

## Correlations between stones composition, dietary and comorbidities context of the lithiasic patient

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### Abstract

The incidence of nephrolithiasis is in full expansion, its etiology being frequently associated with lifestyle changes. The objective of this retrospective study, carried out between April and December 2019, was to identify the correlations of the known lithogenic factors with the chemical structure of the calculi in the patients from the North-Eastern region of Romania. The results obtained after the data analysis of our LAMPA questionnaire (L – liquids, A – antecedents, M – medication, P – associated pathologies, A – aliments) made in evidence a statistically relevant relationship between the heredocollateral history of lithiasis and calcium oxalate dihydrate (COD) calculi, hypertension and calcium oxalate monohydrate (COM) stones, uric lithiasis and diabetes, COD, and obesity, between predominantly uric lithiasis and meat or meat-derived products consumption, between frequent potato consumption and COD stones and the frequently consume of dairy products and predominantly COM calculi. The authors concluded that the use of a complex questionnaire, like LAMPA, together with Fourier-transform infrared (FTIR) spectroscopic and morphological analysis are essential steps for developing an efficient metaphylaxis.

**Keywords:** kidney stones, FTIR, dietary, comorbidities, lithogenic factors.

### Introduction

The incidence of nephrolithiasis is in full expansion, its etiology being frequently associated with lifestyle changes, including high protein and saline intake in conjunction with inadequate water intake and metabolic alterations [1].

Nephrolithiasis is a frequent urological problem and constitutes a significant burden on the health care systems worldwide. Kidney stones are highly prevalent worldwide with rates ranging from 7% to 13% in North America, 5–9% in Europe, and 1–5% in Asia, according to Sorokin *et al.* [2]. Urolithiasis in young patients is a public health issue due to the increased risk of relapse. Nutrition plays an important role in the etiology of nephrolithiasis.

The composition of urinary calculi represents a crucial step in establishing the etiology of lithiasis, thus providing information on the renal environment in which calculi are formed. Moreover, the identification of crystalline structures from the composition of the stone allows the personalized metaphylaxis of recurrent renal lithiasis [3, 4] The assessment of data obtained from the morphological and spectroscopic analysis together with the information provided by the LAMPA questionnaire (L – liquids, A – antecedents, M – medication, P – associated pathologies, A – aliments) used in the clinic to evaluate the lithiasic patient allowed us to create the first complex analysis of lithiasic patients in the North-Eastern part of Romania.

The pathogenesis of renal calculi indicates a multifactorial and complex interaction between environmental, metabolic, and genetic factors. A key element widely recognized to influence the risk of kidney stone formation is nutrition. Dietary habits can be assessed with food frequency questionnaires (FFQs). According to Shim *et al.*, FFQ enables the assessment of long-term dietary intakes in a relatively simple, cost-effective, and time-efficient manner [5]. Certain researchers' question, however, the importance of using FFQs in epidemiological studies because they generate large amounts of data difficult to be analyzed, the answers can be subjective, or the participants may misinterpret the questions.

### Aim

This is a retrospective study, carried out between April and December 2019, to identify the correlations of the known lithogenic factors with the chemical structure of the calculi in the patients from the North-Eastern region of Romania, therefore creating the premises for contouring the general profile of the lithiasic patient in this area.

### Patients, Materials and Methods

#### Patients

Between April and December 2019, the first 100 patients

were consecutively evaluated in an observational study in the Michel Daudon Center for Morphological and Spectroscopic Analysis of Reno-Ureteral Lithiasis, Iași, Romania. Patients with reno-ureteral lithiasis ranged in age from 19 to 73 years (mean age of 48.6 years), the ratio of men to women being 1.5:1. There were no exclusion criteria in this study.

Patients were informed about the study procedures and signed the informed consent. The study was approved by the Ethics Committee of Dr. C. I. Parhon Clinical Hospital, Iași.

### Study design

Patients with reno-ureteral lithiasis were evaluated in the Department of Urology and submitted to an extraction method (extracorporeal shock wave lithotripsy – ESWL, retrograde ureteroscopy – RURS, percutaneous nephrolithotomy – PCNL, open surgery, expulsion treatment), in agreement with current guidelines [6]. No randomization was done concerning the method used. Additional lab tests were performed to exclude co-morbidities that might change or select the treatment indication (hyperparathyroidism, coagulation disorders, cardiovascular risk, obesity, etc.).

