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The impact of recreational maras powder use on bladder function: a ketamine-bladder-like syndrome

Sami Berk Ozden[1*], Burak Yılmaz[1], Göktuğ Kalender[2] and Meral Filiz Taştekin[1]

Abstract

Background Chronic recreational use of maras powder (minced *Nicotiana rustica* leaves), endemic in Southeastern Turkey and characterized by very high nicotine and alkaloid content, may induce bladder dysfunction analogous to ketamine-induced cystitis. This study investigates the urological impact of chronic maras powder use.

Methods We retrospectively analyzed 400 patients with lower urinary tract symptoms (LUTS) at Osmaniye State Hospital (2024–2025). The case group included 20 chronic Maras Powder users, while 30 age-matched controls had no exposure. Evaluations included urodynamics, cystoscopy, and histopathologic examination. Maras powder exposure was quantified as pack-years (daily frequency × duration).

Results Maras powder users demonstrated significant urodynamic impairments compared to controls: reduced cystoscopic bladder capacity (median 200 mL vs. controls, $p < 0.001$), lower voided volume (79.3 mL vs. controls, $p < 0.001$) on the initial uroflowmetry test, diminished maximum flow rate (Qmax: 5.5 mL/s, $p = 0.007$), and decreased detrusor compliance (11 mL/cmH_2O, $p = 0.007$). Dose-dependent correlations linked higher pack-years to reduced bladder capacity (Pearson's $r = -0.45$, $p < 0.05$). Urge incontinence ($p < 0.05$) and nocturia ($p < 0.05$) were more prevalent in users. Histopathology revealed eosinophilic cystitis, lymphocytic inflammation, lamina propria edema, and vascular dilation.

Conclusions Chronic maras powder use is associated with a ketamine-like bladder syndrome, characterized by contracture, inflammation, and impaired flow. Public health measures and clinician awareness are critical to address this emerging etiology of LUTS.

Keywords Maras powder, *Nicotiana rustica*, Bladder dysfunction, Ketamine-like cystitis, Urodynamics, Tobacco-related uropathy

1 Background

Recreational drug use has been associated with bladder dysfunction, with ketamine-induced cystitis being a well-documented phenomenon [1]. Chronic ketamine abuse leads to bladder contracture, ulceration, and severe lower urinary tract symptoms (LUTS), including urgency, frequency, and stress incontinence [1, 2]. In this study, we present our findings on a group of patients using maras powder plant leaves for recreational purposes.

Maras powder, a tobacco species with exceptionally high nicotine content (9–10 times more nicotine than *Nicotiana tabacum* (common tobacco)), is traditionally consumed in recreational contexts through buccal dipping or chewing (locally known as enfiye or 'maras powder') in the far eastern regions of Turkey (Figs. 1 and 2). The product use is endemic in Kahramanmaras, Osmaniye, Gaziantep, and Adıyaman provinces and can

*Correspondence:
Sami Berk Ozden
s.berkozden@gmail.com
[1] Osmaniye State Hospital, Osmaniye, Turkey
[2] Istanbul Beykoz State Hospital, Istanbul, Turkey

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Fig. 1 Commercial packaging of a typical maras powder sachet (left-hand side), the actual powder released from the sachet (right-hand side)



Fig. 2 Used maras powder package found in the vicinity of Osmaniye State Hospital

be purchased in nylon packages or plastic bags from local groceries [3]. The plant leaves also harbor significantly higher concentrations of alkaloids and their metabolites, which are excreted renally, potentially exposing the bladder mucosa to prolonged irritation. Tobacco-specific nitrosamines like NNN (*N*-nitrosonornicotine) and NNK (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone) can be implicated in urothelial inflammation and rarely carcinogenesis [4, 5]. However, it has not been extensively studied for its urological detrimental effects. Chronic use has been associated with bladder cancer, yet there is no study regarding the functional effects of the substance on the bladder [6]. This study presents comprehensive clinical, cystoscopic, urodynamic, and histopathological findings in patients with lower urinary tract symptoms (LUTS) associated with chronic maras powder use.

2 Methods

2.1 Study design and patients

After ethical approval was obtained from the Osmaniye Korkut Ata University Ethical Committee, we retrospectively analyzed 400 consecutive male patients with lower urinary tract symptoms (LUTS) referred to the urology clinic at Osmaniye State Hospital, Turkey, between January 2024 and January 2025. Of these, 120 patients underwent urodynamic evaluation due to refractory symptoms or suspected bladder dysfunction. After excluding individuals with active urinary infections, a pelvic surgery history, neurogenic bladder, acontractile bladder, bladder outlet obstruction (urodynamically confirmed), urothelial carcinoma, or missing data, 50 patients comprised the final cohort.

