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Original Research Article

A Hospital-Based Study Destemming the Clinical Implication of Serum Uric Acid, Serum Calcium, Serum Creatinine and Serum Electrolytes in Patients with Kidney Stone

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Abstract

Aim: The aim of the present study was to assess the clinical significance of serum uric acid, serum calcium, serum creatinine and serum electrolytes in patients with kidney stone.

Methods: The present study was conducted in the Department of Surgery and 200 patients were included in the study. The patients were divided into two groups according to serum UA levels: the UA-high group with hyperuricemia (serum UA ≥ 7.0 mg/dL) or the UA-low group with normal UA levels (serum UA < 7.0 mg/dL) groups.

Results: Patient background was significantly different between the UA stone patients and the patients with Coax/CaP stones in age, sex, body mass index, HTN, DM, CVD, hemoglobin, serum Alb, serum UA, hyperuricemia, triglyceride, and stage 3 CKD. The UA-low group comprised 50 control subjects and pair-matched 25 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects. The UA-high group comprised 10 patients with UA stones and 20 pair-matched control subjects. There were no statistically significant differences in background between UA stone patients and control subjects. The UA-low group comprised pair-matched 20 patients with CaOx/CaP and 20 patients with UA stones. There were no statistically significant differences in background between UA stone patients and CaOx/CaP patients. The UA-high group comprised 10 patients with CaOx/CaP and pair-matched 10 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects.

Conclusion: Patients with UA stones had significantly worse renal function than controls and CaOx/CaP patients regardless of hyperuricemia. Urolithiasis (CaOx/CaP and UA stone) and hyperuricemia had an association with impaired renal function. Our findings encourage clinicians to initiate intensive treatment and education approaches in patients with urolithiasis and/or hyperuricemia in order to prevent the progression of renal impairment.

Keywords: serum uric acid, serum calcium, serum creatinine, serum electrolytes, kidney stone

Introduction

Kidney stone is a widespread benign urological disorder with overwhelmingly high incidence in the study area. [1] A number of latest multicounty survey studies summarized that the prevalence rate of kidney stones in the US [2] was over 10%, whereas in Europe [3] and China [4], it was 9 and 5.8%, respectively. Furthermore, even after formal treatment, a high recurrence risk of kidney stone still prevailed with a relapse rate of 50% within 10 years. [4] The development of nephrolithiasis is known to be associated with several predisposing factors, which include male, age, race, high sodium intake, hypercalcemia, monogenic hereditary disorders, obesity, pregnancy, and urine-specific gravity. [1,2,5-7] Compounded by the increasing overall prevalence of kidney stones, it is alarmingly becoming a serious public social problem and healthcare burden. [8] Therefore, to ensure targeted prevention of nephrolithiasis formation and recurrence, the identification of novel modifiable risk factors is the need of the hour.

In fact, kidney stone may lead to intra- or extrarenal urinary outflow obstruction to impair renal function, permanent renal damage, and renal failure which are the most serious complications of renal calculi [9]

and creatinine is one of the most common markers in detection and predicting the progression of renal function. The concentrations of UCR can be estimated in both blood and urine. Impaired kidney function affects the serum and urine creatinine (UCR) levels. [10] The influence of nephrolithiasis on creatinine is often discussed at present, but what is the impact of creatinine on renal calculi? As is generally known, nephrolithiasis formation in urinary tubules begins with the supersaturation of urine materials. [11] The previous researches had centralized mainly on the effects of metabolite changes in urine on kidney stone formation. It also suggests that urine plays a crucial role in the production of kidney stones. As a result, our study could focus only on the effects of UCR on kidney stone formation.

Although the precise relationship between hyperuricemia and urolithiasis remains unclear, hyperuricemia-associated symptoms such as hyperuricosuria and acidic urine are well-established contributors to the formation of UA stones. [12,13] These findings indicate that both hyperuricemia and UA stones are potential risk factors for CKD. [14] However, the influence of serum UA levels on renal impairment in patients with urolithiasis is not well known. For example, although hyperuricemia is a risk factor for CaOx/ CaP stones, UA stone patients do not always present with hyperuricemia. Furthermore, urolithiasis patients with impaired renal function do not always present with hyperuricemia.

The aim of the present study was to assess the clinical significance of serum uric acid, serum calcium, serum creatinine and serum electrolytes in patients with kidney stone.

