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Study of Crystalluria and Associated Factors at Amirou Boubacar Diallo National Hospital

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Abstract

Background: Crystalluria is the intermediate stage between urinary biochemical abnormalities and stone formation, which can lead to urological and nephrological complications. Objective: To assess the frequency of crystalluria and associated factors at the Hospital National Amirou Boubacar Diallo (HNABD) in Niamey. Methodology: This was a cross-sectional, prospective, descriptive, and analytical study conducted from February 2023 to June 06, 2023. All urine samples sent to the laboratory during the study period were included. Results: A total of 404 patients' urine samples were included and analyzed during the study period. These urine samples were predominantly from male patients (64.00%; sex ratio = 1.7). The median age of the patients was 15 years, with extremes ranging from 37 days to 89 years. High urine density and medication intake were significantly associated with crystalluria (p-value < 0.05). However, there was no statistically significant association between crystalluria, pH, and bacterial species isolated in this study. In principal component analysis, crystalluria was associated with high urine density, gender, presence of ketone bodies, use of medication, presence of cylinders, parasites, urobilinogen, yeast and history of urinary lithiasis, but in multivariate logistic analysis, no risk factors for crystalluria were found. Conclusion: The frequency of crystalluria at the Hospital National Amirou Boubacar Diallo was relatively low. No risk factors for crystalluria were found in the multivariate logistic analysis. Further studies taking into account patients' clinical characteristics and crystalluria are needed to complete this study.

Keywords

Crystalluria, Calcium Oxalate, Cystine, Phospho-Ammoniaco-Magnesium, Uric Acid, Niger

1. Introduction

Crystalluria refers to the presence of crystals in the urine. It is due to the saturation of urine with one or more poorly soluble substances. It is therefore a marker of the supersaturation of the urine which is observed in normal or pathological urine. The screening and monitoring of crystalluria by analysis informs the clinician about its nature and its characteristics. Crystalluria is not a pathology in itself but rather often a marker of a pathology [1].

The study of crystalluria is of major interest in the detection of certain ions or potentially crystallizable substances (calcium, uric acid, phosphates, oxalate…) of endogenous or exogenous origin abnormally abundant in the urine. It finds its justification both for the diagnosis and for the effectiveness of the therapeutic management of the pathologies responsible for renal crystallization [2].

Diagnostically, certain crystals are significant simply because of their presence, irrespective of any other qualitative or quantitative considerations. Therefore, crystals of this kind are of interest in diagnosing and screening for certain diseases, such as:

- Cystine crystals can reveal congenital cystinuria, revealing an all-too-dangerous and fatal tubulopathy.
- Phosphate crystals at high pH, caused by certain infectious urea germs, often lead to saturation with ammonium manganese phosphate (struvite) and ammonium acid urate.
- Ammonium acid urate crystals which indicate hyperuricuria associated with hyperammoniuria and which depend on urine pH, point either to a urinary tract infection caused by ureasic germs, or to infectious diarrhoea with digestive loss of base and electrolytes in subjects with inadequate phosphorus intakes.

The study of crystalluria is also very important because crystals constitute the intermediate stage between urinary biochemical abnormalities and the formation of stones. These abnormalities may trigger kidney complications such as lithiasis and other crystallogenic pathologies such as gout, oxalosis, calcium pyrophosphate crystal deposition disease, cholesterol crystals.

In Niger, several hospital studies had focused on the renal complications of crystalluria [3] [4]. However, to the best of our knowledge, there are no studies on crystalluria in Niger.

The objective of this study was to evaluate the frequency of crystalluria at the Amirou Boubacar Diallo National Hospital in Niamey.

2. Methodology

2.1. Study Framework

The study took place in the Medical Biology Laboratory ward of the Amirou Boubacar Diallo National Hospital (HNABD) bacteriology unit.

2.2. Type and Period of the Study

The study was cross-sectional, prospective with a descriptive and analytical aim,

over a period of 6 months (from February 06, 2023 to June 06, 2023).

2.3. Study Population

The study population comprises all the patients who requested a cito bacteriological examination of urine (CBEU) at the HNABD during the study period.

2.4. Inclusion Criteria

All patients regardless of age or gender who received a CBEU in the HNABD laboratory were included in this study.