Case Group ($n=20$): patients with documented recreational maras powder confirmed through patient interviews and medical records, who underwent complete urodynamic evaluation and cystoscopic examination, and complete laboratory workup. All patients with refractory LUTS undergoing cystoscopic examination were thoroughly evaluated for suspicious mucosal lesions, such as erythematous patches, ulcers, or flat lesions resembling carcinoma in situ. Following an initial assessment via office-based cystoscopy under local anesthesia and a shared decision-making process with informed consent, cold cup or resection biopsies were obtained consecutively. Random biopsies were not performed on patients without visible lesions. All procedures and subsequent histopathological analyses were conducted as part of the routine standard of care for these patients.

Control Group ($n=30$): age-matched patients without a history of maras powder use, known urological pathologies, or other risk factors for LUTS, who similarly completed a full urodynamic assessment, underwent a cystoscopic examination, and laboratory tests.

2.2 Exclusion criteria

- Patients with active urinary tract infections.
- Patients with neurogenic bladder, acontractile bladder, or bladder outlet obstruction (confirmed via urodynamics).
- Patients with known pelvic surgeries.
- Patients with a known history of stone disease or urinary malignancies.
- Patients with missing laboratory and urodynamic data were excluded from the study.

2.3 Data collection

Demographic, clinical, and urodynamic data were extracted from electronic health records. Variables included age, smoking history (pack-years), maras powder usage frequency and duration, comorbidities, and LUTS-related parameters, namely pollakiuria, nocturia, and urge/stress incontinence. Urodynamic studies assessed detrusor compliance, maximum flow rate (Qmax), average flow rate (Qavg), post-void residual volume, and cystometric bladder capacity. Cystoscopic evaluations recorded bladder capacity and mucosal abnormalities. Laboratory parameters included complete blood count, serum creatinine, PSA, urinalysis, and urine culture.

2.4 Standardization of maras powder use

Maras powder exposure was quantified as "pack-years", calculated by multiplying daily consumption frequency (Exposure = (Daily Frequency [packs/day] × Duration [years])) by the duration of use.

2.5 Statistical analysis

Data analysis was performed using IBM SPSS Statistics v.27 (IBM). Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed data were expressed as mean ± standard deviation (SD) and compared using independent *t*-sample tests. Non-normally distributed variables were reported as median (interquartile range, IQR) and analyzed with the Mann–Whitney *U* test. Categorical variables were presented as frequencies and compared using Pearson's Chi-square test.

Intergroup differences (Case vs. Control) were evaluated using univariate analyses for urodynamic and laboratory parameters. Maras powder exposure was quantified as adjusted pack-years using the formula:

$$\text{Exposure}\left(\text{daily frequency}\left(\text{packs/day}\right) \times \text{duration}\left(\text{years}\right)\right).$$

Correlations between maras powder exposure and continuous outcomes (e.g., detrusor pressure, bladder capacity) were evaluated using Pearson's correlation. A p-value < 0.05 was considered statistically significant.

3 Results

This study analyzed data from 50 participants, comprising 20 chronic users of maras powder and 30 age-matched controls, with a median age of 61 years (52–68.25). Maras powder users reported a median cumulative exposure of 20 pack-years (IQR: 7–30), reflecting prolonged use over the majority of patients. Controls, with no history of maras powder use or preexisting urological conditions, served as the reference group for comparative analyses.

Significant differences were observed between maras powder users and controls across multiple urodynamic and cystoscopic parameters. Users exhibited a median cystoscopic bladder capacity of 200 mL (18–300), markedly lower than controls ($p < 0.001$), consistent with patterns of bladder contracture. Office-based uroflowmetry measurements revealed a median voided volume of 79.3 mL (56.2–88) in users, significantly reduced compared to controls ($p < 0.001$), indicative of impaired voiding efficiency; furthermore, maximum urinary flow rates (Qmax) were notably reduced in users (median: 5.5 mL/s, 3–7; $p < 0.001$).

Detrusor compliance, a measure of bladder elasticity, was also compromised in users (median: 11 mL/cmH_2O, 5–34; $p = 0.007$), suggesting a hyperelastic, stiff bladder wall. Additionally, users experienced earlier sensations of bladder filling, with a median first sensation volume of 30 mL (16–71; $p < 0.001$), concordance with clinical reports of patients with urgency and frequency at initial presentation (Table 1).

