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ORIGINAL PAPER

Adult urolithiasis in a population-based study in Iran: prevalence, incidence, and associated risk factors

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Abstract The aim of this study was to determine the prevalence, incidence, and risk factors of adult urolithiasis in Iran. A total of 8,413 persons aged over 14 years enrolled in this cross-sectional study. They were questioned on the occurrence of urinary stones during their lifetime (prevalence) and on acute urolithiasis in 2005 (incidence) by 62 general practitioners. The subjects were randomly identified from 30 counties of Iran. Data on risk factors for urolithiasis including age, race, education, body mass index, hypertension, and current use of medication were also obtained by self-administered questionnaire. Of the 7,649 participants who provided information, 5.7% (436) [95% confidence interval (CI) 4.2–5.4], reported urinary stones. The prevalence increased from 0.9% in adults aged 15–29 years to 8.2% in those aged 60–69 years (test for trend, $P = 0.001$). Urolithiasis was slightly more frequent and persisted in males (6.1%) than females (5.3%) giving a male-to-female ratio of 1.15:1 [odds ratio (OR) 1.03; 95% CI 0.64–1.36; $P = 0.814$]. The annual incidence of urolithiasis in 2005 was 145.1. The average cumulative recurrence rate was 16% after 1 year, 32% after 5 years, and 53% after 10 years. Urinary stones were more in number among men and women who lived in south central and southwest counties, with odds increasing from west to east and from north to south. A positive association was found between urolithiasis and obesity (OR 1.74; 95% CI 1.21–2.31; $P = 0.04$), diuretic use (OR 1.62; 95% CI 1.18–2.70; $P = 0.03$), hypertension (OR 1.88; 95% CI 1.26–2.18; $P = 0.04$), unemployment (OR 2.10; 95% CI 1.43–2.14; $P = 0.04$), consumption of tea (OR 1.64; 95% CI 1.32–2.62; $P = 0.03$), consumption of cola (OR 1.49; 95% CI 1.23–2.19; $P = 0.02$), and meat consumption (OR 1.38; 95% CI 1.29–2.21; $P = 0.02$). This study provides a quantitative estimate of the prevalence, incidence, and main risk factors for adult urolithiasis in the Iranian population. Further studies are warranted in order to determine the incidence and prevalence of urolithiasis in different ethnic groups.

Keywords Epidemiological study · Urolithiasis · Prevalence · Incidence · Risk factors

Introduction

The prevalence of urolithiasis varies significantly from country to country all over the world. Epidemiological data on the occurrence of urolithiasis ranges between 2 and 20% [1–3]. The annual incidence of stone formation in the industrialized regions is generally considered to be 1,500–2,000 cases per million [4]. Few studies have been done in various countries worldwide on the epidemiology of urolithiasis [5–9]. Urolithiasis prevalence may vary according to cultural, racial, and health variables among countries. Accurate data on the epidemiology of an entity can only be determined if geographical region, socioeconomic status, race, age, sex, climate, nutrition, and other environmental and cultural factors are also considered. One of the important factors accounting for the large differences observed in the prevalence of urinary stones between countries is different epidemiological methods. Most of these studies were not population-based and did not use probabilistic samples representative of the general population. In addition, studies addressing associated family history and risk factors are even scarcer.

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We studied the prevalence and incidence of urolithiasis in the Iranian population over the age of 14 years, addressing risk factors associated with urolithiasis. To our knowledge, this is the first epidemiologic report on urolithiasis from Iran.

Materials and methods

A representative sample of 8,413 persons aged over 14 years from all over Iran enrolled in the cross-sectional study. They were questioned on the occurrence of urinary stones during their lifetime (prevalence) and on acute urolithiasis in 2005 (incidence). A probabilistic two-stage cluster random sampling design was used, with stratification of the primary sampling units. It accounts for about 97% of the population in this age range—roughly 75 million Iranians. The primary sampling units were census sections, the secondary sampling units were dwellings, and the final sampling units were subjects. Subjects were chosen from polling station lists of the electorate in order not to influence the representativeness of the selection. Every tenth voter was included in the selection until the desired sample size was completed. To guarantee a representative estimate of prevalence of urinary stone, a weighting method was used to compute the national estimate of urolithiasis because the survey sample was selected based on stratification and systematic sampling of clusters within strata (counties). That is, a representative sample was obtained within each county. Supplementary information, for instance the reported population size in 1996, was used to calculate stratum weights, corresponding to the amount of the stratum population to the entire national population at the end of 1996.

