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Research Article

Metabolic Profile of Patients with Recurrent Nephrolithiasis: A Hospital Based Cross-Sectional Study from a Tertiary Care Centre in Nepal

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ABSTRACT

Background & Objectives: Nephrolithiasis is a recurrent condition with multifactorial metabolic causes that vary across populations. Identifying metabolic abnormalities among recurrent multiple stone formers is essential for targeted prevention. This study aimed to evaluate the spectrum and frequency of metabolic derangements among patients with recurrent nephrolithiasis including both recurrent single- and multiple-stone formers presenting to a tertiary care center in Nepal.

Material and Methods: This hospital based cross-sectional observational study was conducted in the Department of Nephrology, Bir Hospital, from February 2018 to January 2019. Adult patients (≥18 years) with a history of recurrent or multiple renal stones confirmed by ultrasonography were included. Demographic and clinical data were recorded, and 24-hour urine samples were analyzed for calcium, citrate, oxalate, uric acid, and volume. Serum calcium, phosphate, uric acid, and creatinine were measured. Metabolic abnormalities were defined using standard thresholds, and data were analyzed using descriptive statistics, the Chi-square test, and logistic regression with R version 4.4.1. A p-value <0.05 was considered statistically significant.

Results: A total of 120 patients with recurrent nephrolithiasis were evaluated. Based on ultrasonographic findings at presentation 73 were recurrent multiple-stone formers and 47 were recurrent single-stone formers. Hypocitraturia (81%) and hyperoxaluria (70%) were the most prevalent abnormalities, followed by hypercalciuria (25%) and hyperuricosuria (8%). Multiple metabolic abnormalities were significantly more common among recurrent multiple stone formers (71% vs. 57%, p = 0.009). Serum biochemical parameters and renal function were comparable between groups. On multivariable logistic regression, hyperoxaluria showed a non-significant trend toward higher

odds of multiple nephrolithiasis (aOR = 1.99; 95% CI: 0.88–4.58; p = 0.10).

Conclusion: Patients with recurrent or multiple nephrolithiasis in our population exhibit a high burden of metabolic abnormalities, particularly hypocitraturia and hyperoxaluria. Comprehensive metabolic evaluation and tailored interventions such as alkali therapy, adequate hydration, and dietary counselling are essential to reduce recurrence and long-term disease burden.

Keywords: Hypocitraturia; Hyperoxaluria; Metabolic abnormalities; Nephrolithiasis; Nepal; Recurrent renal stones

INTRODUCTION

Nephrolithiasis is a common global health problem with a significant economic and clinical burden. Its prevalence exceeds 12% in the general population and is influenced by gender, ethnicity, and dietary habits [1]. A particularly challenging aspect of the disease is its high recurrence rate which approaches 50% over ten years without targeted medical management [2]. The impact of nephrolithiasis extends beyond the kidneys, as it is independently associated with an increased risk of systemic conditions, including hypertension, coronary artery disease, stroke, and metabolic syndrome [3–5]. This underscores nephrolithiasis not merely as an isolated urological issue, but as a potential marker of broader metabolic dysregulation. The etiology of kidney stones is multifactorial involving a complex interplay of genetic predisposition (e.g., cystinuria, renal tubular acidosis), anatomical anomalies, dietary factors (such as low fluid intake, high sodium, and animal protein consumption), and environmental influences [6].

Crucially, specific metabolic abnormalities are well-established risk factors for stone formation. These include hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, and abnormal urine pH (low for uric acid stones, high for calcium phosphate stones) [7]. Consequently, comprehensive metabolic evaluation is considered a cornerstone in the management of nephrolithiasis, as it allows for targeted medical and dietary interventions that can significantly reduce the risk of recurrence [7–9]. The clinical landscape of nephrolithiasis is evolving. With the increased use of computed tomography, multiple stones are now more frequently detected at the time of initial presentation [10]. Emerging evidence suggests that patients with multiple stones, even at their first episode, represent a distinct high-risk group. They exhibit a higher prevalence of metabolic abnormalities, particularly hypocitraturia, and face a significantly greater risk of recurrence compared to single-stone formers. This has led to the recommendation that such patients should undergo prompt metabolic evaluation and be considered for preventive therapies like potassium citrate [11].