The bladder volume at the first strong desire to void also differed significantly between groups (median: 154 mL, 90–243; $p < 0.001$), further reinforcing the clinical relevance of a hyperelastic and stiff bladder. A dose-dependent relationship has been observed, with maras powder exposure (pack-years) inversely correlated with bladder capacity (Pearson's $r = -0.45$, $p = 0.045$), suggesting progressive damage with prolonged use (Fig. 3).

The Mann–Whitney *U* test was conducted to examine the relationship between maras powder exposure and various urinary symptoms. A significant difference was observed in urge incontinence, with participants reporting the symptom having a significantly higher exposure to maras powder ($n = 14$, $M = 30.84$, $p < 0.05$) compared to those who did not report urge incontinence (Fig. 4). Similarly, a significant difference was found concerning

Table 1 Comparison of patient characteristics and examination findings

Variables	Groups		
	Maras powder non-users (*n* = 30)	**Maras powder users (*n* = 20)**	***p* value**
Age (year)	59 (50–66.3)	62 (59–69.8)	0.102
Concurrent cigarette smoking	18 (60)	18 (90)	**0.026**
Cigarette smoking (pack-years)	15 (0–26)	20 (7–30)	0.198
Prostate volume	27 (22–35)	33 (20–53)	0.389
ICIQ-SF Score	6 (4–10)	14 (8–19)	**< 0.001**
ICIQ-SF Score Severity			**< 0.001**
1	15 (50)	1 (5)	
2	11 (36.6)	9 (45)	
3	4 (13.3)	3 (15)	
4	0 (0)	7 (35)	
Storage phase (overall, %)			
Frequency	20 (66.6)	17 (85)	0.197
Nocturia	20 (66.6)	16 (80)	0.353
Urgency	20 (66.6)	19 (95)	**0.033**
Urge urinary incontinence	12 (40)	14 (70)	**0.048**
Stress urinary incontinence	7 (23.3)	8 (40)	0.345
Voiding Phase (overall,%)			
Hesitancy	7 (23.3)	7 (35)	0.552
Straining	16 (53.3)	12 (60)	0.773
Cystoscopic bladder capacity	270 (198–312)	110 (91.3–202.5)	**< 0.001**
Free uroflowmetry findings			
Qmax (ml/sn)	14 (10.1–18.4)	5.5 (3–7)	**< 0.001**
Voiding volume (ml)	172 (146–233)	79.3 (56.2–88.8)	**< 0.001**
Urodynamic findings			
Compliance	30 (20–40)	11 (5–34)	**0.007**
First sensation	106 (91–133)	30 (16–71)	**< 0.001**
Urodynamic strong desire	259 (197–309)	154 (80–243)	**< 0.001**
Urodynamic maximum capacity	272 (203–318)	159 (98–334)	**0.009**
Painful abortion of the procedure	0 (0)	11 (55)	**< 0.001**
Hydronephrosis at initial presentation	0 (0)	5 (25)	**< 0.001**

Data were expressed as median (interquartile range) or number (percentage) whenever appropriate. *PVR* post-void residual volume; *ICIQ-SF* International Consultation on Incontinence Questionnaire Short Form

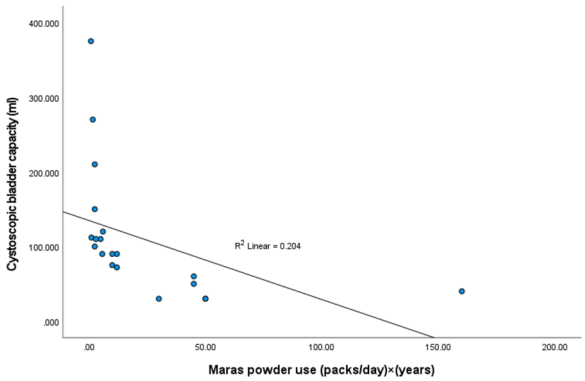


Fig. 3 Dose-related correlation graph between maras powder use and bladder capacity

