Scientific Research Publishing

Open Journal of Nephrology, 2023, 13, 104-115
https://www.scirp.org/journal/ojneph
ISSN Online: 2164-2869
ISSN Print: 2164-2842

The CALVIH Study: How to Handle Renal Stones in Persons Living with HIV_1?

Corinne Isnard Bagnis[1*], Hassimiou Diallo[2], Isabelle Tostivint[1], Marie-Paule Dousseaux[1], Nassima Mansour[2], Jessica Palmyre[2], Anne Simon[3], Marc-Antoine Valantin[4], Myriam Kirstetter[4], Roland Tubiana[4], Christine Katlama[4]

[1]Departement of Nephrology, Assistance Publique-Hôpitaux de Paris, and Sorbonne University, Paris, France
[2]Department of Clinical Research, Assistance Publique-Hôpitaux de Paris, and Sorbonne University, Paris, France
[3]Department of Internal Medicine, Assistance Publique-Hôpitaux de Paris, and Sorbonne University, Paris, France
[4]Department of Infectious Diseases, Assistance Publique-Hôpitaux de Paris, and Sorbonne University, Paris, France
Email: *Corinne.bagnis@aphp.fr

How to cite this paper: Bagnis, C.I., Diallo, H., Tostivint, I., Dousseaux, M.-P., Mansour, N., Palmyre, J., Simon, A., Valantin, M.-A., Kirstetter, M., Tubiana, R. and Katlama, C. (2023) The CALVIH Study: How to Handle Renal Stones in Persons Living with HIV_1? *Open Journal of Nephrology*, **13**, 104-115.
https://doi.org/10.4236/ojneph.2023.132012

Received: March 30, 2023
Accepted: June 13, 2023
Published: June 16, 2023

Abstract

Background: Renal stone (RS) is a highly prevalent disease in our societies and is mostly secondary to lifestyle habits. HIV_1 patients often experience RS, although specific risk factors are not known. Despite other priorities, comprehensive work-up should be offered to avoid recurrences (50% risk in 5 years). **Purpose and Methods:** The aim of the study is to describe how to handle RS in persons living with HIV_1 and to suggest how the understanding of mechanisms involved in stone composition helps customize therapy and prevent recurrences. We prospectively performed a complete work-up in a cohort of 23 prevalent HIV_1 patients referred to our highly-specialized center by HIV physicians. **Results:** Inclusion was secondary to a colic episode with spontaneous elimination of the stone (74%), bilateral (67%), not obstructive (67%); 53% underwent urologic interventions. Mean age was 34 ± 16 years old and BMI was 22.5 ± 3 (one-third with metabolic syndrome). History of RS showed only one episode (22%), >one (74%) or >4 (4%). Estimated GFR was 78 ± 24 ml/min/1.73m^2 (mean Cr 101 ± 24 µmol/L), and 5 were classified CKD stage 3. Stone analysis was only available for 7 patients and in 6/7 patients, and calcium metabolism was fully explored (2 absorptive hypercalciuria, 4 renal primitive hypercalciuria). Retained mechanism for RS was uric acid dependent for one, oxalic acid dependent for three and calcium dependent for three. Very few patients were exposed to known environmental risk factors for RS, 3 were/had been exposed to darunavir and 3 to atazanavir, 1 to efavirenz, 1 to acetazolamide, 2 to allopurinol. **Conclusion:** RS in HIV_1 patients is mostly not related to ARV. Understanding of renal stone composition is critical to prevent recurrences by offering specific dietetic counselling

and therapy. The role of HIV physicians is important due to the high prevalence of RS in the context of HIV disease.

Keywords

Hypercalciuria, Metabolic Syndrome, Urolithiasis, Uric Acid, HIV Infection

1. Introduction

Renal stone (RS) is a highly prevalent disease in our societies and is mostly secondary to lifestyle changes [1]. RS generates a strong burden of pain, interventional urology and disability, and may lead to chronic kidney disease [2] (up to 1.82 times more likely). Persons living with HIV_1 may experience RS as anyone else, although their specific risk factors for RS are not clearly established, apart from some drug exposition [3].

