medical College Srinagar, India

²DNB, Resident, Department of Urology, Government Medical College Srinagar, India

³MCH, Scholar, Department of Urology, Government Medical College Srinagar, India

⁴Senior Resident, Department of General Surgery, Government Medical College Srinagar, India

⁵Consultant, Department of Obstetrics and Gynaecology, Directorate of Health Kashmir, India

⁶Postgraduate Scholar, Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India

Corresponding Author*

Annam Qayoom

Postgraduate Scholar, Department of Anesthesiology & Critical Care, Govt. Medical College, Srinagar, India. E-mail: annam.qayoom@gmail.com

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Abstract

Background: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a debilitating disease that induces mental stress, lower urinary symptoms, and pelvic pain, therefore resulting in a decline in quality of life. The present diagnosis and treatments still lead to unsatisfactory outcomes, and novel diagnostic and therapeutic modalities are needed.

Aim & Objectives: The assessment on improving the utility of clinical phenotyping in interstitial cystitis/painful bladder syndrome.

Methods: This prospective observational study includes the profile of 62 patients in the Department of urology at Super speciality Hospital Srinagar, one of the associated hospitals of government medical college Srinagar. Patients with CPPS were prospectively classified in each domain of our UPOINT system and the symptoms were measured using the Chronic Prostatitis Symptom Index. Statistical analysis was done using IBM SPSS Statistics for Windows from IBM Corp. (released 2020, Version 27.0. Armonk, NY, USA). Categorical variables were shown in the form of frequencies and percentages. Independent t-test was used. All values were discussed at a 5% level of significance ($p < 0.05$).

Results: The percentage of patients positive for the each domain urinary, psychosocial, organ specific, infection, neurologic/systemic, and tenderness domains, respectively was 100%, 69.1%, 100%, 27%, 57.5%, and 29%. Of the 62 patients, 25% were positive for only 1 domain, and a significant stepwise increase was found in the total Chronic Prostatitis Symptom Index score as the number of positive domains increased. A symptom duration of

>2 years was associated with an increase in positive domains ($P < 0.01$). Comparing the total Chronic Prostatitis Symptom Index score with the presence of each domain revealed significantly increased symptoms in patients positive for the urinary, psychosocial, organ specific and neurologic/systemic domains. The mean decrease in ICSI was 13 ± 4 points. Significant clinical improvement (>35%-55% decrease in ICSI-29.8 and >50% decrease in ICSI-71.3%) was observed in 91.4% compared with initial baseline visit. Significant improvement was seen after UPOINT directed treatment with the symptoms of interstitial cystitis/painful bladder syndrome.

Conclusion: Multimodal therapy using UPOINT leads to significant improvement in symptoms and quality of life. CP/CPPS is a heterogeneous condition and, much like with prostate cancer, optimal therapy can only be achieved by classifying patients into clinically meaningful phenotypic groups and letting the phenotype drive therapy.

Keywords: Chronic bladder pain • Interstitial cystitis • Pathophysiology • UPOINT • Clinical phenotype • Treatment

Introduction

Defined as a chronic inflammatory condition with a bacterial infections of the bladder, Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is characterized by symptomatic frequency and urgency, as well as chronic pelvic pain [1-4]. Although non-lethal, IC/BPS afflicts millions of individuals worldwide, while its potential mechanism is unknown. It is a disease of unknown aetiology, with a poorly understood pathophysiological mechanism. BPS is more common in women than men, with a prevalence of 2%-6%. [5] The disease phenotype is varied, some patients display a mild form of the disease and treatment can be undertaken in the outpatient setting, whereas others have a debilitating disease, requiring repeated hospital visits. The treatment objective is therefore focused on restoring function, preventing relapse of symptoms and improving quality of life [5,6].

A multidisciplinary approach to management is key to success, where patients are reviewed in dedicated clinics, including specialists in psychology, pain management, urology and urogynaecology.

Research into BPS over the last 30 years has resulted in a new understanding of the bladder urothelium and the impact of urothelial injury on the symptoms experienced by patients with BPS. Research continues into discovering new biomarkers to better subtype patients. The stratification of patients into BPS subtypes is important to determine the treatment modalities or targets that would be most effective. Several novel therapies have shown promise in small clinical trials [7].

BPS/IC is contemporarily seen as a biopsychosocial disorder necessitating a multidisciplinary approach in the clinical management. The use of a multidisciplinary phenotyping system, UPOINT (urinary, psychosocial, organ-specific, infection, neurologic and/or extrapelvic/systemic pain, and tenderness of pelvic floor), is recommended to better characterize what domains are involved in each patient with the hope of directing multimodal therapy and improving patient outcomes [8,9].