The subjects were divided into six age groups, including ages 15–29, 30–39, 40–49, 50–59, 60–69, and $\geq$70 years. For population density, three levels were considered, including fewer than 500,000, 500,001–1,000,000, and more than 1,000,000 inhabitants. The secondary sampling units or dwellings were selected using the random route procedure and a computer-generated random number list. Extensive discussions on the sampling design and evaluations of sample and data quality are found in the book by Laumann et al. [10]. They were identified by 62 general practitioners from the national population in 30 counties, and invited to a confidential interview. The number of subjects who could be interviewed by a single physician was limited to five per day. They were educated by the one urologist (M.R.S.) on the general information regarding urolithiasis and on the items included in the survey. Sample sizes were determined for the 95% confidence interval (CI) with a design effect of 1.1. Using this assumption, a sample size of 7,648 would be required. With a projected subject dropout rate of 10% the total number of subjects required for study was determined to be 8,413. Interviewers made second visits in cases in which those being interviewed were not available. Study participants provided their age at recruitment, their education level, personal and family anamnesis, eating habits, current health conditions and their race, or ethnicity. Self-reported weight and height were used to calculate body mass index (BMI). In addition, data about the use of any medications with especial attention to antihypertensive, and diuretics use, were also collected. Consumption of beverages, including tea, coffee, milk, diet drinks, and soft drinks, was assessed using a food frequency questionnaire. The main survey questionnaire of the study included items on the past or present presence of stone, treatment modalities, preventive measures from the formation of new stones and whether stones had developed for the first time in that patient's life. The following questions were asked:

1. Has any doctor found you to be suffering from kidney stones, bladder stones, and stones lodged in the renal duct (any stone in the upper and lower urinary tract collecting system) in the year 2005 or before?
2. Have you noticed spontaneous passage of urinary stones?
3. How often had you had urinary stones prior to the year 2005?
4. Did you have radiologically demonstrated urinary stones?
5. Did you have urinary stones for the first time in 2005, or had you had them before?
6. Did you have a past history of renal colic?
7. How old were you when your physician first diagnosed urinary stones?
8. How were your urinary stones treated?
   - Operative removal
   - Using shock waves (lithotripsy)
   - Using an endoscopic procedure, i.e., cystoscopic inspection of the bladder or ureter, or percutaneously via the skin
   - Spontaneous passage of the stones
   - No treatment
9. What are you yourself doing to prevent formation of new stones?
   - I drink a lot of fluid
   - I take regular medication
   - I have reorganized my dietary and drinking habits
   - None

Recurrence was defined as new symptoms due to urinary stone formation or detection of new urinary stones after a stone-free period among subjects who had been reported to have urinary stones.

We also assessed the influence of two indices of environmental exposure. The first was the mean annual temperatures of the major weather-reporting cities in each county to allocate an annual average ambient temperature for that county. The second was the annual sunlight level based on measured ultraviolet radiation levels for each county.

Concerning medical history, whenever useful, information given by the patient was checked by his/her general practitioner with medical records. Interviewers matched respondents on various social attributes, for an interview averaging 45 min. The average number of interviews for each general practitioner was 33 (range 7–79). After the study had been explained to the participants, all subjects gave their written informed consent before entering the study, which was conducted in accordance with the Declaration of Helsinki. The blanket approval was obtained from the "Urology Nephrology Research Center" Ethical Committee. The study protocol did not include any clinical or diagnostic procedures. The main resulting statements on prevalence and incidence were confirmed in the individual cycles, so that the final result led to highly valid data.

Analysis

Analyses performed in this study were made by use of logistic and multinomial logistic regression. For assessing the prevalence of urolithiasis across demographic characteristics, we performed logistic regressions for each symptom. This approach produced adjusted odds ratios (ORs), which indicate the odds that members of a given social group (e.g., graduated) reported the urolithiasis relative to a reference group (e.g., none educated). To examine the relations between temperature and sunlight indices and stones prevalence, five categories of exposure were defined using quintile cut points. For each exposure level, the odds of ever having had a urinary stone divided by the odds in a reference exposure category (lifetime prevalence OR) were determined [11]. Levels demonstrating the least exposure to personal and environmental exposures were used as the reference categories in these analyses. The annual incidence was calculated as the estimated number of first episode stone formers per 100,000 of the general population in the survey year.

