e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(7); 60-66

Original Research Article

# Serum Calcium Does Not Reflect Stone Calcium Burden: An Observational Study

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**Received: 27-04-2026 / Revised: 28-05-2026 / Accepted: 29-06-2026**

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**Conflict of interest: Nil**

**Abstract:**

**Introduction:** Urolithiasis is a common and recurrent condition influenced by metabolic, dietary, and environmental factors, with calcium-containing stones accounting for the majority of cases. Although calcium plays a central role in stone formation, the relationship between serum calcium levels and the calcium content of urinary stones remains unclear. This study aimed to evaluate whether serum calcium can serve as a reliable indicator of stone calcium burden in patients with urolithiasis.

**Methodology:** A cross-sectional observational study was conducted over one year (November 2024 to October 2025) at KPC Medical College, Kolkata. A total of 70 patients aged 18–80 years with diagnosed urolithiasis were included. Urinary stones were collected post-surgically, processed, and analyzed qualitatively and quantitatively using standard biochemical methods. Serum calcium levels were estimated using the OCPC method on an full-automated analyzer. Statistical analysis, including Spearman correlation, was performed using SPSS version 23.

**Results:** The study population had a mean age of 45.57 ± 17.17 years, with a male predominance (47 males, 23 females). Most patients were overweight or obese (mean BMI: 27.24 ± 4.14 kg/m²). The mean stone weight was 2.93 ± 2.55 g, with a mean calcium content of 0.74 ± 0.73 g. Serum calcium levels were within the normal range (9.32 ± 0.9 mg/dL). Correlation analysis revealed a very weak negative and statistically insignificant relationship between serum calcium and stone calcium content ($r_s = -0.05$, $p = 0.69$).

**Conclusion:** Serum calcium levels do not correlate with the calcium content of urinary stones and are not a reliable marker for assessing stone burden. These findings highlight that urolithiasis is primarily driven by urinary and metabolic factors rather than systemic calcium levels. Comprehensive metabolic evaluation, particularly urinary analysis, is essential for effective management and prevention of stone disease.

**Keywords:** Urolithiasis, Serum Calcium, Stone Calcium Content, Calcium Oxalate Stones, Metabolic Factors.

**DOI:** 10.25258/ijcpr.18.7.10

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## 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]. This disease affects roughly 12% of the global population [2]. In India, the prevalence is similar, though higher rates of up to 15% have been reported in northern regions of the country [3.4]. Urolithiasis is a multifactorial disorder influenced by a complex interplay of genetic predisposition, metabolic abnormalities, dietary habits, and environmental factors. In recent years, it has also been increasingly recognized as a potential marker of underlying

systemic disorders, including metabolic and cardiovascular diseases. Clinically, urolithiasis most often presents with acute flank pain, abdominal discomfort, or haematuria, significantly impacting patient quality of life. The formation of urinary stones is primarily associated with low urine volume and increased urinary concentration of stone-forming constituents such as calcium, oxalate, uric acid, and phosphate, along with reduced levels of natural inhibitors like citrate [5-7]. These conditions promote supersaturation of urine, leading to crystal nucleation, growth, and aggregation within the renal system. Although a single episode may not result in permanent damage, recurrent stone formation can lead to progressive renal injury by causing tubular obstruction, inflammation, and damage to renal epithelial cells. Over time, this may contribute to a decline in kidney function. Therefore, early diagnosis and appropriate management are essential to prevent recurrence and long-term complications. Management strategies depend on the size, composition, and location of the stone. While smaller stones may pass spontaneously with conservative treatment, larger or obstructive stones often require intervention. Procedures such as extracorporeal shock wave lithotripsy (ESWL) or 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 calcium levels and calcium content in urinary stones, and to evaluate whether serum calcium serves as a reliable indicator of stone calcium burden in patients with urolithiasis.