Materials and Methods

The present study was conducted in the Department of Surgery, Government Medical College and Hospital, Bettiah, Bihar, India for one year and 200 patients were included in the study. The patients were divided into two groups according to serum UA levels: the UA-high group with hyperuricemia (serum UA ≥ 7.0 mg/dL) or the UA-low group with normal UA levels (serum UA < 7.0 mg/dL) groups.

Evaluation of Variables

The analyzed pre-treatment variables were age, sex, body mass index, history of hypertension (HTN), blood pressure, diabetes mellitus (DM), cardiovascular disease (CVD), renal function, hemoglobin, serum albumin (Alb), serum UA, dyslipidemia (total cholesterol [Tcho] and triglyceride [TG]) and type of stones (Calcium oxalate [CaOx], Calcium phosphate [CaP], CaOx/CaP mixed, UA containing stone, magnesium ammonium phosphate [struvite stone, NH4MgPO4], and cystine). CVD was defined as a positive history of cardiac surgery, angina, myocardial infarction, or stroke or taking any cardiotonic agents or coronary vasodilators. Stage 3 and 3B CKD was defined as eGFR < 60 and <45 mL/min/1.73 m2, respectively.

Outcome Measurements

To adjust the background differences, they were matched to the study patients using propensity-score matching. [15] We compared background characteristics, eGFR, and number of stage 3 CKD individuals between control individuals and patients with UA stones.

Statistical Analysis

Statistical analyses were conducted using SPSS v. 24.0 (IBM Corporation, Armonk, NY, USA) and GraphPad Prism v. 5.03 (GraphPad Software, San Diego, CA, USA). Categorical variables were presented as percentages and compared using Fisher's exact test or Chi-square test. Quantitative data were expressed as the mean ± standard deviation. Differences between groups were compared using Student's t-test (data with a normal distribution) or Mann-Whitney U-test (data with a non-normal distribution). The correlation between two parameters was analyzed using Spearman's correlation coefficient. Probability (P) values < 0.05 were considered statistically significant.

Results

Table 1: Clinical characteristic of the population

			Eligible patients	
	Ctrl	**Stone former**	**Non-UA stone**	**UA stone**
Number, n =	200	80	30	10
Age, years (IQR)	55 (44–66)	56 (46–68)	58 (48–68)	72 (61–79)
Sex, male, n	76	52	12	8
Body mass index (kg/m2)	21.7 (19.8–21.5)	21.3 (18.9–23.4)	23.7 (21–25.4)	24.6 (21.8–26.6)
Blood pressure (mmHg)				
Systolic	126 (114–140)	131 (120–140)	131 (120–140)	132 (122–150)
Diastolic	78 (68–85)	79 (70–80)	79 (70–80)	80 (70–81)

Hypertension (HTN), n	72	28	12	7
Diabetes mellitus (DM), n	15	6	5	3
Cardiovascular disease (CVD), n	16	8	3	2
Hemoglobin (Hb) (g/dL)	13.4 (12.7–14.8)	13.6 (12.5–15.1)	13.7 (12.7–15.1)	13.1 (11.8–14.6)
Serum Albumin (Alb) (g/dL)	4.4 (4.3–4.7)	4.3 (3.9–4.4)	4.1 (3.9–4.4)	4.0 (3.7–4.2)
Serum uric acid (UA) (mg/dL)	4.6 (3.9–5.8)	5.5 (4.5–6.5)	5.2 (4.3–6.3)	6.3 (5.3–7.5)
Hyperuricemia (UA ≥ 7.0 mg/dL), n	9	7	4	3
UA value unknown, n	0	80	0	0
eGFR (mL/min/1.73m2)	78.2 (69.8–88.9)	68.2 (57.7–84.1)	71.4 (55.5–86.4)	55.5 (36.0–67.4)
Stage 3 CKD, n	8	20	10	6
eGFR value unknown, n	0	80	0	0
Total cholesterol (Tcho) (mg/dL)	204 (181–226)	192 (166–218)	191 (169–216)	188 (162–220)
Triglyceride (TG) (mg/dL)	79 (57–113)	108 (77–153)	106 (76–145)	112 (830177)
Dyslipidemia (Tcho >220, or TG >140 mg/dL), n	68	32	12	5
Tcho or TG value unknown, n	0	65	0	0
Stone information available, n		40	30	10
Type of stone, n				
Calcium oxalate (CaOx)		16	20	0
Calcium phosphate (CaP)		4	2	0
CaOx/CaP mixed		12	12	0
Uric acid containing stone		8	0	10
Ammonium magnesium phosphate (NH4MgPO4)		3	0	0
Cystin		2	0	0
Stone information unavailable, n		40	0	0

Patient background was significantly different between the UA stone patients and the patients with CaOx/CaP stones in age, sex, body mass index, HTN, DM, CVD, hemoglobin, serum Alb, serum UA, hyperuricemia, triglyceride, and stage 3 CKD.