After the sample was weighted by the specified design the percent or prevalence and population estimates of the degree of urinary stones in the population and the corresponding standard errors were obtained to construct the 95% CI. Statistical analysis was performed using the computer statistical package SPSS/10.0 (SPSS, Chicago, IL, USA) and SAS/6.4 (SAS Institute Cary, NC, USA).

Results

Study population

In cases where the information was incomplete, the results of the survey were excluded from the final analysis.

The age and sex distribution of the study subjects is shown in Table 1. Of the 8,413 participants that were interviewed, 764 (9.1%) were excluded from the analysis due to missing data (588) and if the response was not completed personally (176). A total of 7,649 subjects (3,748 men and 3,901 women) of the 8,413 contacted completed the interview, with an overall response rate of 90.9%. Baseline average age of the 7,649 persons in the analysis sample was 40 ± 4.7 years (range 15–79) (95% CI 3.22–7.42). Those participants excluded from study did not significantly differ from the study group in regard to sociodemographic characteristics. There were 3,748 (49%) males and 3,901 (51%) females.

Prevalence of urolithiasis and impact of age and sex

Of the 7,649 participants who provided information, 5.7% (436) (95% CI 4.2–5.4), reported urinary stones. The prevalence of urolithiasis increased with age (linear Chi-square 198.176, one degree of freedom, $P = 0.001$). Table 1 lists the distribution of the incidence and prevalence of urolithiasis by age groups. The prevalence increased from 0.9% in adults aged 15–29 years to 8.2% in those 60–69 years (test for trend, $P = 0.001$). The oldest cohort of participants (age $\geq$70 years) is more than 5.7 times as likely to experience urolithiasis (95% CI, 2.1–4.2) in comparison to adults aged 15–29 years.

After adjustment for age, urolithiasis was slightly more frequent and persisted in males (6.1%) than females (5.3%), giving a male-to-female ratio of 1.15:1(OR 1.03; 95% CI

Table 1 Prevalence and incidence of urolithiasis

Group	Number	Prevalence *n* (%)	Incidence[a]	Recurrence
Male	3,748 (49)	229 (6.1)	147.2	82 (36)
Female	3,901 (51)	207 (5.3)	129.6	58 (28)
Age group (years)				
15–29	1,332 (17.4)	12 (0.9)	79.5	3 (24)
30–39	1,282 (16.8)	44 (3.4)	161	15 (36)
40–49	1,330 (17.4)	74 (5.6)	164.5	23 (32)
50–59	1,300 (17)	107 (8.2)	154.5	32 (30)
60–69	1,212 (15.8)	100 (8.2)	146	33 (33)
≥70	1,193 (15.6)	99 (8.3)	125	34 (35)
Total	7,649 (100)	436 (5.7)	138.4	140 (32)

[a] Incidence (per 100,000) of first-episode urinary tract stones in survey year (2005)

0.64–1.36; $P = 0.814$). For patients over the age of 50 the prevalence was 8.7% for males and 7.7% for females (Fig. 1). Analysis of the age when urolithiasis occurred for the first time amongst all stone patients interviewed in 2005 revealed a marked increase in both females and males aged above 29 years (Fig. 2).

Most of the stones were located at the kidney and/or ureter. Presentation with the classic combination of renal colic and microscopic hematuria was common. The most common clinical presentation at the time of diagnosis was flank pain (68%), followed by abdominal pain (32%), dysuria (20%), and hematuria (11%). Over 35% of subjects with urolithiasis stated that they had suffered from urolithiasis a number of times (Table 2). Over 7% had had five or more stone episodes.

Incidence of urolithiasis

The annual incidence of urolithiasis in 2005 was 145.1. Of these, 56% were first occurrences and 37% were recurrences. In 14% of patients the stones were apparently asymptomatic and fortuitously detected. The incidence was higher in males than in females (Table 3).