### The LAMPA questionnaire

Before the patient underwent an extraction method, we asked to complete a questionnaire. The LAMPA questionnaire is made of 76 questions, most of which are focused on the dietary habits of lithiasic patients (the quantity of water consumed, the types of water preferred, the intake of proteins, food rich in oxalates, consumption of citrus fruits, etc.), on the comorbidities (high blood pressure, diabetes mellitus, malabsorption syndrome, history of recurrent urinary tract infections, excessive sweating, etc.), but also the chronic medication received.

### Samples' preparation

The calculi from each patient were cleaned with demineralized water, according to international standards [7], dried and stored in an environment with controlled parameters (away from the direct action of sun rays, in a dry place, at a temperature between 20–22°C). At the time of their processing, each calculus was morphologically examined using the Olympus SZ61TR stereomicroscope, equipped with a high-resolution 2592×1944 pixels camera, which was used to identify special structural elements (Randall's plaque, crystalline conversion elements). After the acquisition of these images, calculi in one piece with dimensions over 8 mm were sectioned to identify the core of the stone. We analyzed fragments both from the stone surface and separately from the nucleus.

### Samples' analysis

Calibration before the actual analysis of the sample, the background spectrum measurement was performed by creating a sample consisting exclusively of potassium bromide, which was introduced into the Bruker Alpha II Fourier-transform infrared (FTIR) spectrophotometer. Subsequently, the samples made according to the previously described protocol were introduced in the spectrophotometer; for each sample, the device performed

12 scans, and the result obtained was compared to the 5000 variants of the software.

### Data analysis

Statistical analyses were performed using the  $\chi^2$  (chi-squared) test posted on [www.socscistatistics.com](http://www.socscistatistics.com) and  $p < 0.05$  was considered statistically significant.

### Results

We noted that most of them came from the elimination of the calculus ( $n=48$ ), followed by PCNL ( $n=36$ ), RURS ( $n=13$ ), ESWL ( $n=2$ ), and only one through ureterolithotomy.

Table 1 presents the cases referring to the proportion of the dominant biochemical constituent(s).

**Table 1 – Classification of the calculi in our group according to the main composition**

Stone category	Main component(s)	No. of stones
Pure calculi in which the main component accounts for 100% ( $n=2$ )	COD	1
	UA	1
	COM + COD	8
	COM + CA	3
	COM + UA	1
Almost pure calculi in which the main component constitutes between 80–99% of its total mass ( $n=34$ )	COD + COM	7
	COD + CA	6
	UA + COM	3
	Struvite + CA	3
	Struvite + COM	1
	CY + COM	1
	BR + CA	1
	COM + COD	9
	COM + CA	6
	COM + COD + CA	3
Complex calculi in which the main component is between 60–79% ( $n=45$ )	COM + BR	1
	COD + COM	7
	COD + CA	7
	COD + COM + CA	2
	UA + COM	3
	UA + CA	2
	CA + Struvite	3
	Struvite + COM	1
	BR + COM	1
	COM + CA	8
Complex calculi in which the main component is between 50–59% ( $n=19$ )	COD + COM	3
	Sodium urate + CA + COD	2
	COD + COM + CA	2
	Struvite + COM	1
	COD + CA + Struvite	1
	COM + Sodium urate + Struvite	1
COD + CA	1	

BR: Brushite; CA: Carbapatite; COD: Calcium oxalate dihydrate; COM: Calcium oxalate monohydrate; CY: Cystine;  $n$ : No. of patients; UA: Uric acid.

We observed that only 2% were pure calculi, many stones falling into the 60–79% category. Regardless of the group analyzed, it was shown that the largest proportion

of calculi consists of calcium oxalate (COM – calcium oxalate monohydrate, COD – calcium oxalate dihydrate), in its two forms, followed by infection lithiasis (IL) (struvite and carbapatite – 18 cases) and 9% of stones being composed mainly of UA.

We found that, on average, 63% of patients can pass calculi through the urinary tract. Compared to other categories of calculi, we found that patients with stones formed from calcium oxalate had more frequent first-degree relatives diagnosed with renal lithiasis, in comparison to the other groups of patients, the difference between these groups is statistically significant ( $p=0.042$ ).

This finding implies that the referral to the urologist was delayed, allowing the increase in the size of the calculus, implying difficulties in the therapeutic possibilities and meaning higher costs incurred by the health insurance system.

