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Comorbidity and socio-demographic factors associated with renal lithiasis in persons aged 40 to 65: A cross-sectional study☆

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ABSTRACT

Background and objective: Renal lithiasis is one of the most important urological diseases. It seems to be related to different socio-demographic and climatic factors, lifestyle and pre-existing comorbidity. The aim of this study was to examine the relationship between socio-demographic variables, certain risk factors and chronic diseases and the renal lithiasis.
Patients and method: A cross-sectional population-based study was carried out, selecting the Spanish population aged from 40 to 65 years, combining 2 random samples (PreLiRenA and PreLiRenE studies). Data were collected by personal telephone surveys, gathering information on socio-demographic variables and perceived morbidity. Data on annual average temperatures in each Spanish region were also collected. A bivariate and multivariate analysis was performed.
Results: A total of 4894 subjects were surveyed; 51.3% were women; 25% were aged 40–45 years, 36% had primary school education and 31.4% were of low social class. The overall prevalence of renal lithiasis was 15.0% (95% confidence interval [95% CI] 14.5–15.5). By means of multivariate analysis, the variables that showed a strong statistical relationship with the presence of renal lithiasis were: older age (61–65 years; OR = 1.39; 95% CI 1.06–1.80), high social class (OR = 1.98; 95% CI 1.29–2.62), family history of renal lithiasis (OR = 2.22; 95% CI 1.88–2.65), high blood pressure (OR = 1.68; 95% CI 1.39–2.02) and overweight/obesity (OR = 1.31; 95% CI 1.12–1.54). A correlation was observed between renal lithiasis and average annual temperatures in the Spanish regions ($r = 0.59$; $p = 0.013$).
Conclusions: A relationship was observed between renal lithiasis and older age, belonging to higher social classes, the existence of a family history of urolithiasis, and hypertension and overweight or obesity. The prevalence of renal lithiasis is greater in warmer climate zones.

Comorbilidad y factores sociodemográficos asociados a litiasis renal en personas de 40 a 65 años: estudio transversal

Palabras clave:
Litiasis renal
Epidemiología
Factores asociados

RESUMEN

Fundamento y objetivo: La litiasis renal es una de las enfermedades urológicas más importantes. Parece estar relacionada con factores sociodemográficos y climáticos, estilos de vida y comorbilidad preexistente. El objetivo de este trabajo fue examinar la relación entre variables sociodemográficas, ciertos factores de riesgo y enfermedades crónicas, y la litiasis renal.

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Pacientes y método: Se realizó un estudio transversal, seleccionando a población española de 40 a 65 años, combinando 2 muestras aleatorias (PreLiRenA y PreLiRenE). Los datos fueron recogidos por encuestas telefónicas personales, recopilando información sobre variables sociodemográficas y la morbilidad percibida. También se recogieron datos sobre las temperaturas medias anuales en cada región española. Se realizó un análisis bivariado y multivariado.
Resultados: Fueron encuestados 4.894 sujetos; el 51,3% eran mujeres; el 25% tenían entre 40 y 45 años; el 36% tenían educación primaria y el 31,4% eran de clase social baja. La prevalencia global de litiasis renal fue del 15,0% (intervalo de confianza al 95% [IC 95%] 14,5–15,5). Por medio del análisis multivariado, las variables que mostraron una fuerte relación estadística con la presencia de litiasis renal fueron: edad avanzada (61-65 años, OR = 1,39; IC 95% 1,06-1,8), clase social alta (OR = 1,98; IC 95% 1,29-2,62), antecedentes familiares de litiasis renal (OR = 2,22; IC 95% 1,88-2,65), hipertensión arterial (OR = 1,68; IC 95% 1,39-2,02) y sobrepeso/obesidad (OR = 1,31; IC 95% 1,12-1,54). Se observó una correlación entre la litiasis renal y las temperaturas medias anuales en las regiones españolas ($r = 0,59$; $p = 0,013$).
Conclusiones: Existe relación entre litiasis renal y edad avanzada, pertenecer a clases sociales altas, existencia de antecedentes familiares de urolitiasis, y tener hipertensión y sobrepeso/obesidad. La prevalencia de la litiasis renal es mayor en las zonas climáticas más cálidas.

