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Original Research Article

# A Study of the Prevalence of Metabolic Abnormalities in Urolithiasis in A Tertiary Care Centre in Bihar

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## Abstract

**Aim:** Study of the prevalence of metabolic abnormalities in a tertiary care centre in Bihar region.

**Methods:** This was a prospective observational study conducted in the Department of Urology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India for 10 months. Total 50 patients over 18 years old were included in this study.

**Results:** Metabolic abnormalities were found in 94% patients (Confidence Interval 95%: 87.2–99.8%). Almost a quarter (26% [CI95%: 16.0–36.8%]) only had one metabolic abnormality, and 68% patients CI95%: 56.9–79.4%) had multiple metabolic abnormalities. Hypercalciuria was the most commonly observed metabolic abnormality and was found in 54% (CI95%: 43.5–67.6%) of patients. Other significant metabolic abnormalities were hyperoxaluria (34% [CI95%: 22.4–49.8%]), hyperuricosuria (32% [CI95%: 21.9–44.7%]) and hypomagnesuria (30% [CI95%: 21.3–44.2%]). several sociodemographic and clinical variables with the most frequent metabolic abnormalities found in our study (hypercalciuria, hyperoxaluria, hyperuricosuria and hypomagnesuria). Patients with hypercalciuria were older (55.8 ±12.9 years vs. 48.8 ±6.8 years, p = 0.022), family history of stone disease was significantly more frequent among patients with hyperoxaluria (70% vs. 30%, p = 0.011) and there was a higher prevalence of present and former smokers among patients with hyperoxaluria (p = 0.012).

**Conclusion:** Immediate metabolic evaluation is the key for a better and individualized management, guiding the selection of proper pharmacological and dietary measures to prevent recurrent stone formation and to relieve all clinical and economic burdens behind this condition.

**Keywords:** Metabolic Abnormalities, Urolithiasis, Stone.

## Introduction

The lifetime risk of stone formation in an individual is estimated at 5−10% [1,2]. The recurrence rate after formation of an initial stone is reported to be as high as 50% at 5 yr and 80−90% at 10 yr [3]. People who form stones are more likely to have urinary metabolic abnormalities compared to a healthy population (level of evidence [LE] III/C) [4], while patients who form recurrent stones tend to have more significant metabolic abnormalities than those with a single stone episode (LE III/C) [5]. Beyond the immediate effects of an acute stone event, long-term effects such as loss of renal function are rarely taken into account in cost estimates of stone disease. Indeed, a French study of over 1300 new cases of end-stage renal disease requiring dialysis found that in 3.2% cases renal failure was a direct result of stone disease [5]. In addition to the morbidity of an acute stone event, upwards of 50% of patients with symptomatic upper tract stones ultimately require surgical intervention [6,7]. As such, the goal of medical treatment is to prevent disease progression and recurrence, and potentially to reduce stone burden [8]. Indeed, after experiencing an initial episode of renal colic, most patients are receptive, at least in the short term, to preventive measures recommended by their physicians [9].

In light of these goals, a variety of environmental and genetic risk factors have been identified that may be targeted for medical intervention. There are a variety of approaches to the metabolic evaluation of stone formers. Although there is no uniformity in the literature regarding the optimal evaluation and treatment program, several European consensus conference statements have been published on this subject [10,12].

## Material and methods:

This was a prospective observational study conducted in the Department of Urology, Indira Gandhi Institute of Medical Sciences Patna, Bihar, India for 10 months.

90 patients over 18 years old admitted in the urolithiasis outpatient clinic of a tertiary centre.

40 patients were excluded due to their medication chart, concerning allopurinol, citrate or thiazides, which could change the urinary metabolic pro- file, or due to the unavailability of assessment of the 24-hour urine samples.