**Background:** Urolithiasis occurs when substances in the urine crystallize and form stones. This can result from various factors, including anatomical abnormalities that cause urinary stasis, low fluid intake, diets high in oxalate or sodium, urinary tract infections, systemic acidosis, certain medications, or, in rare cases, inherited conditions such as cystinuria [9,10]. The majority of kidney stones (75%–85%) are calcium-based, mostly composed of calcium oxalate—either monohydrate or dihydrate—or calcium phosphate. Other common stone types include uric acid stones (8%–10%), struvite stones (calcium magnesium ammonium phosphate, 7%–8%), and cystine stones (1%–2%). Among these, uric acid and cystine stones are particularly prone to recurrence [11]. Low urine volume and inadequate hydration are major contributors to stone formation. Chemically, four key factors promote stone development: elevated urinary calcium (hypercalciuria), oxalate (hyperoxaluria), or uric acid (hyperuricosuria), and reduced citrate levels (hypocitraturia) [12,13]. Certain medications, such as atazanavir, guaifenesin, indinavir, silicate, sulfonamides, and triamterene, can also increase the risk of kidney stones [14-20]. Genetics may play a role as well, with evidence showing that in some families, mutations can impair the kidney's ability to regulate calcium and other stone-forming substances, increasing susceptibility to stone formation [11,21].

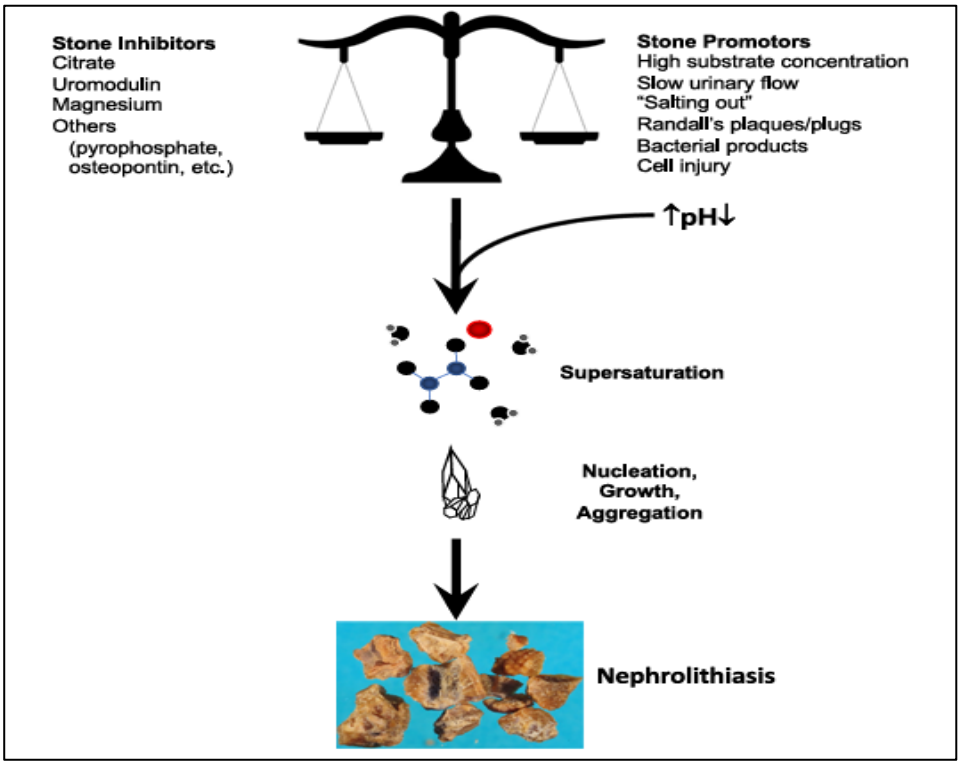


**Figure 1: Overview of the pathogenesis of urolithiasis/nephrolithiasis [22].**

**Methodology:**

This study was conducted in the Department of Biochemistry in collaboration with the Department of Urology at KPC Medical College, Jadavpur, Kolkata, India. The research 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 performed involving patients diagnosed with urolithiasis.

**Sample Size:** A total of seventy (70) patients with urolithiasis were selected from the Urology Department. The sample size was determined based on the reported prevalence of urinary stones in India [4].

**Selection of Study Subjects:**

- **Inclusion Criteria:** Patients of either sex, aged 18–80 years, diagnosed with urinary stone disease, regardless of symptom status.
- **Exclusion Criteria:** Pregnant or lactating women, patients with malignancies or collagen vascular disorders, critically ill or unconscious individuals, patients younger than 18 or older than 80 years, and those who did not provide consent.

**Data Collection and Laboratory Procedures:** Urinary stones were obtained from the Urology Operation Theatre following surgical removal, after informed consent was obtained from the patients or their relatives and approval from the operating surgeon. The stones were washed with water to remove blood and tissue debris and then dried using filter paper. External characteristics, including size, shape, and weight, were recorded.

