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Prevalence of renal stones in an Italian urban population: a general practice-based study

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Abstract Kidney stones represent a common condition characterized by significant morbidity and economic costs. The epidemiology of kidney stones is not completely understood and may vary substantially based on geographic, socioeconomic and clinical factors; the present study aims at defining the prevalence and diagnostic patterns of kidney stones in a cohort representative of the general population in Florence, Italy. A sample of 1,543 adult subjects, all Caucasians, was randomly selected from a population of over 25,000 subjects followed by 22 general practitioners (GPs). Subjects were administered a questionnaire requesting the patient's age and sex, any history of kidney stones and/or colics and the prescription of kidney ultrasound (US) examination. GPs data-bases were also interrogated. Crude and adjusted prevalence proportions and ratios (PRs) with corresponding 95 % confidence intervals (CIs) were computed. Furthermore, the association between the practice pattern of each physician with respect to US prescription and the prevalence of kidney stones was investigated. The overall prevalence of kidney stones was 7.5 % (95 % confidence interval 6.2, 8.9 %), increasing with age until 55–60 years and then decreasing. About 50 % reported recurrent disease. There were no significant differences in prevalence among males and females. GPs who tended to prescribe more US examinations were more likely to have more patients with kidney stones (adjusted PR 1.80, 95 % CI 1.11, 2.94; $p = 0.020$). The present study confirms both the high prevalence and the regional variability of kidney stones. Practice patterns may be involved in such variability.

Keywords At-risk groups · Case management · Chronic disease · Community medicine · Diagnostic tests · Primary care

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Introduction

Nephrolithiasis is a common disease, typically occurring between 30 and 60 years of age [1, 2]. Among the disorders of the urinary tract, kidney stones are a major cause of morbidity. Idiopathic calcium nephrolithiasis, which constitutes 70–85 % of all stones, emerged as a health problem in western countries at the beginning of the 20th century. Indeed, the prevalence of nephrolithiasis is very frequent ranging from 4 to 20 % in different studies and countries [3, 4]. In a population study in Italy, the reported prevalence in the 80's was 6 % [5]. In the majority of patients, the symptoms and the consequences are not life threatening, but stones in the urinary tract are a major cause of morbidity, hospitalisation and days lost from work [6]. In Italy for example, the number of patients receiving hospital treatment has greatly increased between 1988 and 1993, from 60,000 to 80,000 per year [7].

These statistics are outdated and often derived from hospital data. However, this condition similar to other complex diseases is very much influenced by environmental and dietary factors which have changed dramatically in the last few decades (global warming, increasing use of industrial foods, increased intake of calories and protein, etc.). On the other hand, hospital-based statistics grasp only the clinically significant episodes requiring in-hospital treatments so that (probably) the majority of asymptomatic stone cases or those treated in the general practitioner (GP) office are missed.

A precise knowledge of the prevalence of stone disease in the general population should be very important, however, for a number of reasons: (1) obtaining a precise figure of the incidence of the disease, which unfortunately is based on only very rough estimates, needs, as a prerequisite, the cross-sectional investigation of a certain cohort to be sure that the new stones are truly the incident rather than the prevalent ones; (2) a better understanding of the relationship between environmental and dietary factors and the stone disease; (3) the exact estimation of social and medical costs of the disease.

This study describes results on the prevalence of renal stones in a group of GP practices in Florence.

Methods

Study design

In the period January–May 2011, 22 GPs in Florence were enrolled in the study and instructed to administer a questionnaire to a sample of their Caucasian patients ≥18 years by January 1st, 2011 (1,543 subjects out of over 25 thousands) randomly chosen from GP's lists. In Italy, all citizens receive a free health insurance from the National Health System. To this aim all are included in the list of patients of GPs of their own choice. Thus, drawing participants from the GP's lists is like drawing them directly from the community. The questionnaire included information regarding the patient's age and sex, a history of kidney stones and/or colics and the prescription of kidney ultrasound (US) examinations. The interrogation of GPs databases allowed to collect further data and to verify the questionnaire self-reported informations.

