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ORIGINAL ARTICLE

# Examining vaginal and vulvar health and sexual dysfunction in patients with interstitial cystitis (UNICORN-1 study)

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## Abstract

**Introduction and hypothesis** The Vaginal Health Index Score (VHIS) and vulvodynia swab tests are used to assess vaginal health and vulvodynia. However, few studies have used these tests in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). IC/BPS is a chronic, debilitating disorder, characterised by urinary frequency, urinary urgency and pelvic pain. It adversely affects organs adjacent to the urinary system, leading to complications of sexual dysfunction. This study was aimed at understanding sexual dysfunction in patients with IC/BPS, as well as deterioration of vaginal health and vulvodynia.

**Methods** This study compared the vaginal health of IC/BPS patients with that of asymptomatic control individuals. The Pain Urgency Frequency (PUF) score, Female Sexual Function Index (FSFI), VHIS, and vulvodynia swab tests, were used as tools. The PUF and FSFI are questionnaire-based surveys of bladder symptoms and sexual function respectively. VHIS evaluation and vulvodynia swab tests are performed by physicians. The PUF was used to assess baseline IC/BPS symptoms to validate the patient population, and FSFI, vulvodynia swab tests and VHIS were used to determine between-group differences.

**Results** Thirty-seven patients were recruited in each group. The IC/BPS group had a higher PUF score (18.19±3.51 vs 3.56±2.35; $p<0.05$), worse total FSFI (15.72±4.46 vs 26.3±4.93; $p<0.05$), and worse vulvodynia swab test and total VHIS (11.59±2.87 vs 22.05±3.05; $p<0.05$) scores than those of the control group.

**Conclusions** Asian women with IC/BPS experienced greater sexual dysfunction, worsened vaginal health and increased vulvodynia compared with control individuals. Information on vaginal and vulva health is very useful in evaluating IC/BPS patients.

**Keywords** Bladder pain syndrome · Interstitial cystitis · Sexual dysfunction · Vaginal health · Vulvodynia

## Introduction

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic disease of the urological organs that is characterised by urinary frequency, urinary urgency and pelvic pain [1], with an estimated prevalence of approximately 300 cases per 100,000 women [2]. The typical age at onset of IC/BPS is between 32 and 49 years [1]. Female patients with IC/BPS may share multiple comorbidities, such as worsened vaginal health and vulvodynia [3–5], and female sexual dysfunction (FSD) [6]. There are many studies on IC/BPS and dyspareunia [7, 8]; however, these studies do not fully explain the causal relationship between IC/BPS and dyspareunia. Interestingly, the tissues involved in the bladder, urethral, and vestibular pain syndrome, come from the same embryonic urogenital sinus, respond similarly to the trigger of dysfunction, and may mutually enhance pain perception [9]. Therefore, vaginal health and vulvodynia are considered important when evaluating dyspareunia in patients with IC/BPS.

To evaluate this condition, many studies have used the Vaginal Health Index Score (VHIS) and vulvodynia swab tests for determining vaginal health and systemically or locally induced vulvodynia respectively [10, 11]. However, vaginal and vulvar health and sexual dysfunction in IC/BPS have primarily been evaluated mainly in white women [5,

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12], and limited data are available in Asian patients [13]. The present paper reports data regarding both vaginal health and sexual function obtained in a longitudinal control study conducted in Asian women with IC/BPS.

## Materials and methods

This case–control study was conducted at a single centre from 1 October 2019 to 31 January 2022. The research was designed to compare vulvovaginal health and sexual function in women diagnosed with IC/BPS (IC/BPS group) with those in normal asymptomatic women (control group).

This study was approved by the Ethical Review Board of Kanagawa Association of Medical and Dental Practitioners (19005) and followed the provisions of the Declaration of Helsinki (revised, Edinburgh, 2000). The research was registered in University Hospital Medical Information (R000053098) and abbreviated as the Urinary-Incontinence (UNICORN)-1 study. All patients registered in this study provided written consent regarding both the use of data collected for research and publication and disclosure of information on a UNICORN study joint website for patients (https://unicorn-study.net/). The data were registered as open access in the Harvard Dataverse and can be obtained at https://doi.org/10.7910/DVN/HVIR7H.

The inclusion criteria were Asian ethnicity; age > 18 years; pain in the lower abdomen and/or genitourinary area over at least 3 months [14]; and at least one of the lower urinary tract symptoms urinary frequency, nocturia and urinary urgency [8]. Patients with other diagnosable medical conditions that could cause these symptoms were excluded [8].

