

Preliminary analysis of serum electrolytes and body mass index in patients with and without urolithiasis

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Abstract

Objectives: To compare body mass index (BMI); serum parameters; and urine parameters between patients with and without urolithiasis.

Methods: Data from 1164 patients admitted to our Department of Urology from January 2011 to July 2013 were retrospectively reviewed; 714 patients (age, 5–87 years; male:female ratio, 1.8:1) exhibited urolithiasis, and 450 patients (age, 12–94 years; male:female ratio, 3.8:1) did not. Blood and urine were collected from patients the morning after hospital admission. Serum and urine parameters were checked by an automatic biochemistry analyzer. Statistical analysis included the Mann–Whitney U test and binary logistic regression.

Results: Serum sodium, potassium, chloride, calcium, phosphorus, and carbon dioxide combining power significantly differed between groups. In male patients, serum sodium, calcium, and phosphorus levels were higher in the urolithiasis group, whereas serum potassium and urine pH levels were lower. In female patients, serum sodium was higher in the urolithiasis group. BMI was higher in the urolithiasis group in all patients, male and female. Respective β -values of serum sodium and BMI in male patients were 0.077 and 0.084; in female patients, these values were 0.119 and 0.102.

Conclusions: Changes in serum sodium and BMI may be involved in the pathogenesis and treatment of urolithiasis.

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Keywords

Urinary calculus, electrolyte, serum sodium, body mass index, serum chloride, serum phosphorus, serum carbon dioxide, serum potassium, serum calcium, serum pH

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Introduction

Urolithiasis is a frequently occurring global disease. The incidence of urolithiasis is increasing in Europe and the United States¹⁻⁴ and ranges from 0.12% to 6.02% in China.⁵ In China, there is a significant regional difference in the incidence of urolithiasis, such that it is higher in the south than in the north.⁶ China is one of three regions with a high incidence of urolithiasis (the other regions comprise the United States and Europe); moreover, urolithiasis is one of the most common diseases in China. In addition, there is a growing epidemic of overweight worldwide. Several studies have analyzed the relationship between body weight and abnormal levels of various urinary constituents of stone promoters and inhibitors (e.g., urinary calcium, citrate, sulfate, phosphate, oxalate, uric acid, and pH).⁷⁻⁹ Taylor et al.¹⁰ first demonstrated the elevated risk of incident urolithiasis in both men and women with increasing body mass index (BMI). However, little is known regarding the association of serum electrolyte constituents with urinary stone formation among individuals with urolithiasis. Serum electrolyte ions (e.g., calcium, phosphorus, sodium, chloride, and potassium) may contribute to formation of urinary stones.^{11,12} The present study was performed to compare serum calcium, phosphorus, potassium, sodium, chloride, and carbon dioxide combining power (CO₂CP), as well as urine pH, urine specific gravity (SG), and BMI between patients with and without urolithiasis.

Patients and methods

Study population and selection criteria

This retrospective study was approved by the institutional review board of The Affiliated Hospital of Qingdao University, which waived the requirement for informed consent. This study constituted a retrospective review of a series of consecutive patients admitted to the Department of Urology from January 2011 to July 2013. Inclusion criteria for the urolithiasis group consisted of a diagnosis of “calculus of kidney,” “calculus of ureter,” or “calculus of bladder and urethra.” These diagnoses were confirmed by the presence of ultrasonographic or radiographic evidence (e.g., X-rays of kidney, ureters, and bladder), as well as intravenous pyelography. A search for “uric acid calculus” diagnoses was performed among ultrasonography or computed tomography records. Patients with renal colic, abnormal pain, hematuria, interrupted micturition, and urinary sediment were also included. The non-urolithiasis group included all other patients admitted to the Department of Urology during the same time period. Patients with a confirmed personal or family history of urolithiasis, metabolic abnormality, endocrine abnormality, rheumatological abnormality, gastrointestinal abnormality, surgical genitourinary reconstruction, or traumatic disease were excluded to avoid confounding bias.

Methods

All study participants were evaluated with the same standard protocol during normal

dietary intake. Blood and urine were collected from patients on the morning after hospital admission. During the collection period, the urine was kept in sterile, closed containers at 4°C without addition of preservatives; all measurements were conducted within 4 hours after the end of the collection period. Following urine sample collection, blood sample collection was performed. For each blood sample, the following serum parameters were measured by standard laboratory technique using a Beckman Synchron CX5 automatic biochemistry analyzer (Beckman Instruments, Brea, CA, USA): calcium, phosphorus, potassium, sodium, chloride, and CO₂CP. Urine samples were analyzed to determine pH and specific gravity using a commercial kit (Boehringer Mannheim, Mannheim, Germany). BMI was calculated as weight in kilograms (kg/m²) from self-reported patient height and weight values at admission.