2.5. Exclusion Criteria

The CBEUs carried out as part of the patients' follow-up treatment were excluded from the study to avoid duplicates.

2.6. Conducting the Analysis of Urine Samples

For each urine sample, the laboratory analysis was carried out in five steps (Figure 1). In a nutshell, a macroscopic analysis of urine was performed first. We use a polarized light microscope to recognize the different types of urinary crystals. The urine samples were then cultured on CLED agar. A 10-parameter test strip was then dipped into the urine. The reading of the strip was carried out according to the manufacturer's recommendations.

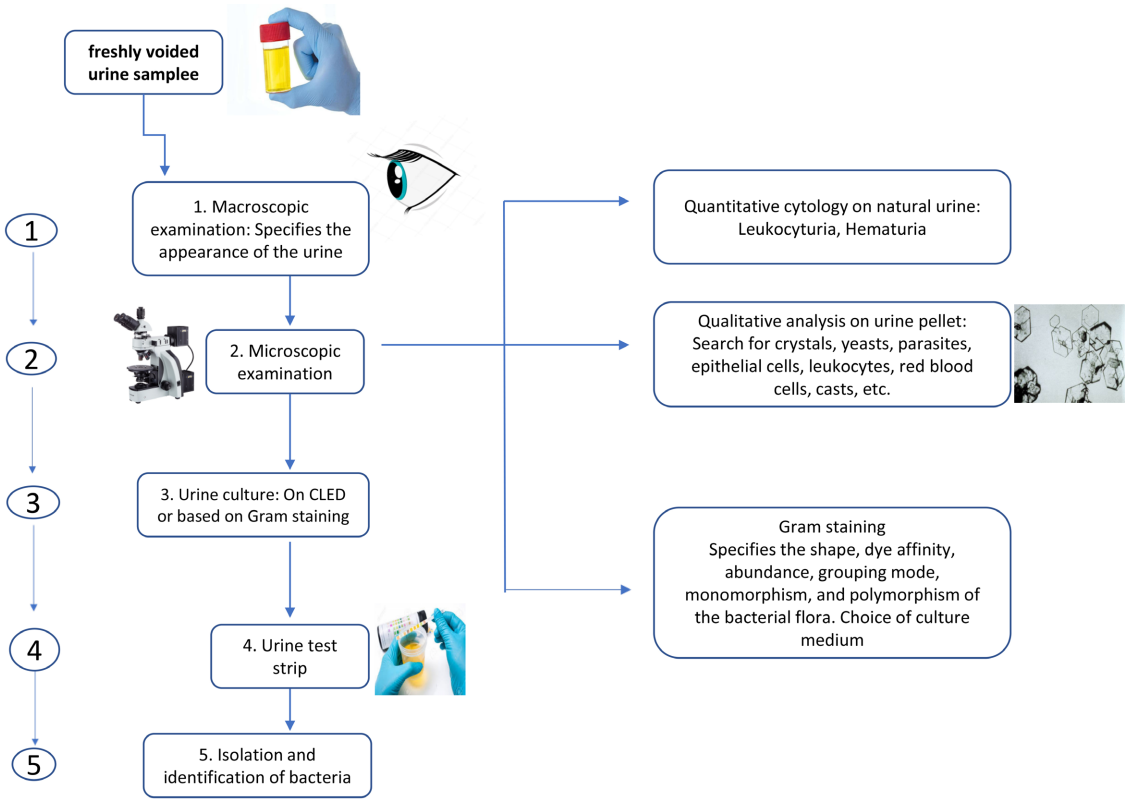

Figure 1. Schematic summary of the sample processing.

2.7. Collection Support

A pre-established individual survey sheet was used to collect data on gender, sex, geographical origin, pathology, medications used, history of lithiasis, age and biochemical parameters.

2.8. Statistical Analysis of Data

The data entry was done using EXCEL 2013. The data analysis was performed using Epi info version 7.2.5.0 and the RStudio software version 4.0.4. The Chi-square comparison test (or, failing that, the Exact Fisher test) was used for the comparison of qualitative variables. A univariate and multivariate logistic analysis was carried out to determine the risk factors associated with the presence or absence of crystals in the urine. The multivariate logistic regression model was constructed from univariate analyses whose *p*-values were ≤0.1. The data were presented in the form of tables and figures. A *p*-value of less than 0.05 was considered significant. A Principal Component Analysis (PCA) was carried out in order to highlight the relationships between crystalluria and the risk factors examined. To determine the risk factors associated with crystalluria, a multivariate logistic analysis was performed. The model was constructed from univariate analyses whose *p*-values were ≤0.2.