The stones were then crushed into fine powder (Fig. 2), which was used for subsequent qualitative analysis using standard biochemical techniques in the Postgraduate Biochemistry Laboratory of KPC Medical College [23].

For quantitative analysis, 20mg of the powdered stone will be dissolved in 2ml of 50% HCl (v/v), by warming, and diluted to 10ml in a volumetric flask [24]. This solution is used for further quantitative analysis of the composition of urinary stones by standard biochemical laboratory procedures (colorimetric) by using UV- Spectrophotometer. Commercially available standardized calcium kit was acquired from reagent suppliers.

Estimation of serum calcium was performed by the OCPC method using our fully automated analyzer – DIASYS 400 (reference value - 8.7 -11.0 mg/dl).

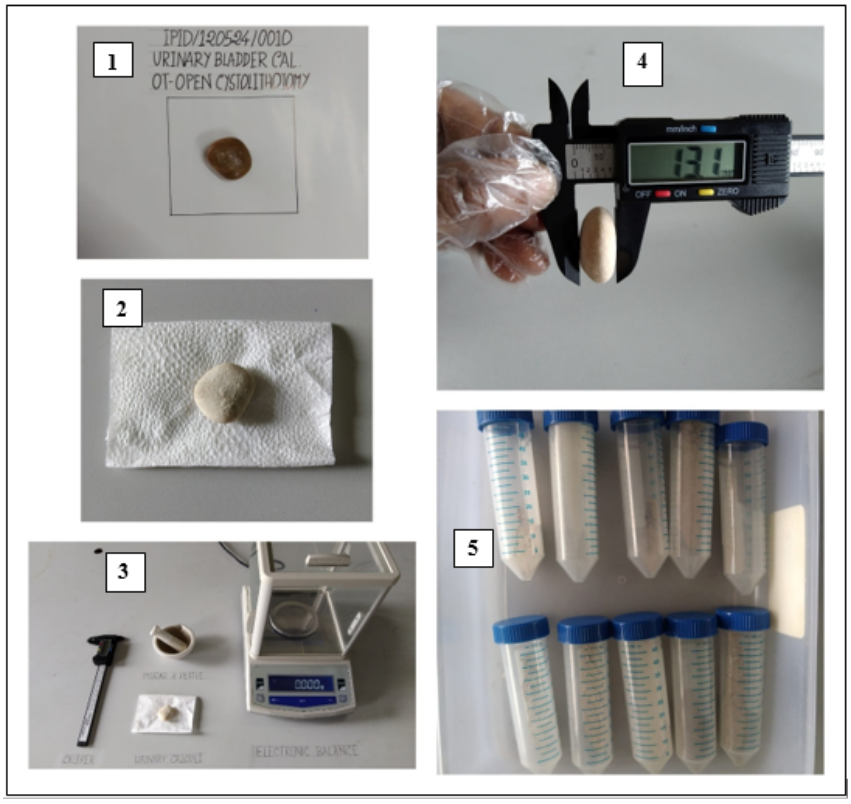


**Figure 2: Urinary stone collection and processing for analysis:**

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.