Statistical analysis

Statistical data were analyzed with SPSS Statistics, version 19.0 (IBM Corp., Armonk, NY, USA). Results were expressed as mean ± standard deviation; *p* values <0.05 were considered to be statistically significant. Student's *t*-test and the non-parametric Mann–Whitney *U* test were used for comparisons between two groups. Binary logistic regression was used to further analyze the effects of serum electrolyte levels, urine pH, urine SG, and BMI on urolithiasis, compared between men and women. Multiple linear regression was used to analyze associations of BMI with serum electrolyte level, urine pH, and urine SG in patients with urolithiasis.

Results

The final study population included 1164 patients; 714 patients exhibited urolithiasis

(463 male patients and 251 female patients). The remaining 450 patients did not exhibit urolithiasis (358 male patients and 92 female patients). Patient age in the urolithiasis group ranged from 5 to 87 years (mean age, 50.6 ± 14.7 years); the male:female ratio was 1.8:1. Patient age in the non-urolithiasis group ranged from 12 to 94 years (mean age, 61.8 ± 16.4 years); the male:female ratio was 3.8:1.

Among 714 patients with urolithiasis, 405 had kidney stones (145 patients had bilateral kidney stones). Moreover, two patients had a single kidney, six patients had sponge kidney, and 307 patients had ureteral stones, including 16 patients who had bilateral ureteral stones; 29 patients had both kidney and ureteral stones; 33 patients had bladder stones, including eight patients who had benign prostatic hyperplasia, one patient who had ureteral stones, and three patients who had kidney stones. There were significant differences in serum sodium, potassium, chloride, calcium, phosphorus, and CO₂CP levels between the urolithiasis and non-urolithiasis groups (*P* < 0.05). In male patients, serum sodium, calcium, and phosphorus levels were significantly higher in the urolithiasis group than in the non-urolithiasis group (*P* < 0.05); serum potassium and urine pH levels were significantly lower in the urolithiasis group than in the non-urolithiasis group (*P* < 0.05). In female patients, the serum sodium level was higher in the urolithiasis group than in the non-urolithiasis group (*P* = 0.083). BMI was significantly higher in the urolithiasis group than in the non-urolithiasis group in all patients, male patients, and female patients (*P* < 0.05). Characteristics of serum electrolytes, urine pH, urine specific gravity, and BMI in patients with and without urolithiasis are shown in Tables 1, 2, and 3.

A backward Wald method was used for binary logistic regression analysis. For male patients, variables kept in the model were

Table 1. Serum parameters, urine parameters, and BMI in patients with and without urolithiasis.

Variable	Urolithiasis group (n = 714)	Non-urolithiasis group (n = 450)	P value
Serum sodium (mmol/L)	140.91 ± 2.62	140.37 ± 2.65	0.018
Serum potassium (mmol/L)	3.96 ± 0.41	4.05 ± 0.45	0.001
Serum phosphorus (mmol/L)	1.20 ± 0.35	1.13 ± 0.24	<0.001
Serum calcium (mmol/L)	2.31 ± 0.17	2.29 ± 0.17	0.025
Serum chloride (mmol/L)	105.12 ± 3.32	104.60 ± 3.26	0.025
Serum CO ₂ CP (mmol/L)	25.88 ± 2.60	26.29 ± 2.58	0.018
Urine pH	6.12 ± 0.78	6.18 ± 0.88	0.283
Urine SG	1.02 ± 0.01	1.02 ± 0.01	0.972
BMI	24.61 ± 3.86	23.61 ± 3.63	<0.001

Abbreviations: CO₂CP, carbon dioxide combining power; BMI, body mass index.

Table 2. Serum parameters, urine parameters, and BMI in male patients with and without urolithiasis.

Variable	Urolithiasis group (n = 463)	Non-urolithiasis group (n = 358)	P value
Serum sodium (mmol/L)	140.96 ± 2.70	140.46 ± 2.54	0.040
Serum potassium (mmol/L)	3.97 ± 0.39	4.08 ± 0.45	<0.001
Serum phosphorus (mmol/L)	1.18 ± 0.26	1.12 ± 0.24	<0.001
Serum calcium (mmol/L)	2.31 ± 0.16	2.30 ± 0.16	0.031
Serum chloride (mmol/L)	104.88 ± 3.11	104.52 ± 3.22	0.204
Serum CO ₂ CP (mmol/L)	26.11 ± 2.60	26.40 ± 2.56	0.152
Urine pH	6.04 ± 0.76	6.18 ± 0.87	0.023
Urine specific gravity	1.02 ± 0.01	1.02 ± 0.01	0.529
BMI	25.00 ± 3.69	23.84 ± 3.62	<0.001

Abbreviations: CO₂CP, carbon dioxide combining power; BMI, body mass index.