While the high rate of metabolic abnormalities in recurrent multiple stone formers is well-documented in various populations[12–18] the specific metabolic profile within our local population remains uncharacterized. Distinct regional variations in diet, ethnicity, and environment can significantly influence the pattern of urinary risk factors [19]. Therefore, data from other regions may not be directly applicable to guiding clinical practice here. This study aims to address this critical knowledge gap by establishing the spectrum and frequency of metabolic abnormalities in patients with recurrent or multiple nephrolithiasis in our population. Identifying the predominant risk factors will provide a vital evidence base for implementing personalized medical

management and specific dietary restrictions, ultimately working to reduce the substantial burden of this recurrent disease. Therefore, this study aimed to evaluate the spectrum and frequency of metabolic abnormalities among patients with recurrent or multiple nephrolithiasis presenting to a tertiary nephrology center in Nepal.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted in the Department of Nephrology, Bir Hospital, Kathmandu, Nepal, from February 2018 to January 2019. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of the National Academy of Medical Sciences (IRB/NAMS Approval reference number: 709). Written informed consent was obtained from all participants prior to enrolment, and the study adhered to the ethical principles of the Declaration of Helsinki. The study included 120 participants, based on the census sampling of estimated number of eligible patients attending the nephrology clinic during the one-year period.

Study Population

Adult patients (≥18 years) attending the Nephrology or Urology outpatient departments (OPD) with a history of urinary stone disease or presenting with new-onset loin pain, recurrent urinary tract infection, or persistent haematuria were screened using ultrasonography (USG) of the abdomen and pelvis. Patients were eligible for inclusion if USG demonstrated multiple renal or ureteric stones, or a single stone with a previously documented stone at a different site, consistent with recurrent or multiple nephrolithiasis. Patients with incomplete urine collection, active urinary tract infection, or known systemic disorders affecting mineral metabolism (such as hyperparathyroidism or gout) were excluded.

Data Collection

A structured proforma was used to collect demographic and clinical data, including age, sex, dietary pattern, family history, and history of kidney stones. All participants were instructed in detail on the correct procedure for 24-hour urine collection using pre-medicated containers provided by the laboratory. Samples with a total volume <1000 mL were considered inadequate, and repeat collection was requested.

Laboratory Analysis

Adequate 24-hour urine samples were analyzed for volume, calcium, citrate, oxalate, and uric acid. Simultaneously, serum calcium, phosphate, uric acid, and creatinine levels were measured from fasting venous blood samples. Serum and urine calcium, phosphate, uric acid, and creatinine were estimated by standard colorimetric methods. Urinary oxalate and citrate were quantified using enzymatic spectrophotometric techniques. The following cut-off values were used to define metabolic abnormalities: hypocitraturia (<320 mg/24 h), hypercalciuria (>300 mg/24 h), hyperuricosuria (>800 mg/24 h in men and >750 mg/24 h in women), hyperoxaluria (>40 mg/24 h), and low urine volume (<2000 mL/24 h). These cutoff values were used to categorize participants for comparative analysis.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) and

compared using the student's *t*-test for independent samples. Categorical variables were summarized as frequency and percentage and analyzed using the Chi-square test or Fisher's exact test, as appropriate. A *p*-value <0.05 was considered statistically significant. Missing or incomplete data were excluded from analysis. Statistical analysis was performed using R version 4.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 120 patients with recurrent nephrolithiasis were included, comprising 73 recurrent multiple-stone formers and 47 recurrent single-stone formers, categorized according to the number of stones detected at presentation. Table 1 Shows the mean age was comparable between the two groups (42.7 ± 15.7 vs. 42.5 ± 16.8 years, $p > 0.9$). The male-to-female ratio was 1.5:1 in both cohorts, with no significant sex difference observed ($p > 0.9$). Mean body mass index (BMI) was similar between recurrent multiple and single stone formers (22.6 ± 1.6 vs. 22.6 ± 1.9 kg/m^2, $p > 0.9$).

A positive family history of nephrolithiasis was reported in 8.2% of patients with multiple stones compared to 4.3% among single-stone formers ($p = 0.6$). The distribution of chronic kidney disease (CKD) stages and stone location did not differ significantly between groups ($p > 0.7$ for both), with most stones located in the kidney (92% vs. 89%) as shown in table 1.

