Original Article

Beyond Calcium Stones: Predictors of Uric Acid and Struvite Urolithiasis Among Surgically Treated Patients in The Kumaun Himalayan Region

Lakshman Singh Pal[1], Nishant Bisht[2], Avanish Kumar Singh[3]

[1]Associate Professor, Department of Urology, GMC Haldwani, Uttarakhand, India. [2]Assistant Professor, Department of General surgery, SSJGIMSR Almora, Uttarakhand, India. [3]Senior Resident, Department of General Surgery, SSJGIMSR Almora, Uttarakhand, India

Abstract

Background: Calcium stones dominate most urinary stone series, but uric acid and struvite stones require distinct metabolic and infection-focused preventive approaches. Identifying patient characteristics associated with these non-calcium phenotypes may support earlier targeted evaluation. The objective is to identify sociodemographic, environmental, and lifestyle characteristics associated with uric acid and struvite stones, using calcium stones as the reference phenotype, among surgically treated patients in the Kumaun Himalayan region. **Material and Methods:** This secondary analysis used aggregate data from a hospital-based cross-sectional study of 200 symptomatic patients with urolithiasis who underwent extracorporeal shock-wave lithotripsy, endoscopic surgery, or open surgery over 18 months. Retrieved stones were classified by qualitative chemical analysis as calcium, struvite, or uric acid. Global associations were reassessed using Pearson's chi-square test. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated separately for struvite versus calcium and uric acid versus calcium; Fisher's exact test was used for pairwise comparisons. **Results:** Calcium stones accounted for 114 (57.0%) cases, uric acid stones for 47 (23.5%), and struvite stones for 39 (19.5%). Stone phenotype differed across age categories (P=0.002). Compared with patients aged 21–40 years, those aged 0–20 years had higher odds of struvite (OR 7.25; 95% CI 1.77–29.68) and uric acid stones (OR 4.83; 95% CI 1.23–19.04). Patients aged 61–80 years also had higher odds of struvite (OR 6.04; 95% CI 1.97–18.49) and uric acid stones (OR 4.03; 95% CI 1.38–11.74). Marital status showed a global association (P=0.014), but estimates for unmarried patients were imprecise because only 14 participants were unmarried. Sex, residence, education, smoking, family history, dietary pattern, alcohol use, and drinking-water source were not associated with stone phenotype. **Conclusion:** Age at both extremes emerged as the principal unadjusted predictor of non-calcium stone composition in this surgically treated cohort. The apparent association with unmarried status was based on sparse data and may reflect age confounding. Patient-level data and modern compositional analysis are required to validate independent predictors.

Keywords: Urolithiasis; uric acid stone; struvite; infection stone; stone composition; Himalaya; Uttarakhand.

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Introduction

Urolithiasis is a recurrent, heterogeneous disorder whose frequency and composition vary substantially between populations. Increasing incidence, recurrent symptoms, surgical requirements, and long-term renal consequences make stone disease an important clinical and public-health problem, particularly in regions undergoing dietary, metabolic, and climatic transition.[1]

Uttarakhand has a documented hospital burden of urinary stone disease, with young and middle-aged adults contributing a large proportion of cases. A 13-year study from the state reported that approximately 90% of retrieved stones were renal and predominantly composed of calcium oxalate, demonstrating the importance of locally generated compositional data.[2]

Calcium oxalate is also the dominant constituent in large northern Indian surgical series. However, less common phenotypes should not be merged indiscriminately with calcium stones because their pathogenesis and preventive management differ; uric acid stones are linked to persistently acidic urine, whereas struvite stones usually indicate infection with urease-producing organisms.[3]

Age and sex can substantially alter the probability of different stone compositions. In a large laboratory series, uric acid stones became more prominent with advancing age, while struvite stones were more frequently submitted by women, showing that the overall frequency of stone disease does not necessarily predict its mineral phenotype.[4]

Uric acid nephrolithiasis is closely related to low urinary pH and is commonly associated with insulin resistance, obesity, type 2 diabetes, and metabolic syndrome. Accurate recognition matters because pure uric acid stones may be amenable to dissolution and recurrence prevention through urinary alkalinisation and metabolic risk modification.[5]

Address for correspondence: Dr. Lakshman Singh Pal, Associate Professor, Department of Urology, GMC Haldwani, Uttarakhand, India. E-mail: lakshman.pal @gmail.com

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Struvite stones represent an infection-associated phenotype and can cause rapid stone growth, recurrent urinary infection, obstruction, and sepsis. Their occurrence varies geographically, and conventional midstream urine culture may not identify infection in every patient with struvite-containing calculi.[6]

