

## CLINICAL STUDY

# Metabolic abnormalities in patients with recurrent stone formation in a hot territory

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**Abstract:** *Objective:* This was a cross-sectional study of 150 consecutive patients (105 males and 44 females) with nephrolithiasis. Serum and urine metabolic evaluations were performed.

*Results:* 70 percent (n=105) of patients were males. Sixty patients (40 %) had hypertension. The urine volume of 114 subjects (76 %) was less than 1 liter/day. There was an inverse correlation between urine pH and weight of patients ( $r=-0.48$ ,  $p=0.001$ ). The prevalence of hypophosphatemia, hypokalemia, hyperuricemia and hypercalcemia was 11 % (n=17), 12.6 % (n=19), 20 % (n=30), and 5 % (n=8), respectively. The prevalence of hypercalciuria and hyperuricosuria was 24 % (n=36) and 14 % (n=21), respectively. The urine calcium significantly correlated with urine sodium ( $r=0.3$ ,  $p<0.001$ ) and uric acid ( $r=0.43$ ,  $p<0.001$ ). Serum phosphate concentrations were inversely correlated with urine calcium concentrations ( $r=-0.37$ ,  $p=0.016$ ).

*Conclusion:* Our findings suggest that lower urine volume has an important role in nephrolithiasis in hot areas. Higher urine sodium and uric acid and lower serum phosphor correlate with higher urine calcium in stone formers. However, further cohort studies should be performed to establish these findings (Tab. 2, Fig. 3, Ref. 26). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: nephrolithiasis. hypophosphatemia. hypercalciuria.

Kidney stone is a common problem (1) and the population prevalence of renal stones has increased from 3.8 % to 5.2 % during one decade (2).

The evaluation of patients with nephrolithiasis consists of radiographic imaging along with blood and urine testing. Although there is general agreement that a complete metabolic evaluation is indicated in all patients with recurrent stone formation, some studies have shown medical evaluation is not cost-effective for patients who have only formed one stone (3).

Metabolic abnormalities such as hypercalciuria, hyperuricosuria and low urine volume that cause stone disease varies in different population and environmental and genetic factors might result in these differences (4, 5, 6).

The aim of this study is to evaluate the metabolic abnormalities in patients with recurrent stone formation in a hot territory in our country.

## Materials and methods

Between October 2006 and March 2007, we performed a cross-sectional study in 150 consecutive patients with recurrent

renal calculi. The metabolic evaluation for renal stones consisted of both serum and urine testing. All of these evaluations were performed two months after passing stone.

A routine chemistry blood tests included measurement of serum calcium, uric acid, potassium, phosphorus and creatinine. Twenty-four hour urine collections were obtained with measurement of urine volume, pH and excretion of calcium, uric acid, sodium, potassium and creatinine. Measurement of creatinine excretion permitted assessment of the completeness of the 24-hours collection. The normal rate of urinary creatinine excretion in patients under the age of 50 is 20 to 24 mg/kg of lean body weight in men and 15 to 20 mg/kg of lean body weight in women. The upper limit of normal urine calcium and uric acid was <300 mg for men, <250 mg for women and <800 mg for men, <750 mg for women, respectively.

At first urine specific gravity (SG) was measured. Both of serum and urine tests were obtained in the outpatient setting when the patients were on their usual diet and physical activity. The history of renal stones in first degree relatives was considered as familial history of stone.

**Tab. 1. Demographic data of patients with renal stones.**

Age	40±12 (18–73)
Sex (male/female)	105 (70 %) /44 (30 %)
Weight (kg)	73±13.2 (47–120)
Family history	100 (67 %)

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**Tab. 2. Serum and urine analysis data of patients with renal stones.**

Serum		
Creatinine		1.09±0.37 (0.56–2.6)
Calcium		8.9±0.90 (4.50–11.30)
Phosphorus		3.7±0.73 (2.3–6.4)
Potassium		4±0.57 (2.60–5.70)
Uric acid		5.1±2.10 (2–20)
Urine		
Specific gravity (SG)	1010>	12 (8 %)
	1010–1020	48 (32 %)
	>1020	90 (60 %)
	<5.5	115 (77 %)
pH	>5.5	35 (23 %)
	1000>	33 (22 %)
Volume	1000–2000	81 (54 %)
	>2000	36 (24 %)
Uric Acid		467.03±223.6 (116–2000)
Sodium (Na)		160.4±81.4 (24–500)
Potassium (K)		42.13±28 (15–250)
Calcium (Ca)		165±68.1 (63–420)
Creatinine (Crea)		1153.9±383.2 (450–2500)

### Statistical analysis

All data were analyzed with SPSS 15. Data are expressed as mean values±SD. Correlations between numerical values were assessed by Pearson analysis. A value of  $p < 0.05$  was considered statistically significant.