Related to water consumption, we found that 59% of patients reported reduced consumption (less than 2 L liquids/day), without a statistically significant difference between the four groups of studied calculi ( $p=0.2$ ), and also there was no relationship between chronic alcohol consumption or water origin (tap or bottled) and a certain type of composition (Table 2).

**Table 2 – Liquid consumption related to calculi composition**

Risk factor	COM (n=40)	COD (n=35)	UA (n=9)	IL (n=13)
Low water consumption	25 (62.5%)	21 (60%)	7 (77.7%)	8 (61.5%)
Chronic alcohol consumption	1 (2.5%)	2 (5.71%)	2 (22.2%)	1 (7.7%)
Tap water	3 (7.5%)	3 (8.6%)	2 (22.2%)	3 (23%)
Frequent consumption of carbonated water	–	–	1 (11.1%)	2 (15.4%)
Working environment with high ambient temperatures	9 (22.5%)	9 (25.7%)	–	1 (7.7%)

COD: Calcium oxalate dihydrate; COM: Calcium oxalate monohydrate; IL: Infection lithiasis; n: No. of patients; UA: Uric acid.

Patients with COM calculi from our group are diagnosed more frequently with hypertension compared to patients with COD stones ( $p=0.03$ ). However, this relationship is not confirmed for the other types of calculi ( $p>0.05$ ). We found that diabetes–uric acid (UA) connection is statistically significant ( $p=0.001$ ), but this relationship could not be proven for the rest of the stones in this group ( $p=0.35$ ).

Regarding the relationship between the composition of the calculi and the malabsorption syndromes, we did not find statistically significant differences ( $p=0.76$ ), neither for the chronic treatments with calcium or vitamin D declared by the patient, between the four groups of patients in our group.

In our group, 15% of patients are known to be hypertensive, all receiving treatment.

In the studied group, 15% of the patients are diabetics under specific treatment. Most of the patients in whom we identified uric lithiasis (77%) had diabetes, from this point of view is the only relation with statistical significance ( $p=0.001$ ).

Our study did not found a statistically relevant relationship between the calculi composition and the malabsorption syndromes.

We found that those patients who reported frequent consumption of oxalate-rich foods (chocolate, spinach, dehydrated fruits, grapes) had predominantly calcium oxalate ( $p=0.014$ ) or infection calculi ( $p=0.041$ ) in comparison to patients diagnosed with UA stones.

Excessive salt consumption is an important lithogenic risk factor, but within this group, there were no significant differences between abusive salt consumption and a certain composition ( $p>0.05$ ). Frequent consumption of dairy products was more common in patients diagnosed with COM stones than in those with COD calculi ( $p=0.008$ ). The consumption of proteins of animal origin, other than those derived from the consumption of dairy products, correlates in our group with the formation of UA calculi ( $p=0.029$ ). Frequent potato consumption in our group of patients was statistically correlated with stones made of COM ( $p=0.04$ ) (Table 3).

**Table 3 – Food excesses related to the calculi composition**

Risk factor	COM (n=40)	COD (n=35)	UA (n=9)	IL (n=13)
Frequent consumption of foods rich in oxalates	22 (55.0%)	21 (60%)	1 (11.1%)	7 (53.8%)
Increased salt consumption	21 (52.5%)	14 (40%)	3 (33.3%)	4 (30.7%)
Increased consumption of foods high in animal protein	18 (45%)	18 (51.4%)	8 (88.8%)	4 (30.7%)
Frequent potato consumption	25 (62.5%)	11 (31.4%)	3 (33.3%)	7 (53.8%)
Frequent consumption of dairy products	25 (62.5%)	13 (37.1%)	8 (88.8%)	8 (61.5%)
Low citrus fruits consumption	34 (85%)	29 (82.8%)	7 (77.7%)	12 (92.3%)
Weight loss diet	–	2 (5.7%)	–	1 (7.7%)

COD: Calcium oxalate dihydrate; COM: Calcium oxalate monohydrate; IL: Infection lithiasis; n: No. of patients; UA: Uric acid.

Also, we found that 70% of patients had calculi consisting of calcium oxalate in its two forms, 18% had IL, and 9% UA stones. The pattern of incidence of calcium oxalate calculi does not differ from that reported by most authors in different geographical areas, which states similar percentages of calcium oxalate stones with those found by us in this group of patients.

