Original Article

Study of urinary stone composition in a university-based hospital

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Abstract

Objective: Knowing the composition of a urinary stone is valuable in its treatment, helping to define stone etiology, guide management, and prevent stone recurrence. This study aims to identify the incidence of various stone compositions in a university-based, tertiary care hospital.

Material and Method: This retrospective study was conducted at King Chulalongkorn Memorial Hospital. Data of stone composition by infrared spectroscopy were collected from all patients undergoing upper urinary tract stone removal surgery from January 2015 to December 2018. Demographic data including age, gender, comorbidities, and stone characteristics were also collected.

Results: A total of 173 stone analyses were included in this study. The main stone composition was calcium oxalate monohydrate (whewellite 49.7%), calcium carbonate apatite (dahllite 34.1%), calcium oxalate dihydrate (weddellite 5.2%), magnesium ammonium phosphate (struvite 4%), and ammonium hydrogen urate (2.9%). A small proportion of uric acid (1.7%), cystine (1.7%), and calcium phosphate (brushite 0.6%) was also found. No correlation was found between stone composition and age, gender or occupation. Multivariate analysis revealed that calcium oxalate stones were more common in males than females (odds ratio=2.21, 95%CI: 1.91-4.12; p-value=0.01). Phosphate-containing stones (struvite, dahllite and brushite) were more common in patients with a history of urinary tract infection (odds ratio=3.06, 95%CI: 1.18-7.92; p-value=0.02).

Conclusion: Calcium oxalate and calcium carbonate apatite were the most common stone compositions found in this study. Male gender was a risk factor for oxalate stone, and a history of urinary tract infection was a risk factor for phosphate-containing stones.

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Introduction

Urinary tract stone is a common urological problem. One study from the United States revealed that a lifetime incidence of stone disease was more than 12% in males and more than 6% in females, and approximately one-third of patients had recurrence within 5 years[1]. The peak incidence of stone disease occurs in the sixth decade of life[2,3]. There is an association between stone prevalence and geographic area, which is demonstrated by the increased incidence in the southern and eastern regions of the United States[4]. Moreover, stone disease also correlates with body mass index (BMI), diabetes mellitus type 2 (T2DM), metabolic syndrome, and cardiovascular disease[5].

Various chemical compositions are found in an upper urinary tract stone. They include calcium oxalate, calcium phosphate, magnesium ammonium phosphate, and uric acid[6]. Knowing the stone composition is valuable for patient management, either with medical or surgical intervention. Additionally, stone composition helps imply the etiology and prevent stone recurrence[7]. Identification of stone composition can be accomplished through various methods, including urine crystal analysis and chemical analysis of the stone fragments. Nevertheless, stone analysis with Fourier-Transform Infrared Spectroscopy (FTIR) is the most accurate method[8]. In Thailand, however, stone analysis is not commonly performed, and the data of stone composition are still lacking. Thus, we proposed this study in order to examine the composition of the stones available from the upper urinary tract and explore whether there is any association between stone composition and clinical characteristics.

Material and Method

This was a retrospective study performed in a tertiary care, university-based hospital. We included all upper urinary tract stone patients who underwent stone removal surgery or passed the stone spontaneously from January 2015 to December 2018. Patient demographics and clinical data were collected, including age, gender, nationality, BMI, occupation, region of residence, comorbidities, clinical presentation, and stone removal operation. Stone characteristics were reviewed from imaging and included stone location, laterality, and configuration. Stone composition was determined using FTIR In short, the stone specimens derived from the patients were broken into small pieces by mortar, and the pure stone was analyzed by FTIR without potassium bromide (KBr). Stone composition was classified into 4 categories: calcium oxalate stone (calcium oxalate monohydrate - whewellite and calcium oxalate dihydrate - weddellite), phosphate - containing stone (calcium phosphate - brushite, calcium carbonate apatite - dahllite and magnesium ammonium phosphate - struvite), uric acid stone, and other stone types.

Data analysis was performed using Stata version 15.1 (College Station, TX, USA) and presented with median and interquartile range (IQR). Patient characteristics and clinical presentation were analyzed with the chi-square test for qualitative variables and the Kruskal Wallis test for quantitative variables. The association between clinical factors and stone composition was analyzed with logistic regression. Factors with p-value < 0.15 were subsequently included in a multivariate analysis model, and significance was indicated at p-value < 0.05.