The diagnosis of IC/BPS was based on the guidelines of the Global Interstitial Cystitis Bladder Pain Society [14]. Each woman was evaluated using cystoscopy with hydrodistension under general anaesthesia at low pressure (60 to 80 cmH2O) and for less than 10 minutes [15, 16].

Hunner's lesion, defined as a distinctive inflammatory lesion with characteristic central fragility, presents as a deep rupture through the mucosa and submucosa when bladder distention is provoked [17]. We compared the PUF scores of IC patients with Hunner's lesion (Hunner patients) and patients without Hunner's lesion (non-Hunner patients) using *t* test.

Detailed medical history was noted and laboratory tests were performed for each patient. We performed urinalysis, urine culture, urine cytology, and obstetrics and gynaecology cytology to rule out urinary tract infections and malignancies. Pelvic ultrasound was performed to rule out pelvic cancer and diseases of the uterus, ovaries and ureter [8].

For the control group, we recruited twice as many individuals as the expected number of patients with IC/BPS. The controls were selected under the following criteria: sexually active women; age 30–50 years; no urological and gynaecological complaints; and similar educational and socioeconomic backgrounds to the IC/BPS patient group [8].

The Pelvic Pain and Urgency/Frequency (PUF) symptom score is used in many studies as one of the indicators of the course of care for patients with IC/BPS [18–20]. In our study, patients with IC/BPS and controls were compared for sign severity using PUF scores [18]. We asked questions in Japanese, Chinese and English according to the patient's language. The PUF Patient Symptom Scale (English [18], Japanese [19], Chinese [20]) is a self-reported questionnaire-based diagnostic tool used to screen patients with chronic pelvic pain. The questionnaire has 12 items that can be divided into the two domains of symptom and bother scores [18–20]. Each question is scored in a range from 0 to 3, 1 to 3, or 0 to 4. The increase in severity of each item is represented by the increase in score. The total score ranges from 0 to 35, with scores >15 indicating significant symptoms [18–20].

The Female Sexual Function Index (FSFI) is a 19-item self-assessment questionnaire used to evaluate FSD [21]. We used the questionnaire according to the patient's language (English [21], Japanese [22] and Chinese [23]). This questionnaire assesses six areas of female sexual function: desire, arousal, lubrication, orgasm, satisfaction and pain. Responses to these questions are scored with respect to sexual activity over the previous 4 weeks. The individual domain score is calculated by multiplying the individual domain questions with the domain factors. Adding the scores for each domain yields the total score. Scores vary from a minimum of 1.2 to a maximum of 36. Scores below 26.55 are classified as FSD [8].

We also used the VHIS [10], a tool for objectively diagnosing vaginal health. Determining the VHIS involves evaluating the five items of overall elasticity, fluid secretion characteristics, vaginal pH range, epithelial mucosa, and moisture, on a scale of 1 (none), 2 (poor), 3 (fair), 4 (good) and 5 (excellent). A total VHIS score of less than 15 is considered to indicate poor vaginal health [10].

The vulvodynia swab test is used to determine systemically or locally induced vulvodynia [5]. To execute this test, pressure is systematically applied to different parts of the vulva (vestibule, clitoris, etc.) to assess the degree and characteristics of pain. For this study, the test was performed at the cardinal positions, 2:00, 4:00, 6:00, 8:00, 10:00 and 12:00, with 12:00 being upward to the urethral orifice and 6:00 being downward to the perineal body. For positions where pain was reported, the patient was asked to quantify the pain while referencing a visual analogue score from 0 (no pain) to 10 (severe pain) [5].

As past studies have shown that different procedures produce different results, it was important for us to ensure uniform pressure application in all patients [5, 11]. Moreover, we performed strength suppression in healthy women who could not feel pain [5].

The VHIS and vulvodynia swab tests were evaluated separately by two doctors, with the same two nurses present to ensure that there were no differences in the procedure. The two doctors had performed over 200 tests each year over the past 3 years, and the two nurses had assisted in over 100 examinations. Prior to this study, both doctors performed the two tests on 40 women, including healthy women and patients with genitourinary syndrome of menopause, vulvovaginal atrophy, stress urinary incontinence and urgency urinary incontinence patients, and we confirmed that there was no difference in the results obtained by both doctors (data not shown).