In the general population, causes for RS vary with gender, age and lifestyle. 10% of the population will experiment with one colic once in their life with a recurrence risk of 35% to 50% over 5 years. Men are more often exposed than women. Recent results from the National Health and Nutrition Examination Survey (NHANES) showed that the prevalence of stone disease in men and women is 11.9% and 9.4%, respectively, in the 2017-2018 cycle in the USA [4]. Risk increases with ageing. Oxalo calcic stone is the most frequently encountered [5]. With ageing, uric acid stones become more prevalent in men and women especially if metabolic syndrome or diabetes is present.

Drug-induced stones are very rare (less than 1% of all stones) and nowadays mostly observed with antiretroviral (mainly protease inhibitors) [2] [6] [7]. Epidemiology of drug-induced RS is biased by underreporting due to lack of collection of stones and the delay between treatment and occurrence of colic.

Being exposed to long-term therapy, among which some may induce RS or acute intra tubular precipitation and often suffering from chronic diarrhea [8], risk for RS is important to consider in the context of HIV, while protecting kidney function is essential. HIV_1-infected patients have a high prevalence (20 to 30%) of metabolic syndrome, hyperinsulinemia, diabetes and hypertension [9], all conditions increasing the risk for uric acid renal stones.

Because RS is a hyperalgesic situation, emergency teams are involved when RS occurs and provide emergency therapy (**Figure 1**). Once the acute phase is over, the renal colic is often poorly documented, the stone itself being very rarely analyzed, and the optimal screening for risk factors for recurrence is insufficiently performed. Therefore, preventive strategies are not initiated with a high risk for recurrence. Ultimately, since RS has been associated with a decrease in glomerular filtration rate [2] in the general population, it could specifically enhance renal risk in HIV_1 patients. HIV physicians should be able to initiate the minimal appropriated work-up in case of RS and provide patients with counselling and