Results

During the study period, 168 stone specimens from the upper urinary tract were collected. Males (58.3%) slightly predominated females (41.7%). The mean age was 56 years, and the most common age range of the patients was 45-55 years old (27.2%). Most patients were Thai (96.4%), with a small proportion of other nationalities, including Cambodian, Burmese, Guinean and Italian. Most of the Thais resided in the central region (79.6%), followed by the northern region (6.8%). Data of comorbidities revealed hypertension

in 47.6%, diabetes mellitus in 27.4%, dyslipidemia in 22%, chronic kidney disease in 11.3%, coronary artery disease in 3.6%, cerebrovascular disease in 3.6% and gout in 3% of all patients. According to univariate analysis, stone composition did not correlate to age group, nationality, region of residence or comorbidities. The details of patient characteristics and stone composition are presented in Table 1.

Table 1. Patient characteristics.

	Total (N=168)	Oxalate (N=94)	Phosphate (N=63)	Uric (N=8)	Others (N=3)	P-value
Median (IQR) Age in years	56 (48-66)	57 (49-66)	55 (48-68) (36.5-63.5)	53 (45-63)	48.5	0.58
Sex, N (%)						0.02
• Female	70 (41.7)	30 (31.9)	33 (52.4)	7 (87.5)	0 (0)	
• Male	98 (58.3)	64 (68.1)	30 (47.6)	1 (12.5)	3 (100)	
Race, N (%)						0.90
• Non-Thai	6 (3.6)	4 (4.3)	2 (3.2)	0 (0)	0 (0)	
• Thai	162 (96.4)	90 (95.7)	61 (96.8)	8 (100)	3 (100)	
Region of Thai patients, N (%)			0.23			
• Non central	33 (20.4)	15 (16.7)	15 (24.6)	2 (25)	1 (33.3)	
• Central	129 (79.6)	75 (83.3)	46 (75.4)	6 (75)	2 (66.7)	
Median (IQR) BMI (kg/m^2)	25.2 (22.6-28.1)	25 (22.5-27.4)	26.1 (23.9-29.7)	22.9 (22.9-22.9)	20 (18.5-21.5)	0.09
Body mass index group, N (%)						0.28
• < 25 kg/m^2	24 (51)	14 (50)	7 (29.1)	2 (8.3)	1 (4.2)	
• ≥ 25 kg/m^2	23 (49)	14 (50)	9 (39.1)	0 (0)	0 (0)	
Diabetes mellitus, N (%)	46 (27.4)	29 (30.9)	13 (20.6)	4 (50)	0 (0)	0.38
Hypertension, N (%)	80 (47.6)	48 (51.1)	27 (42.9)	5 (62.5)	2 (66.7)	0.30
Gout, N (%)	5 (3.0)	3 (3.2)	2 (3.2)	0 (0)	0 (0)	0.95
Dyslipidemia, N (%)	37 (22.0)	24 (25.5)	11 (17.5)	2 (25)	0 (0)	0.61
Coronary artery disease, N (%)	6 (3.6)	5 (5.3)	1 (1.6)	0 (0)	0 (0)	0.60
Cerebrovascular disease, N (%)	6 (3.6)	3 (3.2)	3 (4.5)	0 (0)	0 (0)	0.79
Chronic kidney disease, N (%)	19 (11.3)	9 (9.6)	8 (12.7)	2 (25)	0 (0)	0.37
History of urinary tract infection, N (%)	22 (13.1)	7 (7.4)	14 (22.2)	1 (12.5)	0 (0)	0.04
Visible stone from film plain KUB, N (%)	137 (81.5)	76 (80.9)	53 (84.1)	5 (62.5)	3 (100)	0.31

The most common clinical presentation was flank pain (48.8%), followed by incidental findings (23.2%), and gross hematuria (20.8%). Renal stones were found in 54.2% and ureteral stones were found in 45.8% of all cases. Stone removal procedures included ureteroscopy (URS, 45.8%), percutaneous nephrolithotomy (PCNL, 30.6%), shockwave lithotripsy (SWL, 6.9%), open stone surgery (4.2%) and nephrectomy (3.6%). Spontaneous stone passage, with or without medical expulsive therapy, was found in 7.7% of all patients. Clinical presentations and stone removal procedures are summarized in Table 2.

