Original Article

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 hypernatriuria (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

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Received: 19.04.2012, **Accepted:** 11.06.2012

Access this article online	
Quick Response Code:	Website: www.advbiores.net
	DOI: 10.4103/2277-9175.100193

INTRODUCTION

Kidney stone formation (Nephrolithiasis) is a major public health problem resulting in high morbidity and economic burden. The incidence and prevalence of nephrolithiasis is globally increasing in both sexes.[1,2] Nearly 10% of the world's population are expected to develop kidney stones in their lifetime, and this

How to cite this article: Emami-Naini A, Eshraghi A, Shahidi S, Mortazavi M, Seyrafian S, Roomizadeh P, *et al.* Metabolic evaluation in patients with nephrolithiasis: A report from Isfahan, Iran. Adv Biomed Res 2012;1:65.

lifetime risk is suggested to be even higher in certain regions of the world including the Middle-East.[3]

Although nephrolithiasis was previously considered as a mere kidney disorder, there is now growing evidence suggesting that kidney stone formation may originate from a wide range of underlying metabolic abnormalities; among which hypercalciuria is the most frequent.[4-6] It is believed that metabolic derangements can alter the urinary composition in a manner that increases risk of stone formation, and even its recurrence, if remain untreated.[3,4] In this respect, serum and urine evaluation in patients with nephrolithiasis can provide insights about the underlying metabolic causes, and offer implications for more appropriate treatment and preventive measures.

As far as we are aware, to date, there is no data concerning frequency of metabolic abnormalities in patients with nephrolithiasis from central parts of Iran. In our review of the literature, we could find two previous reports from Iran; however, their results cannot be attributed to the entire country, since they were conducted in some regions with special climates.[7,8] This is the first large study investigating the frequency of metabolic and electrolyte abnormalities among patients with nephrolithiasis in central part of Iran.

MATERIALS AND METHODS

Study area

This cross sectional study was performed in Isfahan, a large central province of Iran, located between latitudes 30 and 34 degrees north of the equator and longitude 49-55 degrees east. According to 2006 national census data, Isfahan has a population of 4,559,256. Its climate is dry with a mean daily temperature of 5.3 C in January and 27.2 C in August (reference period: 1972-2000).

Patients

In the time period between March 2009 and August 2010, we consecutively enrolled 437 Isfahani nephrolithiasis patients who referred to urology and nephrology wards of the Isfahan University of Medical Sciences, the main health support organization of the region. The inclusion criteria were: (i) age at onset of 18 years and above, (ii) confirmed diagnosis of nephrolithiasis by one of the three methods as follows: (a) imaging (ultrasonography, kidney-ureter-bladder radiography, Intravenous pyelography or computed tomography scan), (b) stone analysis in cases with spontaneous passage of stone, and (c) surgical or endoscopic nephrolithotomy. Notably, during the study, patients consumed their typical diet and were not hospitalized.Cases with renal failure, defined as glomerular filtration rate below 60 mL/min/1.73 m^2 (based on Cockcroft-Gault equation[9]), and also those who were under medications that could affect the metabolic status or urinary excretion were excluded. Demographic features and clinical data of eligible subjects were extracted retrospectively by reviewing their medical records. These data included age, sex, previous history for nephrolithiasis and history for any concurrent diseases including diabetes mellitus, hypertension, gout and hyperparathyroidism.

Metabolic assessments

Metabolic evaluation was performed by obtaining a 24-hours urine sample and fasting venous blood draw. We analyzed 24 hours urine samples for volume, creatinine, calcium, citrate, oxalate, uric acid, sodium, and cystine. Fasting blood sample was taken to assess serum calcium, phosphorus, sodium, potassium, uric acid, albumin, creatinine and blood urea nitrogen.

The following definitions were considered in our study, as they are generally accepted in population studies:[6,7]Hypercalciuria: urine calcium excretion over 300 mg/day in males, and over 250 mg/day in females; Hyperoxaluria: urine oxalate excretion over 45 mg/day; Hypocitraturia: urine citrate excretion below 320 mg/day; Hyperuricosuria: urine uric acid excretion over 800 mg/day in males, and over 750 mg/day in females; Hypernatriuria: urine sodium excretion over 200 mEq/day; Cystinuria: urine cystine excretion over 200 mg/day; Low urinary volume: urine volume below 1000 ml/day; Hypercalcemia: serum calcium levels over 10.5 mg/dl; Hyperuricemia: serum uric acid levels over 8 mg/dl in males and over 6 mg/dl in females; Hypernatremia: serum sodium levels over 145 mEq/l; Hypokalemia: serum potassium levels below 3.5mEq/L; and Hypophosphatemia: serum phosphorus level below 2.5 mg/dL

Ethics and consent

All subjects provided written informed consent before enrolment. They were assured for the anonymity of their information. The study protocol was reviewed and approved by the institutional ethics committee of Isfahan University of Medical Sciences.