Patient demographic data were obtained from medical records and during the medical appointment, including age, sex, tobacco (non-smoker, former or present smoker; pack-years) and alcohol (yes/ no) consumption, physical exercise (no exercise, 1–3 days/ week, 4–5 days/week, 6–7 days/week), weight and height to calculate the body mass index (BMI), co-morbidities such as hypertension, diabetes mellitus type 2 and dyslipidaemia, medical or surgical history (including past history of urologic interventions such as extracorporeal shock wave lithotripsy, ureteroscopy laser stone fragmentation or nephrolithotomy), medication chart, personal history and family stone history. Initial evaluation of every patient also included: urinalysis, 24-hour urine sample (with analysis of urinary calcium, oxalate, phosphate, uric acid, sodium and magnesium), bacteriologic examination of urine, serum analysis of creatinine, urea, ionised calcium and parathyroid hormone (PTH) and non-contrast computerized tomography (CT). Hydrochloric acid (HCl) was added into the container for oxalate measurement in the 24-hour urine sample. For the other measurements, patients received an empty container and were instructed to keep it in a cool place during the collection. We considered the following metabolic abnormalities: hyperoxaluria, hypercalciuria, raised PTH, hypercalcemia, hyperuricosuria, hypomagnesuria and hyperphosphaturia.

Reference laboratory values for urine and serum biochemical parameters in adults were made according to the European Association of Urology (EAU) Guidelines for Urolithiasis [13]. Since the reference values for serum PTH and urinary sodium are not given in these guidelines, we used those from our hospital laboratory (high levels for serum PTH was 65 pg/ml and 220 mmol/day for urinary sodium).

Statistical analysis was performed using the soft- ware Statistical Package for the Social Sciences (SPSS), version 25.0. Descriptive statistics were calculated for the sociodemographic, clinical and metabolic abnormalities. We used t-test for independent samples and nonparametric Mann-Whitney U test for comparisons between categorical and continuous variables, Chi-square for categorical variables and linear correlation for assessment between continuous variables. We considered statistically significant results for a p value <0.05.

**Results:**

The majority of the population was women, making a female/male ratio of 1.5:1. The median age at the time of the consultation was 50 years old, with most patients between 41 and 58 years of age. Frequencies of smoking and alcohol consumption and physical activity are shown in Table 1.

As depicted in Table 1 for clinical characterization, 2% of patients were underweight, 38% presented normal BMI and 60% were overweight or obese. Taking other comorbidities into account, 24% had hypertension, 14% had diabetes mellitus and 28% presented with dyslipidaemia. Almost 70% of patients admitted had personal history of lithiasis, with a median age of 44 years at first episode. Regarding past lithiasic intervention, 20% of patients presented with positive history. According to family history of urolithiasis, 40% of patients only referred one first degree relative while 10% mentioned two or more first degree relatives.

**Frequency and type of metabolic abnormality in patients with urolithiasis**

Metabolic abnormalities (considering any of these hyperoxaluria, hypercalciuria, raised PTH, hypercalcemia, hyperuricosuria, hypomagnesuria or hyperphosphaturia) were found in 94% patients (Confidence Interval 95%: 87.2–99.8%). Almost a quarter (26% [CI95%: 16.0–36.8%]) only had one metabolic abnormality, and 68% patients CI95%: 56.9–79.4%) had multiple metabolic abnormalities. Hypercalciuria was the most commonly observed metabolic abnormality and was found in 54% (CI95%: 43.5–67.6%) of patients. Other significant metabolic abnormalities were hyperoxaluria (34% [CI95%: 22.4–49.8%]), hyperuricosuria (32% [CI95%: 21.9–44.7%]) and hypomagnesuria (30% [CI95%: 21.3–44.2%]), as shown in Table 2. As for other urinary parameters, the median of the 24-hour urinary volume was 1680 ml, with 64% of patients presenting a 24-hour urinary volume be- low 2000 ml. The majority of urinary samples had a pH between 5.5 and 6.5 – almost a third (30%) of patients with a urinary pH less than 5.5 and 18% higher than 6.5. Approximately one-sixth (16%) of patients presented a positive urinary bacteriologic exam, with Escherichia coli as the most frequent isolated agent (5 in 9).