Introduction

Renal lithiasis (RL) currently represents one of the nephro-urological pathologies of greatest magnitude, with increasing prevalence and incidence, due to its clinical and social significance, its direct and indirect costs.[1,2] Although RL has traditionally been considered an exclusively kidney-related problem, there is evidence to suggest that it is a systemic disorder, being associated with epidemiological factors, other health problems such as type II diabetes mellitus (DM), high blood pressure (HBP), obesity and overweight (individually or as part of accompanying factors that constitute metabolic syndrome, with which it seems to share certain biochemical processes), gout, primary hyperparathyroidism, stress and their consequences.[3] Similarly, it seems that lifestyles (mainly diet and exercise) and environmental factors, such as the hardness of drinking water or climate, could be related to the likelihood of suffering renal lithiasis.[4] It is accepted that RL episodes occur more frequently during the warmer months of the year, due to increased perspiration, leading to a more concentrated urine and a higher probability of crystalluria. An exception to this rule has been reported in some studies conducted in countries with colder climate where these conclusions cannot be drawn.[5] Because RL is a complex disease, an understanding of the epidemiology, particularly the interactions among different factors, may help lead to approaches that reduce the risk of stone formation.[6]

The aim of this study was to determine the relationship with RL of certain epidemiological factors, both socio-demographic and comorbidity and climate-related factors, in the Spanish population aged 40–65 years. For this purpose, we based our conclusions on data from two population-based studies carried out by our team in Spain: the PreLiRenA study[7] (conducted in Andalusia, a region in southern Spain); and the PreLiRenE study[8] (a study that covered the entire country). In this way, we sought to obtain a large sample in order to check more consistent and accurate relationships from the statistical standpoint between the factors studied and RL.

Materials and methods

Design

This was an observational, cross-sectional, population-based survey conducted by telephone. The prevalence results obtained in the PreLiRenA study[7] and the PreLiRenE study[8] have been published. To analyze the relationship between average temperature by region and the prevalence of RL, an ecological correlation study was performed.

Participants

The selection criteria in both studies were similar: Spanish subjects of both sexes, aged between 40 and 65 years. The exclusion criteria were as follows: inability to communicate, foreigners, or refusal to participate in the study.

Sample size

To estimate sample size in the PreLiRenA study, consideration was given to an expected proportion of RL of 5.0% (prevalence study by Sánchez-Martín,[9] a confidence level of 95%, an accuracy of $\pm 1.1\%$, and a non-response rate of 25%; the estimated size was 2432 subjects.

To calculate the sample size of the PreLiRenE study, we used the prevalence result reported in the PreLiRenA study[7]: an expected proportion of 16.4%, setting a precision level of $\pm 1.6\%$ and a non-response rate of 25%, yielding a sample size of 2449 subjects.

The fieldwork for these studies was conducted from September 2011 to June 2012 in the PreLiRenA study, and from May 2013 to November 2014 in the PreLiRenE study.

Sources of information and sampling

In the PreLiRenA study a stratified random sample was conducted by Andalusian provinces, sex and five-year age groups, while in the PreLiRenE study this was done by region, sex and five-year age groups. The subjects in the PreLiRenA sample were obtained from the Andalusian Health Service Users Database. The sample data from the PreLiRenE study were extracted from the continuous census of the Spanish population of the National Statistics Institute (www.ine.es). An ad hoc questionnaire was prepared; the same questionnaire was used for both studies.

To collect data on weather variables, statistics on the study of the physical environment from the National Statistics Institute were used, together with those provided by the State Meteorological Agency (www.aemet.es).

The information was obtained through personal telephone interviews using the Andalusian Health Service Users Database in the PreLiRenA study, while in the PreLiRenE study the CATI (Computer Assisted Telephone Interviewing) system was used, which makes a random selection of telephone numbers and manages data obtained in the survey using the Gandia Integra programme (http://www.tesigandia.com/en/gandia-integra-catinet/), which can be used for conducting online surveys, in addition to guaranteeing anonymity, completion of the sampling plan and improved reliability of the coding of responses. When a telephone

number was selected, if no response was received, the system made successive attempts to make contact by telephone up to a limit of 30 calls. Prior to the interview and applying the protocol established for this purpose, the respondent was informed of the purpose of the study, and asked for their verbal informed consent.