RESULTS

Among our 437 subjects, 226 were females (51.7%) and 211 were males (48.3%). The mean age was 46 ± 13.8 years (rang: 18-87). Two hundred and twenty patients (50.3%) had history of previous

nephrolithiasis and 78 (17.8%) were previously hospitalized due to nephrolithiasis. The family history for nephrolithiasis was present in 180 (41.2%). Further demographic and history characteristics of the patients are represented in Table 1. Urinary abnormalities observed in 24 hours urine analysis were as follows: hypocitraturia in 177 (40.5%), hypernatriuria in 139 (31.8%), hyperoxaluria in 126 (28.8%), low urine volume in 71(16.2%), hyperuricosuria in 58 (13.3%), hypercalciuria in 40 (9.2%), and,cystinuria in 8 (1.8%). In addition, fasting venous blood results revealed the following metabolic derangements: hypercalcemia in 55 (12.6%), hyperuricemia in 46 (10.5%), hypernatremia in 21 (4.8%), hypokalemia in 19 (4.3%), and hypophosphatemia in 16 (3.7%). Figure 1 summarizes the frequency of metabolic abnormalities. The mean (± SD) values for each metabolic evaluation are brought in Table 2.

Table 1: Demographic and clinical characteristics of the patients

Age (years)	46 ± 13.8 (18-87)
Sex (male (%), female (%))	211 (48.3), 226 (51.7)
Weight (kg)	73 ± 15 (59-115)
Family history for nephrolithiasis (%)	180 (41.2)
Recurrence nephrolithiasis (%)	220 (50.3)
Previous hospitalization due to nephrolithiasis (%)	78 (17.8)
History of significant disease	
Hypertension (%)	176 (40.3)
Diabetes mellitus (%)	40 (9.2)
Gout (%)	5 (1.1)
Hyperparathyroidism (%)	3 (0.7)

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

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

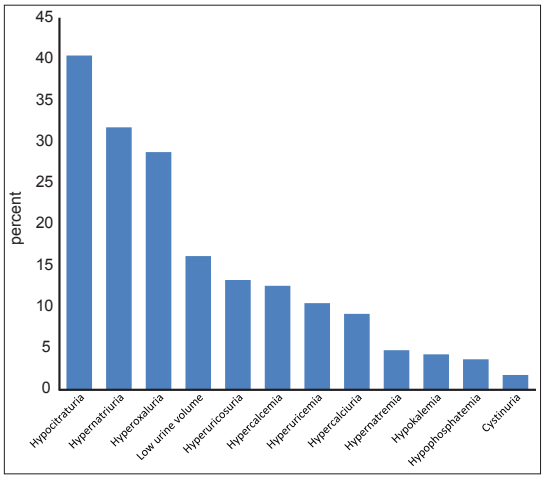

Figure 1: Frequency of metabolic abnormalities among patients

DISCUSSION

This is the first large study concerning urinary and serum analysis of nephrolithiasis patients in Isfahan, a large central province of Iran. All recruited patients were adults with ages ranging from 18 to 87 years and about 50% were first-time stone formers. Hypocitraturia was the most common metabolic abnormality in our cases (40.5%). In the literature, the frequency of hypocitraturia varies from 20%-60% in patients with nephrolithiasis.[10] It is firmly established that a dietary habit rich in protein and sodium but low in vegetables can reduce the urinary citrate excretion.[4,11] one possible explanation for the high frequency of hypocitraturia in this study is major shifts in the nutritional patterns of our population which have led to increased consumption of animal protein and sodium salt.[12]

Hypercalciuria was relatively infrequent in our subjects (9.2%); while in similar studies, it was the leading metabolic abnormality among nephrolithiasis patients.[5,6] One explanation for this discrepancy could be the well-documented high prevalence of vitamin D deficiency in Isfahan province, that reaches to as much as 50.8% in the adult population.[13] Of note, Berlin *et al.*[14] showed positive correlations between serum vitamin D status and increased risk of hypercalciuria and nephrolithiasis. Furthermore, there are a number of studies in the literature that demonstrated an association between vitamin D intake and kidney stone disease.[15,16] In this respect, we postulate that the low mean level of serum vitamin D in the adult population of our province might be the cause for the lower frequency of hypercalciuria among adult Isfahani nephrolithiasis patients.

Dehydration and reduced urinary volume are well-known risk factors for kidney stone formation.[3,4] In this study we observed low urinary volume in approximately 16% of the cases, which was lower than the values reported from two other regions of Iran (58.2% and 76%), where climate is warmer.[7,8]

We acknowledge limitations of our study, which may

have affected the outcomes of the report. Of most importance, the kidney stone types were not outlined in our study, since we were unable to extract the data of stone analysis in a group of the cases.

CONCLUSION

In conclusion, studies from various regions of the world are controversial in reporting the frequency of metabolic abnormalities among patients with kidney stone disease. These variations are generally due to diverse climates, ethnicities, nutritional patterns and even cultural issues. Our 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. These observations might be due to high prevalence of vitamin D deficiency and also nutritional transitions in Isfahan province.

ACKNOWLEDGMENTS

We kindly appreciate the excellent help and assistance of Dr. Azita Ebrahimian during this study.

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Source of Support: Nil, **Conflict of Interest:** None declared.