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Research article

The correlation between demographic factors and upper urinary tract stone composition in the Thai population

Noppon Arunkajohnsak, Tawatchai Taweemonkongsap, Sunai Leewansangtong, Sittiporn Srinualnad, Kantima Jongjitaree, Ekkarin Chotikawanich *

Division of Urology, Department of Surgery, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

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ABSTRACT

Objective: To identify the correlation between demographic factors and upper urinary tract stone composition in the Thai population.

Method: A retrospective observational study of first-time upper urinary tract stone former patients aged over 18 years who underwent stone surgery was performed in a tertiary referral university hospital from January 2013 to May 2018. Collected data included demographic information and stone composition information, which were analysed by the Fourier Transform-Infrared Spectroscopy (FTIR) method. The correlation between the demographic factors and major upper urinary tract stone composition was analysed using Fisher's exact test.

Results: A total of 480 patients were included in this study. The stones were 319 (66.5%) renal calculi and 161 (33.5%) ureteric calculi. There were 248 (51.7%) single composition stones and 232 (48.3%) mixed composition stones. The major stone compositions were 288 (60.0%) calcium oxalate (CaOx), 125 (26.0%) calcium phosphate (CaP), 40 (8.3%) uric acid (UA), 19 (4.0%) magnesium ammonium phosphate (MAP), five (1.0%) cystine, and three (0.6%) ammonium hydrogen urate (AHU). Gender was correlated with the major stone composition. In females, a correlation was found between the major stone composition and age, diabetes mellitus (DM), and glomerular filtration rate (GFR). The study showed no significant correlation between the major stone composition and dyslipidemia (DLP), hypertension (HT), gout, and body mass index (BMI) in both genders.

Conclusion: Gender, age, DM, and GFR were the factors affecting the stone composition.

1. Introduction

Urolithiasis is a common disease with a prevalence that ranges between 7-13% in North America, 5–9% in Europe, and 1–5% in Asia [1]. The differences among countries including age, gender, geographic variation, climate, dietary habits, fluid intake, occupation, education, socio-economic status, and genetic and metabolic diseases are factors for lithogenesis [1, 2]. Compared to the past, the prevalence of urolithiasis has increased in most countries over recent decades because of changes in the living standards and dietary habits, as well as improvements in clinical diagnosis procedures [3, 4, 5, 6, 7]. Furthermore, the composition of stones has varied across gender, age, and country due to different risk factors [6, 8, 9, 10, 11, 12]. The most frequently found minerals have been calcium oxalate (CaOx), calcium phosphate (CaP), and uric acid (UA), but these also vary among countries [6, 8, 9, 10, 11, 12]. Moreover, in recent decades, the composition of the stone types has changed with an increase in CaOx and decrease in the infected stones [8].

Understanding the correlation between stone composition and patients' status is important to provide the etiology of lithogenesis, and the management and prevention of urinary stones [9, 11]. In Thailand, there have also been changes in dietary habits and living standards due to urbanisation and industrialisation over recent decades, which has resulted in changes in patients' status and increases in the metabolic syndrome, which could affect the composition of urinary tract stones. Therefore, the aim of this study was to identify the correlation between stone composition and patients' status that could aid in the prevention and treatment planning in urological services and provide a better understanding of the lithogenesis process.

2. Objective

The objective of this study was to identify the correlation between stone composition and patients' status including age, gender, body habits, and underlying medical conditions; such as, hypertension (HT), diabetes

* Corresponding author.
E-mail address: ekkarinc@yahoo.com (E. Chotikawanich).

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mellitus (DM), dyslipidemia (DLP), gout, and glomerular filtration rate (GFR), which affect the upper urinary tract stones in the Thai population.

3. Methods

This was a retrospective observational study, which was performed in a tertiary referral university hospital from January 2013 to May 2018 and approved by the Ethics Committee of the institute.

The sample size was estimated based on the comparison of the proportion of CaOx between males and females. A previous study [8] of the Norwegian population in 2018 revealed that CaOx was more common in males (75.7%) than females (63.1%). With the expected similar difference of 13%, two-sided type I error of 0.05 and 85% power, the required number of males and females would be 240:240. Therefore, a sample of 480 participants was needed.

