

## ORIGINAL RESEARCH

# Prevalence of urolithiasis in rural Thebes, Greece

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## A B S T R A C T

**Introduction:** Worldwide, urolithiasis is the third most common urological disease affecting both males and females. Both genetic and environmental factors contribute to stone formation. The recurrence rate is approximately 50%, rising to 70% within 10 years and this condition represents a significant healthcare cost burden. An unusually frequent history of urolithiasis has been observed among patients from the rural area of Thebes, Viotia, Greece. Objective: To determine the prevalence of urolithiasis in Thebes.

**Methods:** A representative sample of persons from the rural area of Thebes was questioned about the occurrence of urinary stones during their lifetime, and acute urolithiasis in 2005. A logistic regression model was used to contrast individuals with lithiasis to those without lithiasis.

**Results:** A total of 422 subjects participated in the study. We found a 15% prevalence of urolithiasis in the rural population of Thebes. The rate was slightly higher in men than in women in almost all age groups questioned, although this was not statistically significant. No case of urolithiasis was found in subjects under the age of 17 years. The prevalence of urolithiasis appeared to increase with age in both men and women. Those drinking bottled water were less likely to have lithiasis.



**Conclusion:** The life time prevalence rate of urolithiasis observed in the rural area of Thebes was higher to that reported in other studies performed among males and females in the general population of Europe.

**Key words:** prevalence, rural population, urolithiasis.

## Introduction

Urolithiasis is the third most common urological disease affecting both males and females; it is predominant among males in a proportion of approximately 2:1<sup>1</sup>. The recurrence rate reaches approximately 50%<sup>2</sup>, rising to 70% within 10 years<sup>3</sup>. Because recurrence is common, this condition that impacts on the economically active population represents a significant healthcare costs burden, as it is associated with restricted activity and/or hospitalization. Although new and effective therapeutic methods to treat nephrolithiasis have been introduced recently, urinary stones continue to occupy an important place in everyday urological practice. The incidence of this condition varies worldwide, affecting from 1 to 20% of the population<sup>1</sup>. In Greece, the incidence of urolithiasis is generally estimated at between 5 to 15%<sup>4</sup>; however, no national data exists and only estimates are possible.

Both genetic and environmental factors contribute to stone formation. Factors believed to predispose to sporadic urinary lithiasis include hygienic-dietetic issues, occupation, geographic and climatic aspects, as well as the special characteristics of drinking water<sup>5,6</sup>. The observation of an unusually frequent history of urolithiasis among patients from the rural area of Thebes, Viotia, Greece, prompted a study aimed at determining the prevalence of urolithiasis in the rural area of Thebes.

Thebes lies in the fields of the Viotia region of Greece. The population of the Viotia region is almost 58 300. Of those, 19 509 live in the city of Thebes and 13 204 live in the rural area of Thebes. Most of the residents of the rural area of Thebes (approximately 80%) are farmers who cultivate

cotton, potatoes, onions, grapes and tomatoes. The climate is typically Mediterranean. To our knowledge, the ‘hardness’ of the drinking water in the rural area of Thebes is one of the highest countrywide. In addition we investigated the following factors associated with the incidence of the disease: the sex ratio, seasonal frequency, and the kind and the amount of water intake. Considering that prognosis is always better than therapy, knowledge of the prevalence of urolithiasis is of utmost importance, because assessment and intervention regarding hygienic aspects could modify the incidence of lithiasis.

## Methods

### *Study population*

We performed an epidemiological, cross-sectional study of the prevalence of urolithiasis in a representative sample of subjects, which included men and women 14 years of age and over, from the general population of the rural area of Thebes. Residents of the urban area of Thebes were excluded from the study. Data on the number, sex and age distribution of the population of the rural area of Thebes were obtained from the National Statistic Service. Assuming a 2% precision estimation and a 95% confidence level, 500 subjects were to be surveyed in order to obtain a simple random sampling. The method used to gather basic information was a self-administered questionnaire about the present or past history of urolithiasis. The questionnaire was handed to visitors to the General Hospital of Thebes between 8.30 am and 1.30 pm from 15th April to 15th June 2006. Subjects were questioned on the occurrence of urinary stones during their lifetimes, and on acute urolithiasis in 2005.