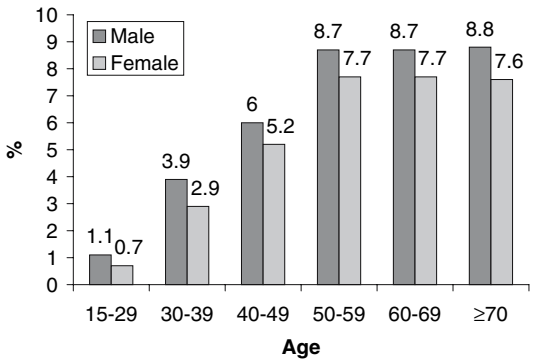

Fig. 1 Prevalence of adult urolithiasis 2005, age-distribution and sex

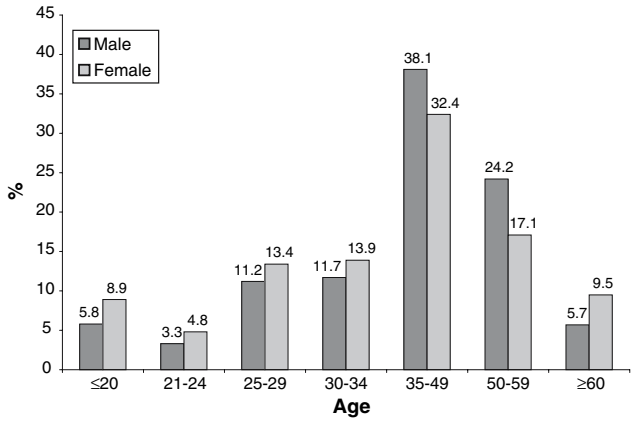

Fig. 2 Age at the first stone episode, $n = 436$

Table 2 Frequency of urolithiasis (%), $n = 436$

Once	56.3
Twice	18.2
Three times	8.7
Four times	2.3
Five times or more	7.9
Do not know	6.6

Table 3 Annual incidence (per 100,000) of first-episode urinary tract stones in the year 2005

Age (years)	Men	Women	*P* value
15–29	87	72	0.04
30–39	168	154	0.07
40–49	173	156	0.04
50–59	167	142	0.02
60–69	159	133	0.03
≥70	129	121	0.06
Total	147.2	129.6	0.04

Recurrence rate

The recurrence rate of urinary stones was 32%. In 2005, the largest number (36%) of stone recurrences was found in the 30- to 39-year age group. Disease recurrence occurred at 11–162 months (median 21) after the initial diagnosis of urolithiasis. The average cumulative recurrence rate was 16% after 1 year, 32% after 5 years, and 53% after 10 years.

Race and ethnicity

Due to different racial residents in a specific geographic area, a simultaneous ethnicity, geographical location, and urolithiasis analysis was not possible. Therefore, two separate covariance analyses were performed. The first looked at race (Black, White, etc.) effects within one geographical location and the second analysis looked at geographical effects between all 30 counties. No effect of race was detected; neither the intercept (analysis of covariance $P = 0.36$) nor the slope of the age relationship was influenced by race (analysis of covariance $P = 0.41$). The interaction terms between ethnicity (Arab, Fars, Kurd, etc.) and other covariates in the model were not significant at the 0.05-level.

Types of treatment

The types of treatment administered are summarized in Table 4. Data for types of treatment were gathered from stone formers ($n = 148$) who had stone episodes between 1994 and 2005. Multiple reports were permitted. Of

Table 4 Types of treatment for stone removal

ESWL	72
Endoscopic procedures	35
Percutaneously (PCNL)	15.5
Spontaneous discharge	18
Open surgery	5.5
None	11.5
Not known	2.5

subjects with urolithiasis, 5.5% stated that their stone was removed by open surgery.

Prophylactic precautions

Subjects with urolithiasis were asked to explain the type of prophylactic measures adopted to prevent recurrences, and they explained them as follows (Table 5):

- High fluid intake (drinking; 82.3%)
- Change in diet (19.3%)
- **Took any regular medication (12%)
- None (7%)

Prevalence of urolithiasis and risk factors

Regional distribution

The prevalence and incidence of urinary stone were different between different races and ethnicities, but not "*statistically*" significant ($P > 0.05$). For prevention from any bias and accuracy of results, statistical analysis was done after adjustment for race and ethnicity. After adjustment for age, race, and ethnicity the odds of ever having had urinary stones were greater among men and women who lived in South central (Kerman and Hormozgan) and Southwest (Fars, Boushehr, Khoozestan, Ilam, and Chaharmahal va Bakhtiari) counties, with odds increasing from west to east and from north to south (Table 6). The odds of stones among participants who resided in the South central were nearly twice that of those living in the Northwest (Ardabil, East Azarbayjan, and West Azarbayjan) counties (OR = 1.8, men and women). After the simultaneous effects of all the studied risk factors that were considered, regional associations with stone prevalence were moderately diminished for men and women.

