World Journal of Urology (2022) 40:2099–2103
https://doi.org/10.1007/s00345-022-04058-4

ORIGINAL ARTICLE

Are there seasonal variations in renal colic in uric acid stone formers in Germany?

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Received: 26 January 2022 / Accepted: 16 May 2022 / Published online: 11 June 2022

Abstract

Purpose Seasonal variations in renal colic have been described by many authors for different countries worldwide. In most studies, there was no differentiation with regard to stone composition. Recently, we demonstrated that there was no seasonal variation in renal colic and urine chemistry for calcium oxalate stone formers in Germany. As we have many uric acid stone formers (UASFs) in our region, we were interested in learning the situation of this type of stone.

Methods We studied 286 consecutive UASFs with symptoms of renal colic. We divided them into four groups according to the quarters of the year. For stone analysis, X-ray diffraction/polarizing microscopy was used. Additionally, the following general parameters were examined in all patients: age, BMI, blood pressure, stone frequency, diabetes mellitus; blood: creatinine, glucose, uric acid, calcium, sodium and potassium; urine: pH, volume, calcium, uric acid, citrate, ammonia, and urea. Using the statistical program Prism 5 (GraphPad Software, San Diego, USA), significant differences between the four groups were calculated by the Kruskal–Wallis test.

Results We observed significantly more UASFs with renal colic in the third and fourth quarters of the year. This is in contrast to our findings in calcium oxalate patients. However, there was no variation in metabolic parameters.

Conclusion The reasons are unclear; different temperatures are not a sufficient explanation, as one quarter is in the warm season and the other one is in the cold season. Unfortunately, no data have been reported in the literature thus far. Further studies are required to better understand these findings.

Keywords Renal colic · Urolithiasis · Uric acid · Seasonal variations · Climate · Urine composition

Introduction

Urolithiasis affects approximately 5% of the population, and the lifetime risk of passing a stone in the urinary tract is estimated to be 8–10% [1, 2]. Urinary stone formation is highly variable, and certain risk factors, such as age, sex, anatomic abnormalities, and metabolic diseases, have been identified. The prevalence of renal calculi in the United States as well as Germany [3] has risen over the past decades. It is assumed that the gradual and long-term increase in ambient temperatures due to global warming via greenhouse gases will induce a rise in urolithiasis-related morbidity [4, 5]. This has been confirmed recently in the United States, where the incidence of urolithiasis rose from 0.6% in 2005 to 0.9% in 2015 [6].

However, the trend of increasing prevalence of urinary stones in hot climates is not necessarily universal. The incidence of urinary stones is quite low in Nigeria [7] but extremely high in Middle Eastern Gulf states, such as Kuwait, the United Arab Emirates, and Saudi Arabia [8].

Seasonal variations in renal colic have been described by many authors for different countries worldwide [1, 9–13]. Recently, we demonstrated that there was no seasonal variation in renal colic and urine chemistry for calcium oxalate stone formers in Germany [14]. In most studies, there was no differentiation with regard to stone composition. As we have many uric acid stone formers (UASFs) in our region [15], we were interested in learning the situation of this type of stone.

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Materials and methods

A total of 286 consecutive uric acid stone formers (UASFs) with symptoms of renal colic treated from 2015 to 2017 in the Department of Urology and Paediatric Urology at the Regiomed-Klinikum in Coburg, Germany, were studied. The catchment area of our department comprises approximately 500,000 inhabitants, which is half of the population of Upper Franconia.

Stone analysis was performed via polarization microscopy and X-ray diffraction.

According to the quarter of the year of the acute stone episode, patients were divided into four groups.

Furthermore, a detailed history including the number of stone episodes was recorded. Arterial blood pressure (BP) was measured according to the recommendations of the World Hypertension League while the patient was sitting after 5 min at rest.

The metabolic evaluation was performed 1–4 weeks after spontaneous stone passage or endourological stone removal. The following parameters were measured in all patients: urine pH profiles on 3 consecutive days in the morning (fasting), noon (postprandial) and evening (postprandial). For urine pH measurements, dipsticks, which allowed pH measurements in 0.1 steps (Madaus GmbH, Cologne, Germany), were used. The mean urinary pH was calculated in every patient.

Blood was drawn to determine creatinine (Jaffé reaction, Dade Behring Marburg, Germany), potassium (atomic absorption), calcium (indirect ion sensitive electrode), glucose (postprandial; hexokinase-glucose-6-phosphate dehydrogenase method, Flex™ Siemens Healthcare Diagnostics Newark, DE, USA) and uric acid (modified uricase method, Dade Behring Marburg, Germany) levels. A 24 h urine specimen was collected to measure the excretion of citrate (citrate lyase method, Boehringer Mannheim, Germany), creatinine (Jaffé reaction, Dade Behring Marburg, Germany), calcium (indirect ion sensitive electrode), uric acid (modified uricase method, Dade Behring Marburg, Germany), ammonia (modified glutamate dehydrogenase method using NADPH, test kit Ammonia Flex™, Dade Int., Newark, DE, USA) and urea (urease-glutamate dehydrogenase, Dade Behring Marburg, Germany) as markers for protein intake.