## Questionnaire

The questionnaire was divided into three sections. The first section gathered information about the characteristics of the interviewee (sex, date of birth and residence), while the second section gathered information about the interviewee's history of urolithiasis. The questionnaire was introduced as follows: 'There is a disorder called urolithiasis. Calculi may occur anywhere in the urinary tract and are common causes of renal colic and bleeding'. The specific questions were: 'Do you have or did you have renal colic, or bleeding? Do you have or did you have a renal calculus passed in the urine? Do you have or did you have a renal calculus diagnosed by ultrasonographic or radiographic image or diagnosed by a physician? How often have you had this disorder prior to 2005? Did you have urinary stones for the first time in 2005? If yes, specify the season of the year. How old were you when you were first diagnosed with a urinary stone? Have other members of your family had lithiasis? How was the lithiasis treated? What are you doing to prevent new stones?'

The third section gathered information about the quantity and sources of drinking water (bottled or tap water). Because there was no intention in this survey to specify special characteristics of the disease, such as the anatomical position and the consistency of the stone, no other information was requested in the questionnaire. Subjects who were not able to read or to understand the questions were assisted to fill in the questionnaire.

## Statistical analysis

After completing the necessary number of questionnaires to obtain a statistical analysis, we entered the data into an electronic database for further analysis using SPSS (SPSS Inc; Chicago, IL, USA) and STATA (STATA Corp, College Station, TX, USA) statistical programs. Percent prevalence rates and their 95% confidence intervals were presented by age; 2x2 tables with  $\chi^2$  tests were used to examine differences in proportions. Odds ratios contrasting those with lithiasis with those without, by gender (males, females; categorically), age groups (nine age groups; ordered), type of

water (tap, bottled; categorically) and quantity of water (up to 1 L, 1–2 L, over 2 L; categorically), and inheritance (no, yes; categorically) were estimated by modelling the data through multiple logistic regression.

## Results

Of the 500 initially administered questionnaires, 21 were not returned while 57 out of the remaining 479 questionnaires were only partially responded to and so omitted from the study. Of the remaining 422 subjects, 194 (46%) were men and 228 (54%) were women. Of these, 313 (74.2%) responded that they had never suffered from urinary stones, while 109 (25.8%) stated that they had experienced an episode of a renal colic or bleeding. Ninety-six (55 males and 41 females) out the 109 had experienced an episode of a colic pain in 2005, while 74 had experienced colic in the previous years. Fifty-one out of the 74 subjects (29 males and 22 females) suffered from colic occasionally, while the remaining 23 subjects (9 males and 14 females) stated that they had suffered from possible renal colic more than three times per year. Colic was more frequent in spring and summer (especially in July and August).

### *Incidence and prevalence of urolithiasis in the rural population of Thebes*

The diagnosis of urolithiasis was established in 62 subjects. It was either confirmed when a renal calculus was passed in the urine, or was revealed on a radiographic image, or diagnosed by symptomatology and clinical examination. More precisely, in 18 out of 109 (16.5%) subjects who reported current or past renal colic, the calculus had been seen either radiographically or ultrasonographically, and in 44 subjects (40.36%), stones were diagnosed by a physician or passed spontaneously in the urine. The remaining subjects, who had non-typical pain rather than renal colic and/or did not have an established diagnosis of urolithiasis, were considered negative. Only 19 (30.6%) of responders



with a confirmed stone in the urinary tract had a family history of urolithiasis.

The prevalence rates of urolithiasis in the rural population of Thebes increased gradually with age in both men and women, varying from 4.8% in the younger group (<20 years) to 42.1% in the ≥90 year age group ( $p$  for trend <0.001) (Table 1). The difference in the prevalence rate of lithiasis between age groups 1-3 and 7-9 was statistically significant ( $p$ <0.001) overall, and for men ( $p$ <0.001), and marginally significant for women ( $p$  = 0.06) at a 95% level of significance (Table 2). For subjects with confirmed urolithiasis, the prevalence rate was slightly higher in men than in women in most age groups studied, but not of statistical significance, except for the group 40-49 years ( $p$  = 0.026).

In 12 cases (19.35%) lithiasis was first diagnosed in 2005. The diagnosis of urolithiasis in subjects younger than 20 years was established in 2005. Analysis of the age when urolithiasis first occurred revealed a relatively earlier onset in females at the age of 17 years, while in the case of males the earliest manifestation reported was at the age of 22 years.