2.9. Ethical Considerations

A research authorization (N˚ 000226/2023) had been issued by the Faculty of Health Sciences of Abdou Moumouni University, Niamey, Niger. Anonymity and confidentiality had been ensured for all information collected during the study.

3. Results

3.1. Patients General Profile

Male patients were the most represented with a count of 259. The sex ratio was 1.7. The median age of the patients was 15 years (interquartile range: 2.08 - 41 years). The 0 to 5 age group was the most represented (n = 149 or 38.2%). Inpatients were the majority with 70.79% (n = 286) while outpatients accounted for 29.21% (n = 118). One patient (0.25%) with a history of urolithiasis was included. The patients who were not on drug treatment at the time the samples were taken were the most represented with a total of 338 or 84%. Among the patients who were on drug treatment at the time of sampling, erythromycin (n = 18 or 4%) was the most commonly used drug, followed by omeprazole (n = 10 or 2%) and ciprofloxacin (n = 9; 2%).

3.2. Frequency of Crystalluria

In total, the crystals were found on 38 samples, *i.e.* a frequency of 9.4% of the study population. Among the various crystals found in the urine, calcium oxalate crystals were the most represented with a count of 29, *i.e.* 76.3%. The other crystals

observed were uric acid crystals (10.5%), calcium carbonate (5.3%), cystine (2.6%), and phosphoammonium-magnesium (PAM) (5.3%) (Figure 2).

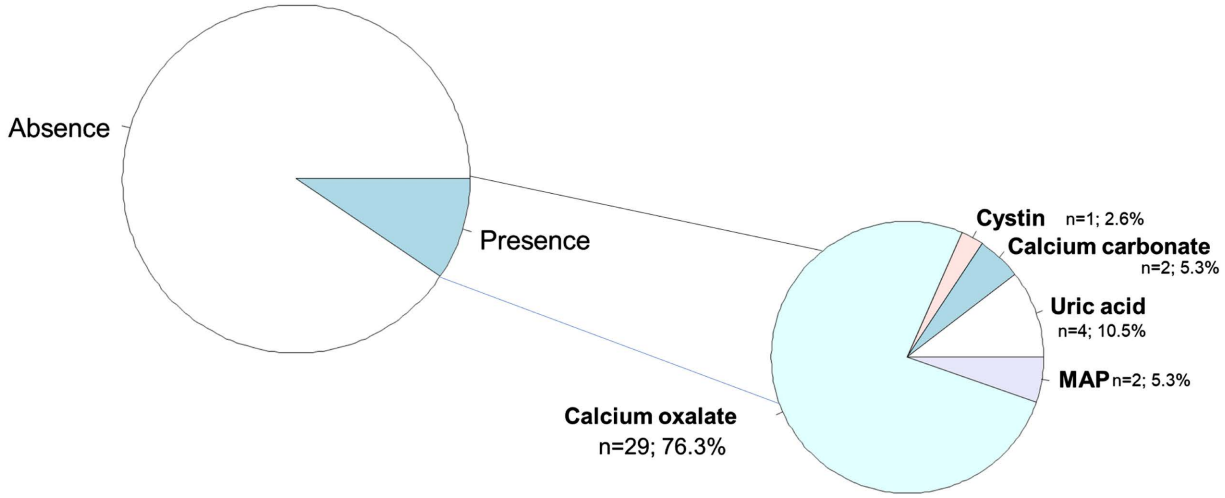

Figure 2. Frequency of different crystal types.

3.3. Exploratory Analysis of the Variables Associated with Crystalluria

Overall, all the variables form two clusters. Crystalluria clustered with a high urinary density, gender, the presence of ketone bodies, medication intake, the presence of cylinders, parasites, urobilinogen, yeasts, and a history of urolithiasis (Figure 3).

