

In The Name of God

Etiology of Nephrolithiasis in Iran

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MD., RESEARCH ASSISTANT

Keywords

- Nephrolithiasis
- Renal stone
- Kidney stone
- Urolithiasis
- Etiology
- Metabolic abnormalities
- Iran

Scientific resources

- PubMed
- Scopus
- Web of science
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Metabolic disorder in patients with urinary stone

Hossein Mahmoudi *

Abstract: (6500 Views)

Background : Urinary stones are quite frequent problems of urinary system that encompass different metabolic disorders. The present study was conducted on patients referring to Naghavi hospital in Kashan during 2000-2001 with urinary stone to find out their different metabolic disorders.

Materials and methods : For this descriptive study, all candidates aged 15 or more were included. Urinary stones were diagnosed using sonography and /or IVP. Meanwhile, the level of Ca, uric acid, creatinine, Na, K, 24-hour urine analysis, and patients' demographic characteristics were determined.

Results : The study population included 55 males and 24 females. The most common disorders were oliguria (78.4%), hypercalciuria (27.8%), hyperuricosuria (11.3%), hyperuricemia (8.8%), and hypercalcemia (2.5%).

Conclusion : Oliguria is by far the most common problem that occur due to excessive heat, excessive sweating, and loss of liquid intake. Necessary educative programs can be helpful.

Keywords: Urinary stone, Metabolic disorder, Prevention

Methods and materials

- A cross sectional study
- 2000-2001
- **Kashan**
- **79** patients with nephrolithiasis
- ≥ 15 yrs.
- Blood sample: Cr, Na, K, Ca, Uric acid
- Urine sample
- 24-hour urine: Cr, Ca, Uric acid

Results

- Male: 55 (70%)
- The most common metabolic abnormalities:
 - Low urine volume 78.4%
 - Hypercalciuria 27.8%
 - Hyperuricosuria 11.3%
- Hyperuricemia 8.8% & hypercalcemia 2.5%

Conclusion

- **Low urine volume** was by far the most common problem that occurred due to excessive heat, excessive sweating & loss of fluid intake.

Metabolic abnormalities in patients with nephrolithiasis: comparison of first-episode with recurrent cases in Southern Iran

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Abstract

Background Metabolic disorders are one of the etiologic factors in renal stone formation. The aim of present study was to evaluate prevalence of metabolic disorders in patients with renal stone.

Methods From 572 patients referring to our urologic clinics, 376 patients participated in the study. Patients were divided to first time stone former (group A) and recurrent renal stone (group B). Twenty-four hour urine specimens were obtained for urinary calcium, oxalate, magnesium, citrate, uric acid, phosphor and 24-h urine volume. Venous blood samples were obtained evaluating serum phosphate, uric acid, and calcium. The prevalence of each metabolic disorder was detected, and two groups were compared regarding metabolic disorders.

Results The prevalence of renal stone in male patients was 63.04% versus 36.96% in female

hyperuricosuria (15.15%). Hyperuricemia was found in 6 first time stone former patients and 14 patients with recurrent renal stone ($P = 0.04$). There was no statistically significant difference between group A and B in other metabolic abnormalities ($P > 0.05$).
Conclusion Low 24-h urine volume was the most common abnormalities in patients with nephrolithiasis in our region. Metabolic evaluation must be performed in all patients with renal stone even those with first time stone formation.

Keywords Metabolic abnormalities ·
Renal stone · First time stone former ·
Recurrent renal stone

Methods and materials

- A cross sectional study
- Feb 2007- Feb 2008
- **Shiraz**
- **376** patients with nephrolithiasis
- 3 to 81 yrs.
- Blood sample: CBC, BUN, Cr, Na, K, Ca, Ph, Uric acid
- Urine sample: U/A, U/C
- 24-hour urine: Volume, Ca, Ph, Mg, Oxalate, Citrate, Uric acid
- Questionnaire: Age, Gender, UTI history, FH of nephrolithiasis, History of ESWL/PCNL/TUL