### ***Treatment and prophylactic measures***

Conservative therapy was by far the most common treatment for patients with urinary stones from the rural area of Thebes. The reason for this was two-fold: first, most patients (34/54.8%) reported spontaneous expulsion of the stone; and second, there was no urological department in the regional hospital. Extracorporeal shock-wave lithotripsy was the second most popular method for the treatment of urinary stones, while only 18 subjects reported a history of surgical therapy. As for prophylactic measures taken by patients themselves to prevent lithiasis, 50 subjects (80.6%) reported a high fluid intake; seven subjects (11.3%) reported taking a herbal therapy occasionally; and only six subjects (9.6%) reported a shift in dietary patterns. Although none of the responders reported permanent medical prophylaxis, several reported a daily intake of soda water. It is worth mentioning

that few (2/62) subjects with established stone disease drank bottled water, while most (60/62) drank water from the public water supply. Most reported an average daily intake of 1 to 1.5 L, but no statistically significant difference in average daily intake of water was found between subjects with and without lithiasis ( $p$  = 0.964).

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**Table 1: Categorisation of subjects according to age and stone disease**

Age group in years	n	With lithiasis n (%)	Without lithiasis n (%)
<20	63	3 (4.8)	60 (95.2)
20-29	36	2 (5.6)	34 (94.4)
30-39	44	5 (11.4)	39 (88.6)
40-49	79	10 (12.7)	69 (87.3)
50-59	62	9 (14.5)	53 (85.5)
60-69	58	10 (17.2)	48 (82.8)
70-79	24	5 (20.8)	19 (79.1)
80-89	37	10 (27.0)	27 (73.0)
≥90	19	8 (42.1)	11 (57.8)
Total	422	62 (15.2)	360 (84.8)

**Table 2: Prevalence of lithiasis by age group and sex**

Age group	Total	Male			Female			P value
		n	With lithiasis n (%)	Without lithiasis	n	With lithiasis n (%)	Without lithiasis	
<20	63	25	0 (0.0)	25	38	3 (7.9)	35	0.150
20-29	36	28	2 (7.1)	26	8	0 (0.0)	8	0.437
30-39	44	21	2 (9.1)	19	23	3 (17.4)	19	0.448
40-49	79	30	7 (23.3)	23	49	3 (6.1)	46	0.026
50-59	62	21	2 (9.1)	19	41	7 (17.1)	34	0.425
60-69	58	27	6 (25.9)	20	31	4 (12.9)	27	0.207
70-79	24	15	4 (26.7)	11	9	1 (11.1)	8	0.364
80-89	37	20	7 (35.0)	13	17	3 (17.6)	14	0.236
≥90	19	7	3 (42.9)	4	12	5 (41.7)	7	0.960
Total	422	194	32 (17.5)	160	228	30 (13.2)	198	0.213
P for trend	-	<0.001	-	-	0.015	-	-	-

### Epidemiological data

Table 3 shows multiple logistic regression-derived, mutually adjusted odds ratios (and 95% confidence intervals) contrasting individuals with lithiasis with those without lithiasis by gender, age groups, type of water and quantity of water, and inheritance. The prevalence of lithiasis appeared to increase with age and to be higher among those who had

family members with lithiasis. Those drinking bottled water were less likely to have lithiasis. With respect to gender, no statistically significant differences occurred between men and women. Moreover, no statistically significant differences were observed among the different quantities of daily water intake.



**Table 3: Mutually adjusted odds ratios (and 95% confidence intervals) contrasting individuals with lithiasis with those without lithiasis by gender, age group, type of water, quantity of water and inheritance**

Independent variables	Odds ratio	95% CI Lower, Upper
Gender		
Men	Referent category	
Women	0.70	0.40 to 1.24
Age Group (ordered)	1.33	1.18 to 1.51
Type of water		
Tap	Referent category	
Bottled	0.21	0.07 to 0.65
Quantity of water		
Up to 1 L	Referent category	
1–2 L	0.70	0.37 to 1.34
Over 2 L	0.77	0.34 to 1.73
Inheritance		
No	Referent category	
Yes	2.59	1.37 to 4.89

## Discussion and Conclusions

Urolithiasis in its different forms is the third most common disease afflicting the urinary tract<sup>7</sup>. Although new and effective therapeutic methods have been introduced recently, urolithiasis remains a frequently encountered condition. It has been apparent for several years that the incidence rates of lithiasis vary dramatically, not only from continent to continent, but also between adjacent regions of a country, even if one allows for differences in methodology and criteria selection among epidemiology studies<sup>8,9</sup>. Because epidemiological data on the occurrence of urolithiasis ranges between 2% and 20% worldwide<sup>10,11</sup> (being most common in south and south-eastern regions of the USA, as well as in central Europe and the Mediterranean, India and northern Pakistan, northern Australia and China<sup>12</sup>) variations in climatic zone, differences in eating and drinking habits, as well as genetic factors have been proposed as risk factors.

