

Overactive bladder with urodynamic study-induced bladder pain

An overactive bladder subtype with symptoms similar to those of interstitial cystitis/painful bladder syndrome

Hsueh-Yu Mu, MD^a, Ming-Ping Wu, MD, PhD^b, I-Te Wang, MD^a, Jeng-Cheng Wu, MD^c, Hung-Yen Chin, MD^{a,*} 

Abstract

Overactive bladder (OAB) and interstitial cystitis/painful bladder syndrome (IC/PBS) are 2 lower urinary tract disorders with urgency and bladder pain for diagnosis and with several other shared symptoms. Because of their overlapping symptoms, precise differential diagnosis of OAB and IC/PBS remains difficult. Thus, we characterize a subgroup of OAB with bladder pain (OAB-BP) that can be differentiated from OAB alone by urodynamic study (UDS) findings. We also further examined the clinical presentations and urodynamic parameters of OAB alone, OAB-BP, and IC/PBS. Data were collected between September 2018 and April 2019. Patients were categorized into 3 groups, OAB-alone (no bladder pain during UDS, $n = 39$), OAB-BP (with bladder pain during UDS, $n = 35$), and IC/PBS (the comparator, $n = 39$). Chi-square tests were used to compare OAB alone, OAB-BP, and IC/PBS with respect to their clinical presentations and urodynamic parameters. Factors with $P < .05$ were further analyzed through post hoc comparisons with Bonferroni adjustment. A unique subgroup of OAB patients was identified (i.e., OAB-BP), bladder pain can only be induced at maximal cystometric capacity during UDS. We also identified that the case histories and UDS parameters (e.g., low first desire, normal desire, and maximum cystometric capacity) of the OAB-BP group were more similar to those of the IC/PBS group than to those of the OAB-alone group. The OAB-BP group and the IC/PBS group reported more intrusive, longer-lasting symptoms before their final diagnoses, more extensive family history of urinary tract disorder, and more associated comorbidities (e.g., irritable bowel syndrome, and myofascial pain) than the OAB-alone group. The UDS assessment induced bladder pain in the OAB-BP group to reveal their hidden symptoms. Careful attention to patient history and sophisticated UDS evaluation may help to identify this unique OAB group.

Abbreviations: FD = first desire, IBS = irritable bowel syndrome, IC/PBS = interstitial cystitis/painful bladder syndrome, MCC = maximum cystometric capacity, OAB = overactive bladder, OAB-BP = overactive bladder with urodynamic study induced bladder pain, UDS = urodynamic study.

Keywords: cystoscopy, interstitial cystitis/ bladder pain syndrome (IC/PBS), overactive bladder syndrome (OAB), overactive bladder syndrome with bladder pain (OAB-BP), urgency, urodynamic study (UDS)

1. Introduction

Overactive bladder syndrome (OAB) and interstitial cystitis/painful bladder syndrome (IC/PBS) have similar symptoms, including urinary urgency, frequency, and nocturia; therefore, differentiating between the 2 on the basis of clinical presentation alone is challenging.^[1] The International Continence Society defined OAB as “urgency, with or without

urge incontinence, usually with urinary frequency, and nocturia.”^[2] IC/PBS is defined as a chronic and debilitating disorder of unknown etiology that is characterized by chronic pelvic pain with the symptoms of urinary frequency, urgency, or nocturia.^[3]

In clinical practice, different conditions may share similar symptoms or a single disorder may present with multiple symptoms. Driscoll et al^[4] and Parsons et al^[5] have reported

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All data generated or analyzed during this study are included in this published article [and its supplementary information files]; The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^a Department of Obstetrics and Gynecology, Taipei Medical University Hospital, and School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, ^b Division of Urogynecology, Department of Obstetrics and Gynecology, Chi Mei Medical Center, Tainan and College of Medicine, Fu-Jen Catholic University, Taipei, Taiwan, ^c Department of Urology, Taipei Medical University Hospital and School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan.

* Correspondence: Hung-Yen Chin, Department of Obstetrics and Gynecology, Taipei Medical University Hospital and School of Medicine, College of Medicine, Taipei Medical University, No.252, Wuxing Street, Taipei City 110, Taiwan, Republic of China (e-mail: chin671009@gmail.com).

