

Updated epidemiologic study of urolithiasis in Turkey. I: Changing characteristics of urolithiasis

Ahmet Yaser Muslumanoglu · Murat Binbay ·
Emrah Yuruk · Tolga Akman · Abdulkadir Tepeler ·
Tarik Esen · Ahmet Hamdi Tefekli

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Abstract The worldwide prevalence and epidemiologic characteristics of urolithiasis appear to have changed in the last decade. This study aims to update the current understanding of the disease in Turkey. A representative sample, totalling 2,468 participants between 18 and 70 years of age from 33 Turkish provinces, was enrolled in this cross-sectional study conducted with a professional market investigation company. Participants were evaluated with face-to-face interviews by medical students using a standard questionnaire. Of the 2,468 participants, 274 (11.1%) reported a history of urinary stone disease diagnosed by a physician and an additional 52 (2.1%) had at least one lifetime episode of colic pain. The annual incidence of urolithiasis in 2008 was 1.7%. The male:female ratio was 1:1 in participants with urolithiasis. A family history of urolithiasis was found in 28.5% of the first-degree relatives of the stone formers, compared to 4.4% of the first-degree relatives of the stone-free participants ($p = 0.01$). Compared to other ethnic groups, the population of Turkish origin had a statistically significant decreased risk of urolithiasis ($p = 0.006$). Though not statistically significant ($p > 0.05$), urolithiasis showed a trend toward a geographical distribution within the country, in which south-eastern Anatolia and the Aegean regions had higher frequencies compared to the Black Sea, and central Anatolian and eastern Anatolian regions. Urinary stone disease

is a severe problem in Turkey, with high prevalence and incidence rates, which differ significantly between ethnic groups. Moreover, current findings demonstrate a demographic shift, with an increased prevalence of stone disease in female subjects.

Keywords Epidemiology · Urolithiasis · Prevalence · Gender distribution

Introduction

Urolithiasis is the third most common urological disease affecting the urinary tract, after urinary infection and prostatic pathology [1]. The prevalence of urolithiasis varies between 2 and 20% throughout the world and appears to depend on the geographic and socioeconomic characteristics of different populations [2, 3]. Urolithiasis is accepted to be endemic in Turkey with a prevalence of 14.8%, which is supported by the nationwide epidemiological study performed in 1991 [4]. However, the worldwide prevalence of this disease appears to have increased in the last quarter of the twentieth century in both men and women [5, 6]. Furthermore, gender distribution has significantly changed, and there is an increased number of obese female patients with urolithiasis today. This study aims to update the current understanding of urolithiasis in Turkey and thus to provide some data that could be used in the treatment and prevention programs.

Materials and methods

A sample of 2,468 randomly selected persons aged 18–70 years in 33 Turkish provinces was enrolled in this

A. Y. Muslumanoglu (✉) · M. Binbay · E. Yuruk ·
T. Akman · A. Tepeler · A. H. Tefekli
Department of Urology,
Haseki Training and Research Hospital, Istanbul, Turkey
e-mail: ymuslumanoglu56@hotmail.com

T. Esen
Department of Urology,
Istanbul University Istanbul Medical Faculty, Istanbul, Turkey

cross-sectional study. A&G, a professional market investigation company, conducted this research. The enrolled population was representative of Turkey in its demographic and socioeconomic characteristics, according to the State Institute of Statistics. The formula $n = \frac{N^2pq}{d^2(N-1)+t^2pq}$ was used for the determination of sample quality, where the prevalence of urolithiasis in Turkey was estimated to be $10 \pm 5\%$ [4]. Given the possibility of non-responders to our survey, the target figure for the number of households to be surveyed was set at 2,468, which is 103% of the actual target figure for the number of subjects and sampling number. Our study was able to estimate the actual prevalence of urolithiasis within $\pm 1.5\%$ standard deviation.