A descriptive publication from the present cohort reported the overall distribution of calcium, struvite, and uric acid stones across several demographic categories. The present secondary analysis addressed a distinct question by estimating effect sizes for candidate predictors of uric acid and struvite stones using calcium stones as the reference phenotype.[7]

Materials and Methods

Study design and setting: This was a secondary analysis of aggregate data from an 18-month hospital-based cross-sectional study conducted in the Department of General Surgery, Government Medical College and Dr. Susheela Tiwari Government Hospital, Haldwani, Uttarakhand. The hospital serves patients from the Kumaun Himalayan region and adjoining plains. Reporting was structured according to the STROBE recommendations for cross-sectional studies.[8]

Participants: The original study used total enumeration of symptomatic patients with urolithiasis who required an intervention and underwent extracorporeal shock-wave lithotripsy, endoscopic surgery, or open surgery during the study period. Patients unwilling to participate and asymptomatic stone formers were excluded. The final reported sample comprised 200 participants.

Variables and outcome definition: The outcome was the predominant reported stone phenotype: calcium, struvite, or uric acid. Candidate explanatory variables with complete and internally consistent cross-tabulations were age group, sex, hilly or plain residence, educational status, marital status, smoking, reported family history or genetic predisposition, vegetarian or non-vegetarian diet, alcohol use, and tap or natural drinking-water source. Variables whose aggregate cross-tabulations could not be independently reconciled were not included in the effect-size analysis.

Stone collection and compositional assessment: Stones retrieved during intervention were softened, crushed, dissolved in distilled water, and assessed by qualitative chemical reactions for uric acid, carbonate, oxalate, phosphate, calcium, and magnesium. The original report subsequently grouped stones as calcium, struvite, or uric acid. Because wet chemical analysis has limited ability to identify mixed and minor components, the reported categories were treated as operational phenotypes rather than definitive crystallographic diagnoses.[9]

Statistical analysis: Counts and percentages were summarized by stone phenotype. Global associations were recalculated from the reported contingency tables using Pearson's chi-square test. Calcium stones were used as the reference outcome. For each candidate factor, crude ORs and 95% CIs were calculated separately for struvite versus calcium and uric acid versus calcium. Fisher's exact test was used for pairwise comparisons because several cells were sparse. All tests were two-sided, and $P<0.05$ was considered statistically significant. Adjusted multinomial regression was not performed because verified patient-level joint covariate data were unavailable.

Ethical considerations: Ethical approval was obtained from the Institutional Ethics Committee, Government Medical College, Haldwani, before commencement of the study. Written informed consent was obtained from all participants.

Results

Stone phenotype distribution: Among 200 surgically treated patients, 114 (57.0%) had calcium stones, 39 (19.5%) had struvite stones, and 47 (23.5%) had uric acid stones. Patients aged 21–40 years constituted 88 (44.0%) of the cohort, females 131 (65.5%), residents of hilly areas 129 (64.5%), and tap-water users 142 (71.0%). The complete distributions and recalculated global association tests are shown in [Table 1].

Candidate predictors of struvite and uric acid stones: Age was the principal candidate predictor of both non-calcium phenotypes. Relative to patients aged 21–40 years, those aged 0–20 years had 7.25-fold higher crude odds of struvite stones and 4.83-fold higher crude odds of uric acid stones. Patients aged 61–80 years had 6.04-fold higher odds of struvite stones and 4.03-fold higher odds of uric acid stones. Estimates for the 41–60-year category did not differ from the reference group.

Unmarried participants had higher crude odds of struvite and uric acid stones relative to calcium stones; however, only 14 participants were unmarried, producing wide confidence intervals. None of the remaining candidate factors showed statistically significant crude associations with either non-calcium phenotype.

Table 1: Distribution of candidate factors according to stone phenotype

Factor	Category	Calcium n=114	Struvite n=39	Uric acid n=47	Total n=200	Global P
Age	0–20 years	4 (3.5)	6 (15.4)	6 (12.8)	16 (8.0)	0.002
	21–40 years	58 (50.9)	12 (30.8)	18 (38.3)	88 (44.0)	
	41–60 years	44 (38.6)	11 (28.2)	13 (27.7)	68 (34.0)	
	61–80 years	8 (7.0)	10 (25.6)	10 (21.3)	28 (14.0)	
Sex	Male	41 (36.0)	15 (38.5)	13 (27.7)	69 (34.5)	0.509
	Female	73 (64.0)	24 (61.5)	34 (72.3)	131 (65.5)	
Residence	Hilly	73 (64.0)	27 (69.2)	29 (61.7)	129 (64.5)	0.759
	Plain	41 (36.0)	12 (30.8)	18 (38.3)	71 (35.5)	
Education	Literate	87 (76.3)	28 (71.8)	36 (76.6)	151 (75.5)	0.835
	Illiterate	27 (23.7)	11 (28.2)	11 (23.4)	49 (24.5)	
Marital status	Married	111 (97.4)	33 (84.6)	42 (89.4)	186 (93.0)	0.014
	Unmarried	3 (2.6)	6 (15.4)	5 (10.6)	14 (7.0)	
Smoking	Smoker	30 (26.3)	10 (25.6)	16 (34.0)	56 (28.0)	0.571

