## Comparative Analysis of Stone Composition and Risk Factors in First-Time vs Recurrent Urinary Stone Formers: A Prospective Study of 200 Cases

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# Abstract

**Background:** Urinary stone disease is a prevalent urological condition with high recurrence rates. Identifying differences in stone composition and associated risk factors between first-time and recurrent stone formers is essential for targeted prevention.

**Objective:** To compare stone composition patterns and clinical, metabolic, and lifestyle risk factors in first-time versus recurrent urinary stone formers.

**Methods:** This prospective observational study  included 200 patients presenting with upper urinary tract calculi over 24 months from JAN 2023 to JAN 2025 conducted in department of urology, Stanley medical College, chennai. Patients were categorized into **first-time (n = 120)** and **recurrent stone formers (n = 80)**. All patients underwent standardized metabolic evaluation and stone analysis using Fourier-transform infrared spectroscopy (FTIR). Demographic, biochemical, radiological, and clinical data were recorded and compared.

**Results:** Calcium oxalate was the predominant stone type in both groups, but mixed calcium oxalate–phosphate stones were significantly higher in recurrent stone formers (45% vs 28%, p = 0.01). Hyperoxaluria (32.5% vs 18.3%, p = 0.02), hypocitraturia (40% vs 22.5%, p = 0.01), and hyperuricosuria (21.3% vs 10.8%, p = 0.04) were more common in recurrent cases. Recurrent patients had higher mean BMI (27.1 ± 3.8 vs 25.2 ± 3.4 kg/m², p = 0.001) and family history of stones (31% vs 14%, p = 0.004). Multivariate analysis showed hypocitraturia, hyperoxaluria, and family history as independent predictors of recurrence.

**Conclusion:** Recurrent stone formers demonstrate a higher prevalence of metabolic abnormalities and mixed-composition stones. These findings highlight the importance of rigorous metabolic evaluation and individualized preventive strategies to reduce recurrence.

**Keywords:** renal stone, urolithiasis, recurrence, stone composition, metabolic abnormalities, FTIR.Introduction

Urolithiasis affects 12–15% of the global population, with recurrence rates approaching 50% within 5 years. Understanding differences between first-time and recurrent stone formers may guide personalized treatment and preventive measures. While stone composition plays an important role in recurrence risk, metabolic abnormalities such as hyperoxaluria, hypercalciuria, hypocitraturia, and hyperuricosuria significantly influence stone formation.

This study prospectively compares stone composition, clinical characteristics, and metabolic risk factors in first-time versus recurrent urinary stone formers in a tertiary care center.

# Materials and Methods

## Study Design

Prospective observational study conducted over 24 months at a tertiary urology department.

## Sample Size

Total: **200 patients**
• First-time stone formers: **n = 120**
• Recurrent stone formers: **n = 80**

## Inclusion Criteria

- Adults aged 18–70 years
- Radiologically confirmed upper urinary tract stones
- Stone fragments retrieved surgically or spontaneously passed

## Exclusion Criteria

- CKD stage ≥ 4
- Urinary tract anomalies
- Primary hyperparathyroidism
- Cystinuria or struvite stones in isolation
- Pregnancy

## Clinical Evaluation

- Detailed history
- BMI, family history
- Dietary and fluid intake
- Comorbidities: diabetes, hypertension, metabolic syndrome

## Laboratory Evaluation

- Serum calcium, uric acid, creatinine, electrolytes
- 24-hour urine analysis: calcium, oxalate, uric acid, citrate, sodium, volume
- Urinalysis & culture

## Stone Analysis

Performed using **FTIR spectroscopy**.

## Statistical Analysis

SPSS v23 used.
$p < 0.05$ considered significant.
Multivariate logistic regression performed to identify recurrence predictors.