All interviewers were selected from amongst senior medical students. A single urologist (MB) taught the interviewers general information regarding urolithiasis and also explained all items included in the survey. All persons interviewed were informed that this was an epidemiological study of urinary stone disease. Using a specially designed questionnaire, participants were assessed via personal interviews at their homes. The study was designed in two parts; the first part aimed to establish the epidemiologic characteristics of urolithiasis in Turkey and the second part aimed to clarify the relation between metabolic syndrome components, dietary habits and urolithiasis. In the first part of the survey questionnaire, participants were asked about their age, ethnicity, educational level, personal and family histories, past or present presence of stone disease, and whether they were currently using treatment modalities or preventative measures.

Participants who had spontaneously passed stones, undergone operations for urolithiasis (including shock wave lithotripsy) or had radiologically demonstrated stone disease at the time of clinical symptoms were defined as having “definitive urolithiasis”. Participants who had a past history of renal colic without a physician diagnosis were defined as having “possible urolithiasis”. Only participants with definitive urolithiasis were taken into consideration for evaluating the relations between urolithiasis and other factors.

Analysis was made using Chi-square tests. Odds ratios (OR) were calculated and statistical determinations were within the 95% confidence interval (CI). All p values were two tailed, and $p < 0.05$ was considered to be statistically significant. The data were analysed with an SPSS (SPSS version 13.0, Chicago, IL) statistical software package.

Results

Of the 2,468 participants, 274 (11.1%) reported a history of definitive urolithiasis and 52 (2.1%) had possible

urolithiasis. The prevalence rates of urolithiasis in Turkey increased gradually with age in both men and women, varying from 8% in the younger group (<25 years) to 26.6% in the 45- to 55-year age group (Fig. 1). The prevalence of urolithiasis amongst participants aged ≥ 40 years was significantly higher than participants aged <40 years (19.4 vs. 7.6%, OR: 2.53, CI: 1.9–3.2, $p = 0.000$). The male:female ratio was 1:1 (Table 1). The annual incidence of urolithiasis in 2008 was 1.7%. Of these incidences, 54.4% were first occurrences and 45.6% were recurrences. The incidence was higher in females than in males (1.9 vs. 1.4%). Figure 1 shows the prevalence of urolithiasis by age group.

In 2008, the largest number of stone recurrences was found in the 45- to 54-year age group. The average cumulative recurrence rate was 16.7% after 1 year and 35.7% after 5 years. In 1.9% of participants, the stones were apparently asymptomatic and coincidentally detected. Asymptomatic stones were mostly detected in the 35- to 44-year age group. The relationship between symptoms and urolithiasis diagnosis is detailed in Fig. 2.

The prevalence of urinary stone disease differed with race and ethnicity. In comparison with other ethnic groups, people of Turkish origin had a statistically significant decreased risk of urolithiasis (9.8 vs. 13.1%, $p = 0.006$, OR: 1.43). The prevalence of urolithiasis in various ethnic groups in Turkey is shown in detail in Table 2.

Though not statistically significant ($p > 0.05$), urolithiasis showed a trend towards a geographical distribution, in which southeastern Anatolia and Aegean regions had higher frequencies compared to Black Sea, and central Anatolian and eastern Anatolian regions (Fig. 3).

The occurrence of stone disease was associated with a family history of urinary stone disease. A family history of urolithiasis was found in 28.5% of the first-degree relatives of stone formers, compared to 4.4% in stone-free participants ($p = 0.01$). Having a child with urolithiasis was the

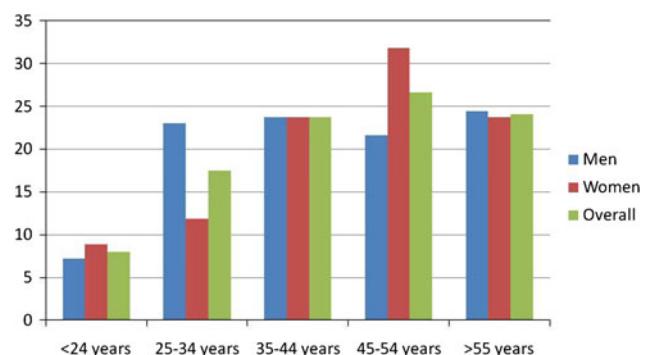


Fig. 1 Distribution of urolithiasis according to age and gender (x axis: years of age and y axis: stone prevalence)