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that IC/PBS causes variable symptoms in its early stage, consequently, and diagnosis is frequently delayed until the more obvious symptoms appear. Our previous study indicated that some patients with IC/BPS had an average onset time of 6 years before their diagnosis was verified.^[6] An extended duration between the onset of urinary symptoms and the final diagnosis of IC/BPS was also reported by Driscoll et al.^[4] Because the symptoms of IC/PBS overlap with those of OAB, sophisticated differential diagnosis of both conditions is crucial for further proper management.

Although the value of a urodynamic study (UDS) for diagnosing IC/PBS remains unclear, UDS parameters provide some useful information about IC/PBS.^[1,7,8] For example, the values for first sensation, normal desire, strong desire, and maximum cytometric capacity (MCC) during filling cytometry were significantly lower in patients with IC/PBS than in those with OAB, including those with severe OAB.^[7] Moreover, UDS can induce bladder pain in patients with a relatively low MCC.^[1] Accordingly, we hypothesized that some patients with OAB may have hidden bladder pain, which could be unveiled during UDS. Furthermore, the clinical histories and UDS parameters of OAB with hidden bladder pain (OAB-BP) may track more closely with IC/PBS than with OAB alone.

This study aimed to identify a distinct subgroup of OAB, with hidden bladder pain discernable only through the UDS procedure. We subsequently examined the clinical presentations and urodynamic parameters among patients with OAB-alone, OAB-BP, or IC/PBS.

2. Methods

This study's protocol was approved by the Taipei Medical University-Joint Institutional Review Board and the Ethics Committee at Taipei Medical University Hospital in Taiwan (No: N201908059). Data were collected between August 2019 and August 2020. A total of 113 female patients met the inclusion criteria for this study. All procedures were carried out in accordance with the relevant guidelines and regulations.

2.1. Inclusion and exclusion criteria

Women aged > 20 years were eligible for inclusion if they had OAB symptoms – specifically, urgency to urinate lasting > 6 months, with or without associated urinary frequency, nocturia, or urge incontinence.^[2] All the participants had previously been treated with antimuscarinic agents at other hospitals but had failed to respond. For the comparator group, we recruited women with IC/PBS who had chronic (>6 months) suprapubic pain accompanied by at least 1 other urinary symptom like persistent urge to void or frequency.^[3,9] Cystoscopy was arranged for these patients, glomerulation was noted in all patients and classified as 2X type of ESSIC classification. We instructed all patients to complete a 3-day urinary diary for us to identify those who voided more than 8 times per day (frequency), those who woke up 2 or more times to void during the night (nocturia), and those who had no fluid overload throughout the day. All patients expressed concern about these lower urinary tract symptoms, which affected their quality of life.

Subsequently, all patients underwent UDS. We performed a multichannel UDS assessment comprising free uroflowmetry, urethral pressure profilometry, and filling cytometry. Briefly, the UDS was performed with the patient in the supine position by using water media and a UDS machine (UD-2000; Medical Measurement Systems, Enschede, the Netherlands). A triple-lumen urethral catheter (8 Fr) was inserted into the urethra and then pulled at a speed of 2 mm/s. For uroflowmetry, each patient was seated on a micturition chair for the assessment. A typical uroflow pattern was defined as 1 with a smooth single curve with a maximum flow rate of > 15 mL/s

and a voided volume of > 250 mL. Abnormal void patterns were defined as those with an abnormal low flow rate and with curves that were not smooth and that had multiple interrupted peaks, as defined in our previous article.^[10] Patients with OAB who experienced no bladder pain during the UDS procedure were enrolled in the OAB-alone group, whereas those who experienced bladder pain were enrolled in the OAB-BP group.

We excluded patients with ketamine addiction or exposure to ketamine; those who refused to receive a UDS; and those with pathological conditions such as urinary tract infection, urogenital tract malignancy, pelvic mass or malignancy, urethral diverticulum, a history of urinary tract stone, or intravesical lesion. No participant exhibited a significant increase in uterine size or pelvic mass during the sonographic examination.

2.2. Statistical analysis

SAS software (version 9.4, SAS Institute, Cary, NC) was used for data management and statistical analysis. Continuous variables are presented as means and standard deviations; categorical variables are presented as counts and percentages. An analysis of variance and chi-square test were used to compare the IC/PBS, OAB-BP, and OAB-alone groups. Factors with $P < .05$ were further analyzed through post hoc comparisons with Bonferroni adjustments. The significance level was set at $P < .05$.

