Changes in kidney stones type according to sex and age in Tunisian patients

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PALABRAS CLAVE
Piedra; Espectrofotometría; Rínón; Niños; Adultos;

Abstract
Background: Studies that evaluate the effect of age and gender on the stone composition are scarce. The aim of this study is to highlight the modification of epidemiological characteristics of this pathology according to patients’ sex and age.
Patients and methods: We studied 1269 urolithiasic patients ranging from 6 months to 92 years old and known as having urinary stones (752 males and 517 females). Stone analysis was performed respectively using a stereomicroscope and infrared spectroscopy to determine, respectively, the morphological type and molecular composition of each.
Results: The annual average incidence of new stone formation was 30.25 per 100,000 inhabitants. In 1041 patients (81%), calculi were located in the upper urinary tract. Children and old men were more affected by bladder stones. Calcium oxalate monohydrate remains the most frequent stone component even if its frequency fell according to age (63.2% in teenagers and 40.6% in the elderly [p<0.05]) in favor of the increase of uric acid stones (3.5% in teenagers and 41.5% in the elderly [p<0.05]). Struvite stones were rare (3.5%) and more frequent in children.
Conclusion: The analysis of these data shows that urinary stones in Tunisia are tending to evolve in the same direction as in industrialized countries.
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Cambios en el tipo de cálculos renales según sexo y edad en pacientes tunecinos

Resumen
Objetivos: Los estudios que evalúan el efecto de la edad y el género sobre la composición de las piedras renales son escasos. El objetivo de este estudio es subrayar la modificación de las características epidemiológicas de esta patología de acuerdo con el sexo y la edad de los pacientes.

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Material y métodos: Estudiamos a 1.269 pacientes con urolitiasis de edades comprendidas entre 6 meses y 92 años y que se conocía que tenían cálculos urinarios (752 varones y 517 mujeres). Se realizó un análisis de las piedras usando un microscopio estereoscópico y espectroscopia infrarroja para determinar respectivamente el tipo morfológico y la composición molecular de cada una.

Resultados: La incidencia anual promedio de formación de nuevas piedras fue de 30,25 por cada 100.000 personas. En 1.041 pacientes (el 81%) los cálculos estuvieron localizados en el tracto urinario superior. Los niños y ancianos fueron más afectados por piedras en la vejiga. El monohidrato de oxalato de calcio sigue siendo el componente más frecuente de los cálculos, a pesar de que su frecuencia cae en relación con la edad (63,2% en adolescentes y 40,6% en ancianos \(p < 0.05\)). Las piedras de estruvita fueron raras (3,5%) y más frecuentes en niños.

Conclusión: El análisis de estos datos muestra que los cálculos urinarios en Túnez tienden a evolucionar en la misma dirección que en países industrializados.

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Introduction

Since 1980, the urban expansion that followed the economic development has broken the traditional ties and created new social and cultural environments in our country.\(^1\) Westernization of the lifestyle and improved medical care\(^2\) increase life expectancy, which inevitably leads to an increase in the number of patients with lithiasis in relation to age. Only a few reports to date have suggested that relation between stone composition and age of the patient.\(^1,3,4\)

In 1995, Daudon et al.\(^3\) reported an increased frequency of uric acid stones in relation to the patient’s age, which reaches its peak in the range of 60–70 years. In Japan, Koide et al.\(^4\) reported that the peak frequency of calcium oxalate urolithiasis was observed between 40 and 50 years of age.

Urolithiasis in developing countries was considered very different from that observed in industrialized countries.\(^6\) In Tunisia, the studies evaluating the epidemiological characteristics of urolithiasis are scarce, and they were based on a limited number of patients.\(^1\)

This study is a pioneer in Tunisia, because it examines 1269 patients with stones over 10 years in order to examine the relation between age and composition of the calculi.

Materials and methods

Between July 2000 and September 2010, 1269 patients with stones were diagnosed at the departments of Pediatrics and Urologic Surgery of the University Hospital of Monastir. The ages of these patients were between 6 months and 92 years; 752 were men and 517 women. In order to make our work easier and CLEVER, we divided our patients into 5 groups according to age: children, teenagers, young adults, adults, and elderly people.