Table 1 Prevalence and incidence of urolithiasis

Group	Number (%)	Prevalence (%)	Prevalence female/male	Incidence (%)	<i>p</i>
Female	1232 (49.9)	139 (11.2)	–	24 (1.9)	>0.05
Male	1236 (50.1)	135 (10.9)	–	18 (1.4)	

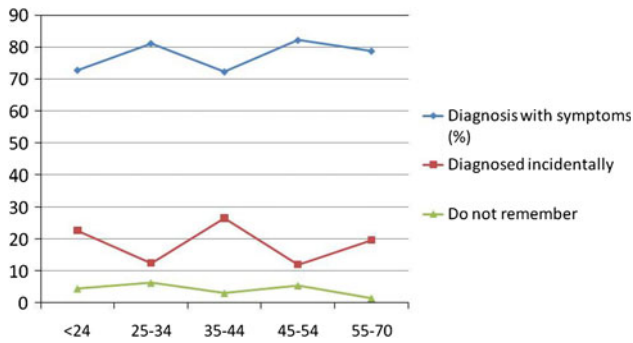


Fig. 2 The age-matched relationship between diagnosis of urolithiasis and symptoms (x axis: years of age and y axis: percent of participants with urolithiasis)

most predictive factor of urolithiasis, increasing the risk of a urolithiasis diagnosis by 3.93 times (Table 3).

The prevalence of urolithiasis amongst illiterates and/or primary school graduates was found to be 15.6%, but was only 8.2% in high school and/or university graduates (*p* = 0.000) (Table 4).

Socioeconomical status was not significantly related to urolithiasis (*p* > 0.05). The prevalence of stone disease was 12.0% for people living in cities and 13.4% for those living in rural areas (*p* > 0.05). For those working in offices, prevalence was 9.1 versus 11.2% for people predominantly working manually (*p* > 0.05). Most stones were passed spontaneously (54.3%); shock wave lithotripsy (SWL) was the most common type of active treatment intervention (50.4%).

Table 2 Prevalence of urolithiasis amongst different ethnic groups in Turkey

	Population (%)	Participants with urolithiasis (%)	<i>p</i>	Odds ratio	CI (95%)
Turkish	1561 (63.2)	154 (56.2)	0.006	1.43	1.10–1.84
Other ethnic groups					
Kurdish	341 (13.8)	48 (17.5)			
Zaza Population	64 (2.6)	11 (4.0)			
Arabic	59 (2.4)	9 (3.3)			
Georgian	51 (2.0)	3 (1.1)			
Circassian	37 (1.5)	6 (2.1)			
Emigrant from the Balkans	119 (4.8)	17 (6.2)			
Laz	127 (5.1)	11 (4.0)			
Others	52 (2.1)	7 (2.5)			
Unknown	57 (2.3)	8 (2.9)			

Discussion

Most previous epidemiological studies on urolithiasis were based on hospital statistics, general practice surveys or selected group surveys. These are easier to perform with less effort and expenditure compared to community-based studies, but, as 30–80% of stones pass spontaneously and these patients do not require medical attention, these studies underestimate the true prevalence of urolithiasis [7]. Therefore, a community-based study is mandatory to precisely characterise the epidemiologic features of urinary stone disease in the general population. Community-based epidemiologic studies frequently use a questionnaire to detect patients with urolithiasis. However, such studies raise the possibility of over- or underestimation of the actual disease prevalence due to their limited diagnostic accuracy. To improve the accuracy of our study, we conducted the investigation with the assistance of a professional marketing research company, the success of which was shown in other similar investigations. The questionnaires used in this study were completed by medical students during face-to-face interviews instead of by mail or phone response. Moreover, urolithiasis was considered in those who had spontaneous passage of stones, stones demonstrated with imaging methods, history of operative removal of stones including shock wave lithotripsy and those with clinical findings judged by a physician at the time of symptoms. We aimed to detect the absolute prevalence of urolithiasis, but did not take into consideration participants with a history of renal colic in the absence of a definitive physician’s diagnosis, a group which totalled