In the patients from our group, we identified 18% infection calculi with the incidence peak overlapping with that reported by most authors, respectively 40–50 years.

In our research, we found that there is a statistically relevant correlation between the patients who declared a high intake of meat and meat products and the appearance of uric lithiasis.

In our study, we showed that 59% of patients declared that they consumed less than 2 L of water per day, but without this aspect being correlated to the certain chemical composition.

In our study, we found that although there was no statistically relevant link between increased salt intake and a certain compositional type, however, 39% of patients in the group reported increased salt consumption, and more than that, 45.7% of patients in the oxalic lithiasis subgroup have been shown to consume large amounts of salt.

In our study, we found a statistically significant correlation between the consumption of foods rich in

oxalates and the occurrence of calculi made of calcium oxalates. Thus, out of the 70 patients who presented oxalic calculi, 39 reported frequent consumption of foods rich in oxalates, mainly represented by spinach, chocolate, and grapes. A special category in the case of the increased consumption of oxalates, in our study, is represented by the abundant diet in potatoes. The frequent consumption and in large quantities, specific to our region, have led to the creation of a relationship statistically relevant between the consumption of this vegetable and the calculi formed of COM ( $p=0.04$ ).

In our group of patients, we found that in patients with frequent consumption of dairy products, the most common type of lithiasis was COM.

Regarding the peaks of maximum incidence of different types of composition, in the female gender, we find that:

- for COM calculi: peaks of maximum incidence in the category 31–40 years;
- for COD calculi: peaks of maximum incidence in the category 41–50 years;
- for stones of UA: the peak of maximum incidence in the category 51–60 years;
- for calculi made of struvite and carbonate-apatite: the peak of incidence at 41–50 years.

Regarding the peaks of maximum incidence of different types of composition, in the male gender, we find that:

- for COM calculi: peaks of maximum incidence in categories 51–60 and 61–70 years;
- for COD calculi: peaks of maximum incidence in categories 41–50 and 51–60 years;
- for stones of UA: the peak of maximum incidence in the category of 61–70 years;
- for calculi made of struvite and carbonate-apatite: the peak of incidence at 41–50 years.

In our group of patients, we found that lithiasis was more frequently diagnosed and treated in male patients, with the male/female ratio being 1.5/1.

We found that in this group the obese patients mainly had calculi made of COD ( $p=0.02$ ), but in normal-weight and overweight patients we did not find statistically relevant differences between the distinct biochemical types of lithiasis (Table 4).

**Table 4 – Distribution of stone' types according to the BMI**

	COM (n=40)	COD (n=35)	UA (n=9)	IL (n=13)	CY (n=1)	BR (n=2)
BMI less than 25 kg/m <sup>2</sup>	9	5	–	–	–	–
BMI between 25–29 kg/m <sup>2</sup>	24	13	7	8	1	1
BMI over 30 kg/m <sup>2</sup>	7	17	2	5	–	1

BMI: Body mass index; BR: Brushite; COD: Calcium oxalate dihydrate; COM: Calcium oxalate monohydrate; CY: Cystine; IL: Infection lithiasis; n: No. of patients; UA: Uric acid.

In our group, we found that 51% of patients are overweight and more than 33% are obese. In other words, 84% of the patients in whom we performed the morphological and spectroscopic analysis of the calculi were overweight. Knowing the composition of the stone, we compared with statistical significance the relationship between obesity and the appearance of COD calculi ( $p=0.002$ ).

In our study, we found that 63% of patients had another lithiasis episode in their lifetime.

Analyzing the heredocollateral history of renal lithiasis, we observed that almost 31% of patients declared that they had first-degree relatives diagnosed with the same disease. Moreover, we found that for patients in whom spectroscopic COD was identified, the heredocollateral history is statistically significant ( $p=0.042$ ). A positive family history of renal lithiasis is associated with the increased risk of developing the disease, but this relationship is not completely understood, the genetic penetrability of the disease is taken into consideration, as well as behavioral and eating factors acquired within the family.

