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ORIGINAL PAPER

Clinical characteristics of adult cases with urolithiasis from Turkey: A regional epidemiological study

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Summary *Objective: To evaluate the metabolic and clinical characteristics of adult cases with stone disease from a regional part of Turkey.*

Methods: The study included 2348 adult patients with sonography and/or computed tomography-proven urinary stones. All cases were given a questionnaire about the epidemiological features of urolithiasis. Aside from the type and severity of stone-forming risk factors, both patient (age, gender, BMI, associated comorbidities, first onset of stone disease, positive family history, educational level) and stone-related (size, number, location, chemical composition, previous stone attacks) factors have been thoroughly assessed. The data were evaluated in multiple aspects to outline the epidemiological features.

Results: The overall mean age value of the cases was 43.3 years, and the M/F ratio was 1.34. The first onset of the disease was found to vary between 15-57 years, with a mean value of 32.4 years. While most of the stones were located in kidney and ureter, calcium-containing stones constituted the most common type (CaOx 69%, CaOxPO^4 7%). More than 42% of the cases suffered from multiple stone attacks; positive family history waspresent in 31.6%. Among the associated comorbidities, hypertension was the most common pathology (45.8%), and the BMI index value was > 30 in 31.3% of the cases. 57.7% of the patients had just one stone attack, and 42.2% had recurrent stone formation.

Conclusions: Our findings clearly show that important implications may be extracted from epidemiologic data acquired from local scale research to implement an effective preventative program and closely monitor the patients.

KEY WORDS: *Urinary stones; Epidemiology; Kidney stones.*

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INTRODUCTION

As an endemic problem in certain parts of the world, urolithiasis constitutes an evident risk to the healthcare system and a certain burden on the economy. The etiology of the disease is multifactorial, and an increase in incidence and prevalence ranging from 7% to 13% in North America, 5-8 % in Europe, and 1-5% in Asia has been reported (1). Environmental and dietary factors, lifestyle, and some individual personal factors, such as age, gender, *body mass index* (BMI), and familial anamnesis, seem to play a critical role in the course of the disease (2).

Considering the urolithiasis-related epidemiological factors as an important parameter, gender-based prevalence has been subjected to several studies where the male-to-female ratio ranged from 1.3 to 3 (3). On the other hand, as a precious predictive factor, positive family history is a significant risk factor for stone formation in individuals with family members suffering from urolithiasis (4). Geographic conditions are also important, and factors including climate, socioeconomic status, diet, and comorbidities may further affect the prevalence of stone formation (2, 5). Components of metabolic syndrome like diabetes mellitus, hypertension, or obesity have also been implicated in constituting an additional risk for urinary stone formation (6). Related to metabolic problems, in addition to less fluid intake, hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia are the most common urinary stone-forming risk factors identified, particularly in recurrent cases (7, 8). The dietary habits of the community, both in developing countries and in developed ones, are essential in stone formation by altering urine composition and increasing relevant risk status (9, 10). Lastly, despite some contradictory reports, education might play a role in urolithiasis. Some studies show that a lower education level may be a possible reason for stone formation (11, 12).

In this present study, we aimed to assess certain clinical and metabolic factors to update epidemiological risk factors in the Turkish population in a regional evaluation-based manner.

METHODS

Ethics committee approval was obtained for the study from the Local Ethics Committee with the number 2023/4203 on 17 February 2023. While conducting this study, the Declaration of Helsinki and international ethical standards were taken into consideration at every stage.

A total of 2348 adult patients referring to the urology departments of different hospitals in the same region with sonography and/or computed tomography-proven stones were included in the study program. Following close collaborative work with epidemiologists, our team designed a simple questionnaire and conducted a face-to-face survey. Staff nurses and resident doctors in urology wards

completed each form after interviewing study participants prior to medical or surgical management of stones.
Regarding the questions with respect to the established epidemiological features of urinary calculi, in addition to the type and severity of stone-forming risk factors, both patient-related factors (such as age, gender, BMI, associated comorbidities, the first onset of stone disease, positive family history, educational level) and stone related factors (such as size, number, location, chemical composition, previous stone attacks) have all been evaluated and recorded. Obtained data were assessed from multiple aspects to outline the epidemiological features in our patients.

