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Analysis of urinary stone types' distribution in Turkey according to the geographical regions where patients were born and live: A cross-sectional single-center experience

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ABSTRACT

Aims: To evaluate the stone composition and the distribution of the stone types in the geographical regions of Turkey according to where patients were born and where patients live.

Methods: The patients who were treated for urinary system stone disease in our hospital between January 2011 and March 2019 were included in the study. Stone samples were collected by endoscopic stone surgery methods or shock wave lithotripsy. Stone analyses were made with manual chemical analysis methods. Stone types and distribution were recorded according to geographical regions of Turkey.

Results: A total of 706 patients who were treated for urolithiasis were included in the study. Calcium oxalate (CO) stones were at the highest rates for both genders [127 (68.6%) and 359 (68.9%), for females and males, respectively]. There were no statistically significant differences in terms of stone types between genders (p=0.323). There were statistically significant more CO (297), uric acid (17), mixed stones (78) in the Anatolian (central) region than the other regions according to the geographical region where patients were born (p<0.001, for each). Additionally, there were significantly more calcium phosphate stone formers (25) in the Anatolian region according to the geographical region where patients lived (p<0.001).

Conclusions: CO is the most common stone type in Turkey independently of where patients were born or where patients live. Higher prevalence rates of stone disease and CO stones were seen in Central Anatolia. Both geographic origin and dietary habits affect the incidence of urinary system stone disease.

Introduction

Urolithiasis is one of the most common urologic pathology that affects the urinary tract with a high prevalence rate between 2% and 20% (1,2). The prevalence and incidence are increasing in different parts of the world for both men and women (3). The higher incidence and prevalence rates were found to be related to dietary habits, socioeconomic conditions, water consumption, water quality and hot climate (4). Metabolic disorders like overweight/obesity, hyperlipidemia, hyperuricemia, and hyperglycemia have a role in the recurrence of urolithiasis (5). In Turkey, urolithiasis is an endemic disease and has a high incidence rate (15%) and it is more common in the south and southeast parts of the country (3). Stones can be seen in any location of the urinary tract and the mechanism of its formation is still unknown (6). Clinical conditions and the treatment choices mainly depend on the size, location of stones, degree of obstruction and the chemical composition of the stone (7,8). Many factors were found to be related to the stone composition as the body weight, metabolic syndrome, hypertension, body mass index and renal function (1,9,10). In addition, it has been shown that stone composition is one of the most important factors which is associated with the recurrence of stone disease (11).

Several *in vivo* and *ex vivo* methods were described in the literature in order to analyze the urinary stone types (12,13). Defining the stone type is very important for both the management and prevention of stone disease. Changing dietary habits and water intake are some of the key points for preventing stone disease (14). In the present study, we aimed to evaluate our single-center results in terms of stone composition and the distribution of the stone types in Turkey according to geographical regions of where patients were born and live. Secondly, we aimed to evaluate and compare if stone types were affected by changing the geographical regions of patients.

Methods

We retrospectively reviewed the medical records of the patients who were diagnosed with urinary system stone disease and treated with endoscopic (percutaneous nephrolithotomy, ureterorenoscopic laser lithotripsy, cystolithotripsy), laparoscopic nephrolithotomy or extracorporeal shock wave lithotripsy (SWL) at University of Health Sciences Turkey, Gülhane Training and Research Hospital, Clinic of Urology between January 2011 and March 2019 in the study. Informed consent was not obtained from participants because of the retrospective nature of the study. Stone samples were collected during the stone surgery methods mentioned above and with SWL. Patients treated with SWL were requested to micturate into a bowl for collecting stone fragments after SWL sessions. Patients whose stone analysis data were missing, who could not collect stone fragments after SWL or who were unwilling to participate in the study were excluded. The study protocol was approved by the University of Health Sciences Turkey, Gülhane Training and Research Hospital, Ethics Committee for Non-Interventional Research (protocol no: 2020/169). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographics of the patients, stone locations, stone analysis results and distribution of stone analysis results according to the regions of Turkey [Anatolia (central), Marmara (north-west), Aegean (west), Black Sea (north), Mediterranean (south), Eastern Anatolia, Southeastern Anatolia] were recorded. The regions where patients lived and where they were born were both noted.

