Risk factors of renal stone in patients with recurrent nephrolithiasis: A case-control study

Ali Ghorbani[1], Heshmatollah Shahbazian[1] and Leila Moradi[2]

[1]Department of Nephrology, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences

[2]Department of Internal Medicine, Sina Hospital, Ahvaz Jundishapur University of Medical Sciences

Corresponding Author: Ali Ghorbani, Department of Nephrology, Golestan Hospital, Golestan Blvd, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
Fax: +98 611 374 3013 Tel: +98 611 374 3013 E-mail: dralighorbani@yahoo.com

Abstract: Renal stone disease is common and caused by a variety of conditions. The overall lifetime rate of renal stone in the general population is approximately 5-12%. The aim of the present study was to determine the prevalence of recurrence rate and metabolic changes present in patients with urinary lithiasis. Patients with renal stone, who attended the nephrology clinics in Ahvaz, Iran, were enrolled into the study. One hundred and forty patients and 60 control cases were recruited to the study. Predominance observed for male gender, with 2.1:1 ratio. There were also 33 men and 27 women in control group. Mean age was 36.8±14.3 and 40.5 ± 14.5 years for patients and control group respectively. Frequency of diabetes mellitus (p = 0 .90), urinary tract infection (p = 0.125) and cystinuria (p = 0.181) did not significantly differ among patients and control cases. Mean body mass index, daily fluid intake, serum fasting glucose, potassium, sodium, magnesium, calcium, alkaline phosphates, parathormone and cholesterol show no statistically significant difference between patients and control group. Mean serum BUN, creatinine, phosphorus, uric acid, and triglyceride levels were significantly higher in patients compared to control group. Mean of 24-hour urine volume, excreted sodium, uric acid, and citrate were significantly higher in patients group too. We concluded that evaluation of recurrent stone formers by examining their blood and urine samples, especially 24-hour urine sample, is beneficial to find underlying metabolic disorder.
[Ali Ghorbani, Heshmatollah Shahbazian and Leila Moradi. **Risk factors of renal stone in patients with recurrent nephrolithiasis: A case-control study.** Life Sci J 2012;9(4):3038-3043] (ISSN:1097-8135). http://www.lifesciencesite.com. 446

1. Introduction

Renal stone disease is common and caused by a variety of conditions (1, 2). The overall lifetime rate of renal stone in the general population is approximately 5-12% (2-5).
Renal colic affects approximately 1.2 million people each year and accounts for about 1% of all hospital admissions worldwide (2-5). It is estimated that almost 40% of stone formers will have a recurrence within 3 years (6-8), and 60% of them experience the third episode within 9 years of first episode (9).
Conditions in which there is low fluid intake, high animal protein intake and alcoholism (10, 11), infections, metabolic disorders such as hypercalcemia (3, 7), hypercalciuria, obesity, and diabetes mellitus are now, known to be associated with increased stone risk (8, 12-17). Now there are obvious evidences revealed that medical treatment, especially correction of blood and urine disturbances, can reduce stone formation (5). Assessment of hygienic dietetic aspects and diagnosis of potential metabolic changes are factors on which we can interfere, modifying the progression of this pathology that is characterized by high recurrence (11-17). The aim of this study was to determine the prevalence of metabolic disorders in patients with recurrent nephrolithias in southwest of Iran.

2. Materials and methods

This study was performed in one of the hottest places in Iran, Ahvaz city, where air temperature may exceed 122° Fahrenheit. Patients with renal stone who attended the nephrology clinics in

Ahvaz, were enrolled into the study. Patients receiving medication or diet modification for possible underlying metabolic disorder were excluded. Finally, 140 patients were enrolled into the study. Of referred patients, 60 cases were chosen and adjusted for contributing variables. All of the cases were weighted. Their height was measured and their body mass index (BMI) was calculated. Metabolic evaluation consisted collection of 24-hour urine samples for measuring calcium, magnesium, sodium, phosphorus, citrate, oxalate, uric acid, and cystine. Also serum levels of fasting glucose (FBS), creatinine, uric acid, cholesterol, bicarbonate, phosphorus and parathormone (PTH) were determined. Urinary specific gravity and pH were measured by dipstick. Finally, urine culture was performed to detect urinary tract infection. Renal failure was considered as serum creatinine level higher than 1.4 mg/dL (18-21). Data are presented as the mean ± standard deviation or percentage as appropriate. Null hypothesis was tested by one-sample Kolmogorov-Smirnov procedure. Chi-square test with Yates' correction is used for comparisons of dichotomous data. Comparison of mean between the groups is performed using the one sample independent t test. A *p*-value less than 0.05was considered as significant.