Definitions

The presence of kidney stones was defined by a questionnaire with a reported history of kidney stones based on a positive US exam and/or symptoms (colics, stones expulsion). Of these patients, those who never experienced symptoms were defined as asymptomatic stone formers.

Subjects who had had more than one episode of kidney stones were classified as recurrent stone formers.

Data about US renal prescription were obtained for the previous 3 years.

Physicians were categorized as "high US prescriber" or "low US prescriber" based on the cut-off represented by the median value (corresponding to 29 %) of the patients being prescribed a US examination.

Statistics

We computed the prevalence and exact 95 % confidence interval (CI) of kidney stones for the overall sample and for each category of age and reported their overall values globally and separately for males and females. Furthermore, we analyzed the relationship between the prevalence of kidney stones and age (modelled as a restricted cubic spline with knots at the 25th, 50th and 75th percentile of the distribution), sex and the interaction between age and sex.

We evaluated the relationship between the prevalence of kidney stones and the prescription of kidney US by computing the prevalence of kidney stones in high and low US prescribers as well as the prevalence ratio (PR). This measure of effect is preferable to the odds ratio for its better interpretability and other favourable statistical properties [8]. The model was further adjusted for age and sex.

The statistical testing was done with the Fisher's exact test for crude 2×2 tables and with a log-binomial regression model to estimate the adjusted PRs, using the GLIMMIX procedure [9].

A $p < 0.05$ was regarded as statistically significant.

All the analyses were carried out with SAS 9.3 (Cary, NC, USA).

Sample size

The size of a simple random sample from the general population in Florence (with a total population of 367,500 subjects) was estimated with the following formula:

$$n = \frac{z_{\frac{\alpha}{2}}^{2} Npq}{\left[\delta^{2}(N-1) + z_{\frac{\alpha}{2}}^{2} pq\right]}$$

where N is the total number of subjects in the population, p is the prevalence of subjects with kidney stones, q is the prevalence of subjects without kidney stones, δ is the accepted tolerance on the estimated prevalence, α is the type I error and $z_{\alpha/2}$ is the Z value for a given value of α. With a type I error of 0.05 and an expected prevalence of subjects with kidney stones of 6 % and a 20 % tolerance, the estimated sample size would be of 1,498 subjects.

Patients were randomly chosen from each GP list by random number tables.

Results

All 1,543 subjects were investigated, mean age 52.9 ± 19.9 years, Male to Female ratio 0.79. The overall prevalence of stone disease (either current or previous) was 7.5 % (95 % CI 6.2, 8.9 %) (115 cases). The prevalence of the disease in males was higher than in females (8.5 vs. 6.6 %, respectively); however, the difference was not statistically significant (PR 1.29, 95 % CI 0.91, 1.84; $p = 0.172$). The prevalence of kidney stones in each age category is shown in Table 1. Stone disease showed an increase in prevalence until the 60's and then a decrease.

In the regression models with presence of kidney stones as dependent variable, the overall test for the interaction terms between age and sex was not significant. Furthermore, the main effect of sex was not significant and it did not show any confounding effect on the relationship between stone disease and age, so it was removed from the model together with the interaction terms. The relationship between kidney stones and age was significant ($p < 0.001$) (Fig. 1).

Fifty percent (58 cases) of stone patients had a recurrent disease, and 18 (15.7 % of stone formers) had asymptomatic stones. However, since only 28 % (405 subjects) of non stone formers had undergone kidney US as opposed to 81 % of stone formers, the prevalence of nephrolithiasis in this general population could be higher. Assuming that randomly performed US is capable of detecting all asymptomatic stones, the prevalence of asymptomatic stones in the general population would be 4.4 %. Considering that the prevalence of symptomatic stone disease was 6.3 %, the global prevalence of stone in this general population could be estimated around 10.5 %.

Restricting the analysis to subjects who reported no US exam in the previous three years ($n = 1{,}039$), the prevalence of kidney stones was 2.1 %. This figure may represent an indirect estimate of the 3 years incidence of symptomatic stones.

