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ORIGINAL PAPER

Stone composition of renal stone formers from different global regions

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Summary

Objective: *To study urinary stone composition patterns in different populations around the world.*

Materials and methods: *Data were collected by reviewing charts of 1204 adult patients of 10 countries with renal or ureteral stones (> 18 years) in whom a stone analysis was done and available. Any method of stone analysis was accepted, but the methodology had to be registered.*

Results: *In total, we observed 710 (59%) patients with calcium oxalate, 31 (1%) with calcium phosphate, 161 (13%) with mixed calcium oxalate/calcium phosphate, 15 (1%) with carbapatite, 110 (9%) with uric acid, 7 (< 1%) with urate (ammonium or sodium), 100 (9%) with mixed with uric acid/ calcium oxalate, 56 (5%) with struvite and 14 (1%) with cystine stones. Calcium-containing stones were the most common in all countries ranging from 43 to 91%. Oxalate stones were more common than phosphate or mixed phosphate/oxalate stones in most countries except Egypt and India. The rate of uric acid containing stones ranged from 4 to 34%, being higher in Egypt, India, Pakistan, Iraq, Poland and Bulgaria. Struvite stones occurred in less than 5% in all countries except India (23%) and Pakistan (16%). Cystine stones occurred in 1% of cases.*

Conclusions: *The frequency of different types of urinary stones varies from country to country. Calcium-containing stones are prevalent in all countries. The frequency of uric acid containing stones seems to depend mainly on climatic factors, being higher in countries with desert or tropical climates. Dietary patterns can also lead to an increase in the frequency of uric acid containing stones in association with high obesity rates. Struvite stones are decreasing in most countries due to improved health conditions.*

KEY WORDS: *Urinary calculi; Epidemiology; Gender; Age; Calcium oxalate; Calcium phosphate; Uric acid; Struvite; Cystine.*

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No conflict of interest declared.

BACKGROUND

Most data on chemical stone composition have been collected in the Western world (1-8). It is well known that stone composition is dependent on lifestyle and diet, which in turn is dependent on country, climate and culture. Therefore, it is of interest to establish a more globalised map of chemical stone composition around the globe. U-merge, an association gathering urologists from all over the world, is the ideal platform for this task. For this reason, the scientific office of U-Merge launched a study to collect the results of urinary stone analyses among different populations in the countries of its members.

MATERIALS AND METHODS

All members of U-merge were invited to join in the study. Data were collected by reviewing charts of adult patients (> 18 years) with renal or ureteral stones observed in each participating center who had chemical analysis of the stone available. Gender, age, country and stone composition of each patient were recorded in an Excel data base. Any method of stone analysis was accepted, but the methodology had to be known and registered. A minimum number of 30 patients per center was required. Stones analyzed by wet chemical were classified as *calcium oxalate* (CaOx) (unspecified), *calcium phosphate* (CaP) (unspecified), mixed *calcium oxalate/calcium phosphate* (CaOx/CaP), struvite, *uric acid* (UA), mixed *uric acid/calcium oxalate* (UA/CaOx) and cystine.

Stones analysed by infrared spectroscopy or X-ray diffractometry were classified as CaOx dihydrate (> 50%), CaOx monohydrate (> 50%), CaP (> 50%), mixed CaOx/CaP (if CaP > 10%), struvite (> 50%), carbonate apatite (50%), UA anhydrous (> 50%), UA dihydrate (> 50%), ammonium

	Argentina	Bulgaria	Canada	China	Egypt	India	Iraq	Italy	Pakistan	Poland
N°	300	183	50	90	73	35	36	360	44	33
M	179 (59%)	122 (67%)	28 (56%)	58 (64%)	57 (78%)	26 (74%)	26 (72%)	226 (63%)	38 (86%)	16 (48%)
F	121 (41%)	61 (33%)	22 (44%)	32 (36%)	16 (22%)	9 (26%)	10 (28%)	134 (37%)	6 (14%)	17 (52%)
Age	45+12	48+13	56+14	50+12	40+12	50+12	38+13	56+14	40+8	50+17

Age p = 0.000; M/F p = 0.002.