General parameters and blood and urine values were also grouped according to the quarters of the year.

For statistical analysis, means and standard deviations were calculated. Significant differences between the four groups were assessed using the Kruskal–Wallis test.

Differences were considered significant at $p < 0.05$. For these analyses, the program Prism 9 (GraphPad Software, San Diego, CA, USA) was used. Calculations were performed on a personal computer.

Results

The study population consisted of 182 males and 104 females (sex ratio male: female = 63.6:36.4%). There was no significant difference in the sex ratio between the four quarters. The mean age of our UASFs was 62.4 years, and the mean BMI was 27 kg/m^2. The mean age of our patients was also not different between the four quarters. There was a high percentage of patients with diabetes mellitus (36.9%). Forty-eight percent of our patients were hyperuraemic (males > 7.0, females > 5.7 mg/dl), and 77% were hypocitraturic (< 2.00 mmol/d). The number of stone episodes in this cohort was 2.07. None of these parameters showed significant differences between the four quarters.

Figure 1 shows the number of patients with renal colic treated in the four quarters of the year. In quarters three and four, there were significantly more acute episodes than in quarters one and two.

Tables 1, 2, 3 show the mean values and standard deviations of general, blood and urine parameters (including the risk factors for UA stone disease) in our patients grouped according to the four quarters of the year. Apart from serum creatinine in the first quarter, there were no significant differences throughout the four quarters of the year in any of the parameters examined ($p > 0.05$).

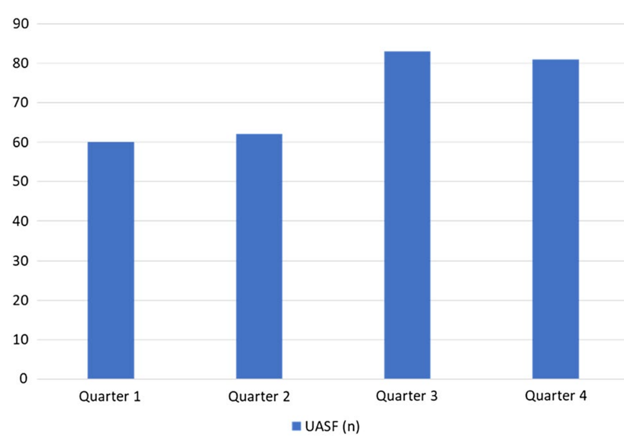

Fig. 1 Distribution of UASFs presenting with renal colic according to the four quarters of the year. Significant differences between quarters 1/2 and 3/4 ($p < 0.05$)

Table 1 Variations in general parameters (means ± standard deviations) according to the four quarters of the year

	Quarter 1	Quarter 2	Quarter 3	Quarter 4
Age (years)	62.6 ± 11.6	63.4 ± 11.6	63.1 ± 14.1	60.4 ± 13.5
BMI (kg/^{2})	31.2 ± 7.3	31.5 ± 4.9	30.3 ± 5.8	31.1 ± 6.1
Diab. mellitus (%)	38.3	30.3	37.4	33.3
Stone episodes (*n*)	2.4 ± 1.8	1.8 ± 1.1	2.0 ± 1.2	2.1 ± 1.5
BP sys (mm Hg)	141 ± 13	144 ± 17	141 ± 14	142 ± 15
BP dia (mm Hg)	83 ± 7	83 ± 8	81 ± 8	82 ± 8

No significant differences ($p > 0.05$)

Table 2 Variations in blood parameters (means ± standard deviations) according to the four quarters of the year

	Quarter 1	Quarter 2	Quarter 3	Quarter 4
Creatinine (mg/dl)	1.1 ± 0.3*	1.4 ± 0.6	1.3 ± 0.3	1.2 ± 0.4
Sodium (mmol/l)	139 ± 3	138 ± 3	140 ± 4	139 ± 3
Potassium (mmol/l)	4.3 ± 0.4	4.2 ± 0.4	4.2 ± 0.5	4.2 ± 0.4
Calcium (mmol/l)	2.3 ± 0.2	2.3 ± 0.1	2.3 ± 0.2	2.2 ± 0.2
Uric acid (mg/dl)	6.4 ± 1.9	6.9 ± 1.9	7.0 ± 1.7	7.0 ± 1.5
Glucose (mg/dl)	134 ± 54	136 ± 43	145 ± 63	151 ± 76

*Significant difference ($p = 0.0061$)

Table 3 Variations in urine parameters (means ± standard deviations) according to the four quarters of the year