Table 5 Prophylactic precautions against recurrence

	%
High fluid intake	82.3
Change in diet	19.3
Regular medication	12
None	7

Sunlight indices

The prevalence of stones in both men and women tended to increase as the average annual temperature increased (OR 2.27; 95% CI 1.73–4.31). A similar increase in stone-prevalence was observed as the sunlight index rose (OR 1.66; 95% CI 1.25–2.23). The increase in the odds of stones adjusted for age and race was observed among both men and women, as with temperature (Table 7).

The average annual temperature varied markedly among the counties, ranging from 8.8°C in Ardabil to 27°C in Hormozgan. The sunlight index ranged from 12.2 in Ardabil County to 44.1 in Hormozgan County. Counties with higher annual temperatures also tended to have higher sunlight indices. The increase in the odds of stones adjusted for age and race was little influenced by further adjustment for personal risk factors for stones (Table 7).

Personal risk factors

A positive association was found between urolithiasis and obesity (OR 1.74; 95% CI 1.21–2.31; $P = 0.04$), diuretic use (OR 1.62; 95% CI 1.18–2.70; $P = 0.03$), hypertension (OR 1.88; 95% CI 1.26–2.18; $P = 0.04$), unemployment (OR 2.10; 95% CI 1.43–2.14; $P = 0.04$), consumption of tea (OR: 1.64; 95% CI 1.32–2.62; $P = 0.03$), consumption of cola (OR 1.49; 95% CI 1.23–2.19; $P = 0.02$), and meat consumption (OR 1.38; 95% CI 1.29–2.21; $P = 0.02$) (Table 6). However, a negative association was found between urolithiasis and consumption of coffee (OR 0.8; 95% CI 0.6–1.2; $P = 0.03$), consumption of dairy products (OR 0.6; CI 0.4–1.3; $P = 0.03$), cereals consumption (OR 0.08; 95% CI 0.06–1.71; $P = 0.02$), and educational level (OR 0.8; 95% CI 0.6–1.2; $P = 0.02$) (Table 6). No positive association was found with fish consumption (OR 1.17; 95% CI 0.66–1.91; $P = 0.072$), vegetable consumption (OR 1.22; 95% CI 0.90–1.81; $P = 0.062$) or consumption of fruits (OR 1.34; 95% CI 0.91–1.67; $P = 0.08$).

Body mass index

We calculated BMI using the ratio between weight in kilograms and height in square meters [12].

Body mass index can be divided into three classes: (A) up to 25, which refers to normal or underweight conditions; (B) between 25.1 and 30, which refers to overweight; and (C) >30, which is considered obesity. About 72% of males and 61% of females with urolithiasis had BMI over 25. In participants without urinary stone, these were 61 and 49%, respectively (OR 2.33; CI 1.77–4.35; $P = 0.02$). Of male and female subjects with urolithiasis, 18.3 and 19.8% were obese (BMI>). These were 11.5 and 10.2% in participants

Table 6 Relations between geographic region of residence, personal risk factors, and history of urolithiasis among adult Iranian population