Results

- Male: 237 (63.04%)
- mean age: 42±8.34
- Group A: 214 patients who diagnosed to have renal stone for the first time
- Group B: 162 patients who diagnosed to have renal stone previously
- **Hyperuricemia** was the only metabolic disorder with statistically significant difference between two groups (P = 0.04)
- The most common metabolic abnormality: **decreased 24-h urine volume** to less than 2 liter (58.24%)
- **Hypercalciuria** was more common than other evaluated metabolic disorder in our study (17.81%)
- **Hyperuricosuria** was the other metabolic disorder which was more common in both groups

Table 2 Metabolic abnormalities and comparison between patient groups A and B

Disorder	Group A	Group B	Total	<i>P</i> -value
24 h UV < 2 l	122	97	219	NS
High 24 h U Ca	34	33	67	NS
High 24 h U u/a	30	27	57	NS
High 24 h U Ox	3	6	9	NS
Low 24 h U Ph	4	9	13	NS
Low 24 h U Cit	2	5	7	NS
Low 24 h U Mg	1	4	5	NS
Hypercalcemia	5	11	16	NS
Hyperuricemia	6	14	20	0.04
Hyperphosphatemia	3	5	8	NS
Total	210	166	376	NS

Conclusion

- **Low 24-h urine volume** was the most common abnormalities in patients with nephrolithiasis in Shiraz.
- Metabolic evaluation must be performed in all patients with renal stone even those with first time stone formation

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 preformed.

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.

Key words: nephrolithiasis. hypophosphatemia. hypercalciuria.

Methods and materials

- A cross sectional study
- Oct 2006 to Mar 2007
- Yazd
- 150 patients with recurrent renal calculi
- 2 months after renal passage, blood and urine sample were collected

Results

- Males: 105 (70%)
- Mean age: 40±12
- Positive FH: 100 (67%)
- Hypophosphatemia 11%, hypokalemia 12.6%, hyperuricemia 20% and hypercalcemia 5%
- The prevalence of **hypercalciuria 24%** and **hyperuricosuria 14%**
- Lower urine volume has an important role in nephrolithiasis in hot areas
- **Higher urine Ca** in stone former correlate with **higher Na and uric acid** and **lower serum Ph**

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		
	1010>	12 (8 %)
Specific gravity (SG)	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)

