Original Article

To study the incidence and preintervention factors associated with acute kidney injury in patients diagnosed with ureteric calculi

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Abstract

Aims and Objectives: The study aims to evaluate the incidence and factors associated with acute kidney injury (AKI) among patients presenting with ureteric calculi. We also intend to study the impact of time delay since first symptom to presentation to our hospital among patients with ureteric calculi and its influence on AKI.

Material and Method: The study is a prospective observational study and included all symptomatic ureteric calculi patients. AKI was defined as per the KDIGO guidelines. All the patients diagnosed with ureteric calculi were grouped into those having an episode of AKI and those without an episode on AKI.

Results: The incidence of AKI in our study was 14.63% (18 patients) among 123 patients of ureteric calculi. Average time delay from time of diagnosis to presentation among patients with AKI was 31.7±6.2 days (mean ± S.D) as compared to 19.5±5.7 (mean ± S.D) days among all cases. Factors which were significantly associated with AKI in patients with ureteric calculi include time delay, diabetes mellitus, bilateral ureteric calculi, stone size greater than 10 mm, solitary functioning kidney and urine culture showing gram negative growth. Fifty percent of the AKI group eventual required nephrectomy of one renal unit.

Conclusion: This study will help us streamline our resources predominantly towards those patients who present with factors associated with increased risk of AKI. As the time delay to presentation in patients with AKI with ureteric calculi is significantly higher, it is imperative to counsel patients with stone disease.

Keywords: Acute kidney injury, calculus, ureter

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Received: 13.07.2018, **Accepted:** 06.03.2019

INTRODUCTION

Urolithiasis forms an integral part of the practice of urology. Over the past few decades, there has been a shift in management of stone disease from open surgery to various endourologic procedures which include percutaneous nephrolithotomy, ureterorenoscopy, and retrograde intrarenal surgery.[1] Despite the advent of minimally invasive surgeries, complications secondary to calculus disease have remained steady. The reported life-threatening complication rate due to stone disease is about 12%.[2] Urolithiasis is the most common surgical cause of acute kidney injury (AKI).[3] Furthermore, 15% of AKI patients secondary to urolithiasis received dialysis.[3] The pathogenesis of AKI due to stone disease may be

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_96_18

How to cite this article: Kamath SU, Patil B, Patwardhan SK. To study the incidence and preintervention factors associated with acute kidney injury in patients diagnosed with ureteric calculi. Urol Ann 2019;11:380-4.

secondary to long-standing obstruction, infection, or previous procedures done on the kidney for removal of stones.[4] AKI secondary to ureteric calculi is a urologic emergency as it requires urgent decompression, either with double-J stenting (DJ stent) or with percutaneous nephrostomy (PCN). Various studies which have evaluated AKI in stone disease have reported recovery rate of renal function ranging from 72% to 100% postprompt management of AKI.[2,5] This highlights the necessity to evaluate factors associated with AKI and their prompt management in patients of ureteric calculi. There have been very few studies which have intended to study these factors, and none have been studied in India to our knowledge. Although the association of time delay in management of obstructive uropathy and eventual outcome has been mentioned, none of the studies to our knowledge have studied it with respect to ureteric calculi and its association with AKI. This study aims to evaluate the incidence and factors associated with AKI among patients presenting with ureteric calculi over the past 1½ year. We also intend to study the impact of time delay since first symptom to presentation to our hospital among patients with ureteric calculi and its influence on AKI.

MATERIALS AND METHODS

The study is a prospective observational study and was conducted in a single tertiary care medical college in a metropolitan city. The study duration was from July 2016 to September 2017 after institutional ethics committee approval obtained in July 2016. Written informed consent was obtained from all patients participating in this study as per ethics protocols. All patients with age >18 years already diagnosed with symptomatic ureteric calculi presenting to the hospital either in the emergency department or outpatient department were included and were evaluated. The presence of ureteric calculi was diagnosed either on ultrasonography or computed tomography (CT) scan. Patients with incomplete data set and those with known chronic kidney disease were excluded. After obtaining an informed consent, data on demographic profile, clinical features (including time delay since first symptom to presentation to our hospital), laboratory investigations, imaging studies, outcome of patients, and the follow-up details were recorded. Clinical features included symptoms at presentation, duration of symptoms, associated comorbidities, and history of prior urologic interventions, if any. The time from diagnosis to the time patient presented to our institution was specifically noted among all the patients with ureteric calculi. These patients were also questioned for the reason for late presentation. On clinical examination, general physical findings such as mental status, cardiorespiratory parameters, and per abdominal findings were assessed. Laboratory variables included a complete hemogram, renal function tests, liver function tests, coagulation profile, urine microscopy, blood culture, urine culture, and sensitivity. AKI was defined as per the KDIGO guidelines. All the patients diagnosed with ureteric calculi were then grouped into two groups – those having an episode of AKI and those without an episode of AKI. Patients who were diagnosed to have AKI were initially managed with diversion procedures which included either DJ stent or PCN. Definitive management was then performed after a patient improved symptomatically and creatinine reached nadir. Patients who did not have an episode of AKI underwent definitive management immediately postdiagnosis. All patients were followed up for a duration of 3 months following stone clearance.