Material and Methods

This prospective observational study was conducted at in the Department of urology at Super speciality Hospital Srinagar, one of the associated hospitals of government medical college Srinagar. Patients with CPPS were prospectively classified in each domain of our UPOINT system and the symptoms were measured using the Chronic Prostatitis Symptom Index. Participants were selected from the patients of either sex who presented with suprapubic pain/ increased frequency of urine/LUTS and diagnosed with IC/BPS.

Patients were assessed by taking a detailed history, examination, routine urine analysis and ultrasound examination (if required) of urinary tract. As per the clinical indications further investigations were performed to exclude any confusable disease. In case of any doubt regarding the diagnosis of BPS, an intravesical lignocaine test was performed to confirm. Severity of the symptoms and response to treatment was assessed and given a 0-35 score based on the proposed scale. Patients were grouped according to

clinical phenotyping and treatment strategies will be given. Patients were categorized into the clinical domains (UPOINT Classification) and treatment given accordingly. The clinical domains are urinary symptoms, psychosocial dysfunction, organ-specific findings, infection, neurologic/systemic, and tenderness of muscles, which produces the acronym UPOINT. Follow up was done at 1 week, 1 month and 2 months. Treatment was adjusted based on patient's response. Responses were stratified into three categories; Unsatisfactory response (decrease of <30% of score), Good response (decrease of >30 to <50% of score) and Excellent response (decrease of > 50% of score). Written informed consent was taken from all the study participants.

Demographics and general health characteristics data were collected. Further information was solicited among individuals with diagnosed bladder pain. The questions included the following: length of time experienced pain, length of time since bladder pain diagnosis, type of diagnosing physician, pain severity, frequency that pain caused urination, type and length of duration of prescription(s) used primarily to treat bladder pain, type of prescribing physician, and satisfaction with treatment (assessed on a 7-point scale, where 1=extremely dissatisfied and 7=extremely satisfied).

All analyses were performed using appropriate statistical software (STATA, SAS, and SPSS). An alpha level of 5% (two-sided) was used for all null-hypothesis tests without adjustments for multiplicity. Data presented as Mean/SD (minimum-maximum) or frequency/ percentage. The change in clinical score from baseline was analysed using Wilcoxon signed rank test. p<0.05 was considered to be statistically significant.

Results

The age of study patients vary from 24 years to 80 years with mean age of distribution was 49.3 years ± 11.21 years. Maximum number of study patients lied between the age of 47 to 57 years. There were more females (75.80%) in the study as compared to males (24.1%) (Table 1).

Table 1. Demographic profile of the study population.

Age (years)	Frequency	(%)
24-35	4	6.45
36-46	9	14.51
47-57	22	35.48
58-68	16	25.8
69-80	11	17.74
Sex M/F	15/47	24.1/75.8
Mean ± SD (Range)=49.3 ± 11.21 (24-80)		

On clinical examination the most commonly observed symptom was pelvic tenderness (11.29%) followed by prostrate grade 2 (3.22%) and Grade 2 cystocele 1.61% (Table 2). With regard to Signs and symptoms on evaluation 100% of patients had complaints of frequency urination, nocturia and urgency (96.77). 30.64% of patients represented with Suprapubic pain followed by haematuria (14.51%), burning micturition (11.29%), dysuria (8.06%), difficulty voiding (4.83) and Fever (3.22%) among the study population (Table 3).

Table 2. Clinical examination.

Clinical examination	Frequency	%
Pelvic tenderness	7	11.29
Prostrate grade 2	2	3.22
Grade 2 cystocele	1	1.61

Table 3. Signs and symptoms among the study population.

Signs and symptoms	Frequency	%
Frequent urination	62	100
Nocturia	62	100
Urgency	60	96.77
Suprapubic pain	19	30.64
Haematuria	9	14.51
Burning micturition	7	11.29
Dysuria	5	8.06
Difficulty voiding	3	4.83
Fever	2	3.22

On routine urine examination and culture characteristics 83.87% patients represented with normal routine urine examination and 35.48% of patients represented with culture positive with *E.Coli* main causative agent among the study population. With regard to hematological and biochemical parameters patients represented within normal ranges except WBC count shows increasing trend (Table 4).

Table 4. Hematological and urine characteristics among the study population.