	Non-smoker	84 (73.7)	29 (74.4)	31 (66.0)	144 (72.0)	
Family history	Yes	19 (16.7)	8 (20.5)	9 (19.1)	36 (18.0)	0.841
	No	95 (83.3)	31 (79.5)	38 (80.9)	164 (82.0)	
Diet	Vegetarian	59 (51.8)	18 (46.2)	20 (42.6)	97 (48.5)	0.539
	Non-vegetarian	55 (48.2)	21 (53.8)	27 (57.4)	103 (51.5)	
Alcohol use	Drinker	53 (46.5)	17 (43.6)	18 (38.3)	88 (44.0)	0.634
	Non-drinker	61 (53.5)	22 (56.4)	29 (61.7)	112 (56.0)	
Water source	Tap	84 (73.7)	27 (69.2)	31 (66.0)	142 (71.0)	0.595
	Natural	30 (26.3)	12 (30.8)	16 (34.0)	58 (29.0)	

Values are n (% within stone phenotype), except the Total column, which shows n (% of total cohort). P values were recalculated using Pearson's chi-square test.

Table 2: Crude associations of candidate factors with non-calcium stone phenotypes

Comparison	Struvite vs calcium OR (95% CI)	P	Uric acid vs calcium OR (95% CI)	P
Age: 0–20 vs 21–40 y	7.25 (1.77–29.68)	0.007	4.83 (1.23–19.04)	0.025
Age: 41–60 vs 21–40 y	1.21 (0.49–2.99)	0.817	0.95 (0.42–2.15)	1.000
Age: 61–80 vs 21–40 y	6.04 (1.97–18.49)	0.002	4.03 (1.38–11.74)	0.019
Female vs male	0.90 (0.42–1.90)	0.848	1.47 (0.70–3.09)	0.361
Hilly vs plain residence	1.26 (0.58–2.76)	0.697	0.90 (0.45–1.83)	0.858
Literate vs illiterate	0.79 (0.35–1.79)	0.668	1.02 (0.46–2.26)	1.000
Unmarried vs married	6.73 (1.59–28.38)	0.009	4.40 (1.01–19.25)	0.047
Smoker vs non-smoker	0.97 (0.42–2.22)	1.000	1.45 (0.69–3.01)	0.342
Family history: yes vs no	1.29 (0.51–3.24)	0.629	1.18 (0.49–2.85)	0.819
Non-vegetarian vs vegetarian	1.25 (0.60–2.59)	0.582	1.45 (0.73–2.87)	0.304
Drinker vs non-drinker	0.89 (0.43–1.85)	0.853	0.71 (0.36–1.43)	0.385
Tap vs natural water	0.80 (0.36–1.78)	0.678	0.69 (0.33–1.44)	0.342

OR: odds ratio; CI: confidence interval. Calcium stones were the reference outcome. Pairwise P values were calculated using Fisher's exact test.

Discussion

This secondary analysis shifted the emphasis from overall prevalence to comparative stone phenotypes. Calcium stones remained the largest group, but more than two-fifths of participants had uric acid or struvite stones. The principal signal was a non-linear association with age: both the youngest and oldest categories had higher crude odds of non-calcium stones than the 21–40-year reference group.

The dominance of calcium stones is consistent with the long-term Uttarakhand experience, in which calcium oxalate accounted for most retrieved stones and the greatest burden occurred among adults aged 21–40 years. The present analysis adds that the composition within a surgical population may become relatively more heterogeneous at the age extremes.[2]

A large northern Indian crystallographic series reported calcium oxalate in more than 90% of stones, with struvite and uric acid forming small minorities. The higher proportions of struvite and uric acid in the present study may reflect referral patterns, selection of symptomatic patients requiring intervention, regional exposures, or differences between qualitative chemical and crystallographic classification.[3]