Study variables

- Socio-demographic variables: age, sex, education level (cannot read or write, no schooling, primary, secondary, university), occupation, social class (based on the respondent's last occupation).[10]
- Clinical variables: RL history, and chronic comorbidity related with its presence in previous studies (hypertension, hypercholesterolemia, diabetes mellitus type – DM – and hyperuricemia).[3,6] In order to examine metabolic syndrome, we created a dichotomous variable with the sum of patients displaying concomitant hypertension, diabetes mellitus, hypercholesterolemia and obesity. They were also asked about their family history of renal lithiasis, weight and height, and in order to weight status of each person their Body Mass Index (BMI = weight in kg/height in m^2) was calculated and the SEEDO classification (http://www.seedo.es/index.php/pacientes/calculo-imc) was used: normal weight (BMI 18.5–24.9), overweight (BMI between 25.0 and 29.9) and obesity (BMI 30 or more).
- Climatological variables: to study the ecological correlation between the weather and the prevalence of RL, data for annual average temperatures recorded by Autonomous Communities registered by the State Meteorological Agency were used corresponding climate in Spain during the period 1981–2010 (www.aemet.es).

Statistical analysis

The databases of both studies were assembled in the SPSS v.17.0 statistical package. Statistical analysis was performed using this programme and the EPIDAT 3.1 programme. A descriptive analysis was performed followed by a bivariate analysis to test the relationship of the independent variables and the presence of renal lithiasis, applying Pearson's Chi-square test or Student's *T* test, after verification of normality by means of the Shapiro–Wilk test. Since the quantitative variables did not follow a normal distribution, Mann–Whitney's test was used. Similarly, prevalence ratios (PRs) (prevalence ratio in subjects exposed to the factor/prevalence rate among those not exposed), with their respective 95% confidence intervals (95% CI), were estimated. Finally, a multivariate analysis (non-conditional multiple logistic regression) was performed. The independent variables were introduced in the model using the "enter" technique of the SPSS programme and the results of the statistical relationship of each variable were analyzed using the Wald test. The goodness-of-fit of the model was verified using the Hosmer–Lemeshow test. To analyze the existence of a correlation between the prevalence of RL and average temperatures in the different Spanish regions, Spearman's rank correlation coefficient was used. Values were considered to be statistically significant when the $p < 0.05$ (two-sided tests).

Ethical and legal aspects

The two research projects were approved by the Ethics and Clinical Research Committee of the Reina Sofia University Hospital in Cordoba.

Results

A total of 4884 subjects were surveyed, 2439 in the PreLiRenA study and 2445 in the PreLiRenE study. The non-response rate was similar in both samples (31.7%). The socio-demographic and clinical characteristics of the subjects in each of the samples and the combination thereof are shown in Table 1. The distributions by age and sex were not statistically different when comparing the two samples; in contrast, a percentage of subjects was observed with a higher level of education and social class in the Spanish sample (PreLiRenE) than in the Andalusian sample (PreLiRenA). 51.3% of the total sample (n = 2504) were women and 48.7% men (n = 2380). It is worth highlighting that 25.0% (n = 1223) were aged between 40–45 years, 36.0% (n = 1795) had completed primary education and 31.4% (n = 1565) belonged to social class IV (the second lowest).

The overall prevalence of RL was 15.5% (95% CI 14.5–15.5); in the PreLiRenA study it was 16.4% (95% CI: 14.8–17.7%), while in the PreLiRenE study, this was 14.6% (95% CI: 13.1–16.0), being 17.5% (95% CI: 13.8–21.2) in the subsample conducted among the Andalusian population. A significantly higher percentage of subjects was observed with a family history of RL, hypertension and hypercholesterolemia in the Andalusian sample, compared to the total Spanish sample (Table 1).