Variables	Mean ± SD	Range
Haemoglobin (g/dl)	11.4 ± 1.3	9.5-14.6
WBC Count (/mm ³)	8325 ± 1800	6458-9256
Serum creatinine (mg/dl)	0.86 ± 0.21	0.50-1.05
Urine routine	Normal/ Abnormal	83.87/16.12
Urine Culture	Positive/Negative	35.48/64.51

On UPOINT score frequency of participants, 100% of patients represented with organ specific and urinary domain followed by 69.1% who had psychological domain. 57.5% participants had neurological/ systemic domain whereas around 27 to 29% had infection and tenderness domain (Figure 1).

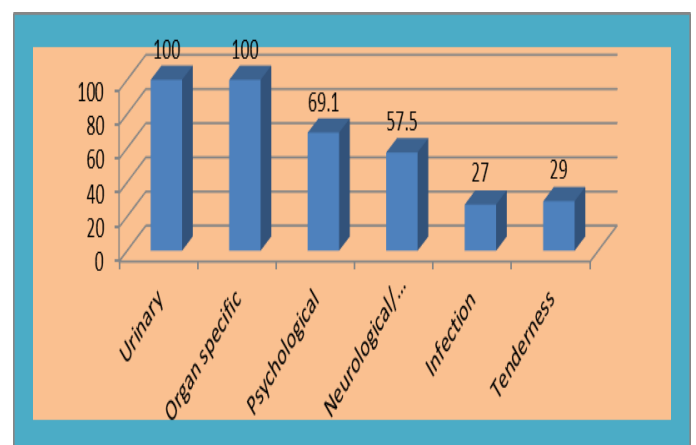


Figure 1. UPOINT score.

With regard to the treatment received by the patients among the study population, majority of patients received B3 agonist followed by PPS, analgesic, behavioural modifications and pregabalin respectively (Figure 2).

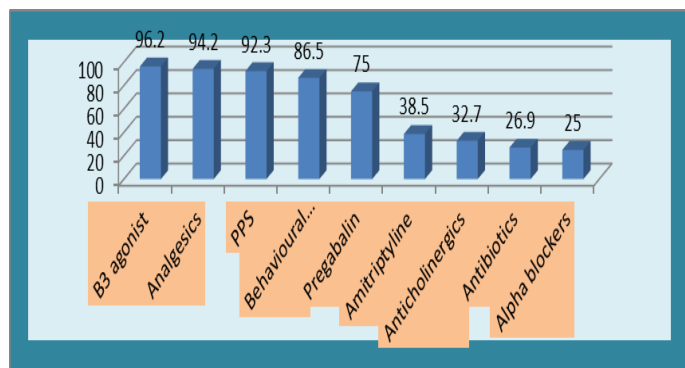


Figure 2. Treatment Received by study population.

Response to treatment received by Study Participants, 66.12% of patients shows excellent results followed by 29.96% patients good results and only 12.9% patients represented with unsatisfactory results among the study population (Figure 3)

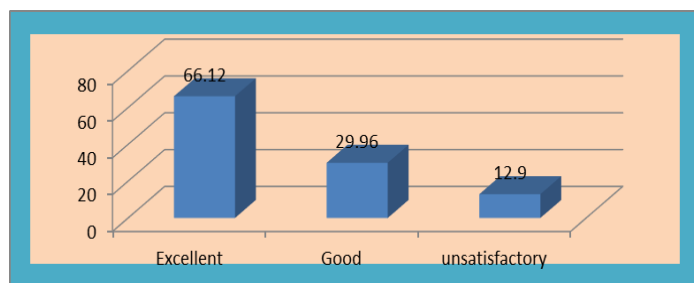


Figure 3. Response to treatment.

Discussion

The prevalence of IC/BPS varies widely since uniform definitions and methods are lacking, and current evidence estimates a rate between 0.01% and 6.5% [10]. Many studies have demonstrated differences in the prevalence of IC/BPS across different regions and ethnicities.

Available treatment options include general relaxation techniques, patient education, behavioral treatments, physical therapy, multimodal pain therapy, oral (amitriptyline, cimetidine, hydroxyzine) and intravesical treatments (heparin, lidocaine, hyaluronic acid and chondroitin sulfate), hydrodistension and other more invasive treatments. Available treatments are mostly not based on a high level of evidence. Lack of understanding of disease mechanisms has resulted in lack of targeted therapies on this area and a wealth of empirical approaches with usually inadequate efficacy [11].

