Original Article

DOI: 10.7860/IJARS/2025/74948.3053

Urology Section

Evaluation of Risk Factors and Stone Composition in Patients with Recurrent Renal Calculus: A Retrospective Descriptive Study from Tamil Nadu, India

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ABSTRACT

Introduction: Renal stone disease is one of the most common occurring conditions in the general population with a prevalence of 12% in India. Recurrent renal stone occurrence is multifactorial and it is observed approximately 98% of patients will develop a recurrent stone within 25 years of the first episode.

Aim: To analyse some of the various risk factors and stone composition in patients with recurrent renal calculi.

Materials and Methods: This was a retrospective descriptive study done with 116 cases of recurrent renal calculi (treated both inpatient and outpatient) coming to the Department of Urology at Meenakshi Medical College, Kanchipuram, Tamil Nadu, India, for two years from May 2022 to April 2024. Various parameters like sex, age, duration of previous stone, stone analysis findings and history of diabetes, hypertension, tobacco/smoking and alcohol consumption (for more than 10 years).

Results: Out of 116 cases, 79 were male (68.1%) and 37 were female (31.9%). Approximately 48.8% of patients were in the age group of 31-50 years, followed by 34.5% in age group of 51-70 years. Around 41.3% of the recurrences occurred within 1-5 years of previous stone episode. Most common component found in stone analysis was calcium (52.3%), followed by phosphate (51.2%). Diabetes was found to have a positive causal association for recurrent stones, 74.1% were found to be diabetic. However, it was found that insulin therapy is associated with a lower risk of stone recurrence. Previous urinary tract surgeries and genitourinary tuberculosis were also found to be a risk factor for recurrence. Descriptive statistics was represented as frequency tables and histogram graph.

Conclusion: Recurrent renal calculus formation is a multifactorial disease with a male preponderance. Metabolic evaluation with stone analysis is mandatory for all recurrent stone formers.

Keywords: Kidney stone disease, Metabolic, Recurrent renal calculus

INTRODUCTION

Kidney stone disease is one of the most common conditions in general population, with a lifetime prevalence estimated at 1% to 15% worldwide [1]. The prevalence in India is approximately 12%, especially in North India, where it rises to 15% [2]. It is a multifactorial disease affected by age, gender, lifestyle and genetics, It is three times more common in men, especially in age group of 40-59 years.

Renal stones have multiple metabolic and genetic causes. In first-time stone formers, these factors are usually not analysed in detail. However, a 13-year hospital-based case study done in India observed that approximately 98% of patients developed a recurrent stone within 25 years of the first episode [3]. Once recurrence occurs, the subsequent relapse risk was raised and the intervals between recurrences shortened, as pointed out in that study. Hence, there developed a necessity to analyse the various causative factors for stones through metabolic evaluation and stone analysis. Currently, these tests are indicated mostly for recurrent stone formers and paediatric patients. A global study done in 2018 by Shin S et al. , for the various confounding factors for stone formation found that, out of the various types of renal stones, calcium oxalate stones form majority of type of recurrent stones 60%, followed by phosphate stones at 30%, uric acid stones 5-10% and cysteine stones 1-3% [4].

Many studies are currently done to assess the various risk factors of stone recurrence. Certain chronic conditions, like diabetes, hypertension and chronic kidney disease, were found as confounding factors to the stone formation and research is going on whether their actual impact on recurrence. Several studies have reported the association between diabetes and the development of kidney stones, with the main pathophysiology involving insulin resistence, prolonged hyperglycemia and glycosuria [5]. Hypertensive patients have a greater risk of renal stone formation, especially when associated with obesity and increased consumption of salt and animal proteins. In hypertensive men and women, oxaluria and calciuria are higher compared to the normotensive [6].

MATERIALS AND METHODS

A retrospective descriptive study was conducted in the Department of Urology at Meenakshi Medical College, Kanchipuram, Tamil Nadu, India, from May 2022 to April 2024. Data analysis was done in May 2024. Ethical approval from the institution (MMCH & RI IEC/ PG/35/ MAY/24) was obtained. As this was an observational data collection study with no hypothesis testing, formal calculation of sample size and statistical power was not performed.

Inclusion criteria: A total of 116 cases of recurrent renal calculi (treated both inpatient and outpatient) were included.

Exclusion criteria: All patients who were first time stone formers were excluded.