### Results

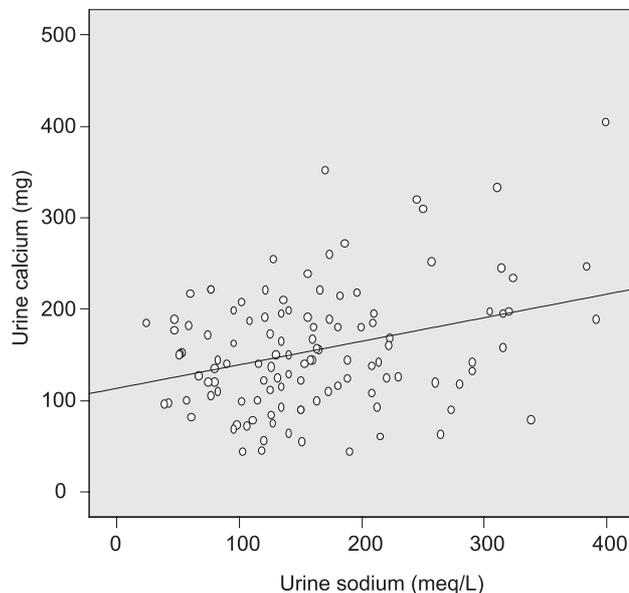
Demographic and metabolic evaluations of patients are shown in Tables 1 and 2, respectively. 70 percent ( $n=105$ ) of patients were males. Sixty patients (40 %) had hypertension. The family history of kidney stone was observed in 100 patients (67 %). The prevalence of hypophosphatemia, hypokalemia, hyperuricemia, and hypercalcemia was 11 ( $n=17$ ), 12.6 ( $n=19$ ), 20 ( $n=30$ ) and 5 ( $n=8$ ) percent, respectively. The prevalence of hypercalciuria and hyperuricosuria was 24 % ( $n=36$ ) and 14 % ( $n=21$ ), respectively.

Urine pH was below 5.5 in 115 patients (77 %). There was an inverse correlation between urine pH and weight of patients ( $r=-0.48$ ,  $p=0.001$ ). The urine calcium significantly correlated with urine sodium ( $r=0.3$ ,  $p<0.001$ ) and urine uric acid ( $r=0.43$ ,  $p<0.001$ ) (Figs 1 and 2). The urine calcium significantly correlated inversely with serum phosphorus ( $r=-0.37$ ,  $p=0.016$ ) (Fig. 3).

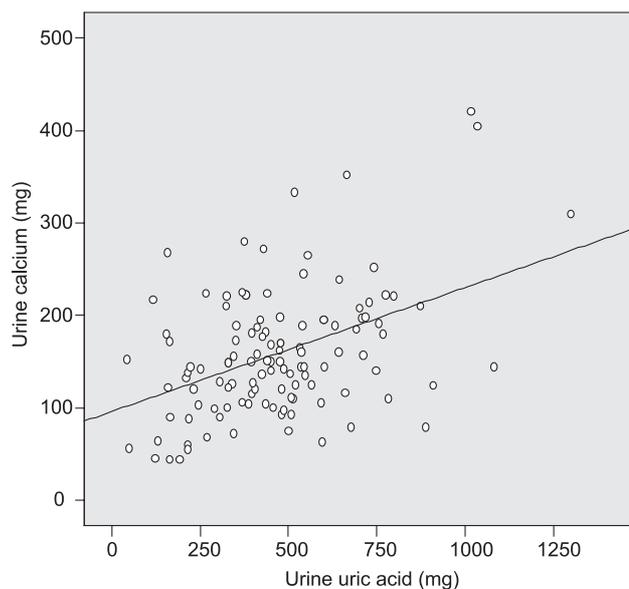
### Discussion

In one study, the ratio of male/female renal stone was 2.3/1, and it is similar to this study that has shown the incidence of renal stones is more common in men than women (1, 2).