The experiments and analyses conducted in our study were approved by the Ethics Committee of the University Hospital of Monastir.

Where possible, we identified the structure of each calculus using a stereoscopic microscope to determine its morphological appearance and to select its representative parts (core, outer section, and external surface), in order to determine its molecular and crystal composition by infrared spectroscopy. From 0.5 to 2 mg was sprayed on each part of the stone with a base in an inert powder (anhydrous potassium bromide) in a proportion of 0.5–2% in an agate mortar. This mixture was transferred to a suitable container and pressed at 10 t/cm\(^2\) to form a transparent sphere of 13 mm in diameter. The spectral region investigated was that of 4000–400 cm\(^{-1}\). The reference spectra were spheres of pure potassium bromide (KBr). The spectra were included using a Bruker Fourier Transform infrared spectrometer IFS25 (Bruker Inc., Wissembourg, France).

An overall powder of the sample was analyzed to quantify the relative proportions of the different components of the stone. Only the qualitative and quantitative compositions obtained from the total powder of the stone were used as study material in this report.

The different compounds were identified by comparison with reference spectra previously published. The results were expressed according to the main crystalline phase found in the stones and they were named as follows: wewelite (calcium oxalate monohydrate), wedelite (calcium oxalate dihydrate), carbapatite (carbonated calcium phosphate crystallized in a hexagonal pattern), struvite (hexahydrate magnesium ammonium phosphate) and calcite (anhydrous calcium carbonate).

The component of the stone was considered the main element if it exceeded the total composition of the calculus. The stones made of a single component were classified as pure stones, and those with more than one component as mixed stones.

The statistical analysis of the data was performed using the SPSS 11.0 for Windows. Statistical significance was determined by the \(\chi^2\) tests. \(p\) values \(< 0.05\) were considered significant.

Results

The average annual incidence of new stone formation was 30.25 per 100,000 inhabitants. The annual incidence was 7 per 100,000 inhabitants in the pediatric age group and 53.5 in both adults and elderly people. The most common method for removal was conventional surgery, with 81.6% of operations versus 13.9% of extracorporeal lithotripsy, 2.8% of spontaneous expulsions, and 1.7% of endoscopies.

Of the 1269 patients with urolithiasis, 752 (59%) were men and 517 (41%) women, with a sex ratio of 1.45:1.
The age of the patients in the presentation was between 6 months and 92 years. Table 1 shows the number of patients stratified by ages and sexes. The greatest number of calculi was observed in age groups 0–9, 40–49, and 50–59 years in men and women, respectively.

There was a family history of stone disease in 51 patients (4%) (15 children, 15 teenagers, and 21 adults). This study showed stone recurrence rates of 22.5% after 20 years of age (285 cases). The incidence of recurrence of calculi in patients who were radiographically free of stones after extracorporeal shock wave lithotripsy was 34%.

Five hundred and forty cases (42.6%) had obstructive stones. In 1041 patients (81%), the calculi were located in the upper urinary tract (kidney and ureter). Children and elderly people were the most affected by bladder stones (Fig. 1), without noticeable difference between the sexes. Prostatic hyperplasia was associated with the finding of bladder stones in 10 elderly males.

As shown in Table 2, the most common components of the urinary calculi determined by infrared spectroscopy were wedelite (66.1%) and wedelite (31.3%). However, their frequencies vary according to age. The wedelite was significantly more common in teenagers (38.6%) and young adults (35.6%) than in the elderly (p < 0.05). The proportion of uric acid of all the stones was 22.7%, and it was more prevalent in the elderly than in other age groups (p < 0.001). While the ammonium urate was predominant in children (p < 0.001), the stones containing carbapatite and struvite were more frequent in children and teenagers than in the other age groups (p < 0.001).

Calcium oxalate was the main component in 59.3% of the cases (Fig. 2). Fig. 3 shows the relative proportion of the main components of the stones observed in men and women. The calcium oxalate monohydrate (wedelite) was the most common major component in the stones of all age groups, and it was more abundant in female patients than in their male counterparts in the first two decades (p < 0.2). The struvite stones were more common in boys than in girls (p < 0.001).

