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Assessment of Kidney Function and 24-Hour Urine of the Patients with Renal Stone; Women Have Lower Urine Volume and Higher Urine Citrate

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Abstract

Background: Nephrolithiasis is a worldwide health problem.
Objectives: This study investigated the frequency of urinary and serum metabolic abnormalities and their association with demographic characteristics in patients with nephrolithiasis.
Methods: In this cross-sectional study, we assessed 376 patients with nephrolithiasis who referred to Motahari Medical Center, Shiraz from March 2017 to June 2017. Patients' history, 24-hour urine analysis (for volume, calcium, uric acid, sodium, citrate, phosphate, and oxalate), and serum tests (for calcium, uric acid, and parathyroid hormone) were recorded in a data gathering sheet. P value < 0.05 was considered statistically significant.
Results: The most common abnormality was a low volume of 24-hour urine (< 2000 mL), (73.7%), followed by hypercalciuria (23.9%), and hyperoxaluria (19.4%). Low 24-hour urine volume was more frequent in women (80.0% vs. 64.3%, P < 0.001), while hypercalciuria (37.0% vs. 18.3%, P < 0.001), and hyperphosphaturia (6.0% vs. 1.7%, P = 0.03) were more frequent in men. Moreover, hypercalciuria was more frequent in outdoor workers (39.7% vs. 21.1%, P = 0.003), whereas low urine volume was more frequent in indoor workers (79.0% vs. 61.1%, P = 0.006). Metabolic abnormalities were not different in terms of patients' family history.
Conclusions: Multiple factors affect the frequency and type of nephrolithiasis. Since these parameters are also influenced by race, culture, and dietary habits; thus each region must determine its own demographic features of renal stone. Based on our results, women had lower urine volume and higher urine citrate than men. Moreover, water intake is one of the most important factors that correlate with renal stone formation.

Keywords: Nephrolithiasis, Demography, Occupation, Renal Stone, Sex

1. Background

Urolithiasis or renal stone is a common health problem, accounting for almost 2 million office visits, and the annual cost of 2 billion dollars in the United Sates (1). The prevalence of urolithiasis has markedly increased over the past few decades, especially in industrialized countries (2), hypothesized to be caused by profound changes in living standards, dietary habits, and climate warming (3, 4). A cross-sectional study that was conducted in Iran in 2005, reported the prevalence of 5.7% (5). Many factors such as race, climate, nutrition, age, and gender affect the prevalence of urolithiasis (5). Except for the severe pain, urolithiasis can cause tragic outcomes such as infection, obstruction, and finally leads to end-stage renal disease (ESRD) (6, 7).

Identifying risk factors and the pathogenesis of stone formation can be a helpful effort in the prevention and early diagnosis of nephrolithiasis (8). In addition, recent studies suggest metabolic abnormalities as a cause of nephrolithiasis; accordingly, it is suggested to evaluate urinary metabolic profile of renal stone formers to better understand the pathogenesis, prevent recurrence, and adopt more appropriate therapeutic approach (9).

2. Objectives

The present study investigated the frequency of urinary metabolic abnormalities and serum parameters and their association with demographic characteristics in the patients with nephrolithiasis in a referral center.

3. Methods

3.1. Population Study

This cross-sectional study was conducted in Motahhari Clinics affiliated to Shiraz University of Medical Sciences from March 2017 to June 2017. We included all the patients who had one of the criteria as follow; bilateral renal stone, recurrent renal stone, symptomatic renal stone, and history of urologic intervention [extracorporeal shock wave lithotripsy (ESWL), transurethral lithotripsy (TUL), and percutaneous nephrolithotomy (PCNL)]. Also, we excluded the patients with chronic kidney disease (CKD) stage 3 - 5, consumption of potassium citrate, vitamin C, vitamin B6, allopurinol, and calcium (Ca) supplement during a month before study, and patients who could not collect 24-hour urine correctly (24 hour creatinine (Cr) < 20 mg/kg in men and < 15 mg/kg in women).

3.2. Data Collection and Sampling

We prepared a data gathering sheet for each patient containing questions about age, gender, occupation, history of urologic intervention, and family history. We classified tasks into two groups; the first group was indoor jobs (e.g., housewives, teachers, secretary, and office personnel, and the second one was outdoor jobs (e.g., workers, farmers, and drivers). After teaching the patients how to collect a 24-hour urine sample, we sent them to the laboratory for taking urine and blood samples. We assessed and documented the results of Ca, oxalate (Ox), citrate, uric acid (UA), volume, creatinine (Cr), sodium (Na), and phosphorus (P) of 24-hour urine and also serum level of Ca, UA, parathyroid hormone (PTH), albumin (Alb), blood urine nitrogen (BUN), and Cr in a preformed sheet.

