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## Childhood trauma perpetrated by close others, psychiatric dysfunction, and urological symptoms in patients with interstitial cystitis/bladder pain syndrome



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#### ABSTRACT

*Background:* A psychosocial phenotype of interstitial cystitis/bladder pain syndrome (IC/BPS), a urogenital condition without known organic causes, was proposed. While psychosocial variables, including interpersonal maltreatment and negative affect, were studied in association with IC/BPS, the specificities of the relationships between childhood trauma by close others, psychiatric dysfunctions (negative affect and post-traumatic psychopathology), and urogenital symptoms have not been established.

Methods: 94 IC/BPS patients were recruited together with 47 patients with acute cystitis who served as clinical controls. Standardized scales were used to assess various potentially traumatizing events in childhood and adulthood as well as psychiatric (dissociation and negative affect) and urogenital symptoms.

*Results*: Among the potentially traumatizing events, those perpetrated by close others during childhood were found to be the most salient features discriminating the IC/BPS group from the control group. When divided into 2 subgroups according to their history of childhood trauma by close others, only IC/BPS patients with childhood trauma by close others had more dissociative and anxiety symptoms compared with the control group. These two subgroups did not differ in urogenital symptom severity.

Conclusions: Childhood trauma by close others, rather than other types of interpersonal trauma, was a differentiating characteristic in IC/BPS patients, and a childhood trauma related psychosocial phenotype with a distinct clinical profile of dissociation and anxiety proneness was identified. Future studies should investigate whether a distinct set of pathogenic factors exists in IC/BPS patients with a history of childhood trauma by close others, even if this subgroup is not readily differentiated by urogenital symptoms.

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#### 1. Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a complex urogenital condition characterized by (1) chronic unpleasant sensations (pain, pressure, and discomfort) over the bladder or pelvic area and (2) lower urinary tract symptoms, such as persistent urge to void, frequent urination, and nocturia [1]. Several hypothetical organic causes of IC/BPS have been proposed, including urothelial inflammation (mastocytosis [2,3], nerve growth factor [4,5], antiproliferative factor [6,7], and gene expression [8,9]), bladder afferent hypersensitivity (autonomic dysfunction [10]), systemic dysregulation (comorbid disease [11,12]), and central sensitization [13,14]. However, empirical findings have been inconsistent, with some studies documenting supportive evidence [2,4,6,8,10–13] and others reporting null results [3,5,7,9,14]. The

lack of reliable findings on organic causes has led to the speculation that IC/BPS may be a functional somatic syndrome (FSS [15]).

FSSs are characterized by persistent bodily complaints with little or no identified organic basis or that are inconsistent with or disproportional to existing organic causes [15,16]. Several FSSs have been identified, such as chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia. According to the traditional view of psychosomatic medicine, FSSs may reflect intensified bodily tensions occurring in conjunction with unregulated affective states [17]. Individuals with an FSS are considered to have difficulty with affect regulation, including lower emotional awareness, reflected by decreased capacity for symbolizing emotional reactions and processing the psychological meaning of emotional experiences [18]. This reduced affect regulation capacity may result from childhood interpersonal experiences with caregivers, as apperception of affective states may be disrupted by insufficient or inadequate responses to a child's needs [19]. In the context of lowquality parent-child interactions, such as being raised in an abusive family [20], children may not acquire the knowledge and skills to reflect

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their mental states, thereby impeding the attribution of bodily symptoms concurrent with affective states.

Some factors identified within the psychosomatic model have been observed in patients with IC/BPS, with IC/BPS patients reporting more frequently unregulated emotional states, including intensified anxiety and depression, than healthy controls [21,22]. Furthermore, stressful interpersonal experiences have been found to be prevalent in patients with IC/BPS. Although the prevalence rates varied due to differences in measurement, 26%, 25%, and 27% of IC/BPS patients were reported to have experienced lifetime sexual, physical, and emotional maltreatment, respectively [23–25]. Only two studies have reported the rates of interpersonal maltreatment during childhood among these patients, suggesting that 27%, 33%, and 36% of study participants had experienced sexual, physical, and emotional maltreatment, respectively [24,26]. Of note, the only case-control study previously conducted on this topic showed that between-group differences in the rates of childhood interpersonal maltreatment reached significance for sexual abuse [26]. These results provide initial support for the psychosomatic account, at least in a subgroup of patients with IC/BPS.

Of note, the role of childhood trauma by close others in IC/BPS remains poorly understood because of inconsistent findings and methodological limitations. The previously observed effects have varied with different trauma types. The potential role of sexual abuse has been emphasized, as this trauma may be associated with a localized peripheral sensitization effect on genitourinary areas [27]. However, various types of maltreatment have been found to be interrelated [20], and some studies have assessed other types of interpersonal maltreatment. The results of these studies were twofold. While one study demonstrated a specific effect of sexual abuse [26], others reported that physical and emotional abuse also had an impact [25,28]. More importantly, two critical features of childhood interpersonal trauma, the abuser-victim relationship, and the age of onset have been ignored. If a developmental arrest in the apperception of affective states is the mechanism underlying the association between childhood maltreatment and FSSs [18,19], then childhood trauma by close others (i.e., caregivers) should characterize patients with IC/BPS. However, the abuser-victim relationship has not been addressed [23-26], and interpersonal maltreatment perpetrated by trusted others [29,30] was not discriminated from non-interpersonal maltreatment involving non-close others in previous studies. The most critical period for interpersonal traumas (i.e., childhood) has also not been specified [25] or compared to interpersonal traumas in adulthood [26].