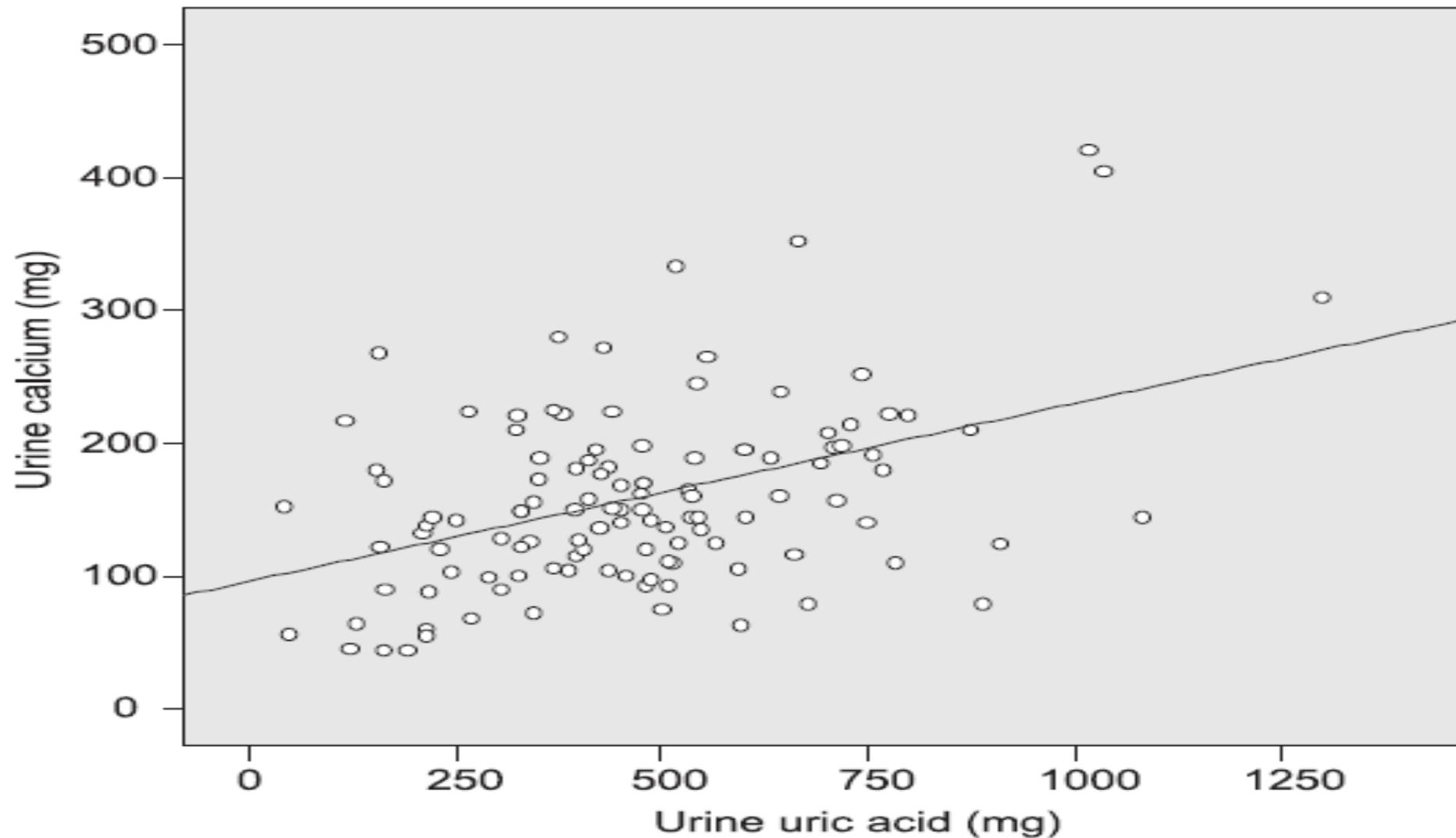


Fig. 2. Correlation between urine calcium and urine uric acid.

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.

Original Article

**Comparison of 24-Hour Urinary Citrate Excretion in Stone Formers
and Healthy Volunteers**

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ABSTRACT. Low urinary citrate excretion is a risk factor in stone formers (SF). This study aimed to measure the urinary citrate excretion in SF and healthy volunteers at our center from 12 June 2008 to 20 August 2009. There were 28 SF patients (18 males and ten females) and 27 (18 males and nine females) age-matched healthy adult volunteers who participated in this study. Both groups had a similar living environment, extrinsic factors, diet and genetic descent. After collecting 24-h urine, citrate was measured using an enzymatic kit. Routine urinalysis and 24-h creatinine and uric acid were also performed. There was a significant difference in urinary citrate excretion level among SF (mean 310, SD 260 mg/L) and normal volunteer subjects (mean 800, SD 300 mg/L). By applying the previously defined normal values (320 mg/24 h) of urinary citrate in the local population, 43% of the SF in our study group was hypocitric, and none among the controls. We conclude that prevalence of hypocitraturia in stone formers was higher than that in healthy volunteers in our population.

Methods and materials

- A case-control study
- Jun 2008 to Aug 2009
- 28 patients
- **Hamadan**
- Inclusion criteria: at least 2 times hx of renal stone removal during the last 2 years
- Exclusion criteria: any medication during the collection of the urine, UTI
- 27 matched normal individuals were the control group
- U/A and 24-hour urine (citrate, uric acid and Cr)

Results

- Mean age: study group (34.7±14.5) & control group (39.9±12.6)
- Male to female ratio: study group (18/10) & control group (18/9)
- There were no significant differences in demographic parameters between both groups
- **Calcium phosphate** and **calcium oxalate** were the most prevalent stones (82%) in the study group
- The means of citrate concentration in urine and urinary excretion of citrate were **lower** in the **study group** (P <0.001)
- **43%** of the urolithiasis patients were **hypocitraturic**

Table 2. Urine characteristics in stone formers and healthy subjects.

Urine parameters	Stone former patients (<i>n</i> = 28)	Healthy controls (<i>n</i> = 27)
Urine volume (mL/24 h)	1489 ± 575.5*	1198 ± 401
Specific gravity	1023 ± 8.4*	1024 ± 7.25
Urine creatinine (g/24 h)	1.6 ± 0.9*	1.8 ± 0.7
Urine pH	6.12 ± 0.53*	5.93 ± 0.67
Urine uric acid (mg/24 h)	651 ± 158*	681 ± 147

Table 3. Urinary citrate in terms of concentration, daily excretion and excretion rate per gram of creatinine in stone formers and healthy subjects.