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# Results

## 1. Demographics

| Parameter | First-Time (n=120) | Recurrent (n=80) | p-value |
|---|---|---|---|
| Mean age (years) | 41.2 ± 11.5 | 43.8 ± 10.9 | 0.12 |
| Male:Female | 2.1:1 | 2.4:1 | 0.48 |
| BMI (kg/m$^2$) | 25.2 ± 3.4 | **27.1 ± 3.8** | **0.001** |
| Family history | 14% | **31%** | **0.004** |

## 2. Stone Composition

| Stone Type | First-Time (%) | Recurrent (%) | p-value |
|---|---|---|---|
| Calcium oxalate monohydrate | 42 | 35 | 0.28 |
| Calcium oxalate dihydrate | 18 | 12 | 0.21 |
| Mixed CaOx + CaP | 28 | **45** | **0.01** |
| Uric acid | 8 | 5 | 0.42 |
| Struvite | 4 | 3 | 0.78 |

## 3. Metabolic Abnormalities

| Abnormality | First-Time (%) | Recurrent (%) | p-value |
|---|---|---|---|
| Hyperoxaluria | 18.3 | **32.5** | **0.02** |
| Hypercalciuria | 16.6 | 22.5 | 0.18 |
| Hypocitraturia | 22.5 | **40** | **0.01** |
| Hyperuricosuria | 10.8 | **21.3** | **0.04** |
| Low urine volume (<1.5 L/day) | 36.7 | 41.3 | 0.51 |

## 4. Logistic Regression

Independent predictors of recurrence:

- **Hypocitraturia** (OR 2.2, p = 0.02)
- **Hyperoxaluria** (OR 1.9, p = 0.03)
- **Family history** (OR 2.8, p = 0.01)

## Figure 1: Stone Composition Comparison
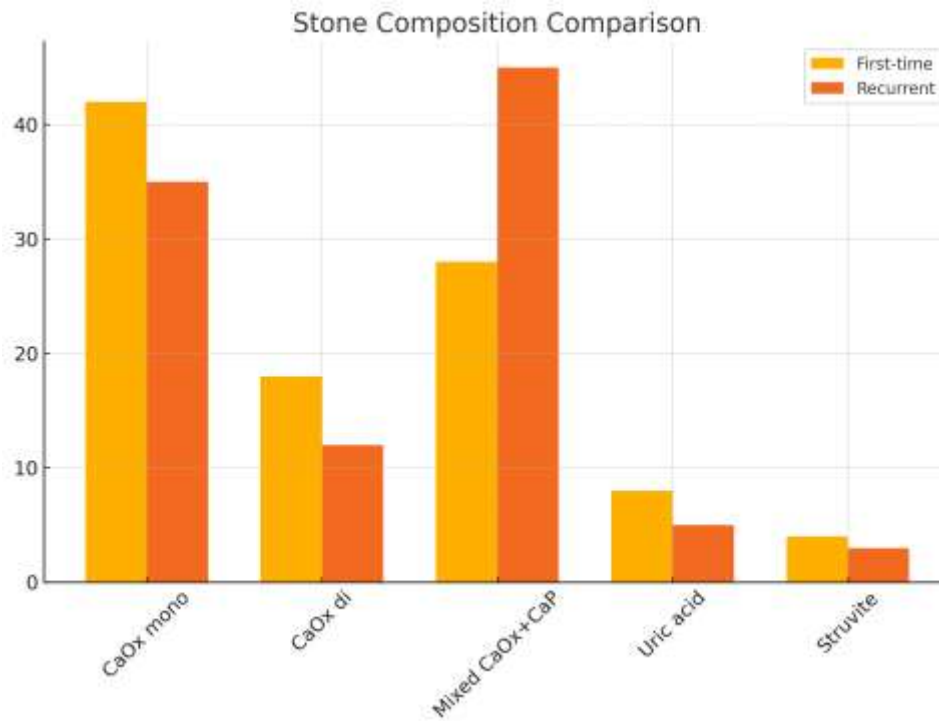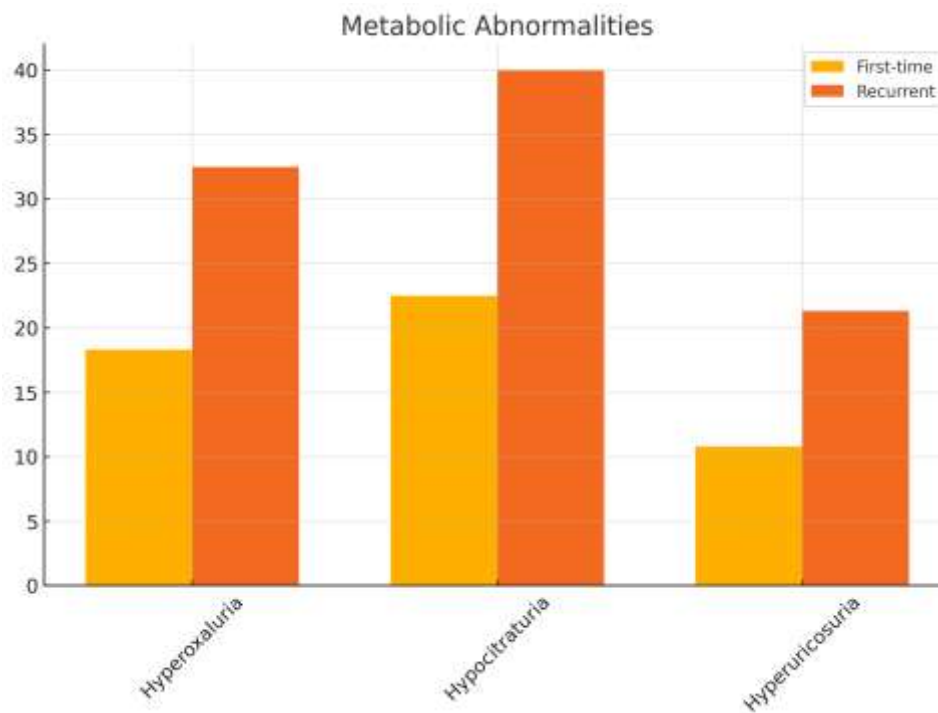