3. Results

A total of 113 patients were included in the final analysis: 39, 35, and 39 patients in the IC/PBS, OAB-BP, and OAB-alone groups, respectively. Figure 1 presents a flowchart of the patient recruitment process.

3.1. Demographic comparison among OAB-alone, OAB-BP, and IC/PBS

The personal information and medical history data collected in this study (Table 1), revealed that the patients experienced symptoms of lower urinary tract for approximately 2 to 7 years before receiving a final diagnosis. The mean duration of onset differed significantly among the 3 groups ($P < .01$; Table 1). The mean durations of onset in the OAB-BP and IC/PBS groups (7.23 and 5.27 years, respectively) were significantly higher than that in the OAB-alone group (2.17 years, Bonferroni adjusted $P < .001$, $P = .028$). The durations between onset and diagnosis in the OAB-BP and IC/PBS groups were similar (Bonferroni adjusted $P = .32$) and significantly longer than that in the OAB-alone group, respectively.

3.2. Clinical symptom comparison among the IC/PBS, OAB-BP, and OAB-alone groups

Urinary frequency differed significantly among the 3 groups (Table 1; mean frequencies in the daytime: 13.38, 11.63, and 8.38, $P < .001$). The mean urinary frequency in the OAB-BP group was similar to that in the IC/PBS group (mean frequencies in the daytime: 11.63 ± 4.89 , 13.38 ± 5.56 , and Bonferroni adjusted $P = .34$), and both were significantly higher than that in the OAB-alone group (OAB-BP vs OAB-alone and IC/PBS vs OAB-alone: Bonferroni adjusted $P = .012$ and $P < .001$, respectively).

Table 1 reveals that the proportions of IC/PBS-related comorbidities, comprising pelvic floor muscle pain, irritable bowel syndrome (IBS), and myofascial pain syndrome, differed significantly among the 3 groups ($P = .027$, $P < .001$, and $P < .001$).