Each patient underwent two VHIS evaluations and two vulvodynia swab tests. An average of the ratings from the two doctors was selected. Both doctors assessed the VHIS and the vulvodynia swab test results independently. One doctor knew whether the patients had IC/BPS or were controls; the other doctor was not informed of the results in advance.

Women reportedly underestimate questions involving sexual function [24]; therefore, FSFI and PUF were performed by female therapists who were not informed of the patient's diagnosis [24].

The sample size was calculated for a hypothesis test between the two means. The minimum effect size to be calculated was 0.8, the power was 80% and the alpha error was 5%. Using data from the research by Ottem et al. [25], the calculated sample size was 27 for each arm [9]. All analyses used the statistical software R version 2.15.1 (R Core Team, Vienna, Austria) and Microsoft Excel version 1911 (Microsoft Corp., WA, USA) on the Windows 10 version 1903 (Microsoft Corp.) operating system. We used an independent Student's *t* test for statistical comparisons and considered $p<0.05$ to be statistically significant.

## Results

Overall, 44 patients were diagnosed with IC/BPS during the research period. Seven patients were excluded from the study: 4 reported having had no sexual activity in the previous 4 weeks, and 3 refused to participate because of the psychological burden of sexual function assessments. A total of 37 patients were included in the IC/BPS group. In the IC/BPS group, 5 (42.6 ± 3.26 years old) and 32 (41.8 ± 4.37 years old) women were diagnosed as Hunner and non-Hunner patients respectively. The total PUF scores of Hunner and non-Hunner patients were 20.67 ± 4.46 and 17.71 ± 3.17 respectively; no significant difference was observed between the two groups ($p=0.058$). The total FSFI of Hunner and non-Hunner patients were 13.21 ± 4.67 and 16.21 ± 4.32 respectively; no significant difference was observed between the two groups ($p=0.134$). Based on these data, we decided not to distinguish between the two groups, and combined them into one group.

In the control group, 89 women were registered. Eighty-two women matched the inclusion criteria. Eight women were rejected owing to the psychological burden, and 6 women did not visit the clinic because of the presence of other diseases before the sexual function assessments (5 with respiratory infections, 1 with gastric cancer). Finally, 68 women joined this study, and the first 37 eligible women—based on their registration order—were selected for the control group.

The two groups of patients mentioned were mutually exclusive. All women were Asians, with the following nationalities: Japanese, 60 people; Chinese, 13 people; Filipino, 1 person. There were no significant differences in age between the two groups ($p=0.954$). Other characteristics of the two groups are shown in Table 1. Each evaluation item is shown in Table 2.

The IC/BPS group had a significantly higher total PUF score than the control group (18.19±3.52 vs 3.76±2.35). The total FSFI score of the IC/BPS group was significantly lower than that of the control group (15.98±4.62 vs 26.35±4.95). The IC/BPS group had significantly lower scores than the control group in all six domains of the FSFI (i.e. desire, arousal, lubrication, orgasm, satisfaction and pain). Using the cut-off score of ≤26.55 [8] for the total FSFI score, 91.9% ($n=34$) of the IC/BPS group was diagnosed with FSD, whereas only 40.5% ($n=15$) of the control group was diagnosed with the same.

The VHIS showed a significantly lower median total score of vaginal health in the IC/BPS group compared with that in the control group (12.03±3.36 vs 22.05±3.90), as well as in all five domains of the VHIS (i.e. overall elasticity, fluid secretion characteristics, vaginal pH range, epithelial mucosa and moisture).

Using the cut-off score of 15 points or less for the total VHIS score [10], 86.49% ($n=32$) of the IC/BPS group was diagnosed with worsened vaginal health, whereas only 40.5% ($n=15$) of the control group was diagnosed with the same.

The positive rate of vulvodynia swab tests is shown in Fig. 1. In the IC/BPS group, 18.92% ($n=7$) and 67.56% ($n=25$) patients reported spontaneous or induced vulvodynia respectively, whereas neither was reported in the control group ($p<0.001$).

Furthermore, 16.21% ($n=6$) reported overall vulvodynia, and 70.21% ($n=26$) reported localised pain in the IC/BPS group. Regarding the location of pain, 59.5% of patients ($n=22$) reported severe pain in the 12:00 position of the vagina, which is around the urethral orifice, and 45.9% ($n=17$) reported pain in the 10:00 to 2:00 positions.

## Discussion

The present study demonstrates that IC/BPS patients have significantly lower vulvovaginal health and poorer sexual activity than women without IC/BPS.