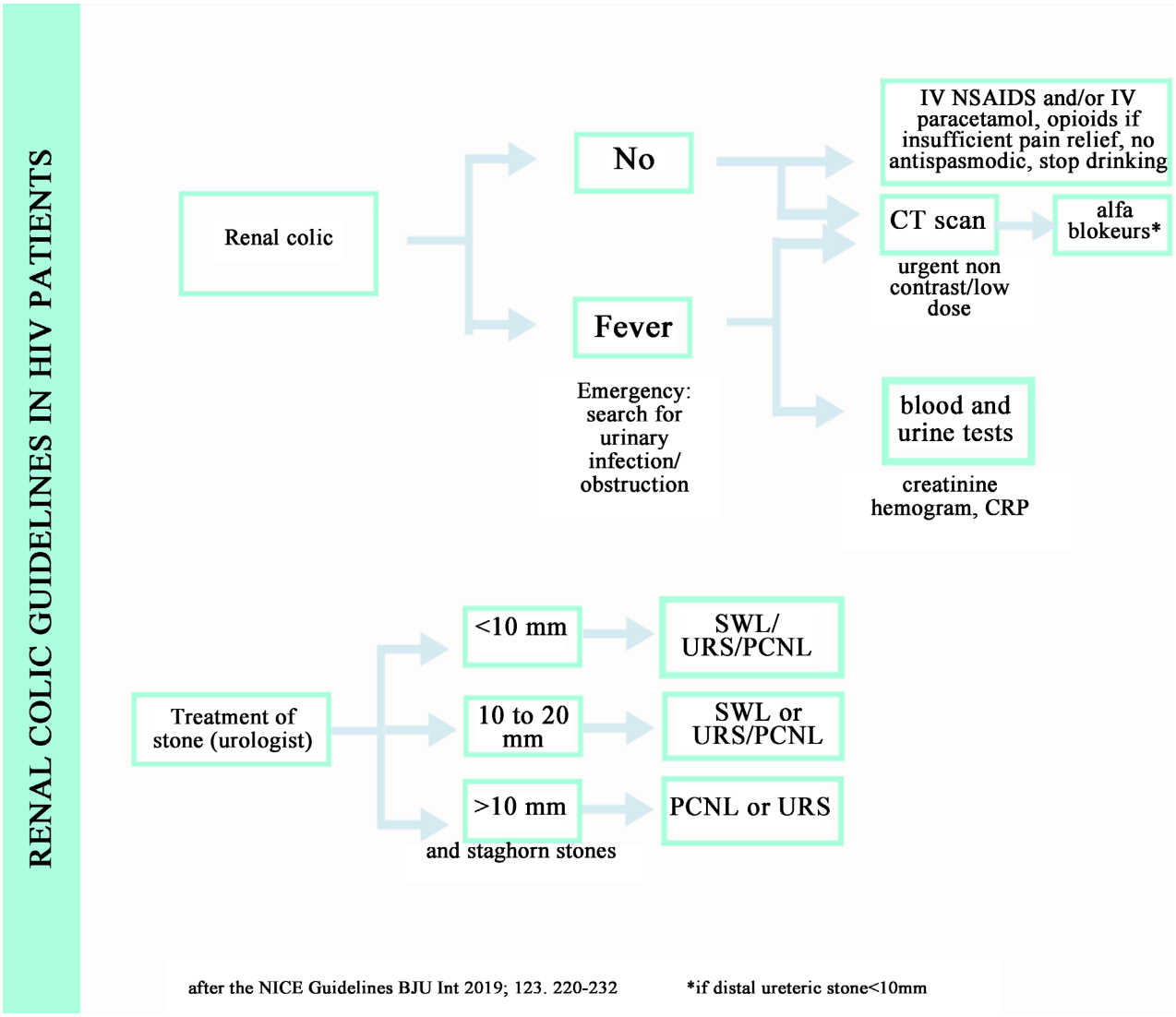

Figure 1. Tutorial for colic management in the HIV patient.

dietetic support.

Describing our experience with a cohort of 23 HIV patients consecutively admitted in our renal stone center, we tried here to summarize an experienced-based, clear and specific overview of usual care for RS that any HIV physician could follow.

2. Patients and Methods

This study aimed at describing the cause of RS and the risk pattern for recurrence (any kind of stones) in HIV_1 patients referred to our center. Our primary objective was to establish the *cause* of renal stone based on stone composition (if stone is available) or on biochemical analysis of urines, cristalluria, low dose renal CT (stone density), patient history, family history… Four main causes of stones were individualized (oxalic, calcic, uric, drug-induced).

The study was conducted in accordance of the Declaration of Helsinki. Ethical

approval was obtained from Sorbonne University Ethical Committee for Research (September 17th, 2013) N˚ IRB: 20133500001072. The study was registered in the Clinical trials system under the reference NCT02457494. All authorizations were obtained (CCTIRS N˚ 13 639 *Advisory Committee on Information Processing in Material Research in the Field of Health* and CNIL N˚914011 *Personal data protection*).

We defined risk profile for stone recurrences estimated on risk factors (**Table 1**) based on plasma and urinary parameters, nutritional profile and drug exposure.

The secondary objectives were to describe the follow-up outcome of HIV_1 patients over one year to identify prevalence of recurrences or complications, observe changes in risk profile pattern during the educational program and describe urological management of stones.

Adult male or female HIV_1 infected patients willing to participate were included if they have experienced a RS episode within the past six months or are living with a RS. All patients gave oral consent. Patient not willing to participate to the study, unable to undergo renal CT low dose scan (no contrast media), unavailable for 12 months follow up were excluded.

A tutorial for colic management (based on the recommendations from the Society for Emergency Medicine) (**Figure 1**) had been sent to infectious disease departments in Ile de France together with an information sheet on the protocol to promote referral to our team for inclusion in the CALVIH study. HIV physicians screened patients on the clinical and/or radiological basis of a history of stone in the past six months and referred the patient to our outpatient department for inclusion and following investigations.

A nephrologist investigator, with expertise in RS care, offered a work-up to the patient specifically to his/her medical story. Treatment was provided according to the standard of care and based on the physicians' judgment. Clinical, biological, and radiological assessments were performed as necessary. Patients met the dietician to evaluate their food/drink consumption. The following visits were programmed as needed with in any case a six-month visit including clinical, biological

Table 1. Risk factors for RS in the general population (after Khan A. Prevalence, pathophysiological mechanisms and factors affecting urolithiasis. Int Urol Nephrol. 2018; 50(5):799-806. doi: https://doi.org/10.1007/s11255-018-1849-2).