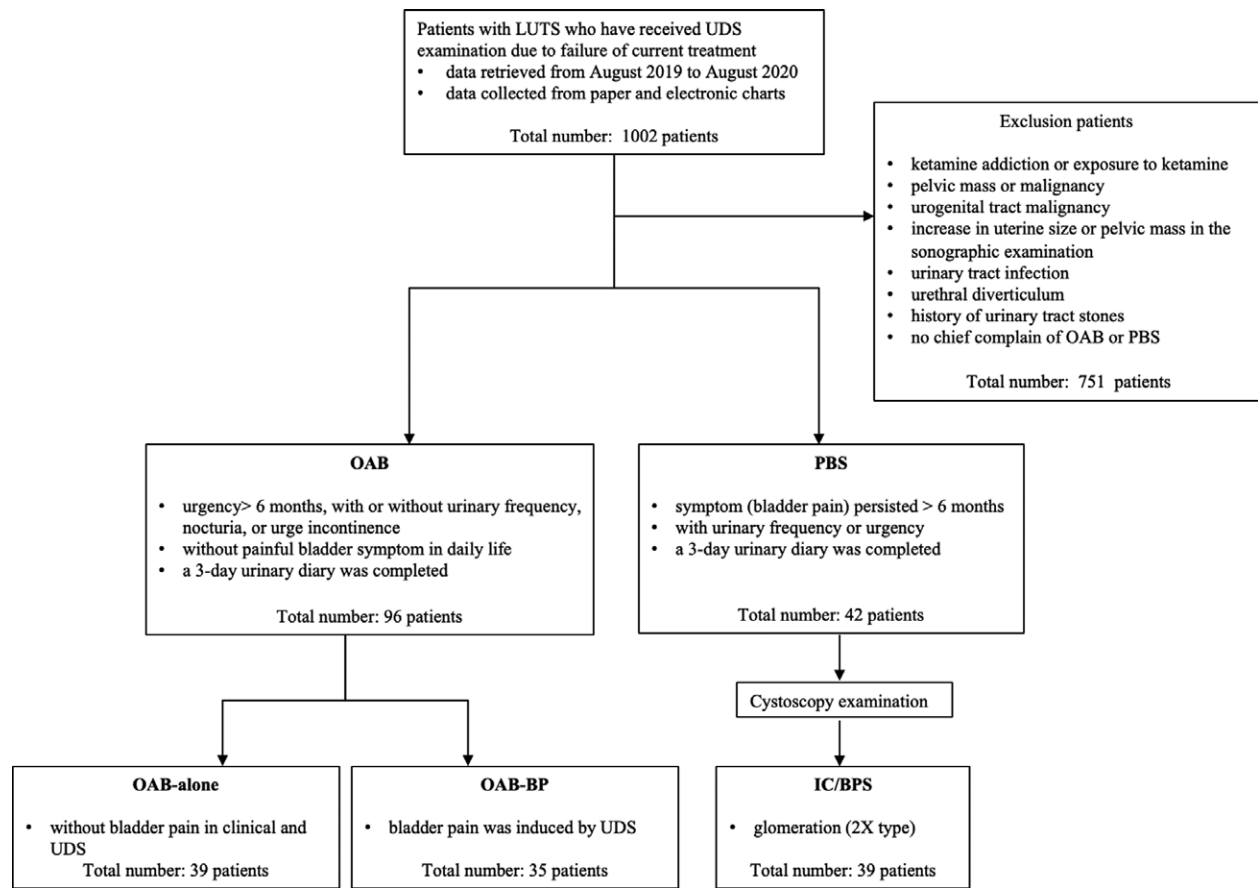


Figure 1. Flowchart of patient inclusion and exclusion.

Table 1
Demographic and clinical symptom for the interstitial cystitis/painful bladder syndrome, overactive bladder with urodynamic-study-induced bladder pain, and overactive bladder alone groups.

	OAB-BP (n = 35)	IC/PBS (n = 39)	OAB alone (n = 39)	P value	OAB-BP vs IC/PBS	OAB-BP vs OAB-alone	IC/PBS vs OAB-alone
Age (mean ± SD)	47.06 ± 15.39	43.62 ± 13.78	46.90 ± 12.47	.48b			
Duration of onset (yr) (mean ± SD)	7.23 ± 7.95	5.27 ± 4.47	2.17 ± 1.08	<.001b	0.32c	<0.001c	0.028c
Urinary frequency (mean ± SD)	11.63 ± 4.89	13.38 ± 5.56	8.38 ± 3.60	<.001b	0.34c	0.012c	<0.001c
Nocturia of urine (mean ± SD)	2.57 ± 1.46	2.85 ± 2.89	1.90 ± 1.45	.12b			
Urgency (n, %)	26 (74.29%)	39 (100.00%)	39 (100.00%)	.86a			
Family history of PBS (n, %)	4 (11.43%)	12 (30.77%)	1 (2.56%)	.002a	0.13c	0.55c	0.002c
Pelvic floor pain (n, %)	16 (45.71%)	20 (51.28%)	9 (23.08%)	.027a	1.00c	0.12c	0.030c
Irritable bowel syndrome (n, %)	16 (45.71%)	24 (61.54%)	4 (10.26%)	<.001a	0.52c	0.002c	<0.001c
Myofascial pain history (n, %)	21 (60.00%)	27 (69.23%)	4 (10.26%)	<.001a	1.00c	<0.001c	<0.001c

^a Chi-square test;

^b analysis of variance;

^c P values of post hoc comparisons with Bonferroni adjustment.

IC/PBS = interstitial cystitis/painful bladder syndrome, OAB = overactive bladder, OAB-BP = overactive bladder with urodynamic-study-induced bladder pain, SD = standard deviation.

Pairwise comparisons with Bonferroni adjustment for the proportions of pelvic floor muscle pain, IBS, and myofascial pain among the 3 groups revealed no significant differences between the IC/PBS and OAB-BP groups (Bonferroni adjusted $P = 1$, $P = .52$, and $P = 1$ for pelvic floor muscle pain, IBS, and myofascial pain, respectively). However, the proportions of comorbidities in the IC/PBS and OAB-BP groups were significantly higher than those in the OAB-alone group (all Bonferroni adjusted $P < .05$). Thus, the OAB-BP group had a similar proportion of comorbidities as the IC/PBS group.