Stone Composition Comparison

## Figure 2: Metabolic Abnormalities



# Discussion

The present prospective study provides a comprehensive comparison between first-time and recurrent urinary stone formers, highlighting several clinically significant differences in stone composition, metabolic abnormalities, and patient characteristics. These findings reinforce the multifactorial nature of urolithiasis and emphasize the importance of individualized evaluation and prevention strategies.

**Stone Composition Patterns**

Calcium oxalate (CaOx) remained the most common stone type in both first-time and recurrent patients, consistent with epidemiological data from global and Indian cohorts. However, a notable finding in this study is the significantly higher prevalence of mixed calcium oxalate–calcium phosphate (CaOx+CaP) stones among recurrent stone formers. Mixed stones have been associated with persistent metabolic derangements, higher urinary pH, suboptimal dietary habits, and inadequate preventive strategies after the first stone episode.

The increased proportion of mixed stones in recurrent patients may also reflect the progressive crystallization phenomenon, where recurrent stone formers show a gradual shift from pure CaOx stones toward mixed compositions due to chronic subclinical metabolic imbalance. This progression is well documented in long-term metabolic studies, suggesting that mixed stones may serve as an early indicator of impending recurrence.

**Metabolic Abnormalities and Recurrence**

Metabolic evaluation revealed significant differences between the two groups. Recurrent stone formers exhibited higher rates of:

Hypocitraturia

Hyperoxaluria

Hyperuricosuria

These abnormalities are known critical drivers of lithogenesis.

Hypocitraturia

Citrate acts as a potent chelator of calcium, binding free calcium ions, reducing supersaturation, and inhibiting crystal aggregation. The significantly higher hypocitraturia observed in recurrent stone formers aligns with previous studies indicating that citrate deficiency is one of the strongest predictors of recurrence. Hypocitraturia may result from chronic dehydration, high sodium intake, persistent metabolic acidosis, or underlying renal tubular disorders. This finding underscores the need for early intervention with potassium citrate supplementation and diet modification.

Hyperoxaluria

Hyperoxaluria was notably higher in recurrent stone formers, contributing to increased CaOx supersaturation. The cause is usually multifactorial—dietary oxalate excess, low calcium intake, fat malabsorption, or genetic predisposition. Persistent hyperoxaluria suggests inadequate lifestyle modification or poor adherence to dietary advice after the initial stone episode, highlighting the need for structured dietary counseling.