Table 2: Clinical characteristic of pair-matched subjects

	UA-low (<7 mg/dL) group			**UA-high (≥7 mg/dL) group**		
Pair-matching (2:1)	**Ctrl**	**UA stone**	***P value***	**Ctrl**	**UA stone**	***P value***
n	50	25		20	10	
Age, years	66 ± 15	64 ± 16	0.624	62 ± 14	65 ± 15	0.816
Sex, male, n	40	20	0.812	18	8	0.480
Body mass index (kg/m2)	22 ± 2.6	23 ± 3.6	0.743	23 ± 1.8	23 ± 3.2	0.512
Hypertension (HTN), n	33	17	0.950	12	5	0.555
Diabetes mellitus (DM), n	14	7	0.840	6	2	0.525
Cardiovascular disease (CVD), n	8	4	0.713	4	2	0.220
Hemoglobin (Hb) (g/dL)	13.6 ± 1.5	13.7 ± 1.6	0.943	13.9 ± 1.6	13.6 ± 1.2	0.164
Serum Albumin (Alb) (g/dL)	4.2 ± 0.4	4.3 ± 0.4	0.920	4.3 ± 0.4	4.3 ± 0.4	0.916
Serum uric acid† (UA) (mg/dL)	5.7 ± 0.8	5.6 ± 1.2	0.125	8.2 ± 0.8	8.4 ± 1.2	0.733
Total cholesterol† (Tcho) (mg/dL)	196 ± 32.6	208 ± 43.5	0.222	216 ± 34	217 ± 33	0.931
Triglyceride† (TG) (mg/dL)	138 ± 162	136 ± 74.6	0.712	194 ± 212	184 ± 136	0.820
Type of stone, n						
Pure-UA stone		12			14	
UA mixed stone		10			4	

The UA-low group comprised 50 control subjects and pair-matched 25 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects. The UA-high group comprised 10 patients with UA stones and 20 pair-matched control subjects. There were no statistically significant differences in background between UA stone patients and control subjects.

Table 3: Clinical characteristic of pair-matched subjects

	UA-low (<7 mg/dL) group			UA-high (≥7 mg/dL) group		
Pair-matching (1:1)	**CaOx/CaP**	**UA stone**	***P value***	**CaOx/CaP**	**UA stone**	***P value***
n	20	20		10	10	
Age, years	66 ± 14	69 ± 14	0.939	58 ± 12	63 ± 17	0.820
Sex, male, n	16	17	0.312	9	8	0.623
Body mass index (kg/m2)	24 ± 4.8	23 ± 3.8	0.212	25 ± 4.2	23 ± 3.7	0.184
Hypertension (HTN), n	12	14	0.055	4	6	0.212
Diabetes mellitus (DM), n	5	6	0.245	1	4	0.170
Cardiovascular disease (CVD), n	1	4	0.220	1	3	1.000
Hemoglobin (Hb) (g/dL)	13.6 ± 1.6	13.5 ± 1.8	0.525	13.7 ± 2.2	13.8 ± 1.6	0.720
Serum Albumin (Alb) (g/dL)	3.8 ± 0.6	4.2 ± 0.4	0.140	4.2 ± 0.6	4.2 ± 0.5	0.840
Serum uric acid (UA) (mg/dL)	5.2 ± 1.2	5.5 ± 1.3	0.320	8.0 ± 0.7	8.2 ± 1.0	0.644
Total cholesterol (Tcho) (mg/dL)	185 ± 35	194 ± 36	0.124	196 ± 34	208 ± 42	0.316
Triglyceride (TG) (mg/dL)	126 ± 82	134 ± 86	0.525	159 ± 72	192 ± 134	0.316
Type of stone, n						
Pure-UA stone		11			5	
UA mixed stone		9			4	

The UA-low group comprised pair-matched 20 patients with CaOx/CaP and 20 patients with UA stones. There were no statistically significant differences in background between UA stone patients and CaOx/CaP patients. The UA-high group comprised 10 patients with CaOx/CaP and pair-matched 10 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects.