Study Procedure

A recurrent stone former was defined as a patient who presents with symptomatic urinary tract stone plus a significant past history of a previous stone formation. This includes a history of passing a stone, presence of a stone on a previous Computed Tomography (CT) scan or ultrasound, history of operation for urinary tract stone.

The following parameters were evaluated: sex, age, duration of previous stone, stone analysis findings, history of diabetes, history

of hypertension and history of tobacco use/smoking and alcohol consumption for more than 10 years.

STATISTICAL ANALYSIS

Descriptive statistics with calculation of maximum number of occurrences of each parameter, was assessed and was represented as frequency tables and histogram graph.

RESULTS

Out of 116 cases, 79 were male (68.1%) and 37 were female (31.9%). Majority of patients were in the age group of 31-50 years (48.8%), followed by age 51-70 years (34.5%) [Table/Fig-1].

Age	Males	Females	n (%)
19-30 years	9	6	15 (12.9)
31-50 years	37	19	56 (48.8)
51-70 years	30	10	40 (34.5)
>70 years	3	2	5 (3.8)

[Table/Fig-1]: Age distribution of the patient.

It was found that 41.3% (48 patients) had a recurrence of stone within 1-5 years of previous presentation, followed by 31.8% (37 patients) within 5-10 years of their previous presentation [Table/Fig-2].

Duration of previous stone	Male	Female	n (%)
Less than 1 year	7	4	11 (9.7%)
1-5 years	36	12	48 (41.3%)
5-10 years	24	13	37 (31.8%)
More than 10 years	12	8	20 (17.2%)

[Table/Fig-2]: Distribution of patients regarding duration of previous stone. N=116

Out of the 116 patients, 86 (74.1%) were found to be diabetic. A total of 18 patients were on insulin therapy (20.9%), while the remaining were on oral hypoglycemic agents. A total of 80 out of 86 patients were diagnosed diabetes for more than five years and was on treatment. Contrastingly, only 24 patients out of 116 (20.6%) were diagnosed of hypertension, out of which 11 were on treatment for more than five years on dual antihypertensives.

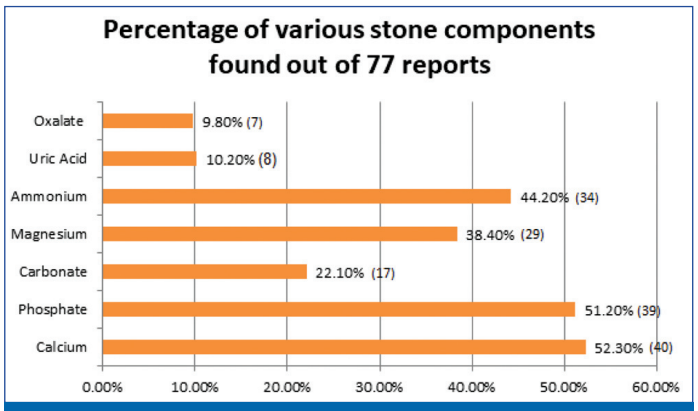
Patients with history of continuous alcohol and nicotine consumption (in the form of smoking or oral tobacco) for more than five years were documented. A total of 38 out of 116 patients (32.7%) had chronic history of nicotine exposure and 39 out of 116 patients (33.7%) had history of alcohol consumption.

In the present study, of 116 patients, only 12 (10%) were managed conservatively with medical expulsion therapy. The remaining patients underwent surgical management of stones, depending upon position and size of stone and surgeon's preference. The most common procedure done was Ureteroscopic Lithotripsy (URSL) at 35.5%, followed by Percutaneous Nephrolithotomy (PCNL) at 30.1%. [Table/Fig-3] shows the different surgical procedures done on the patients.

Stone analysis were sent for 77 patients (66.3%) out of the 116. In patients who were managed conservatively and in some patients who had underwent ureteroscopic pneumatic lithotripsy and laser lithotripsy, stone analysis could not be done as stone could not retrieved or had been expelled out. Most common component found in analysis was calcium (52.3%), followed by phosphate (51.2%) [Table/Fig-4].

S.No.	Type of Procedure	n (%)
1	Ureteroscopic Lithotripsy (URSL)	41 (35.3)
2	Retrograde Intrarenal Surgery (RIRS)	11 (9.4)
3	Percutaneous Nephrolithotomy (PCNL)	35 (30.1)
4	Cystolithotripsy	13 (11.2)
5	Open cystolithotomy	1 (0.86)
6	Open pyelolithotomy	2 (1.72)
7	Open ureterolithotomy	1 (0.86)

[Table/Fig-3]: Various procedures done for the patients.