40 % of our patients had hypertension. We had no control group, but according to the prevalence of hypertension in adult group in Iran that is 15 % (7) it seems that the prevalence of hypertension in our study is higher than in general population. In a cohort study, Borghi et al (8) have shown hypertension increases 5.5 times in stone formation. They explained that exces-



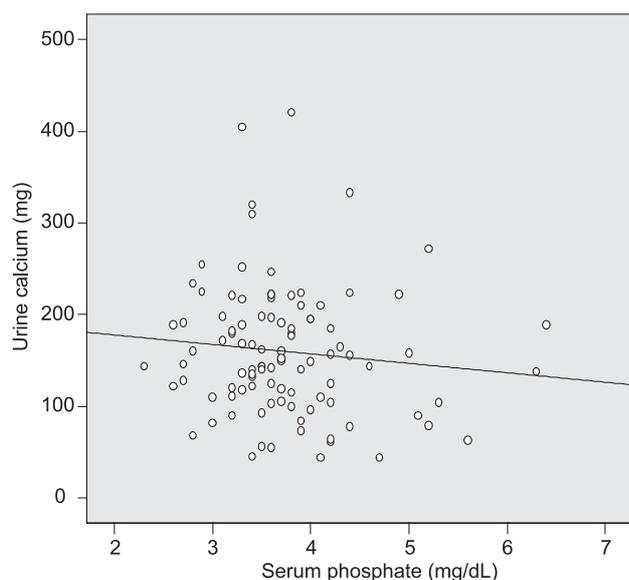
**Fig. 1. Correlation between urine calcium and sodium.**



**Fig. 2. Correlation between urine calcium and urine uric acid.**

sive weight and consumption of salt and animal proteins in hypertensive patients may cause renal stone formation. Some studies have reported that stone formers experienced 69 % increase in odds of hypertension that was significantly more than non stone formers (9).

Although we had no control group, our data support that the patients who have suffered from kidney stone have 23 % of family history of kidney stones. Some reports show the relationship between family history and risk of kidney stone formation. Gray et al have shown over an eight years period, individuals with a positive family history had a relative risk of 2.6 of experiencing a stone as compare with those without such history (10). Famil-



**Fig. 3. Correlation between urine calcium and serum phosphate.**

ial aggregation has also been noted in Italy (11). Family history data don't distinguish between genetic and environmental features. However, there is evidence of genetic susceptibility to development of calcium stone disease (12, 13).

Low urine volume is an important risk factor of formation of renal stones (14). Levy et al (15) have reported that 15 % of stone formers have low urine volume (<1 L) and in our study 33 % and 60 % of patients had low urine volume and specific SG, respectively. And the explanation is that our territory is in hot areas.

In our study, the prevalence of hypercalcemia was 5.6 % of patients; however, we did not measure PTH. Our result is similar to a study performed in 1132 patients with nephrolithiasis (16). They reported 4.2 % of hypercalcemia with hyperparathyroidism. Karmar et al have shown that a history of gout independently increases the risk for incident kidney stones in men. In our patients, however, the prevalence of hyperuricosuria was 20 %; but only 5 % of them had history of gout arthritis.

We did not measure citrate and oxalate of urine and it might be a shortage of our study. However, we found a prevalence of 12.7 % of hypokalemia and it might correlate with relation between potassium and urine citrate (17) and potassium and urine calcium (18).

The prevalence of hypercalciuria and hyperuricosuria was 27 % and 14 %, respectively. Some studies have shown that hypercalciuria and hyperuricosuria are risk factors of renal stones formation (19) (20). Levy et al (15) have also reported that hypercalciuric calcium nephrolithiasis accounted for 60 % of patients and hyperuricosuric calcium nephrolithiasis accounted for 36 % of patients. In our study, however, the prevalence of these abnormalities was lower than in Levy's and the explanation was that in our cases, nephrolithiasis was not just calcium type.

We found that stoners with higher weights had lower urinary pH. Maalouf et al (21) has also showed urinary pH is in-

versely related to body weight among patients with stones, and their results confirmed that obesity may sometimes cause uric acid nephrolithiasis by producing excessive uric acid due to insulin resistance.

We found that the urine calcium correlated with urine sodium (Fig1). A high sodium intake will enhance the excretion of calcium, a relationship that has been thought to be due in part to the reabsorption of calcium passively following that of sodium and water in the proximal tubule (22). Sakhaee et al (23) have also shown that high urine sodium correlate with high urine calcium.

In our study, the prevalence of hypophosphatemia was 11.5 % and we also found that the patients with lower serum phosphor correlate with high urine calcium (Fig. 3). Some studies have shown that hypophosphatemia has the effects that can promote stone formation including reduced tubular calcium reabsorption (24, 25, 26).

In summary, lower urine volume has an important role in nephrolithiasis in hot areas. Higher urine sodium and uric acid and lower serum phosphor correlate with higher urine calcium in stone former. However, further cohort studies should be performed to establish these findings.

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