Stone locations were divided into three groups as kidney, ureter, and bladder. Manual chemical analysis was used to identify stone compositions. Stone analyses were made with wet chemical analysis method, firstly described by Uldall, (15), in the University of Health Sciences Turkey, Gülhane Training and Research Hospital, Biochemistry Clinic's metabolism laboratory. All analyses were carried out in the same laboratory by two experienced biochemistry specialists. Stone types were classified as calcium oxalate (CO), calcium phosphate (CP), uric acid (U), cystine (C), magnesium ammonium phosphate (MAP) and the mixed types. The calcium components and the infectious components were also analyzed because of the importance of prophylaxis. The seven regions of Turkey were analyzed statistically in detail according to the distribution of stone analysis results, calcium components and infectious components of stones. In addition, CO stones were compared according to the patient's geographical origin and location to evaluate if the changing the geographical region affected the incidence.

Statistical Analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in median, minimum and maximum, number and frequency. The normal distribution of the quantitative data was analyzed using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to compare two groups of quantitative variables showing abnormal distribution. The Pearson chi-square and Fisher's exact tests were used to compare qualitative data. A p value of <0.05 was considered statistically significant.

Results

A total of 706 patients were included in the study. Of the patients, 521 (73.8%) were male and 185 (26.2%) were female. The median age of the female patients was 44 (19-78) years and it was 41 (3-85) years for male patients. There was no statistically significant difference in terms of age and gender ($p>0.05$, for each). There were no statistically significant differences in terms of stone localization and stone types between the genders ($p=0.053$ and $p=0.323$, respectively). Only 16 (3.1%) male patients had stones in the bladder (Table 1). CO stones were at the highest rates for both genders [127 (68.6%) and 359 (68.9%), for females and males, respectively] (Table 1). The calcium component was observed in 166 (89.7%) female patients and 484 (92.9%) male patients, there was no statistically significant difference ($p=0.171$). In addition, there was no statistical difference in terms of the infectious component between the genders ($p=0.127$). The infectious component was observed in 16 (8.6%) female patients and 67 (12.9%) male patients (Table 1).

While evaluating the regions where people were born, CO, U, and mixed stone forms displayed statistically significantly higher prevalence in the Anatolian (central) region than in other regions ($p<0.001$) (Table 2). CO stones were the most observed stone type in the Anatolian (central) region (Table 2, 3). The calcium component was positive and the infectious component was negative in most of the patients in all regions. There was no statistical difference in infectious components according to geographical regions where patients were born ($p=0.313$) (Table 2).

While evaluating the region where patients lived, most of our patients were from Anatolia (central) region as it was

expected because our hospital is located in that region. There was an approximately similar number of patients from other geographical regions. When we compared the stone types according to regions where patients lived, there were statistically significantly more CO, CP, U and mixed stones in Anatolian (central) (p<0.001, for each) (Table 3).

When we compared the CO stone formers according to the patient's geographical origin and location, there was a statistically significant difference between the regions and we realized that migration had an impact on urinary system stone disease (Table 4).

Discussion

The overall incidence of urolithiasis is rising worldwide, including the United States and Northern Europe in the latest years (16,17). Turkey is among the countries with a high incidence of urolithiasis. Evaluating the regions of Turkey, it has a higher prevalence rate in the south and southeastern parts (3,18). The common features of these two regions are that they have similar hot climates and the nearest side of the country to the equator. In addition, people who live in these regions have similar dietary habits (oxalate-rich foods, high animal protein, high salt intake, etc.). The amounts of oxalate and calcium consumed in the diet are significant factors in the development of CO stone disease (19). Positive relation has been demonstrated between kidney stones and the consumption of oxalate-rich foods (20). Oxalate does not have a functional role in humans and is derived from the diet as an unnecessary product of metabolism (19). Therefore, the oxalate intake directly affects urinary oxalate concentration. As we have mentioned in the introduction section, a high fluid intake seems to be the most evidence-based measure for the prevention of idiopathic oxalate stone formation. A high fluid intake which guarantees a diuresis of 2 L/day seems together with some dietary oxalate and Na^+ restriction to be an appropriate measure to prevent idiopathic Ca nephrolithiasis. However, a consensus has not been reached yet for this to be an acceptable strategy for CO stone formation (21).