Univariate analysis was done and the two groups were compared, and thereby, factors significantly associated with AKI were evaluated. Chi-square test was used to evaluate the categorical variables and unpaired *t*-test for normally distributed continuous variables. $P < 0.05$ was considered statistically significant. All statistical analysis was done using SPSS software 16.0 (IBM-SPSS, Chicago, Illinois, U.S.A.).

RESULTS

The mean age of patients diagnosed with symptomatic ureteric calculi was 37.46 ± 1.43 (mean ± standard deviation [SD]). Seventy-one (57.72%) patients among them were females. The most common presenting feature was ureteric colic which was present in 107 patients (86.66%). Among all patients diagnosed with ureteric calculi, 87 patients (70.73%) had no growth on urine culture, 20 (16.26%) patients had *Escherichia coli*, 9 (7.31%) had *Klebsiella*, and 7 (5.69%) had polymicrobial growth on urine culture. The average stone size of ureteric calculi on CT scan was 11.13 ± 3.90 (mean ± SD), and the most common site was upper ureter.

The incidence of AKI was 14.63% (18 patients) among 123 patients of ureteric calculi. Among the patients with AKI, the most common presenting feature was vomiting in 11 patients (61.11%). Fifteen patients (83.33%) had a positive urine culture and the most common organism was *E. coli* seen in six patients (33.33%). The average stone size among patients with AKI was 15.05 ± 3.13 (mean ± SD), and the most common site in this group as well was upper ureter. The average time delay from time of diagnosis to presentation among patients with AKI was 31.7 ± 6.2 days (mean ± SD) as compared to 19.5 ± 5.7 days (mean ± SD) among all

cases. Graph 1 shows time delay among patients with AKI and non-AKI patients with ureteric calculi. The reason for delay was documented to be resorting to alternative medication (54%), unawareness about the disease (15%), and financial constraints (12%).

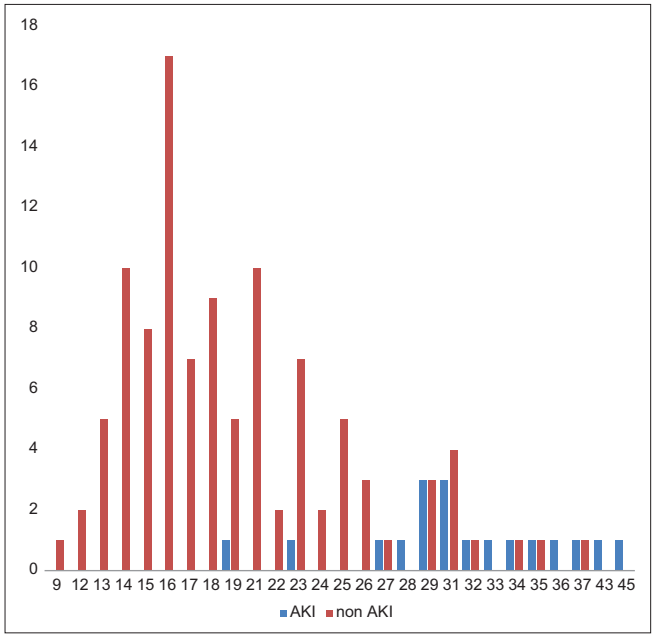
Factors which were significantly associated with AKI in patients with ureteric calculi include diabetes mellitus, bilateral ureteric calculi, stone size >10 mm, solitary functioning kidney, and urine culture showing Gram-negative growth. Table 1 shows the details of various factors significantly associated with AKI in patients of ureteric calculi.

DISCUSSION

The prevalence of stone disease ranges from 1% to 20% across the various geographic location.[6] AKI is one of the most dreaded complications of stone disease. Untreated ureteric calculi lead to progressive interstitial fibrosis and tubular injury, which leads to substantial decrease in renal function over weeks to months.[7] This, thereby, emphasizes the need to evaluate the incidence of AKI in a particular geographic location and to assess the factors which predict the risk of AKI among patients with ureteric calculi so as to treat them promptly.

The incidence of AKI in our study was 14.63% (18 patients) among 123 patients of ureteric calculi. A study conducted by Wang *et al*. in 2011 among Chinese population identified only 15 cases of AKI among 2073 patients (0.72%) over a period of 8 years.[8] Another study conducted in Pakistan reports the incidence of AKI as 8.2% among patients with ureteric calculi.[2] A large observational study conducted in India identified the incidence of CKD to be 17.2%; however, this study did not evaluate the incidence of AKI and its association with stone disease.[9] Only symptomatic ureteric calculi were included in our study which may be the reason for higher incidence of AKI in our study. Another reason for the increased incidence in both studies from the Indian subcontinent could be an increased threshold to seek medical attention for stone disease.

