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Crystallographic analysis of urolithiasis in patients treated at Centro Médico ABC

Análisis cristalográfico de urolitiasis de pacientes tratados en Centro Médico ABC

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Abstract

Background: *Urinary lithiasis is a chronic disease with increasing prevalence, which generates a great socioeconomic impact. Numerous factors inherent to human biology and sociodemographic variables have been identified, which favor the development of urinary stones (US). The analysis of the chemical composition of US through crystallography with the Fourier technique is a useful tool to know the chemical components of the US and thus understand the causal mechanisms in order to focus on a therapy for lithiasis. Therefore, the exclusive elimination of the US, without an adequate investigation of the causes that led to its formation, only means suppressing the expression of a disease that often causes new episodes.* **Objective:** *The objective is to describe the analysis by crystallography with the Fourier technique of urinary stones from adult patients treated with lithotripsy at the Centro Médico ABC in Mexico City.* **Material and methods:** *With the authorization of the local ethics committee of the American British Cowdray Medical Center in Mexico City with number CMABC-24-52, a descriptive, observational, cross-sectional and retrospective case series was carried out from 2013 to 2023 of adult patients, of either sex and over 18 years of age, post-lithotripsy, with analysis of the urinary stone by crystallography with the Fourier transform technique at the Mayo Clinic in the United States of America. The records of patients with chronic urinary lithiasis and with known calcium and urea alterations were excluded. Those with incomplete measurements, inability to analyze the urinary stone or with loss of the record were eliminated. The sample size was for convenience, being a total of 314 records. For statistical analysis, mean and standard deviation, as well as frequency and percentages, were used.* **Results:** *A total of 314 patient records with lithotripsy were studied, of which 69% were male with an average age of 46 + 14 years. Crystallographic analysis showed that 60% were of single composition, mainly consisting of calcium oxalate monohydrate. 40% were of mixed composition mainly consisting of calcium oxalate plus apatite carbonate.* **Conclusions:** *The importance of crystallographic analysis is essential for the medical treatment of patients with urinary lithiasis because it allows the recognition of diseases associated with its components and therefore, its adequate treatment and prevention.*

Keywords: *Urinary lithiasis. Crystallography. Lithotripsy.*

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Resumen

Antecedentes: *La litiasis uriaria es una enfermedad crónica con prevalencia cada vez mayor, lo que genera un gran impacto socioeconómico. Se han identificado numerosos factores inherentes a la biología humana y variables sociodemográficas, que favorecen el desarrollo de litos urinarios (LU). El análisis de la composición química de los LU a través de la cristalografía con técnica de Fourier es una herramienta útil para conocer los componentes químicos del LU y así entender los mecanismos causales para poder enfocar una terapéutica de la litiasis. Por lo que la eliminación exclusiva del LU, sin una investigación adecuada de las causas que llevaron a su formación, solo significa suprimir la expresión de una enfermedad que muchas veces provoca nuevos episodios.* **Objetivo:** *Describir el análisis por cristalografía con técnica de Fourier de litos urinarios en pacientes adultos tratados de litotripcia en el Centro Médico ABC de la Ciudad de México.* **Material y métodos:** *Con autorización del comité de ética local del Centro Médico American British Cowdray de la Ciudad de México, con número CMABC-24-52, se realizó una serie de casos, descriptivo, observacional, transversal y retrospectivo de expedientes del 2013 al 2023, de pacientes adultos, de cuaquier sexo y mayores de 18 años, postoperados de litotripcia, con análisis del lito urinario por cristalografia con técnica de transformada de Fourier en la Clínica Mayo en Estados Unidos de Norteamérica. Se excluyeron los expedientes de los pacientes con litiasis urinaria crónica y con alteraciones conocidas de calcio y urea. Se eliminaron a aquellos con mediciones incompetas, imposibilidad de analizar el lito urinario o con pérdida del expediente. El tamaño de muestra fue por convenencia, siendo un total de 314 expedientes. Para el análisis estadístico se utilizó promedio y desviación estándar, así como frecuencia y porcentajes.* **Resultados:** *Se estudiaron un total de 314 expedientes de pacientes con litotripcia, de los cuales el 69% fueron masculinos con edad promedio de 46 ± 14 años. El análisis cristalográfico demostró que el 60% fueron de composición única principalmente por monohidrato oxalato de calcio. El 40% fueron de composición mixta, principalmente conformado por oxalato de calcio más carbonato de apatite.* **Conclusiones:** *La importancia del análisis cristalográfico es esencial para el tratamiento médico de los pacientes con litiasis urinaria porque permite reconocer enfermedades asociadas a los componetes del mismo y, por ende, a su adecuado tratamiento y prevención.*

Palabras clave: *Litiasis urinaria. Cristalografia. Litotripcia.*

Introduction

Urolithiasis has become a chronic disease with a significant impact on the quality of life and work situation of those who suffer from it. Its prevalence and recurrence rates are increasingly high, generating a significant socioeconomic impact in any country by affecting the health care system.