Risk factors	Men				Women			
	No.	% with stones	Odds ratio[a]	95% CI	No.	% with stones	Odds ratio[a]	95% CI
Region								
Northwest	1,250	4.4	1.0	–	1,294	3.8	1.0	–
North central	862	5.1	1.1	1.0–1.2	952	4.6	1.1	1.1–1.3
Northeast	105	5.7	1.2	1.1–1.3	110	4.9	1.2	1.2–1.4
Central counties	625	6.7	1.5	1.3–1.6	620	6.0	1.5	1.3–1.7
Southwest	590	8.4	1.7	1.4–1.8	638	7.7	1.8	1.4–2.0
South central	190	9.0	1.8	1.4–2.0	175	8.0	1.8	1.4–2.2
Southeast	126	10.3	2.0	1.4–2.6	112	9.0	2.2	1.6–2.8
Obesity								
No	2,982	5.3	1.0	–	3,241	4.4	1.0	–
Yes	766	6.9	1.62	1.2–2.1	660	6.2	1.84	1.2–2.5
Diuretic use								
No	3,362	5.1	1.0	–	3,606	4.1	1.0	–
Yes	386	7.1	1.52	1.16–2.5	295	6.5	1.90	2.1–3.3
Hypertension								
No	3,059	5.1	1.0	–	3,251	4.5	1.0	–
Yes	689	7.1	2.0	1.4–2.2	650	6.1	1.8	1.2–1.8
Consumption of tea (>2 cup/day)								
No	975	5	1.0	–	1,872	4.9	1.0	–
Yes	2,773	7.2	1.8	1.42–2.81	2,029	5.7	1.4	1.2–2.4
Consumption of cola soft drinks								
None	1,424	5.6	1.0	–	1,911	4.8	1.0	–
Any	2,324	6.5	1.6	1.42–2.42	1,990	5.8	1.4	1.21–2.18
Consumption of non-cola soft drinks								
None	2,345	5.8	1.0	–	2,652	5	1.0	–
Any	1,403	6.4	1.2	1.1–1.4	1,249	5.7	1.2	1.1–1.3
Consumption of diet soft drinks								
None	3,070	5.8	1.0	–	2,925	5	1.0	–
Any	678	6.4	1.2	1.13–1.46	976	5.6	1.2	1.12–1.52
Consumption of dairy products								
None	1,202	6.9	1.0	–	1,095	6.1	1.0	–
Any	2,546	5.3	0.5	0.3–1.5	2,806	5.5	0.7	0.5–1.2
Consumption of coffee								
None	3,290	6.8	1.0	–	3,588	5.9	1.0	–
Any	458	5.4	0.9	0.7–1.2	313	4.7	0.7	0.5–1.2
Consumption of cereals								
None	2,330	6.5	1.0	–	2,496	5.7	1.0	–
Any	1,418	5.7	1.1	1.05–1.2	1,405	4.9	1.2	1.1–1.3
Consumption of meat								
≤40 g./day	2,910	5.2	1.0	–	2,886	4.6	1.0	–
>40 g./day	838	7	1.4	1.2–2.4	1,015	6	1.4	1.3–2
Family history								
Negative	1,050	4.5	1.0	–	1,093	3.1	1.0	–
Positive	2,698	7.7	3.3	2.0–5.4	2,808	7.5	3.0	1.8–5.2
Educational level								
≤High school	2,923	6.6	1.0	–	2,928	5.7	1.0	–
>High school	825	5.6	0.8	–	0.6–1.2	4.9	0.8	0.7–1.2

CI confidence Interval

[a] Odds ratios are adjusted for age and race

Table 7 Relations between mean annual temperature and sunlight index and history of urolithiasis among Iranian men and women

Risk factors	No. of respondents	Respondents with stones		Crude odds ratio[a]	95% CI	Adjusted odds ratio[b]	95% CI
		No.	%				
Men							
Mean annual temperature (°C)							
<15	1,250	55	4.4	1.0	–	1.0	–
15–17	862	44	5.1	1.2	1.1–1.24	1.1	1.1–1.20
17–19	105	6	5.7	1.4	1.2–1.6	1.3	1.2–1.5
20–22	625	42	6.7	1.6	1.4–1.7	1.4	1.3–1.5
22–24	590	50	8.4	1.7	1.5–1.8	1.5	1.4–1.7
24–26	190	17	9	1.9	1.7–2.1	1.7	1.6–2.0
>26	126	13	10.3	2.1	1.8–2.5	1.9	1.7–2.2
Sunlight index							
<15	918	38	4.1	1.0	–	1.0	–
16–20	644	31	4.8	1.2	1.1–1.3	1.1	1.06–1.2
21–25	156	9	6.0	1.3	1.1–1.4	1.2	1.1–1.3
26–30	500	35	7.1	1.5	1.3–1.7	1.3	1.2–1.6
31–35	519	47	9	1.6	1.3–1.8	1.5	1.3–1.7
36–40	111	15	10.3	1.9	1.4–2.2	1.7	1.4–1.9
>40	104	12	11.6	2.1	1.6–3.0	1.9	1.5–2.4
Women							
Mean annual temperature (°C)							
<15	1,294	49	3.8	1.0	–	1.0	–
15–17	952	44	4.6	1.1	1.0–1.2	1.1	1.0–1.2
17–19	110	5	4.9	1.2	1.1–1.4	1.2	1.1–1.3
20–22	620	37	6	1.3	1.2–1.5	1.2	1.1–1.4
22–24	638	49	7.7	1.4	1.3–1.6	1.3	1.2–1.5
24–26	175	14	8	1.5	1.3–1.7	1.4	1.3–1.6
>26	112	10	9	1.6	1.4–2.2	1.5	1.3–1.9
Sunlight index							
<15	864	18	2.1	1.0	–	1.0	–
16–20	644	21	3.2	1.2	1.1–1.3	1.1	1.1–1.2
21–25	90	4	4.4	1.2	1.1–1.4	1.2	1.1–1.3
26–30	440	23	5.2	1.3	1.1–1.5	1.2	1.1–1.4
31–35	480	27	5.6	1.4	1.2–1.6	1.3	1.2–1.5
36–40	122	7	6	1.6	1.4–2.0	1.4	1.3–1.8
>40	142	10	7	1.9	1.4–2.6	1.6	1.4–2.2