**Comparison between clinical and metabolic abnormalities**

Several sociodemographic and clinical variables with the most frequent metabolic abnormalities found in our study (hypercalciuria, hyperoxaluria, hyperuricosuria and hypomagnesuria). Patients with hypercalciuria were older (55.8 ±12.9 years vs. 48.8 ±6.8 years, p = 0.022), family history of stone disease was significantly more frequent among patients with hyperoxaluria (70% vs. 30%, p = 0.011) and there was a higher prevalence of present and former smokers among patients with hyperoxaluria (p = 0.012). Urinary volume was higher in patients with hypercalciuria (1879.4 ±637.9 ml vs. 1457.3 ±716.1 ml, p = 0.014) and hyperuricosuria (1956.2 ±685.2 ml vs. 1561.8 ±719.7, p = 0.041).

Body mass index was associated with urinary calcium and urinary pH. There was a positive linear relationship between BMI and urinary calcium (r = 0.251, p = 0.44) and a negative linear relationship between BMI and urinary pH (r = −0.251, p = 0.041). There was also a positive linear relationship between urinary calcium compared with urinary sodium (r = 0.519, p < 0.0001), uricosuria (r = 0.524, p <0.0001), magnesuria (r = 0.522, p <0.0001) and phosphaturia (r = 0.659, p <0.0001).

**Table 1: Sociodemographic and clinical characterization. Absolute and relative frequency of sociodemographic and clinical variables**

| Parameter | Number | % |
|---|---|---|
| Age | 50(41-58) | |
| Gender | | |
| Male | 20 | 40 |
| Female | 30 | 60 |
| Smoker (including former smoker) * | | |
| Below 10 pack years | 27 | 54 |
| 11-20 pack years | 7 | 14 |
| Above 20 pack years | 16 | 32 |
| Alcohol consumer (Yes)* | 21 | 42 |
| Physical exercise | | |
| NO | 25 | 50 |
| 1-3 days per week | 15 | 30 |
| 4-5 days per week | 4 | 8 |
| 6-7 days per week | 6 | 12 |
| BMI ($kg/m^2$) | | |
| Underweight | 1 | 2 |
| Normal | 19 | 38 |
| Overweight | 21 | 42 |
| Obesity | 9 | 18 |
| Hypertension (yes) | 12 | 24 |
| Diabetes mellitus (yes) | 7 | 14 |
| Hyperlipidemia (yes) | 14 | 28 |
| Personal history of lithiasis (yes) | 20 | 40 |
| Past lithiasic intervention | | |
| None | 40 | 80 |
| SWL | 4 | 8 |
| URS | 3 | 6 |
| SWL + URS | 1 | 2 |
| SWL + PNL | 1 | 2 |
| URS+PNL | 1 | 2 |

**Table 2: Blood and urine parameters.**

| Metabolic abnormality | Number (%) | CI 95% (%) |
|---|---|---|
| Hypercalciuria (>5 mmol/day) * | 27(54) | 43.5–67.6 |
| Hyperoxaluria (oxalate >0.5 mmol/day | 17(34) | 22.4–49.8 |
| Hyperuricosuria (>4 mmol/day<br>in women and >5 mmol/day in men) | 16(32) | 21.9–44.7 |
| Hypomagnesuria (<3 mmol/day) | 15(30) | 21.3–44.2 |
| Hyperphosphaturia (phosphate level>1.3 g/dl) | 9(18) | 7.8–28.4 |
| Elevated PTH (>65 pg/ml) | 8(16) | 5.8–24.3 |
| Hypercalcemia (ionised calcium >1.32 mmol/L) | 4(8) | 1.4–16.3 |