The lifetime risk of urinary stone (US) formation is around 10-15% in developed countries, but can reach 25% in the Indian subcontinent, the Middle East, and in parts of South America and Africa, with a recurrence rate close to 50%[1-3]. In Mexico, in 1984, the Mexican Social Security Institute[4] reported a urolithiasis prevalence of 2.4 cases/10,000 inhabitants, mainly in the states of Yucatán, Puebla, and Quintana Roo, with 5.8 cases/10,000 inhabitants.

The formation and development of crystals in urine depend on the level of supersaturation and the amount of metabolic promoters and inhibitors. Numerous factors inherent to human biology and some sociodemographic variables have been identified that favor the development of US[5,6].

The analysis of US has been established to identify their composition and prevent their formation, using various techniques ranging from the simplest, such as radiological analysis, to the most advanced and modern, such as crystallography, which is responsible for the qualitative and quantitative identification of US[3].

Crystallographic analysis using the inverse Fourier technique is a technique that uses the Fourier transform to analyze the solid structure of crystals, which helps to understand their properties[7]. The Fourier transform is a mathematical tool used to represent the distribution of atoms in a crystal. To apply the Fourier transform in crystallography, it is performed using infrared spectroscopy, which is the most common technique in the study of the structure of solid materials. Through this analysis, precise information is obtained about the cause of urolithiasis by identifying and quantifying the crystalline phases using physical analysis methods to collect US from different urological treatments[8].

In different parts of the world, there is research related to the analysis of US. For example, Daudon et al. in 2009[9] in France described that the crystalline organization is inversely proportional to the resistance to fragmentation by shock waves. Giannossi et al. in 2012[10] in Italy determined the mineralogical and morphological compositions of US, where calcium oxalate stones were the most frequent. In Belgium, Castiglione et al. in 2018[11] identified that the components of US were calcium oxalate monohydrate (COM) and dihydrate,

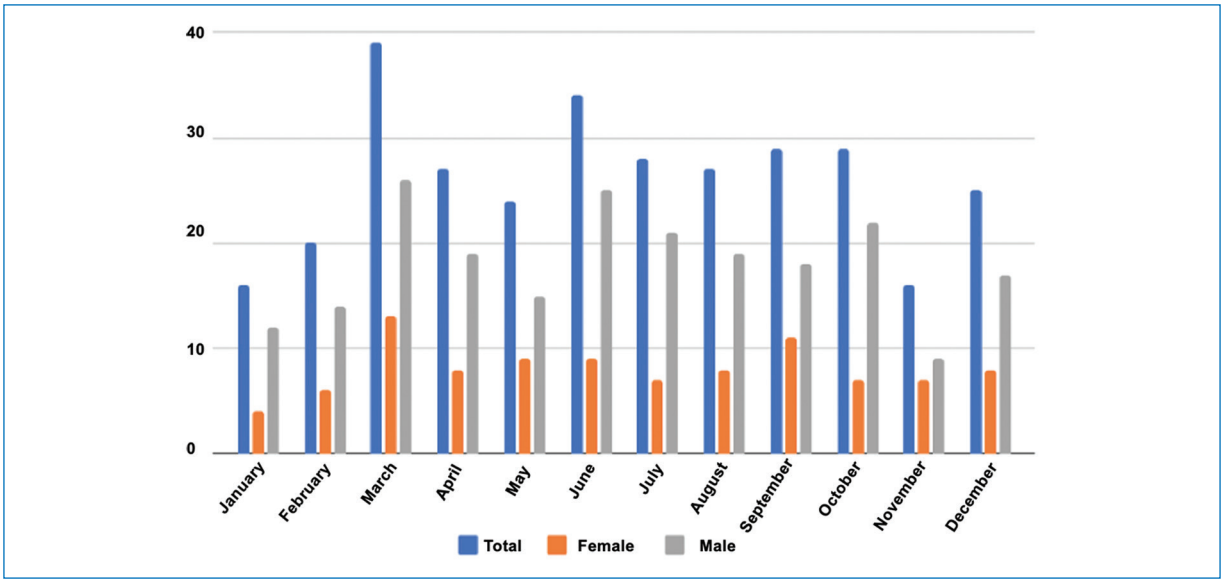

Figure 1. Distribution by month and gender.

anhydrous and dihydrate uric acid (UA), apatite, struvite, brushite, and other components. In Monterrey, Mexico, in 2013, Aragon-Tovar et al. in 2013[12] determined that the prevalence of US increases in summer, and that 80% of US had a mixed composition, with calcium oxalate plus calcium phosphate being the most frequent.