Regarding chronic morbidity (Table 1), 23.7% reported having HBP, 30.9% hypercholesterolemia, 7.0% DM, 4.8% hyperuricemia (high uric acid), and 57.7% excess weight or obesity, these diseases being more frequent (except DM) in men than in women, as shown in Table 2. The mean BMI was 25.62 ± 5.43 (SD). Significant differences in gender (Mann–Whitney test, $p < 0.001$) were found, the average BMI being 25.85 ± 5.63 in men and 25.40 ± 5.22 in women. There was also a greater prevalence of hypertension, hypercholesterolemia, hyperuricemia and overweight or obesity in men than in women (Table 2).

26.3% of the respondents (n = 1286) had a family history of renal lithiasis, predominantly among the women surveyed (29.8%) than among the men (22.6% test Chi-square; $p < 0.001$).

As reflected in Table 3, bivariate analysis revealed a higher prevalence of RL among older persons, and among those in the highest social group. No relationship between sex or education level and RL was observed. On the other hand, a family history of renal lithiasis, hypertension, hypercholesterolemia, hyperuricemia or overweight or obesity were found to be associated with a higher prevalence of RL, but no relationship was observed, however, with the existence of DM nor the combination of hypertension, diabetes, hypercholesterolemia and obesity.

By means of multivariate analysis (Table 4), the variables that showed a statistically significant association with the presence of renal lithiasis were: being aged between 51 and 55 years or between 60 and 65 years, belonging to the upper social class, family history of RL, HBP, or overweight or obesity.

Finally, as shown in Fig. 1, a direct correlation between the prevalence of RL and average annual temperatures in the Spanish regions (Spearman's correlation coefficient; $r = 0.59$, $p = 0.013$) was observed.

Discussion

It is a proven fact that the prevalence and incidence of renal lithiasis is increasing worldwide, especially in developed countries. This is attributed, among other factors, to the rise in living standards, changes in dietary habits of the population, particularly the increase in calorie intake and abusive consumption of animal proteins and salts (precooked foods), as well as advances in diagnostic and therapeutic procedures that have improved diagnosis.[1,2]

Table 1
Socio-demographic and clinical characteristics of the population surveyed in both studies.

Variables	PreLiRenA (Andalusia) n = 2439		PreLiRenE (Spain) n = 2449		PreLiRenE (subsample Andalusia) n = 429		Total (PreLiRenA and PreLiRenE) n = 4884		*p*-Value[a]
	n	%	n	%	n	%	n	%	
Age groups									
40–45	629	25.8	594	24.3	120	28.0	1223	25.0	0.536
46–50	534	21.9	545	22.3	94	21.9	1079	22.1	
51–55	419	17.2	524	21.4	92	21.4	943	19.3	
56–60	404	16.6	376	15.4	58	13.5	780	16.0	
61–65	453	18.6	406	16.6	65	15.2	859	17.6	
Sex									
Male	1187	48.7	1193	48.8	213	49.7	2380	48.7	0.930
Female	1252	51.3	1252	51.2	216	50.3	2504	51.3	
Education level									
Uneducated	168	6.9	99	4.0	26	6.1	267	5.5	0.048
Primary	803	32.9	992	40.6	188	43.8	1795	36.8	
Secondary	791	32.4	751	30.7	121	28.2	1542	31.6	
University	603	24.7	677	27.8	94	21.9	1280	26.2	
Social class									
I (highest)	115	4.7	416	17.1	25	5.8	531	10.9	<0.001
II	315	12.9	204	8.4	39	9.1	519	10.6	
III	557	22.8	441	18.1	80	18.6	998	20.4	
IV	710	29.0	855	35.1	137	31.9	1565	32.0	
V (lowest)	748	30.6	523	21.4	148	34.5	1271	26.0	
Family history of renal lithiasis	707	29.0	579	23.7	129	30.1	1286	26.3	<0.001
Renal lithiasis	399	16.4	356	14.6	75	17.5	755	15.5	0.082
HBP	655	26.9	504	20.6	104	24.2	1159	23.7	<0.001
DM	158	7.1	170	7.0	25	6.1	328	7.0	0.885
Hypercholesterolemia	827	33.9	682	27.9	124	28.9	1509	30.9	<0.001
Hyperuricemia	126	5.2	110	4.5	26	6.1	236	4.8	0.308
Weight									
Normal weight	1050	43.1	977	41.6	144	34.9	2027	42.3	0.379
Overweight	955	39.2	1030	43.9	192	46.5	1985	41.5	
Obesity	434	17.8	341	14.5	77	18.6	775	16.2	

HBP: high blood pressure; DM: diabetes mellitus.
[a] Chi-square test, comparative analysis between the sample and the PreLiRenE and PreLiRenA studies.