Results

Evaluation of our data revealed the following findings. The mean age value of the 2348 adult cases was 43.3 years (15-69), and the gender distribution was 1346 males and 1002 females with an M/F ratio of 1.34.
The first onset of the disease was found to vary between 15-57 years, with a mean value of 32.4 years (Table 1).

Table 1.
Evaluation of the patient characteristics and stone-related factors by gender.

	Male	Female
Total number of cases (n)	1346	1002
Mean age of the cases (years)	42.6 ± 9.8	44.3 ± 11.3
First onset of the disease (years)	31.7 ± 10.2	33.5 ± 12.8
Stone size (mm)	1.3 ± 0.8	1.1 ± 0.6
Height (cm)	170.1 ± 9.7	165.7 ± 10.2
Body weight (kg)	75.0 ± 9.4	79.2 ± 10.2
Body mass index (BMI) (kg/m^2)	25.7 ± 8.8	26.8 ± 9.2

The majority of the stones were located in the kidney (62.3%) and ureter (35.2%), and calcium-containing stones constituted the most common type (CaOx 69%, CaOxPO4 7%) (Table 2).
On referral, 57.7% of the cases had the first stone attack; 42.2% had recurrent stone formation. Regarding the previous interventions for stone removal, pyelolithotomy was present in 12 patients (0,5%), cystolithotomy in 14 (0,6%), PCNL in 108 (4,6%), ureterorenoscopy in 213 (9%), and lastly SWL in 284 cases (12 %) (Table 2). A positive family history was present in 743 patients (31.6%) (Table 2).
Positive family history was strongly associated with the mean age of the cases at first presentation and the disease's number of stone attacks (recurrence).
Stones are formed at younger ages in these cases, with more recurrent stone formation than those with no family history.
Of the clinical presentation symptoms noted, while the majority of the cases referred with colic pain (n:1902, 81%), 50.3% (n:1181) of the patients had microscopic hematuria, and 7.2% (n:169) presented with macroscopic hematuria. High-grade hydronephrosis (Grade 3-4) was present at first presentation in 14.2% of the cases, and 53.3% had no dilatation (Table 3).
Among the associated comorbidities evaluated, while hypertension was present in 45.8% of the cases, diabetes was present in 2.8%, hypercholesterolemia in 27.6%, and obesity in 31.3% (in 735 cases, BMI index value was 30-35). While the mean BMI was 25.7 ± 8.8 in male patients, this value was 26.8±9.2 in female cases (Table 3).

Table 2.
Urolithiasis characteristics of the patients at first presentation.

	Total		Male		Female	
	n	%	n	%	n	%
Stone analysis data	1945	82.8	981	72.9	964	96.2
Calcium oxalate	1342	69	703	71.7	639	66.3
Calcium phosphate	136	7	74	7.5	62	6.4
Infection stones	233	12	86	8.8	147	15.2
Uric acid	156	8	83	8.5	73	7.6
Cystine	78	4	35	3.5	43	4.5
Number of stone episodes						
One episode	1355	57.7	731	54.3	624	62.3
2-4 episodes	647	27.6	388	28.8	259	25.8
5 and more	346	14.7	227	16.9	119	11.9
Stone localization at the first presentation						
Kidney	1463	62.3	786	58.4	677	67.5
Single	696	29.6	372	27.6	324	32.3
Multiple	767	32.7	414	30.8	353	35.2
Ureter	826	35.2	437	32.5	389	38.8
Bladder	59	2.5	59	4.4	0	0
Previous interventions						
Pyelolithotomy	12	0.5	7	0.5	5	0.5
Uretrorenoscopy	213	9	134	10	79	7.9
PCNL	108	4.6	53	3.9	55	5.5
Cystolithotomy	14	0.6	14	1	0	0
SWL	284	12	123	9.1	161	16.1
Family history						
Positive	743	31.6	331	24.5	412	41.1

Table 3.
Clinical characteristics of the patients at first presentation.