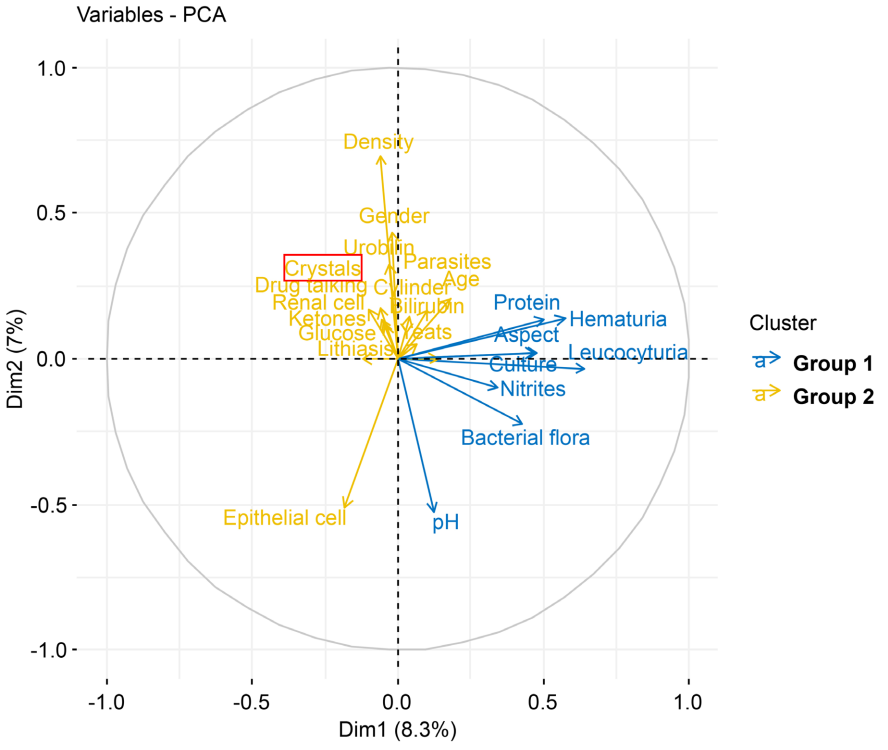

Figure 3. Exploratory analysis of the different variables using principal component analysis.

3.4. Crystalluria and Identified Bacteria

Crystalluria was by far more represented in patients with a negative uroculture with a frequency of 89.47% (n = 34). Among the patients with a positive uroculture, *Escherichia coli*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Proteus mirabilis* were the bacteria identified.

3.5. Risk Factors for Crystalluria

In the univariate logistic analysis, crystalluria was significantly associated with bacterial flora (odds ratio = 0.35; 95% CI = 0.17 - 0.73; p-value = 0.004). The other explanatory variables such as age, sex, history of medication intake, the appearance of urine, the pH, Nitrites, leukocyturia, hematuria, urine density, proteinuria, and culture were not associated with crystalluria (Table 1).

Table 1. Factors associated with Crystalluria in univariate analysis.

Variables		Odds ratio	95% CI	p value
Sexe	Female			
	Male	0.96	0.48 - 1.95	0.898
Age	(0, 40]			
	(40, 100]	1.06	0.47 - 2.19	0.890
Medication	No			
	Yes	1.16	0.42 - 2.73	0.755
Urine appearance	Normal			
	Colored/cloudy	1.73	0.70 - 3.82	0.201
Leukocyturia	Negative			
	Positive	1.11	0.53 - 2.57	0.788
Hematuria	Negative			
	Positive	0.82	0.32 - 1.83	0.651
Bacterial flora	Negative			
	Positive	0.35	0.17 - 0.73	0.004
pH	Non-acidic			
	Acidic	0.61	0.24 - 1.88	0.339
Proteinuria	Negative			
	Positive	0.94	0.46 - 1.86	0.865
Nitrites	Negative			
	Positive	0.60	0.20 - 1.46	0.301
Density	Normal/reduced			
	High	1.72	0.87 - 3.57	0.128
Culture	Negative			
	Positive	0.69	0.30 - 1.46	0.360

In the multivariate logistic analysis, as in univariate analysis only bacterial flora was significantly associated with crystalluria (adjusted odds ratio = 0.37; 95% CI = 0.18 - 0.80; *p*-value = 0.009) (Figure 4).