## ▣ Discussions

One of the best-documented studies on the epidemiology of urinary lithiasis in the United States has been conducted by Lieske *et al.* [8]. The authors assessed the evolution of renal lithiasis for 30 years in Rochester, Minnesota. In the case of men, there was a decrease in the incidence from 155.1 ( $\pm 28.5$ )/100 000 inhabitants in 1970 to 105.0 ( $\pm 16.8$ )/100 000 inhabitants in the year 2000, resulting in a decrease of 1.7% per year. In the case of women, however, there was an increase from 43.2 ( $\pm 14.0$ ) in 1970 to 68.4 ( $\pm 12.3$ )/100 000 inhabitants in 2000, which means an increase of 1.9% per year. According to these data, the ratio between the genders (men/women) suffered a decrease from 3.1/1 in 1970 to 1.3/1 in 2000.

With the increase in the incidence and prevalence of lithiasis, the cost for the treatment determined by this disease has increased. If for the year 1984, worldwide, 900 million dollars were spent, 30 years later, in 2014, the direct costs of treatment for lithiasis amounted to 5.3 billion dollars [9].

Obesity [10], diabetes [11], hypertension, and metabolic syndrome [12] are considered risk factors for lithiasis, and reciprocally the stone formers are predisposed to high blood pressure and chronic kidney disease. Beside some anatomical abnormalities like pyeloureteral syndrome [13] or autosomal dominant polycystic kidney disease (ADPKD) [14], where up to 20% of patients could develop kidney stones [15], several other nutritional factors could be involved, as is vitamin D status [16, 17], thyroid function [18], or insulin resistance [19]. All statistics show that renal lithiasis should be perceived in the context of dramatic changes in dietary habits.

Knowing the epidemiology allows us to understand the extent to which the practice of metaphylactic therapy can prevent the recurrence of lithiasis, and today we can no longer speak of a personalized and efficient metaphylaxis without knowing, on the one hand, the most precise composition of the calculi and, on the other hand, the eating habits, including the daily liquid intake of the lithiasis patient. Infrared spectroscopy is currently recommended as the first intention to determine the composition of the stone, given that the determination by chemical methods is considered to be outdated, due to the low reliability [6].

In our group, 15% of patients are known to be hypertensive, all receiving treatment. Pak *et al.* first described the relationship between renal lithiasis and hypertension [3], and Cappuccio *et al.* demonstrate that in normotensive patients the incidence of renal lithiasis was 13.4%, in

untreated hypertensive patients it was 20.3%, and in hypertensives treated 32.8% [20]. Thus, we find an important discrepancy between the percentage found in our group and the one stated by Cappuccio *et al.* [20], but Borghi *et al.* find a percentage similar to that identified by us, respectively of 14% for hypertensive patients, compared with 3% in patients without hypertension [21].

In the studied group, 15% of the patients are diabetics under specific treatment. Most of the patients in whom we identified uric lithiasis (77%) had diabetes, from this point of view is the only relation with statistical significance ( $p=0.001$ ). Daudon *et al.* identified in a group of 272 diabetic patients the presence of 35.7% UA stones, the discrepancy between the two mentioned percentages probably coming from the size differences of the two compared groups [22].

In the patients from our group, we identified 18% infection calculi, while Kravdal *et al.* [23] report, in Norway, on the previously mentioned group, that 4.1% of cases were struvite stones, finding a decrease of this type of lithiasis from the 6.6% reported by Otnes in the same country and Lieske *et al.* in the United States, at the level of 2010, finds only 3% struvite stones, associated with urinary infections with urea germs [24]. All the above-mentioned authors find that IL predominantly represents the female gender, but in our group of patients, there were no significant differences between the two genders. However, also in the group studied by us, the incidence peak of IL overlaps with that reported by most authors, respectively 40–50 years. Also identifying the bacteria in a urine culture is of significant importance according to a study that highlights the significant correlation between bacterial species found both in the calculi and in the urine [25].

Uric lithiasis represents lithiasis that has experienced the most galloping rhythm of emergence, this being the consequence of adopting the western lifestyle, with a high protein diet. Kravdal *et al.* notes that in the last 40 years, the rate of this type of lithiasis has increased from 2% to 9.1% in Norway [20] a percentage similar to that identified in patients in our group (9% UA stones). Knoll identify in Germany 11.7% UA calculi, but unlike our group where the peak of incident incidence was located at 51–60 years, Knoll places the incidence peak of this type of lithiasis in category 60–69 years [26].