**Discussion:**

In our series, the most striking finding was the very high prevalence of metabolic abnormalities (94%), resembling the findings of several other studies, which considered metabolic abnormalities as one of the most important factors for stone formation [14,16]. Nevertheless, in some studies, a predominance of other abnormalities such as hyperoxaluria [14]. or hypo- magnesuria was found. These disparate results may be explained by climate, seasonal, dietary or life-style variations, which highlights the importance of studying the prevalence of different metabolic changes in each population. This matter assumes a preponderant role, given the ability to modify these metabolic abnormalities with preventive (metaphylatic) measures, including diet and lifestyle changes along. Hypercalciuria (detected in 54% of patients) was the most frequent metabolic abnormality, followed by hyperolaxuria (34%) and hyperuricosuria (32%), a finding also observed in larger studies, most of them with patients with recurrent stone formation history [14,18]. We included 17 patients with first self-reported episode of stone disease and, interestingly, all of them presented at least one metabolic abnormality. It is known that obesity and weight gain increase the risk of stone formation. In our study, the majority (60%) of patients was overweight or obese and the increase of BMI was associated with a higher urinary calcium excretion. These patients may benefit from nutritional counseling for weight loss, aiming for the reduction of stone recurrence and decreasing cardiovascular risk. We also observed that BMI was inversely related to urinary pH, explained by the hypothesis that obesity may induce excessive production of acidic urine secondary to insulin resistance [20]. Almost a third (28%) of patients presented a urinary pH less than 5.5, a documented risk for uric acid nephrolithiasis. Patients with persistently low urinary pH benefit from urine alkalization.2019]. With the introduction of some pharmacological options (i.e. allopurinol, citrate or thiazides) that might prevent urinary stone formation [14]. There is great variability in the literature regarding the prevalence of urolithiasis according to gender. Our sample revealed a predominance of women (1.5:1), the same ratio pointed by Amaro et al [15]., but different from other studies, with a gender ratio male/female of 1.5–2.5 across the world. The gender ratio discussion of this study is precluded by the methods of patients' referral which influences our outpatient clinic representativeness of the general population. Patients with hypercalciuria were older than those without this metabolic abnormality, with a median age around 50 years. Otto et al. also observed that middle-aged patients are more likely to be hypercalciuric [21]. The higher prevalence of present and former smokers among patients with hyperoxaluria sustains the studies of Hamano et al. The authors suggested an interplay between cigarette smoking and arginine vasopressin, resulting in a further decrease of urinary output and enhancing stone formation. There- fore, smoking cessation can be effective in reducing calcium stone recurrence [22]. According to the European Association of Urology Guidelines for Urolithiasis [13], one preventative risk for stone formation relies on a higher fluid in- take, 2.5–3.0 l/day, in order to maintain a urinary volume between 2 and 2.5 l/day. We observed that 62.7% of patients presented a lower 24-hour urine output (<2 l in 24 h) and recommending an increased fluid intake should be considered the first option as a general treatment of these patients. Despite our findings, in clinical practice the implementation of an extensive metabolic evaluation is still controversial. In our opinion, given the high prevalence of metabolic abnormalities in our population, it seems to be worth performing an extended metabolic evaluation in all patients admitted to the urolithiasis clinics in a tertiary hospital. In fact, this work-up has prompted the prescription of preventive measures and drugs in a significant number of patients. We believe that this work-up is also cost effective, with a reduction of new stone-related events, such as admission to the Emergency Department (ER) and possible need for urgent surgical intervention, follow-up consultations and future non-invasive or minimally invasive procedures. Whether or not this proactive attitude should be extended to primary health care level remains to be elucidated. Despite being an important ionic molecular inhibitor, our laboratory was unable to measure urinary citrate which is an important limitation of this study. Also, some urine samples did not present oxalate measurement due to unexpected laboratory technical problems. We decided to perform just one 24-hour urine collection for the sake of the patient's convenience and adherence, and in fact the need for one versus two 24-hour urine collections during the initial metabolic evaluation is still an unsolved issue [23].

## Conclusion:

This immediate metabolic evaluation is the key for a better and individualized management, guiding the selection of proper pharmacological and dietary measures to prevent recurrent stone formation and to relieve all clinical and economic burdens behind this condition.