Citrate	Stone former patients (<i>n</i> = 28)	Healthy controls (<i>n</i> = 27)
Concentration (mg/L)	310 ± 260* (CI** = 393.1–44.8)	800 ± 300
Excretion (mg/g creatinine)	363 ± 337*** (CI = 654.4–227.2)	582 ± 305.6
Daily excretion (mg/24 h)	460 ± 375* (CI = 625.5–322.4)	901 ± 414

P* < 0.001 compared with the healthy group, **CI = 95% confidence interval, **P* = 0.015 compared with the healthy group.

Conclusion

We conclude that prevalence of **hypocitraturia** in stone formers was higher than that in healthy volunteers in our population

Metabolic evaluation in patients with nephrolithiasis: A report from Isfahan, Iran

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Abstract

Background: Nephrolithiasis is a major public health problem worldwide. In recent years, growing evidence suggest that this disease may originate from underlying metabolic disorders. This is the first study that reports the frequency of different metabolic abnormalities among patients with nephrolithiasis in Isfahan, a large central province of Iran.

Materials and Methods: From the time period between March 2009 and August 2010, 437 nephrolithiasis patients in Isfahan province enrolled in this study. Metabolic evaluation was performed by obtaining a 24-hours urine sample and fasting venous blood draw. We analyzed urine samples for volume, creatinine, calcium, citrate, oxalate, uric acid, sodium, and cystine. Fasting blood samples were assessed for serum calcium, phosphorus, sodium, potassium, uric acid, albumin, creatinine and blood urea nitrogen.

Results: The mean age was 46 ± 13.8 years (rang: 18-87). Nearly 50% were first time stone formers. The most common metabolic abnormalities were hypocitraturia (40.5%) and hypernatruria (31.8%) that was followed by hyperoxaluria (28.8%). Hypercalciuria was detected only in 9.2% of the cases.

Conclusion: Although, high calcium excretion was the most frequent metabolic derangement in several similar studies, in our province with considerably high prevalence of vitamin D deficiency, it is not frequent among nephrolithiasis patients. Instead, other metabolic risk factors were in higher frequencies.

Key Words: Metabolic abnormalities, hypercalciuria, nephrolithiasis, Isfahan, Iran

Methods and materials

- A cross sectional study
- Mar 2009 to Aug 2010
- 437 nephrolithiasis patients
- **Isfahan**
- Inclusion criteria: age \geq 18 yrs. & confirmed diagnosis of nephrolithiasis
- Exclusion criteria: eGFR $<$ 60 ml/min/1.73m² & those who are on medications
- Age, sex, hx of nephrolithiasis and any concurrent diseases collected from medical records
- 24-hour urine & fasting blood sample

Results

- Males: 211 (48.3%)
- Mean age: 46 ± 13.8 yrs.
- PMH of nephrolithiasis: 220 (50.3%)
- Positive FH of nephrolithiasis: 180 (41.2%)
- In contrast to other similar studies, **hypercalciuria** was **not** a frequent metabolic abnormality among nephrolithiasis patients (9.2%)
- **Hypocitraturia** and **hyperoxaluria** were more frequent (40.5% & 28.8%)

Table 2: The mean \pm SD values of serum and 24 hours urine analysis in patients

Variable	Male	Female	Total
Serum analysis			
Calcium (mg/dl)	9.42 \pm 0.57	9.33 \pm 0.54	9.4 \pm 0.55
Sodium (mEq/l)	139.9 \pm 3.2	139.6 \pm 3.2	139.8 \pm 3.2
Potassium (mEq/l)	4.14 \pm 0.04	4.1 \pm 0.41	4.1 \pm 0.4
Uric Acid (mg/dl)	5.9 \pm 1.6	4.9 \pm 1.3	5.4 \pm 1.5
Phosphorus (mg/dl)	3.47 \pm 0.64	3.44 \pm 0.64	3.5 \pm 0.64
24 hrs urine analysis			
Volume (ml)	1882 \pm 736	1651 \pm 734	1793 \pm 745
Calcium (mg)	173 \pm 94	159 \pm 82	165 \pm 88
Sodium (mEq)	200 \pm 86	164 \pm 68	181 \pm 79
Oxalate (mg)	44.5 \pm 33	43.8 \pm 43	44 \pm 39
Citrate (mg)	367 \pm 153	381 \pm 193	375 \pm 174
Uric acid (mg)	638 \pm 663	516 \pm 183	575 \pm 482
Cystine (mg)	30.3 \pm 42.5	27.5 \pm 44.4	28.8 \pm 43.4

