



Computed tomographic characterization of urinary stones in patients with urolithiasis from Southeast Mexico

Katy Sánchez-Pozos^{a,1}, Abraham Adolfo Ramírez-Jurado^{b,1}, Martha Medina-Escobedo^c, Ángel Gabriel Garrido-Dzib^c, Lizeth Araceli González-Rocha^c, Ana Ligia Gutiérrez-Solis^c, Azalia Avila-Nava^c, Roberto Lugo^{c,*}

^a Research Division, Hospital Juárez de México, Av. Instituto Politécnico Nacional 5160, Magdalena de las Salinas, Delegación Gustavo A. Madero, 07760. Ciudad de México, México

^b Department of Radiology, Hospital Regional de Alta Especialidad de la Península de Yucatán, Calle 7 por 20 y 22 Num 433, Fracc. Altavista, 97130, Mérida, México

^c Research Unit, Hospital Regional de Alta Especialidad de la Península de Yucatán, Calle 7 por 20 y 22 Num 433, Fracc. Altavista, 97130, Mérida, México

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ABSTRACT

Urolithiasis (UL) is a severe public health concern in southeastern Mexico. Computed tomography (CT) is the first-line diagnostic method for patients with suspected UL. The present study aimed to characterize stones in the entire urinary system using CT and to contribute to personalized treatment in patients with UL. Patients >18 years of age with suspected UL were enrolled. Characteristics of UL included stone size, location (kidney, ureters, and bladder), composition of the stone in Hounsfield units (HU), presence of staghorn stone(s), and obstructive uropathy. Patients were stratified according to sex and age to determine whether stone size and HU were dependent on hormonal factors in females and on prostatic hyperplasia in males. The Mann–Whitney *U* test was used to compare median values. Frequencies are expressed as percentages and were analyzed using the Mantel–Haenszel chi-squared test. A total of 1150 patients were included in this study, of whom 744 (64.7 %) had UL in only 1 anatomical location in the urinary system, and 406 (35.3 %) had stones in ≥ 2 anatomical locations. Localization and stone size differed between males and females ($p < 0.05$). Additionally, males exhibited differences in HU ($p = 0.024$) and frequency of obstructive uropathy ($p = 0.10$) when stratified according to age (≤ 50 and > 50 years). In addition, females exhibited statistical differences in HU ($p = 0.010$) and kidney stone size ($p = 0.047$) dependent on age (≤ 47 and > 47 years). In conclusion, findings suggest that HU and stone size differ in different anatomical structures of the urinary system. In addition, differences in stone size and composition may be associated with age and sex.

1. Introduction

Urolithiasis (UL) is a serious public health problem worldwide [1–3]. The prevalence of UL in Mexico is estimated to be 2.4/10,000

* Corresponding author.

E-mail address: roberto.lugo.gomez@gmail.com (R. Lugo).

¹ These authors contributed equally to this work.

inhabitants; however, in the state of Yucatán, it is higher than the national average (5.8/10,000 inhabitants) [4]. Another study indicated that the prevalence in the state of Yucatan was 9.4/10,000 inhabitants [5]. For this reason, Southeast Mexico is considered to be an endemic region in the country, reporting the highest number of hospital admissions for UL across the country [6]. Acute recurrence, pain, and chronic urinary infections are the most common symptoms of UL, and their progression can lead to chronic renal dysfunction and organ resection [7]. Obesity (OB), diabetes mellitus (DM), hypertension (HTN), genetics, and nutritional and dietary alterations are risk factors for the development of UL [8]. In fact, OB, DM, and HTN are the most prevalent comorbidities in Southeast Mexico, showing not only high risk for the development of UL but also a high risk for disease recurrence with rapid progression [9,10].

Ultrasonography is the first-line modality used to diagnose UL. This method has several advantages, including accessibility, low cost, and lack of ionizing radiation. However, its sensitivity and specificity are low (approximately 84 % and 53 %, respectively), and its interpretation depends on the operator, patient body mass, and stone size (stones <5 mm cannot be reported) [11,12]. The best imaging method to diagnose UL is computed tomography (CT) because its sensitivity and specificity are higher than those of other methods (approximately 95 % and 98 %, respectively). In addition, it can be used to identify small stones (approximately 1 mm in size) in different regions of the urinary tract [11,13]. CT enables the evaluation of stone density in Hounsfield Units (HU), which has gained importance as a diagnostic tool because it can predict stone composition [14]. Moreover, CT can be used to determine the appropriate treatment for each patient (medical or surgical) according to the stone characteristics (size, location, and tomographic density).