According to the scientific literature reviewed[1–4,11] several factors are related to this disease that are usually displayed to a greater or lesser extent by patients with renal lithiasis and which are somehow interrelated; hence, this condition should be treated as a systemic disorder related to other health problems rather than as an isolated disease. There is sufficient evidence that renal lithiasis is associated with chronic health problems such as cardiovascular disease and hypertension, DM, high BMI or the presence of metabolic syndrome, and although unclear, the causes of this association seem to lie in metabolic processes underlying and common to all of them.[4,11]

In our study, being aged between 51 and 55 or between 61 and 65, belonging to the highest strata of society, having a family history of urolithiasis, suffering from hypertension, overweight or obesity or hyperuricemia, were associated with renal lithiasis, while DM, hypercholesterolemia or the combination of hypertension, diabetes, hypercholesterolemia and obesity (important processes that are part of the metabolic syndrome, since other factors such as hypertriglyceridemia were not included, and should be considered only as an approximation to that disease) did not reach a statistically significant association with renal lithiasis. The small number of patients with this pluripathological syndrome (only 8 of the 4884 respondents) restricted the obtainment of sufficiently accurate statistical results, and therefore relevant findings from the epidemiological standpoint.

The results of our study are consistent with those reported in published literature regarding the importance of having a family history of renal lithiasis for there to be a greater likelihood of

Table 2
Prevalence of morbidity by sex.

Morbidity	Men, No. = 2380			Women, No. = 2504			Total, No. = 4884			*p*-value[a]
	n	%	(95% CI)	n	%	(95% CI)	n	%	(95% CI)	
HBP	660	27.7	(25,9–29.5)	550	21.9	(20.3–23.6)	1159	24.3	(23.1–25.6)	0.003
DM	170	7.5	(6.1–8.2)	159	6.6	(5.4–7.3)	328	6.7	(6.0–7.4)	0.192
Hypercholesterolemia	782	32.9	(30.9–34.8)	727	29.0	(27.2–30.8)	1509	30.9	(29.6–32.2)	0.004
Hyperuricemia	180	7.6	(6.5–8.6)	56	2.2	(1.6–2.8)	236	4.8	(4.2–5.4)	<0.001
Overweight	1018	44.5	(40.8.44–8)	914	37.9	(34.6–38.4)	1932	41.2	(38.2–40.9)	<0.001
Obesity	394	17.2	(10.0–18.1)	341	13.6	(12.3–14.9)	735	16.6	(14.0–16.0)	<0.001
HBP, DM, hypercholesterolemia and obesity	39	1.6	(1.1–2.2)	26	1.0	(0.6–1.5)	65	1.3	(1.0–1.7)	0.067

HBP: high blood pressure; DM: diabetes mellitus; 95% CI: 95% confidence interval.
[a] Chi-square test.

Table 3
Relationship between socio-demographic characteristics and the pathologies considered and renal lithiasis by bivariate analysis.