Table 1.
Average age and M/F ratio of RSFs from different countries.

urate (> 50%), sodium urate (> 50%), mixed UA/CaOx, cystine.
The *Statistical Package for the Social Sciences* (SPSS) version 11.5 for Windows was used for statistical analysis. Comparisons were considered to differ significantly if $p < 0.05$.

Results

In total, 1204 renal stone formers (RSFs) were considered (776 males, 428 females) from 10 countries (*Argentina, Bulgaria, Canada, China, Egypt, India, Iraq, Italy, Pakistan* and *Poland*).
Twelve institutions from 10 countries have joined the survey as listed below:

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- *Acibadem City Clinic Tokuda Hospital, Sofia (Bulgaria)*
- *Department of Urology and Nephrology, Military Medical Academy, Sofia (Bulgaria)*
- *CHU de Québec, Laval University, Québec City (Canada)*
- *Dep of Urolotgy, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai (China)*
- *Urology Department, Assiut University, Assiut (Egypt)*
- *Department of Urology, Kasturba Medical College, Manipal, Karnataka (India)*
- *Urology Department, Sulaymaniyah Surgical Teaching Hospital, Sulaymaniyah (Iraq)*
- *Shar Teaching Hospital, Sulaymanyah City (Iraq)*
- *Department of Urology, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan (Italy)*
- *City Hospital Pakpattan, Pakpattan (Pakistan)*
- *Private Medical Center Klinika Wisniowa, Zielona Gora (Poland)*

The average age of patients was 49.3+14.4 and the M/F ratio was 1.81. The number, average age and M/F ratio of RSFs from different countries are shown in Table 1. The average age of RSFs in *Italy* and *Canada* was greater than that of the RSFs of *Argentina* (p = 0.000), *Bulgaria* (p = 0.000 and p = 0.001), *Egypt* (p-0.000), *Iraq* (p = 0.000, and *Pakistan* (p = 0.000). The average age of RSFs in Italy was higher than that of the RSFs in *China* (p = 0.011). The lowest average age was observed in *Egypt*, *Iraq*, and *Pakistan*, where the average age of RSFs was lower than those of RSFs in *Canada* (p = 0.000), *Italy* (p = 0.000) and *China* (p = 0.000, p = 0.000 and p = 0.001). In *Egypt* and *Iraq*, the average age of the RSFs was also lower than in *Bulgaria* (p = 0.001, p = 0.002), *Poland* (p = 0.020, p = 0.007) and *India* (p = 0.009 and p = 0.004). The frequency of the disease was slightly higher in women in *Poland* (52%), whereas it tended to be higher in men in *Canada* (56%), *Argentina* (59%), *Italy* (63%), *China* (64%) and *Bulgaria* (67%). Highest rates in men were observed in *Pakistan* (86%), *Egypt* (78%), *India* (74%) and *Iraq* (72%).

Table 2.
Spectrum of stone composition by gender and age.

	Gender		Age class			
	Males	Females	18-39	40-59	> 60	Total
CaOx	461 (59%)	249 (58%)	200 (59%)	318 (57%)	192 (62%)	710 (59%)
COM	223	105	73	136	119	328
COD	52	23	20	34	21	75
CaOx/CaP	89 (11%)	72 (16%)	46 (13%)	80 (14%)	35 (11%)	161 (13%)
CaP	18 (2.3%)	13 (3.0%)	12 (3.5%)	14 (2.5%)	5 (1.5%)	31 (3%)
Carbapatite	4 (0.5%)	11 (2.5%)	5 (1.5%)	8 (1.5%)	2 (0.5%)	15 (1%)
Ca-containing	572 (74%)	345 (80%)	263 (77%)	420 (76%)	234 (76%)	917 (76%)
UA	84 (11%)	26 (6%)	22 (6.4%)	49 (8.8%)	39 (12.6%)	110 (9%)
Urate	4 (0.5%)	3 (0.7%)	0 (0%)	4 (0.5%)	3 (1%)	7 (0.5%)
UA/CaOx	75 (10%)	25 (6%)	25 (7%)	55 (10%)	20 (6%)	110 (9%)
UA-containing	163 (21%)	54 (13%)	47 (14%)	108 (19%)	62 (20%)	217 (18%)
Struvite	33 (4.2%)	23 (5.4%)	23 (7%)	22 (4%)	11 (3.5%)	56 (5%)
Cystine	8 (1.1%)	6 (1.4%)	8 (2.5%)	4 (0.5%)	2 (0.5%)	14 (1%)
Total	776	428	341	554	309	1204