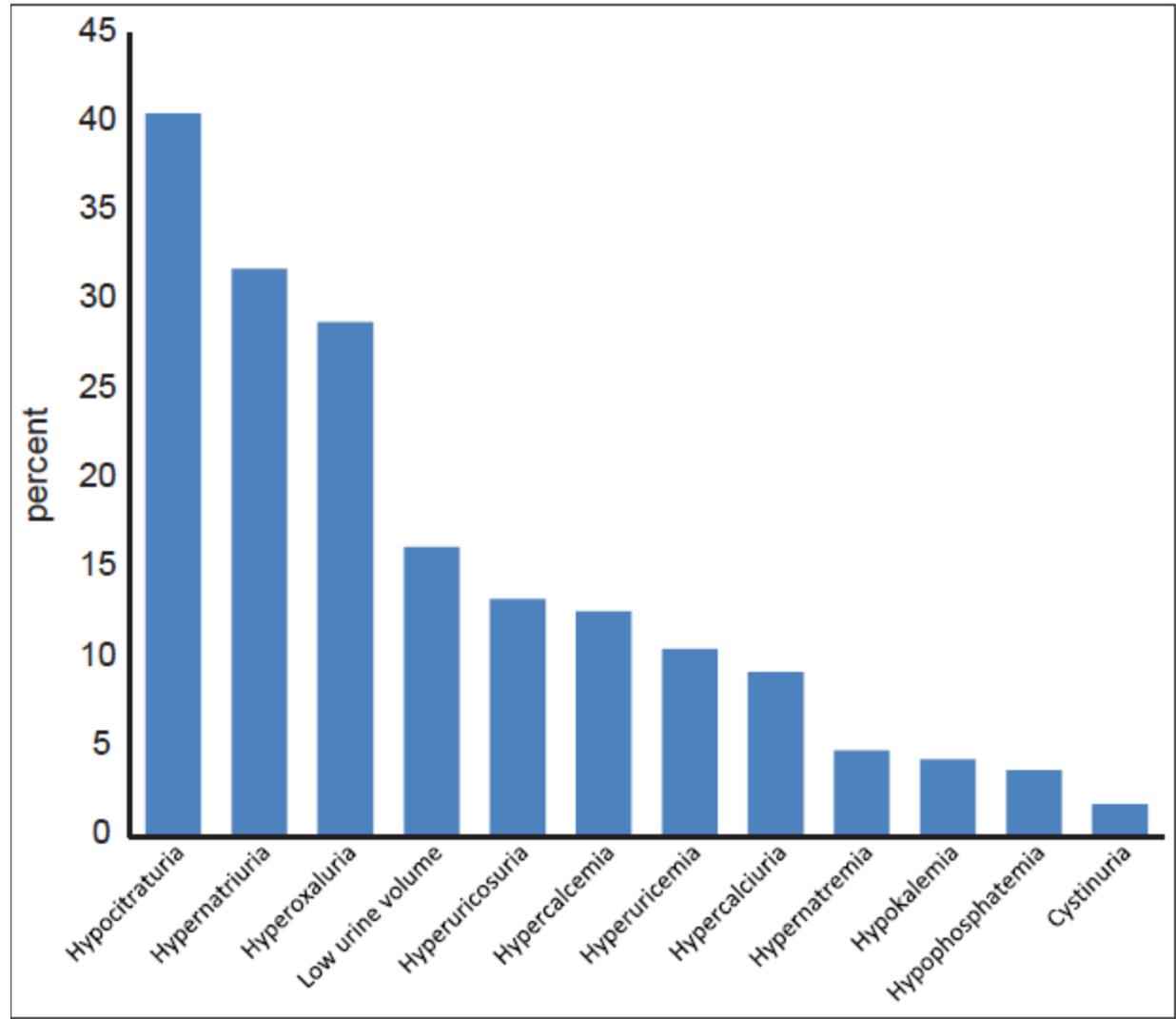


Figure 1: Frequency of metabolic abnormalities among patients

Conclusion

- Results revealed that in contrast to other similar studies, hypercalciuria is not a frequent metabolic abnormality among nephrolithiasis patients in our region.
- Instead, **hypocitraturia and hyperoxaluria** were in higher frequencies.

Study of Urine Composition of Patients With Recurrent Nephrolithiasis in Lorestan, Iran

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Keywords. recurrent urinary
calculus, urine biochemistry,
nephrolithiasis

Introduction. Nephrolithiasis is one of the most common urinary tract diseases. After the first episode of urinary calculus, the risk of recurrence is nearly 40% to 50% at 5 years. Nephrolithiasis is a systemic disease that is associated with some metabolic disorders. This study aimed to provide a picture of the frequency of metabolic abnormalities in patients with nephrolithiasis from west part of Iran. **Materials and Methods.