CI confidence interval

[a] Crude odds ratios are adjusted for age (5-year levels) and race

[b] Odds ratios are adjusted for age (5-year levels), race, hypertension, education, beverage consumption, body mass index, and diuretic use, using logistic regression

of the same age without urinary stones (OR 1.87; CI 1.22–2.98; $P = 0.04$).

Family history

Urolithiasis was significantly associated with a positive family history of urinary stones (Table 6). The OR was highly significant (3.1, 95% CI 1.8–5.1) for a family history of urolithiasis in siblings. The family history of urolithiasis was found in 28.5% of first-degree relatives, compared to 4.4% in the stone-free participants ($P = 0.01$). A positive family history of urolithiasis was one of the strongest predictors in the logistic model. There are no significant differences with respect to two other chronic diseases: hypertension and diabetes. In these cases, the frequency rate in the families' subjects affected by urolithiasis is the same as for the stone-free families.

Discussion

Large differences are present in the prevalence of urolithiasis between countries. The prevalence rate of urinary stones has been variably reported to be 3.5–18.5%, depending on

the countries or regions in which the surveys were performed [2, 6, 8, 9, 13–18]. In our study the overall prevalence of urolithiasis was 5.7%. Most epidemiological studies of urolithiasis were based on hospital statistics, general practice surveys, or selected group surveys [19, 20]. A direct comparison between different studies is hampered by the lack of a uniform validated questionnaire, and differences in the characteristics of the study population, in the method of assessment (self-applicable questionnaire, personal interview, phone interview, mailed surveys) and in the definitions of urolithiasis. These variables underscore the problems pertaining to epidemiological studies. The samples should be representative of the entire population. In large countries, variations in climatic zone, differences in eating and drinking habits, different degrees of industrialization, different sunlight indices, and different mean annual temperature pose additional problems for epidemiological studies. As the prevalence of urolithiasis reported in recent studies has been higher than in earlier ones, the prevalence of urolithiasis may be greater than we have previously considered [2, 21]. Changes in dietary habits, however, play a pivotal role in increasing the prevalence and incidence of urinary stones. Within a period of 10 years (1975–1985), Yoshida et al. detected a rise in the prevalence of urolithiasis from 4 to 5.4%, and attributed this to increasing industrialization and westernization of life-style in Japan [6]. The prevalence of urolithiasis in Iran does not match the prevalence rates of the surrounding geographical countries but almost equals the rates of Western Europe. This can be attributed to increasing industrialization and westernization in Iran, and socioeconomic factors, such as dietary habits and lifestyle. In addition, questions regarding the true accuracy of the reported studies without a properly designed protocol are valid. A representative survey of the incidence and prevalence of a disease is only possible using randomly selected samples of the general population questioned in face-to-face interviews. Other likely explanations for these differences may be due to variations in climate, nutrition, occupation, or the prevalence of comorbid conditions that may affect the risk of stones. A population-based study is mandatory to determine the precise epidemiologic details of urinary stone disease in the different regions. The questionnaires used in our study were completed by well-trained general practitioners instead by mail response to improve the confidence of the study. We used a two-stage cluster random sampling design, because this is a nationally representative cross-sectional investigation that specifically addresses the likelihood of urolithiasis.