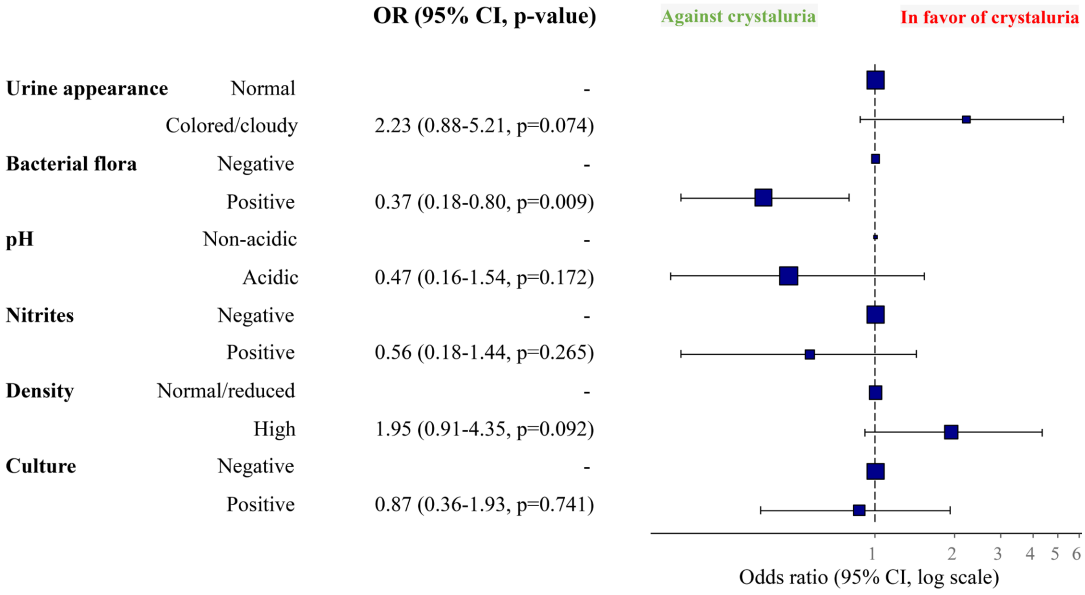

Figure 4. Multivariate logistic analysis of risk factors associated with crystalluria.

4. Discussion

The study of crystalluria is of major interest in the detection of some ions or potentially crystallizable substances (calcium, uric acid, phosphates, oxalate...) of endogenous or exogenous origin abnormally abundant in the urine. It finds its justification both for the diagnosis and for the effectiveness of the therapeutic management of pathologies responsible for renal crystallization.

It emerges from this study which involved 404 patients that 259 are men and 145 women respectively representing 64.1% and 35.9% of the total sample. The sex ratio was 1.7. Berrahal and Mohamed Bachir [5] in Algeria in 2021 also reported a male predominance in their study with 64% and 36% respectively. Ouédraogo I *et al.* [6] in Burkina Faso in 2015 also demonstrated a male predominance with 89.55%. This predominance can be explained on the one hand by the fact that men are sedentary and practice several activities thus increasing the risk of infection and on the other hand the length of the urethra (retention factor) in boys while the brevity of the female urethra and the power of the urinary jet allow girls to eliminate certain germs more easily.

In the present study, it appears that one patient with a history of lithiasis represented 0.25% (n = 1) of the patients included. In Mali, Ouattara [7] in 1993, had observed 146 cases of all ages combined. In 2006 in Tunisia, 205 pediatric cases were collected in 14 months by Jallouli *et al.* [8] compared to 420 pediatric cases in 6 years in France by Daudon *et al.* [9] in 1983. This difference can be explained by the fact that urolithiasis, in children as in adults, has a great variability in fre-

quency depending on the country. In our study, among the patients who were on drug treatment at the time of sampling, erythromycin (n = 18; 4%) was the most commonly used drug, followed by omeprazole (n = 10; 2%) and ciprofloxacin (n = 9; 2%). Chopra *et al.* [10] in 2000 in New Jersey reported that a patient had developed obstructive uropathy due to massive precipitation of ciprofloxacin crystals in the distal ureters and bladder, after a 24-day treatment at a dose of 500 mg twice a day.