Variables	Renal lithiasis, n (%)	PR (95% CI)	*p* value[a]
Socio-demographic characteristics			
Age (years)			
40–45	154 (12.6)	Reference category	0.012
46–50	168 (15.6)	1.28 (1.01–1.62)	
51–55	155 (16.4)	1.36 (1.03–1.74)	
56–60	123 (15.8)	1.30 (1.01–1.68)	
61–65	155 (18.0)	1.53 (1.20–1.95)	
Sex			
Men	363 (15.3)	0.97 (0.83–1.13)	0.697
Women	392 (15.7)		
Level			
Uneducated	39 (14.6)	Reference category	
Primary	296(15.5)	1.15 (0.80–1.66)	0.467
Secondary	225 (14.6)	1.00 (0.69–1.66)	
University	195 (15.2)	1.05 (0.72–1.52)	
Social class			
I (highest)	104 (19.6)	1.36 (1.09–1.69)	0.021
II	78 (15.0)	1.04 (0.82–1.33)	
III	154 (15.4)	1.07 (0.88–1.31)	
IV	236 (15.1)	1.05 (0.88–1.25)	
V (lowest)	183 (14.4)	Reference category	
Comorbidity			
Family history of RL	310 (24.1)	2.25 (1.91–2.65)	<0.001
HBP	259 (22.3)	1.87 (1.59–2.15)	<0.001
DM	54 (16.5)	1.11 (0.82–1.50)	0.496
Hypercholesterolemia	270 (17.9)	1.30 (1.10–1.53)	0.002
Hyperuricemia	55 (23.3)	1.71 (1.25–2.34)	0.001
Weight			
Normal weight	274 (13.5)	Reference category	0.001
Overweight	317 (16.4)	1.29 (1.08–1.53)	
Obesity	126 (17.1)	1.38 (1.11–1.73)	
HBP, DM, hypercholesterolemia and obesity	8 (12.3)	1.25 (0.65–2.42)	0.479

n = 4884; PR: prevalence ratio; 95% CI: 95% confidence interval; RL: renal lithiasis; HBP: high blood pressure; DM: diabetes mellitus.
[a] Chi-square test.

Table 4
Relationship between the socio-demographic variables and the pathologies considered and renal lithiasis by multivariate analysis (n = 4787).

Variables	OR	95% CI	*p* value[a]
Age (years)			
40–45	Reference category	–	–
46–50	1.27	0.99–1.62	0.056
51–55	1.31	1.02–1.69	0.036
56–60	1.20	0.92–1.58	0.182
61–65	1.39	1.06–1.80	0.015
Sex (male)	0.94	0.79–1.12	0.494
Level			
Uneducated	Reference category	–	–
Primary	1.37	0.94–2.01	0.103
Secondary	1.11	0.74–1.65	0.619
University	0.93	0.59–1.45	0.741
Social class			
I (highest)	1.84	1.29–2.62	0.001
II	1.45	1.00–2.10	0.048
III	1.29	0.98–1.68	0.065
IV	1.12	0.89–1.41	0.327
V (lowest)	Reference category	–	–
Family history of renal lithiasis	2.22	1.88–2.65	<0.001
HBP	1.68	1.39–2.02	<0.001
DM	1.04	0.88–1.23	0.604
Hypercholesterolemia	1.10	0.92–1.31	0.310
Hyperuricemia	1.39	0.99–1.95	0.056
Overweight/obesity	1.31	1.12–1.54	0.001
HBP, DM, hypercholesterolemia and obesity	0.76	0.36–1.61	0.481

95% CI: 95% confidence interval; DM: diabetes mellitus; HBP: high blood pressure; OR: odds ratio.
[a] Wald Test; Hosmer–Lemeshow Test: 11.950; $p = 0.153$; Omnibus Test: 155.072; $p < 0.001$.