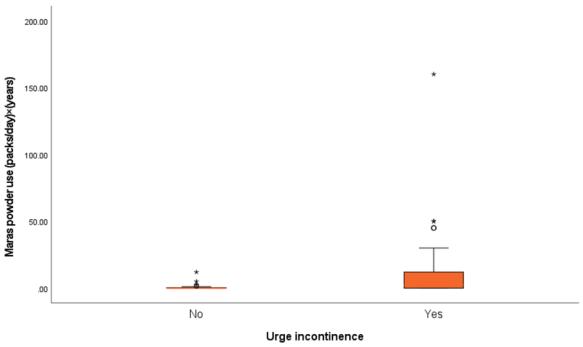


Fig. 4 Distribution of urge incontinence patients among maras powder users. Comparison was performed using the Mann–Whitney *U* test

nocturia, with those experiencing nocturia showing greater maras powder exposure ($n=16$, M = 27.36, $p<0.05$) than those without nocturia. These findings indicate that higher levels of maras powder exposure may be associated with the presence of urge incontinence and nocturia (Fig. 5). Multiple linear regression models were also constructed to identify nocturia and urge incontinence as independent predictors (Table 2). The initial inclusion of cystoscopic bladder capacity resulted in variance inflation factor (VIF) values exceeding 10 (range: 10.3–10.5), denoting significant multicollinearity with other parameters. Hence, cystoscopic bladder capacity was omitted from the final models to maintain the validity of the regression analysis. After its removal, all remaining variables demonstrated VIF values below the threshold of 10, rendering no multicollinearity (Table 2).

3.1 Pathological findings

Among the 20 maras powder users who underwent cystoscopic evaluation, ten cases underwent bladder biopsy for histopathological analysis. Microscopic examination revealed distinct inflammatory patterns. Eosinophilic cystitis was observed in 2 cases (Fig. 6a, b), and general lymphocytic cystitis was identified in a single case (Fig. 6c, d). The urothelium lining was found intact in all cases; however, the lamina propria demonstrated edema and vascular dilation, suggesting marked inflammation in all cases.

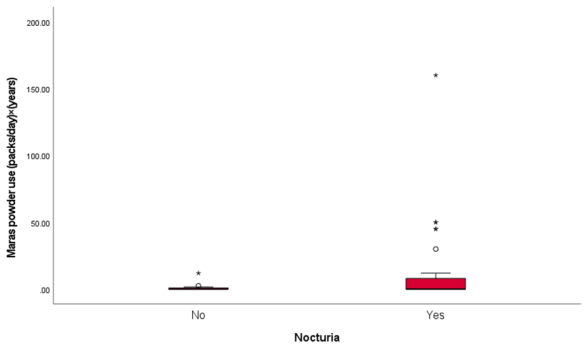


Fig. 5 Distribution of urge incontinence patients among maras powder users. Comparison was performed using the Mann–Whitney *U* test

4 Discussion

This study provides strong evidence that chronic use and abuse of maras powder is associated with significant bladder dysfunction, similar to ketamine-induced cystitis. Our findings align with previous reports linking high nicotine and alkaloid exposure to urothelial damage, while introducing insight into functional bladder impairment caused by this endemic substance.

Study revealed statistically significant differences between maras powder users and controls, most notably in cystoscopic bladder capacity ($p<0.001$) and diminished uroflowmetry voided volume (controls; $p<0.001$) at admittance, consistent with bladder contracture observed in ketamine cystitis [1–4]. Urodynamic detrusor compliance was markedly lower in users (median: 11 mL/cmH2O; $p<0.05$), suggesting impaired bladder elasticity, which we propose may be due to chronic irritation.

The strong inverse correlation between maras pack-years and bladder capacity ($\rho=-0.45$, $p=0.045$) signifies a dose-dependent relationship, reinforcing the cause-and-effect relationship.

Results yielded a clinically significant relationship between maras powder exposure and the development of urge incontinence and nocturia. Participants reporting urge incontinence demonstrated markedly higher maras powder exposure (mean: 30.84 pack-years) compared to asymptomatic individuals, while those with nocturia exhibited similarly elevated exposure levels

Table 2 Multiple linear regression for nocturia and urge incontinence

Predictor	Nocturia model			Urge incontinence model		
	B (SE)	*p*-value	VIF	B (SE)	*p*-value	VIF
(Constant)	0.676 (0.382)	0.1	–	1.254 (0.312)	0.001	–
Package per year (Cigarette)	0.009 (0.008)	0.271	1.199	−0.008 (0.006)	0.227	1.199
Maras powder years used	0.010 (0.009)	0.299	1.857	0.001 (0.008)	0.914	1.857
Maras powder exposure	0.001 (0.003)	0.808	1.481	0.002 (0.003)	0.51	1.481
Uroflowmetry Qmax	−0.017 (0.022)	0.442	2.294	−0.046 (0.018)	0.022	2.294
Detrusor compliance	0.004 (0.011)	0.722	3.054	−0.006 (0.009)	0.52	3.054
Prostate volume	−0.005 (0.005)	0.388	1.565	0.000 (0.004)	0.953	1.565
Model fitness						
R^2	0.32			0.32		
Adjusted R^2	0.006			0.006		