In the present observational study, a profile of 62 patients included of which 75.80% patients were female and 24.1%, that accordance to study of Clemens et al, 2005 in which prevalence of IC/BPS of female to male ratio observed was 5:1. Out of 174 patients, 19 (10.9%) were male in Taneja et al study [12,13]. In the present study, the mean age was 49.3 years ± 11.21 years with minimum age of 24 years and maximum age of 70 years among the study population. This is accordance the study conducted by Nickel et al., were the mean age recorded was 45.2 years ± 17.4 years. Out of the 174 patients in Taneja et al, (2019) study the overall age ranged from 25 years to 75 years, with a mean of 46.5 years [14].

The main symptom of IC/BPS is pelvic pain with or without urinary symptoms, and the clinical pattern among young patients is dominated by urgency, frequency, dysuria, dyspareunia, and external genital pain, while that of elderly patients is dominated by nocturia, urinary incontinence, and Hunner lesions [2,15]. In addition, IC/BPS is more common in women than men, with a female-to-male ratio in incidence rates of approximately five to one [16].

In the present study on evaluation 100% of patients had complaints of frequency urination, nocturia and urgency (96.77). 30.64% of patients represented with Suprapubic pain followed by haematuria (14.51%), burning micturition (11.29%), dysuria (8.06%), difficulty voiding (4.83) and Fever

(3.22%) among the study population which is quite similar to studies done by Nickel et al [14,17].

On UPOINT score frequency of participants, 100% of patients represented with organ specific and urinary domain followed by 69.1% who had psychological domain. 57.5% participants had neurological/ systemic domain whereas around 27% to 29% had infection and tenderness domain, which is quite similar to Nickel et al, 2009 study. Unlike male CP-CPPS, in which approximately 52% and 61% were categorized in the urinary and organspecific domains, respectively. Treatment for these two domains was anticholinergics, alpha blockers, Beta-3 Agonist (Mirabegron) and Pentosan Polysulfate. With the development of Mirabegron, which is selective for urinary bladder is safe and effective to control frequency, urgency and nocturia than usage of anticholinergics, which has little more side effects profile.[17] In our participants of IC/BPS, (35.48%) patients were included in infection domain, which was comparable to study of Nickel, 2005 that included 35 % patients in infection domain. All the 35.48% of patients were treated with short course of antibiotics directed against uropathogenic organism mainly *E.Coli* according to culture report [17]. The major psychosocial domain considerations identified in patients with IC/PBS included depression and social problems. In our study we had 69.1% of patients with psychosocial domain. In the present study 79.9% received behavioral modifications in the form of counseling that shows treatment not only focusing on psychosocial domain, but it helps in curing other domains and 38.5% received Amitriptyline acting as an antidepressant. In our study 57.5% of patients included in neurologic domain. In our study 75% received Pregabalin and 38.5% received Amitriptyline. These two drugs other than neurological treats psychosocial and tenderness domain also [17]. Patients identified in the tenderness domain had pelvic, perineal and/or abdominal muscle (or ligament) pain/tenderness, and trigger points on physical examination, that included 25% of patients in our cohort. Therapy for this domain would include counselling, analgesics and various forms of physical therapy [17].

BPS/IC is contemporarily seen as a biopsychosocial disorder necessitating a multidisciplinary approach in the clinical management. The use of a multidisciplinary phenotyping system, UPOINT (urinary, psychosocial, organ-specific, infection, neurologic and/or extrapelvic/systemic pain, and tenderness of pelvic floor),] is recommended to better characterize what domains are involved in each patient with the hope of directing multimodal therapy and improving patient outcomes [8,9]. In a one study, conducted by Nickel JC, Irvine-Bird K, Jianbo L, et al. designed as , Phenotype-directed management of interstitial cystitis/bladder pain syndrome, demonstrated that a phenotype directed approach resulted in clinically significant improvement in BPS/IC symptoms at 1 year follow-up [9]. Also, there is evidence to suggest that improvement in one domain can lead to a favorable effect in the others [18]. These results are similar to our study in which out of 62 patients 66.12% of patients shows excellent results followed by 29.96% patients good results and only 12.9% patients represented with unsatisfactory results among the study population Our result shows significant improvement in patients's response towards clinical UPOINT directed treatment and improves quality of life.

The update is on account of the emphasis on mutual and in-depth communication between patients and clinicians, personalized factors, and evaluations. Meanwhile, other guidelines also advocate for a similar multimodal treatment system on the basis of shared decision-making to cope with the complexity of IC/BPS [19,20].

Conclusion

Multimodal therapy using UPOINT leads to significant improvement in symptoms and quality of life. CP/CPPS is a heterogeneous condition and, much like with prostate cancer, optimal therapy can only be achieved by classifying patients into clinically meaningful phenotypic groups and letting the phenotype drive therapy.

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