Hyperuricosuria

The higher incidence of hyperuricosuria in recurrent patients supports the known role of uric acid crystals as heterogeneous nucleators, accelerating CaOx stone formation. This finding supports consideration of allopurinol in appropriate subsets of patients with recurrent stones.

Absence of Significant Hypercalciuria Differences

Although hypercalciuria was slightly higher among recurrent patients, the difference was not statistically significant. This trend is consistent with several contemporary studies suggesting that hypercalciuria alone may not distinguish recurrence risk unless accompanied by other metabolic abnormalities such as low citrate or high oxalate levels.

**Obesity and Lifestyle Factors**

The significantly higher BMI in recurrent stone formers indicates a strong interplay between metabolic syndrome and stone recurrence. Obesity is associated with:

Increased urinary excretion of calcium, oxalate, and uric acid

Insulin resistance leading to reduced ammoniagenesis and acidic urine

Increased risk of mixed CaOx+CaP stones

These mechanisms explain the higher recurrence rates among overweight individuals. This reinforces the importance of weight reduction and metabolic correction as part of stone prevention protocols.

**Family History and Genetic Predisposition**

Family history emerged as an independent predictor of recurrence, consistent with the genetic heritability of stone formation (estimated at 40–50%). Genetic predisposition influences urinary citrate excretion, oxalate metabolism, and renal tubular transport of calcium, contributing to early and recurrent stone episodes. This finding emphasizes the need for proactive metabolic screening among individuals with a positive family history.

**Clinical Implications**

The findings of this study have several important clinical implications:

1. All recurrent stone formers should undergo complete metabolic evaluation, as selective screening risks missing significant abnormalities.

2. Mixed stones warrant closer follow-up, as their presence strongly indicates metabolic instability.

3. Hypocitraturia and hyperoxaluria should be aggressively corrected to prevent recurrence.

4. Targeted education on hydration, dietary oxalate reduction, and sodium restriction is essential.

5. Patients with high BMI require metabolic counselling, lifestyle advice, and comorbidity screening.

Comparison With International Literature

Our observations are in agreement with major prospective studies from the U.S., Europe, and Asia, which consistently identify hypocitraturia and hyperoxaluria as the strongest predictors of recurrence. The stone composition patterns in our cohort are comparable to those reported in Indian studies, which often note a high prevalence of CaOx stones but a rising incidence of mixed CaOx–CaP stones in recurrent cases.

**Strengths and Limitations**

**Strengths**

Prospective design

Uniform metabolic evaluation

FTIR-based stone analysis for accuracy

Subgroup analysis between first-time vs recurrent cases

**Limitations**

Single-center study

Limited follow-up beyond the immediate postoperative period

Dietary evaluation not quantified using validated tools

Lack of 24-hour urine volume correction for seasonal variation

Future multicenter studies with longer follow-up would help validate these findings and develop tailored recurrence prevention algorithms.

## Conclusion

Recurrent stone formers demonstrate a clearly distinct clinical and metabolic profile marked by a higher prevalence of mixed stones, hypocitraturia, hyperoxaluria, and obesity. These factors play pivotal roles in recurrent stone formation and demand proactive, targeted intervention. Early identification and aggressive correction of metabolic abnormalities, combined with structured patient education, remain the cornerstone of effective long-term stone prevention.

This prospective study highlights distinct differences between first-time and recurrent stone formers. Mixed calcium oxalate–phosphate stones were significantly more common among recurrent stone formers, consistent with increased metabolic instability and repeated stone formation.

Metabolic abnormalities—especially hypocitraturia, hyperoxaluria, and hyperuricosuria—were substantially more prevalent among recurrent patients. Citrate is a well-known natural inhibitor of crystallization, and its deficiency strongly predisposes to stone formation. Similarly, elevated urinary oxalate significantly increases calcium oxalate supersaturation.

The higher BMI among recurrent stone formers aligns with global evidence linking obesity and metabolic syndrome to stone recurrence. Genetic influence, reflected through a higher rate of family history, also emerged as an independent predictor of recurrence.

Overall, these findings underscore the need for **comprehensive metabolic screening** and **tailored preventive therapy**—including dietary modification, adequate fluid intake, potassium citrate therapy (when indicated), and long-term follow-up.

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