Family History and Age at the Onset of Upper Urinary Tract Calculi

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Introduction: The aim of this study was to evaluate the effect of family history on the age of urinary calculus formation and its relation with characteristics of the calculi and patients.

Materials and Methods: In a cross-sectional study in Tabriz, a total of 210 patients with upper urinary tract calculi were evaluated. Their demographics and clinical characteristics and detailed information on their family history were recorded.

Results: Of the patients, 28.6% had a positive family history for urinary calculi. Siblings were the majority of the affected family members (71.1%). The rate of a positive family history was slightly higher in women than in men (30.0% versus 28.1%; $P = .20$). The mean age at the disease onset of the men with and without a positive family history was 37.2 years versus 39.3 years, respectively ($P = .20$). Such a difference was not detected in the female patients, either ($P = .63$). In general, the calculi were more detected on the left renal unit, but more prevalent on the right side in patients with a positive family history ($P = .008$). No relation was found between the number and size of the calculi and the family history.

Conclusion: About one-third of the patients with urinary calculi had a positive family history too. Men with affected family members are slightly more susceptible to the disease at younger ages. There might be differences in the side of the calculi and family members with a history of disease that warrants further studies.

Keywords: urinary calculi, family history, age, inheritance

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INTRODUCTION

Urinary calculi are more prevalent between 20 and 40 years of age and men are affected 3 times more than women.[1] Age is one of the factors evaluated in association with the risk of calculus formation. In a prospective study on patients with urinary calculus in Italy, the authors found that patients who had 2 or more calculi during the follow-up were younger at the onset of the disease than those who had only 1 calculus or no recurrence.[1] Having a positive family history of urinary calculus and its effect on different factors is another important issue in this condition. It has been shown that a positive family history is more common in patients with calculi than healthy individuals.[2,3] Among patients with a positive family history, the prevalence rate of the disease reaches 25%.[4] Also, recurrence of the calculi is more common in these patients and occurs faster.[2] Although could be related to the genetic factors, patients' relatives may be at risk of common environmental factors participating in calculi formation.[2,5] The cause (either genetic or environmental) put the family in a higher risk of calculus formation. We designed a study to evaluate the relationship between

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upper urinary tract calculi and family history of urinary calculi and sex of the patients.

MATERIALS AND METHODS

In a cross-sectional study performed between November 2003 and May 2003, we evaluated 210 patients. They had presented to the urology clinic of Imam and Sina hospitals in Tabriz, Iran, and were between 25 and 55 years old. The cause of referral was a diagnosed upper urinary tract calculus or flank pain that was found to be due to upper urinary tract calculi in our diagnostic evaluation. Patients with systemic disorders and those who were receiving medical therapy were excluded. Informed consent was obtained from all eligible patients. Demographic and clinical characteristics of the patients including sex, age, occupation, place of living during the last 10 years, previous episodes of urinary calculi, the age at the onset of the first discovered calculus, and documented history of calculi in the patients or their first-degree relatives (father, mother, sister, and brother) were recorded. To confirm the collected data, a second interview was planned for the patients who were not sure of their information. Characteristics of the calculi including location, number, and size were recorded according to the results of ultrasonography and plain abdominal radiography. If there was more than 1 calculus, the largest one was evaluated.

The patients were categorized based on the family history of urinary calculus. For evaluating the differences between the two groups in age and calculus size, the independent sample *t* test was used. The chi-square and Mann-Whitney tests were used for the evaluation of the relation of the patients' sex, location of the calculi, and number of the calculi with the family history. Continuous variables were shown as mean ± standard deviation and the 95% confidence interval was calculated. A *P* value less than .05 was considered significant.

RESULTS

Of 210 patients, 60 (28.6%) had a positive family history for urinary calculus formation. Thirteen patients (21.7%) had the history in more than one person in their family. The affected family members were 30 brothers (39.5%), 24 sisters (31.6%), 14 fathers (18.4%), and 8 mothers (10.5%). Therefore, a positive family history was more detected in patients' siblings.