Table 2. Clinical presentation, stone characteristics, and operation performed for stone removal.

	Total (N=168)	Oxalate (N=94)	Phosphate (N=63)	Uric (N=8)	Cystine (N=3)	P-value
Presentation, N (%)						
• Flank pain	82 (48.8)	46 (48.9)	32 (50.8)	3 (37.5)	1 (33.3)	0.52
• Urinary tract infection	22 (13.1)	7 (7.4)	13 (20.6)	0 (0)	2 (66.7)	0.04
• Lower urinary tract symptoms	2 (1.2)	2 (2.1)	0 (0)	0 (0)	0 (0)	0.79
• Microscopic hematuria	5 (3.0)	2 (2.1)	2 (3.2)	0 (0)	1 (33.3)	0.40
• Gross hematuria	35 (20.8)	22 (23.4)	12 (19.0)	0 (0)	1 (33.3)	0.78
• Incidental finding	39 (23.2)	24 (25.5)	12 (19.0)	4 (50)	0 (0)	0.18
• Passing stone	14 (8.3)	7 (7.4)	6 (9.5)	1 (12.5)	0 (0)	0.38
Staghorn, N (%)	27 (16.1)	8 (8.5)	16 (25.4)	0 (0)	3 (100)	0.01
Location, N (%)			0.19			
• Renal calculi	91 (54.2)	46 (48.9)	37 (58.7)	5 (62.5)	3 (100)	
• Ureteral calculi	77 (45.8)	48 (51.1)	26 (41.3)	3 (37.5)	0 (0)	
Side, N (%)						0.10
• Left	87 (51.8)	53 (56.4)	32 (50.8)	2 (25)	0 (0)	
• Right	72 (42.9)	38 (40.4)	25 (39.7)	6 (75)	3 (100)	
• Unknown	7 (4.2)	2 (2.1)	5 (7.9)	0 (0)	0 (0)	
Operation, N (%)						0.63
• Percutaneous nephrolithotomy	53 (31.5)	26 (27.7)	22 (34.9)	2 (25)	3 (100)	
• Ureteroscopy with lithotripsy	77 (45.8)	47 (50)	25 (39.7)	5 (62.5)	0 (0)	
• Passing stone	13 (7.7)	10 (10.6)	3 (4.8)	0 (0)	0 (0)	
• Extracorporeal shock wave lithotripsy	12 (7.1)	5 (5.3)	6 (9.5)	1 (12.5)	0 (0)	
• Open stone surgery	7 (4.2)	6 (3.6)	4 (4.26)	2 (2.13)	3 (4.8)	
• Nephrectomy	4 (6.3)	0 (0)	0 (0)	0 (0)	0 (0)	

The main stone compositions were calcium oxalate monohydrate (whewellite 50.6%), calcium carbonate apatite (dahllite 32.7%), calcium oxalate dihydrate (weddellite 5.4%), magnesium ammonium phosphate (struvite 4.2%), and ammonium hydrogen urate (3.0%). A small proportion of uric acid (1.8%), cystine (1.8%) and calcium phosphate (brushite 0.6%) was also found. All data are presented in Table 3 and Figure 1.

Interestingly, calcium oxalate stones were significantly more common in males than females with an odds ratio of 2.28 (95% CI: 1.23-4.24; p-value= 0.01). This difference was still statistically significant from the multivariate analysis, controlling for the coronary artery disease factor (odds ratio=2.21, 95% CI: 1.91-4.12; p-value=0.01). Moreover, the incidence of phosphate-containing stones (struvite, dahllite and brushite) was more common in patients with a history of urinary tract infection (odds ratio=3.06, 95%CI: 1.18-7.92; p-value=0.02), after controlling for the gender factor in the multivariate analysis (Tables 5, 6).