In our research, we found that there is a statistically relevant correlation between the patients who declared a high intake of meat and meat products and the appearance of uric lithiasis. Proteins of animal origin occupy a higher place in the food pyramid, and the consumption of meat and derived products has increased significantly in the last decades. Because the animal proteins contained higher sulfur amino acids compared to the proteins of plant origin, the consumption of meat causes the decrease of the urinary pH, increasing the risk of lithogenesis by decreasing the excretion of urinary citrate and increasing the excretion of oxalate. On the other hand, animal proteins with high purine content cause hyperuricosuria and consequently the formation of UA calculi [27]. We found that those patients who reported frequent consumption of oxalate-rich foods (chocolate, spinach, dehydrated fruits, grapes) had predominantly calcium oxalate ( $p=0.014$ ) or infection calculi ( $p=0.041$ ) in comparison to patients diagnosed

with UA stones. In addition, patients from general population of young adults may have more risk factors for metabolic syndrome, enhancing the importance of understanding nutrition principles which play an important role in stone formation [28].

Despite the advances in endourology [29, 30], the majority of analyzed stones were passed spontaneously.

Although in some studies, the role of food oxalate in the process of lithogenesis remains controversial because of the difficulties of evaluating the intake and the variability of the instinctive absorption of this principle, in our study we found a statistically significant correlation between the consumption of foods rich in oxalates and the occurrence of calculi made of calcium oxalates. Thus, out of the 70 patients who presented oxalic calculi, 39 reported frequent consumption of foods rich in oxalates, mainly represented by spinach, chocolate, and grapes. Pak *et al.*, in a study on 2209 patients concluded that urinary oxalate, as well as the level of urinary calcium, creates favorable conditions for precipitation of salts in patients with oxalic lithiasis [31].

In our group of patients, we found that lithiasis was more frequently diagnosed and treated in male patients, the male/female ratio being 1.5/1, conclusions that are supported by other studies – data provided by *US Nationwide Inpatient Sample* reveals a ratio of 1.7/1 for 1997 but this ratio tends to decrease, in 2002 was 1.3/1. In other studies, *e.g.*, the *South Eastern Group for Urolithiasis Research* (SEGUR) study, for Romania the ratio of the two genders was almost equal, being 1.03/1 at the level of 2015 [32].

In our group, we found that 51% of patients are overweight and more than 33% are obese. In other words, 84% of the patients in whom we performed the morphological and spectroscopic analysis of the calculi were overweight. Knowing the composition of the stone, we compared with statistical significance the relationship between obesity and the appearance of COD calculi ( $p=0.002$ ). Taylor *et al.* [11] and Curhan *et al.* [33] find important differences between the composition of the urine in patients with lithiasis and overweight history as compared to the normal ponderal ones. The participants included in this study had lower urinary pH values and a higher level of urinary excretion of oxalate, UA, sodium, and phosphate compared to the normal ponderal population. A positive correlation between body mass index (BMI) and calcium excretion could only be demonstrated in males [11, 33]. Negri *et al.*, examining a population of 700 lithiasis patients, find that 61% of them had a BMI of over 25 kg/m<sup>2</sup> and also demonstrated the presence of increased urinary excretion of oxalate, UA, and sodium, both in the female gender, as well as in the male one [34]. In contrast to our study, in which we found the prevalence of COD lithiasis in obese patients, Daudon *et al.* discovered, in a group of 2000 patients, the prevalence of uric lithiasis for this category of patients [4].

## ☞ Conclusions

Our ongoing study, the first in Romania, even if it includes only 100 patients, it has concluded that within our geographical area, oxalic lithiasis is the most common

type. IL is in the second place, most likely secondary to incorrect or incomplete treatment of urinary infections, unlike most European countries where uric lithiasis is in this place. We found a statistically relevant relationship between the heredocollateral history of lithiasis and COD lithiasis, the presence of hypertension and COM calculi, uric lithiasis, and the presence of diabetes, COD and obesity, between predominantly uric lithiasis and meat or meat-derived products consumption, between frequent potato consumption and COD and that those who frequently consume dairy products have predominantly COM stones. On the other hand, we could not find a statistically relevant connection between the appearance of a certain type of lithiasis and the malabsorption syndromes or the administration of multivitamins, as otherwise, we could not find a relation between the abusive salt consumption and the tendency to develop a certain biochemical type. We consider that the use of a complex questionnaire, like LAMPA, together with FTIR spectroscopic and morphological analysis are essential steps for developing an efficient metaphylaxis.

### Conflict of interests

There were no sources of funding received for this study. The authors confirm that there is no conflict of interests.

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