Discussion

Urolithiasis is among the most common urologic diagnoses globally, with considerable burden and cost on healthcare systems worldwide. The most relevant risk factors include diet and lifestyle trends, common diseases such as diabetes and obesity, and global warming. [16] The worldwide prevalence, incidence, and composition of calculi vary according to geographical area, with prevalence ranging from 7 to 13% in North America, 5–9% in Europe, and 1–5% in Asia. [17] The recurrence rate without preventive treatment is approximately 10% at one year, 33% at five years, and 50% at ten years. Kidney stone recurrence rates vary by the underlying metabolic cause. Eligible patients including recurrent active stone formers and single-stone formers with individual risk factors, are considered for full metabolic evaluation that relies on 24-hour urine collection to diagnose metabolic abnormalities and future pharmacologic therapy to prevent a recurrence. [18]

Patient background was significantly different between the UA stone patients and the patients with CaOx/CaP stones in age, sex, body mass index, HTN, DM, CVD, hemoglobin, serum Alb, serum UA, hyperuricemia, triglyceride, and stage 3 CKD. The UA-low group comprised 50 control subjects and pair-matched 25 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects. Chronic inflammation caused by MetS in patients with UA stone may be a possible explanation. The previous report indicated that patients with UA stones have chronic, low grade, and systemic inflammatory diseases. [19]

Another study reported that patients with UA stones had significantly higher rates of aortic calcification [20], which is a surrogate marker of arterial degradation. Furthermore, aortic calcification is directly correlated with CKD severity in renal transplant recipients [21], renal cell carcinoma patients who underwent radical nephrectomy [22] and urolithiasis patients [23], suggesting a potential surrogate marker for diminished renal reserve capacity. Although the mechanisms by which aortic calcification might influence glomerular microcapillary degeneration remain unclear, it is not hard to anticipate that vascular damage occurs first and more severely in small vessels such as afferent arterioles and glomeruli. Therefore, chronic inflammatory disease might play a key role in arterial degradation, thereby promoting the deterioration of renal function. However, the precise mechanism underlying the contribution of chronic inflammatory disease to renal impairment remains unclear. Further studies are necessary to address the detailed association between Mets, chronic inflammation, aortic calcification, UA stone, and CKD. The UA-high group comprised 10 patients with UA stones and 20 pair-matched control subjects. There were no statistically significant differences in background between UA stone patients and control subjects. The UA-low group comprised pair-matched 20 patients with CaOx/CaP and 20 patients with UA stones. There were no statistically significant differences in background between UA stone patients and CaOx/CaP patients.

The UA-high group comprised 10 patients with CaOx/CaP and pair-matched 10 patients with UA stones. There were no statistically significant differences in background between UA stone patients and control subjects.

Chronic asymptomatic hyperuricemia (even in the normal ranges) may promote development of CKD and formation of UA stones. However, the lack of biomarkers for UA accumulation within the body remains an unmet need in patients with hyperuricemia. As efforts to improve chronic asymptomatic hyperuricemia are applied to patients with gout, this might be also a valuable therapeutic approach for patients with a combination of UA stones, insulin resistance, and MetS. [24] Optimal treatment of chronic asymptomatic hyperuricemia requires long-term reductions in serum UA levels. Urate-lowering agents used to treat renal impairment, including the xanthine oxidase inhibitors allopurinol, oxipurinol, and febuxostat, might also prevent CKD. A meta-analysis demonstrated that allopurinol and febuxostat might slow the progression of CKD; however, the results were inconclusive due to the small size of the studies analyzed. [25,26] There is currently no definitive evidence to support the recommendation of urate-lowering agents for asymptomatic hyperuricemia in patients with CKD and urolithiasis. Large scale, randomized, and placebo-controlled trials are required to assess the effect of these agents in patients with CKD and urolithiasis.

Conclusion

Patients with UA stones had significantly worse renal function than controls and CaOx/CaP patients regardless of hyperuricemia. Urolithiasis (CaOx/CaP and UA stone) and hyperuricemia had an association with impaired renal function. Our findings encourage clinicians to initiate intensive treatment and education approaches in patients with urolithiasis and/or hyperuricemia in order to prevent the progression of renal impairment.

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