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Association Between Serum Uric Acid and Uric Acid Composition of Urinary Stones: An Observational Study

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Type of Publication: Original Research Article

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Abstract

Introduction: Uric acid is an important contributor to urinary stone formation and is associated with metabolic and dietary risk factors. However, the relationship between serum uric acid levels and uric acid content of urinary stones remains incompletely defined.

Methodology: A cross-sectional observational study was conducted from November 2024 to October 2025 at KPC Medical College, Kolkata, involving 70 patients aged 18–80 years with urolithiasis. Surgically retrieved stones were processed and analyzed for biochemical composition using standard methods. Serum uric acid

was estimated, and correlation with stone uric acid content was assessed.

Results: The mean age was 45.57 ± 17.17 years, with a male predominance (47 males, 23 females). Mean BMI was 27.24 ± 4.14 kg/m² and mean stone weight was 2.93 ± 2.55 g. The mean uric acid content of stones was 1.40 ± 1.11 g, while mean serum uric acid was 5.86 ± 1.62 mg/dL. Serum uric acid showed a positive, and statistically significant correlation with stone uric acid content ($r = 0.63$, $p < 0.001$).

Conclusion: Serum uric acid was significantly associated with the uric acid content of urinary stones, suggesting that systemic uric acid status may contribute to uric acid stone formation. Serum uric acid may therefore serve as a useful metabolic marker in patients with uric acid-containing urolithiasis.

Keywords: Urolithiasis; Uric acid stones; Serum uric acid; Stone composition; Metabolic risk factors.

Introduction

Urolithiasis, derived from the Greek words “ouron” (urine), “oros” (flow), and “lithos” (stone), refers to the formation of calculi within the urinary tract [1]. It affects approximately 12% of the global population [2], with a comparable prevalence in India and rates of up to 15% reported in northern regions [3,4]. Urolithiasis is a multifactorial disorder resulting from the complex interaction of genetic predisposition, metabolic abnormalities, dietary habits, and environmental factors, and is increasingly recognized as a potential marker of underlying metabolic and cardiovascular disorders. Clinically, it commonly presents with acute flank pain, abdominal discomfort, or haematuria, significantly affecting quality of life. Stone formation is primarily associated with low urine volume and increased urinary concentrations of stone-forming constituents such as calcium, oxalate, uric acid, and phosphate, along with reduced levels of natural inhibitors such as citrate [5–7]. These conditions promote urinary supersaturation, leading to crystal nucleation, growth, and aggregation within the renal system. Although a single episode may not cause permanent damage, recurrent stone formation can result in progressive renal injury through tubular obstruction, inflammation, and renal epithelial cell damage, potentially contributing to declining kidney function. Therefore, early diagnosis and appropriate management are essential to prevent recurrence and long-term complications. Management depends on the size, composition, and location of the stone; smaller stones may pass spontaneously with conservative treatment, whereas larger or obstructive stones often require intervention. Procedures such as extracorporeal shock wave lithotripsy (ESWL) and percutaneous nephrolithotomy are commonly employed, particularly in complicated cases, including those associated with infections such as pyonephrosis [8].

The aim of the study is to investigate the relationship between serum uric acid levels and uric acid content in urinary stones, and to evaluate whether serum uric acid serves as a reliable indicator of uric acid stone burden in patients with urolithiasis.