Fig. 3 Regional distribution of participants with urolithiasis in Turkey



Table 3 The presence of stone disease amongst relatives in participants with urolithiasis compared to the whole sample (p^* : Chi-square test)

Relatives with urolithiasis	All participants n (%)	Participants with urolithiasis n (%)	p^*	Odds ratio	CI (95%)
Child	63/2468 (2.6)	20/274 (7.3)	0.000	3.93	2.28–6.80
Mother	173/2468 (7.0)	38/274 (13.8)	0.000	2.45	1.67–3.60
Father	192/2468 (7.8)	44/274 (16.0)	0.000	2.64	1.83–3.80
Sister, brother	176/2468 (7.1)	49/274 (17.9)	0.000	3.54	2.48–5.06
Grandmother/grandfather	62/2468 (2.5)	10/274 (3.6)	>0.05	–	–
Uncle, aunt	115/2468 (4.7)	16/274 (5.8)	>0.05	–	–

Table 4 The relation of educational status with urolithiasis development

	Population n (%)	Participants with urolithiasis (%)	p	Odds ratio	CI (95%)
Illiterates/primary school (8 years)	1252 (57.1)	196 (71.5)	0.000	2.028	1.54–2.67
High school–university	942 (42.9)	78 (28.5)			

2.1% of the participants. Moreover, participants with asymptomatic stones who were not diagnosed before the study could not be detected; thus, we conclude that the true prevalence of urolithiasis in Turkey is higher than 11.1%. As in many previous surveys, we did not include persons younger than 18 years of age because the risk of stone formation is lowest in the paediatric age group.

Finlayson reviewed several worldwide geographic surveys and found that areas of high stone prevalence included the USA, British Isles, Scandinavian and Mediterranean countries, northern India and Pakistan, northern Australia, Central Europe, portions of the Malay and China [8]. Our survey has revealed an overall prevalence of urinary stone disease of 11.1% in Turkey. This is a much higher figure than the prevalence of 3.5% in Korea [9], 4.7% in Germany [6], 5.7% in Iran [10], 7% in Japan [11] and 8% in USA [5]. Generally viewed, it is clear that Turkey is a country with a relatively high prevalence of urolithiasis.

However, the prevalence of urolithiasis appears to have increased worldwide in the last quarter of the twentieth century [5, 13]. This apparent increase may reflect an actual

increase in stone disease, or it may stem from increased detection of asymptomatic stones discovered with the greater use and higher sensitivity of imaging studies. Ageing populations in these countries may also contribute to the increased stone disease prevalence. Compared to previous epidemiologic studies performed in Turkey, the prevalence of urolithiasis seems to have decreased from 14.8 to 11.1%, but we have to highlight that in the previous study participants with urolithiasis were detected with questionable criteria by non-medical interviewers. As such, the previous study probably overestimated the true prevalence and incidence of the disease in 1991.

According to previous studies, the prevalence of urolithiasis in the male population was approximately 1.5–3 times that in the female population [1, 2]. However, in recent years, various studies have commented on the changing gender prevalence of stone disease [5, 12]. In our study, the number of female participants with urolithiasis was slightly higher than the male participants with urolithiasis. Similar to our findings, Safarinejad et al. [10] from Iran reported a comparable male to female ratio of

1.15:1 in 2007. Compared to the previous epidemiologic study of urolithiasis in Turkey, we recognise that the ratio of males to females diagnosed with urolithiasis changed from 1.5:1 in 1991 to 1:1 in 2009. Based on self-reports of stone disease in the USA, Stamatelou et al. [5] showed a larger increase in stone disease in women than in men between 1976 and 1994. More recently, Scales et al. [12] documented a shift in the prevalence of treated stone disease in female inpatients from a male to female ratio of 1.7:1 to 1.3:1 during a 5-year period. The responsible factor underpinning the shift in the gender distribution of urolithiasis is thought to be a more rapid increase in body mass index in women than in men. Increases in metabolic risk factors have been linked to increasing body mass index, and obesity has also been linked to recurrent stone disease [14]. In the USA, obesity has increased more rapidly in women than in men from 1960 to 2002, coincident with the increase in stone disease in women [15].