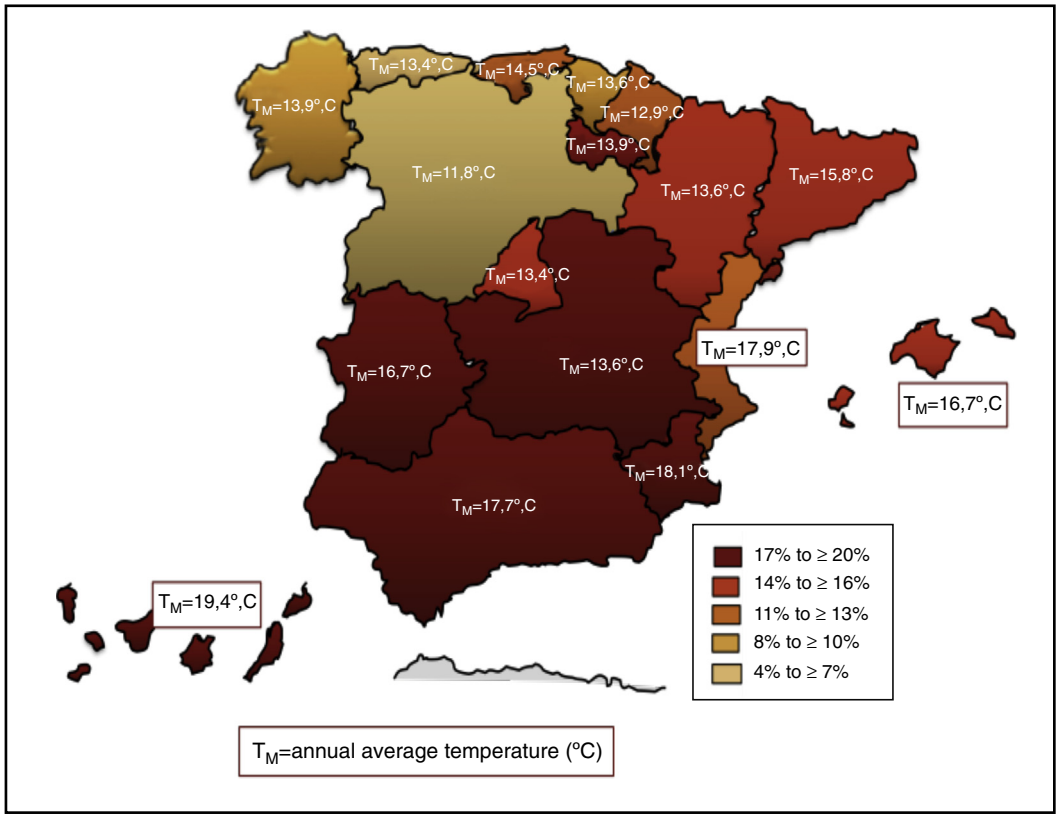

Fig. 1. Cartographic representation of the correlation between the prevalence of urolithiasis and the annual average temperature in the different regions of Spain.

developing this disease. Thus, Koyunku et al.,[12] in a study of 1595 patients with urolithiasis recruited to assess the possible effect of family history of RL on the age of onset of this disease and frequency of recurrences, found no association between both factors, such that in male patients with a background of this disease, the age of onset of nephrolithiasis was earlier than in those who did not have this, the number of recurrences also being significantly higher. These authors concluded that a family history of RL could be a predictor of the course of the disease. In our study, OR was 2.25 (95% CI: 1.91–2.65), i.e. the subjects who reported a family history of RL were more than twice as likely to develop RL as those who did not have such a family history of this disease. Other authors have estimated that a family history of RL increases the risk of suffering RL threefold.[3]

Regarding social class, Scales et al.[2] when analysing data from the NHANES 2007–2010 study, a stratified, multistage probability survey of the non-institutionalized US population, found an association between income level and the presence of RL, although in this study, unlike in ours, the risk was higher in persons of lower socioeconomic status. Social class may be a confounding factor, and what really plays a relevant role is the type of diet prevailing in each culture (the diet of North American society is very different to that of Spanish society), and the amount of daily calorie intake.[13]

Regarding the association between RL and metabolic syndrome, several cross-sectional retrospective studies have investigated this relationship.[3,14–21] The various silent features of the metabolic syndrome, including type 2 diabetes, increased BMI, hypertension and dyslipidaemia, are becoming progressively more recognized and independently associated with an increased risk of kidney stone formation. Thus, Obligado et al.,[3] among others, in a review performed to assess the association between nephrolithiasis, HBP and obesity, considered, based on the results of the studies analyzed, that the three pathologies probably share common pathophysiological mechanisms, which are conveyed through metabolic syndrome. Similarly, Daudon[22] found an increased risk of kidney stones due to uric acid in patients with DM, even concluding that nephrolithiasis could perhaps be considered as a marker of insulin resistance, mainly in obese patients, recommending DM screening in patients with kidney stones. Similar conclusions were reached by Taylor et al.[23] in their study of DM and risk of RL. In our study, no association was observed between DM and renal lithiasis, although an association was observed between the latter and hyperuricemia in the bivariate analysis, and although no significant difference was observed when adjusting other variables in the multivariate analysis, the *p* value remained very close to the established statistical threshold (OR = 1.39; $p = 0.056$).