Table 3. Serum parameters, urine parameters, and BMI in female patients with and without urolithiasis.

Variable	Urolithiasis group (n = 251)	Non-urolithiasis group (n = 92)	P value
Serum sodium (mmol/L)	140.81 ± 2.47	140.03 ± 3.06	0.083
Serum potassium (mmol/L)	3.95 ± 0.45	3.94 ± 0.45	0.898
Serum phosphorus (mmol/L)	1.25 ± 0.46	1.19 ± 0.21	0.154
Serum calcium (mmol/L)	2.31 ± 0.19	2.27 ± 0.21	0.289
Serum chloride (mmol/L)	105.54 ± 3.65	104.90 ± 3.41	0.149
Serum CO ₂ CP (mmol/L)	25.48 ± 2.55	25.87 ± 2.65	0.348
Urine pH	6.27 ± 0.79	6.19 ± 0.92	0.467
Urine specific gravity	1.02 ± 0.01	1.01 ± 0.01	0.780
BMI	23.94 ± 4.05	22.71 ± 3.55	0.020

Abbreviations: CO₂CP, carbon dioxide combining power; BMI, body mass index.

serum sodium, serum potassium, pH, age, and BMI, with respective β -values of 0.077 ($P=0.045$), -0.611 ($P=0.013$), -0.221 ($P=0.081$), -0.055 ($P<0.001$), and 0.084 ($P=0.028$). For female patients, variables kept in the model were serum sodium, serum CO_2CP , age, and BMI, with respective β -values of 0.119 ($P=0.050$), -0.114 ($P=0.081$), -0.031 ($P=0.005$), and 0.102 ($P=0.014$). Notably, elevated serum sodium and BMI were positively associated with development of urolithiasis. Factors associated with urolithiasis in binary logistic regression are shown in Tables 4 and 5.

In multiple linear regression analysis, increasing BMI was positively associated with serum phosphorus and negatively associated with serum potassium and urine pH in male patients with urolithiasis (all $P<0.05$). In female patients with urolithiasis, increasing BMI was negatively associated with urine pH and positively associated with age (both $P<0.05$). Multiple linear regression results regarding BMI, serum electrolytes, urine pH, and urine SG in patients with urolithiasis are shown in Table 6.

Table 4. Binary logistic regression analysis of factors associated with urolithiasis in male patients.

Factors	β	P value	EXP (B)	95% CI
Serum sodium	0.077	0.045	1.080	1.002–1.164
Serum potassium	-0.611	0.013	0.543	0.336–0.878
Urine pH	-0.221	0.081	0.802	0.626–1.027
Age	-0.055	<0.001	0.947	0.935–0.959
BMI	0.084	0.003	1.087	1.029–1.149

Abbreviations: BMI, body mass index; CI, confidence interval.

Table 5. Binary logistic regression analysis of factors associated with urolithiasis in female patients.

Factors	β	P value	EXP (B)	95% CI
Serum sodium	0.119	0.050	1.126	1.000–1.269
CO_2CP	-0.114	0.081	0.892	0.785–1.014
Age	-0.031	0.005	0.969	0.948–0.991
BMI	0.102	0.014	1.107	1.021–1.201

Abbreviations: CO_2CP , carbon dioxide combining power; BMI, body mass index; CI, confidence interval.

Discussion

Previously, numerous studies have focused on metabolic abnormalities, such as hyperparathyroidism and renal tubular acidosis, with respect to stone formation.¹³ The 24-hour urinary excretion of promoters and inhibitors of stone formation are of considerable interest in patients with urolithiasis.¹⁴ However, not all patients with urolithiasis have exactly defined metabolic abnormality syndromes.¹⁵ Several studies have investigated the possible inhibitory or

Table 6. Multiple linear regression analysis of factors associated with BMI in patients with urolithiasis.

	β	P value
Male patients with urolithiasis		
Serum potassium	-1.728	0.002
Serum phosphorus	2.259	0.006
Urine pH	-0.773	0.006
Female patients with urolithiasis		
Age	0.063	0.003
Urine pH	-1.217	0.001

promotive effects of trace elements in urolithiasis. Trace elements influence the external morphology of crystals, as well as hasten or slow the stone formation process.^{16,17} For instance, zinc and magnesium have inhibitory effects on calcium oxalate stone formation. However, iron and copper may promote calcium oxalate stone formation.¹¹ To the best of our knowledge, little is known regarding the associations of serum electrolyte constituents with urinary stone formation. In the present study, we investigated serum parameters, urine parameters, and BMI in patients with and without urolithiasis. The reasons for different findings in male and female patients are unclear, although we presume that sex, hormones, and dietary factors contributed to these associations.