	Total		Male		Female	
	n	%	n	%	n	%
Total number of cases	2348	100	1346	57.9	1002	42.1
Associated morbidities						
Hypertension	1075	45.8	623	46.3	452	45.1
Diabetes Mellitus	66	2.8	29	2.2	37	3.7
Hypercholesterolemia	648	27.6	403	29.9	245	24.5
Obesity (BMI of > 30)	735	31.3	347	25.8	388	38.7
Presence of urinary tract infection (UTI)	802	34.2	114	8.5	688	68.6
Presence of obstruction (sonographic findings)						
None	1252	53.3	883	65.6	369	36.8
Grade I	356	15.2	124	9.2	232	23.2
Grade II	406	17.3	226	16.8	180	18
Grade III	187	8	52	3.9	135	13.5
Grade IV	147	6.2	61	4.5	86	8.5
Presence of hematuria						
Microscopic	1181	50.3	671	49.9	510	50.9
Macroscopic	169	7.2	87	6.5	82	8.2
Presence of pain *						
No	446	18.9	253	18.8	193	19,3
Mild (VAS 1-3)	680	29	408	30.3	272	27,1
Moderate (VAS 4-6)	483	20.6	267	19.8	216	21,6
Severe (VAS ≥ 7)	739	31.5	418	31.1	321	32

* *Evaluation according to visual Analogus sclala 0-10.*

When the education level of the cases was evaluated, 36.4% (n = 856) were primary school graduates, 14.3% (n = 335) were secondary school graduates, 34.5% (n = 810) were high school graduates, and 14.8% (n = 347) were college graduates.

Discussion

Urinary system stone disease is an endemic pathology in many parts of the world, which poses an evident risk to the healthcare system with a significant burden on the economy. The etiology of the disease is multifactorial, consisting of several risk factors evaluated in detail so far. Regarding the evident differences among several regions and countries of the world, variations in specific etiologic parameters like age, gender, dietary preferences, fluid consumption, the climate they live in, their occupation, level of education, socioeconomic status, and genetic and metabolic factors have been considered to be responsible (2, 9).

On the other hand, the formation of new stones based on the present metabolic and other risk factors is commonly observed, particularly in recurrent stone-forming cases. Studies on this aspect have revealed that after the initial stone passage, the rate of stone recurrence in patients with previous urolithiasis was reported to be 40% at five years and 75% at 20 years, respectively (13).

Considering all these facts, it is clear that data from regional epidemiological studies will help us assess the prevalence and underlying etiological factors, which will support developing policies for effective metaphylaxis and treatment of the disease appropriately. In other words, in light of reported evident geographic differences in the prevalence of urolithiasis, well-conducted local/regional studies may provide a detailed understanding of the disease nationwide.

When we look at the studies examining the effect of gender on kidney stone formation, several gender-based studies have shown that although infection stones were more commonly reported in women, the general incidence of urinary calculi tends to be more frequent in men (14, 15). Statistics show that males tend to indulge in higher amounts of alcohol and coffee as well as meat consumption compared to females. Moreover, it has been observed that testosterone can increase the likelihood of stone formation, whereas estrogen plays a role in inhibiting stone formation by regulating the synthesis of 1.25-dihydroxy-vitamin D (5). Stone formation is often linked to anatomical factors, with infravesical obstruction being a common risk factor. This obstruction is usually caused by benign prostatic hyperplasia or urethral stricture (16). In many countries, it has been observed that the ratio in favor of females is increasing while the ratio in favor of males is decreasing. Changes observed in the living standards resulting in the differences in diet, lifestyle, and occupations of the female population could be responsible for the decreased ratio (17).