In the present study, we found that CO is the most common stone type in Turkey, independently of where patients were born or live. In Turkey, the central and western parts of the country are usually taking emigrants from the other regions of the country. Local food varieties and dietary habits of each region are so different in reality. For example, Mediterranean cuisine is dominated in the western regions while the consumption of red meat and animal proteins are common feeding habits in the south and east regions. In our cohort, CO stone formers' number and frequency were higher according to patients' location than patients' origin (450, 92.6% vs. 297, 61.1%, p<0.001). This difference can help to explain that migration has an impact on

Table 1. Demographics and stone characteristics of the patients

Variables		Gender		
		Female (185, 26.2%)	Male (521, 73.8%)	
		n (%)	n (%)	p value
Age (year) [median (minimum-maximum)]		44 (19-78)	41 (3-85)	0.437[a]
Stone localization	Kidney	117 (63.2)	314 (60.3)	0.053[b]
	Ureter	68 (36.8)	191 (36.7)	
	Bladder	0	16 (3.1)	
Stone type	Calcium oxalate	127 (68.6)	359 (68.9)	0.323[b]
	Calcium phosphate	9 (4.9)	20 (3.8)	
	Uric acid	12 (6.5)	16 (3.1)	
	Cystine	2 (1.1)	8 (1.5)	
	Magnesium ammonium phosphate	5 (2.7)	13 (2.5)	
	Calcium oxalate + calcium phosphate	12 (6.5)	27 (5.2)	
	Calcium oxalate + uric acid	7 (3.8)	24 (4.6)	
	Calcium oxalate + magnesium ammonium phosphate	11 (5.9)	54 (10.4)	
Calcium component	None	19 (10.3)	37 (7.1)	0.171[b]
	Exist	166 (89.7)	484 (92.9)	
Infectious component	None	169 (91.4)	454 (87.1)	0.127[b]
	Exist	16 (8.6)	67 (12.9)	

[a]Mann-Whitney U test
[b]Chi-square test

Table 2. Stone characteristics according to the geographical region where patients were born

Variables		Geographical Region								
		Anatolia (Central) (419, 59.3%)	Marmara (North-West) (43, 6.1%)	Aegean (West) (n, %=40, 5.7%)	Black Sea (North) (68, 9.6%)	Mediterranean (South) (49, 6.9%)	Eastern Anatolia (56, 7.9%)	Southeastern Anatolia (25, 3.5%)	Abroad (6, 0.8%)	
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	p value
Stone type	Calcium oxalate	297 (70.9)	33 (76.7)	29 (72.5)	43 (63.2)	28 (57.1)	36 (64.3)	16 (64.0)	4 (66.7)	<0.001[a]
	Calcium phosphate	14 (3.3)	6 (14.0)	1 (2.5)	1 (1.5)	5 (10.2)	2 (3.6)	0	0	
	Uric acid	17 (4.1)	0	3 (7.5)	5 (7.4)	0	2 (3.6)	0	1 (16.7)	<0.001[a]
	Cystine	4 (1.0)	0	0	3 (4.4)	1 (2.0)	2 (3.6)	0	0	
	Magnesium ammonium phosphate	9 (2.1)	1 (2.3)	1 (2.5)	2 (2.9)	2 (4.1)	1 (1.8)	2 (8.0)	0	
	Calcium oxalate + calcium phosphate	23 (5.5)	0	2 (5.0)	4 (5.9)	2 (4.1)	5 (8.9)	3 (12.0)	0	<0.001[a]
	Calcium oxalate + uric acid	18 (4.3)	1 (2.3)	0	7 (10.3)	5 (10.2)	0	0	0	<0.001[a]
	Calcium oxalate + magnesium ammonium phosphate	37 (8.8)	2 (4.7)	4 (10.0)	3 (4.4)	6 (12.2)	8 (14.3)	4 (16.0)	1 (16.7)	<0.001[a]
Calcium component	None	30 (7.2)	1 (2.3)	4 (10.0)	10 (14.7)	3 (6.1)	5 (8.9)	2 (8.0)	1 (16.7)	
	Exist	389 (92.8)	42 (97.7)	36 (90.0)	58 (85.3)	46 (93.9)	51 (91.1)	23 (92.0)	5 (83.3)	
Infectious component	None	373 (89.0)	40 (93.0)	35 (87.5)	63 (92.6)	41 (83.7)	47 (83.9)	19 (76.0)	5 (83.3)	0.313[a]
	Exist	46 (11.0)	3 (7.0)	5 (12.5)	5 (7.4)	8 (16.3)	9 (16.1)	6 (24.0)	1 (16.7)	