B unstandardized coefficient; *SE* standard error; *VIF* variance inflation factor

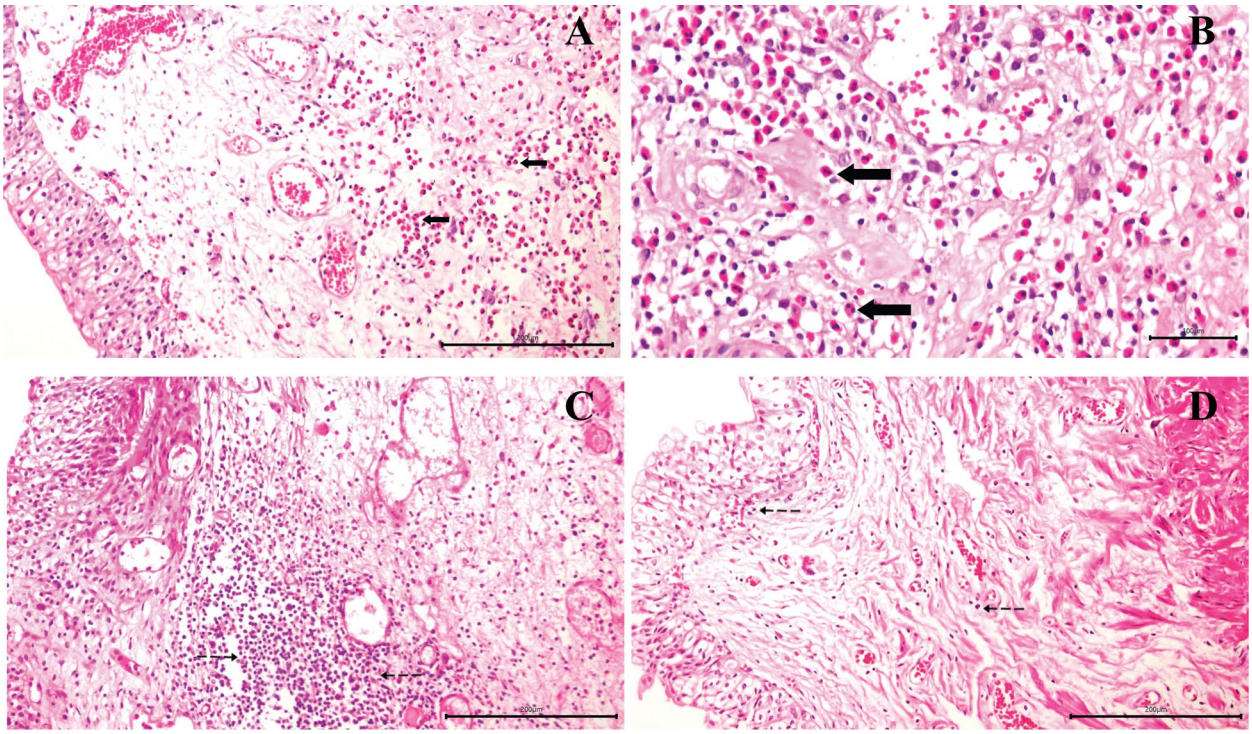


Fig. 6 Histopathological sections of bladder mucosa from patients using maras powder. **A** Urothelial epithelium is noted in the bottom right corner. The lamina propria in other areas contains edema, dilated capillaries, and numerous eosinophilic leukocytes. H&E, × 20. **B** Higher magnification view of the lamina propria, highlighting dilated capillaries and a dense infiltrate of eosinophilic leukocytes (H&E, × 40). **C** and **D** The urothelial epithelium exhibits reactive changes and edema. The lamina propria shows dilated, congested capillaries and a mixed inflammatory infiltrate composed of lymphocytes, plasma cells, and eosinophils. H&E, × 20 and × 40. Bold arrows indicate representative eosinophilic leukocytes. Dashed lines demarcate areas of dense perivascular lymphocytic infiltration