As shown in table 2, Metabolic evaluation revealed a high prevalence of abnormalities in both groups. Hypocitraturia was the most frequent abnormality, present in 81% of multiple and 83% of single-stone formers ($p > 0.9$). Hyperoxaluria occurred in 70% of multiple versus 57% of single-stone formers ($p = 0.2$), while hypercalciuria and hyperuricosuria were less common and

Table 1. Baseline Characteristics of Recurrent Nephrolithiasis Patients by Number of Stones

Characteristic	**Recurrent Multiple-Stone Formers** N = 73[1]	**Recurrent Single-Stone Formers** N = 47[1]	**p-value**[2]
Age (years)	42.7 ± 15.7	42.5 ± 16.8	>0.9
Sex			>0.9
Female	29 (40%)	19 (40%)	
Male	44 (60%)	28 (60%)	
Body Mass Index (BMI)	22.6 ± 1.6	22.6 ± 1.9	>0.9
Family History of Kidney Stone	6 (8.2%)	2 (4.3%)	0.6
CKD Stage (Grouped)			0.8
Stage 1-2	62 (85%)	42 (89%)	
Stage 3	8 (11%)	4 (8.5%)	
Stage 4-5	3 (4.1%)	1 (2.1%)	
Stone Location			0.9
Both	3 (4.1%)	2 (4.3%)	
Renal	67 (92%)	42 (89%)	
Ureteral	3 (4.1%)	3 (6.4%)	
[1]Mean ± SD; n (%)			
[2]Welch Two Sample t-test; Pearson's Chi-squared test			
Abbreviation: Mean ± SD or n (%)			

Table 2. Prevalence of Metabolic Abnormalities among Recurrent Nephrolithiasis Patients by Number of Stones

Characteristic	Recurrent Multiple-Stone Formers N = 73[1]	Recurrent Single-Stone Formers N = 47[1]	p-value[2]
Hypocitraturia	59 (81%)	39 (83%)	>0.9
Hypercalciuria	18 (25%)	15 (32%)	0.5
Hyperuricosuria	6 (8.2%)	2 (4.3%)	0.6
Hyperoxaluria	51 (70%)	27 (57%)	0.2
Low urine volume	9 (12%)	6 (13%)	>0.9
Number of Metabolic Abnormalities			0.018
0	6 (8.2%)	0 (0%)	
1	15 (21%)	20 (43%)	
2	32 (44%)	17 (36%)	
3	16 (22%)	7 (15%)	
4	4 (5.5%)	1 (2.1%)	
5	0 (0%)	2 (4.3%)	
Metabolic Abnormality Category			0.009
Multiple	52 (71%)	27 (57%)	
None	6 (8.2%)	0 (0%)	
Single	15 (21%)	20 (43%)	

[1]Definitions: Hypocitraturia (<320 mg/24h), Hypercalciuria (>300 mg/24h), Hyperuricosuria (>800 mg/24h men, >750 mg/24h women), Hyperoxaluria (>40 mg/24h), Low urine volume (<2000 mL/24h)

[2]Pearson's Chi-squared test

showed no significant intergroup difference (p = 0.5 and p = 0.6, respectively).

However, when the number of concurrent metabolic abnormalities was analyzed, a significant difference emerged. Patients with recurrent multiple stones exhibited a higher burden of metabolic derangements (p = 0.018), with 71% categorized as having multiple abnormalities compared to 57% among recurrent single-stone formers at presentation (p = 0.009) as depicted in table 2.

Table 3 depicts that the mean 24-hour urine volume was slightly lower in patients with multiple stones (3,229.9 ± 1,137.2 mL) compared to single-stone formers (3,534.5 ± 1,188.1 mL), though this difference did not reach statistical significance (p = 0.2).