Our Hospital in Southeast Mexico receives patients from all parts of the Yucatan Peninsula with multiple urinary complications, such as renal stones, obstructive processes, abscesses, and chronic infections, all of which are in the advanced stages of UL, such as chronic kidney disease. Thus, CT characterization of urinary system stones will enable the prediction of the type of stone and subsequent therapeutic management. Generated knowledge could establish a basis for proposing specific treatments directed at our population and increase the current understanding of UL.

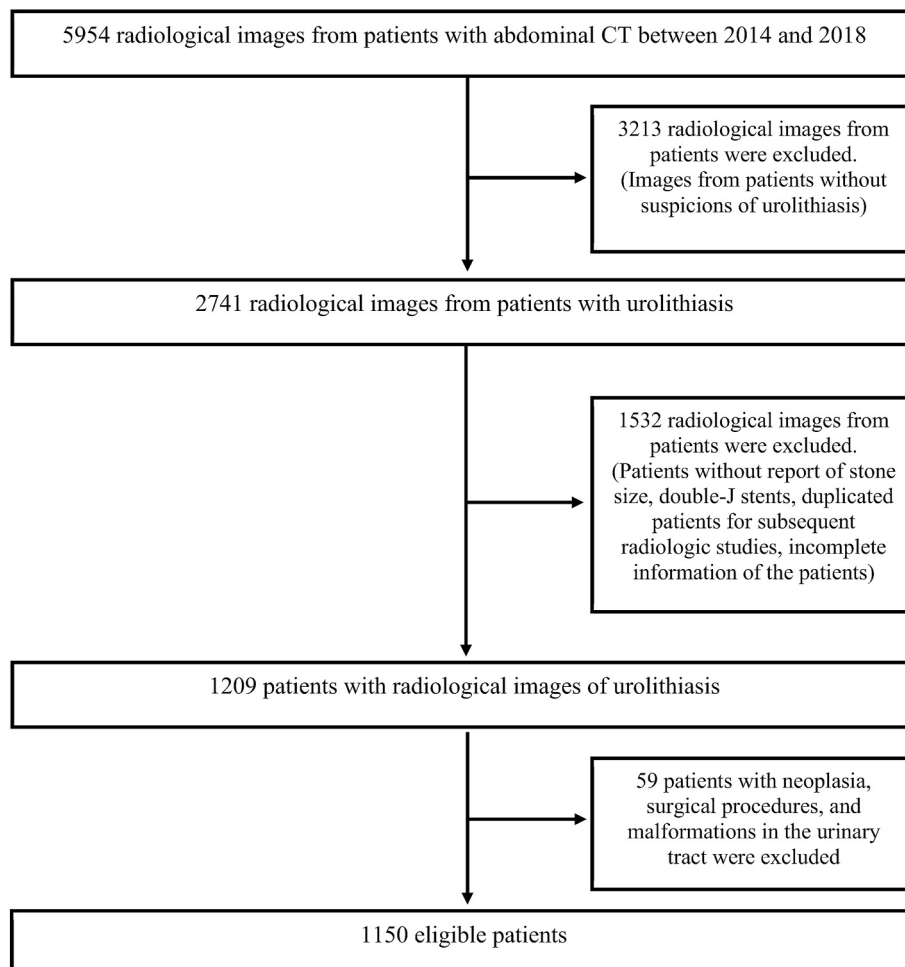


Fig. 1. Scheme of the sample selection.

2. Materials and methods

The study was an observational, descriptive, and cross-sectional conducted according to the guidelines of the Declaration of Helsinki and approved by the Research Committee (DG/1162/2019) and the Ethics Committee (CEI/021/2019) of the Hospital Regional de Alta Especialidad de la Península de Yucatán, Mexico, in connection with the research project (protocol identification: 2019-009).

2.1. Population

Participants were selected according to the following criteria: age >18 years; suspected UL; and abdominal CT performed using the same equipment between January 2014 and December 2018. Only the first CT scan of each patient was considered, and subsequent studies were excluded. In addition, patients with cancer, malformations of the urinary tract, double-J stents, or surgical procedures before the abdominal CT scan were excluded.