**Results:**

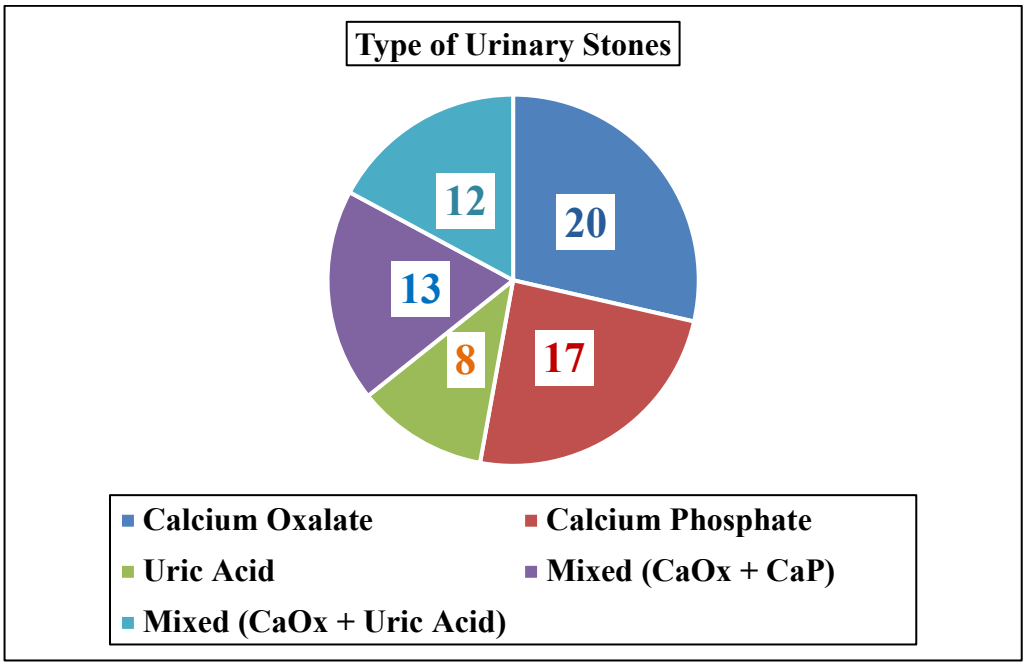


**Figure 3: Description of type of urinary stones (n=70)**

**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 calcium in stone (gm) | 0.74 ± 0.73 |
| Serum calcium (mg/dL) | 9.32 ± 0.9 |

**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 |

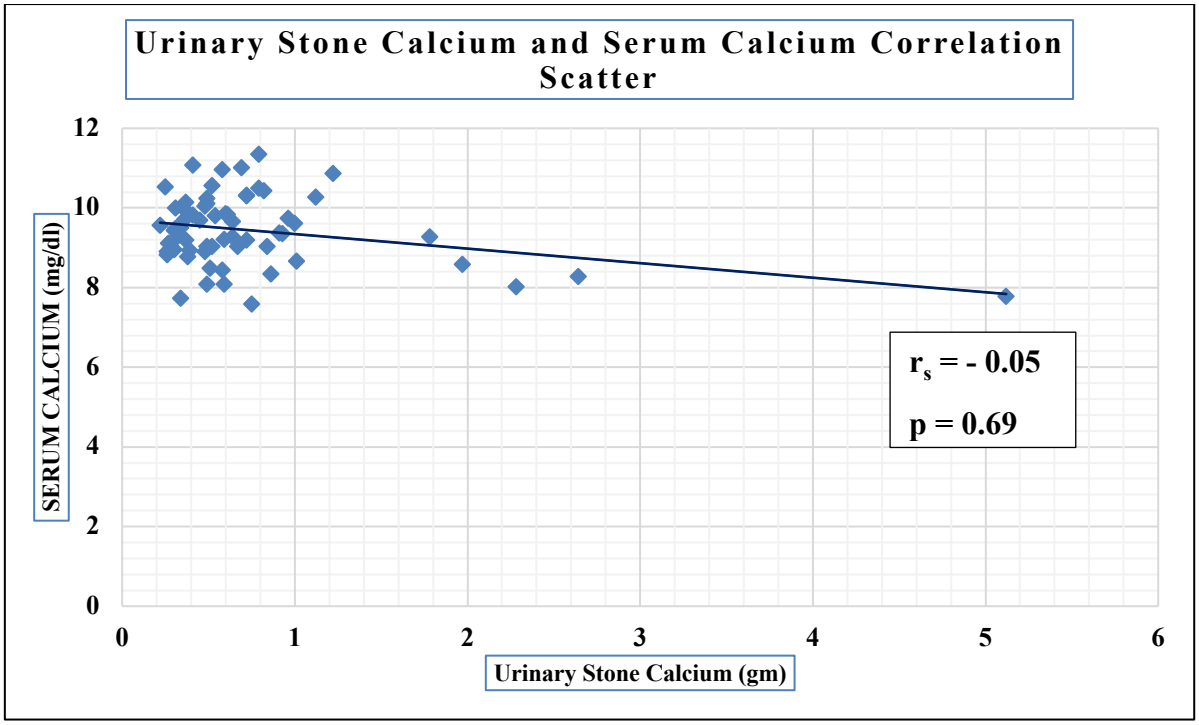


**Figure 4: Urinary stone calcium and serum calcium correlation scatter**

The study included 70 patients with urolithiasis, 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, indicating that most patients were overweight or obese, which was further supported by BMI distribution showing higher frequency in overweight (n=29) and obese (n=22) categories. The mean weight of urinary stones was 2.93 ± 2.55 g, with mean calcium content of 0.74 ± 0.73 g. The average serum calcium level was within the normal range (9.32 ± 0.9 mg/dL). The correlation (spearman) between urinary stone calcium content and serum calcium showed a very weak negative relationship ($r_s$ = - 0.05), indicating that there is no statistically significant association between these parameters (p = 0.69).