All charts of the upper urinary tract stone patients aged over 18 years who underwent stone surgery during the study period were collected by a systematic randomised approach by computer. Only the first time stone formers were included in the study. Demographic information (age, gender, body mass index (BMI), HT, DM, DLP, gout, and GFR) and stone composition information, which were analysed by the Fourier Transform- Infrared Spectroscopy (FTIR) method, were collected. The GFR status was determined as the baseline of the patients; therefore, less GFR represented the existing CKD. All stone compositions were analysed in terms of frequency and percentage. The major stone composition was described by the composition amounting to more than 50% in each stone. The correlation between the demographic factors and major upper urinary tract stone composition was analysed using Fisher's exact test.

4. Results

A total of 480 patients were included in this study. The demographic data included 252 males and 228 females (52.5%:47.5%); 227 (47.3%) HT; 105 (21.9%) DM; 131 (27.3%) DLP, and 16 (3.3%) gout. The average age was 56.5 years (males = 55.9 years; females = 57.1 years), while the BMI was 26.1 kg/m^2, and GFR was 75.2 mL/min/1.73 m^2 (Table 1). There was 59/252 (23.4%) of men with low GFR, and 53/228 (23.2%) of women with low GFR.

The stones were 319 (66.5%) renal calculi and 161 (33.5%) ureteric calculi. There were 248 (51.7%) single composition stones and 232 (48.3%) mixed composition stones (Table 2).

The single composition stones were classified into six types, which were composed of 148 (59.7%) CaOx, 44 (17.7%) CaP, 33 (13.3%) UA, 18 (7.3%) magnesium ammonium phosphate (MAP), four (1.6%) cystine, and one (0.4%) ammonium hydrogen urate (AHU).

The mixed composition stones were classified into 13 types (Table 2). In considering the major stone composition in the mixed composition stones, the composition type which was greater than 50% was acknowledged as the major composition. These were classified into six types comprising 140 (60.3%) CaOx, 81 (34.9%) CaP, seven (3.0%) UA, one (0.4) MAP, one (0.4%) cystine, and two (0.9%) AHU.

In combining both the single and mixed composition stones, the results of the major stone compositions were 288 (60.0%) CaOx, 125 (26.0%) CaP, 40 (8.3%) UA, 19 (4.0%) MAP, five (1.0%) cystine, and three (0.6) AHU (Table 3 and Figure 1).

There was correlation between the gender and major stone compositions; females had more major stone compositions of CaP, MAP, and AHU than males (Figures 1 and 2). In females, there was also a correlation between the major stone composition and age, DM, and GFR (Figures 3, 4, and 5). There was no difference in the stone incidence and composition in the males with low GFR and normal GFR.

Female patients older than 60 years had more UA as the major stone composition than the younger patients, while the younger patients had more CaP with a significant p-value < 0.001 (Figure 3).

Females with DM had the major stone composition which comprised UA more significantly than the non-DM patients. On the contrary, CaP and MAP were found more significantly in non-DM patients than in the DM patients with a p-value $= 0.001$ (Figure 4).

Females with GFR <60 mL/min/1.73 m^2 had more UA than the group of GFR ≥ 60 mL/min/1.73 m^2 with a p-value $= 0.002$ (Figure 5).

The study showed no significant correlation between the major stone composition and DLP, HT, gout, and BMI in both genders.

5. Discussion

The stone analysis and major stone composition provided valuable information into how the stones were formed. The American Urological Association (AUA) guidelines on the medical management of kidney stones recommend obtaining a stone analysis at least once when one is available to help classify the patients and guide prevention [13]. The two most widely recommended and used methods of stone analysis are x-ray diffraction or FTIR [14].

This study presented that the major composition of the upper urinary tract stones in the Thai population was CaOx followed by CaP and UA, respectively. In the single stone compositions, CaOx was found to comprise the majority (59.7%). In the mixed stone compositions, CaOx + CaP was the majority (85.3%). Liu et al. reported the incidence of CaOx (75–90%), CaP (6–13%), and UA (5–20%) among various Asian countries [2]. Likewise, Kravdal et al. stated that CaOx (71.3%) was the most common stone composition in Norway [8], while the incidence of CaP equalled 10.8%, and UA equalled 8.9%.

The number of upper urinary tract stones in this study was found most frequently in the age groups of 50–59 years and 60–69 years, respectively. This could be compared to another study of upper urinary tract stone composition in Thailand in 2008, in which the frequency was found mostly in the age group of 50–59 years and 40–49 years, respectively

Table 1. Demographic data.