2.2. Identification of samples using CT

A CT scanner (Revolution EVO, GE Healthcare, Madison, WI, USA) equipped with a 64-row detector was used to identify the location, size, and HU of patients with suspected UL. CT parameter settings were as follows: collimation, 5 mm; voltage, 120 kV; and current, 180 mA. The images were visualized using RadiAnt DICOM viewer 4.6.4 software, using the soft tissue of the abdomen with a window width of 400 and a window level of 50. Characteristics of UL assessed included stone size, location (kidney, ureters, and bladder), composition of the stone in terms of HUs (media obtained from all stones in the specific UL structure), presence of staghorn stones (>50 mm), and obstructive uropathy. In all cases, if a patient had >1 stone at the same location, only the largest stone was considered.

2.3. Statistical analyses

Statistical analyses were performed using Jamovi software version 1.6 (Jamovi Project 2021, Sydney, Australia). The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. The Mann–Whitney *U* test was used to compare median values. Data are expressed as median and quartiles. Frequencies are expressed as percentages and were analyzed using the Mantel–Haenszel chi-squared test. Differences with $p < 0.05$ were considered to be statistically significant.

3. Results

Overall, 1150 patients fulfilled the inclusion criteria (Fig. 1): 391 (34 %) males (mean [$\pm$ SD] age, 43.3 ± 15.0 years; 759 (66 %) females, mean age 46.8 ± 14.1 years). The general characteristics of the urinary stones in patients with UL (stone size, HUs, and obstructive uropathy) are summarized in Table 1. In addition, data reported in Table 1 show that 744 patients (64.7 %) had UL in only 1 anatomical location of the urinary system, and 406 (35.3 %) had stones in ≥ 2 anatomical locations. Larger stones were located in the bladder. HU values indicated that most stones measured 700–868 HU, and bladder stones exhibited a median HU of 675.

Females exhibited larger right kidney stones than males (Fig. 2A). However, males exhibited greater calculi sizes in the right ureter and bladder than females ($p < 0.05$). Moreover, the HU values measured in the right kidney, left ureter, and bladder in females were significantly greater than those in males (Fig. 2B).

Staghorn stones were analyzed separately to avoid bias in kidney stone measurements. The right kidneys of males exhibited larger staghorn stones than in females, exhibiting a statistical difference (median 56.0 mm [IQR 51.5–65.0 mm] vs. 49.0 mm [IQR 41.0–57.0 mm]; $p = 0.035$). Median HU values for staghorn stones exhibited a statistically significant difference between males and females (523

Table 1
General characteristics of the patients with urolithiasis.

Anatomic structure	Patients (n)	Stone size (mm)	Hounsfield units	Obstructive uropathy n (%)
Single site:	744			
Right kidney	347	12.0 [7.0–23.0]	790 [500–1076]	61 (17.5)
Left kidney	270	11.0 [6.0–20.0]	700 [450–1000]	52 (19.2)
Right ureter	52	11.0 [7.5–13.5]	800 [600–1090]	21 (40.3)
Left ureter	58	9.0 [5.0–12.2]	868 [585–1200]	38 (65.5)
Bladder	17	18.0 [9.3–39.0]	675 [500–1090]	2 (11.7)
Various sites:	406			
Bilateral kidney	189	16.0 [8.5–30.0]	648 [445–920]	57 (30.1)
Kidney + ureter	36	18.5 [11.0–29.5]	962 [684–1140]	20 (55.5)
Kidney + bladder	18	20.0 [9.0–36.0]	725 [650–1100]	2 (66.6)
Bilateral ureter	10	12.0 [6.5–22.0]	790 [640–1070]	3 (30.0)
Ureter + bladder	9	26.0 [17.0–89.0]	742 [400–1150]	9 (100.0)
Kidney + ureter + bladder	1	33.0 [33.0–33.0]	482 [482–482]	1 (100.0)

The parameters were analyzed using Mann–Whitney *U* test and expressed by median and IQR.