The present prevalence of urolithiasis (5.7%) is lower than the reported rate of 7% in Japan [22] and 8% in the USA [23] but higher than prevalence rate of 4.7% [9] in Germany, and 3.5% in Korea [15]. In our study, the prevalence was 6.1% for males and 5.3% for females. These numbers are 9.6 and 4.5% in Japan [22], 6 and 1.8% in Korea [15], and 5.5 and 4% in Germany [9], respectively. It is well known that urinary stones have a male preponderance [22, 24]. The male-to-female ratio (1.15:1) in our study is lower than from most of the previous studies [8, 9, 13, 15]. It may reflect regional and ethnical factors, particularly in the setting of the possible presence of eating, drinking, cultural, and racial differences. In addition, the clinical definition used for urolithiasis, type of trial performed (self-applicable questionnaire, mailed questionnaire, interview by phone, personal interview), and the characteristics of samples (general population vs. clinics) studied are among the confounding factors in reported prevalences of urolithiasis. In a nation-wide study, the following selection criteria must be considered: age structure, gender, place of residence, occupation, climatic zone, eating habits, environmental factors, lifestyle, different degrees of industrialization, etc. The samples should be representative of the entire population. It is difficult to do a community-based study including whole age groups. The age groups must be selected carefully, because the prevalent age group is different according to the nature of the disease. In this study, the main resulting statements on prevalence and incidence were confirmed in the individual cycles, so that the final result led to highly valid data. However, there is every chance that, due to undiagnosed stones, the true prevalence and incidence lie quite a bit higher than was found in our study.

The average cumulative recurrence rate was 16% after 1 year, 32% after 5 years, and 53% after 10 years in our study. In a community-based survey, Ljunghall et al. [25] reported a recurrence rate of 31.5, 49, and 72% after 5, 10, and 20 years, respectively. The lifetime recurrence rate in our study was 32%. According to studies carried out in Italy, there has been an increase in recurrence rates 7 years after extracorporeal shock wave lithotripsy as compared with those who had surgical removal (41% vs. 30%) [26], although the former treatment undoubtedly has advantages.

People who have had stones are more likely to have a first-degree relative with stones than those without such a history [27]. Thun et al. [18] also found a high prevalence of stones among the relatives of stone formers. Defects in urine acidification can be inherited [28] and polygenic factors, as well as household diet and environmental factors, can play a role [23, 29, 30]. In this survey, we found that first-degree relatives of those with stones have twice as high a chance of stone disease. Robertson et al. [31] were the first to detect a link between rising protein consumption and stone formation. We also studied the influence of diet on the risk of urinary stone formation, and confirmed the increasing risk from protein-rich diets producing strong acidification of the urine. Meat consumption is higher among subjects affected by urolithiasis than in the rest of

the population of the same age, whereas cereals, milk, and dairy products are eaten less. Water is consumed less often among urolithiasic subjects than among the rest of the participants. Tea consumption may have been changed by an event of stones. Prior to 1982, people who experienced urinary stones were commonly recommended to avoid sources of oxalate such as tea [32]. If subjects with stones limited tea consumption, then the positive association between tea and stones would be underestimated. The regional odds of stones in the Northwest region were reduced after accounting for several of the studied risk factors. Individual adjustment for ambient temperature, sunlight index, and beverage intake each resulted in a decrease in the regional odds of stones. Each of these factors accounted for a similar degree of regional variation among both men and women. Higher temperature is positively associated with stone prevalence. Parry et al. [33] reported that urinary calcium levels increased among soldiers transferred to warmer climates during summer but not winter months. They concluded that exposure to sunlight might influence stone formation. Dehydration from inadequate fluid intake during exposure to high ambient temperatures increases the concentration and acidity of urine, which promotes stone formation [34, 35]. In our study, among both men and women, sunlight level increased the odds of stones. The effect of sunlight was as strong on the regional odds for women as for men. Sunlight increases production of 25-hydroxycholecalciferol in the skin, which, after conversion to 1,25-dihydroxy-vitamin D by the kidneys, increases intestinal absorption of calcium. Patients with hypercalciuria have elevated levels of circulating 1,25-dihydroxyvitamin D [36] and excess urine calcium. These linked to stone formation. The effect of sunlight on the regional odds of stones that we seen was not owing to the latitude part of the sunlight index, since adjustment for latitude did not have a similar effect on regional difference in stones as did adjustment for sunlight.

Prevalence of urolithiasis also varies in relation to education level and profession. The prevalence is higher among subjects with lower education levels. The highest rate is among the unemployed; taking into account the employed, the highest prevalence is among agricultural employees.

Conclusion

In this first systematically assessed epidemiologic survey we report the prevalence and incidence of adult urolithiasis in the Iranian population. Better understanding of the epidemiology of urolithiasis is crucial to plan effective treatment and prevention strategies. We found that indices of ambient temperature and sunlight exposure were independently associated with the prevalence of urolithiasis. Further, after adjustment for differences regional variation was mildly reduced for men and women after adjustment for temperature, sunlight, and eating habits. Still more epidemiologic research is crucial to further elucidate the prevalence as well as the incidence of urolithiasis in certain ethnic groups.

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