3.3. Definition

Based on Harrison internal medicine, abnormal findings in 24-hour urine were defined as follow: Hypercalciuria: Urine calcium > 300 mg/d in men and > 250 mg/d in women, hyperuricosuria: Urine uric acid > 750 mg/d in women and > 800 mg/d in men, hyperoxaluria: urine oxalate > 40 mg/day in both women and men, and hypocitraturia: Urine citrate < 320 mg/d. We considered 100 - 260 milli-equivalents to be the normal value of 24-hour urine Na and 400 - 1300 mg as the normal value of 24-hour urine P. Normal ranges of serum contents were as follow; UA: 2.5 to 5.6 mg in women and 3.1 to 7 mg in men, Ca: 8.7 to 10.2 mg, and PTH: 8.0 to 51 picogram/milliliter (10).

3.4. Ethical Consideration

Ethics Committee of Shiraz University of Medical Sciences approved this study (approval number: 93-01-01-8584). At the beginning of the study, we gave complete information about the aim of the study and the process of study to the patients, then we took a written informed consent.

3.5. Statistical Analysis

Data were analyzed by Statistical Package for the Social Sciences software version 18.0 (SPSS Inc. Chicago, IL). Qualitative data are expressed as number and percentage, which were analyzed by the chi-square. Quantitative data were presented as mean and standard deviation and analyzed by independent *t*-test or ANOVA. P value < 0.05 was considered statistically significant.

4. Results

Totally, we gathered 376 patients with the age range of 14 to 81 years and mean age of 43.9 ± 13.6. The mean duration of disease was 88.7 ± 11.8 months. The mean GFR of our patients was 84.4 ± 33.9. Women consisted of 64.3% (242 cases) of the patients and 65.2% (245 numbers) of the cases worked at indoor environments.

Of all the studied population, 29.6% (112) had a positive family history in 1st or 2nd degree family. Generally, 42.3% (159) of the patients experienced bilateral renal stone and 12.5% (47) developed recurrent renal stone. The most common complaint in our patients was renal colic followed by gross hematuria and dysuria occurred in 52.7% (198 cases), 39.9% (150 cases), and 31.1% (117 cases) of the patients, respectively. The most common urologic interventions were ESWL, TUL, and nephrectomy, which were done for 21.3% (80 cases), 17.6% (66 cases), and 2.9% (11 cases) of the patients, respectively. Table 1 showed some demographic data and baseline laboratory tests.

Table 2 revealed the results of 24-hour urine test components and their association with gender, occupation, and family history. As shown in Table 2, the mean urine volume in women was 1437.9 ± 708.1, which was significantly less than men with urine volume 1836.0 ± 801.6 (P < 0.001). Urine volume in the patients with outdoor occupations was also significantly more than the patients with indoor jobs (1903.8 ± 851.1 vs. 1478.8 ± 711.0, P < 0.001). We found no significant difference in urine volume of the patients with and without a positive family history (P = 0.188). Based on our data Cr was higher in men (P < 0.001) and in the patients with outdoor jobs (P < 0.001). Also UA was found more in men (P < 0.001) and outdoor occupations (P = 0.003). Ca, P, and Ox showed the same pattern. The

Table 1. Distribution the Baseline Characteristics in Our Studied Patients[a]

Variables	Value
Age, y	43.9 ± 13.6
Gender	
Female	242 (64.3)
Male	134 (35.7)
Occupation	
Indoor	245 (65.2)
Outdoor	131 (34.8)
Duration of disease, mo	88.7 ± 11.8
Body mass index	27.0 ± 3.2
Glomerular filtration rate	84.4 ± 33.9
Family history	
Positive	112 (29.6)
Negative	264 (70.4)
Past history	
Bilateral renal stone	159 (42.3)
Recurrent renal stone	47 (12.5)
Symptomatic renal stone	198 (52.7)
Renal colic	
Gross hematuria	150 (39.9)
Dysuria	117 (31.1)
Urologic intervention	
ESWL	89 (23.5)
TUL	66 (17.4)
PCNL	6 (1.5)
Nephrectomy	11 (2.9)
No intervention	196 (52.1)
Missing	8 (2.1)
Serum value	
Blood urine nitrogen	14.3 ± 5.1
Cratinine	1.0 ± 0.3
Uric acid	4.6 ± 1.5
Calcium	9.4 ± 0.6
Phosphorus	3.7 ± 0.7
Parathyroid hormone	58.8 ± 59.9
24-hour urine	
Volume	1579.2 ± 265.7
Cratinine	1177.1 ± 447.9
Uric acid	424.9 ± 207.2
Calcium	16.1 ± 102.6
Phosphorus	577.8 ± 522.5
Oxalate	34.0 ± 47.3
Citrate	574.9 ± 418.2
Sodium	137.9 ± 84.0

