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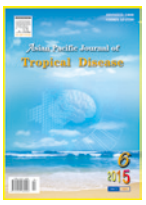

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# Study of correlation of crystalluria and hematuria for lithiasic and non lithiasic subjects

Kheyra Sbahi[1], Brahim Kacem[1*], Ahmed Semmoud[2], Ahmed Addou[1]

[1]*STEVA Laboratory, Research Team Urolithiasis, Department of Biology, Faculty of Natural Sciences and Life, University Abdelhamid Ibn Badis of Mostaganem, Algeria*

[2]*LASIR Laboratory, University of Science and Technology of Lille, Lille, France*

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ABSTRACT

**Objective:** To detect a correlation between crystalluria and symptomatic hematuria, which may be indicative of urological or kidney disease.
**Methods:** A total of 617 first morning urine from 306 patients, including 59 urolithiasic subjects and 247 patients with other urinary tract problems but without lithiasis, were collected and analyzed by a light microscope and urine dipsticks. Meanwhile, 202 urines from 100 healthy subjects were analyzed to compare results.
**Results:** Results show that in patients with hematuria, 81.08% of urolithiasis, 32.39% of patients without urolithiasis and 21.88% of controls had a positive crystalluria. The crystalline species most encountered in urolithiasis was whewellite with 37.84% followed by uric acid dihydrate with 21.62%.
**Conclusions:** In most cases, the formation and growth of a calculi are the result of urinary disorders, metabolic, infectious or anatomical, whose identification can provide prophylactic and preventive measures of recurrence kidney stones.

## 1. Introduction

Urolithiasis is a disease characterized by the presence of stones in the urinary tracts; which are substances that crystallize in the urine under certain conditions. The study of urinary crystals is a means of detecting urinary stone-diseases before they cause kidney complications.

This disease has often little or no symptoms. The classic manifestation of pain, hematuria, and bacteriuria is the most common symptoms[1]. In this study we are only interested in hematuria, as very common biological sign, may reflect the existence of a nephrological or urological disease[2].

Any microscopic or macroscopic hematuria must deserve a thorough investigation in search of a causal direction, hence the interest in our study, which aims to seek a correlation between hematuria and crystalluria, is the intermediate step between urinary biochemical abnormalities and the formation of calculus. For this, we propose a monitoring crystalluria associated with a study of hematuria in different groups.

## 2. Materials and methods

### 2.1. Patients and samples

A total of 617 first morning urine from 306 patients (2.02 samples/patient) were collected under sterile conditions at the laboratories of hospital of Ain Tadelesse (Mostaganem) and Mazouna (Relizane) and at private medical clinics of Mostaganem between February 2011 and November 2011. Among them, 59 patients had calculi (2.46 samples/patient), including 35 men and 24 women ( M/W ratio: 1.46 ); 247 patients didn't have stones (SL sick) but had other problems in the urinary tract (1.91 samples/patient ), 89 men and 158 women, Meanwhile, 202 samples from 100 healthy subjects, 25 men and 75 women were analyzed and considered as control.

### 2.2. Procedure

Once received, the urine is homogenized by inverting the tubes

*Corresponding author: Dr. Brahim Kacem, Department of Biology, Faculty of Natural Sciences and Life, University of Mostaganem, Algeria.
Tel: 0021377893120; 00231554279989
E-mail: kacem1B@voila.fr

then analyzed cytologically and study of crystalluria. Hematuria and pH were determined using multi-reagents Dipstick type "strips urinalysis multi-parameter Medi-Test Combi 10® SGL" and confirmed by cytology.

For each urine sample, a droplet was taken using a Pasteur pipette and placed on a Malassez cell for examination by light microscopy polarization ZEISS. The study of crystals includes the identification of all crystalline species, counting and size determination (for grits, a semi- quantitative estimate is sufficient) The crystals were identified by their morphology and characteristics in polarized light according to the criteria described by other studies[3,4].

## 3. Results

### 3.1. Presence of blood

The results show that blood was present in 30.08 % of SL patient's urine with a higher frequency in women. In urolithiasis, hematuria positive was recorded with almost the same rate in both sexes, the overall rate is 25.52% while in the control group, 15.84% of the urine showed only hematuria, females represented higher rate compared to males (Table 1).

### 3.2. Correlation between the presence of blood and crystalluria

The study of crystalluria subjects with hematuria, allowed us to extract the results summarized in Table 2. Frequencies obtained (81.08% of urolithiasis, 32.39% in patients SL and 21.88% in controls) are higher compared to the overall crystalluria found in the study of all cases whether with or without hematuria (72.41% of urolithiasis, 28.81% in patients SL and 18.32% in controls). It was noted that women accounted for higher than men, while the results of the study of overall crystalluria were reverse except for patients SL frequencies.