(mean: 27.36 pack-years). It is important to note that the small size of the case group ($n = 20$) limits the statistical power of these comparisons. A formal power analysis was not conducted prior to this first study to characterize this specific urological syndrome, and no preliminary data existed to inform such an analysis. Moreover, recruiting a larger cohort presents significant challenges; despite the widespread use of maras powder in the region, patients who are both willing to undergo invasive diagnostic procedures and admit to recreational use of an endemic substance are exceedingly rare. These findings constitute preliminary evidence for future multicenter studies with larger cohorts and are nevertheless in accordance with the established association of nicotine and tobacco-derived nitrosamines with bladder dysfunction. Nicotine, a potent parasympathomimetic agent, binds to nicotinic acetylcholine receptors (nAChRs) in the bladder urothelium and detrusor muscle, potentially inducing hypercontractility and sensory hypersensitivity. Chronic stimulation of nAChRs may disrupt normal afferent signaling pathways, leading to urgency and involuntary detrusor contractions, a plausible explanation for the observed association with urge incontinence [7, 8]. We find the potential confounding effect of concurrent cigarette smoking noteworthy; due to its widespread use among maras powder users in comparison to the control group (90% vs. 60%) and its role as a risk factor for bladder irritation. While the mechanisms may appear synergistic due to shared constituents like nicotine, the markedly higher concentration of nicotine and other alkaloids in Maras powder, coupled with dipping, suggests its effects are likely more potent and direct [7, 8]. However, the specific contribution of Maras powder independent of cigarette smoke remains an important area for future research. Multiple regression models constructed to predict nocturia and urge incontinence in maras powder users were statistically weak. The poor explanatory power, despite significant univariate findings, is likely due to the study's limited sample size. Furthermore, cystoscopic bladder capacity was also excluded due to its significant collinearity with other urodynamic parameters, which would consequently confound the regression model.

Histopathological examination revealed marked leukocytic infiltration within the lamina propria of the bladder. These results parallel the changes seen in ketamine users,

yet through a distinct mechanism involving tobacco-specific nitrosamines rather than NMDA-mediated toxicity [1–3].

The high nicotine content (9–10 × conventional tobacco) and alkaloid-rich composition of maras powder likely drive urothelial toxicity via direct mucosal irritation and oxidative stress. Chronic exposure may inhibit nitric oxide synthase, reduce bladder blood flow, and promote ischemia mechanisms shared with ketamine [4, 9–11]. Unlike ketamine, however, maras powder lacks any known NMDA receptor antagonism, suggesting alternative pathways in bladder remodeling [6, 11].

4.1 Limitations of the study

This study has limitations. Its retrospective design introduces potential selection bias, and the small case group ($n=20$) limits generalizability. Histopathological data were not systematically analyzed, leaving a gap in the physiopathology of the overall entity. Future prospective studies with larger cohorts should investigate histological changes in maras powder users, and comprehensive long-term effects of specific alkaloids and tobacco nicotine-derived nitrosamine ketones on the bladder.

5 Conclusions

Maras powder use is associated with ketamine-like bladder syndrome characterized by reduced compliance, capacity, and obstructive voiding patterns. These findings necessitate public health interventions to regulate maras powder distribution and clinician education on recognizing this emerging etiology of LUTS. Further research should explore therapeutic strategies effective in ketamine cystitis for potential adaptation in maras-related bladder dysfunction.

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Author contributions
SBO: conceptualization, study design, manuscript writing, and project planning. GK: statistical analysis, data interpretation, and methodology. BY: data curation, data collection, and organization of clinical records. MFT: histopathological diagnosis, analysis, and understanding of pathological findings. All authors critically reviewed, edited, and approved the final manuscript.

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Data availability
Due to ethical restrictions and data sensitivity, the datasets generated and/or analyzed during this study are not publicly available. Digital data reside in the controlled digital archive of Osmaniye State Hospital. Urodynamic studies are also stored in the hospital's physical archive as original files/paper records. Requests for access to either digital or physical records should be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
This study was approved by the Osmaniye Korkut Ata University Institutional Review Board (Approval No: OKU.KKO.FR.0024) and conducted by the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants for urodynamic testing, cystoscopy, and bladder biopsy as part of standard clinical care. The ethics committee waived the requirement for additional informed consent for the retrospective analysis of anonymized patient data. Patient confidentiality was strictly maintained.

Consent for publication
Not applicable, as the manuscript does not contain identifiable personal data, images, or details of individual participants.

Competing interests
The authors declare no competing interests.

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