The mean age and sex distribution of the patients are shown in Table 1. The age range of the patients at the onset of urinary calculus disease was 7 to 54 years and 15 to 55 in those with and without a positive family history, respectively. Although not statistically significant, the age at the onset of the disease was 2 years less in the men with a positive family history than the men without a family history. No significant relation was detected between the sex of the patients and the family history of urinary calculi ($P = .20$).

Table 1. Age and Sex Distribution of Patients With and Without a Positive Family History of Urinary Calculi*

Characteristics	Values			*P*
	All Patients	Positive Family History	Negative Family History	
Number of patients	210	60 (28.6)	150 (71.4)	
Male-female ratio	3.2:1	3:1	3:1	.20
Men				
Number of patients	160	45 (28.1)	115 (71.9)	
Mean age (95%CI), y	40.9 ± 8.7	40.6 ± 8.5 (38.1 to 43.1)	41.0 ± 8.8 (39.4 to 42.6)	.89
Mean age at disease onset (95%CI), y	38.7 ± 9.5	37.2 ± 9.3 (34.5 to 39.9)	39.3 ± 9.6 (37.6 to 41.1)	.20
Women				
Number of patients	50	15 (30.0)	35 (70.0)	
Mean age (95%CI), y	39.2 ± 8.9	38.2 ± 8.9 (33.7 to 42.7)	39.5 ± 9.1 (36.4 to 42.5)	.63
Mean age at disease onset (95%CI), y	36.8 ± 10.9	36.8 ± 11.0 (31.6 to 41.9)	36.7 ± 11.0 (33.1 to 40.4)	.99
Single Calculi				
Number of patients	132	41 (31.1)	91 (68.9)	
Mean age at disease onset (95%CI), y	39.0 ± 10.3	36.3 ± 9.3 (33.5 to 39.2)	39.3 ± 9.8 (37.3 to 41.3)	.10
Multiple Calculi				
Number of patients	78	19 (24.4)	59 (75.6)	
Mean age at disease onset (95%CI), y	38.5 ± 9.7	38.6 ± 10.5 (33.9 to 43.3)	37.8 ± 10.3 (35.2 to 40.5)	.77

*Values in parentheses are percents unless otherwise indicated. CI indicates confidence interval.

Table 2. Location of Urinary Calculi*

Calculus Location	Patients		
	All	Positive Family History	Negative Family History
Right kidney	72 (34.3)	27 (45.0)	45 (30.0)
Right ureter	19 (9.0)	8 (13.3)	11 (7.3)
Left kidney	84 (40.0)	17 (28.3)	67 (44.7)
Left ureter	16 (7.7)	4 (6.7)	12 (8.0)
Bilateral	19 (9.0)	4 (6.7)	15 (10.0)

*Values in parentheses are percents.

The most common site for calculus formation was the left kidney, while in the patients with a positive family history of urinary calculi, it was the right kidney (Table 2). The side of the involved renal unit was mostly right in the patients with a positive family history ($P = .008$); however, there was no relation between the bilaterality of the calculi and family history. The number of the calculi was between 1 and 6 in our patients, and 9 patients (4.3%) had undetermined number of the calculi which had been reported to be a complex of calculi on ultrasonography. There was no relation between the family history and the number or the maximum size of the calculi. The mean number of the calculi was 1.6 ± 0.9 and 1.6 ± 1.2 in the patients with and without a positive family history, respectively ($P = .90$). The mean maximum size of the calculi was 12.0 ± 4.5 mm and 13.3 ± 5.6 mm, respectively ($P = .08$).