### 3.3. Hematuria and nature of the crystals

In general, the nature of the chemical and crystalline species present in urolithiasis, SL patients and controls has shown that calcium oxalate dominated in all three groups with a higher frequency in urolithiasis patients (59.31%) compared to patients SL and control (17.16% and 12.87% respectively). In the latter two, the calcium oxalate dihydrate (weddellite or C2) was observed more than calcium oxalate monohydrate (whewellite or C1). The reverse was observed in the case of urolithiasis where whewellite is present in 40% of cases, against 33.1% for weddellite. Phosphates were present in 16.55% of urolithiasis [(5.52% struvite, brushite 8.28%, 11.03% amorphous calcium carbonate phosphate (PACC)]. As for uric acid, were present in urolithiasis, SL patients and control in frequencies of 8.28%, 6.99% and 5.44% respectively.

In urine with hematuria, the most commonly found crystalline in urolithiasis was whewellite with a frequency of 37.84% followed by uric acid dihydrate with 21.62% and 16.22% brushite. In SL patients weddellite was the most common species with a rate of 11.27%, followed by struvite and PACC with 7.04%. In controls, weddellite was present in the majority of analyzed urine with a frequency of 18.75% (Table 3).

**Table 3**

Frequency of different crystalline forms in the urine with hematuria.

| Presence of blood and crystals | pH | Urolithiasis | | SL patients | | Control | |
|---|---|---|---|---|---|---|---|
| | | Nb | (%) | Nb | (%) | Nb | (%) |
| C1 | 6.14 | 14 | 37.84 | 6 | 4.22 | 3 | 9.37 |
| AUD | 5.63 | 8 | 21.62 | 6 | 4.22 | 1 | 3.12 |
| Brushite | 6.76 | 6 | 16.22 | 2 | 1.41 | - | - |
| C2 | 5.76 | 5 | 13.51 | 16 | 11.27 | 6 | 18.75 |
| Struvite | 7.42 | 4 | 10.81 | 10 | 7.04 | - | - |
| PACC | 7.21 | 3 | 8.11 | 10 | 7.04 | - | - |
| UAC | 5.60 | 2 | 5.40 | 8 | 5.63 | - | - |
| AUA | 5.50 | - | - | 1 | 0.70 | - | - |
| Total (Hematuria positive) | | 37 | | 142 | | 32 | |

C1: Calcium oxalate monohydrate (whewellite); AUD: Uric acid dihydrate; Brushite: Calcium hydrogen phosphate dihydrate; C2: Calcium oxalate dihydrate (weddellite); Struvite: Magnesium ammonium phosphate hexahydrate; UAC: Amorphous urate complex; AUA: Uric acid anhydrous.

## 4 . Discussion

The study of crystalluria can bring a helpful aid when it highlights the presence of specific crystals such as cystine crystals, 2.8-dihydroxyadenine of xanthine, uric acid or anhydrous dihydrate or struvite. When the crystalluria test is positive, this could be considered as risk factors of lithogenic roughly asserted by the presence of inducers such as oxalate and cystine crystals[5].

Urinalysis in this work is the study of crystalluria. The results of this study provide information leading to conclude a relationship between

**Table 1**

Presence of blood in urolithiasis, SL patients and controls [*n* (%)].

| Hematuria | Urolithiasis | | | SL patients | | | Control | | |
|---|---|---|---|---|---|---|---|---|---|
| | Males | Females | Total | Males | Females | Total | Males | Females | Total |
| Positive | 13 (25.49) | 24 (25.53) | 37 (25.52) | 31 (18.9) | 111 (36.04) | 142 (30.08) | 5 (8.62) | 27 (18.75) | 32 (15.84) |
| Negative | 38 (74.51) | 70 (74.47) | 108 (74.48) | 133 (81.1) | 197 (63.96) | 330 (69.92) | 53 (91.38) | 117 (81.25) | 170 (84.16) |
| Total | 51 (100.00) | 94 (100.00) | 145 (100.00) | 164 (100.00) | 308 (100.00) | 472 (100.00) | 58 (100.00) | 144 (100.00) | 202 (100.00) |

**Table 2**

Frequency of positive and negative crystalluria in urine containing blood in nephrolithiasis, SL patients and controls [*n* (%)].