More importantly, only negative affect states were specifically assessed in previous studies. Although intensified anxiety and depression may reflect affect regulation failure, another critical construct in the psychosomatic model, dissociative pathology, has been neglected. Dissociation, the disintegration of the processing of cognitive (psychoform) and sensory-motor (somatoform) information [31], is a trauma-related psychiatric dysfunction [32]. This disintegration may reflect atypical cognitive control and monitoring that influences the regulation of mental and somatic representations [33-37], especially in association with unresolved stressful experiences [38]. Dissociative pathology has been found to be another critical factor in FSSs and somatoform disorders [39–43]. Intriguingly, urinary problems and pelvic pain have been observed in traumatized patients and are considered somatic presentations of dissociative pathology [44]. It is unclear whether dissociative pathology is present in patients with IC/BPS. Without this evidence, it is difficult to evaluate the adequacy of the psychosomatic model and advance understanding of the impact of early interpersonal maltreatment on physical and mental health in patients with IC/BPS.

This study aimed to investigate the role of childhood trauma by close others in IC/BPS patients. Specifically, we targeted the relationships between childhood trauma by close others, psychiatric dysfunctions, and urogenital symptoms in patients with IC/BPS. We assumed that IC/BPS may be of multifactorial etiology [45] and posited that a phenotype of

IC/BPS in which psychosocial factors play a vital role may exist [22]. A group of patients with IC/BPS and a clinical control group comprising patients with acute cystitis (AC) were recruited to test our hypotheses. We selected AC as the clinical control because it has similar manifest urogenital symptoms (i.e., pelvic pain, urinary frequency, and urgency of urination), but, in contrast to IC/BPS, with proven organic causes (i.e., pyuria in urinalysis examination and/or positive bacterial findings in urine culture). We predicted that the prevalence rates of childhood trauma by close others would be higher in patients with IC/BPS than in those with AC but that childhood trauma by close others may characterize only a subgroup of IC/BPS patients. Additionally, we predicted that psychiatric dysfunctions would be an exclusive feature of this childhood interpersonal trauma subgroup and that this subgroup would report intensified negative affect states and dissociative pathologies. These psychiatric dysfunctions, however, were not expected to be identified in IC/BPS patients without a history of childhood trauma by close others. Finally, it was unclear whether the two subgroups of IC/BPS patients would differ in urological symptom presentation, as few studies have investigated this issue. Some preliminary findings have suggested that psychiatric dysfunctions may be correlated with quality of life and even urogenital symptoms [22,27,46].

#### 2. Methods

#### 2.1. Participants

#### 2.1.1. IC/BPS

Ninety-four female patients with IC/BPS were recruited. Among these patients, the average age was  $40.6\pm10.0$  years, and the average years of education were  $12.0\pm4.1$ . The inclusion and exclusion criteria for the diagnosis of IC/BPS were adopted from the 2010 guidelines of the American Urology Association. All patients were diagnosed based on the presence of chronic (>6 weeks) unpleasant sensations (pain, pressure, or discomfort) perceived to be related to the bladder and associated with frequent urination and nocturia in the absence of infections or other identifiable causes. Other urogenital diseases including neurogenic bladder, radiation cystitis, urolithiasis, and chronic urinary tract infections were differentiated and excluded. Cystoscopic hydrodistention was performed on all participants, and the bladder was then emptied and inspected for Hunner's ulcers. Participants with Hunner's ulcers were also excluded from the study.

#### 2.1.2. Acute cystitis

Forty-seven female patients with AC were recruited. Their average age was  $43.4\pm9.9$  years, and the average years of education were  $11.5\pm3.9$ . The inclusion criterion for the diagnosis of an acute uncomplicated urinary tract infection was the presence of urogenital symptoms, including dysuria, urgency, and frequency, within the past 7 days. The diagnosis of acute uncomplicated urinary tract infections was made when pyuria was evident via urinalysis. The exclusion criteria were immunosuppressive diseases, a neurogenic bladder, urinary stones, and other definite urogenital diseases. Additionally, patients with chronic recurrent urinary tract infections persisting for >1 year or with indwelled Foley catheters were excluded.

#### 2.2. Instruments

#### 2.2.1. IC/BPS manifest symptoms

Several measures were applied to assess the symptoms of IC/BPS. Two standardized instruments were used to evaluate the manifest symptoms of IC/BPS. The Pelvic Pain and Urgency/Frequency Patient Symptom (PUF) scale is a measure of pelvic pain, dyspareunia, and lower urinary tract symptoms of interstitial cystitis [47]. The scale comprises two parts. The first part includes seven items related to manifest symptoms; the second part includes four items pertinent to symptom-related dysfunctions and distress. A total score is derived to reflect the

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