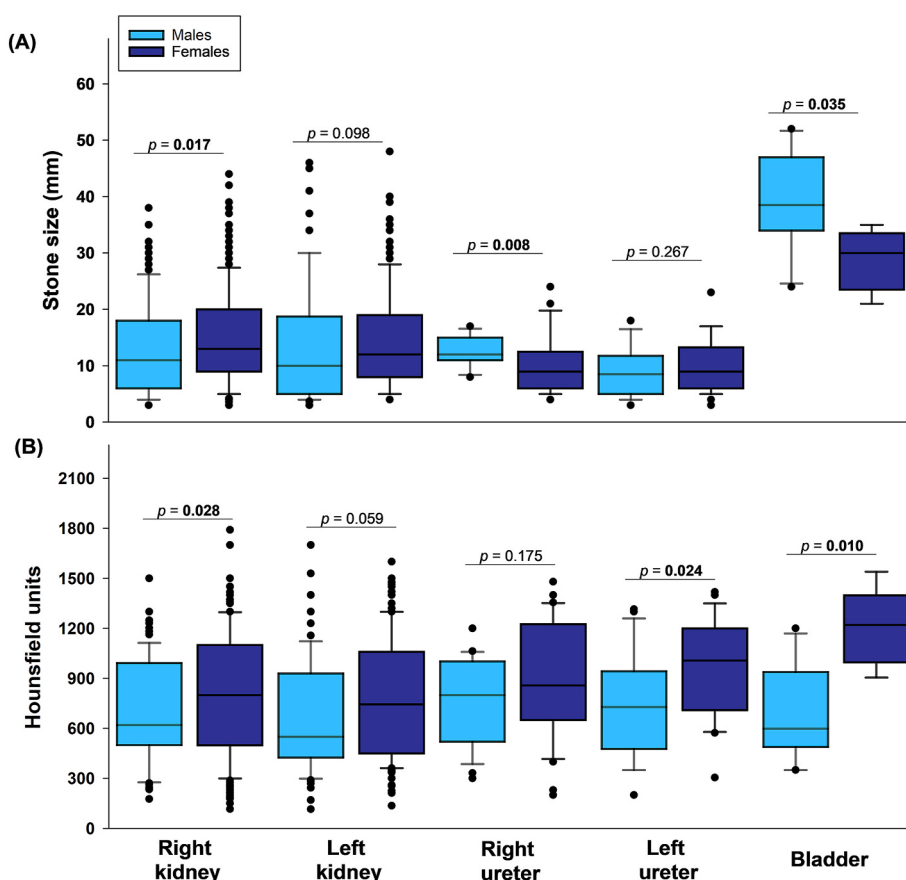


Fig. 2. Characteristics of the stones according to the specific anatomic structure from patients with UL. (A) Stone size expressed in millimeters. (B) Composition of the stones expressed in HU. Males: right kidney (n = 97); left kidney (n = 86); right ureter (n = 21); left ureter (n = 26); bladder (n = 12). Females: right kidney (n = 205); left kidney (n = 172); right ureter (n = 31); left ureter (n = 32); bladder (n = 5). Staghorn stones were excluded.

HU [IQR 449–591 HU] vs. 965 HU [IQR 675–1034 HU]; $p = 0.016$) (Supplementary Fig. S1).

To identify stones in different segments of the urinary system, the urinary system was segmented as follows: the kidney was divided into the upper, middle, and bottom renal collectors; the ureters were divided into the upper, middle, and bottom third; and the bladder was not divided. Stone size and HU according to sex in all segments of the urinary system are presented in Fig. 3.

The right bottom renal collector (median = 11.5 mm versus vs. 15.0 mm; $p = 0.026$), the right middle third (median = 13.0 mm vs. 8.0 mm; $p = 0.039$) and right bottom third (median = 12.5 mm vs. 9.0 mm; $p = 0.046$) of the ureters exhibited statistical differences when comparing stone size between males and females, respectively. In addition, the left middle renal collector (median = 5.0 mm vs. 11.0 mm; $p = 0.041$), left bottom renal collector (median = 10.0 mm vs. 13.0 mm; $p = 0.013$), and left bottom third of the ureter (median = 5.0 mm vs. 10.0 mm; $p = 0.033$) exhibited statistical differences when comparing stone size according to sex.