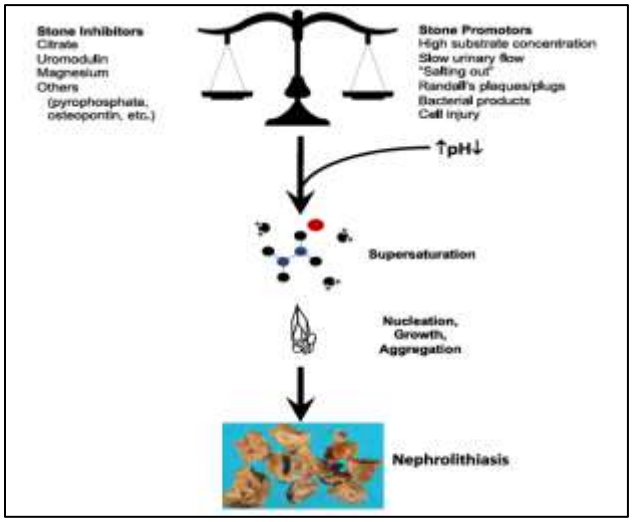
Background

Urolithiasis develops when urinary solutes crystallize and aggregate to form stones. Several factors may contribute to this process, including anatomical abnormalities causing urinary stasis, inadequate fluid intake, diets rich in oxalate or sodium, urinary tract infections, systemic acidosis, certain medications, and, rarely, inherited disorders such as cystinuria [9,10]. Approximately 75%–85% of kidney stones are calcium-based, predominantly composed of calcium oxalate in

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monohydrate or dihydrate forms or calcium phosphate. Other common types include uric acid stones (8%–10%), struvite stones (calcium magnesium ammonium phosphate; 7%–8%), and cystine stones (1%–2%), with uric acid and cystine stones showing a greater tendency for recurrence [11]. Low urine volume and inadequate hydration are important contributors to stone formation. The major urinary risk factors include increased excretion of calcium (hypercalciuria), oxalate (hyperoxaluria), and uric acid (hyperuricosuria), along with decreased citrate excretion (hypocitraturia) [12,13]. Certain medications, including atazanavir, guaifenesin, indinavir, silicate, sulfonamides, and triamterene, may further increase the risk of urinary stone formation [14–20]. Genetic factors may also contribute, as familial mutations can impair renal regulation of calcium and other stone-forming substances, thereby increasing susceptibility to urolithiasis [11,21]

Figure 1: Overview of the pathogenesis of urolithiasis/nephrolithiasis [22].



Methodology

The study was conducted in the Department of Biochemistry in collaboration with the Department of Urology at KPC Medical College, Jadavpur, Kolkata, India. The study was carried out over a one-year period from November 2024 to October 2025, following approval from the Institutional Ethics Committee of KPC Medical College.

Study Design: A cross-sectional observational study was conducted among patients diagnosed with urolithiasis.

Sample Size: A total of 70 patients with urolithiasis were recruited from the Department of Urology. The sample size was determined based on the reported prevalence of urinary stone disease in India[4].

Selection of Study Subjects: Patients of either sex, aged 18–80 years, with diagnosed urinary stone disease, irrespective of symptom status, were included. Pregnant or lactating women, patients with malignancies or collagen vascular disorders, critically ill or unconscious individuals, those younger than 18 or older than 80 years, and patients unwilling to provide informed consent were excluded.

Data Collection and Laboratory Procedures: Urinary stones were collected from the Urology Operation Theatre following surgical removal, after obtaining informed consent from the patients or their relatives and approval from the operating surgeon. The retrieved stones were washed thoroughly with water to remove adherent blood and tissue debris and subsequently dried using filter paper. Their physical characteristics, including size, shape, and weight, were recorded. The stones were then crushed into a fine powder (Fig. 2), which was subjected to qualitative analysis using standard biochemical techniques in the Postgraduate Biochemistry Laboratory of KPC Medical College [23].

For quantitative analysis, 20 mg of powdered stone was dissolved in 2 mL of 50% hydrochloric acid (HCl; v/v) with gentle warming and subsequently diluted to 10 mL in a volumetric flask [24]. The resulting solution was used

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for quantitative estimation of stone constituents, including uric acid, using standard colorimetric biochemical methods with a UV-visible spectrophotometer. A commercially available standardized uric acid reagent kit was used for the estimation.

Serum uric acid was estimated using a standardized enzymatic uricase–peroxidase (Uricase/PAP) method on a fully automated biochemical analyzer (DIASYS 400). The reference range was considered according to the manufacturer's specifications.