The spectrum of stone composition by gender and age is shown in Table 2. In total, we observed 710 (59%) patients with calcium oxalate, 31 (1%) with calcium phosphate, 161 (13%) with mixed calcium oxalate/calcium phosphate, 15 (1%) with carbapatite, 110 (9%) with uric acid, 7 (< 1 %) with urate (ammonium or sodium), 100 (9%) with mixed with uric acid/ calcium oxalate, 56 (5%) with struvite and 14 (1%) with cystine stones.
In the calcium-containing group, calcium oxalate stones accounted for 77% and phosphate or mixed calcium phosphate/calcium oxalate stones for the remaining 23%. The frequency of calcium phosphate or mixed calcium phosphate/calcium oxalate ranged from 9 to 74%.
The great variability depends on the different methods of analyzing stones and reporting the results.
In 403 patients with calcium oxalate stones analyzed by infrared spectroscopy, *calcium oxalate monohydrate* stones (COM) were more frequent than *calcium oxalate dihydrate* (COD) stones.
Frequency of calcium oxalate stones was equal in women and men (58% *vs* 59%), whereas frequency of uric acid containing stones was lower in women than in men (13% *vs* 21%) and frequency of calcium phosphate and mixed calcium phosphate/calcium oxalate stones (21% *vs* 14%) and frequency of struvite stones were higher in women. Frequency of COM stones tended to be higher in men than in women (78 *vs* 71%) and to increase with age (18-39 =78%, 40-59 = 80%, > 60% = 85%).

Table 3.
Spectrum of stone composition in different countries.

	Argentina	Bulgaria	Canada	China	Egypt	India	Iraq	Italy	Pakistan	Poland	Tot
CaOx	239 (80%)	97 (53%)	23 (46%)	65 (72%)	12 (16%)	7 (20%)	16 (44%)	214 (59%)	21 (48%)	16 (49%)	710 (59%)
COM	-	79	-	49	12		11	178		-	
COD	-	18	-	16	0		5	36		-	
CaOx/CaP	12 (4%)	17 (9%)	11 (22%)	11 (12%)	34 (47%)	8 (23%)	7 (20%)	57 (16%)	0 (0%)	4 (12%)	161 (13%)
CaP	7 (2%)	0 (0%)	2 (4%)	6 (7%)	0 (0%)	0 (0%)	0	14 (4%)	2 (4%)	0	31 (3%)
Carbapatite	0 (0%)	3 (2%)	10 (20%)	0 (0%)	0 (0%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0	15 (1%)
Ca-containing	258 (86%)	117 (64%)	46 (92%)	82 (91%)	46 (63%)	15 (43%)	25 (69%)	285 (79%)	23 52%	20 61%	917 (76%)
Ox %	92%	85%	50%	79%	26%	46%	64%	72%	91%	80%	77%
UA pure	27 (9%)	8 (4.5%)	1 (2%)	5 (5%)	0 (0%)	5 (14%)	8 (22%)	39 (10.5%)	11 (25%)	6 (18%)	110 (9%)
UA urate	0 (0%)	6 (3.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.5%)	0 (0%)	0 (0%)	7 (1%)
UA/CaOx	6 (2%)	39 (21%)	1 (2%)	1 (1%)	22 (30%)	7 (20%)	1 (3%)	18 (5%)	0 (0%)	5 (15%)	100 (8%)
UA - containing	33 (11%)	53 29%	2 (4%)	6 6%	22 (30%)	12 (34%)	9 (25%)	58 (16%)	11 (25%)	11 (33%)	217 (18%)
Struvite	9 (3%)	10 (5.4%)	1 (2%)	2 (3%)	4 (5.5%)	8 (23%)	1 (3%)	12 (3,5%)	8 (18%)	1 (3%)	56 (5%)
Cystine	0 (0%)	3 (1.6%)	1 (2%)	0 (0%)	1 (1.5%)	0 (0%)	1 (3%)	5 (1.5%)	2 (5%)	1 (3%)	14 (1%)
Total	300	183	50	90	73	35	36	360	44	33	1204