Risk factors for RS	Drinking and urine volume
	Urinary density
	Hypercalciuria, hyperuricuria, hyperoxaluria
	Urinary pH
	Urinary Na^+, K^+ and urea per 24 hours
	Metabolic syndrome
	Anatomical or genetic disease
	Chronic urinary tract infection
	Pregnancy
	Stone inducing drugs

and radiological assessment. Another visit at month 12 was planned.

During the study, all patients underwent clinical and biological evaluation in our reference ambulatory outpatient center for RS with fresh urine cristalluria, fasting blood estimation of urea, creatinine, calcium, phosphate, bicarbonates, sodium, potassium, chloride, magnesium, uric acid, glucose, cholesterol, triglycerides, parathyroid hormone and 23 hydroxy-vitamin D3. Urinary parameters were analyzed after 24 h urines collection (creatinine, urea, calcium, potassium, uric acid, oxalate, citrate, phosphate, proteinuria) and on fresh urines (pH, density, hematuria, leucocyturia).

Imaging included renal ultrasound and Xray and when necessary, a low-dose no contrast media renal CT scan. An auto interview on food intake was used as well as an individual interview with a specialized dietician. Whenever necessary, genetic tests, PAK test or bone densitometries were performed.

The primary evaluation criterion was the suspected or confirmed cause of RS classified into 4 options: calcium dependent, oxalate dependent, uric acid or phosphate dependent, drug-induced. Criteria used for diagnosis are in Table 2.

Follow-up allowed description of:

- number of new colic over the next year;
- mean glomerular filtration rate (eGFR estimated with MDRD formula) 6 months and after one year follow up;
- type and number of urological intervention if recurrence/complication;
- number of risk factors for lithiasis per patient at the 6 months and 12 month's visits;
- prevalence of cholelithiasis (diagnosed on available data).

3. Statistical Methods

The analysis was descriptive. We express data as mean (SD) and percent for continuous and categorical variables respectively. We used R software for statistical

Table 2. Diagnostic criteria for RS composition (after Frochot V, Daudon M. Clinical value of crystalluria and quantitative morphoconstitutional analysis of urinary calculi. Int J Surg. 2016 Dec; 36(Pt D):624-632. doi: https://doi.org/10.1016/j.ijsu.2016.11.023. Epub 2016 Nov 12. PMID: 27847293.)

Suspected stone composition	Diagnostic criteria		
	CT scan density	RS morphology	Cristalluria
Calcium dependent	>850 - 1000	spiculated surface, bipyramial surface, sharp angles, pame, yellow to brown	weddelite or calcium phosphate crystals
Oxalate dependent	650 - 850	mamillary or budding surface, cream to pale, dark to brown	whewellite crystals
Uric acid	<650	homogeneous smooth or rough, porous, orange to grayish	uric acid crystals
Drug-induced	radiolucent, can be diagnosed by ultrasonography or enhanced CT scan (low density)	variable	drug crystals

analysis.

4. Results

Inclusions began in November 2013 and lasted 18 months. Inclusion's rate was much slower than expected despite many actions (5 meetings in different infectious diseases departments to promote inclusions, 900 health care providers and professionals informed about the study by mail, communication through major patient's associations like AIDS, Act Up-Paris, TRT-5, Sidaction). The difficulty to recruit patients in our study is illustrative of the burden represented by the discovery of a RS, in patients that already have to deal with the viral infection and many comorbidities.

Population description at baseline:

Our study recruited 23 patients (2 women) all infected for HIV_1. Mean age at HIV infection diagnosis was 33.9 ± 9.7 years and mean age at diagnosis of RS disease was 39.9 ± 16.0 years. Mean BMI was 22.5 ± 3 and one third of the patients were classified as having metabolic syndrome.