3.3. Urodynamic study parameter comparison among OAB-alone, OAB-BP, and IC/PBS

As indicated in Table 2, the UDS parameters of first desire (FD), ND, and MCC differed significantly between the 3 groups ($P = .009$, $P = .002$, and $P < .001$, respectively). A pairwise comparisons with Bonferroni adjustment for FD, ND, and MCC among the 3 groups revealed no significant differences between the IC/PBS and OAB-BP groups (Bonferroni adjusted $P = .66$, $P = 1$, $P = 1$ for FD, ND, and MCC, respectively). However,

Table 2**Urodynamic study parameters for interstitial cystitis/painful bladder syndrome, overactive bladder with urodynamic-study-induced bladder pain, and overactive bladder alone groups.**

	OAB-BP (n = 35)	IC/PBS (n = 39)	OAB alone (n = 39)	P value	OAB-BP vs IC/BPS	OAB-BP vs OAB alone	IC/PBS vs OAB alone
Qmax (mL/s) (Mean ± SD)	19.26 ± 9.03	18.62 ± 7.27	18.28 ± 6.67	.86b			
Qave (mL/s) (Mean ± SD)	9.49 ± 4.43	9.38 ± 3.81	9.76 ± 4.12	.92b			
MUCP (cm H ₂ O) (Mean ± SD)	90.31 ± 31.33	97.15 ± 29.64	90.38 ± 34.76	.56b			
FD (mL/s) (Mean ± SD)	106.51 ± 46.88	123.72 ± 51.62	149.90 ± 75.63	.009b	0.66c	0.007c	0.17c
ND (mL/s) (Mean ± SD)	177.20 ± 63.01	177.64 ± 67.03	233.95 ± 101.39	.002b	1.00c	0.008c	0.007c
MCC (mL/s) (Mean ± SD)	301.37 ± 79.96	305.08 ± 87.55	393.87 ± 119.02	<.001b	1.00c	<.001c	<.001c
Detrusor overactivity (n, %)	22 (62.86%)	23 (58.97%)	25 (64.10%)	.89a			
Abnormal void pattern (n, %)	18 (51.43%)	23 (58.97%)	20 (51.28%)	.74a			

^a chi-square test;^b analysis of variance;^c P values of post hoc comparisons with Bonferroni adjustment.

FD = first desire, IC/PBS = interstitial cystitis/painful bladder syndrome, MCC = maximum cystometric capacity, MUCP = maximum of urethral closure pressure, ND = normal desire, OAB = overactive bladder, OAB-BP = overactive bladder with urodynamic-study-induced bladder pain, Qave = average flow rate, Qmax = maximum flow rate, SD = standard deviation.

the parameters differed significantly between the OAB-BP and OAB-alone groups (Bonferroni adjusted $P = .007$, $P = .008$, and $P < .001$ for FD, ND, and MCC, respectively). Furthermore, the parameters differed significantly between the IC/PBS and OAB-alone groups (Bonferroni adjusted $P = .007$ vs $P < .001$). These results indicate that the presentations of bladder capacity were similar between the IC/PBS and OAB-BP groups.

4. Discussion

In this study, we identified a new subtype of OAB, namely OAB-BP, which is characterized by hidden bladder pain that can be unveiled through a UDS assessment. In the previous study, bladder pain can be self-assessed on the basis of daily experience for the purpose of diagnosing IC/PBS.^[3] However, the patient with OAB-BP experienced bladder pain only upon reaching MCC during the UDS examination in our study. OAB patients usually modify their toilet habits to void more frequently for preventing urine leakage or higher bladder volume. Consequently, these patients did not attain a full bladder in daily lives and evoking painful sensation. In addition, the OAB-BP group and IC/PBS group shared more similar clinical symptoms and UDS parameters which were distinct from OAB-alone group.

The indication of bladder pain in the UDS assessment elucidates the temporal relationship between urgency and bladder pain. Because urgency precedes bladder pain in OAB-BP, patients can urinate before reaching a full bladder, thereby avoiding the onset of bladder pain. Hanno et al^[11] reported that some patients with IC/PBS also felt the urgency and urinate early to avoid the pain, pressure, or discomfort associated with a full bladder. Assuming that IC/BPS begins with the mild symptoms of urinary frequency/urgency and progresses to bladder pain, many individuals with undiagnosed IC/BPS may modify their toilet habits in lack of pain experience and the IC/BPS thus remains undetected.^[5]

Our medical records revealed that the patients categorized as OAB-BP used early voiding as a coping strategy to avoid urinary urgency and nonspecific pelvic discomfort associated with full bladder. Therefore, the above coping strategy successfully limited the feeling of bladder pain in daily lives of the patients included in our study and the bladder pain remained unnoticed until induction of MCC during UDS. Whether these patients with OAB-BP will be diagnosed with IC/BPS for the rest of life remains inconclusive and warrants follow-up closely.