Because the incidence of urolithiasis differs according to sex and age, hierarchical analysis was performed in the present study: logistic regression was used to control for bias due to age and sex. Binary logistic regression analysis revealed that elevated serum sodium and BMI were positively associated with the onset of urolithiasis. There is limited research regarding the association of serum sodium level with stone formation. Moreira et al.¹² reported that the predicted risk of calcium oxalate stones was positively associated with serum sodium and chloride levels. Although they did not identify mechanisms to link serum levels of sodium and chloride to a high risk of calcium oxalate stones, their results reinforced the role of sodium chloride in calcium oxalate stone formation. Several studies have shown a potential association between elevated risk of urolithiasis and elevated sodium consumption.^{18–20} A synergistic interaction has been reported among serum sodium, serum potassium, and serum calcium. In particular, because sodium and calcium transport are parallel processes in the proximal renal tubule, elevated urinary sodium levels may

increase the risk of hypercalciuria, thus leading to calcium oxalate stone formation.²¹ A high-sodium diet has been shown to reduce renal tubular reabsorption of calcium and enhance intestinal reabsorption of calcium, leading to an overall increase in serum calcium and eventual increases in urinary calcium.^{22,23} In contrast, a low-salt diet can reduce calcium excretion in patients with known calcium stone disease.²⁴ A high-sodium diet has been shown to increase calcium excretion and decrease citrate excretion. The reduction of citrate excretion is presumably due to a significant reduction in serum bicarbonate concentration.²² In our study, there were no significant differences in serum citrate levels between patients with and without urolithiasis, regardless of sex. Parivar et al.²⁵ suggested that potassium intake was significantly associated with a low risk of stone formation. Our study found serum potassium levels were significantly lower in the urolithiasis group than in the non-urolithiasis group among male patients, but not among female patients. Tieder et al.²⁶ proposed that an imbalanced phosphorus level is an important potential risk factor for urolithiasis. Dagnone and Norman²⁷ reported that serum phosphorus level was not an independent risk factor for urinary stone recurrence or complications. In our study, there were no significant differences in serum phosphorus between the two groups.

Nutrition is regarded as a major environmental risk factor for calcium stone formation. Individuals residing in nations with western and westernized lifestyles are likely to have energy-rich and high-salt diets, which result in high BMI and elevated excretion of urinary lithogenic substances that promote idiopathic urolithiasis.^{10,28,29} High BMI is regarded as a cause of urolithiasis among both male and female patients.³⁰ Patients with high BMI excrete more urinary sodium, oxalate, uric acid,

and phosphorus; they also have lower urine pH. These factors are all presumed to promote calcium oxalate stone formation.²⁸ Notably, a higher uric acid level was found to be more predictive of calcium oxalate stones, which emphasizes the importance of heterogeneous nucleation. Furthermore, a known core aspect of stone formation is the presence of acidic urine.³¹

Our multiple linear regression analysis suggested significant negative associations between BMI and urine pH in both male and female patients with urolithiasis. Consistent with our findings, Maalouf et al.⁷ demonstrated that urine pH was inversely associated with BMI in nearly 5000 patients with urolithiasis at two metabolic stone clinics in the United States. Furthermore, multivariate analyses by Taylor and Curhan⁸ and Seiner et al.²⁸ demonstrated that BMI was significantly negatively associated with pH in both men and women. Daudon et al.³² previously indicated that greater body size was associated with greater risk of uric acid stone formation.

This study had the following limitations. First, data were collected retrospectively, which could have introduced unintentional bias. Second, stone analysis was not performed in this study. Certain stone types are often associated with specific metabolic abnormalities. Third, the study was not community-based. Participants in this study were patients who had been admitted to our hospital for urolithiasis or other urological symptoms; thus, their characteristics might not be generalizable to the overall Chinese population. Finally, many confounding factors that might have affected the results (e.g., dietary habits, sedentary lifestyle, hypertension, and weight change) were not considered.

Because the present study did not strictly use a case-control design, we could not conclude that increasing serum sodium

level and BMI were independent risk factors for urolithiasis. However, our results showed that serum sodium level and BMI were significantly higher in patients with urolithiasis than in patients without urolithiasis; moreover, serum sodium and BMI were positively associated with the onset of urolithiasis in both sexes. Our findings suggest that changes in serum sodium level and BMI may be important in the pathogenesis and treatment of urolithiasis. Further research is needed to clearly define the role of serum sodium level in urolithiasis.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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