Previous studies have shown that the risk of stone formation was approximately 2.5 times greater in individuals with a family history of stone disease [16]. Defects in urine acidification can be inherited and polygenic factors, as well as shared household dietary and environmental risks, can play a role [17, 18]. In the present study, having a mother or father with urolithiasis increased the risk of urolithiasis development approximately 2.5 times, showing similarity with a previously published series. However, we found that having a child with urolithiasis increased this risk 3.9 times.

Recurrence is nearly inevitable during the course of stone disease and many studies have shown that the likelihood of forming another stone after an initial episode was 30–40% at 5 years [19]. These figures from observational studies are similar to recurrence rates documented in the control arms of recently published randomised trials [20, 21]. In a community-based survey, Ljunghall [22] reported a recurrence rate of 31.5, 49 and 72% after 5, 10 and 20 years, respectively. Similarly, the recurrence rate was 16.7% after 1 year, and 35.7% after 5 years in our study. The treatment arms of many of the randomised trials have shown dramatic reductions of 50% or more in recurrence rates [21, 23]. In our survey, most of the participants with urolithiasis were aware of the importance of prophylactic precautions, with 50.4% of them trying to prevent recurrence by increasing water intake and 31.7% using phytotherapy as prophylactic precautions.

Many epidemiologic studies have recorded a geographic variability in the prevalence of urolithiasis and have supported the idea that individuals living in hot climates have an increased lifetime prevalence of urolithiasis secondary to dehydration [24]. Soucie et al. [25] showed that correction for ambient temperature, sunlight and consumption of several beverages eliminated the geographical variation

in lifetime prevalence of urolithiasis. In our survey, although the geographic variability of urolithiasis in Turkey was statistically similar, the Aegean region and the southeastern region of Turkey represented the highest prevalence figures. During the past 20 years, the prevalence of urolithiasis in Marmara and the Aegean region has significantly increased; however, prevalence changes in these regions might be the result of the movement of population mass from the eastern or southeastern regions to the western part of country. Ethnic groups other than of Turkish origin (except Georgian and Laz), such as Kurdish, are more prone to develop urolithiasis. Notably, these people also constitute the largest ethnic group migrating from the southeastern parts of the country to the Marmara region.

Conclusions

Urolithiasis is a severe problem in Turkey, with high prevalence and incidence rates. The disease appears to affect women more often than men during the recent decades, and now there is no longer a male predominance in Turkey. Furthermore, variable prevalence rates amongst ethnic groups underline the importance of genetic, as well as environmental, factors in the pathogenesis of urolithiasis.

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Appendix

1. There is a disorder called urolithiasis. This encompasses kidney stones, bladder stones and stones located in the renal duct. Gallstones are excluded. Have you ever had experience with urolithiasis diagnosed by a physician or have you ever had experience with interventions performed for urolithiasis? (Question to assess definitive urolithiasis).
2. Have you ever had experience with sudden onset of intermittent pain, not improved by changes in position, radiating from the back, down the flank and into the groin, with associated haematuria? (Question to assess possible urolithiasis).

Further questions followed, but only when urolithiasis had been diagnosed by a physician:

3. Did you have urinary stones for the first time in 2008, or had you had them before?
4. How old were you when your doctor first diagnosed urinary stones?

5. How often have you had this disorder prior to the year 2009?
6. Was urolithiasis diagnosed by a doctor when you had symptoms or incidentally at another time?
7. Have you ever had experience with spontaneous stone passage?
8. How was your urolithiasis treated?
 - Using shock waves lithotripsy
 - Using endoscopic procedures
 - Surgically
9. Do you have persons with urolithiasis in your family?
10. What are you yourself doing to prevent recurrence?
 - I drink a lot
 - I have reorganised my diet
 - I drink the juice of some plants

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