[a]Chi-square test

Table 3. Stone characteristics according to the geographical region where patients live

Variables		Geographical Region							
		Anatolia (Central) (648, 91.8%)	Marmara (North-West) (12, 1.7%)	Aegean (West) (11, 1.6%)	Black Sea (North) (12, 1.7%)	Mediterranean (South) (7, 1.0%)	Eastern Anatolia (11, 1.6%)	Southeastern Anatolia (5, 0.7%)	
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	p value
Stone type	Calcium oxalate	450 (69.4)	10 (83.3)	8 (72.7)	5 (41.7)	2 (28.6)	6 (54.5)	5 (100.0)	<0.001[a]
	Calcium phosphate	25 (3.9)	0	0	1 (8.3)	1 (14.3)	2 (18.2)	0	<0.001[a]
	Uric acid	26 (4.0)	1 (8.3)	0	1 (8.3)	0	0	0	<0.001[a]
	Cystine	8 (1.2)	0	0	0	1 (14.3)	1 (9.1)	0	
	Magnesium ammonium phosphate	15 (2.3)	0	1 (9.1)	1 (8.3)	0	1 (9.1)	0	
	Calcium oxalate + calcium phosphate	36 (5.6)	0	1 (9.1)	0	1 (14.3)	1 (9.1)	0	<0.001[a]
	Calcium oxalate + uric acid	28 (4.3)	0	0	3 (25.0)	0	0	0	<0.001[a]
	Calcium oxalate + magnesium ammonium phosphate	60 (9.3)	1 (8.3)	1 (9.1)	1 (8.3)	2 (28.6)	0	0	<0.001[a]
Calcium component	None	49 (7.6)	1 (8.3)	1 (9.1)	2 (16.7)	1 (14.3)	2 (18.2)	0	
	Exist	599 (92.4)	11 (91.7)	10 (90.9)	10 (83.3)	6 (85.7)	9 (81.8)	5 (100.0)	
Infectious component	None	573 (88.4)	11 (91.7)	9 (81.8)	10 (83.3)	5 (71.4)	10 (90.9)	5 (100.0)	
	Exist	75 (11.6)	1 (8.3)	2 (18.2)	2 (16.7)	2 (28.6)	1 (9.1)	0	

[a]Chi-square test

urinary system stone disease. In light of these data, we can say that people maintain their dietary habits when they migrate to another geographical region of the country and both geographical origin and dietary habits have a cumulative effect on the incidence of urinary system stone disease.

There are lots of epidemiological studies that have been conducted in order to analyze the stone types and prevalence. True prevalence would be underestimated because the patients with spontaneous stone passage do not need medical therapy (2). Several community-based studies revealed interesting results in the literature. Epidemiological studies can provide purposeful knowledge for the treatment and prevention of stone disease. Ogawa et al. (7) presented their results for Japan and the annual incidence for the stone disease was detected to be at higher rates as 114.3 (per 100,000) (7). Metabolic evaluation is an important point for stone prevention as some metabolic conditions as hypercalciuria, hypocitraturia, and hypomagnesuria were found to be strongly related to stone formation (22). In our study, we did not evaluate patients in terms of prevention for stone disease by metabolic evaluation. We aimed to show the distribution of stone types according to regions where patients were born and lived. In line with our study results, we have found that the most common stone type was CO in each region of Turkey. Wu et al. (23) reported similar results with our study as they reported the results of 12,846 patients and the most common stone type was CO in China (23). Although the overall incidence rate was lower in the general population, a recent 3-year retrospective study from Norway also showed that CO stones were the most commonly seen stones also in this country (17). Similarly, Jindal et al. (24) reported the results of 90 patients and the most common stone type was