The mean number of patients per GP was 70 (range 55–80). The mean number of total and symtpomatic stone formers per GP was 5 (range 0–12) and 1 (range 0–5), respectively.

The prevalence of the stone condition in each practice was highly variable, from less than 2 % to >16 % (Fig. 2). US prescription among GPs was also highly variable (Fig. 3). Among high US prescribers (i.e., physicians who tended to prescribe more US examinations to their patients) the prevalence of stone disease was significantly higher when compared with low US prescribers (9.8 vs. 5.2 %; PR 1.89, 95 % CI 1.30, 2.73; $p < 0.001$). Adjustment for patients' age and sex did not change the findings substantially (PR 1.80, 95 % CI 1.11, 2.94; $p = 0.020$).

Table 1 Prevalence of stone disease by sex and age category

	Enrolled subjects	Stone disease	Recurrent stone disease[a]
Males			
<30	97	1 (1.0 %)	1 (100 %)
30–39	97	3 (3.1 %)	2 (66.7 %)
40–49	139	11 (7.9 %)	6 (54.6 %)
50–59	100	15 (15.0 %)	7 (46.7 %)
60–69	94	16 (17.0 %)	8 (50.0 %)
70–79	101	7 (6.9 %)	5 (71.4 %)
≥80	51	5 (9.8 %)	0 (0.00 %)
Females			
<30	108	6 (5.3 %)	1 (20.0 %)
30–39	134	9 (6.7 %)	5 (55.6 %)
40–49	135	7 (5.2 %)	2 (28.6 %)
50–59	133	13 (9. 8 %)	7 (53.9 %)
60–69	119	8 (6.7 %)	4 (50.0 %)
70–79	124	9 (7.3 %)	6 (66.7 %)
≥80	110	5 (4.6 %)	2 (40.0 %)

[a] The percentage refers to the proportion of recurrence among stone formers

Discussion

The present study shows that the prevalence of the renal stone condition in the general population older than 18 yrs is approximately 7.5 %, a higher figure than previously reported prevalence in Italy [5]. In a different, though contemporary setting, in a large general Northern Italian population ≥40 years [10], the self-reported prevalence of renal stones was 12.4 % (unpublished) higher than the prevalence observed in subjects 40 years old or more of the present cohort (8.8 %, $p < 0.001$). The difference in prevalence may be due to more rigorous criteria for the definition of stone episodes in the present study. A previous study in North Italy found an incidence of stones comparable with other western European countries [11]. Notwithstanding the prevalence of the disease seems to be definitely higher than in the past in Italy. This data confirms an increasing trend of stones for the Italian population [12].

The prevalence of asymptomatic stones can be estimated in 4.4 %, lower than in a recent study from an American cohort of potential kidney donors (10 %) [13]. The higher prevalence in the latter can be explained by both, a more accurate radiological diagnosis and the higher prevalence of renal stones in the United States [3].

That approximately 50 % of stone formers have a recurrent condition is a well-known notion since, provided that the follow up is sufficiently long, a large percentage of renal stone patients recurs [14].

