



Characteristics and Treatment Outcomes of Ketamine-Induced Uropathy in Wales in 2024: A Pilot Study

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Abstract

Background : Ketamine use is increasingly associated with lower urinary tract symptoms, including ketamine-induced uropathy (KIU). Characterising affected patients and treatment outcomes is essential to guide management.

Method: A cross-sectional study included 20 patients diagnosed with KIU between January and June 2024 at our institution. Urinary symptoms were assessed at presentation and three months after treatment, including frequency, dysuria, urgency, nocturia, incontinence, incomplete emptying, weak stream, and straining. Symptom severity was measured using the International Prostate Symptom Score (IPSS). Statistical analysis was performed using SPSS version 26.0.

Results: Most patients were male (n=15; 75%) and aged 16–21 yr (n=11; 55%). Regular ketamine use was reported by 14 patients (70%), and 15 (75%) had used ketamine for over six years. At presentation, all patients reported urinary frequency and dysuria (100%), and 17 reported urgency (85%). After treatment, significant improvement was observed in dysuria (100% vs 75%; $p=0.016$), urgency (85% vs 40%; $p=0.003$), urinary incontinence (35% vs 10%; $p=0.047$), and incomplete emptying (30% vs 5%; $p=0.037$). IPSS scores shifted from severe to mild symptoms, although this change was not statistically significant ($p=0.546$).

Conclusions: KIU is associated with a high burden of urinary symptoms in young users. Recognition and targeted treatment can significantly improve key urinary outcomes.

Patient summary: Young ketamine users frequently develop bladder symptoms. Symptoms improved following treatment, suggesting intervention may improve quality of life.

Keywords: Ketamine; Uropathy; Urinary Symptoms.

Highlights

- Ketamine-induced uropathy is associated with a significant burden of lower urinary tract symptoms in a predominantly young patient population.
- Urinary frequency, dysuria, and urgency were the most common presenting symptoms, with frequency and dysuria reported in all patients.
- Targeted treatment resulted in statistically significant improvement in dysuria, urgency, urinary incontinence, and incomplete bladder emptying at three months.
- Despite treatment, a proportion of patients continued to experience persistent symptoms, highlighting the chronic nature of the condition.
- These findings emphasise the importance of early recognition and structured management in patients with ketamine-induced uropathy.

INTRODUCTION

Ketamine is a dissociative anesthetic agent that acts as an N-methyl-D-aspartate (NMDA) receptor antagonist. It is used clinically for analgesia and sedation, but has also gained popularity as a recreational drug due to its psychoactive effects. The recreational use of ketamine has increased significantly in recent years, particularly among young adults [1,2].

Ketamine has gained notoriety for its recreational use, particularly among younger populations in the UK. The drug's increasing prevalence, particularly in Wales, has raised concerns regarding its associated health risks, notably ketamine-induced uropathy (KIU). Recent studies have highlighted a troubling rise in ketamine abuse among younger populations in the UK, with reported usage increasing from 1.9% in 2008/2009 to 2.9% in 2018/2019 among individuals aged 16-24 years [3].

Ketamine-induced uropathy (KIU) is an emerging clinical entity characterized by severe lower urinary tract symptoms, small bladder capacity, and pelvic pain in chronic ketamine users. The exact prevalence

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of KIU is unknown, but it appears to be increasing in recent years along with rising recreational ketamine use, especially among young adults in the UK. A systematic review and meta-analysis found the pooled prevalence of frequency, the most common symptom, to be 77.1% in patients with KIU. Other common manifestations include urgency (69.9%) and suprapubic pain (60.4%) [4].

The pathophysiology of KIU is complex and multifactorial. Ketamine's metabolites exert toxic effects on the urinary tract, leading to inflammation, fibrosis, and ultimately, damage to both the bladder and kidneys. Clinical presentations can vary widely, with many patients experiencing lower urinary tract symptoms (LUTS) such as frequency, urgency, and dysuria, while others may present with hydronephrosis, a condition that can result from prolonged ketamine abuse. Reports suggest that a significant proportion of patients with a history of ketamine use exhibit upper urinary tract involvement, which can complicate management and increase the risk of renal failure [5,6].

The outcomes of ketamine-induced uropathy are concerning, particularly given the potential for irreversible damage to the urinary system. Studies have shown that a substantial number of patients may progress to severe complications, including hydronephrosis and impaired renal function. The recognition of KIU as a distinct clinical entity is crucial for timely diagnosis and intervention. Current management strategies emphasize the importance of cessation of ketamine use, alongside symptomatic treatment and monitoring of renal function. However, many patients may be reluctant to disclose their drug use, complicating diagnosis and treatment efforts [7,8].