According to HU, the right bottom renal collector (median = 592 HU vs. 756 HU; $p = 0.033$) and right middle third of the ureters (median = 850 HU vs. 663 HU; $p = 0.033$) exhibited statistically significant differences between sexes. In addition, the left bottom renal collector (median = 523 HU vs. 965 HU; $p = 0.016$) and the left bottom third of the ureters (median = 650 HU vs. 1132 HU; $p = 0.002$) exhibited statistical differences between males and females (complete analysis available in Supplementary Table S1). Staghorn stones were excluded from the analysis in all cases.

Similarly, stone size and HU for multiple ULs were analyzed separately. Regarding stone size, patients with UL in the kidney and ureters (median = 13.0 mm vs. 10.0 mm; $p < 0.001$) and ureter and bladder (median = 10.0 mm vs. 17.5 mm; $p < 0.001$) exhibited statistical differences when compared between males and females, respectively, and only patients with UL in the kidney and ureters (median = 653 HU vs. 950 HU; $p < 0.001$) exhibited statistical differences when HU were compared (data not shown).

Age is considered to be a risk factor for the development of UL. Fifty percent of males >50 years of age develop prostatic hyperplasia [15]. In this context, males were grouped according to age: ≤ 50 years (n = 219) and >50 years (n = 145). Stone size, HU, and frequency of obstructive uropathy in these groups are summarized in Table 2. Characterization of stones in the kidneys, ureters, and bladders in both groups are shown in Supplementary Fig. S2.

Differences in stone size were only observed in the bladder (median = 25.0 mm vs. 42.0 mm; $p = 0.016$). Nevertheless, HU showed