Table 3. Twenty-Four-Hour Urine Metabolic Parameters among Recurrent Nephrolithiasis Patients by Number of Stones

Characteristic	Recurrent Multiple-Stone Formers N = 73[1]	Recurrent Single-Stone Formers N = 47[1]	p-value[2]
24-hr Urine Volume (mL)	3,229.9 ± 1,137.2	3,534.5 ± 1,188.1	0.2
24-hr Urine Calcium (mg)	221.7 ± 146.7	251.2 ± 170.3	0.3
24-hr Urine Oxalate (mg)	55.6 ± 23.7	50.8 ± 23.8	0.3
24-hr Urine Citrate (mg)	149.9 ± 177.2	131.1 ± 179.4	0.6
24-hr Urine Uric Acid (mg)	518.6 ± 224.7	467.3 ± 215.4	0.2
Calcium-Oxalate Product	1.3 ± 1.1	1.3 ± 1.3	0.8

[1]Mean ± SD

[2]Welch Two Sample t-test

Similarly, urinary calcium, oxalate, citrate, and uric acid excretion were comparable between the two groups (all $p > 0.2$). The calculated calcium–oxalate product was identical (1.3 ± 1.1 vs. 1.3 ± 1.3, $p = 0.8$), suggesting no major difference in supersaturation potential.

Table 4 indicates Serum biochemical parameters, including creatinine, calcium, phosphate, and uric acid, were within normal limits and did not differ significantly between groups (all $p > 0.1$). Mean estimated glomerular filtration rate (eGFR) was 83.4 ± 24.8 mL/min/1.73 m^2 among multiple-stone formers and 88.3 ± 23.2 mL/min/1.73 m^2 in

Table 4. Serum Biochemical Parameters and Renal Function among Recurrent Nephrolithiasis Patients by Number of Stones

Characteristic	Recurrent Multiple-Stone Formers N = 73[1]	Recurrent Single-Stone Formers N = 47[1]	p-value[2]
Serum Creatinine (mg/dL)	1.2 ± 0.7	1.0 ± 0.4	0.2
eGFR (mL/min/1.73m²)	83.4 ± 24.8	88.3 ± 23.2	0.3
Serum Calcium (mg/dL)	9.0 ± 0.6	8.8 ± 0.6	0.13
Serum Phosphate (mg/dL)	3.8 ± 0.5	3.7 ± 0.5	0.2
Serum Uric Acid (mg/dL)	5.9 ± 1.4	5.7 ± 1.3	0.5
CKD Stage			0.7
1	34 (47%)	28 (60%)	
2	28 (38%)	14 (30%)	
3	8 (11%)	4 (8.5%)	
4	2 (2.7%)	1 (2.1%)	
5	1 (1.4%)	0 (0%)	
[1]Mean ± SD; n (%)			
[2]Welch Two Sample t-test; Pearson's Chi-squared test			

Table 5. Logistic Regression Analysis for Predictors of Multiple-Stone Formation among Patients with Recurrent Nephrolithiasis

		Univariate			Multivariable		
Predictor	**N**	**OR (95% CI)**	**95% CI**	**p-value**	**aOR (95% CI)**	**95% CI**	**p-value**
Age (per year)	120	1.00	0.98, 1.02	>0.9	1.00	0.97, 1.02	0.9
Sex (Male vs Female)	120						0.7
Female		—	—		—	—	
Male		1.03	0.48, 2.17	>0.9	1.17	0.51, 2.72	
Hypocitraturia	120	0.86	0.32, 2.22	0.8	0.83	0.29, 2.22	0.7
Hypercalciuria	120	0.70	0.31, 1.58	0.4	0.56	0.23, 1.35	0.2
Hyperoxaluria	120	1.72	0.80, 3.71	0.2	1.99	0.88, 4.58	0.10
Family History	120	2.01	0.44, 14.2	0.4	1.37	0.27, 10.2	0.7
CKD Stage ≥2	120	1.57	0.74, 3.45	0.2	1.67	0.72, 4.00	0.2
Abbreviations: CI = Confidence Interval, OR = Odds Ratio							

single-stone formers (p = 0.3). The distribution of CKD stages also showed no significant variation (p = 0.7).

In univariate logistic regression analysis, none of the assessed clinical or metabolic parameters were significantly associated with multiple-stone disease. After multivariable adjustment, hyperoxaluria showed a trend toward increased odds of multiple nephrolithiasis (adjusted OR = 1.99; 95% CI: 0.88–4.58; p = 0.10), although this did not achieve statistical significance. Other factors, including age, sex, hypocitraturia, hypercalciuria, and CKD stage, were not independently predictive (all p > 0.2) as shown in Table 5 above.