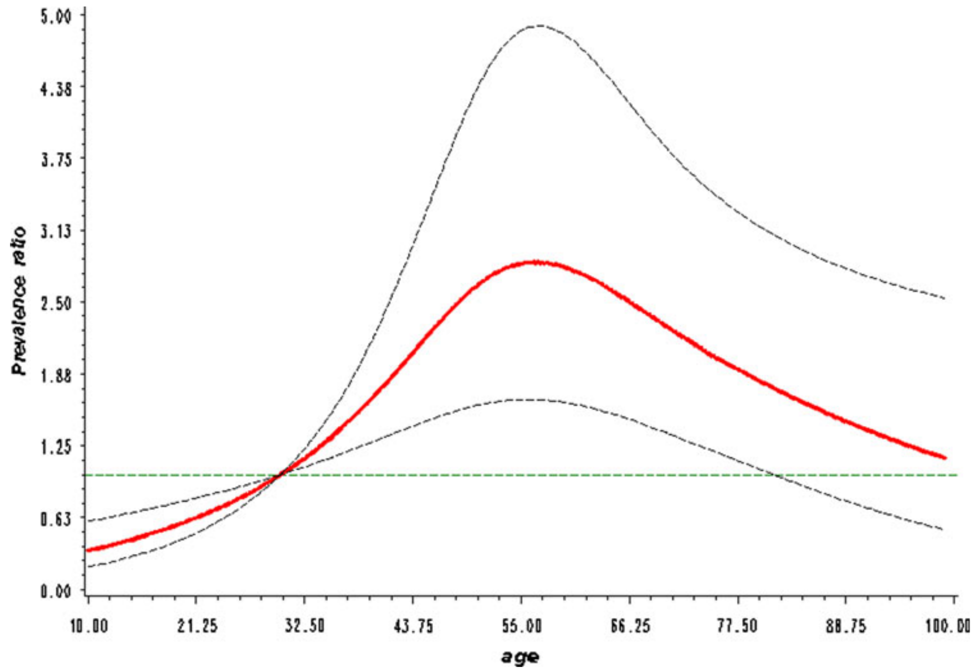

Fig. 1 Prevalence ratio for stone disease associated with age. *Solid line* represents the prevalence ratio (30 years as the reference value); *dotted lines* represent 95 % confidence interval; *horizontal line* represents a prevalence ratio of 1

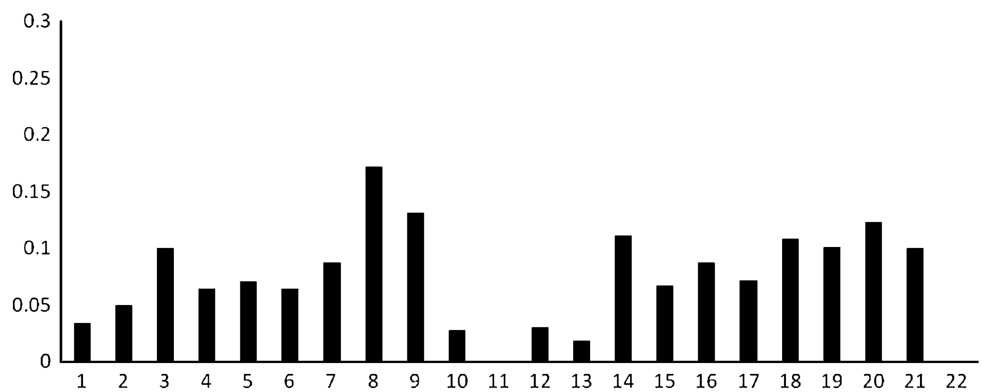

Fig. 2 Differences in stone disease prevalence among physicians. Each *bar* represents the proportion of patients with stone disease for each physician

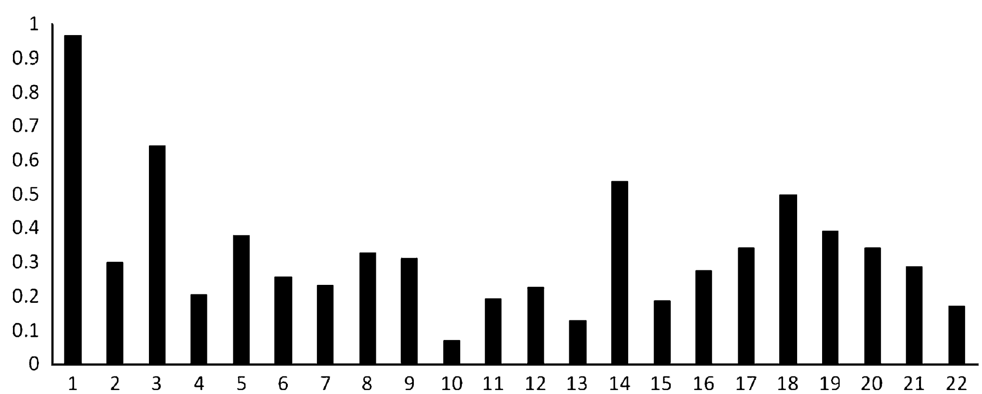

Fig. 3 Differences in US prescription among physicians Each *bar* represents the proportion of patients with US for each physician