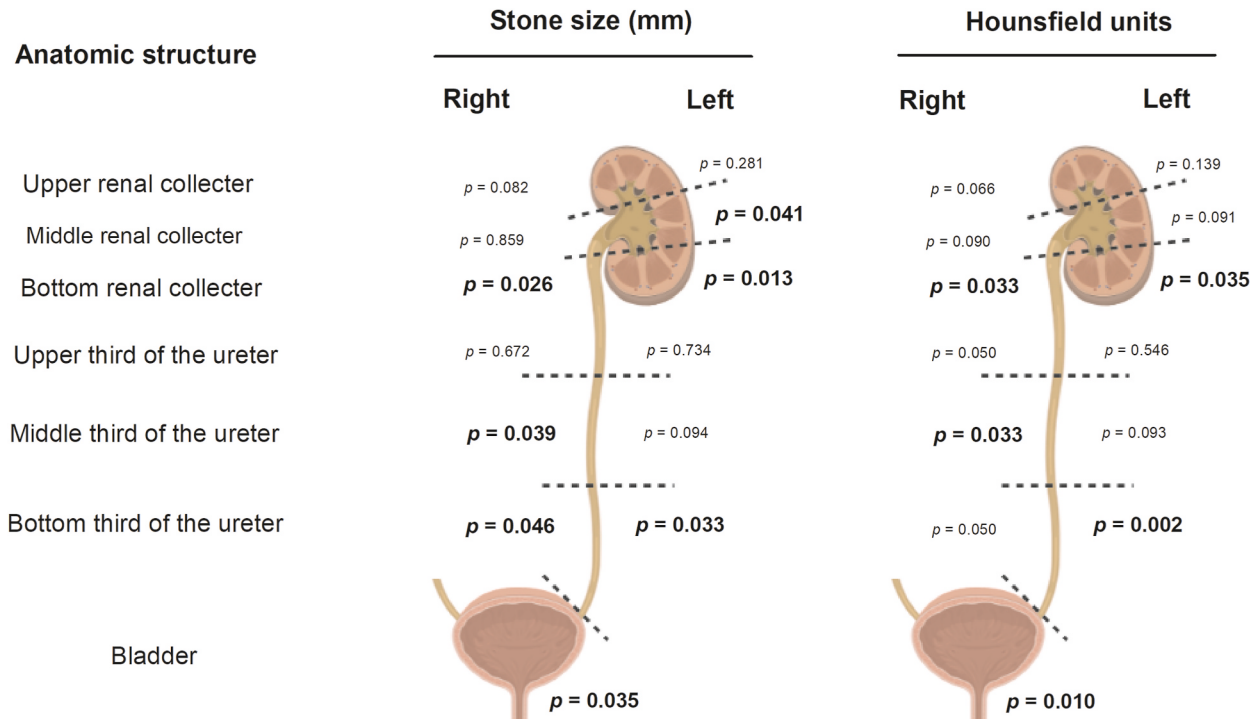


Fig. 3. Comparison of the stone size and HU by different segments of the urinary system between males and females. Males: right upper renal collector (n = 20); right middle renal collector (n = 25); right bottom renal collector (n = 52); upper third of the right ureter (n = 6); middle third of the right ureter (n = 8); bottom third of the right ureter (n = 7); left upper renal collector (n = 13); left middle renal collector (n = 21); left bottom renal collector (n = 49); upper third of the left ureter (n = 7); middle third of the left ureter (n = 3); bottom third of the left ureter (n = 16); bladder (n = 12). Females: right upper renal collector (n = 29); right middle renal collector (n = 58); right bottom renal collector (n = 120); upper third of the right ureter (n = 12); middle third of the right ureter (n = 5); bottom third of the right ureter (n = 14); left upper renal collector (n = 33); left middle renal collector (n = 47); left bottom renal collector (n = 92); upper third of the left ureter (n = 14); middle third of the left ureter (n = 5); bottom third of the left ureter (n = 13); bladder (n = 5).

Table 2
Comparative analysis according to age in male patients with urolithiasis.

Characteristics, n (%)	Age ≤50 Years Old 219 (60.2)	Age >50 Years Old 145 (39.8)	p-Value
Stone size (mm)	11.0 [7.0–20.0]	12.0 [6.0–18.5]	0.598
Kidney	11.0 [6.0–20.0]	11.5 [6.0–18.0]	0.839
Ureter	11.0 [8.0–13.0]	11.0 [5.0–15.0]	0.944
Bladder	25.0 [24.0–33.5]	42.0 [34.5–50.5]	0.016
Hounsfield units	670 [490–990]	581 [428–835]	0.024
Kidney	700 [500–1023]	581 [396–794]	0.017
Ureter	800 [508–1047]	724 [537–856]	0.310
Bladder	401 [350–545]	690 [561–1075]	0.016
Obstructive uropathy	84 (38.3)	36 (24.7)	0.010

The parameters were analyzed using Mann–Whitney *U* test and expressed by median and IQR. The obstructive uropathy was analyzed using the Mantel–Haenszel Chi-square test. Staghorn stones were excluded.

statistical differences in the kidney (median = 700 HU vs. 581 HU; $p = 0.017$) and in the bladder (median = 401 HU vs. 690 HU; $p = 0.016$) in males ≤50 vs those >50 years of age.

Among females, a similar classification was performed, but the division was according to hormonal factors (decalcification through menopause age in the Mexican population): ≤47 years (n = 35 [52.5 %]) and >47 years (n = 324 [47.5 %]); the results are summarized in Table 3. Stone size and HU values in the kidney, ureter, and bladder are presented in Supplementary Fig. S3.

4. Discussion

UL is considered to be a severe public health problem in several countries. Its incidence and prevalence have increased over the past 10 years [1,2,16]. The highest prevalence and incidence have been reported in Southeast Mexico. Furthermore, this population has a

Table 3
Comparative analysis according to age in female patients with urolithiasis.

Characteristics, n (%)	Age ≤47 Years Old 358 (52.5)	Age >47 Years Old 324 (47.5)	p-Value
Stone size (mm)	10.0 [6.0–16.0]	11.0 [7.0–18.0]	0.064
Kidney	10.0 [5.0–16.0]	11.0 [7.0–18.0]	0.047
Ureter	9.0 [6.0–13.0]	8.0 [6.0–12.0]	0.847
Bladder	30.0 [26.0–35.0]	23.5 [21.0–26.0]	0.020
Hounsfield units	900 [566–1199]	700 [520–970]	0.010
Kidney	845 [587–1111]	700 [518–935]	<0.001
Ureter	956 [663–1200]	829 [754–1097]	0.099
Bladder	1221 [905–1540]	1171 [1087–1256]	0.800
Obstructive uropathy	101 (28.2)	87 (26.8)	0.337

The parameters were analyzed using Mann–Whitney *U* test and expressed by median and IQR. The obstructive uropathy was analyzed using the Mantel–Haenszel Chi-square test. Staghorn stones were excluded.

high incidence of disease recurrence in Mexico [10], making it endemic in the population. Yucatan Health Services statistics reported that in 2017, chronic kidney disease (CKD) and related diseases of the urinary system derived from UL were the main causes of surgical procedures and the tenth leading cause of mortality in the state of Yucatan, Mexico [17].