DISCUSSION

This study evaluated the metabolic abnormalities among patients with recurrent nephrolithiasis. All participants had a history of stone recurrence. The main findings were a high prevalence of metabolic derangements, particularly hypocitraturia and hyperoxaluria, and a significantly greater clustering of multiple abnormalities among recurrent multiple-stone formers compared to recurrent single-stone formers. The predominance of hypocitraturia (81%) and hyperoxaluria (70%) is consistent with previous studies from India and South Asia, where similar rates have been observed [14–18]. Western studies report lower frequencies of hypocitraturia (40–60%) [7,11], suggesting possible geographic and dietary variation. Citrate is a potent inhibitor of calcium-oxalate crystallization, and low urinary citrate levels promote supersaturation and recurrent stone formation [8]. Hyperoxaluria, on the other hand, increases the risk of calcium-oxalate precipitation and may be related to oxalate-rich diet, low calcium intake, or enteric hyperabsorption [17,19].

The proportion of patients with multiple concurrent metabolic abnormalities was significantly higher in those with recurrent or multiple stones (71% vs. 57%), similar to the trend reported by Kang et al. [11]. While individual biochemical parameters were not significantly different between groups, the aggregation of metabolic defects may better reflect the overall lithogenic potential than single abnormalities alone [16]. These findings emphasize the multifactorial nature of stone disease and the importance of evaluating the metabolic milieu rather than focusing on isolated risk factors. Serum biochemical parameters and renal function were comparable across groups, aligning with previous evidence that metabolic risk is often independent of overt renal impairment [6,11]. The non-significant trend toward increased odds of multiple stones in patients with hyperoxaluria (aOR = 1.99) is clinically meaningful and warrants further investigation in larger prospective studies.

The pattern of abnormalities in our cohort differs from that seen in Western populations, where hypercalciuria predominates [12]. This regional variation may relate to environmental and dietary factors, including lower fluid intake, high ambient temperature, and dietary patterns rich in oxalate but poor in alkali and calcium sources [19]. Such differences highlight the need for locally relevant preventive strategies. The clinical implications are significant. Identification of correctable metabolic abnormalities provides an opportunity for targeted intervention. Potassium citrate therapy can correct hypocitraturia, while dietary counselling focusing on adequate hydration, reduced oxalate intake, and balanced calcium

consumption can mitigate recurrence [7,15]. These interventions are inexpensive and feasible in resource-limited settings such as Nepal.

This study's strengths include the use of standardized laboratory methods and strict quality control of 24-hour urine collection. Limitations include its cross-sectional design, modest sample size, and lack of stone composition and dietary analysis, which may have provided additional mechanistic insight. Future multicentric studies integrating stone chemistry and dietary assessment are recommended to validate and expand these findings. In summary, patients with recurrent or multiple nephrolithiasis in our population demonstrated a high prevalence of metabolic abnormalities, chiefly hypocitraturia and hyperoxaluria. Although absolute biochemical values were similar between groups, the higher burden of concurrent abnormalities among recurrent stone formers underscores the multifactorial pathogenesis of stone disease. Comprehensive metabolic evaluation and individualized preventive therapy remain essential for effective long-term management and recurrence prevention.

CONCLUSION

This study demonstrated that patients with recurrent or multiple nephrolithiasis exhibit a high prevalence of metabolic abnormalities, predominantly hypocitraturia and hyperoxaluria. Although individual biochemical parameters were comparable between recurrent single- and multiple-stone formers, the greater clustering of metabolic derangements among recurrent multiple-stone formers cases highlights the complex and multifactorial nature of stone disease. Routine metabolic evaluation should therefore be incorporated into the management of all stone formers to identify correctable risk factors. Targeted interventions such as alkali therapy, adequate hydration, and dietary modification could play a crucial role in preventing recurrence and reducing the overall burden of nephrolithiasis in our population.

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Author's Contribution Conceptualized and designed the study, performed data collection, statistical analysis, and manuscript drafting-**KKS**; study design, provided expert input on data interpretation, and critically reviewed the manuscript for important intellectual content-**RH, AB.** All authors read and approved the final version of the manuscript prior to submission.

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