Figure 2: Urinary stone collection and processing for analysis:

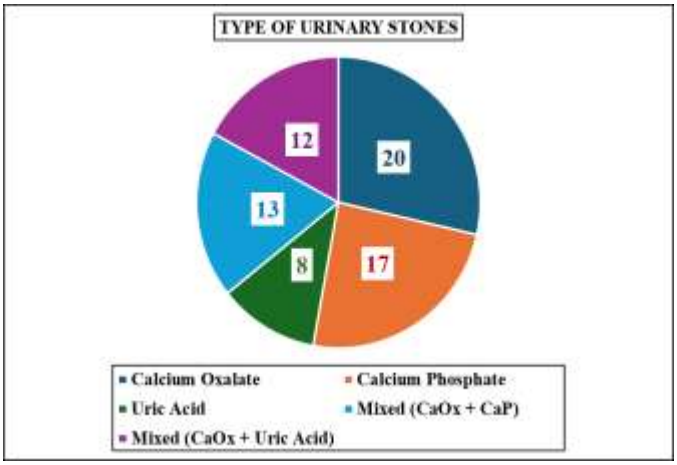


1. Urinary stone (A large urinary bladder calculi) was collected after surgical removal.
2. Stone was washed and cleaned
3. Instruments for measurement and pounding of stones.
4. Measurement of a urinary calculi by electronic calliper
5. Stone dust was collected in containers for analysis after pounding

Statistical analysis: Statistical analysis was performed using IBM SPSS version 23. The online free social science statistics calculator was also used.

Result:

Figure 3: Description of type of urinary stones (n=70)



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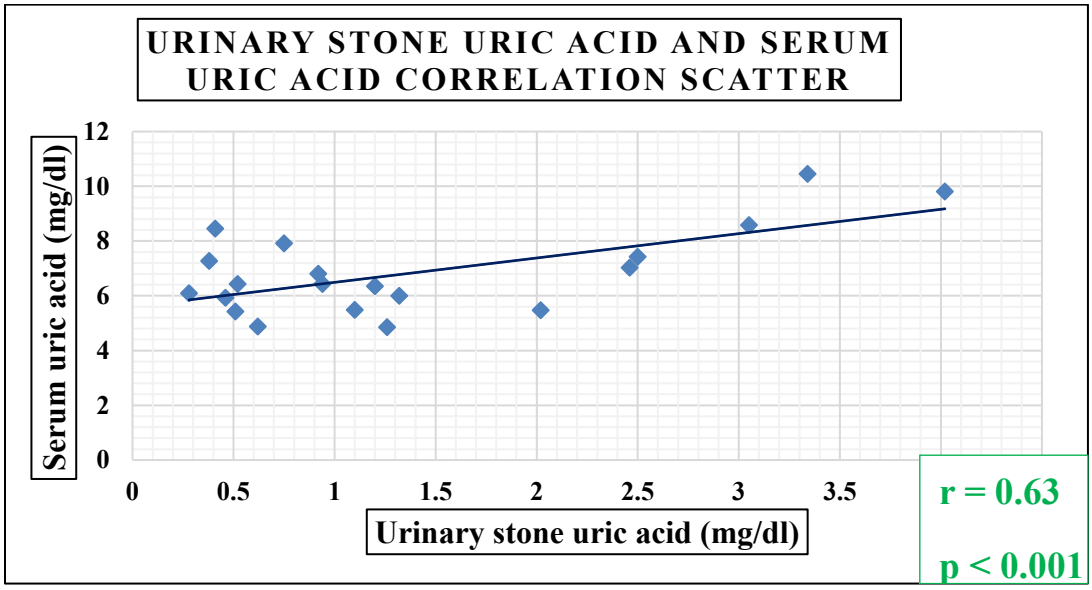
Table 1: Description of clinical and biochemical parameters of cases (n=70).