Timely diagnosis of UL is essential. In this context, CT is the gold standard for prompt diagnosis of UL. Computed tomography (CT) enables clinicians to determine stone size and identify its specific location, even with stone sizes of approximately 1 mm. In addition, with CT, it is possible to determine attenuation of the stone through HU and resolve its composition [11,13].

UL is a multifactorial disease caused by the accumulation of crystals that form stones [18]. Stones are not always located in a single urinary structure. In our study, we identified 741 patients with UL in a single site of the urinary system; more specifically, the right kidney exhibited the greatest frequency, number, and size of stones (Table 1). It is possible that the number and size of stones found in the right kidney could be explained by the relationship between the kidney and the liver in terms of anatomical location (anatomically, the right kidney is 2 cm below the left kidney) [19]. Our results are consistent with those reported in a study by Cruz-Euan et al. [20], who observed that the greatest stone size was found in the right kidney of an endemic population.

In contrast, the left ureter had more stones than the right ureter, although the stones were the smallest. These results may be due to the migration of small kidney stones toward the ureters with the flow of urine [21,22].

HU indicated that all stones were mixed in composition, consisting of calcium oxalate monohydrate (783–1100 HU) and calcium oxalate dihydrate (873–1218 HU) as the main components, except for stones in the bladder, which contained magnesium ammonium phosphate (540–693 HU) as the main component. In addition, HU suggests that the stones may be composed of anhydrous uric acid (367–556 HU) and apatite carbonate (835–1034 HU) [23].

As mentioned, UL with multiple locations was identified in 409 patients, the most prevalent being bilateral kidney stones (46.5 % of all multiple UL), exhibiting larger sizes (median = 16 mm, min = 3 mm, max = 46 mm) compared with UL located only in a single kidney: right kidney (median = 12 mm, min = 3 mm, max = 44 mm) and left kidney (median = 11 mm, min = 3 mm, max = 41 mm). These results could be due to metabolic alterations in the patients and/or the etiology of lithiasis [24]. Stone growth depends on metabolism, dietary habits, and patient anatomy, which increases the risk for the recurrence of UL [9,11]. In addition, the frequency of obstructive uropathy is higher in patients with multiple UL at a single or various sites [25]. Only 1 patient exhibited UL in the entire urinary system, which could decrease quality of life and lead to a poor prognosis.

In this study, we analyzed UL according to sex due to the high prevalence of non-communicable diseases in these populations. Although body mass index (BMI) was not reported in our study, females in the Yucatan Peninsula exhibited greater accumulation of abdominal fat and are shorter than males [9]. Females exhibited the largest number and size of stones in the right kidney and higher HU values than males (Fig. 2). An increase in BMI has been suggested to increase the probability of kidney stone development, which could explain the high number of stones observed in females [26,27]. In addition, stones located in the right ureter were smaller in females than in males, contributing to stone migration to the bladder. In contrast, the left ureter exhibited a significant number and size of stones, which led to more severe obstructive uropathy being observed in the left ureter than in the right ureter (65.5 % vs. 40.3 %, respectively). In addition, the HU of the stones agreed with the composition most frequently reported in southeastern Mexico (calcium oxalate) [23,28].

The largest stones were exhibited by males; however, males had lower HU values than females (Fig. 2), suggesting that these stones were composed of anhydrous uric acid and magnesium ammonium phosphate. The major calculi observed in males could be associated with prostatic diseases and age (mean age of males with UL was 72 ± 8 years). In this context, some studies reported that males have a 3.4:1 probability of developing UL and prostate disease at advanced ages [29,30].

Interestingly, the same results regarding stone size were observed when analyzing specific anatomical sites of the urinary system. As previously discussed, larger stones were located in the right kidneys of females, specifically in the lower renal collector. In males the largest stones were found in the middle and bottom thirds of the ureters and bladders. The HU in both the right and left bottom collectors, the upper third ureter, and the bladder in females suggests calcium oxalate.