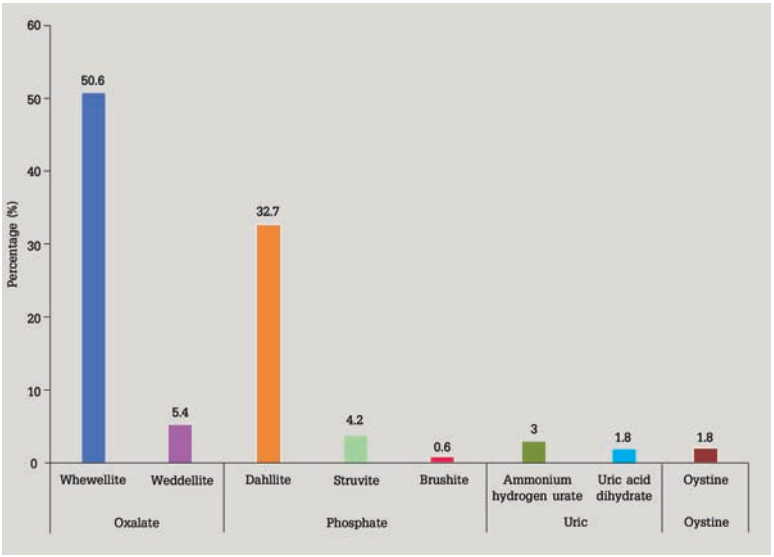

Figure 1.
Percentage of stone composition by group.

Table 3. Stone composition.

	N (Total 168)	%
Oxalate		
• Whewellite	85	50.6
• Weddellite	9	5.4
Phosphate		
• Dahllite	55	32.7
• Struvite	7	4.2
• Brushite	1	0.6
Uric		
• Ammonium hydrogen urate	5	3.0
• Uric acid dihydrate	3	1.8
Cystine		
• Cystine	3	1.8

Table 4. Age and incidence of stones.

Age group (years)	Total (N=168)	Oxalate (N=94)	Phosphate (N=63)	Uric (N=3)	Others (N=8)
<35	12 (7.1)	4 (4.3)	6 (9.5)	0 (0)	2 (25)
35-45	24 (14.3)	12 (12.8)	9 (14.3)	1 (33.3)	2 (25)
46-55	45 (26.8)	25 (26.6)	18 (28.6)	1 (33.3)	1 (12.5)
56-65	42 (25.0)	28 (29.8)	12 (19.0)	1 (33.3)	1 (12.5)
66-75	35 (20.8)	19 (20.2)	14 (22.2)	0 (0)	2 (25)
>75	10 (6.0)	6 (6.4)	4 (6.3)	0 (0)	0 (0)

Table 5. Factors associated with oxalate stone.

	Univariate		Multivariate	
	OR (95%CI)	P-value	aOR (95%CI)	P-value
Age in years				
• < 45	Ref			
• 46-55	1.55 (0.65-3.71)	0.33		
• 56-65	2.19 (0.89-5.38)	0.19		
• > 65	1.49 (0.62-3.58)	0.37		
Sex				
• Female	Ref		Ref	
• Male	2.28 (1.23-4.24)	0.01	2.21 (1.19-4.12)	0.01
Race				
• Non-Thai	Ref			
• Thai	0.6 (0.11-3.36)	0.56		
Region				
• Non-Central	Ref			
• Central	1.38 (0.68-2.79)	0.37		
Body mass index > 25kg/m^2	0.91 (0.29-2.82)	0.87		
Diabetes melitus	1.58 (0.79-3.15)	0.20		
Hypertension	1.2 (0.66-2.19)	0.55		
Gout	1.24 (0.2-7.61)	0.82		
Dyslipidemia	1.55 (0.74-3.24)	0.25		
Ischemic heart disease	4.28 (0.49-37.41)	0.14	3.61 (0.40-32.24)	0.25
Stroke	0.82 (0.16-4.16)	0.81		
Chronic kidney disease	0.71 (0.27-1.85)	0.49		

OR = Odds ratio; aOR = adjusted odds ratio; 95%CI = 95% confidence interval.