Frequency of uric acid stones was higher in males and tended to increase with age.
The distribution of the different types of stones in RSFs in different countries is described in Table 3. Calcium-containing stones were the most common in all countries. Among calcium-containing stones, calcium oxalate stones were more frequent in all countries except in *Egypt* and *India* where the frequency of calcium phosphate or mixed calcium phosphate/calcium oxalate was 74% in *Egypt* and 53% in *India*, respectively. Among calcium oxalate stones, the rate of COM stones was 100% in *Egypt*, 83% in *Italy*, 81% in *Bulgaria*, 75% in *China*, and 69% in *Iraq*. The rate of uric acid containing stones ranged 4 to 34% in most countries with the highest rates observed in *Egypt*, *India*, *Poland*, and *Bulgaria*. Struvite stones were less than 5% in all countries but *India* (23%) and *Pakistan* (16%). Cystine stones were less than 2%.

Discussion

Stone composition by age and sex

In the present study, calcium-containing stones were the most frequent, followed by uric acid-containing stones, while struvite and cystine are less frequent.
In accordance with previous reports (9), uric acid containing stones were more frequent in males and in older ages, whereas phosphate stones were more frequent in women.
The average age of RSFs in different countries varies but these differences reflect those that are observable in the general population of their countries, which averaged about 20 years lower (Figure 1).
M/F ratio is different in countries, being balanced between men and women or slightly in favor of men in the countries of *North America*, *Europe*, *South America* and *China* but heavily weighted in favor of men in *Egypt*, *Pakistan*, *India* and *Iraq*. This finding confirmed the tendency to an increase of stone formation in women of Western countries (9), and more recently of *China* (10), while in *Egypt*, *Pakistan*, *India* and *Iraq* the ratio of males to females is still similar to what was observed in Western countries forty years ago (11). This trend can be explained by the so-called nutrition transition, that is the change in dietary habits across the world with a convergence towards an increased consumption of unhealthy

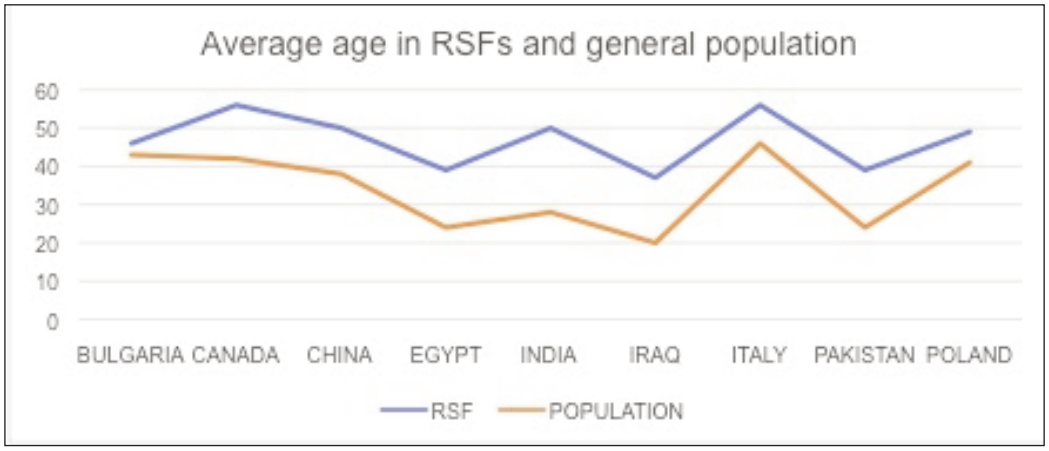


Figure 1.
Average age in RSFs and general population.

foods that is the cause of the increase in non-communicable diseases in almost all regions of the world in both sexes (12). Consumption of unhealthy foods is still limited in some regions of *North Africa* and *South Asia* that maintain dietary patterns with a lower risk of urinary stones forming. Moreover, in some countries the characteristics of family structure and cultural rules still present a nutritional disadvantage for women (13).