- HIV background:

All patients had been diagnosed more than 10 years ago with a mean exposure time of 21 ± l64 years. VHB co-infection was reported for 1 patient and VHC co-infection for 4. At baseline, mean CD4 cell count was 654 ± 373, all but 2 showed negative viral load (two results not available) and all patients were treated with ARV.

- Renal stone disease:

Patients were included in the study if they exhibited either renal colic (n = 12) or asymptomatic discovery of stones (n = 10) or hematuria (n = 1). Stone disease was expressed by more than one episode in 74% of the patients, only one episode in 22% and more than 4 episodes in 4%. Most of them (82%) had no chronic urinary obstruction and no chronic urinary tract infection (94%).

Most patients were included for RS with spontaneous elimination of the stone (76%) although at inclusion, none of the stones had been collected for analysis. 53% of the patients underwent urologic interventions. Most episodes were bilateral (67%). Most stones were not obstructive (67%) and when renal obstruction was evidenced it was mostly partial (2/3 of the cases n = 6). Only 2 patients had anatomical abnormalities (one ureteral bifidity/duplicity, one vesical dysfunction and one urethroprostatic obstacle).

Radiologic assessment was performed for 87% of the patients, with a CT scan in 60% and an ultrasound + Xray in 40%. 40% of the patients exhibited 1 stone, 25% two stones, 20% three stones, 5% four stones, 5% six stones when for 5% of the patients with a pelvic of lumbar pain, no stone was evidenced.

Very few patients were exposed to known environmental risk factors for RS (overheated work environment 4 %, stay in hot countries 4 %, prolonged immobilization 4%, change in diet 4%) except for regular physical activities 26% or familial history 22% (n = 5).

At baseline, 3 patients were exposed to darunavir and 3 to atazanavir, 1 to efavirenz, 1 to acetazolamide, 2 were treated with allopurinol.

Baseline estimated mean glomerular filtration rate was 78 ± 24 ml/min/1.73m^2 with a mean plasma creatinine of 101 ± 24 µmol/L, meaning that 12 patients exhibited normal renal function and 5 were classified CKD stage 3 (for 6 patients, creatinine and therefore GFR were not available at inclusion).

Other biological data showed high calcium blood levels in two patients (but no clear hyperparathyroidism profile), low phosphate in two patients, low HCO_3^- in one patient, uric acid level above normal in three patients and below normal in one. 6 patients exhibited insufficient vitamin D profile.

Baseline urinary analysis showed a mean 24 hours' diuresis volume of 2106 ± 769 ml. 3 patients had a value below 1500 ml/24hours. Mean urinary sodium value was 73 mmol/L and mean 24 hours' sodium excretion was 144 mmol. No hyperoxaluria was evidenced. Hypocitraturia was present in one patient.

Dietetic interviewing showed that even though mean 24 hours' diuresis was around 2000 ml/day, 9 patients didn't have a good volume repartition during the day. Half of the patients (n = 13) drank tap water (which is perfectly fine). In all but 4 patients, daily dietetic calcium intake was below guidelines. In all but 6, daily protein intake was too low. In all but 4, daily intake for carbohydrates was in the expected range. From the interview, the mean estimated amount of daily NaCL was 6 to 10 gr/day, coherent with 24-hour urinary sodium estimation.

Follow up

Second visit (after 6 months) included a one-day hospitalization and third visit was the closing visit (after 1 year). Patients follow up was one year or more.

During follow up, dietetic counselling was offered by a highly-specialized dietitian (expert in stones management). Interviews showed at the second and third visits that a higher proportion of patients had integrated a more balanced repartition of protein intake (68% vs 42%), of carbohydrates (89% vs 68%) and adopted a better balance in calcium intake (58% vs 26%). Water daily intake tended to increase over follow-up (from a mean value of 1650 ml, to 1955 to 2183 ml) as well as optimal intake balance during the day (53%, to 61% to 78% of the patients).

Baseline hypercalciuria was observed in 7 patients but those results are questionable because of the inappropriately low calcium intakes. Therefore, over follow up, concentration hypercalciuria tended to be less frequent (37% at the second visit and 18% at the last visit) due to higher water intake and better repartition. Biological data showed no major changes in the blood or urine data over the follow up. No change in the situation with regard to the HIV infection was observed (CD4 count, viral load).