3. Results

One hundred and forty patients and 60 control cases were recruited to the study. Predominance observed for male gender, with 95 men (67.9%) and 45 women (32.1%), ratio: 2.1:1. There were also 33 (55%) men and 27 (45%) women in control group. Mean age was 36.8 ± 14.3 and 40.5 ± 14.5 years for patients and control group respectively. There was no statistically significant difference between mean age of the patients and control group (p =0 .823). Familial history of nephrolithiasis was positive in 23.6% of patients, but only was 1.7% in control group (p <0 .001). Frequency of diabetes mellitus (p = 0 .90), urinary tract infection (p = 0.125), and cystinuria (p = 0.181) did not significantly differ among patients and control cases. Mean body mass index, daily fluid intake, serum fasting glucose, potassium, sodium, magnesium, calcium, alkaline phosphates, parathormone and cholesterol showed no statistically significant difference between patients and control group, as well in mean level of 24-hour urine magnesium, phosphorus, and oxalate (table 1). Mean serum BUN, creatinine, phosphorus, uric acid, and triglyceride were significantly higher in patients compared to control group. Mean 24-hour urine volume, excreted sodium, uric acid were significantly higher in patients group too (table 1). Mean daily urinary citrate was significantly lower in patients group in comparison to control group ($p=0.045$). Renal failure was found in 10 patients. Hyperuricemia, hyperuricosuria and hypocitraturia were detected in 26 (18.5%), 30 (21.4%), and 83 patients (59.2%) in patients group, respectively.

Table 1: Demographic and laboratory data of patients and control group

	Scale	**Patients**	**Control group**	**p-value**
Age	Year	36.8 ± 14.3	40.5 ± 14.5	0.823
BMI	Kg/m^2	25.6 ± 3.8	26.2 ± 3.1	0.259
Fluid intake	Liter	2.2 ± .5	2.3 + .5	0.85
Fasting blood sugar	mg/dL	92.4 ± 28.1	97.7 ± 47.7	0.386
Serum potassium	mEq/L	4.2 ± .6	4.2 ± .3	0.319
Serum sodium	mEq/L	140.6 ± 5.2	140.7 ± 3.4	0.895
Serum BUN	mg/dL	16.9 ± 6.1	14.7 ± 4.8	0.006
Serum creatinine	mg/dL	1.03 ± .27	.87 ± .22	<0 .001
Serum magnesium	mg/dL	2.2 ± .3	2.1 ± .3	0.64
Serum phosphorus	mg/dL	3.5 ± .8	4.1 ± .6	<0 .001
Serum calcium	mg/dL	9.4 ± .8	9.5 ± .5	0.244
Serum Uric acid	mg/dL	6.1 ± 1.6	5.4 ± 1.3	< 0.001
Serum PTH	pg/ml	49.9 ± 60.1	48.9 ± 15.9	0.84
Serum alkaline phopsphatase	U/L	197.6 ± 85.7	217.5 ± 66.5	0.078
Serum cholesterol	mg/dL	187.8 ± 48.8	184.4 ± 46.7	0.647
Serum triglyceride	mg/dL	205.5 ± 96.8	159.5 ± 84.4	0.001
24-h urine volume	L/24 h	1647.6 ± 676.4	1409 ± 418.5	0.003
24-h urine protein	mg/24 h	103.2 ± 55.2	151.3 ± 231.8	0.108
24-h urine phosphorus	mg/24 h	595.2 ± 236.7	564.5 ± 134.3	0.247
24-h urine magnesium	mg/24 h	60.2 ± 35.5	68.9 ± 39	0.223
24-h urine sodium	mmol/24 h	152.6 ± 75.2	129.2 ± 41	0.005
24-h urine uric acid	mg/24 h	676.6 ± 624.5	545.6 ± 168.6	0.023
24-h urine oxalate	mg/24h	28.8 ± 37.9	27 ± 40	0.766
24-h urine citrate	mg/24h	407.5 ± 272.7	482.7 ± 226.3	0.045
24-h urine calcium	mg/24	165.3 ± 96.4	131 ± 46.5	0.032

4. Discussion

Better understanding of pathophysiology and applicable therapeutic managements, specific therapies in particular, have increased the importance of evaluation of urolithiasis (1,5). Significance of management of underlying medical disorders come clear regarding this fact that kidney stones have a high recurrence rate. In our study, the most frequent metabolic change in patients who with recurrent stones was hypocitraturia, followed by hyperuricosuria and hyperuricemia.