### Comparison with other studies

According to our findings, the prevalence of urolithiasis in the rural area of Thebes found in our study is eight- to nine-

fold higher than the prevalence found by other investigators<sup>13,14</sup>, and significantly higher than that reported at the Consensus Conference 4<sup>15</sup>. Such a difference is possibly related to geographical distribution. It is, however, noteworthy that the prevalence found in our study is higher than the median incidence (10.2%) found in coastal and island regions of Greece<sup>16</sup>. Although geography is proposed to influence the incidence of urinary calculi<sup>11</sup>, the lack of significant variations in the climate between the rural area of Thebes and other regions of southern Greece does not adequately explain the differences in lithiasis prevalence. Moreover, the fact that only 32.2% of responders with confirmed stone disease had a family history of urolithiasis cannot itself justify the differences in incidence of lithiasis among various regions.

A relationship exists between affluence and nephrolithiasis, with a close correlation between the frequency of stone disease and per capita expenditure on foodstuffs<sup>17</sup>. Despite changes in the diet of the Greek population, dietary patterns remain similar throughout the country. Accordingly, the only explanatory factor is probably the water supply. Indeed, the two factors involved in the relationship between water intake



and urolithiasis, are the volume of water ingested (as opposed to that lost by perspiration and respiration) as well as the mineral or trace-element content of the drinking water. Because variations among daily water intake are similar in both groups (with and without lithiasis), the mineral content of water may contribute to the high incidence of stone disease in the rural area of Thebes.

Several authors have demonstrated that lithiasis usually occurs between the third and fourth decades of an individual's life, and that the prevalence rate varies considerably according to age, while the peak incidence of urinary calculi is from the twenties to the forties<sup>18</sup>. However, this was not found in our study. The prevalence of urolithiasis increased with age in both men and women, seeming to be more prevalent in elderly people, while rare in adolescents. This finding was in accordance with other studies<sup>19</sup>.

According to the literature, lithiasis is more common in men than in women; however, the exact rate differs between studies, with several authors reporting that approximately three males are afflicted for every female<sup>20</sup>, while other investigators found variations not very different from that found in the present survey<sup>21</sup>. Moreover, in the present study, no statistically significant differences in the prevalence of lithiasis were found between sexes in all age groups. Our finding of the relatively earlier onset of the disease in females, and the lack of significant difference in prevalence between men and women, is probably due to lifestyle changes in females (working activity, type of diet, fluid consumption etc) which have made them more prone to urolithiasis. The rate of 4.2% found by Robertson *et al.*<sup>22</sup> in men  $\geq 18$  years compares well with the 4.8% seen in our study in the same age group for both sexes. In subjects between 20 and 29 years, the disease prevalence rate was 5.56%. This compares well with those found in northern Italy by Borghi *et al.*<sup>8</sup>, in central Germany by Vahlensieck *et al.*<sup>14</sup>, and in the US by Stamatelou *et al.*<sup>23</sup>. However the prevalence of lithiasis in the rural area of Thebes increases sharply with age, resulting in a four-fold higher mean prevalence than in the aforementioned studies.

## Study implications

This epidemiological study offers better knowledge of the distribution of this condition in our population, allowing an estimation of its impact on society and also better planning of prevention programs. It remains essential to evaluate current knowledge to derive insights, guidelines and recommendations for the diagnosis. In addition, medical and interventional treatment of urinary tract calculi can be evaluated, as can ways of prevention of disease recurrence.

We consider that there is a need for a fully equipped urologic department and clinic in the area of Thebes, to manage the high prevalence of urolithiasis that increases with ageing. According to our conclusions, 60/62 subjects with confirmed stone disease consumed tap water; thus, it is reasonable to question the quality of the public water supply. Water consistency should be examined, biochemical filters used and all appropriate measures taken for better public health.

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