The higher odds of uric acid stones in patients aged 61–80 years are biologically and epidemiologically plausible. Lieske and colleagues observed that uric acid became the second most common composition after approximately 55 years, suggesting that age-related metabolic and urinary changes influence mineral phenotype even when calcium oxalate remains dominant overall.[4]

Studies using modern Fourier-transform infrared spectroscopy have also identified age as a determinant of stone composition. In a surgically treated Thai population, age, sex, diabetes, and renal function were associated with major stone composition, although the pattern differed by sex, illustrating that demographic effects may vary across populations.[10]

Body size and metabolic disease are established correlates of uric acid stones, but these variables could not be evaluated reliably in the present aggregate reanalysis. In a large compositional series, the proportion of uric acid stones increased progressively with body mass index, and both age and body mass index independently predicted uric acid composition.[11]

The pathophysiological link between metabolic syndrome and uric acid stone formation is primarily mediated by persistently low urinary pH and impaired ammonium buffering. Therefore, older patients with uric acid stones should undergo metabolic evaluation rather than receiving only generic hydration advice.[5]

Previous work has demonstrated that metabolic syndrome is associated with a higher prevalence of uric acid stones, although the influence of obesity alone is not uniform across studies. The absence of verified diabetes, urinary pH, and metabolic data in the supplied dataset limits etiological interpretation of the uric acid findings.[12]

The increased proportion of struvite stones in the youngest and oldest age groups requires cautious interpretation. Infection stones are strongly associated with urinary infection, but urine culture may be negative in a substantial minority, and organisms other than classic urease-producing Proteus species may be isolated.[6]

Recent clinical prediction research indicates that struvite stones cannot be identified reliably from a single demographic characteristic; laboratory and radiological information improve discrimination. The present age association should therefore be regarded as a screening signal rather than a diagnostic rule.[13]

The absence of a sex association in this cohort differs from large series reporting more struvite stones among women and more uric acid stones among men. The discrepancy may arise from sample size, referral selection, regional differences, or classification methods rather than indicating that sex has no biological relevance.[14]

Residence and drinking-water source were not associated with composition after the contingency tables were recalculated. Mineral content varies markedly between water sources, but water labels such as tap or natural are insufficient proxies for calcium, magnesium, sodium, bicarbonate, or total fluid intake; direct chemical assessment is needed before attributing stone phenotype to water source.[15]

The apparent association with unmarried status was statistically unstable. Only 14 participants were unmarried, and marital status is strongly related to age in most populations; without patient-level adjustment, the finding may simply mirror the higher representation of non-calcium stones at age extremes and should not be interpreted causally.

A major methodological limitation was the use of qualitative chemical stone analysis. Comparative studies have shown clinically important discordance between wet chemical analysis and Fourier-transform infrared spectroscopy, including poor recognition of minor components and missed struvite or calcium phosphate, which may have affected the phenotype assignments in this study.[9]

Current European guidance recommends reliable stone analysis, preferably using infrared spectroscopy or X-ray diffraction, and tailoring recurrence prevention to stone composition and urinary risk profile. A future regional study should combine validated compositional methods with urine culture, urinary pH, metabolic evaluation, comorbidities, medication history, and quantitative fluid and dietary assessment.[16]

Strengths and limitations: The study addressed a geographically underrepresented Himalayan population and included consecutively treated symptomatic patients over an 18-month period. Recalculation of global tests and reporting of ORs with 95% CIs provided more clinically interpretable effect estimates than simple within-column percentages.

The analysis was limited by its single-centre, cross-sectional design and inclusion only of patients requiring intervention. Aggregate marginal tables prevented adjustment for confounding and assessment of interactions. Sparse cells produced imprecise estimates, particularly for unmarried participants and age extremes. The original source tables and appended master chart were not fully concordant, so only internally consistent variables were analyzed. Qualitative chemical analysis may have misclassified pure and mixed stones, and clinical variables central to uric acid and struvite pathogenesis—urine pH, diabetes, metabolic syndrome, urine culture, renal function, and anatomic abnormalities—were unavailable.

Conclusion

In this surgically treated Kumaun Himalayan cohort, calcium stones were most frequent, while uric acid and struvite stones together accounted for 43% of cases. Age at both extremes was the clearest unadjusted predictor of non-calcium composition. The association with unmarried status was based on sparse data and probably vulnerable to age confounding. Sex, residence, education, smoking, family history, dietary pattern, alcohol use, and broad drinking-water source did not distinguish stone phenotypes. These results support age-directed metabolic and infection evaluation but require confirmation using a verified patient-level dataset and infrared spectroscopic or X-ray diffraction stone analysis.

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Conflicts of interest

There are no conflicts of interest.

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