During follow up, 3 patients experienced a new renal colic episode (2 colic and one discovery of an asymptomatic stone), complicated by acute renal failure in one patient.

In 6 patients, a PAK test [10] was performed to explore calcium metabolism. In two patients, *absorptive hypercalciuria* was observed and in 4 patients *renal*

hypercalciuria was diagnosed (Table 3).

Stone analysis was available only for 7 patients. Most stones had migrated from ureter (n = 4, 57%), from the left kidney (n = 2, 29%) or the right kidney (n = 1, 14%). Nature of the renal stone was uric acid in one, calcium oxalate (whewellite) in two, phosphocalcic in two, and a mix of phosphocalcic and calcium oxalate (whewellite) in two. Retained mechanism for RS was uric acid dependent for one, oxalic acid dependent for 3 and calcium dependent for 3 (Table 4).

5. Discussion

Our study is a large *prospective* cohort describing the outcomes of HIV patients with RS. Precise diagnosis of stone composition was performed in 10 patients out of 23. Despite the fact that the burden of a medical check-up for a comorbidity considered as minor (compared to HIV) induced a high frequency of no shows and a poor adherence to work-up in our study, patient's referral to our group allowed to investigate the causes of RS.

We found that HIV patients in our study exhibit similar risk of underlying conditions than the general population with 4 patients being diagnosed with hypercalciuria of renal origin and two with absorptive hypercalciuria. Of note, these patients all had recurrent stone episodes within a short follow-up (1 to 2 years). In some of them, the first episode had happened in their twenties, sometimes long before HIV infection, showing that nephrolithiasis history may be important to know when choosing ARV, in order to lower the risk for RS.

Nephrolithiasis in HIV patients has not been scientifically explored surprisingly, as demonstrated by the poor literature (200 articles in PubMed over more

Table 3. In our study, PAK test allowed to discriminate, in hypercalciuric patients, between abnormal gut absorption of calcium, abnormal bone release of calcium (mostly because of hyperparathyroidism) or primitive renal calcium leak.

	No symptoms	Renal colic	Total
PAK test:	4	2	6
Absorptive hypercalciuria	1	1	2
Renal leak	3	1	4

Table 4. Retained mechanism for RS occurrence (from 7 patients having collected stones).

Stone analysis (n = 7)	Mechanism retained (n = 7)		
	Uric acid dependent	Oxalic acid dependent	Calcium dependent
Uric acid (N = 1)	N = 1		
Calcium oxalate (whewellite) (N = 2)			N = 2
Phosphocalcic (N = 2)		N = 2	
Mix of phosphocalcic and calcium oxalate (whewellite) (N = 2)		N = 1	N = 1

Figure 2. A clinical strategy for person living with HIV and RS.

than 20 years) for a condition as frequently encountered as in one out of ten patients. Most articles are case reports, focusing on a specific situation mostly supposedly related to HAART [7] [11] [12] [13] [14] when no clear risk factors description is present and no causal link demonstrated. The two largest retrospective cohorts included 41 patients and 25 patients respectively [15] [16]. Raheem *et al.* [7] reported similar prevalence of nephrolithiasis in HIV compared to the non-HIV population, with a lack of consistent comprehensive metabolic evaluations in HIV patients with recurrent nephrolithiasis. Lin *et al.* [11] showed that nephrolithiasis were found both in antiretroviral-naïve and antiretroviral-experienced patients without statistically significant difference, suggesting that there may be other contributing factors in addition to ARV in the HIV-positive population, the overall prevalence in this Taiwanese population being 8.2%.

Paucity of specific guidelines does not help clinicians to offer high quality care to HIV patients with regard to accurate diagnosis, adapted counselling and follow-up or reduction of chronic kidney disease risk.