We explored the possibility that age in males could be associated with urological pathologies; as such, males were classified into age categories ≤50 and > 50 years. Patients >50 years of age exhibited greater stone sizes and HU compared with those ≤50 years of age, demonstrating that age was a risk factor for developing urinary complications in males, such as recurrence of UL, CKD, or prostate

complications not associated with obstructive uropathy [31]. Therefore, in males, the largest stones were found in patients >50 years of age.

Menopause is the physiological period during which females experience hormonal changes caused by a decrease in estrogen and progesterone levels. In industrialized countries, menopause can occur between 51 and 52 years of age. However, studies in the Mexican population have reported that this phase is present in females >47 years of age [32,33]. This stage has many symptoms, such as irregular menstruation, mood changes, weight gain and slowed metabolism and, of note, bone decalcification, among others [33]. In this context, a similar analysis was performed to identify whether menopause can predict the composition of the stones in females ≤ 47 and > 47 years of age. Our results revealed that stone size was larger in the kidneys of females >47 years of age. However, the composition suggested a mixture of magnesium and ammonium phosphate (approximately 700 HU). Moreover, HU observed in females ≤ 47 years of age suggested calcium oxalate dehydrate (approximately 1200 HU) in the kidney and the bladder. These results could explain why during menopause, decalcification is common and calcium is not deposited as crystals during stone formation [34].

CT diagnosis is crucial in patients with suspected UL because this technique offers advantages, such as determining the number, location, and possible composition of the stones. Therefore, CT characteristics of the stones, including number, size, and location, guide the urologist in deciding the surgical approach, whether through percutaneous nephrolithotomy or cystoscopy using a holmium laser, minimally invasive surgery such as laparoscopic procedures, or invasive procedures such as nephrectomies, when the life of the patient is compromised. In contrast, metabolic studies and HUs have addressed stone composition. Based on this, decisions regarding medical treatment, such as a specific drug or dietary plan, are made, and the urologist can predict the hardness of the stones during surgical procedures. This is vital because hard stones are more challenging to fragment, often resulting in a lower stone-free rate after surgical intervention. In addition, multidisciplinary teams, including radiologists, nephrologists, urologists, internists, and nursery staff, are required to understand the disease and implement specific and personalized treatments.

4.1. Limitations

The main limitation of this study was its cross-sectional design; as such, it was not possible to include data such as recurrence of lithiasis and the evolution of patients to correlate CT characteristics with clinical history. Additionally, although we started from 5954 radiological images (2014–2018), 4854 were discarded and, ultimately, only 1150 radiological images remained. Because our institution is a reference hospital, patients from all Southeast counties attend; hence, it is difficult for them to return. Moreover, the majority of patients are low-income individuals, making treatment and follow-up more difficult. Although previous studies have described the radiological characteristics of urinary stones, they did not provide a detailed characterization or consider endemic populations. Therefore, longitudinal studies with large sample sizes that consider etiology and family history are warranted.

5. Conclusion

This study examined CT characteristics of patients with urinary stones admitted to a reference hospital in Southeast Mexico. Our findings highlight the differences in stone sizes in the right kidney, right ureter, and bladder between males and females. Furthermore, the composition of stones in the right kidney, left ureter, and bladder differed between males and females. Additionally, our research showed, for the first time, that UL was identified in various anatomical sites within the urinary system. The data suggest that stone characteristics may be associated with age and sex, as evidenced by the distinct stone size and composition in the bladders of males >50 years of age and in the kidneys of females >47 years of age.

Data availability statement

Data will be made available on request.

Ethics approval and consent to participate

The need for informed consent was waived by the ethics committee of the Hospital Regional de Alta Especialidad de la Península de Yucatán, Mexico, because of the retrospective nature of the study. All protocols were approved by the Hospital Regional de Alta Especialidad de la Península de Yucatán, ethics committee and research committee, and were conducted in accordance with their regulations and guidelines.

CRediT authorship contribution statement

Katy Sánchez-Pozos: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Formal analysis. **Abraham Adolfo Ramírez-Jurado:** Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Conceptualization. **Martha Medina-Escobedo:** Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Ángel Gabriel Garrido-Dzib:** Writing – original draft, Validation, Resources, Investigation. **Lizeth Araceli González-Rocha:** Writing – original draft, Validation, Resources, Investigation. **Ana Ligia Gutiérrez-Solis:** Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Azalia Avila-Nava:** Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Roberto Lugo:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e23547>.

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