Stone composition by country

The spectrum of composition of urinary stones is quite variable in different countries. Differences could be attributable to the different characteristics by age and gender of the populations studied, reflecting the distribution by age and gender in the general population of each country. On the other hand, the modality of stone analysis and reporting in the different centers may be a confounding factor (14). For this reason, the most robust data are those comparing the rates of calcium-containing with those of uric acid containing stones, whereas it is less significant to compare the results of different countries in relation to the specific crystallographic composition, which should be compared between patients whose stones have been analyzed and reported in the same laboratory.

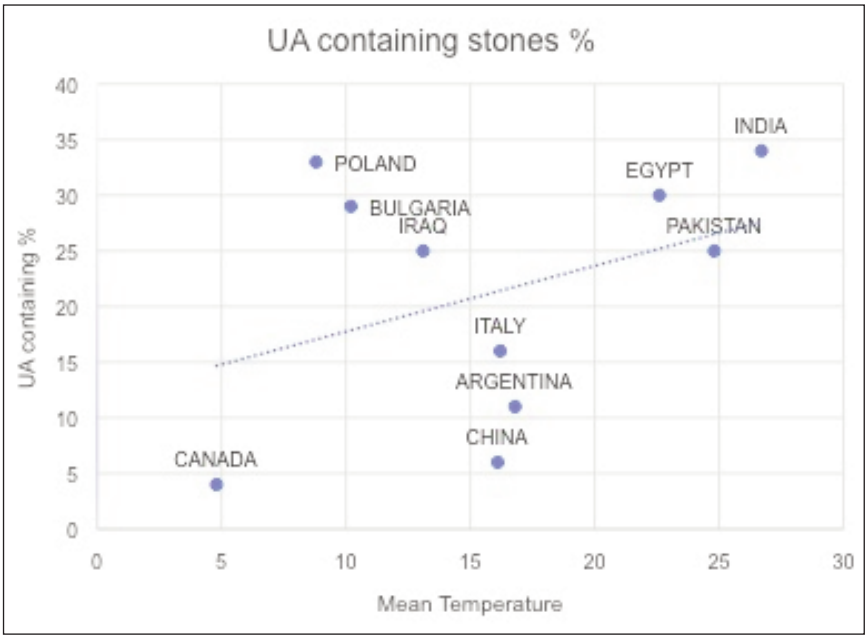
Calcium-containing stones were the most common in vast majority of countries with a rate ranging from 52 to 91%. The highest rates of calcium-containing stones were observed in *North America*, *South America*, *China* and some European countries. In most countries, calcium oxalate stones (in particular, COM stones) were the more frequent calcium-containing stones, although calcium phosphate and mixed calcium oxalate/calcium phosphate stones were more frequent than pure calcium oxalate stones in some countries such as *Egypt* and *India*. This trend agrees with previous observation in North America where a tendency has been reported of an increase in oxalate stones and a decrease in phosphate stones during the last two decades (4, 5).