** Patients with recurrent urinary tract calculi referred to the Nephrology-Urology Clinics in Khorramabad city were recruited. After collection of demographic data of all the patients, 24-hour urine and blood samples were taken to measure biochemical factors.

Results. Of the 232 participants, 125 were males and 107 were females. Hyperoxaluria was seen in 93 (40.1%) of the participants, hypercalciuria in 55 (23.7%), hypocitraturia in 58 (25%), and hyperuricosuria in 33 (14.9%). Hyperoxaluria in the males was significantly more frequent than in the female patients. There were no significant differences between the two groups in other urinary metabolic disorders.

Methods and materials

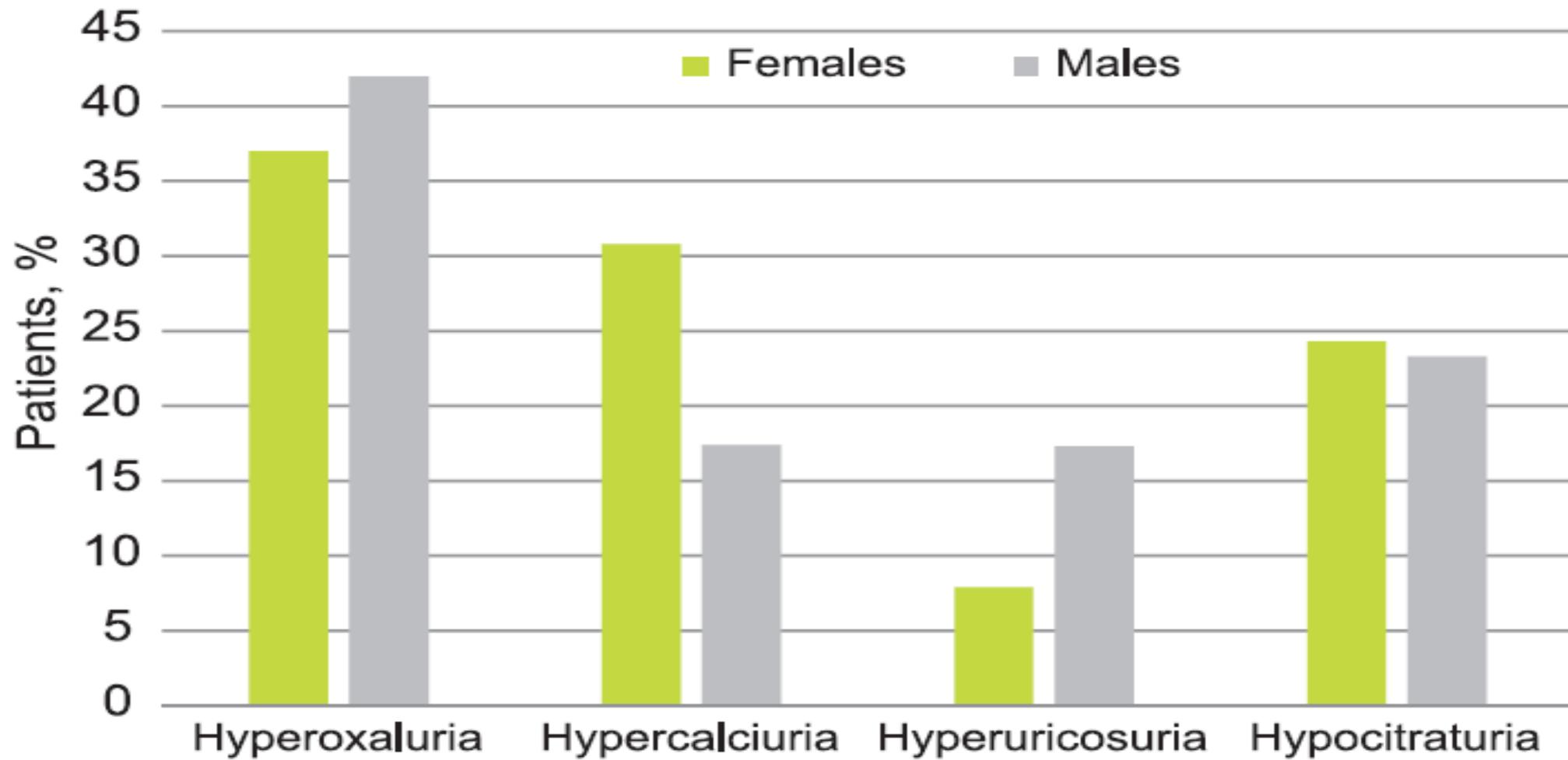
- A cross sectional study
- Jan 2016 to Feb 2016
- **Lorestan**
- 232 patients
- Inclusion criteria: age \geq 14 yrs. & on usual typical diet
- Exclusion criteria: recent hospitalization, hx of calculus passage during the recent 8 weeks, on medical or dietary treatment & first calculus former patients
- 24-hour urine, blood sample, age & gender were collected