	Min	Max	Mean	SD
Age (year)	20	88	56.5	12.5
Height (cm)	105	183	160.6	8.8
BW(kg)	33	120	67.4	13.9
BMI(kg/m^2)	14.5	48.1	26.1	1.6
GFR ((mL/min/1.73 m^2)	11	140	75.2	23.9

	n	%
Male: Female	252:228	52.5:47.5
HT	227	47.3
DM	105	21.9
DLP	131	27.3
Gout	16	3.3
GFR <60	112	22.3

Table 2. Single and Mixed stone Composition.

Stone composition	n	% of single or mixed stone	% of total stone
Single	248	100	51.7
1 CaOx	148	59.7	30.8
2 CaP	44	17.7	9.2
3 UA	33	13.3	6.9
4 MAP	18	7.3	3.8
5 Cystine	4	1.6	0.8
6 AHU	1	0.4	0.2
Mixed	232	100	48.3
7 CaOx + CaP	198	85.3	41.3
8 CaOx + UA	9	3.9	1.9
9 CaOx + MAP	3	1.3	0.6
10 CaOx + Cystine	1	0.4	0.2
11 CaOx + AHU	4	1.7	0.8
12 CaP + MAP	3	1.3	0.6
13 CaP + Cystine	1	0.4	0.2
14 CaP + AHU	4	1.7	0.8
15 CaOx + CaP + UA	3	1.3	0.6
16 CaOx + CaP + MAP	3	1.3	0.6
17 CaOx + CaP + AHU	1	0.4	0.2
18 CaP + UA + AHU	1	0.4	0.2
19 CaP + MAP + AHU	1	0.4	0.2
Total	480	100	100

Table 3. Major stone composition.

	Major stone composition: Number (%)		
	Single stone composition	Mixed stone composition	Total
1 CaOx	148 (59.7)	140 (60.3)	288 (60.0)
2 CaP	44 (17.7)	81 (34.9)	125 (26.0)
3 Uric	33 (13.3)	7 (3.0)	40 (8.3)
4 Struvite	18 (7.3)	1 (0.4)	19 (4.0)
5 Cystine	4 (1.6)	1 (0.4)	5 (1)
6 AHU	1 (0.4)	2 (0.9)	3 (0.6)
Total	248 (100)	232 (100)	480 (100)

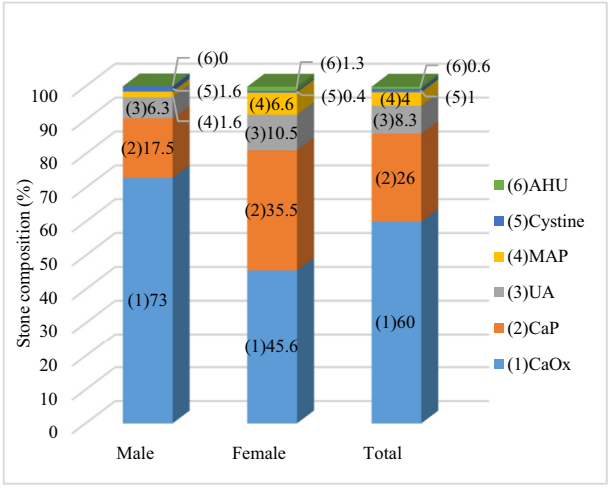

Figure 1. Percentage distribution of major stone composition according to gender (p-value < 0.001).

[12]. This study reported that the stones occurred in older patients after a 10-year interval.

Gender was significantly correlated with the major stone composition; the study showed the proportion of CaP, MAP, and AHU in females was greater than that found in males. All three types of stones were influenced by urinary tract infection, which occurred more in females than males [15]. The percentage of CaP in females (35.5%) was double that of males (17.5%), which correlated with the high urine pH of females, which exceeded that of males [16], causing CaP stone formation [17]. Additionally, Wang et al. demonstrated the prevalence of infected stones among women was two times of that in men (17.22% vs. 8.27%) [18].

Age, DM, and GFR also correlated with the major stone composition but significantly only in females.

Females older than 60 years had significantly more UA than females younger than 60 years. The older subjects were prone to have a metabolic syndrome and different lifestyle than the younger subjects. Low urine pH, which was the predisposing factor to have UA, was also found more commonly in the older age groups [19].