DISCUSSION

Kidney calculus is the third common disease of the urinary system in both men and women, and both genetic and environmental factors influence its development and characteristics.[6] Due to the high prevalence of the calculi in different regions, it has always been an important issue. The prevalence of urinary calculi has been reported to be 5.7% in Tehran, Iran.[7] Due to the diversity of environmental factors, the prevalence of kidney calculus is different in different countries. For example, in Greece, the prevalence of kidney calculus reaches 15%.[6] Many studies have been performed evaluating the relationships between the history of calculus formation and recurrence or between the patients' sex and the characteristics of the calculi.[1,8] The results of our study were in accordance with other studies. However, it should be mentioned that our study was performed in the patients referring to general university hospitals and this may cause the evaluation of the patients in only one socioeconomic class. In a study performed in Tehran, Iran, the prevalence of urinary calculi was different in the east and south of the city in comparison with the north and west.[7]

A family history of urinary calculus was reported in 34.7% of women and 31% of men with the disease in Paris.[9] In our study, it was 30% and 28.1%, respectively, showing a greater likelihood of a positive family history in women. The reason behind such a difference warrants further research. It has also been suggested that this prevalence is influenced by the recurrence rate of the calculi.[8] In the study done in Paris, calculi had been diagnosed about 5 years earlier in men with a positive family history.[9] This figure is in accordance with our results; age at the onset of calculi was 2 years less in the men with a positive family history than the men without a family history, but in the women, such an age difference was not observed.

Kodama and Ohno reported that the prevalence rate of urinary calculi is higher in the brothers and fathers of the patients.[10] Also, in a study by Ljunghall and associates, calculus was more prevalent in the fathers than the mothers of the patients.[8] It has also been shown that the history of calculi is more prevalent in the parents and siblings of the patients with calculi than that in general population, but such a difference is not seen in the spouses, suggesting the predominance of genetic rather than environmental factors.[11] In the present study, brothers and sisters of the patients were the majority of the family members with a history of urinary calculi, and in agreement with other studies, calculi were less prevalent in the mothers of our patients. These differences may be affected by the geographical, social, and racial factors, as well.

In our study, the patients with a positive family

history had a tendency to have the calculi in the right kidney which might be an accidental finding as it has not been reported in the previous studies; however, it needs more evaluations for the probable causes. We did not find a relation between the positive family history and the number of the calculi; the Paris study supports our result.[9] Concerning the type of the calculi, Ljunghall and coworkers showed that the family history was not related to the level of the calcium and uric acid excretion in urine, which is in contrast to the study of Marya and colleagues that showed the higher prevalence of hypercalciuria in patients who had first-degree relatives with a history of calculi in comparison with their spouses. It can be concluded that genetics is a factor more important than the environment.[8,12] More studies in this regard are warranted to come to a clear conclusion

Finally, in our study there was no significant relation between the calculus size and family history. In our search, we found no article on this issue. We did not evaluate the recurrence of urinary calculi; however, most of the studies have a consensus of conclusion on the effect of family history on the recurrence of the disease.[1,2,10,12]

CONCLUSION

The age of the first diagnosis of urinary calculus is slightly less in men with a positive family history than those without a family history. The patients' relatives are recommended to pay attention to the consumption of the calculus-forming foods. More studies are needed to evaluate the risk of calculus formation and its characteristics and complications in the patients' family members.

CONFLICT OF INTEREST

None declared.

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EDITORIAL COMMENT

A Lack of Difference Versus a Lack of Power: Do We Have Enough Soldiers to Liberate the Castle?

Ahmadi Asr Badr and colleagues conducted a cross-sectional study to evaluate the impact of family history on the age of onset and other characteristics of urolithiasis. While the study was based on an interesting question, the authors could not find any significant impact of family history on the age at the onset of the disease, neither in men nor in women. Nevertheless, they discussed the difference both in the text and in the conclusion. Although a nonsignificant result is not conclusive, it seems that this statistical failure in the present study is mainly due to a lack of power rather than a lack of real difference. For instance, given the number of individuals and the mean and standard deviation for the age of onset (Table 1 of the paper), the power of the *t* test for detecting a significant difference is

only 26% in men and 5% in women! The same is also true for the other characteristics. In particular for the single calculi, it seems that increasing the sample size would reach to a significant difference (the current power is 38% for this group).

Patients' recruitment from a public hospital may be a source of selection bias, as discussed by the authors; however, a systematic difference in family history of calculus between the public and private hospitals is unlikely. Therefore, it is not a major issue in this study.

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