Results

- Males: 125 (53.9%)
- Mean age: 46.10
- Hyperoxaluria was seen in 93 (40.1%) of the participants
- **Hyperoxaluria** was the **most common abnormality**
- There were **no** significant differences in the levels of serum **Ca** and **uric acid** between men and women
- Urine metabolic abnormality in recurrent nephrolithiasis and first calculus makers was **not** significantly different

Summary of Demographic and Laboratory Data of Patients With Nephrolithiasis

Parameter	Number of Patients	Mean Value
Age, y	232	46.10 ± 14.39
Urine oxalate, mg/24 h	210	39.19 ± 23.04
Urine sodium, mg/24 h	191	157.86 ± 89.54
Urine calcium, mg/24 h	232	175.69 ± 148.69
Urine citrate, mg/24 h	205	451.96 ± 244.76
Urine uric acid, mg/24 h	222	518.42 ± 258.82
Urine volume, mL	231	1546.09 ± 724.03
Urine pH	232	5.14 ± 0.38
Urine specific gravity	232	1019.70 ± 5.45
Blood calcium, mg/dL	228	9.38 ± 0.53
Blood phosphorus, mg/dL	227	3.76 ± 1.54
Blood uric acid, mg/dL	220	6.59 ± 4.64



Metabolic disorders in male and female patients with nephrolithiasis.

Drinking Water Composition and Incidence of Urinary Calculus

Introducing a New Index

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Keywords. urinary calculi,
water supply, magnesium,
calcium

Introduction. We searched for a pathophysiologically based feature of major water electrolytes, which may define water quality better than the water hardness, respecting urinary calculus formation.

Materials and Methods. Utilizing a multistage stratified sampling, 2310 patients were diagnosed in the imaging centers of the provincial capitals in Iran between 2007 and 2008. These were composed of 1755 patients who were settled residents of 24 provincial capitals. Data on the regional drinking water composition, obtained from an accredited registry, and their relationships with the region's incidence of urinary calculi were evaluated by metaregression models. The stone risk index (defined as the ratio of calcium to magnesium-bicarbonate product in drinking water) was used to assess the risk of calculus formation.