| Crystalluria | Urolithiasis | | | SL patient | | | Control | | |
|---|---|---|---|---|---|---|---|---|---|
| | Males | Females | Total | Males | Females | Total | Males | Females | Total |
| Crystalluria positive | 10 (76.92) | 20 (83.33) | 30 (81.08) | 9 (29.03) | 37 (33.33) | 46 (32.39) | 1 (20.00) | 6 (22.22) | 7 (21.88) |
| Crystalluria negative | 3 (23.08) | 4 (16.67) | 7 (18.92) | 22 (70.97) | 74 (66.67) | 96 (67.61) | 4 (80.00) | 21(77.78) | 25 (78.12) |
| Total (hematuria positive) | 13 (100.00) | 24 (100.00) | 37 (100.00) | 31 (100.00) | 111 (100.00) | 142 (100.00) | 5 (100.00) | 27 (100.00) | 32 (100.00) |

hematurea and the observed crystalline frequency and nature.

The blood was present in the urine of SL patients with a frequency of 30.08% against 25.52% in urolithiasis. In controls, we note that the blood was present in 15.84% of urine. This result is similar to that found in a study of male soldiers who underwent annual examinations of urine sediment over a period of 12 years, the incidence was 16% with microscopic hematuria in more than two examinations[6]. In another study, the transient microscopic hematuria was noted in about 13% of postmenopausal women[7]. It can also be caused by vigorous exercise before urine collection, by sex, by a slight injury, or menstrual contamination. There are no data on the differences between patients with transient microscopic hematuria and those with persistent microscopic hematuria[8].

The study of the correlation between the presence of blood in urine and crystalluria showed that the frequency of the latter rises to 81.08% in urolithiasis. This frequency is higher than those found in other studies where the rates vary between 60% and 70% in idiopathic calcium urolithiasis[9-11]. SL patients and controls, we found frequencies of 32.39% and 21.88% respectively. These are lower than those observed in our urolithiasis and much higher than the 6.4% reported from 5 956 urine urolithiasis non-hospitalized patients showing no uro- nephrological diseases[12].

In urolithiasis with hematuria, whewellite crystals dominated with a frequency of 37.84% followed by uric acid dihydrate with a frequency of 21.62% and 16.22% brushite. There was a sharp increase in the frequencies of uric acid dihydrate and brushite which means that there could be a relationship between their presence and hematuria.

It can be noted from our results that the precipitation of crystals found in the urine with a positive hematuria was influenced by the change of pH[4]. The average pH for uric acid was generally between 5.5 and 5.63. The decrease in urinary pH associated with the simultaneous maintenance of uric acid excretion promote the formation of an excessive amount of undissociated uric acid, which facilitate its crystallization in urine. Maintaining a high uric acid excretion may be related to an increase in uric load filtered by the kidneys in patients with hyperuricemia[13]. For calcium oxalate, the average pH was 5.76 weddellite (C2) and 6.14 whewellite (C1). This crystalline species is less dependent on pH. For phosphates, average pH increased to 6.76 for brushite, 7.21 for the PACC and 7.42 for struvite. They are dependent on the pH and found in the urine with a pH values greater than 6, and sometimes at lower pH if the concentration of calcium and phosphate was very high[4].

Crystalluria reflects supersaturation of urine in one or several substances eliminated by the kidney. The presence of urinary crystals in urine is not, except in special cases, pathological in itself. However, in a urolithiasis, or in certain pathological contexts, crystalluria can be a very useful indicator of the pathology observed. It is possible, for example, to screen for genetic diseases by the identification of urinary crystals, even before renal disease is declared. In a urolithiasis patient, monitoring crystalluria under certain conditions, appears to be an excellent indicator of the effectiveness of medical treatment or otherwise a prognostic marker of the risk of urolithiasis recurrence.

Our work has allowed us to confirm that the examination of the first-morning urine crystalluria remains clinically a very interesting test. Concerning the correlation between crystalluria and hematuria, this study has shown that the presence of blood in urine resulted an increase in the frequency of positive crystalluria and a change of the dominant crystalline forms especially in urolithiasis.

We can thus conclude that although the frequency of crystalluria with uro- nephrological diseases was lower than that of urolithiasis. The frequency remained high and showed that these patients were at risk of crystal formation than normal, leading them to be urolithiasis. As can be inferred there was a strong relationship between crystalluria and hematuria. This confirms that these tests are effective and can help us in the diagnosis, and should be given more importance in our analysis.

## Conflict of interest statement

We declare that we have no conflict of interest.

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