**Table 1** Group characteristics

| Characteristic | | IC/BPS group | Control | Odds ratio | Confidence interval |
|---|---|---|---|---|---|
| Total number | | 37 | 37 | | |
| Average age (years) | | 40.78±4.36 | 40.73±3.7 | | |
| Marital status | Married | 31 (83.7%) | 30 (81.1%) | Ref | |
| | Unmarried | 6 (16.2%) | 7 (18.9%) | 1.210 | 0.36–4.00 |
| Cigarette smoking | Current non-smoker | 34 (91.9%) | 34 (91.9%) | Ref | |
| | Current smoker | 3 (8.1%) | 3 (8.1%) | 1.00 | 0.19–5.31 |
| Alcohol consumption | Never drinker | 4(10.8%) | 4(10.8%) | Ref | |
| | 1–4 times a month | 30 (81.1%) | 29 (78.4%) | 1.61 | 0.53–4.90 |
| | ≥4 times a week | 3 (8.1%) | 4 (10.8%) | 0.935 | 0.56–1.55 |
| History of taking antibiotics for bacterial cystitis in the past month | No | 35 (94.6%) | 36 (97.3%) | Ref | |
| | Yes | 2 (5.4%) | 1 (2.7%) | 2.060 | 0.18–23.7 |
| History of taking antibiotics and antifungal drugs for vaginitis in the past month | No | 37 (100%) | 37 (100%) | Ref | |
| | Yes | 0 (0%) | 0 (0%) | – | – |
| History of taking antipsychotics for mental illness in the past month | No | 37 (100%) | 37 (100%) | Ref | |
| | Yes | 0 (0%) | 0 (0%) | – | – |
| History of bladder cancer | No | 37 (100%) | 37 (100%) | Ref | |
| | Yes | 0 (0%) | 0 (0%) | – | – |
| History of ureteral stones and bladder stones | No | 37 (100%) | 36 (97.3%) | Ref | |
| | Yes | 0 | 1 (2.7%) | 1.03 | 0.65–1.63 |
| Menopause | No | 36 (97.3%) | 36 (97.3%) | Ref | |
| | Yes | 1 (2.7%) | 1 (2.7%) | 1.00 | 0.060–16.6 |
| History of endometriosis | No | 34 (91.9%) | 35 (94.6%) | Ref | |
| | Yes | 3 (8.2%) | 2 (5.4%) | 1.540 | 0.24–9.82 |
| History of cervical cancer | No | 37 (100%) | 37 (100%) | Ref | |
| | Yes | 0 (0%) | 0 (0%) | – | – |
| Previous pregnancies | No | 23 (62.1%) | 22 (59.5%) | Ref | |
| | Yes | 14 (37.9%) | 15 (40.5%) | 0.893 | 0.35–2.27 |
| Vaginal delivery | No | 26 (70.2%) | 24 (64.9%) | Ref | |
| | Yes | 11 (29.8%) | 13 (35.1%) | 0.781 | 0.29–2.07 |
| Caesarean section | No | 34 (91.9%) | 35 (94.6%) | Ref | |
| | Yes | 3 (8.2%) | 2 (5.4%) | 1.540 | 0.24–9.82 |

*IC/BPS* interstitial cystitis/bladder pain syndrome

After we used PUF for comparing baseline IC/BPS symptoms to validate the patient population, the FSFI, vulvodynia swab tests and VHIS were used to determine differences between the IC/BPS and control groups. All examinations showed that the IC/BPS group was significantly different from the control group.

The aetiology of IC/BPS is largely unknown, but it is predicted that urothelial damage, mast cell activation, inflammation and autoimmunity may play a role. Urinary symptoms are quite likely to be debilitating. Moreover, complications of FSD adversely affect quality of life. Our study revealed that the condition of the vagina and vulva are essential aspects to consider in IC/BPS patients.

The higher validated PUF scores in the IC/BPS group (18.19) compared with those in the control group (3.76) demonstrate that patients in the IC/BPS group were accurately diagnosed with IC/BPS and the controls did not have IC/BPS. Kahn et al. reported that the possibility of patients with a PUF score >15 being diagnosed with IC/BPS was over 87% [26]. Our PUF results are similar to those of prior studies of patients with IC/BPS [7, 8].