Usual care should then follow the guidelines edited for the general population [17] [18] [19] [20]. Some patients treated for HIV infection are exposed to a high risk of RS, because of a combination of known risk factors such as metabolic syndrome [21], chronic diarrhea or exposition to drugs. Kidney stones form because of an imbalance of promoters and inhibitors of crystallization in the urine. It is only when appropriated risk factors are identified that useful behavioral (mostly dietetic) changes may be suggested. Therefore, HIV patients should benefit from precise determination of the causes of urolithiasis, allowing to minimize, through adapted and high specialized dietetic counselling, the risk of recurrences. Some conditions, like hydration (both total volume and nyctemeral dispatching), calcium and sodium daily consumption, familial traits (recurrent stones disease in parents, grandparents) or common risk factors (chronic diarrhea or limited water input secondary to urinary symptoms like dysuria or pollakiuria) should be easily screened and treated in renal stones formers to prevent recurrences.

RS physiopathology is very complex though, explaining why few physicians have enough expertise to rule out renal stone diagnosis. That is why referral to a stone clinic is helpful. **Figure 2** gives an overview of a proposed clinical strategy for HIV physicians when facing RS in HIV patients.

Finally, in HIV infected patients, systematic full work-up looking for constitutional abnormalities enhancing RS should be offered when early in life recurrent episodes are documented. ARV is too often considered as responsible without any clear documentation. Only long term dietetic and behavioral counselling may promote life changes favoring appropriated dilution of urines and lack of recurrence.

Funding

The CalVIH study was supported through a Non Interventional Research Agree-

ment AI424-426 from the Bristol Myers Squibb Company. The research agreement was fully signed by Assistance Publique-Hôpitaux de Paris and Bristol-Myers Squibb SARL on February 11th, 2014.

Acknowledgements

We wish to thank all patients and professionals who contributed to this study.

Conflicts of Interest

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

References

[1] Viljoen, A., Chaudhry, R. and Bycroft, J. (2019) Renal Stones. *Annals of Clinical Biochemistry*: *International Journal of Laboratory Medicine*, **56**, 15-27. https://doi.org/10.1177/0004563218781672

[2] Chuang, T.-F., Hung, H.-C., Li, S.-F., *et al.* (2020) Risk of Chronic Kidney Disease in Patients with Kidney Stones—A Nationwide Cohort Study. *BMC Nephrology*, **21**, Article No. 292. https://doi.org/10.1186/s12882-020-01950-2

[3] Izzedine, H., Lescure, F.X. and Bonnet, F. (2014) HIV Medication-Based Urolithiasis. *Clinical Kidney Journal*, **7**, 121-126. https://doi.org/10.1093/ckj/sfu008

[4] Abufaraj, M., Xu, T., Cao, C., *et al.* (2021) Prevalence and Trends in Kidney Stone Among Adults in the USA: Analyses of National Health and Nutrition Examination Survey 2007-2018 Data. *European Urology Focus*, **7**, 1468-1475. https://doi.org/10.1016/j.euf.2020.08.011

[5] Talati, V.M., Soares, R.M.O., Khambati, A., Nadler, R.B. and Perry Jr., K.T. (2020) Trends in Urinary Calculi Composition from 2005 to 2015: A Single Tertiary Center Study. *Urolithiasis*, **48**, 305-311. https://doi.org/10.1007/s00240-019-01151-z

[6] Daudon, M., Frochot, V., Bazin, D. and Jungers, P. (2018) Drug-Induced Kidney Stones and Crystalline Nephropathy: Pathophysiology, Prevention and Treatment. *Drugs*, **78**, 163-201. https://doi.org/10.1007/s40265-017-0853-7

[7] Zhao, A.M. and Angoff, N.R. (2019) Renal Stone Composed of Ritonavir. *BMJ Case Reports*, **12**, e230487. https://doi.org/10.1136/bcr-2019-230487

[8] Siddiqui, U., Bini, E.J., Chandarana, K., *et al.* (2007) Prevalence and Impact of Diarrhea on Health-Related Quality of Life in HIV-Infected Patients in the Era of Highly Active Antiretroviral Therapy. *Journal of Clinical Gastroenterology*, **41**, 484-490. https://doi.org/10.1097/01.mcg.0000225694.46874.fc