The average stone size among patients with AKI (15.05 ± 3.13) was higher in comparison with the average stone size among all patients of ureteric calculi (11.13 ± 3.90). Patients with AKI had a significantly higher number of patients with stone size >10 mm. Majority of patients with ureteric calculi had upper ureteric calculi, and this finding persisted among patients with AKI. This finding has been previously proven by Wang *et al*. in 2011 with the average stone size of 1.35 cm and with majority of patients having upper ureteric calculi in patients with AKI.[8] However, a noteworthy finding was that in the above-mentioned study, >50% of patients in the non-AKI group had lower ureteric calculi with an average stone size of 8 mm. The discrepancy in the non-AKI group



Graph 1: Time delay and association with acute kidney injury

Table 1: Association of various factors with acute kidney injury

Factors	AKI (*n*=18)	Non-AKI (*n*=105)	*P* value
Age (years), mean±SD	41.33±13.9	36.80±10.8	NS
Gender			
Male	11	60	NS
Female	7	45	
History of diabetes mellitus			
Yes	9	20	0.004
No	9	85	
Size of stone at presentation (mm)			
≤10	0	61	0.000
>10	18	44	
Size of stone at presentation			
Upper	12	70	NS
Mid	4	19	
Lower	2	16	
Bilateral calculi			
Yes	7	11	0.002
No	11	94	
Solitary kidney			
Yes	4	2	0.000
No	14	103	
White blood cell counts (/cmm)			
≤13,000	8	57	NS
>13,000	10	48	
Urine culture			
Gram-negative	15	21	0.000
No growth	3	84	
Time delay (days), mean±SD	31.7±6.25	19.5±5.7	0.000

SD: Standard deviation, AKI: Acute kidney injury, NS: Not significant

could again be explained by the fact that only symptomatic patients were included in our study.

Several case reports have highlighted bilateral ureteric calculi as a medical emergency owing to its high risk for AKI as well as persistent metabolic derangements despite relieving obstruction.[10] In our study, patients having bilateral ureteric calculi had a higher incidence of AKI, thereby needing urgent intervention. Patients with solitary kidney presenting with symptomatic ureteric calculi had a significantly higher association with AKI as mentioned by a previous study conducted in China as well as the Indian subcontinent.[8,11]

A peculiar finding among patients with ureteric calculi which has not previously been mentioned in other studies is an association of diabetes mellitus The association of diabetes mellitus could be explained by the fact that these patients already have decreased renal reserve and ureteric calculi, which adds to the insult subsequently causing interstitial and tubular injury and thereby manifestating as AKI.[10] Urinary infection in urolithiasis is a known risk factor for AKI, which has been also proven in our study by an association-positive Gram-negative urine culture with AKI.[12,13]

The importance of time in management of patients in obstructive uropathy has been mentioned time and again. Lucarelli *et al.* evaluated long-term renal outcome among 76 patients with iatrogenic renal injury caused by ureteric obstruction, and their result stated that if outflow was restored in <2 weeks, no evidence of long-term renal damage was observed.[12] In a rodent ureteral obstruction model, the severity of tubular atrophy and interstitial fibrosis linearly increased as the duration of obstruction was extended.[14] In our study, we evaluated the average time delay from diagnosis of stone disease to presentation to our hospital. The time delay was significantly more among patients with ureteric calculi presenting with AKI. Thus, it could be proposed that the time delay in presentation and thereby delay in management among these could significantly contribute to subsequent AKI as per the above-mentioned theory in rat model. On questioning the reason for delay among these patients, majority of the patients gave a history of experimenting with alternative medicine. Not only this leads to delay in definitive management, but also these alternative medications have known to promote nephrotoxicity adding to the existing insult.[15]

The major limitation of this study was a short follow up. Moreover, neither functional studies such as diuretic renogram nor estimated glomerular filtration rate were calculated pre- and post-intervention in all patients. Both these factors contributed to lack of assessment of the eventual outcome. This study needs to be followed up by a large multi-institutional prospective study to confirm the above-mentioned factors associated with AKI.

AKI secondary to ureteric calculi predominantly is associated with a younger earning population, which adds to the economic burden to our country. AKI in these patients is easily avoidable and is associated with almost 72%–100% recovery with timely management.[2,5] With a report mentioning that 12% of men and 6% of women will have ureteric colic once in their lifetime and there are limited resources to tackle stone disease in India, it becomes essential to prioritize patients needing early management.[11] This study will help us streamline our resources predominantly toward those patients who present with factors associated with increased risk of AKI. This would mean that fewer patients with stone disease need dialysis and diversion procedures. As the time delay in presenting to our tertiary care hospital in patients with ureteric calculi is significantly higher among patients with AKI, it is imperative to counsel patients with stone disease at grass-root level about the complications of stone disease as well as the necessity to undergo prompt management. This may also contribute to decrease the incidence of AKI among patients with urolithiasis.

CONCLUSION

Preintervention factors predicting AKI in patients with ureteric calculi include diabetes mellitus, bilateral ureteric calculi, stone size >10 mm, solitary functioning kidney, and urine culture showing Gram-negative growth. Time delay since first symptom to presentation to our hospital among patients with ureteric calculi is significantly associated with AKI.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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