Various medications have been used for symptomatic relief, including anticholinergics and pain medications. However, data on the efficacy of these treatments is limited. A large case series from a single UK center reported using oral medications in addition to intravesical therapies and surgery in 81 patients with KIU. However, the specific oral medications used and their outcomes were not detailed. Given the increasing prevalence of KIU and the paucity of data on treatment outcomes, further research is needed to characterize the oral pharmacological management of this condition. This thesis aims to evaluate the prevalence of KIU in a large cohort of chronic ketamine users and assess the efficacy of various oral medications used in its management [9].

Despite the growing body of evidence surrounding KIU, there remains a paucity of data specifically addressing the characteristics and treatment outcomes of patients in Wales. This gap underscores the need for comprehensive research to evaluate the prevalence of KIU and the effectiveness of various oral treatment strategies within this population. This study aims to provide a detailed examination of the characteristics and treatment outcomes of KIU in Wales, thereby contributing to the development of more effective management protocols and formal treatment guidelines for affected patients.

MATERIAL AND METHODS

A cross-sectional study included 20 patients diagnosed with KIU between January and June 2024 at our institution. Urinary symptoms were assessed at presentation and three months after treatment, including frequency, dysuria, urgency, nocturia, incontinence, incomplete emptying, weak stream, and straining. Symptom severity was measured using the International Prostate Symptom Score (IPSS). Statistical analysis was performed using SPSS version 26.0.

Study Design

This is a retrospective cross-sectional hospital-based study enrolled 20 KIU individuals in our institution, during the period from January to June 2024. The inclusion criteria include ketamine users aged 16 years old or above. Any with a history of significant urological conditions or prior surgeries affecting the urinary tract were excluded.

Data Collection Tools and Methods

Data at admission after 3 months of treatments were collected retrospectively from hospital's computer data base by using a pre-designed structured questionnaire composed of demographic characteristics (age, gender, smoking), ketamine usage details (the person who guided you to use ketamine, duration of use, regularity of use, amount per day, other substances with ketamine), duration of treatment, urological evaluation by radiological modalities (ultrasound-US and computed tomography-CT), renal evaluation by eGFR, and symptom assessment before and after the treatment.

All the patients were treated orally with Tamsulosin 400 µg and Solifenacin 5 mg once daily for one month in addition to Pentosan polyphosphate 100 mg three times a day for three months up to 6 months.

International Prostate Symptom Score (IPSS) was used to assess LUTS. The IPSS questionnaire consists of 7 questions that evaluate the sensation of incomplete emptying, frequency of urinating at intervals of ≤2 hours, intermittency of the urinary stream, difficulty postponing urination characterized as urinary urgency, weakness of urinary stream (weak stream), the need to push or strain to urinate (straining), and the need to awaken at night to urinate (nocturia). The overall IPSS ranges from 0 to 35 and categorized as mild when score from 0 to 7, moderate 8-19 and severe from 20-35 [10].

Statistical analysis

Data analyzed by using statistical package for social sciences (SPSS; IBM, version 26.0). The results showed in tables and figures designed by Microsoft Excel 2010. The Chi-Square test was employed for significance testing, with a p-value of less than 0.05 considered statistically significant (two-sided).

RESULTS

Most patients were male (n=15; 75%) and aged 16-21 yr (n=11; 55%). Regular ketamine use was reported by 14 patients (70%), and 15 (75%) had used ketamine for over six years. At presentation, all patients reported urinary frequency and dysuria (100%), and 17 reported urgency (85%). After treatment, significant improvement was observed in dysuria (100% vs 75%; p=0.016), urgency (85% vs 40%; p=0.003), urinary incontinence (35% vs 10%; p=0.047), and incomplete emptying (30% vs 5%; p=0.037). IPSS scores shifted from severe to mild symptoms, although this change was not statistically significant (p=0.546).

A total of 20 participants were included in the study, with 15 males (75%) and 5 females (25%). The majority of participants 11(55%) were aged from 16-21 years. Most participants 14(70%) were regular ketamine users, with duration of use above 6 years in 15(75%) cases. The amount of ketamine used per day was mostly between 1-2 grams by 14(70%) cases. The majority of participants 16(80%) still using ketamine even after being diagnosed with uropathy, and 13(65%) received treatment for 1-3 months. Radiological imaging modalities used included CT in eight (40%) and US in six (30%) cases. The estimated glomerular filtration rate (eGFR) was greater than 90 ml/min in 16(80%) participants and between 80-90 ml/min in four (20%) cases. The baseline characteristics were detailed in Table 1.

Pretreatment, the most common symptoms were urinary frequency (n=20; 100%), dysuria (n=20; 100%) and urgency (n=17; 85%). After three months of treatment, there was significant reduction in dysuria [at admission= 20(100%) vs post-treatment= 15(75%); P= 0.016], urgency [at admission= 17(85%), post-treatment= eight (40%); P= 0.003], urine incontinence [at admission= seven (35%), post-treatment= two (10%); P= 0.047] and incomplete emptying [at admission= six (30%), post-treatment= one (5%); P= 0.037] as illustrated in Table 2.