Results. No correlation was found between the urinary calculus incidence and the amount of calcium, bicarbonate, or the total hardness of the drinking water. In contrast, water magnesium had a marginally significant nonlinear inverse relationship with the incidence of the disease in the capitals ($R^2 = 26\%$, $P = .05$ for a power model). The stone risk index was associated nonlinearly with the calculus incidence ($R^2 = 28.4\%$, $P = .04$).

Conclusions. Urinary calculus incidence was inversely related with drinking water magnesium content. We introduced a new index constructed on the foundation of a pathophysiologically based formula; the stone risk index had a strong positive association with calculus incidence. This index can have therapeutic and preventive

Methods and materials

- This study is a part of a nationwide epidemiological research conducted at 787 radiology centers in 24 provinces of Iran
- Between 2007 to 2008
- Of 6127 imaging-proven cases of urinary calculi detected out of 117 956 referrals to the radiology centers of all provinces, 2310 were diagnosed in the imaging centers of the provincial capital

Results

- **No** correlation was found between the urinary calculus incidence and the amount of **calcium, bicarbonate, or the total hardness of the drinking water**
- No significant relationship between the incidence of urinary calculi and water minerals concentrations in different regions of Iran
- Although **magnesium** content of water had a marginally inverse correlation with calculus incidence

Evaluation of biochemical urinary stone composition and its relationship to tap water hardness in Qom province, central Iran

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Purpose: The aim of this study was to evaluate the biochemical stone composition in general population of Qom province, central Iran, and its relationship with high tap water hardness.

Materials and methods: In a prospective study, from March 2008 to July 2011, biochemical analysis of urinary stones in patients living in Qom province for at least 5 years was performed. Stones were retrieved by spontaneous passage, endoscopic or open surgery, and after extracorporeal shockwave lithotripsy. Demographic findings and the drinking water supply of patients were evaluated and compared with biochemical stone analysis.

Results: Stone analysis was performed in 255 patients. The most dominant composition of urinary stones was calcium oxalate (73%), followed by uric acid (24%), ammonium urate (2%), and cystine (1%). The peak incidence of urinary stone was in patients in their forties. Overall male to female ratio was 4.93:1.

Conclusion: The dominant stone composition in inhabitants of central Iran, where tap water hardness is high, was calcium oxalate stones. On the basis of this study, biochemical urinary stone composition of Qom does not differ from other regions of Iran with lower water hardness.

Keywords: stone analysis, water hardness, urinary stones, stone composition

Methods and materials

- Mar 2008 to Jul 2011
- **Qom**
- Renal or ureteral stones were sent for biochemical analysis
- Inclusion criteria: Residents of Qom for at least 5 years, and all consumed city tap water
- Exclusion criteria: Bladder stone cases and pediatric patients
- Gender and age of patients, water source, and composition of stones were analyzed
- A total of 255 stones were obtained from 255 adult patients
- These patients were 14 to 84 yrs.

Results

- Males: 212 (83%)
- Mean age: 45±11.87
- **Calcium oxalate** was the most prevalent type of calculi overall
- The most frequent major component of stones was **calcium oxalate** (73%), followed by **uric acid** (24%), **ammonium urate** (2%), and **cystine** (1%)
- **No** significant difference in biochemical stone analysis distribution between Qom province and other provinces with softer drinking water was found
- There is no relationship between the quality of tap water and the distribution pattern of urinary stones
- Although, there is a conflict between water hardness and incidence of urinary stone formation

	Author	Year	Design	Population	Place	Most common abnormality
1	Mahmoudi H	2000-2001	Cross sectional	79	Kashan	1. Low urine volume 2. Hypercalciuria 3. Hyperuricosuria
2	Hosseini MM, et al.	2010	Cross sectional	376	Shiraz	1. Low urine volume 2. Hypercalciuria 3. Hyperuricosuria
3	Nouri-Majalan N, et al.	2010	Cross sectional	150	Yazd	1. Hypercalciuria 2. Hyperuricemia
4	Goodarzi MT, et al.	2012	Case control	28	Hamadan	Hypocitraturia
5	Emami-Naini A, et al.	2012	Cross sectional	437	Isfahan	1. Hypocitraturia 2. Hyperoxaluria
6	Hadian B, et al.	2018	Cross sectional	232	Lorestan	Hyperoxaluria

Thank you