The proportion of uric acid increased continuously with age from 5.5% in the age group 6 months–19 years to 41.5% in the patients of 70 years or more. The uric acid was more prevalent in female patients than in males in the age groups of adults and elderly people.

Discussion

Changes in socioeconomic conditions have led to variations in the incidence and types of urolithiasis in terms of both

| Age groups | Age (years) | Men | | | Women | | | Total | | |
|------------|-------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Children   | 0–9         | 137 | 18.2| | 81  | 15.7| | 218 | 17.2|
| Teenagers  | 10–19       | 26  | 3.5 | | 31  | 6   | | 57  | 4.5 |
| Young adults| 20–29       | 51  | 6.8 | | 41  | 7.9 | | 92  | 7.2 |
| Adults     | 30–39       | 60  | 8   | | 56  | 10.8| | 116 | 9.1 |
| Adult      | 40–49       | 130 | 17.3| | 77  | 14.9| | 207 | 16.3|
| Adults     | 50–59       | 125 | 16.6| | 82  | 15.9| | 207 | 16.3|
| Adults     | 60–69       | 92  | 12.2| | 63  | 12.2| | 155 | 12.2|
| Elderly people | 70–79 | 90  | 12  | | 55  | 10.6| | 145 | 11.4|
| Elderly people | ≥80    | 41  | 5.5 | | 31  | 6   | | 72  | 5.7 |
| Total      |             | 752 | 100 | | 517 | 100 | | 1269| 100 |

Figure 1 Changes in the location of the calculi according to age and sex (n=1269). F: female; M: male.
location and chemical composition of the calculi. Important variations have been described in the occurrence of urolithiasis worldwide depending on geographical areas and historical periods.5

We found that the annual incidence of new stone formation in Tunisian patients was 30.25 per 100,000 Tunisians. This rate is similar to that reported in England (22 per 100,000 inhabitants)6 and Kuwait (23.9 per 100,000). It is, however, significantly different from that described in Sweden (140 per 100,000 inhabitants),9 Italy (168 per 100,000 inhabitants),10 and the U.S.A. (277 per 100,000 inhabitants).11

In Europe, the urinary calculi are primarily located in the upper urinary tract, and the bladder calculi ratio does not exceed 10%.3,12 It has been found that bladder stones are more common in the elderly, as reported by some studies,13 but not by others.12 According to Daudon et al.,40% of the patients are men over 80 years.13 In our study, 19% of the stones were bladder calculi and the elderly men were the most affected (31.3%). Prostatic hyperplasia, considered a common cause of distal bladder obstruction, is common in old men and it could be a possible explanation for the high frequency of bladder stones in the elderly.13,14 Women were also exposed to lower urinary tract calculi (25.6%), suggesting other risk factors, such as changes in bladder function in the elderly, associated with relaxation of toxicity of the smooth muscle, which could reduce the efficiency of bladder emptying and promote urinary stasis.13

The pattern of urolithiasis in adult patients is not different from that observed globally.15 The composition of the stones has changed substantially over the last decades, with a progressive increase in the frequency of calcium oxalate stones, representing 70–80% of the stones.16 According to Daudon et al.,17 in the case of developing countries, the calcium oxalate stones occur mainly in North Africa and Asia Minor. In our study, calcium oxalate stones were found in 59.3% of the cases. This rate is comparable with other French,5 Brazilian,18 and Spanish19 studies.