Abbreviations: ESWL, extracorporeal shock wave lithotripsy; PCNL, percutaneous nephrolithotomy; TUL, transurethral lithotripsy.
[a]Values are expressed as mean ± SD or No. (%).

mean Ca, P, and Ox levels were significantly more in men ($P < 0.001$) and outdoor jobs ($P < 0.001$). Also women showed a higher amount of citrate in their urine ($P = 0.026$). However, no significant difference was found between our two groups of occupation in level of citrate ($P = 0.351$). According to our data, the amount of Na in urine did not correlate with gender, occupation, and family history. No significant difference was found in none of the 24-hour urine criteria of patients with and without a positive family history ($P > 0.05$).

The prevalence of 24-hour urine component abnormality in our total population, regarding gender and occupation, were described in Table 3. The most common abnormalities were a low volume of 24-hour urine (< 2000 mL) (73.7%), followed by hypercalciuria (23.9%) and hyperoxaluria (19.4%).

Low volume (urine volume 1000 - 2000 mL/24h) and very low volume (< 1000 mL/24h) were seen in 57.4% (139) and 21.9% (53) of women while 53.7% (72) and 9.7% (13) of men showed low volume and very low volume ($P < 0.001$ for both). Also low and very low volumes were seen significantly more in patients with indoor jobs ($P = 0.006$). Hypercalciuria, hyperphosphaturia, and hyperoxaluria occurred in a greater percentage of men and patients with an outdoor job ($P < 0.003$). There were no differences in hyperuricosuria, hypocitraturia, and Na excretion among both genders and both occupations ($P = 0.05$).

5. Discussion

The present study was conducted to find out the conditions that predispose the cases to renal stone formation. To obtain this goal, we gathered 376 proven cases of renal stone referred to Motahhari Clinic for follow up.

In the present study, the most common abnormalities were a low volume of 24-hour urine followed by hypercalciuria, and hyperoxaluria while most non–Iranian studies have reported hypercalciuria as the most common abnormality (11, 12). This difference reflects the diversity of demographic characteristics of the studied population, dietary habits, and climate of the place of the studies. Since the urine volume greatly depends on the amount of water and liquids intake (13, 14), the results of the present study, which were in favor of previous studies, can be a warning for Iranian population to consume more water in a day (15, 16).

In this study, we observed that UA, Ca, P, and Ox were significantly higher whereas the urine volume and citrate were significantly lower in men than women. There was no significant difference in the level of urine Na between men and women. One previous study reported the same results for UA, Ca, and Ox (16). Curhan and his colleagues conducted a study on patients with and without a history of renal stone. They reported no gender difference for citrate. On the other hand, in the same weight UA, Ca, and Ox

Table 2. Frequency of Some Quantitative Characteristics of 24-Hour Urine Relation to Gender, Occupation and Family History in Studied Patients[a]

24-Hour Urine, N = 376	Volume	Cratinine	Uric acid	Calcium	Phosphorus	Oxalate	Citrate	Sodium
Gender								
Men	1836.0 ± 801.6	1437.4 ± 463.7	493.8 ± 199.9	185.6 ± 112.1	798.4 ± 640.1	55.0 ± 34.4	536.6 ± 278.9	135.9 ± 86.6
Women	1437.9 ± 708.1	1032.0 ± 366.6	388.3 ± 201.9	147.5 ± 94.7	474.3 ± 418.6	43.0 ± 36.9	596.0 ± 477.3	139.0 ± 82.8
P value	0.01	< 0.001	< 0.001	0.001	< 0.001	0.05	0.026	0.752
Occupation								
Indoor	1478.8 ± 711.0	1092.8 ± 413.5	409.4 ± 208.1	153.0 ± 97.5	518.2 ± 428.3	44.7 ± 30.9	555.2 ± 361.4	145.2 ± 87.8
Outdoor	1903.8 ± 851.1	1469.1 ± 447.1	498.1 ± 201.5	186.9 ± 89.6	868.8 ± 781.0	56.7 ± 38.7	597.2 ± 435.7	129.4 ± 70.2
P value	0.01	< 0.001	0.003	0.008	< 0.001	0.023	0.351	0.153
Family history								
Positive	1538.0 ± 724.3	1204.1 ± 429.3	464.3 ± 212.7	166.6 ± 116.4	569.7 ± 509.9	49.8 ± 27.5	577.2 ± 421.4	464.3 ± 212.7
Negative	1724.0 ± 634.1	1159.5 ± 459.3	432.4 ± 208.9	180.2 ± 120.4	589.4 ± 518.7	52.4 ± 24.0	581.0 ± 412.2	432.4 ± 208.9
P value	0.188	0.349	0.311	0.312	0.106	0.447	0.41	0.313

[a]Values are expressed as mean ± SD.