As another important factor affecting the prevalence of stone disease, geographic conditions may also affect the occurrence of urolithiasis (2, 5). Differences in factors such as climate, socioeconomic status, race, genetics, dietary habits, and the presence of other medical conditions may contribute to significant variations in the prevalence of kidney stone formation in a particular geographic or regional area. This scenario has the potential to mirror the urolithiasis problem at a national and even global level. Apart from commonly diagnosed urinary tract infections, patients with urolithiasis frequently present with the component pathologies of metabolic syndrome like diabetes mellitus, hypertension, or obesity, which could potentially be another factor that increases the risk for urinary stone formation (2, 18). The involved patients' associated comorbidities and metabolic factors play a specific role in the presence and severity of urinary stone-forming risk factors. Related to this important subject, in addition to reduced fluid intake, decreased urine output, hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia are the most commonly reported risk factors for stone formation in adults and children (7, 8). Based on this fact, a comprehensive metabolic evaluation seems mandatory in risk group cases prone to form recurrent stones requiring interventional procedures for a stone-free status.

Considering the formation of metabolic risk factors in these cases, apart from the lifestyle playing a significant role in the formation of stones, the dietary habits of the community have a more critical role. While cereals and vegetables contain high levels of oxalate and its precursors are widely consumed in developing countries, in the western part of the world, a Westernized diet containing excessive protein, lipid, calcium, and sodium is also important in stone formation, changing the urine composition and increasing the associated risk status (9, 19). Among the dietary risk factors evaluated so far, in addition to excessive calcium and oxalate-rich food consumption, a high sodium intake may increase calcium absorption into the blood or decrease absorption from urine into renal tubular cells, resulting in hypercalciuria. On the other hand, higher consumption of animal protein can also lead to urine acidification (10).

Last but not least, education might play a role in urolithiasis. In support of this, Data from studies in Iran and Turkey suggest that lower education levels may contribute to kidney stone formation (11, 20). However, some studies also show a negative relationship between the incidence of stone disease and the education level or occupation (12, 21).

Taking all the above facts, we believe that significant implications could be derived from the epidemiologic data obtained from local scale studies. With this aim to update urolithiasis epidemiological data by examining certain epidemiological risk factors in the Turkish population, we conducted this study.

Our findings revealed valuable data showing useful clinical implications that could be derived from our trial. The majority of the stones were located in the upper tract and were calcium-containing stones. The number of stone attack episodes was an important issue, and most cases did present with the first attack (57.7%), where a limited percentage had high recurrence rates with more than five attacks (14.7%). Men were affected by the disease at relatively younger ages than women. Hypertension was the most common co-morbidity. Additionally, as another important component of metabolic syndrome, BMI values

were well evaluated, and 31.3% of the cases had severe obesity with BMI values of > 30. On the first presentation, most cases presented with persistent microscopic hematuria (50.3%), and recurrent infection, colic pain were the other presenting symptoms. 26.8% of the patients have a previous stone-related intervention. A considerable percentage of the cases have severe (Grade III-IV) obstruction at first evaluation. Last but not least, positive family history was a critical and predictive parameter noted where 1/3 of all cases did have this history, and men were more likely to have this anamnesis. This parameter affected the course of the disease, and mean age at first onset was less in these cases. Also, stone attacks were higher in these cases than in patients without family history.

Our study is not free of limitations. The number of patients evaluated may be limited, and the need for a control group may constitute another critical drawback. However, taking limited information regarding the epidemiological data on stone disease, particularly in a regional evaluation-based manner, we believe our findings will be contributive to a greater extent. Additionally, taking the endemic nature of the stone disease in our country, these values coming from a regional part of the country will give further insights into the epidemiologic features of the disease.

Conclusions

In light of the data published so far and our findings obtained in adult cases with urinary stones, we may say that local and regional epidemiological studies focusing on personal, environmental, and metabolic risk factors could be critical. These data can be used to derive practical, predictive clinical implications from limiting the risk of stone recurrence, lowering the economic burden of the disease, and outlining the most rational treatment alternative.

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