Marangella et al. found that renal stones induce a clear-cut influence in accelerating the natural worsening of glomerular filtration rate (22). Similarly in showed that patients with urolithiasis had higher serum levels of BUN and creatinine. In our study, patients experienced hyperuricemia and hyperuricosuria, more than control group. It is in concordance with previous studies which demonstrated hyperuricemia and hyperuricosuria as the risk factors for stone formation (23). There is dominancy in plasma triglyceride in patients group compared to control group as mentioned in table 1. Orzaki et al noticed that 24-hour urine volume decreased in 39.7% of patients with recurrent renal stone (24), but in contrast, mean 24-h urine volume was significantly lower in patients group in comparison to control group. We found natriuresis as a risk factor of urolithiasis in 17.8% of patients. It may be a result of high salt diet in Ahvaz city, especially in hot days. Stone risk is greater in those who had hypercalciuria, reported as high as 50% in recurrent episodes (24-26). We found hypercalciuria in 12 (9%) patients. Of them, one had hyperparathyroidism. Genetic, dietary and climate diversity may justify the difference. Similar to our results Mortazavi et al. found that 60% of children with urinary stones had hypercalciuria with unknown origin (27). In contrast to previous studies, rate of hypercalciuria is lower in our patients, maybe due to dietary habits. As discussed earlier, hypocitraturia is the most frequent metabolic changes in our patients. Despite the results found by Mithani et a.l in Pakistan (28), many authors noted hypocitraturia as a major risk factor for stone formation (23-29). Pathogenesis of hypocitraturia remained unclear (23, 24, 28, 29). Regarding to the diversity of genetic, dietary and climate factors and the fact that correction of biochemical disturbance can prevent stone formation (30-36), we concluded that the evaluation of recurrent stone formers by examining their blood and urine samples, especially 24-hours urine sample, is beneficial to find underlying metabolic disorder.

Acknowledgements: This study was performed as the residency thesis of Dr. Leila Moradi and supported by a grant from Ahvaz Jundishapur University of Medical Science.

References

1- Soucie JM, Coates RJ, McClellan W, Austin H, Thun M. Relation between geographic variability in kidney stones prevalence and risk factors for stones. Am J Epidemiol. 1996 Mar 1;143 (5): 487- 95.

2-Sahni N, Gupta KL. Dietary antioxidents and oxidative stress in predialysis chronic kidney patients. J Nephropathology. 2012; 1 (3): 134-142.

3-Maghsoudi AR, Baradaran-Ghahfarokhi M, Ghaed-Amini F, Nasri H, Dehghani Mobarakeh M, Rafieian-Kopaei M. Renal failure and sub mental lymphadenopathy in a 68 years old woman. J Nephropathology. 2012; 1 (3): 198-201.

4-Kalantar E. Minimizing potential resistance among bacteria causing urinary tract infection. J Nephropathology. 2012; 1 (1): 11-12.5-Wilson DR, Strauss AL, Manuel MA. Comparison of medical treatments for the prevention of recurrent calcium nephrolithiasis. Urol Res. 1984; 12: 39-40.

6-Ghorbani A, Ehsanpour A, Roshanzamir N, Omidvar B. Alterations in antibiotic susceptibility of urinary tract infection pathogens. J Nephropathology. 2012; 1 (1): 43-48.

7-Solati M, Mahboobi HR. Paraoxonase enzyme activity and dyslipidemia in chronic kidney disease patients. J Nephropathology. 2012; 1 (3): 123-125.

8-Johri N, Cooper B, Robertson W, Choong S, Rickards D, Unwin R. An Update and Practical Guide to Renal Stone Management. Nephron Clin Pract. 2010 Jul 2; 116 (3): c159-c171.

9-Whalley NA, Martins MC, Van Dyk RC, Meyers AM. Lithogenic risk factors in normal black volunteers, and black and white recurrent stone formers. BJU Int. 1999 Aug; 84 (3): 243-8. PMID: 10468714.

10-Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and

other nutrients and the risk of symptomatic kidney stones. N Engl J Med. 1993 Mar 25; 328 (12): 833-8.

11-Siener R, Ebert D, Nicolay C, Hesse A. Dietary risk factors for hyperoxaluria in calcium oxalate stone formers. Kidney Int. 2003; 63 (3): 1037-43.

12- [No authors listed]. Consensus conference. Prevention and treatment of kidney stones. JAMA. 1988 Aug 19; 260 (7): 977-81.

13-Assadi F. The epidemic of pediatric chronic kidney disease; the danger of skepticism. J Nephropathology. 2012; 1 (2): 61-64.