Thus, it is not surprising that different clinical guidelines on urolithiasis, published in recent years, do not hesitate to point out stone analysis as an essential element and starting point in the study of the disease[13,14].

Therefore, the exclusive elimination of the US, without an adequate investigation of the causes that led to its formation, only means suppressing the expression of a disease that often causes new episodes. Thus, crystallographic analysis of the US is a useful tool to understand the causal mechanisms, as well as the therapeutic approach to lithiasis.

The objective of this study is to describe, through crystallography with the inverse Fourier technique, the chemical composition of US from adult patients treated with lithotripsy at the Centro Médico ABC in Mexico City.

Material and methods

With authorization from the local ethics committee of the American British Cowdray Medical Center in Mexico City under No. CMABC-24-52, we conducted a descriptive, observational, cross-sectional, and retrospective case series of records from 2013 to 2023, including adult patients of any gender, older than 18 years, who underwent lithotripsy and had their US analyzed by crystallography with the Fourier transform technique at the Mayo Clinic in the United States of America. Records of patients with chronic urolithiasis and known calcium and urea alterations were excluded. Those with incomplete measurements, impossibility of analyzing the US, or loss of the record were eliminated.

The size of the sample was by convenience, totaling 314 records.

For statistical analysis, mean and standard deviation, as well as frequency and percentages, were used.

Table 1. Gender distribution by age group

Variables	Age groups (years)				
	f (%)				
	< 20	20 a 39	40 a 59	60 a 79	> 80
Female	5 (1.6)	36 (11.5)	41 (13)	13 (4.1)	2 (0.6)
Male	0	88 (28)	95 (30)	32 (10.2)	2 (0.6)
Total	5 (1.6)	124 (39.5)	136 (43)	45 (14.3)	4 (1.2)

f: frequency.

Results

From 2013 to 2023, a total of 314 patients underwent lithotripsy, of whom 217 patients (69%) were men with

a mean age of 46 ± 14 years; the rest were women with a mean age of 44 ± 16 years, resulting in a male-to-female ratio of 2.2-1.

Regarding the age group, the most frequent was 40-59 years with 43%, followed by 18-39 with 39.5%, then 60-79 with 14.3%, and the rest older than 80 years (Table 1).

In relation to the months of presentation of urolithiasis (US), a homogeneous distribution was maintained from March to October, with a slight increase in March and July (Fig. 1).

Regarding the crystallographic analysis, 60% (188 stones) had a unique composition. Of these, 46% were composed of COM; 11% by calcium oxalate dihydrate (COD), 2.7% by brushite (BS), and 2.1% by UA (Fig. 2).

Calcium oxalate (CO) was the basis of the mixed composition of the stones, of which 27% were composed of a base plus carbonate apatite (CO + CA), 5.5% of a base plus UA (CO + UA), 5.5% of a base plus magnesium ammonium phosphate (CO + MAP), 1.3% of a base plus calcium phosphate (CO + CP), 2% of a base plus carbonate apatite plus UA (CO + CA + UA), 0.9% was formed of a base plus ammonium acid urate (CO + AAU), and the rest of a base plus cystine (CO + CYS) (Table 2).

Discussion

Urolithiasis is a common disease that represents a healthcare burden with associated risk factors. This study collected information from patients treated for urolithiasis for the 1st time, with a male/female ratio of 2-1, which is consistent with what Awedew et al. reported[15] worldwide and Aragon-Tovar in Mexico[12].

The age range with the highest frequency was 40-59 years, with a mean age of 46 ± 14 years. This result is consistent with Arias[16] and Awedew[15] who report that urolithiasis develops most frequently between the fourth and sixth decades of life.

Regarding the month of presentation of lithiasis, it occurred homogeneously from March to October, which does not correspond to that reported by the Instituto Mexicano del Seguro Social[17], by Aragon[12] who states that the incidence rate of US increased in the hottest months.

An adequate analysis of the US through crystallography is essential to initiate the diagnostic process of the underlying metabolic alteration. Reports on the composition of the stones mostly indicate that > 70% have a mixed composition[12,17], but in our study, only 40% were of mixed origin, with those of unique composition predominating.

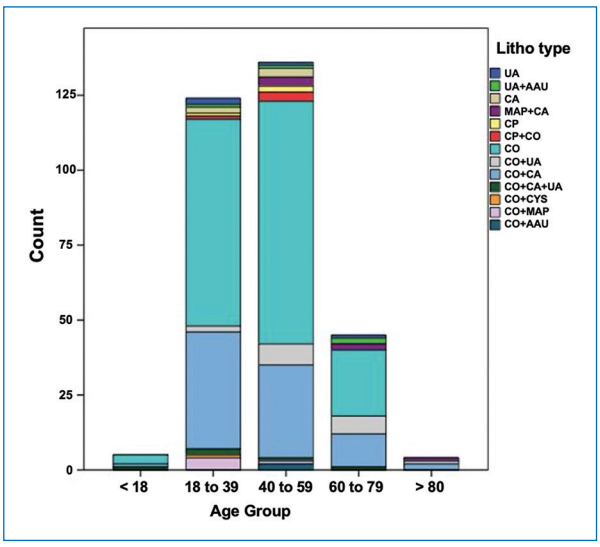

Figure 2. Distribution by type of composition and age group.