Table 4. Comparisons of calcium oxalate stones according to patients' geographical origins and locations

Variables	Geographical region where patients born n (%)	Geographical region where patients live n (%)	p value
Anatolia (Central) (n=486)	297 (61.1)	450 (92.6)	<0.001[a]
Marmara (North-West) (n=486)	33 (6.8)	10 (2.1)	<0.001[b]
Aegean (West) (n=486)	29 (6.0)	8 (1.6)	<0.001[b]
Black Sea (North) (n=486)	43 (8.8)	5 (1.0)	0.006[b]
Mediterranean (South) (n=486)	28 (5.8)	2 (0.4)	1.000[b]
Eastern Anatolia (n=486)	36 (7.4)	6 (1.2)	<0.001[b]
Southeastern Anatolia (n=486)	16 (3.3)	5 (1.0)	<0.001[b]
Abroad (n=486)	4 (0.8)	-	-

[a]Chi-square test
[b]Fisher's exact test

CO in eastern India (24). Karabacak et al. (3) reported that the most common stone type was CO in Turkey when they evaluated the stone compositions according to gender and region (3). In concordance with our results, Karabacak et al. (3) reported that the prevalence of CO stones was higher in the Central Anatolia region (3). The explanation of this situation may be that both of our institutes are in the same region. In contrast, Akinci et al. (18) reported a higher prevalence of the stone disease in the southern and southeastern regions of Turkey (18). We think the reason for these similarities and differences is the different patient profiles of the institutes. When we consider the gender distribution of urinary stone patients in our study, we find that 73.8% of the patients were male and 26.2% of the patients were female. This is actually the expected ratio because higher levels of testosterone in males can be thought of as an independent risk factor for urolithiasis. This can be explained by the suppression of renal osteopontin expression by testosterone and causing increased urinary oxalate excretion. On the other hand, estrogen seems to inhibit stone formation by increasing osteopontin levels and decreasing oxalate formation (25). The stone compositions were found to be relevant to the kidney functions (9). U stones were found to be related to lower glomerular function rates (GFR) and CP stones were found to be associated with higher GFR levels (9). Several prevention strategies as changing dietary habits, higher water consumption and protection from hot climate could be taken according to the distribution of stone types in regions. In our study cohort, there were not many patients with U and CP stones, multicenter and prospective studies could provide more clear results for these stone types.

Nonetheless, this study has some limitations. First, it has a retrospective design and the inherent retrospective and non-randomized nature may have led to selection bias. Because of the limitations of stone types number in each region, we could not compare the regions in terms of C and MAP stones. Larger patient populations, multicentric and prospective studies are necessary for getting more information about the distribution of stone compositions in each region of Turkey. Finally, we did not evaluate patients in terms of recurrent disease or prevention methods. Nevertheless, our study is in concordance with several epidemiologic studies.

Conclusion

CO is the most common stone type in Turkey, independently of where patients were born or live. Higher prevalence rates of stone disease and CO stones were seen in Central Anatolia. The calcium composition was also detected at higher rates. Both geographic origin and dietary habits affect the incidence of urinary system stone disease. If the stone type distribution of each region is better understood, various prevention strategies such as patient-specific nutrition can be applied. Prospective and multicentric studies with larger patient populations are necessary for getting more information about the distribution of stone compositions in each geographical region of Turkey.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Turkey, Gülhane Training and Research Hospital, Ethics Committee for Non-Interventional Research (protocol no: 2020/169).

Informed Consent: Informed consent was not obtained from participants because of the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.B., T.Ö., Design: S.B., T.Ö., Data Collection or Processing: N.K., E.S., Analysis or Interpretation: S.S., Ç.Y., E.S., E.K., T.E., T.Ö., N.K., Literature Search: S.B., T.Ö., Writing: S.S., N.K., Ç.Y.

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