The highest rates of acid uric containing stones were observed in *Iraq*, *Pakistan*, *India*, *Egypt* and *Poland* and *Bulgaria*. In general, uric acid-containing stones should be more frequent in older male patients, but surprisingly in our study the highest rates of uric acid-containing stones were observed in two countries with the lowest mean age, namely *Egypt* and *Iraq*. This result can be explained by the finding that the frequency of a type of stone is not a measure of the prevalence of the disease in the population, but is the result of the prevalence of different types of urinary stones. In other words, a high frequency of uric acid stones may be due to an increase in the prevalence of uric acid stones but, alternatively, a lower prevalence of other types of stones in the population studied. On the other hand, the impact of environmental factors could be decisive, considering that high temperatures and high humidity cause a decrease of urinary volumes and urinary pH values resulting in an increase of urinary uric acid saturation and of the incidence of uric acid stones (15, 16). In fact, the highest values of uric acid-containing stones were observed in countries with high mean temperatures (17) and tropic or hot desert climates such as *Egypt, India, Pakistan* and *Iraq* (Table 4) (Figure 2). Our data confirm previous evidence in the literature showing a high rate of uric acid-containing stones in *Pakistan, Egypt*, and *Iraq* (18-21). In the present

Table 4.
Mean temperature, precipitation fall and climate classification in the countries involved in the study.

Country	Town	Temperature mean	Precipitation fall	Climate	Köppen-Geiger climate classification system
Argentina	Buenos Aires	16.8 °C.	1040 mm	Warm temperate	Cfa
Bulgaria	Sofia	10.2 °C	581 mm	Warm temperate	Cfb
Canada	Quebec	4.8 °C.	1101 mm	Cold temperate	Dfb
China	Shanghai	16.1 °C.	1066 mm	Warm temperate	Cfa
Egypt	Asyut	22.6 °C.	2 mm	Hot desert	BWh
India	Karnataka	26.7 °C	4866 mm	Tropical	Am
Pakistan	Pakpattan	24.8 °C	234 mm	Hot desert	BWh
Iraq	Sulaymaniyah	16.2 °C	906 mm.	Warm temperate	Csa
Italy	Milan	13.1°C	1013 mm	Warm temperate	Cfa
Poland	Zielona Gora	8.8 °C	572 mm	Warm temperate	Cfb

Figure 2.
Rate of uric-acid containing stones and mean temperature.



study, the prevalence of uric acid containing stones was also high in Southern India in accordance with previous reports. In fact, the frequency of uric acid-containing stones was reported low (4.28%) or very low (< 1%) in *North Western India* (22, 23), but higher in *Southern India* (24). This difference can be explained by different regional eating habits: in the Northern and Western regions, a more traditional vegetarian diet is consumed with exclusive consumption of fruit, vegetables and legumes, whereas in the Southern regions the consumption of sweets, snacks and pork meat is common (25). On the other hand, in our study the lowest rate of uric acid containing stones was observed in *Canada*, the country with the lowest mean temperature. Intermediate rate values were observed in countries with a temperate climate, such as *China* and *Italy*. The high frequency of uric acid-containing stones in *Poland* is less easily explained, mainly because it contrasts with previous findings showing lower rates of uric acid stones in a series of stones analyzed by infrared spectroscopy (26). Possible explanations are high obesity rate of the population (45%) and unfavorable dietary patterns (27). In fact, the adherence to the traditional Polish dietary pattern, characterized by high intake of refined grains, potatoes, sugar and sweets is associated with a higher risk of abdominal obesity and hypertriglyceridemia (28). Similarly, in Bulgaria the frequency of uric acid-containing stones is associated with obesity rates which are among the highest in *Europe* (46%) (27), and with an unhealthy nutritional pattern characterized by high consumption of fatty meats and meat products, high-fat milk and a high alcohol intake (29).

The rate of struvite stones is generally lower than described in the past, due to improved health conditions and early diagnosis and treatment of urinary tract infections by urease-producers, although in some countries such as Pakistan and India it still accounts for a quarter of cases. Cystine stone rates are similar in all countries, with similar rates than those reported in the literature. In conclusion, the frequency of different types of urinary stones varies from country to country. Calcium-containing stones are the most frequent in all countries, with frequencies of up to 90%. The frequency of uric acid containing stones seems to depend mainly on climatic factors, being more frequent in warmer countries with desert or tropical climates although dietary patterns can also lead to an increase in the frequency of uric acid containing stones in association with high obesity rates. Struvite stones are decreasing in most countries except India and *Pakistan*.

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