[9] Vargas-Pacherrez, D., Cotrim, H.P., Pires, L., *et al.* (2020) Metabolic Syndrome in HIV-Patients in Antiretroviral Therapy. *Current HIV Research*, **18**, 388-395. https://doi.org/10.2174/1570162X18666200609115615

[10] Pak, C.Y., Kaplan, R., Bone, H., Townsend, J. and Waters, O. (1975) A Simple Test for the Diagnosis of Absorptive, Resorptive and Renal Hypercalciurias. *New England Journal of Medicine*, **292**, 497-500. https://doi.org/10.1056/NEJM197503062921002

[11] Grant, M.T., Eisner, B.H. and Bechis, S.K. (2017) Ureteral Obstruction Due to Radiolucent Atazanavir Ureteral Stones. *Journal of Endourology Case Reports*, **3**, 152-154. https://doi.org/10.1089/cren.2017.0096

[12] Vavassori, A., Lanza, P., Izzo, I., *et al.* (2017) Litiasi biliare e renale in paziente con

coinfezione HIV e HCV genotipo 4 in corso di terapia con daclatasvir/sofosbuvir + ribavirina e atazanavir/ritonavir + abacavir/lamivudina: Caso clinico [Biliary and Kidney Lithiasis during Treatment with Daclatasvir/Sofosbuvir/Ribavirin and Atazanavir/Ritonavir + Abacavir/Lamivudine in an HIV/HCV Genotype 4-Infected Patient: A Case Report]. *Recenti Progressi in Medicina*, **108**, 98-100.

[13] Khalil, C., Mohanty, M.J., Kaatz, G. and Abu-Hamdan, D. (2016) Efavirenz-Associated Urinary Matrix Stone—A Rare Presentation. *The American Journal of the Medical Sciences*, **351**, 213-214. https://doi.org/10.1016/j.amjms.2015.11.020

[14] Wang, L.C., Osterberg, E.C., David, S.G. and Rosoff, J.S. (2014) Recurrent Nephrolithiasis Associated with Atazanavir Use. *BMJ Case Reports*, **2014**, Article ID: Bcr2013201565. https://doi.org/10.1136/bcr-2013-201565

[15] Raheem, O.A., Mirheydar, H.S., Palazzi, K., *et al.* (2012) Prevalence of Nephrolithiasis in Human Immunodeficiency Virus Infected Patients on the Highly Active Antiretroviral Therapy. *Journal of Endourology*, **26**, 1095-1098. https://doi.org/10.1089/end.2011.0639

[16] Lin, K.-Y., Liao, S.-H., Liu, W.-C., *et al.* (2015) Cholelithiasis and Nephrolithiasis in HIV-Positive Patients in the Era of Combination Antiretroviral Therapy. *PLOS ONE*, **10**, e0137660. https://doi.org/10.1371/journal.pone.0137660

[17] Quhal, F. and Seitz, C. (2021) Guideline of the Guidelines: Urolithiasis. *Current Opinion in Urology*, **31**, 125-129. https://doi.org/10.1097/MOU.0000000000000855

[18] Jiang, P., Xie, L., Arada, R., *et al.* (2021) Qualitative Review of Clinical Guidelines for Medical and Surgical Management of Urolithiasis: Consensus and Controversy 2020. *Journal of Urology*, **205**, 999-1008. https://doi.org/10.1097/JU.0000000000001478

[19] Tiselius, H.-G., Daudon, M., Thomas, K. and Seitz, C. (2017) Metabolic Work-up of Patients with Urolithiasis: Indications and Diagnostic Algorithm. *European Urology Focus*, **3**, 62-71. https://doi.org/10.1016/j.euf.2017.03.014

[20] NICE Guideline (2019) Renal and Ureteric Stones: Assessment and Management. https://www.nice.org.uk/guidance/ng118/resources/renal-and-ureteric-stones-assessment-and-management-pdf-66141605137093

[21] Besiroglu, H., Otunctemur, A. and Ozbek, E. (2015) The Metabolic Syndrome and Urolithiasis: A Systematic Review and Meta-Analysis. *Renal Failure*, **37**, 1-6. https://doi.org/10.3109/0886022X.2014.976133