Variables	Cases (n=70), MEAN ± SD
Age (in years)	45.57 ± 17.17
Gender (M/F)	47/23
BMI (kg/m2)	27.24 ± 4.14
Weight of urinary stone (gm)	2.93 ± 2.55
Weight of uric acid in stone (gm)	1.40 ± 1.11
Serum uric acid (mg/dL)	5.86 ± 1.62

Table 2: Distribution of Urinary Stones According to Body Mass Index (BMI) (n=70)

BMI→	Underweight < 18.5	Normal 18.5 – 24.9	Overweight 25 – 29.9	Obese ≥ 30
Number of urinary stones	0	19	29	22

Figure 4: Urinary; stone uric acid and serum uric acid correlation scatter



The study included 70 patients with urolithiasis, Uric acid-containing stones were identified in 20 cases, comprising 8 cases of pure uric acid stones and 12 cases of mixed uric acid–calcium oxalate stones. with a mean age of 45.57 ± 17.17 years and a male predominance (47 males, 23 females). The mean BMI was 27.24 ± 4.14 kg/m², with a higher proportion of patients being overweight (n=29) or obese (n=22). The mean urinary stone weight was 2.93 ± 2.55 g, with a mean uric acid content of 1.40 ± 1.11 g. The mean serum uric acid level was 5.86 ± 1.62 mg/dL. The correlation (pearson) between urinary stone uric acid content and serum uric acid showed a strong positive relationship ($r = 0.63$, $p < 0.001$), indicating statistically significant association between these parameters.

Discussion

In the present study, calcium-containing stones, particularly calcium oxalate stones, were the predominant type, in agreement with previous reports indicating that calcium stones account for approximately

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75–85% of urinary calculi. This predominance may be attributed to metabolic abnormalities such as hypercalciuria and hyperoxaluria, along with dietary and environmental influences [25]. The age distribution showed that urolithiasis was more common among middle-aged individuals, with a mean age of approximately 45 years, consistent with the reported peak incidence during the third to fifth decades of life [26]. A clear male predominance was observed, which is consistent with global patterns and may be related to differences in lifestyle and hormonal factors, although this gender disparity appears to be narrowing. Testosterone has been proposed to promote stone formation, whereas estrogen may exert a protective effect by increasing urinary citrate excretion [27]. Another notable finding was the higher proportion of overweight and obese individuals among patients with urolithiasis. Obesity may increase the risk of stone formation through mechanisms including insulin resistance, altered renal handling of calcium and uric acid, and reduced urinary pH [27].

The uric acid content of urinary stones demonstrated a strong positive correlation with serum uric acid levels ($r = 0.63$, $p < 0.001$), indicating a statistically significant association between systemic uric acid status and the uric acid composition of urinary stones. This finding is biologically plausible because increased circulating uric acid can result in greater renal uric acid filtration and urinary excretion, thereby increasing urinary urate concentration and the potential for supersaturation. However, the formation of uric acid stones is influenced not only by the total amount of uric acid excreted but also by urinary pH and urine volume. Persistently acidic urine markedly reduces uric acid solubility, favouring conversion of soluble urate to poorly soluble undissociated uric acid and promoting crystal nucleation and aggregation. Low urinary volume further increases urinary uric acid concentration and enhances supersaturation, thereby facilitating stone formation.

Conclusion

This study demonstrates that urolithiasis is more common among middle-aged individuals, with a clear male predominance and a higher frequency among overweight and obese patients, highlighting the contribution of metabolic and lifestyle factors. A key finding was the significant positive correlation between serum uric acid levels and the uric acid content of urinary stones, suggesting an association between systemic uric acid status and uric acid stone burden. These findings emphasize the importance of assessing serum uric acid as part of the metabolic evaluation of patients with uric acid-containing urolithiasis. However, stone formation is influenced by multiple factors, particularly urinary pH, urine volume, and urinary uric acid excretion. Therefore, comprehensive metabolic evaluation, including appropriate urinary analysis, dietary assessment, and monitoring of serum uric acid, may aid in the prevention, early identification, and management of uric acid stone disease.

Limitations

This study has several limitations that should be considered. The relatively small sample size and single-center design may limit the generalizability of the findings to a broader population. As the study was cross-sectional in nature, a causal relationship between serum uric acid levels and uric acid content of urinary stones cannot be established. Furthermore, important urinary parameters, including 24-hour urinary uric acid excretion, urinary pH, urine volume, and citrate levels, were not assessed, which could have provided a more comprehensive understanding of uric acid stone

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formation. Dietary intake, particularly purine and animal-protein consumption, as well as other lifestyle factors, were not evaluated in detail.

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