Whereas the increasing prevalence of the renal stone condition in the 4th and 5th decades observed in this study was expected because of both cumulative cases and the known increasing incidence of the disease [4], the noteworthy decrease in subjects older than 70 years is puzzling. We may advance two possible explanations. The first is that we are observing the long tide of the changes in nutritional behaviours favouring nephrolithiasis which occurred in our population too in those who were teenagers in the 60–70s [15], while people older than 70 was not affected by these changes. The second is that people older than 70 years are the "healthy survivors" of a population in which, according to recent studies [16, 17], the stone formers seem to have a higher cardiovascular risk than non-stone formers.

Interestingly, our data confirm what have been described by others [18], i.e. a trend toward equal overall prevalence between genders possibly because of nutritional changes in females.

The analysis of data of single GPs disclosed a positive relationship between prevalence of stone formers and use of US imaging. The interpretation of this datum is double faced. With the limitation that the questionnaire did not investigate the temporal relationship, if any, between stone episodes and the US request, it is self-evident that stone episodes (i.e. colics, gross hematuria) often lead to requesting US. So, the higher the number of stone patients, the higher the demand for US. On the other hand, a systematic use of abdominal US may disclose stones that have not yet given any manifestation. Our data would support the hypothesis of US prescription leading to diagnosis of stone disease as opposed to that of patients with stones being prescribed US more often, since the prescription of US in stone-negative patients followed by high US prescribing GPs was substantially higher when compared with stone-negative patients followed by low US prescribing GPs (48.5 vs. 19.9 %; $p < 0.001$). If one would hypothesize that the number of US prescriptions be driven by stone patients, one would expect that the number of US exams in stone-negative patients be comparable. Instead, these differences suggest different policies among GPs in requesting US (Fig. 3) and a different proportion of subjects with stone disease as a consequence. However, none of these explanations fully elucidate our data. It is interesting to note that the prevalence of the disease was dramatically different among GPs, ranging from less than 2 % to values higher than 16 %. These differences are so huge that they cannot be explained by different policies in prescribing US, or by different age profile of patients in each practice. Certainly, numbers of investigated subjects per doctor were low, so that a type 2 error cannot be ruled out. Furthermore, possible familial clusters of the disease could occur in some specific GP cohort. However, as previously observed, the study discloses very different policies between GPs in asking for US. Since the practices were all in the Florence area where imaging investigations, and specifically US are freely available in Hospitals of the National Health Service, the highly variable demand by doctors of US deals with their specific diagnostic styles. This unexpected issue is of potential great interest and needs further research.

The study has a number of limitations. The relatively small case population does not provide deeper insights into the data analysis in reference to some aspects of the disease (recurrent cases, gender effect, etc.). The precise prevalence can only be estimated since not all subjects performed an US. Furthermore, the diagnostic performance of US in detecting urinary stones is suboptimal [19]. Thus, the prevalence of the renal stone condition could be even higher than the estimated one. Although self-reported episodes were verified by the GPs, not all episodes were recorded in the GPs' data-bases or had a clinical documentation. Thus the study is largely based on self reports and is retrospective. This is one more reason for which the prevalence estimation is not precise and it explains why it was not possible to investigate the prevalence according to the chemical nature of stones and analyse data in reference to this aspect. Furthermore, the accuracy of US for diagnosing small kidney stones is fairly low, another element that might have led us to understimate the true prevalence of this condition.

In our study, one GP had the highest rate of US prescription and also a very low prevalence of patients with stones. It is difficult to explain such an inconsistency; however, the analysis should not be biased by this outlier since the rate of US prescription has been analyzed as a dichotomous variable (e.g., above or below the median US prescription for the GP population).

In conclusion, the present study confirms the high prevalence of the renal stone disease in an urban Italian population, supporting the idea that its prevalence has increased over the last decades particularly in females. The study also discloses different policies between GPs in the diagnostic use of US.

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