	Quarter 1	Quarter 2	Quarter 3	Quarter 4
pH	5.9 ± 0.2	5.9 ± 0.2	5.9 ± 0.3	6.0 ± 0.2
Volume (l/d)	2.4 ± 1.3	2.5 ± 1.1	2.4 ± 1.9	2.4 ± 1.1
Calcium (mmol/d)	2.7 ± 1.8	2.9 ± 2.2	3.0 ± 2.4	3.4 ± 2.6
Uric acid (mmol/d)	3.4 ± 1.6	3.5 ± 1.7	3.4 ± 1.5	3.6 ± 1.7
Citrate (mmol/d)	1.5 ± 1.3	1.3 ± 1.2	1.3 ± 1.2	1.6 ± 1.2
Urea (mmol/d)	355 ± 166	366 ± 166	362 ± 135	353 ± 164
Ammonia (mmol/d)	41 ± 23	39 ± 21	39 ± 19	39 ± 26

No significant differences ($p > 0.05$)

Discussion

This is the first study on seasonal variations in acute episodes in UASFs in Europe. Our results are based on a large number of UASFs, as uric acid stones are very common in individuals living in our region of Upper Franconia [15]. Contrary to our study on calcium oxalate stone formers [14], regarding UASFs, we observed significantly more people with renal colic in the third and fourth quarters of the year. This observation is in accordance with the report of Baker et al., who described an increased incidence of uric acid calculi in summer and autumn in individuals in South Australia [16]. To the best of our knowledge, there are no further studies on seasonal variations in acute episodes in UASFs.

For renal stone disease in general, however, a close relationship among the four seasons and the incidence of acute stone episodes has been shown in various regions of the world, e.g., in Japan [10, 17], Taiwan [5], the United States [4, 18], New Zealand [9], Italy [19], and Iran [20], where the temperatures fluctuate widely throughout the seasons [13]. In many countries, the incidence peaks in summer, which corresponds to July–September [5] and January–March [9] in the northern and southern hemispheres, respectively. These trends have been demonstrated to exist regardless of patient age, sex [5], and race [9].

These findings are partially in accordance with our results in UASFs in Germany. We found a significantly increased incidence in the third quarter of the year, which represents the summer months in Germany. However, the incidence was similar in the fourth quarter, which includes autumn and early winter. The reasons for this peak in the colder season are unclear.

The climate data in Coburg (2015–2017) did not show remarkable differences when compared to previous years and long-term mean temperatures. (www.wetterkontor.de).

Another possible explanation for seasonal differences in the incidence of renal colic could be seasonal variations in urine composition. Authors from the USA [18], UK [21], Finland [22] and Poland [23] have described seasonal changes in calcium excretion, daily urine volume (diuresis) and urine supersaturation.

In contrast to these findings, we did not find fluctuations in urine composition (metabolic urinary stone risk factors) throughout the year. This finding is in accordance with our findings in individuals with calcium oxalate urolithiasis [14].

We explain the constant urine composition throughout the year by the lack of seasonal variations in our diet. All investigations from the UK, Finland and Poland were conducted in the late 1970s or early 1980s, when globalization had not reached the levels of today; hence, the availability of certain dietary products indeed depended on their seasonal growth. Currently, due to hypermarketization, every dietary product is available at all times of the year. However, to date, no data have been published with respect to this question.

Conclusion

For UASFs, there are seasonal variations in the incidence of acute stone episodes, showing peaks in summer and autumn. This has been described consistently for individuals in South Australia by Baker et al. [16] and in Germany in our study. The reasons remain unclear. Temperature differences are not a sufficient explanation, as there was one peak in the warm season and another in the cold season. Furthermore, the climate data in our region did not show remarkable differences when compared to other years (www.wetterkontor.de). If temperature plays an important role, we would have seen similar relations for calcium oxalate stone formers, as temperature mainly influences urine volume. However, as we showed recently, in calcium oxalate stone formers, there was no seasonal variation during the same time period [14].

Metabolic reasons and dietary factors are also implausible, as we did not observe a different urine composition throughout the year. Unfortunately, in the study by Baker et al. [16], which showed similar variations in the incidence of UA stones, no metabolic data were reported, as we observed.

Further studies are required to elucidate the causes of the seasonal variations in renal colic in UASFs. One approach could be to conduct a multicentre study with a similar design in various regions to determine whether this seasonal variation also exists in other regions. However, it will not be easy to recruit study centres, as almost no centre in Germany evaluates stone formers in such an extensive way anymore. Another approach could be to analyse the urinary concentrations of uric acid in 24 h urine and calculate risk indices (e.g., Tiselius Indices, BONN Risk Index, and Robertson Risk Factor Algorithms).

Author contributions WLS: protocol/project development, data collection or management, data analysis, manuscript writing/editing. JB-Ö: data collection or management, data analysis, manuscript writing/editing.

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article. The authors did not receive support from any organization for the submitted work.

Ethical approval This is an observational study. According to the laws in Germany, approval from an ethics committee is not needed, as it is a retrospective study based on completely anonymized data that cannot be traced back to individual patients. This study was exempt from approval by the Regiomed-Kliniken Institutional Review Board, as it used only deidentified patient data.

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