With regard to obesity and overweight, and consistent with findings reported in other studies,[3,14,17–21] we also found a relationship between these two pathologies. Semins et al.[18] concluded that although the risk of nephrolithiasis grows as BMI increases, the magnitude of risk appears to have stabilized in the population with morbid obesity, defined as persons with a BMI≥30, contradicting the findings reported by Trinchieri et al.[1] in their updated study. Meanwhile, in a study on obesity as a risk factor for gallstone recurrence, although a significant relationship between BMI and gallstone multiplicity was found, the same findings were not observed for recurrence.[15]

Finally, it seems undeniable that climate (temperature, humidity, hours of sunlight) plays an epidemiological role in the development of RL, resulting in their greater frequency in geographical areas with warm climates.[5,24–26] Our findings corroborate this phenomenon, as we found a positive correlation of moderate intensity between the average temperatures in each region (higher the further south they lie) and the prevalence of RL in those regions. It has been confirmed that RL episodes occur more frequently during the warmer months of the year, due to increased perspiration.

This implies a more concentrated urine and a greater likelihood of crystalluria.[27]

This study has some limitations that must be taken into account when assessing the validity of the results. The study was based in probabilistic samples using formal stratification and random selection of interviewers, something rather uncommon in this type of surveys which represents a remarkable attribute. The non-response rate was rather high (31.7%), which could have caused a selection bias in the sample. Obviously, the amount of non-response is a problem. Given that the sample obtained reproduces with good fidelity the characteristics of the population in the variables gender, age, level of education or social class, we believe that the absent data could have been distributed at random, so that these losses would not have generated a bias important. Future efforts should be take this difficulty into account: proper weights to manage absent data and, possibly, the use of imputation techniques could be implemented to tackle de problem. To try to increase participation before finally discarding a selected subject, up to 30 more attempts were made to locate them. The prevalence of hypertension, diabetes, overweight/obesity and hypercholesterolemia found in our study was similar to that reported in the Spanish National Health Survey in 2011–2012, for the population aged between 45 and 64,[28] which gives consistency to our data in terms of their representativeness and external validity. On the other hand, potential information bias attributable to the observer was minimized through prior training provided to the interviewers. Moreover, these professionals already had broad and extensive prior experience in conducting sociological or epidemiological studies.

Another aspect to consider and which can also generate information bias is the validity of self-reported morbidity. Although surveys are considered to be a reliable and valid method for obtaining data on health problems in the population, rarely is information provided by patients during telephone surveys contrasted with clinical data. Studies have been carried out in our country to determine the validity of the self-declaration of other morbid processes,[29] in which the validity and reliability of self-referenced BMI in the National Spanish Health Survey are evaluated, concluding that information self-reported by subjects constitutes a valid (and also efficient) method for obtaining the data required to calculate BMI. Another example is the study by Fernández-Montero et al.[29] which analyses the validity of the components of self-declared metabolic syndrome in a cohort where the authors found an acceptable correlation between the data measured objectively in patients and self-referenced data. We also have our own data indicating that the information patients provide is reasonably reliable. In the PreLiRenA[7] study, the diagnostic agreement between interviewers and an urology expert was 93.1% (95% CI: 77.23–99.15). In the PreLiRenE study, inter-observer agreement was 70% (Kappa = 0.70; 95% CI: 0.40–0.90), which can be considered as good, thus endorsing the reliability of the method used to collect data in both studies.

The fact that women have larger renal lithiasis antecedents than men is certainly surprising. The only plausible explanation seems to be that women tend to remember their health problems than men; this could also explain the higher rates for low social class persons than those in low social class. However, this is rather speculative and could be matter of future investigation.

In conclusion, our results are in line with the available evidence certifying that risk factors such as hypertension or obesity or overweight – metabolic syndrome components – play an important role in the genesis of renal lithiasis. Family history increases the risk of renal lithiasis two-fold. There is a clear correlation between renal lithiasis and climate, being more prevalent in warmer geographical areas.

Further studies need to be carried out, ideally of a prospective nature and based on the general adult population, in order to establish causal relationships, demonstrating biological and epidemiological plausibility, between components (either together or isolated) of metabolic syndrome, dietary factors and others deriving from lifestyles, and the risk of developing renal lithiasis.

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Conflict of interest

The authors declare that they have no conflict of interest.

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