[Table/Fig-4]: Chart showing data on various stone components.

There were other significant past history findings noted in some patients. A total of 11 out of 116 patients (9.4%) were found to have history of tuberculosis (pulmonary and extrapulmonary) for which they had undergone a full course of anti-tubercular therapy.

DISCUSSION

Men are found to have greater incidence and prevalence rate of recurrent renal stones than women. This male preponderance is observed in recent studies, like Chew Ben H et al. in 2024, (where the prevalence of 53.6% in males [7]. This difference may be due to anatomical differences in the urinary tract of males and females, as postulated in a study by Muhbes FJ [6]. Due to the long urethra in men, there is stagnation and accumulation of urine in the bladder, resulting in stone formation.

In the present study, it was found that majority of the patients had recurrent stones between age groups 31 to 50 years. This finding is consistent with an Iranian study by Kalani L et al., which found the mean age of stone recurrence among 519 patients to be 47.2 years [8]. The reason posited is that majority of patients who turn up to the hospital and get evaluated were falling under this age group, hence more procedures and more analysis get done in this age bracket.

Recurrence of Kidney Stone (ROKS) nomogram data, created from the Rochester Epidemiology Project and studied from 1984 to 2003, showed symptomatic recurrence rates after the initial stone event at the following time points: 11% in two years, 20% in five years, 31% in 10 years and 39% in 15 years [9]. The nomogram can individualise the risk of symptomatic recurrence at 10 years for most patients, ranging from 12% for the lowest-risk quintile to 56% for the highest-risk quintile.

As per recent study from Germany by Siener R et al., the maximum prevalence of recurrent calcium oxalate stones was noted at 71.4%, followed by carbonapatite stones at 10.2% and uric acid stones at 8.3% [10]. A high-volume centre study done in China in 2021 by Zhang S et al. indicated that calcium oxalate (CaOx) and uric acid (UA) stones were more commonly encountered in men, but calcium phosphate (CaP), Magnesium Ammonium Phosphate (MAP) and Carbonate Apatite (CA) stones were more prevalent in women [11]. In a recent global study by Halinski A et al. examining stone composition across different regions, calcium-containing stones were the most common in all countries, ranging from 43% to 91%. Oxalate stones were more common than phosphate or mixed phosphate/oxalate stones in most countries, except Egypt and India. The rate of uric acid-containing stones varied from 4% to 34%, being higher in countries such as Egypt, India, Pakistan, Iraq, Poland and Bulgaria. Struvite stones occurred in less than 5% in all countries, except in India (23%) and Pakistan (16%) [12].

In India, Saurashtra region is considered as the stone belt, with maximum incidence of calcium oxalate stones (75%), followed by calcium phosphate (15%) and uric acid stones (7%), based on a recent 2020 study by Shah P and Patel A [13]. However, in the present study, there was more of calcium ammonium phosphate stones (struvite stones) was found rather than oxalate stones. The reason posited is that such patients may have an indolent urinary tract infection in the form of asymptomatic bacteriuria, which could have led to the formation of infected stones. However, the authors could not get data on the urine culture reports of all these patients and hence could not elaborate on why these stone compositions were predominant in this cohort compared to other studies.

Several studies reported the association between diabetes and recurrent renal stones. A retrospective cohort multivariate analysis done by Prasanchaimontri P and Monga M on the predictive factors for stone recurrence in Type 2 Diabetes revealed that body mass index, urinary pH, glycosylated haemoglobin levels, presence of microangiopathy, insulin therapy and potassium citrate therapy were all significant predictors of stone recurrence, with a median time to recurrence of 64 months [14]. It was also found that insulin therapy is specifically associated with a lower risk of stone recurrence. This is comparable to the present study, where only 21% of the diabetic patients were on insulin therapy. Certain studies like Lange JN et al., have also found that diabetic stone formers have increased urinary calcium, phosphate and oxalate excretion [15]. Consequently, they tend to have more acidic urine, leading to development of uric acid stones [16]. Chronic diabetic nephropathy also leads to defects in renal ammoniagenesis, causing hypocitraturia, which is an important risk factor for calcium stone formation.