Daudon et al.,1 using a multivariate approach based on the correspondence factor analysis, confirmed the relation between the composition of the stones and the age of the patients. However, some variations have been described depending on geographical areas. In 1993, Baker et al.,20 reported that, in Australia, the peak frequency of calcium oxalate urolithiasis was observed between 50 and 60 years. Studies in Europe had shown that calcium oxalate stones were more common in people between 40 and 50 years old.3,19,21 In Asia, apparently, the peak frequency of calcium oxalate stones occurs at younger ages (30–50 years).4 In our study we found a peak frequency of calcium oxalate urolithiasis between 10 and 39 years, which has also been noted in neighboring countries to ours.22

The monohydrated form (wewelite) was 2.1 times more abundant than the dihydrated form (wedellite). The wedelite calculi occurred at younger ages in women than in men patients, and they decreased in frequency according to age, which is similar to the publications of Algeria4 and France.7 The smaller decrease in wedellite calculi in women might be related to changes in calcium metabolism during menopause, to demineralization and, therefore, to hypercalcuria.5,19 Abrams et al. reported that both vitamin D deficiency and a decreased ability to absorb dietary

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**Table 2** Distribution of stone components according to age.

<table>
<thead>
<tr>
<th>Composition</th>
<th>Children 0–9 years</th>
<th>Young adults 20–39 years</th>
<th>Adolescents 10–19 years</th>
<th>Adults 40–69 years</th>
<th>Elderly people ≥ 70 years</th>
<th>Total (n = 1269)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amount</strong></td>
<td><strong>%</strong></td>
<td><strong>Amount</strong></td>
<td><strong>%</strong></td>
<td><strong>Amount</strong></td>
<td><strong>%</strong></td>
<td><strong>Amount</strong></td>
</tr>
<tr>
<td>Wewelite</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Wedellite</td>
<td>138</td>
<td>63.3</td>
<td>67</td>
<td>20</td>
<td>29</td>
<td>1.8</td>
</tr>
<tr>
<td>Uric acid</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Carbonate</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Ammonium urate</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Oxalate</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Cystine</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
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<td>0</td>
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</tr>
<tr>
<td>PACC</td>
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<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Calcium</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Sodium ammonium</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Xanthine</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Valerate</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Aragonite</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Changes in kidney stones type according to sex and age in Tunisian patients

Calcium were more prevalent in the elderly. This could partly explain the decrease in frequency of wedellite and wewellite in old individuals. In fact, a greater amount of dietary calcium remains available in the intestine to bind to the oxalate and, thus, reduce the absorption of oxalate and the subsequent concentration of oxalate in urine.

The uric acid stones were the second most common in both sexes. The frequency of uric acid calculi (21.4%) was from two to three times higher than that reported in studies of Algeria (8.8%) and France (6.9–10.7%). As reported in industrialized countries, our data show a clear increase in the proportion of uric acid stones depending on age in both sexes. According to the well-established dependence of uric acid urolithiasis on pH, the increasing proportion of uric acid with age could be a progressive defect in the genesis of urinary ammonia which occurs with age, an important factor causing a low urinary pH in uric acid stone formers.

According to Daudon et al., diabetic patients are more likely to be affected by uric acid calculi. Additionally, recent studies have suggested an increase in the prevalence of urolithiasis by year and in the recurrence associated with obesity, elevated urinary excretion of calcium, uric acid, and oxalate. Now we know that overeating, which contributes to the development of obesity, is strongly involved in diabetes, kidney stones, and hypertension. These risk factors, such as obesity, diabetes, and hypertension, will have to be taken into account by epidemiological research.
in order to avoid confusion with the influence of age on the composition of the calculi, and to have representative data.

Struvite remains the best marker of urinary tract infections by bacteria that produce ureases. Stones related to the infection were observed in 3.5% of the cases, which is comparable with the European data,\textsuperscript{1,35} but lower than what reported by the publication of Algeria.\textsuperscript{22} The struvite stones were more common in men than in women, and they were slightly more frequent in the extreme ages of life, especially in children and young people.

**Conclusion**

Although the data about kidney stones in Tunisia are scarce, our data provide an idea about their epidemiological characteristics. The calcium oxalate stones remain the most frequent component in all age groups, even when their frequency decreases in the elderly. As described in other studies, the uric acid stones increase in proportion with age, and the stones related to infection are rarely seen in adults. The analyses of these data show that urinary calculus in Tunisia tend to evolve in the same direction as in industrialized countries.

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**Conflict of interest**

The authors declare that they have no conflict of interest.

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