In the present study, in total, the crystals were found on 38 samples, *i.e.* a frequency of 9.4% of the population. Among the various crystals found in the urine, calcium oxalate crystals were the most represented with a strength of 29/38 or 76.32%. The other crystals observed were uric acid crystals, calcium carbonate, cystine, and phospho-ammoniaco-magnesium (PAM).

A frequency (8.20%) of the crystalluria close to that obtained in this study was reported by Verdesca *et al.* [11] in 2011 in France. According to these authors, the most frequent crystals were calcium oxalate crystals (75.9%), uric acid crystals (25.9%), amorphous urate crystals (7.9%) [11].

Berrahal and Mohamed Bachir [5] in Algeria in 2021 reported 40% oxalocalcium crystalluria [5]. Ouédraogo I *et al.* [6] in Burkina Faso in 2015 also reported a predominance of calcium oxalate crystals which represented 74.17% followed by ammoniacomagnesian phosphates (4.11%) [6].

This predominance of calcium oxalate crystals can be explained by the frequent saturation of urine with calcium oxalate.

In this study, *Escherichia coli*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Proteus mirabilis* were the bacteria identified in patients with a positive uroculture. Berrahal and Mohamed Bachir [5] in Algeria in 2021 had isolated *Proteus Mirabilis*, *Staphylococcus aureus*, *Pseudomonas spp*, *Escherichia coli* and *Enterobacter cloacae* complex in patients with crystalluria.

In our study, crystalluria was more represented in male patients with a workforce of 24, or 63.16%. In Algeria Flih Amel and Fahem Kadija [12] in 2020 also reported a predominant crystalluria in the female sex with 43.47% (n = 23) against 38.46% (n = 13) in the opposite sex.

In our study, crystalluria was more represented in the age groups of 0 - 5 years and 40 - 65 years with a respective percentage of 39% and 15%.

In Algeria Flih Amel and Fahem Kadija [12] in 2020 reported a predominance in the age group of 61 to 75 years.

This result could be explained by the fact that the age group of 0 - 5 years was by far the most represented in our study.

In our study, crystalluria was by far more represented in patients with high urinary density than those with low density and normal density, with 65.79%.

Stoerman C. and Deffert C. [13] in 2021 reported in France a density ranging from 1.004 to 1.014.

This difference could be explained by the fact that some crystalline species have more molecular weight than others.

In our study, crystalluria was by far more represented in patients with an acidic pH than those with a neutral and basic pH, with 86.84%. Jamme *et al.* [14] in 2019 in France reported a low urinary pH (OR = 0.79 [0.62 - 0.94]). This situation could be explained by the fact of the sensitivity of the crystalline species to the pH.

5. Limitations of the Study

Since this study is monocentric, the generalization of these results to the entire country must be done with caution. Also, in this study, markers for studying crystalluria such as the determination of crystalline facies, the counting of crystals by crystalline species, the measurement of the average and maximum sizes of crystals, the counting of aggregates as well as the measurement of the average and maximum sizes (aggregates) and finally the calculation of the aggregation coefficient were not carried out.

However, this study provided basic information necessary for future research work with regard to crystalluria.

6. Conclusion

It emerges from this study that the frequency of crystalluria at the Amirou Boubacar Diallo National Hospital was relatively low. Calcium oxalate crystals were by far the most frequently observed in urine. Although in the main component analysis, crystalluria clustered with a high urinary density, gender, the presence of ketone bodies, medication intake, the presence of cylinders, parasites, urobilinogen, yeasts, and history of urolithiasis, no risk factors for crystalluria were found in multivariate logistic analysis. Additional studies taking into account the clinical characteristics of the patients and crystalluria are necessary to complete this study.

7. State of Knowledge on the Subject

*Crystalluria is not a pathology in itself but rather often a marker of a pathology;

*crystalluria is the intermediate stage between urinary biochemical abnormalities and the formation of the stone at the origin of renal complications such as lithiasis and other crystallogenic pathologies such as gout, oxalosis, …

8. Contribution of Our Study to Knowledge

•This study evaluated the frequency and associated factors of crystalluria at the Amirou Boubacar Diallo National Hospital, Niamey, Niger;

•This work demonstrated that the frequency of crystalluria at the Amirou Boubacar Diallo National Hospital was relatively low;

*Calcium oxalate crystals were by far the most frequently observed in urine;

•No risk factors for crystalluria were found in the multivariate logistic analysis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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