## Reference:


1. Pearle MS, Calhoun EA, Curhan GC. Urologic Diseases of America Project. Urologic diseases in America project: urolithiasis. J Urol 2005; 173:848‒57.
2. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976‒1994. Kidney Int 2003; 63:1817‒23.
3. Uribarri J, Oh MS, Carroll HJ. The first kidney stone. Ann Intern Med 1989; 111:1006‒9.
4. Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. Kidney Int 2001; 59:2290‒8.
5. Robertson WG. A risk factor model of stone-formation. Front Biosci2003;8: s1330‒8.
6. Krepinsky, J., Ingram, A.J., and Churchill, D.N. (2000) Metabolic investigation of recurrent nephrolithiasis: compliance with recommendations. Urology **56**, 915.
7. Glowacki, L.S., Beecroft, M.L., Cook, R.J., et al. (1992) The natural history of asymptomatic urolithiasis. J. Urol.**147**, 319.
8. Shekarriz, B. and Stoller, M.L. (2002) Uric acid nephrolithiasis: current

concepts and controversies. J. Urol. **168**, 1307.
9. Grampsas, S.A., Moore, M., Chandhoke, P.S. (2000) 10-year experience with extracorporeal shockwave lithotripsy in the state of Colorado. J. Endourol. **14,** 711.
10. Tiselius, H.G. (2001) Possibilities for preventing recurrent calcium stone formation: principles for the metabolic evaluation of patients with calcium stone disease. BJU Int. **88**, 158.
11. Consensus conference (1988) Prevention and treatment of kidney stones. JAMA **260**, 977.
12. Osther, P.J., Grenabo, L., Haraldsson, G., et al. (1999) Metabolic evaluation and medical management of upper urinary tract stone disease. Guidelines from the Scandinavian Cooperative Group for Urinary Stones. Scand. J. Urol. Nephrol. **33**, 372.
13. Türk C, Neisius A, Petrik A, et al. EAU Guidelines on Urolithiasis 2017.ISBN 978-90-79754-91-5. EAU Guidelines Office, Arnhem, The Netherlands. 2017
14. Ahmad I, Pansota MS, Tariq M, Tabassum SA. Frequency of metabolic abnormalities in urinary stones patients. Pak J Med Sci. 2013; 29: 1363-1369
15. Amaro CR, Goldberg J, Damasio PC, et al. An update on metabolic assessment in patients with urinary lithiasis. World J Urol. 2015; 33: 125-129.
16. Parvin M, Shakhssalim N, Basiri A, et al. The most important metabolic risk factors in recurrent urinary stone formers. Urol J. 2011; 8: 99-106.
17. Karabacak OR, Ipek B, Ozturk U, Demirel F, Saltas H, Altug U. Metabolic evaluation in stone disease metabolic differences between the pediatric and adult patients with stone disease. Urology. 2010; 76: 238-241.
18. Shah S, Calle JC. Dietary and medical management of recurrent nephrolithiasis. Cleve Clin J Med. 2016; 83: 463-471.
19. Abdel Goad EH, Bereczky ZB. Metabolic risk factors in patients with renal stones in KwaZulu Natal: an inter-racial study (Asian and Whites). BJU Int. 2004; 93: 120-123.
20. Maalouf NM, Sakhaee K, Parks JH, Coe FL, Adams-Huet B, Pak CYC. Association of urinary pH with body weight in nephrolithiasis. Kidney Int. 2004; 65: 1422-1425.
21. Otto BJ, Bozorgmehri S, Kuo J, Canales M, Bird V, Canales BK. Age, BMI, and Gender Predict 24 Hour Urine Parameters in Recurrent Idiopathic Calcium Oxalate Stone Formers. J Endourol. 2017: 31: 1335-1341.
22. Hamano S, Nakatsu H, Suzuki N, Tomioka S, Tanaka M, Murakami S. Kidney stone disease and risk factors for coronary heart disease. Int J Urol. 2005; 12: 859-863.
23. Alruwaily AF, Dauw CA, Bierlein MJ, et al. How Much Information is Lost When You Only Collect One 24-Hour Urine Sample during the Initial Metabolic Evaluation? J Urol. 2016; 196: 1143-1148.