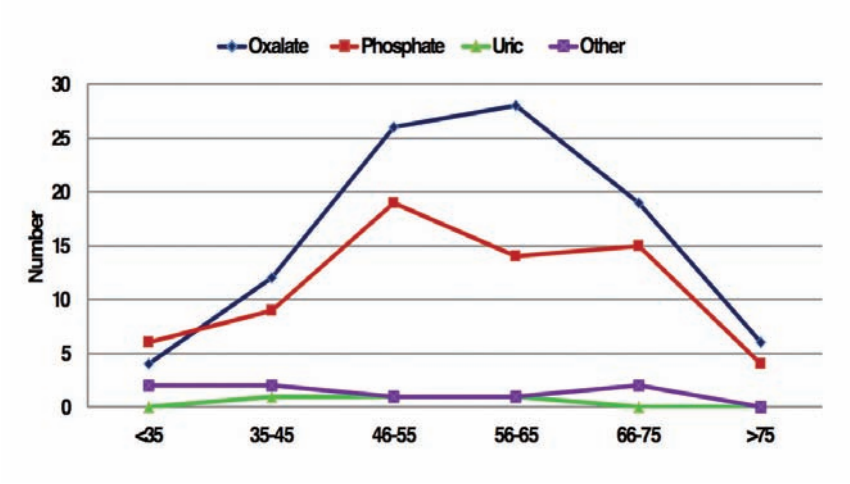

Figure 2.
Incidence of stones in different age groups.

Table 6. Factors associated with phosphate-containing stones.

	Univariate		Multivariate	
	OR (95%CI)	P-value	aOR (95%CI)	P-value
Age in years				
• < 45	Ref			
• 46-55	0.95 (0.39-2.3)	0.91		
• 56-65	0.65 (0.26-1.64)	0.36		
• >65	0.99 (0.41-2.39)	0.97		
Sex				
• Male	Ref		Ref	
• Female	1.81 (0.97-3.38)	0.06	1.48 (0.77-2.86)	0.23
Race				
• Non-Thai	Ref			
• Thai	1.27 (0.23-7.16)	0.78		
Region				
• Non-Central	Ref			
• Central	0.75 (0.37-1.54)	0.44		
Body mass index > 25 kg/m^2	1.91 (0.58-6.23)	0.28		
Diabetes Mellitus	0.53 (0.26-1.11)	0.19		
Hypertension	0.69 (0.37-1.28)	0.24		
Gout	1.06 (0.17-6.49)	0.95		
Dyslipidemia	0.67 (0.31-1.44)	0.31		
Ischemic heart disease	0.31 (0.03-2.68)	0.29		
Stroke	1.61 (0.32-8.22)	0.57		
Chronic kidney disease	1.17 (0.45-3.08)	0.75		
History of urinary tract infection	3.53 (1.41-8.88)	0.01	3.06 (1.18-7.92)	0.02

OR = Odds ratio; aOR = adjusted odds ratio; 95%CI = 95% confidence interval.

Discussion

The data of urinary stone composition in Thai patients are limited because the FTIR machine is available only in tertiary or university-based hospitals, and stone analysis is not commonly performed. Our institution, however, has a designated specialized stone clinic which has been routinely analyzing stone composition since January 2015. During a four-year study period, calcium oxalate and phosphate-containing stones were predominantly found in nephrolithiasis patients. This finding was similar to others. Tanthanuch et al. showed that calcium oxalate and phosphate-containing stones were predominant in southern Thai patients[9]. However, our study found a larger ratio of phosphate-containing stones (38%) compared to their study (19%). In contrast, the incidence of uric acid stones was less common in ours (5%) compared to the southern Thais (27%).

In addition, our study found that urinary stones were more common in males than females with a peak incidence between 45 and 55 years, which is similar to other studies. There was no correlation between the incidence of stone and region of residence, BMI, and patient comorbidities. However, this negative finding may have been caused by the relatively small number of patients included in this study and its single-institution research design.

Our study demonstrated that phosphate-containing stones were more common in patients with a history of urinary tract infection. Similarly, Holmgren et al. reported an association between phosphate-containing stones in patients and *E. coli* urinary tract infection, and between magnesium ammonium phosphate stones and Proteus infection10. Miano et al. hypothesized that these stone compositions were related to infections with urease-producing pathogens[11]. Urease hydrolyzes urea in the urine, and products of this reaction are ammonium ions and bicarbonate, which subsequently lead to urine alkalization and stone formation[11].

We also found a significant epidemiological correlation between the male gender and calcium oxalate stones. An earlier study showed that the amount of oxalate required to initiate crystallization was lower in healthy males than in females[12]. However, there are various factors involved in the pathogenesis of urinary stone formation. Further studies should be conducted in order to support this finding.

Conclusion

Calcium oxalate and phosphate-containing stones were the most common stone compositions found in this study. Male gender was associated with oxalate stones, and a history of urinary tract infection was associated with phosphate-containing stones. Further studies should be conducted to verify the findings on a larger scale.

Conflict of interest

The authors declare no conflict of interest.

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