14-Sakhaee K. Nephrolithiasis as a systemic disorder. Curr Opin Nephrol Hypertens. 2008 May; 17 (3): 304-9.

15-Ardalan MR, Samadifar Z, Vahedi A. Creatine monohydrate supplement induced interstitial nephritis. J Nephropathology. 2012; 1 (2): 117-120.

16-Rahimi Z. ACE insertion/deletion (I/D) polymorphism and diabetic nephropathy. J Nephropathology. 2012; 1 (3): 143-151.

17-Daudon M, Traxer O, Conort P, Lacour B, Jungers P. Type 2 diabetes increases the risk for uric acid stones. J Am Soc Nephrol. 2006 Jul; 17 (7): 2026-33.

18-Kari J. Epidemiology of chronic kidney disease in children. J Nephropathology. 2012; 1 (3): 162-163.

19-Baradaran A. Lipoprotein (a), type 2 diabetes and nephropathy; the mystery continues. J Nephropathology. 2012; 1 (3): 126-129.

20-Nasri H. Sudden onset of acute renal failure requiring dialysis associated with large B-cell lymphoma of colon. J Nephropathology. 2012; 1 (3): 202-206.

21- Nasri H. Hypertension and renal failure with right arm pulse weakness in a 65 years old man. J Nephropathology. 2012; 1 (3): 130-133.

22-Marangella M, Bruno M, Cosseddu D, Manganaro M, Tricerri A, Vitale C, et al. Prevalence of chronic renal insufficiency in the course of idiopathic recurrent calcium stone disease: risk factors and patterns of progression. Nephron. 1990; 54 (4): 302-6.

23-Hess B, Hasler-Strub U, Ackermann D, Jaeger P. Metabolic evaluation of patients with recurrent idiopathic calcium nephrolithiasis. Nephrol Dial Transplant. 1997; 12 (7): 1362-8.

24-Orakzai N, Hanbury DC, Farrington K. Screening for biochemical abnormalities in urolithiasis patients. J Ayub Med Coll Abbottabad. 2004; 16 (2): 60-3.

25-Wikstrm B, Backman U, Danielson BG, Fellstrm B, Johansson G, Ljunghall S. Ambulatory diagnostic evaluation of 389 recurrent renal stone formers. A proposal for clinical classification and investigation. Klin Wochenschr. 1983 Jan 17; 61 (2): 85-90.

26-Morton AR, Iliescu EA, Wilson JW. Nephrology: 1. Investigation and treatment of recurrent kidney stones. CMAJ. 2002 Jan 22; 166 (2): 213-8.

27-Mortazavi F, Mahboobi L. Clinical manifestations and risk factors of urolithiasis in children. Iranian J Pediatr. 2007; 17 (2): 129-133

28-Mithani S, Zaidi Z. Comparison of 24 hours urinary citrate levels in urolithiasis patients and healthy controls. J Pak Med Assoc. 2005 Sep; 55 (9): 371-3.

29-Usui Y, Matsuzaki S, Matsushita K, Shima M. Urinary citrate in kidney stone disease. Tokai J Exp Clin Med. 2003; 28 (2): 65-70.

30-Gheissari A, Mehrasa P, Merrikhi A, Madihi Y. Acute kidney injury: A pediatric experience over 10 years at a tertiary care center. J Nephropathology. 2012; 1 (2): 101-108.

31-Gheissari A, Hemmatzadeh S, Merrikhi A, Fadaei Tehrani S, Madihi Y. Chronic Kidney Disease in Children, A report from a tertiary care center over 11 years. J Nephropathology. 2012; 1 (3): 159-164.

32-Tayebi Khosroshahi H. Short history about renal transplantation program in Iran and the world: Special focus on world kidney day 2012. J Nephropathology. 2012; 1 (1): 5-10.

33-Tolou-Ghamari Z. Nephro and neurotoxicity, mechanisms of rejection: A review on Tacrolimus and Cyclosporin in organ transplantation. J Nephropathology. 2012; 1 (1): 23-30.

34- Rafieian-kopaei M, Baradaran A, Nasri H. Association of hyperparathyroidism with malnutrition and Infammation in maintenance hemodialysis patients. Life Sci J. 2012; 9(3): 1871-8

35-Yousefi P, Firouzifar MR, Cyrus A. Correlation between sacral ratio and primary enuresis. J Nephropathology. 2013; 2 (4): 183-187.

36-Einollahi B. Are acquired cystic kidney disease and autosomal dominant polycystic kidney disease risk factors for renal cell carcinoma in kidney transplant patients? J Nephropathology. 2012; 1 (2): 65-68.

11/24/2012