The International Prostate Symptom Score (IPSS) showed a slight



Table 1: The baseline characteristics (N= 20)

	N	%
Gender		
• Male	15	75.0
• Female	5	25.0
Age (Years)		
• 16-21	11	55.0
• 22-27	8	40.0
• 27-32	1	5.0
Smoking (yes)	19	95.0
The person who guided you to use ketamine		
• Friends	9	45.0
• School peer	6	30.0
• Both	5	25.0
Duration of use (Years)		
• <1	1	5.0
• 1-3	3	15.0
• 4-6	1	5.0
• >6	15	75.0
Regularity of use		
• Regular	14	70.0
• Occasional	6	30.0
Amount per day (gm)		
• <1	2	10.0
• 1-2	14	70.0
• >2	2	10.0
• Don't know	2	10.0
Use other substances with ketamine	1	5.0
Still use ketamine after uropathy diagnosis	16	80.0
Duration of treatment (months)		
• <1	2	10.0
• 1-3	13	65.0
• >3	5	25.0
Radiological Imaging modalities		
• CT	8	40.0
• US	6	30.0
• None	6	30.0
eGFR (ml/min)		
• >90	16	80.0
• 80-90	4	20.0



Table 2: The symptoms before and after ketamine induced uropathy (KIU) treatment (N= 20)

	pretreatment; n(%)	3 months posttreatment; n(%)	P. value
Urinary frequency	20(100%)	18(90%)	0.147 ^a
Dysuria	20(100%)	15(75%)	0.016 ^{a*}
Urinary urgency	17(85%)	8(40%)	0.003 ^{a*}
Nocturia	7(35%)	6(30%)	0.735 ^a
Urinary incontinence	7(35%)	2(10%)	0.047 ^{a*}
Incomplete emptying	6(30%)	1(5%)	0.037 ^{a*}
Weak stream	3(15%)	1(5%)	0.291 ^a
intermittency	2(10%)	2(10%)	0.999 ^a
Straining	2(10%)	1(5%)	0.548 ^a

shift from severe symptoms to mild symptoms after treatment, but this change was not statistically significant ($P=0.546$) as demonstrated in Figure 1.

DISCUSSION

In this study ketamine was markedly used by males 15(75%), which supported by previous study of Merikangas et al., who is indicating a male predominance in substance use disorders [11]. The age distribution showed that 55% of participants were aged 16-21 years, and 40% were aged 22-27 years. This finding is consistent with Andrew et al., study where the younger adults are more likely to engage in recreational drug use, including ketamine [12].

A striking 70% ($n= 14$) of participants were regular ketamine users, with 75% ($n= 15$) having used the drug for over six years. Corresponding, Mak S et al., reported symptoms related KIU were significantly higher for ketamine use for more than 24 months [13]. This indicating that KIU is duration-dependent condition. A Taiwanese study of 106 ketamine users found that the prevalence of lower urinary tract symptoms (LUTS) was

84%, with symptoms beginning at a mean of 24 months after starting daily use. The study shat that all symptom severity scores (overactive bladder symptom score, international prostate symptom score, interstitial cystitis symptom / pain index) correlated with the duration of ketamine abuse [14].

Among our cohorts, the daily consumption of ketamine was 1-2 grams by 14(70%) participants also reflects a pattern seen in other research, which suggests that high doses are common among KIU patients. A review by Tsai and Kuo discussed the relationship between ketamine usage patterns and the development of ketamine-induced cystitis. The authors noted that higher doses and prolonged use are associated with increased risk of urinary symptoms, including frequency and urgency. They suggested that the toxic effects of ketamine and its metabolites on the bladder epithelium contribute to these symptoms.

Before treatment, the most common symptoms reported were frequency, dysuria and urgency. These findings are consistent with previous literature that identifies these symptoms as prevalent among individuals with uropathy related to ketamine use [4].