Our study identified FSD in 91.9% ($n$=34) of IC/BPS patients and in only 40.5% ($n$=15) of control individuals. This is similar to the results by Agrawal et al. who found FSD in 90.62% ($n$=29) of IC/BPS patients and in only 31.25% of control individuals [8].

The FSD of the control group in our study was anticipated to be higher than that in past studies [5, 8]. As only a few studies have focused on this problem in Asia [27], this prevalence is difficult to assess.

Pain is the most common symptom of IC/BPS and the most common cause of avoidance of sexual activity in

**Table 2** Pain Urgency Frequency (*PUF*) score, Female Sexual Function Index (*FSFI*) and Vaginal Health Index Score (*VHIS*)

| Questionnaire | Domain | Score range | IC/BPS group (mean±SD) | Control (mean±SD) | *p* value |
|---|---|---|---|---|---|
| PUF | Total | 0–38 | 18.19±3.52 | 3.76±2.35 | <0.0001 |
| FSFI | Desire | 1.2–6.0 | 2.64±0.77 | 3.79±0.53 | <0.0001 |
| | Arousal | 0.0–6.0 | 2.50±0.70 | 3.965±0.60 | <0.0001 |
| | Lubrication | 0.0–6.0 | 2.70±0.87 | 4.69±1.02 | <0.0001 |
| | Orgasm | 0.0–6.0 | 2.46±0.85 | 4.24±0.87 | <0.0001 |
| | Satisfaction | 0.8–6.0 | 2.76±0.99 | 4.70±1.00 | <0.0001 |
| | Pain | 0.0–6.0 | 2.92±1.00 | 4.96±1.41 | <0.0001 |
| | Total | 2.0–36.0 | 15.98±4.62 | 26.35±4.95 | <0.0001 |
| VHIS | Overall elasticity | 0–5 | 2.34±0.71 | 4.54±0.63 | <0.0001 |
| | Fluid secretion | 0–5 | 2.59±0.83 | 4.41±0.81 | <0.0001 |
| | Ph | 0–5 | 2.57±0.79 | 4.35±0.89 | <0.0001 |
| | Epithelial mucosa | 0–5 | 2.47±0.77 | 4.38±0.86 | <0.0001 |
| | Moisture | 0–5 | 2.11±0.60 | 4.38±0.86 | <0.0001 |
| | Total | 0–25 | 12.03±3.36 | 22.05±3.90 | <0.0001 |

*IC/BPS* interstitial cystitis/bladder pain syndrome

*$p < 0.0001$ for each domain and for total score, between the IC/BPS group and the control group

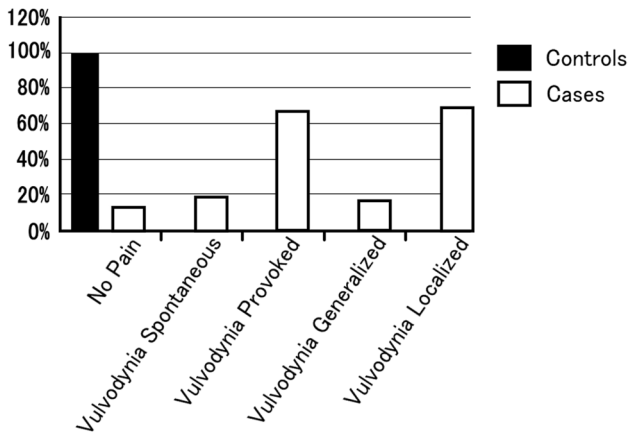


**Fig. 1** Vulvodynia rating in interstitial cystitis cases and controls. $p < 0.0001$ for each diagnosis

women [8, 12]. In our study, pain was experienced during sexual activity by 70.3% of the IC/BPS group and only 37.87% of the control group. Similarly, in previous studies, Agrawal et al. [8] reported values of 65.25% and 31.25% respectively; and Peters et al. [28] reported values of 67.2% and 39.8% respectively. These results are in agreement with those in the present study.

In our study, the mean FSFI score of the IC/BPS group was worse in all domains, including desire, arousal, lubrication, orgasm, satisfaction and pain, as well as the total score. Similar results have been reported by Ottem et al. [25]; their study of 75 patients with IC/BPS showed that sexual function in women was significantly low across all six domains. Ottem et al. reported that the total FSFI scores differed between patients with IC and controls (20.2±9.6 and 29.0±6.8 respectively, $p < 0.001$). Additionally, research by Agrawal et al. [8] and Gardella et al. [5] reported similar results.