In females with DM, the major stone composition was UA (21.2%), which was 2.9 times greater when compared with females of the non-DM group (7.4%). This was a result from the low urine pH in DM patients caused by insulin resistance, which decreased renal ammonia genesis, ammonium excretion, and the activity of the Na^+/H^+ exchange channel,

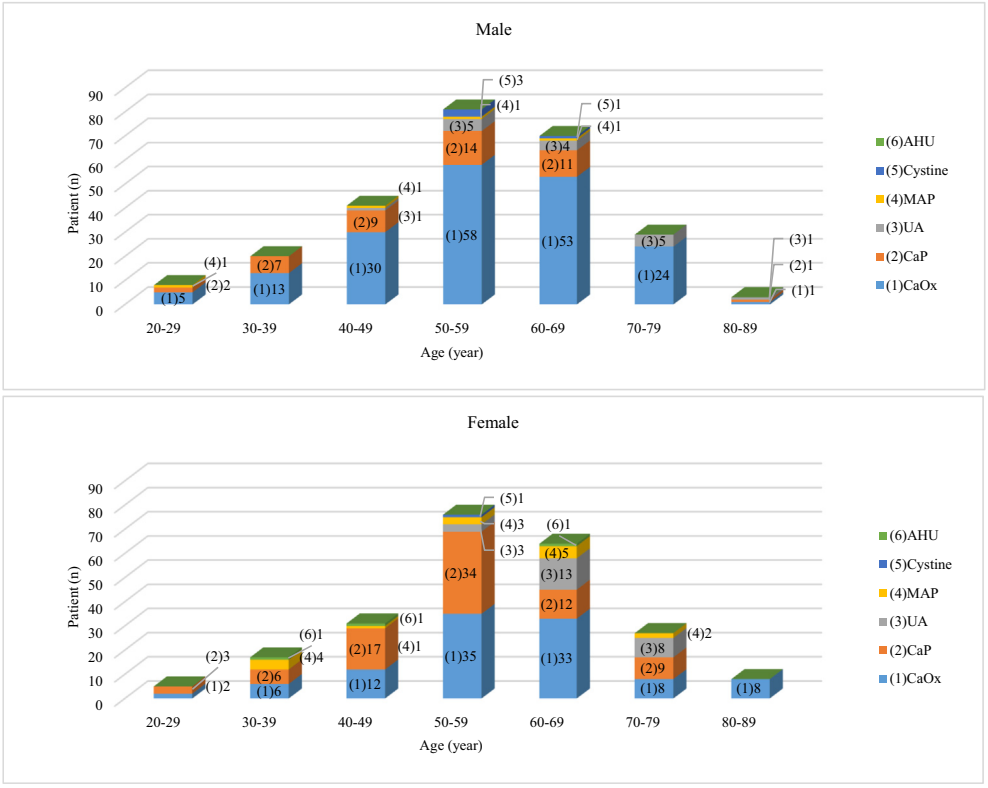

Figure 2. Distribution of frequency and major stone composition according to age in male (n = 252) and female (n = 228).

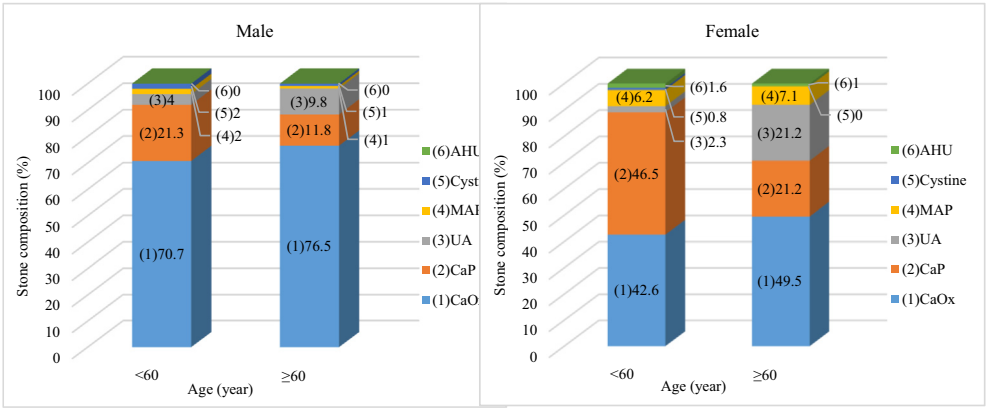

Figure 3. Percentage distribution of major stone composition according to age in male (p-value = 0.099) and female (p-value < 0.001).

leading to an increase in free H^+ ions within the renal tubule [20]. On the other hand, non-DM females significantly exhibited CaP and MAP, which was associated with infection and a high urine pH to a greater extent than in females with DM. In spite of the fact that the incidence of urinary tract infection in DM patients was higher than in non-DM patients, 46.9 per 1000 persons-years (95% CI; 45.8–48.1) vs. 29.9 (95% CI; 28.9–30.8) for patients without diabetes [21], the result of the low urine pH caused by insulin resistance had more effect on the composition of the stones than the infection. Furthermore, the DM subjects had significantly higher 24-hour urine volumes, lower urine calcium, and lower magnesium excretions than non-DM subjects [22]. Thus, DM patients might have some protective factors that could decrease calcium stone formation.