Table 3. Frequency of Some Qualitative Characteristics of 24-Hour Urine Relation to Gender and Occupation in Studied Patients[a]

24-Hour Urine	Stone Prevalence, N = 376	Gender			Occupation		
		Women, N = 242	Men, N = 134	P Value	Indoor, N = 245	Outdoor, N = 131	P Value
Volume							
Low	180 (47.8)	139 (57.4)	72 (53.7)	< 0.001	144 (58.7)	36 (49.3)	0.006
Very low	56 (14.8)	53 (21.9)	13 (9.7)	< 0.001	48 (19.5)	8 (10.9)	0.006
Total	277 (73.6)	192 (79.3)	85 (63.4)	< 0.001	192 (78.3)	44 (60.2)	0.002
Uric acid	17 (4.5)	8 (3.3)	9 (6.7)	0.120	8 (3.2)	6 (8.2)	0.086
Calcium	90 (23.9)	43 (17.7)	47 (35.0)	< 0.001	50 (20.4)	27 (36.9)	0.003
Phosphorus	12 (3.2)	4 (1.6)	8 (5.9)	0.022	6 (2.4)	5 (6.8)	0.034
Oxalate	73 (19.4)	37 (15.2)	36 (26.8)	0.008	44 (17.9)	19 (26.0)	0.052
Citrate	69 (18.4)	46 (19.0)	23 (17.1)	0.776	46 (18.7)	14 (19.1)	0.721
Sodium	57 (15.2)	42 (17.3)	15 (11.1)	0.171	45 (18.3)	8 (10.9)	0.347

[a]Values are expressed as No. (%).

were higher in men. This may explain more incidence rate and prevalence of urinary stone in men (12, 17).

Despite our thoughts, we found that indoor employees had lower urine volume, though all the other variables of 24-hour urine such as UA, Ca, P, and Ox were significantly higher in the patients with outdoor occupations. Basiri et al. who worked on 6,089 imaging-proven cases from 12 ecologic zones across Iran, classified occupations to indoor, high activity outdoor and low activity outdoor. They reported indoor employees had renal stone more than others. Previous studies revealed the role of weather in stone formation and this factor mainly influences patients with an outdoor job, this might be as a result of significant lower urine volume of indoor patients based on our results. Although we do not have the amount of liquid intake of each patient, the lower urine volume in an indoor employee can be due to the amount of water intake.

In spite of the previous study conducted on 37,999 men that reported more excretion of Ca and citrate in urine of patients with positive family history, we did not find any significant difference in 24-hour urine tests of patients with positive and negative family history (18, 19). Ljunghall et al. reported that the prevalence of hypercalciuria and hyperuricosuria were not different in patients with positive and negative family history (19).

Like a cross-sectional study which was also done in Iran

in 2005, ESWL was the most common intervention in the treatment of our patients (5). Also Pearle et al. in 2005, reported ESWL as the most common modality for renal stone in the USA followed by ureteroscopy (20).

The main strength of the present study was the assessment of a wide range of data, including demographic characteristics such as age, gender, occupational exposure, and family history of renal stone formers and their association with urinary metabolic abnormalities. Nevertheless, there were some limitations in the present study, such as the fact that we did not asses the stone compositions and the amount of liquid intake.

5.1. Conclusions

In conclusion, the results of the study suggested low urine volume as the most common abnormality in stone formers of Shiraz, which is interestingly different from other countries and other cities in Iran. In our study, the women had lower urine volume and higher urine citrate than men. As a result, clinicians must warn their patients about liquid intake. Discrepancies among studies show the multifactorial nature of nephrolithiasis and the necessity to study the underlying factors in each community separately and plan the educational strategies, and prevention measurements based on the results in that region.

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Footnotes

Authors' Contribution: Maryam Pakfetrat and Leila Malekmakan: Contributed to design, contributed to analysis, drafted the manuscript, final approval, and accepts accountability for the overall work. Taraneh Tadayon: Contributed to data collection, revised the manuscript, final approval, and accepts accountability for the overall work. Amin Nikfar: Contributed to design, contributed to analysis, revised the manuscript, final approval, and accepts accountability for the overall work. Afshin Mansourian: Contributed to data collection, revised the manuscript, final approval, and accepts accountability for the overall work.

Conflict of Interests: The authors declare that they have no conflict of interest.

Ethical Approval: This manuscript was in accordance with the ethical standards of the institution. Ethics Committee of Shiraz University of Medical Sciences approved this study (approval number: 93-01-01-8584).

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