In our study, the mean VHIS of the IC/BPS group was affected across all five domains. The values were greatly decreased relative to those in the control group. Gardella et al. [5] conducted a cross-sectional study of 47 patients with a control group and showed that the total mean VHIS score of the IC/BPS group was 12.55±2.78. The total VHIS score in our study was 12.03±3.36, and it was confirmed that the value decreased to a similar level. All subscale values were similarly affected.

Vulvodynia was confirmed using vulvodynia swab tests, and was found only in the IC/BPS group. The incidence of spontaneous or induced vulvodynia was similar to that found by Gardella et al. [5]. Gardella et al.'s study shows that overall, spontaneous or provoked vulvodynia was reported by 23.4% (11 out of 47) or 74.5% (35 out of 47) of IC cases respectively, and in none of the controls ($p<0.001$). Gardella et al. reported that vulvodynia was localised in 38 (80.9%) and generalised in 8 (17%) cases [5].

The present study suggested that sexual dysfunction, worsened vaginal health and vulvodynia in IC/BPS may be correlated. Previously, Gardella et al. [12] hypothesised that a sex hormone-dependent mechanism that regulates vulvar and vaginal health might be involved in IC/BPS based on the worsened PUF, FSFI, VHIS and vulvodynia swab tests in the IC/BPS group. They reported that 12 weeks of local oestrogen therapy (LET) improved vaginal health and urinary/bladder pain symptoms in women with IC/BPS.

Similarly, Nickel et al. reported that a positive correlation was observed between the mean change scores of sexual functioning and physical and mental quality-of-life components. In their study, IC/PBS patients were treated with 300 mg/day pentosan polysulfate sodium for 32 weeks [29].

Our previous research [30] also showed that urinary/bladder pain symptoms improved after performing vaginal erbium:YAG laser (VEL) treatment [31], which has been reported to improve urinary incontinence and vaginal health in patients with IC/BPS when administered monthly for 1 year. However, the vaginal health status was not investigated; therefore, the basis for improvement by VEL was unknown.

Our study has certain limitations. The first is that it was a single-centre study. Additionally, we only investigated patients who had been sexually active within the preceding 4 weeks. As a result, we were not able to rule out the possibility of underreporting the degree of sexual dysfunction.

In the present study, one of the two doctors was aware of whether a patient had IC/BPS or was enrolled as a control. Thus, the validity of this metric could be compromised as patients known to have IC/BPS might have inadvertently received lower scores.

Furthermore, the causes of worsened vaginal health are multifactorial, and this study only investigated the effects of IC/BPS; thus, the causal relationship between IC/BPS and worsened vaginal health has not been established. Therefore, bladder pain may also be related to the vaginal environment. However, further research is needed to clarify this.

Based on research on animal models, it is suggested that there is an interaction between the vagina–vulva and the bladder. Sex hormones are key players in that interrelationship. Stimulation of both the lower abdominal and pelvic nerves of female rats elicits a neural response that causes oestrous cycle fluctuations [32]. Furthermore, the neuromodulatory role of oestrogen in the transmission of pain in multiple sites is highly recognised [33]. A significant decrease in oestrogen receptor beta (ERb) in the bladder of rats with chemically induced cystitis has already been reported [34]. In an ERb knockout female mice model, development of a bladder phenotype resembling human interstitial cystitis occurred [35]. In these ERb knockout female mice, oestrogen deficiency leads to bladder-wall stiffness by reducing some components of the extracellular matrix of the urothelial surface [36].

The results of these animal studies also suggest that sex hormone-dependent mechanisms may be involved in the association between vulvar–vaginal status and bladder pain, even in premenopausal women [12]. Evidence from PUF, VHIS and vulvodynia swab tests may be an effective tool in seeing the therapeutic effect of pain syndromes.

Based on our research, future areas of investigation should include the use of VEL [30] in patients with IC/BPS while recording the results of the VHIS and vulvodynia swab tests. Prior studies for patients with overactive bladder have shown improvement in urgency, frequency and VHIS [37], and a combination of VEL and neodymium laser in the vulva and vagina improves superficial dyspareunia [38].

In conclusion, among sexually active women between the ages of 30 and 50 years, patients with IC/BPS had significantly worsened PUF, FSFI, VHIS, and vulvodynia swab tests, compared with patients in the control group. IC/BPS is thought to be a combination of FSD, worsened vaginal health and vulvodynia. This is the first report of its kind that considers IC/BPS in Asian women.

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## Declarations

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