**Discussion**

In this study, calcium-containing stones—predominantly calcium oxalate—were the most common, consistent with existing literature (75–85%), likely due to metabolic abnormalities such as hypercalciuria and hyperoxaluria along with dietary and environmental factors [25].

The age distribution in this study shows that urolithiasis predominantly affects middle-aged individuals, with a mean age of around 45 years, consistent with the peak incidence reported in the third to fifth decades of life [26].

In the sex distribution, there is a clear male predominance, consistent with global trends, likely due to lifestyle and hormonal factors, although the gender gap is gradually narrowing. Testosterone has been suggested to promote stone formation, whereas estrogen may have a protective role by enhancing urinary citrate excretion [27].

Another important observation in our study is the predominance of overweight and obese individuals among stone formers. Obesity has been linked to increased risk of urolithiasis through mechanisms such as insulin resistance, altered renal handling of calcium and uric acid, and decreased urinary pH [27].

The present study demonstrates that serum calcium levels do not significantly correlate with the calcium content of urinary stones, indicating that serum calcium is not a reliable marker for estimating stone calcium burden in patients with urolithiasis. Despite the majority of urinary calculi being calcium-based, the mean serum calcium levels in our study population remained within the normal reference range, while the calcium content of stones showed considerable variability. This finding highlights the complex and multifactorial nature of stone formation, where local urinary factors play a more decisive role than systemic serum calcium levels. Stone formation is primarily driven by urinary supersaturation of calcium salts, particularly calcium oxalate and calcium phosphate, rather than elevated serum calcium levels. Factors such as hypercalciuria, hyperoxaluria, hypocitraturia, and low urine volume are well-established contributors to stone formation and growth. Even in individuals with normal serum calcium, increased urinary excretion of calcium can occur due to dietary influences, renal tubular handling abnormalities, or metabolic conditions, leading to stone formation without systemic hypercalcemia [25,26]. Our

findings are consistent with previous studies that have reported a lack of direct association between serum calcium and urinary stone composition. For instance, Worcester and Coe (2010) emphasized that kidney stone disease is largely a disorder of urine chemistry rather than serum biochemical abnormalities [26]. Similarly, Curhan et al. (1997) demonstrated that dietary and urinary factors, rather than serum calcium, are stronger predictors of nephrolithiasis risk [28]. These observations support the concept that serum calcium homeostasis is tightly regulated by hormonal mechanisms involving parathyroid hormone, vitamin D, and calcitonin, thereby maintaining levels within a narrow physiological range even in the presence of ongoing stone formation.

**Conclusion:**

This study shows that calcium-containing stones, especially calcium oxalate, are the most common type of urinary stones, with a higher occurrence in middle-aged individuals and a clear male predominance. The greater frequency among overweight and obese patients further highlights the influence of metabolic and lifestyle factors in the development of urolithiasis. A key finding of this study is that serum calcium levels do not reflect the calcium content of urinary stones, making them an unreliable marker for assessing stone burden. This suggests that stone formation is more closely related to urinary and metabolic factors rather than systemic calcium levels. Therefore, a detailed metabolic workup, particularly urinary analysis, is essential for better understanding, prevention, and management of urolithiasis.

**Limitations:** This study has a few limitations that should be considered. The sample size was relatively small and the study was conducted at a single center, which may limit how well the findings apply to a larger population. Since the study design was cross-sectional, it is not possible to establish a cause-and-effect relationship between serum calcium and stone calcium content. In addition, important urinary parameters, such as 24-hour urine analysis, were not included, which could have provided deeper insight into stone formation. Dietary patterns and lifestyle factors were also not explored in detail, although they are known to play a significant role in urolithiasis.

**Ethics Statement:** The study was conducted following approval from the Institutional Ethics Committee of KPC Medical College & Hospital, Jadavpur (Approval No. KPCMCH/IEC/2024/211; dated 04/06/2024).

**Data Availability Statement:** All data analysed during this study are contained within this article. Patient identity has not been disclosed.

**Author contributions:** All authors contributed equally to the conception, design, data collection, analysis, drafting, and revision of this manuscript. All authors approved the final version.

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