Table 2. Distribution of single and mixed stone components by gender

Type of composition	Male (%)	Female (%)	Total (%)
Single composition			
COM	108 (34.4)	36 (11.6)	144 (46)
COD	31 (9.9)	4 (1.1)	35 (11)
Bru	3 (1.05)	2 (0.65)	5 (1.7)
UA	4 (1.1)	0	4 (1.1)
Mixed composition			
CO + CA	56 (13)	29 (9)	85 (27)
CO + UA	14 (4.4)	3 (1.1)	17 (5.5)
CO + MAP	6 (1.9)	1 (0.4)	7 (2.3)
CO + CA + UA	2 (0.65)	4 (1.3)	6 (2)
CO + CP	2 (0.65)	2 (0.65)	4 (1.3)
CO + AAU	0	3 (0.95)	3 (0.95)
CO + CYS	3 (0.95)	0	(0.95)

COM: calcium oxalate monohydrate, COD: calcium oxalate dihydrate, Bru: brushite; UA: uric acid, CO + CA: calcium oxalate + apatite, CO + UA: calcium oxalate + uric acid; CO + MAP: calcium oxalate + ammonium magnesium phosphate (struvite), CO + CA + UA: calcium oxalate + apatite + uric acid; CO + CP: calcium oxalate + calcium phosphate; CO + AAU: calcium oxalate + ammonium acid urate; CO + CYS: calcium oxalate + cysteine.

In stones of unique composition, the highest percentage in men was COM, which is generally associated with idiopathic hypercalciuria[18].

COD was more prevalent in the group of women, which is associated with a deficiency of crystallization inhibitors (phytates) and a greater presence of heterogeneous nucleants in the urine, which are organic matter induced by diseases more prevalent in this group, such as arterial hypertension and hyperuricemia, and to a lesser extent, hyperglycemia and hypercholesterolemia[19].

UA stones followed, which are associated with a disorder of purine metabolism caused by a hereditary deficiency of the xanthine dehydrogenase/oxidase enzyme, leading to an increase in xanthines; finally, brushite stones are associated with primary hyperparathyroidism or primary tubular acidosis[20].

It is known that mixed component stones are due to heterogeneous nucleation phenomena (urate nuclei) with a calcium oxalate base, which is produced daily in the liver or through diet. Calcium oxalate kidney stones form when urine contains more of these substances than the fluid can dilute them; when this occurs, calcium and oxalate form crystals, and if at that moment the urine lacks the substances that prevent the agglutination of crystals, then the ideal environment for the formation of kidney stones is created. The consumption of nuts, chocolate, Vitamin C, and dietary supplements has a high oxalate content. Furthermore, intestinal bypass surgery, excessive use of calcium-based antacids and laxatives, and certain drugs used to treat migraines or depression increase calcium oxalate levels[20].

In this study, the base of the mixed component stones is calcium oxalate, with the most frequent combination, in both men and women, being calcium oxalate plus carbonate apatite (CO + CA); apatite is the type of crystal found in bones, formed from the union of ammonium and carbonate radicals with phosphate in the urine, and is more common in middle-aged men. It is related to hyperparathyroidism.

Following in frequency are calcium oxalate plus UA (CO + UA) stones, presenting more frequently in men. Next are calcium oxalate plus magnesium ammonium phosphate (CO + MAP) stones; magnesium ammonium phosphate (struvite) stones are often called “infection stones” because they are closely related to urinary tract infections caused by organisms that break down urea. They can grow rapidly over a period of weeks to months and, if not treated properly, can become staghorn or branched stones that fill the entire collecting system of the kidney. If left untreated, they can lead to impaired kidney function and end-stage renal disease[21].

The most important aspect of the present study is to offer a description of the type of stone components that patients treated in a private tertiary-level hospital present, paving the way for prospective studies where, in addition to knowing the components of the stones, comorbidities, diet type, etc., are associated, since kidney stones are sometimes the initial clinical signs of other diseases.

Conclusion

The importance of crystallographic analysis is essential for the medical treatment of patients with urolithiasis because it allows the recognition of diseases associated with the components of the stone and therefore, their adequate treatment and prevention.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed. Due to the type of study, clinical records were reviewed, which required authorization from the local Ethics Committee of the American British Cowdray Medical Center in Mexico City under No. CMABC-24-52.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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