In patients with decreasing GFR, the incidence of stones was less than those patients with normal GFR in both genders. Females with GFR <60 mL/min/1.73 m^2 (27.5%) had significantly higher UA than those with GFR ≥60 mL/min/1.73 m^2 (5.4%). This finding could be from the decreasing ammonium excretion in renal insufficiency, which occurred in patients regarding the decrease in GFR and metabolic disease [20, 23, 24].

In addition, the study showed that demographic factors affected the stone composition. Metabolic disorders caused by DM and chronic kidney disease were able to alter the composition compared with healthy individuals of a similar gender and age. Understanding the factors that affect the stone composition could support the prevention of stone formation and recurrence.

6. Conclusion

In concluding, it was found that gender, age, DM, and GFR were the factors affecting the stone composition.

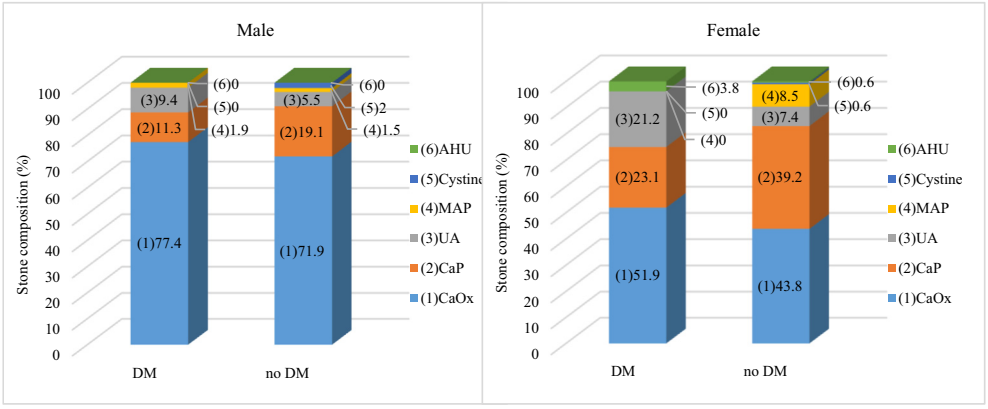

Figure 4. Percentage distribution of major stone composition according to DM in male (p-value = 0.427) and female (p-value = 0.001).

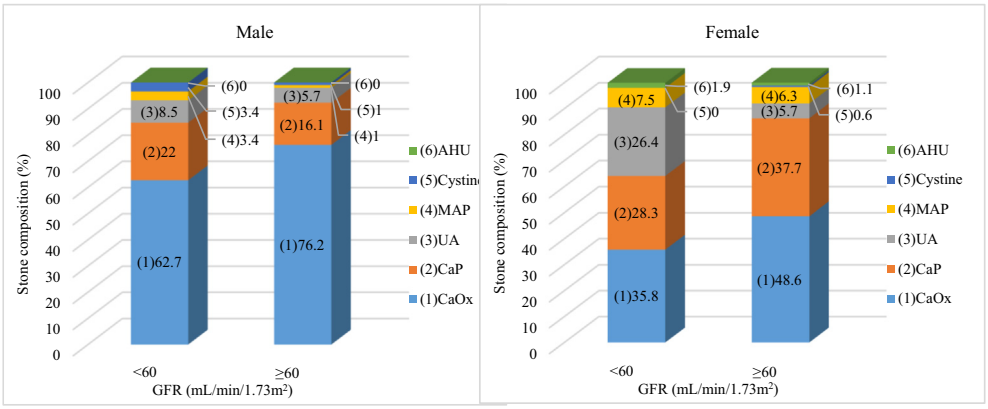

Figure 5. Percentage distribution of major stone composition according to GFR in male (p-value = 0.138) and female (p-value = 0.002).

Declarations

Author contribution statement

Noppon Arunkajohnsak and E. Chotikawanich: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tawatchai Taweemonkongsap, S. Leewansangtong, S. Srinualnad and K. Jongjitaree: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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