The OAB-BP and IC/PBS groups shared similar clinical histories, which differed from those of the OAB-alone group. Specifically, patients in the IC/PBS and OAB-BP groups reported more invasive symptoms than patients in the OAB alone group; had a longer delay (5 to 7 years) before receiving a diagnosis; had a broader family history of urinary tract disorders; and had

more associated comorbidities, such as IBS and myofascial pain (Table 1).

MacDiarmid et al^[1] also reported overlapping lower urinary tract symptoms such as urgency, frequency, and nocturia between OAB patients and IC/PBS patients. According to some reports,^[1,12–14] urinary urgency is also a key clinical symptom among some patients with IC/PBS. In our study, we observed that 74% of the patients with IC/PBS presented with urgency. Because urgency is the core symptom of OAB, these patients with IC/PBS might have been misdiagnosed. According to previous studies, it has been suggested that the cause of urgency was different between OAB (due to fear of urine leakage) and IC/PBS (avoidance of bladder pain when the bladder is full). Consequently, a detailed history taking is necessary for more accurate diagnosis.

UDS parameters in the OAB-BP group were similar to IC/BPS, such as smaller first desire, normal desire and maximal cytometric capacity, but not in the OAB-alone group. MacDiarmid et al^[1] reported painful sensory urgency was commonly observed in IC/PBS during UDS. In addition to the above findings, our study is the first to report that bladder pain in women with OAB can be revealed by cytometric capacity measurements during UDS rather than by daily experience.

Bladder pain can either manifest in typical means in patients with IC/PBS, or it can be induced by a UDS in patients with hidden OAB-BP women. Some women with IC/PBS might not experience bladder pain during their daily lives due to their coping strategies. Ito et al^[13] demonstrated that only 46% of women with IC/PBS presented classic bladder pain that was worsened with bladder filling and was ameliorated after bladder emptying. Likewise, Parsons et al^[5] observed only 43% of 100 women presenting with classic bladder pain in their study. Conversely, Macdiarmid et al^[1] pointed out that in addition to inducing elevated resting urethral closure pressures and a dyssynergic voiding pattern in women with IC/PBS, UDS can also induce a painful sensory urgency of pain. Our study demonstrated that the OAB-BP and IC/PBS groups shared similar UDS parameters, including lower ND and MCC, compared with the OAB-alone group (Table 2). Since the clinical and UDS findings were similar between the OAB-BP and IC/PBS groups, we hypothesized that OAB-BP was an earlier form of IC/PBS, or overlapping with the progression IC/PBS. Although differentiating IC/PBS from OAB based on clinical symptoms remains a difficult task, UDS may offer some clues for better diagnosis.

Some limitations of this study were worth to notice. Firstly, this was a retrospective study with a relatively small number of patients. Secondly, although all the patients completed a 3-day urinary diary once, keeping a urinary diary twice may be appropriate to reduce record error.

In summary, we identified a subtype of OAB that shares more features with IC/PBS than with OAB per se and may not respond to conventional OAB therapy.^[1] The OAB-BP and IC/PBS groups exhibited a high degree of similarity in their clinical and urodynamic findings. Urgency and a family history of PBS were the key characteristics collected from the case histories, and the UDS assessment revealed the additional characteristic of hidden bladder pain in patients with OAB-BP. Larger studies with more participants are warranted to verify these results before definitive conclusions can be made concerning treatment strategies.

Author contributions

Conceptualization: Hung-Yen Chin.

Formal analysis: Hsueh-Yu Mu.

Data curation: Ming-Ping Wu.

Resources: I-Te Wang.

Investigation: Jeng-Cheng Wu.

Project administration: Hung-Yen Chin.

Writing – original draft: Hsueh-Yu Mu.

Writing – review & editing: Ming-Ping Wu, Hung-Yen Chin.

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