A study by Alexander RT et al., which compared various antihypertensives and their risk for stone recurrence, found that thiazides were associated with a lower risk of kidney stones (Hazard Ratio (HR) 0.76; 95% Confidence Interval (CI) 0.68-0.84), while Angiotensin-Converting Enzyme Inhibitors (ACE) inhibitors/ Angiotensin II Receptor Blockers (ARBs) showed a borderline decreased risk (HR 0.90; 95% CI 0.83-0.98) and calcium channel blockers were associated with a comparable risk (HR 1.02; 95% CI 0.92-1.13) [17]. However, the present study could not provide any significant results, as there were only 24 patients who were known to be hypertensive.

A study by Chmiel JA et al. regarding the association between tuberculosis and stone disease postulated that there is enhanced oxidative stress and increased levels of lipid peroxidation in patients on anti-tubercular therapy, causing membrane disintegrate in nephrons favoring the retention of microliths. This can be prevented by administering Vitamin E in such patients, as told in that study [18].

Recurrent bladder calculi are formed secondary to Bladder Outlet Obstruction (BOO), most commonly due to benign prostatomegaly. Transurethral resection Of Prostate (TURP) has a protective effect in preventing recurrence. A study by Mekke S et al. showed that there is a risk reduction of 72% in need for re-cystolithotripsies when TURP is operated along with first-time bladder stone formers [19]. However, despite medical or surgical management of prostatism, recurrences can occurs when there is underlying BOO due to neurogenic bladder. In the present study, six patients who had previously undergone TURP experienced a recurrence of bladder calculi. Post-surgery, urodynamic assessments were conducted for those patients and was found to have functional BOO; they are on regular follow-up and medical management.

The role of smoking as an independent risk factor for recurrent stones is still controversial. Logistic regression analysis done in an Iranian study by Tamadon showed that smoking was significantly associated with urinary stones (OR= 2.06, 95% CI: 1.06-4.01, P= 0.034) [20]. Several theories were explained in that study regarding the pathogenesis. It was proposed that increased serum cadmium levels associated with cigarette smoking may be a risk factor for calculus. Significant increases in plasma arginine vasopressin levels associated with cigarette smoking may further decrease urinary output and trigger stone formation. Alcohol consumption is not significantly associated with the prevalence of kidney stones. As per logistic regression analysis done by Zhou Z et al., using National Health and Nutrition Examination Survey (NHANES) datasets of nine years, there was no significant association between the amount and frequency of alcohol consumption and the prevalence of kidney stones, even among heavy drinkers [21]. The present study also does not provide any concrete association between smoking or alcohol consumption and recurrent renal stone due to lack of significant number of patients with positive history. A long-term, multicentric, prospective analytical study with multiple variables related to metabolic evaluation is ideal to be conducted in a large population to provide a more systematic approach to evaluating the various risk factors for stone recurrence.

Limitation(s)

It was a retrospective study done with only limited patients in a short stipulated time period. It is only a descriptive study without any quantitative variable to substantiate a causal association with a risk factor. There are no reports on the individual complete metabolic evaluation of the patients, which is a significant lacuna in the present study, especially considering risk factors of recurrence. The authors reason for that is that metabolic evaluation for stone formers is supposed to be done after six weeks of stone clearance. Those patients were lost to follow-up after being discharged from hospital (or following the removal of the Double-J stent). Certain variables such as smoking and alcohol consumption, failed to demonstrate any definitive causal association with stone recurrence due to low sample size, restricted time period and retrospective recall bias.

CONCLUSION(S)

Recurrent renal calculus formation is a multifactorial disease. It is more common in males, especially in the fourth decade of life. The majority of recurrences occur within 10 years of the first episode. Metabolic evaluation, along with stone analysis, is mandatory for all recurrent stone formers. In India, struvite stones secondary to chronic urinary infection and uric acid stones are the most common types of recurrent stones. Early detection of plausible risk factors in the first stone episode, combined with adequate preventive measures, will help prevent recurrences in the near future.

Acknowledgement

The authors thank the medical records department of Meenakshi Medical College for the conduct of the retrospective study

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 17, 2024
- Manual Googling: Mar 10, 2025
- iThenticate Software: Mar 12, 2025 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 16, 2024**
Date of Peer Review: **Dec 04, 2024**
Date of Acceptance: **Mar 14, 2025**
Date of Publishing: **May 01, 2025**