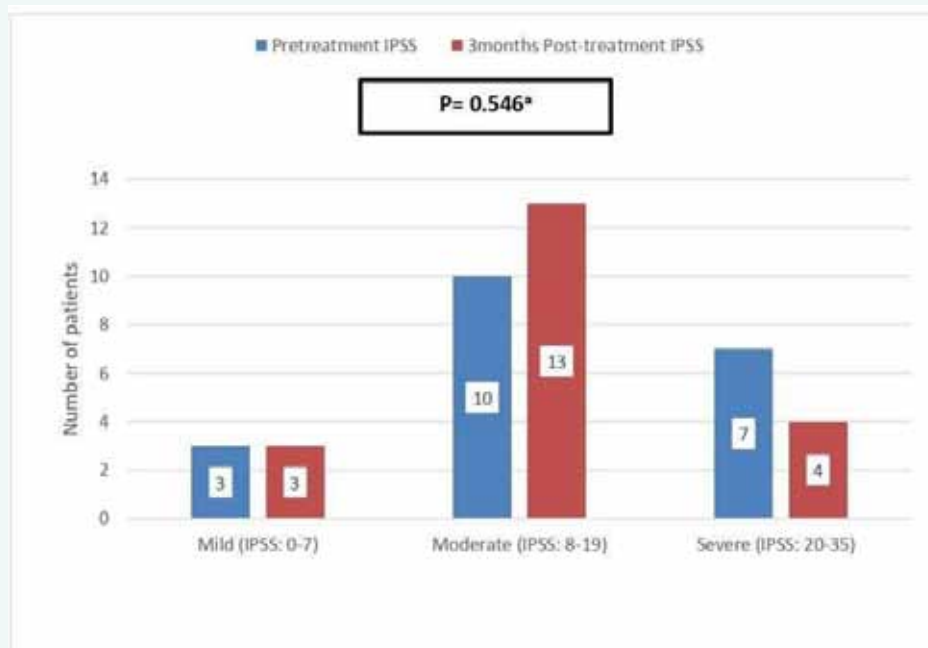


Figure 1: Bar chart showing Patient distribution according to the severity of IPSS (N=20)



After three months of treatment, the prevalence of frequency, dysuria and urgency decreased to 90% (n= 18), 75% (n= 15), and 40% (n= 8), respectively. Also, notable improvement was observed in incontinence, which decreased from 35% (n= 7) to 10% (n= 2), with a statistically significant P. value of 0.037. Similarly, incomplete emptying decreased from 30% (n= 6) to 5% (n= 1), with a P. value of 0.047. These results support findings from the comprehensive review of Li et al and systematic review of Zhou et al those reported non-invasive therapies, including the use of oral anti-inflammatories and anticholinergics, can also lead to improvements in urinary symptoms. These treatments, combined with ketamine cessation, contribute to symptom relief and improved bladder function.

The IPSS results indicated a shift from severe symptoms to mild symptoms three months post-treatment, but this change was not statistically significant (P=0.546). This finding agreed with studies that have shown that while treatment can lead to symptom improvement. In the work of Li et al., who surveyed ketamine users in Taiwan and compared IPSS-S scores between treated and non-treated groups. They found that the non-treated group had lower IPSS-S scores compared to the treated group (5.14 ± 4.36 vs. 7.31 ± 6.71 , $p=0.0055$), suggesting that treatment may have led to a slight improvement in storage symptoms (14). Chu et al., conducted a systematic review and meta-analysis on ketamine-associated uropathy. They found that the pooled prevalence of storage symptoms, as measured by the IPSS storage subscore (IPSS-S), was 69.9% (95% CI=48.8%-87.3%). However, the review did not specifically report on changes in IPSS scores after treatment [4].

While this study provides valuable insights, several limitations should be acknowledged; firstly, the study comprises a relatively small sample size of participants, which may limit the generalizability of the findings to the broader population. Secondly, the cross-sectional nature of the study restricts the ability to establish causal relationships between variables. Longitudinal studies are needed to understand the progression of KIU and its impacts over time. Thirdly, the reliance on self-reported data may introduce bias, as participants may underreport or overreport their symptoms and experiences.

Despite these limitations, the study has several strengths including that; this study specifically ketamine abusers, a demographic often underrepresented in research, thereby filling a critical gap in the literature, the inclusion of various factors such as demographic characteristics, symptomology, and treatment outcomes provides a holistic view of the challenges faced by this population, and conducting the study within the Walsh context allows for culturally relevant insights that can inform local health policies and interventions.

CONCLUSION

In conclusion, this study provides valuable insights into the demographic and clinical characteristics of ketamine users with uropathy. While significant improvements were noted in certain symptoms, particularly dysuria, urgency, incontinence and incomplete emptying, the overall changes in symptomatology were not uniformly statistically significant. Future research should focus on larger sample sizes and longer follow-up periods to better understand the long-term effects of treatment on uropathy symptoms in this population.

ETHICS STATEMENT

Ethical approval was obtained from center's ethical committee. Both verbal and written consents to publish this information were gained from the patients.

TRANSPARENCY STATEMENT

Fares Alzubair Basheer Idrees, the lead author, declares that this manuscript is an honest, accurate, and transparent. He also clarifies that

significant aspects of this study were not excluded and any discrepancies from the planned study have been explicitly explained.

CONSENT TO PUBLISH

All authors gave their approval for publication.

Availability of Data and Materials, Ethical Approval, Informed Consent, Author Contributions, Declaration of Interests, and Funding.

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