ARTICLE ORIGINAL

Adult urolithiasis in Western Algeria: a study of 1104 cases

Lithiase urinaire chez l'adulte dans l'ouest algérien : A propos de 1104 cas

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RÉSUMÉ

Introduction: La lithiase urinaire constitue un problème de santé de plus en plus fréquent dans le monde et en Algérie, mais avec peu de données. Notre objectif était de déterminer, pour la première fois, les aspects épidémiologiques de cette pathologie dans l'ouest algérien.
Méthodes : Nous avons déterminé les paramètres sociodémographiques, les données cliniques et ceux concernant les calculs de 1104 patients adultes (2012-2019).
Résultats: Nous avons confirmé la prévalence de la lithiase urinaire chez les hommes (sex-ratio = 1,9). Il y'avait 57.2% patients en surpoids ou obèses, 56.7% vivaient dans des zones urbaines et 53,2% avaient un faible niveau d'éducation. Le taux de consanguinité était de 25% et 33.9% avaient des antécédents familiaux. Il y avait 51.1% de récidives. Les calculs étaient situés dans le haut appareil dans 89% et expulsés spontanément dans 51.9%. La chirurgie ouverte a permis d'extraire 19.7% alors que 15.5% étaient traités par endourologie ou lithotripsie extracorporelle. Le composant majoritaire des calculs était l'oxalate de calcium (75%). Les phosphates de calcium constituaient 8,9%, l'acide urique 10.2% et la struvite, indice d'infection urinaire, 3.4%, avec une présence dans 16.9%. Les hommes avaient plus d'instruction, un taux de consanguinité plus élevé et plus de récidives que les femmes.
Conclusion: Le profil épidémiologique qui ressort est proche de celui décrit au Maghreb et dans les pays industrialisés. Il y'a une nette amélioration du niveau socio-économique dans notre pays, mais les techniques modernes d'ablation des calculs doivent être plus utilisées.
Mot clés : Lithiase urinaire, Adultes, Epidémiologie, Analyse des calculs, Ouest algérien.

SUMMARY

Abstract Introduction: Urolithiasis is a health problem which is increasing all over the world as in Algeria, but with scarce local data. Our objective was to determine, for the first time, the epidemiological characteristics of urolithiasis in western Algeria.
Patients and methods: We determined the socio-demographic parameters, the clinical data and those related to stones of 1104 adult stone formers (2012-2019).
Results: We confirmed the higher prevalence of urolithiasis among males (sex-ratio=1.9). Stone formers were overweight or obese in 57.2% of cases, 56.7% were living in urban areas and 53.1% had a poor educational level. The rate of consanguinity was 25% and 33.9% had a family history. Stone recurrence was 51.1% and 89% of stones were located in the upper urinary tract. Spontaneous expulsion was the most frequent way of elimination (51.9%), open surgery was used in 19.7%, while 15.5% resorted to endourology or extracorporeal shock wave lithotripsy. The predominant component of stones was calcium oxalate (75%), followed by calcium phosphates (8.9%) and uric acid (10.2%). Struvite (urinary infection indices) was in 3.4% of stones but detected in 16.9% and cystine was found in 1%. Males had a higher educational level, a higher consanguinity rate and more recurrences than females.
Conclusion: The epidemiologic profile coming out of this study is close to those described in Maghreb and in industrialized countries. Our data showed that there is an improvement of the socio-economical level, but modern techniques of stone removal should be used more, as well as change in lifestyle.
Keywords: Urolithiasis; Adults; Epidemiology; Stone analysis; Western Algeria.

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INTRODUCTION

Urolithiasis is the result of inherited or acquired metabolic disorders [1]. It is a multifactorial disease with world-wide distribution in rural and urban areas of developed and developing countries and it is increasing in the world [2-4]. It is prevalent among affluent societies and associated with environmental factors, such as climate, season, socio-economic status, diet and composition of water or fluid intake, obesity, race and gender, stress, consanguinity, metabolic and genetic pre-disposition [3, 5-9]. Urolithiasis affects men more often than women [3, 10, 11], but it is on increase more in females [2, 4]. Its financial burden is very costly and it is a critical public health problem due to its recurrence. Episodes of urolithiasis also increase the risk of developing renal insufficiency within a period of approximately eleven years [12]. The only studies carried out in Algeria regarding urolithiasis were on the chemical composition of the calculi in relation to localization, age and sex of stone formers [13-15], and the relationship between urinary infection and crystalluria [16].

Thus, the aim of our study was to determine, for the first time in Algeria, the epidemiological characteristics of urolithiasis in adults.

METHODS

This study was conducted from January 2012 to October 2019, in the West of Algeria which has 15 counties (the country has 48 ones), 441 boroughs and 7,704,102 inhabitants (www.ons.dz). The study is aimed at 1104 stone formers aged at least 18 years and referred by the practitioners to our laboratory center, the only one in the region since 1998.

We recorded these items: age, sex, body mass index (classified as: Normal: BMI< 25 kg/m^2; overweight: 25-30 kg/m^2, Obesity: > 30 kg/m^2), borough of residence, educational level, consanguinity, family history of urolithiasis, medical history, presenting symptoms, anatomical location and mode of stone removal. Two stones were not recovered, 14 were still *in situ* and 26 were microlithiasis. So, we analyzed 1062 stones by Fourier transform infrared spectroscopy and kept the main component and noted the presence of struvite.

Data were analyzed with SPSS 20 software for Windows. Statistical significance was determined by the χ^2 tests. P values < 0.05 were considered significant.

RESULTS

Distribution of stone formers by age and sex

The sex-ratio M/F was 1.9 and the mean age 45.3 ± 13.9 years (age range 18 to 85 years). Among males, the frequency peak was located in the subject's forties; among females, in the fifties and sixties. Patients aged (18 to 30) years were less affected in both genders (Table 1).

Table 1. Epidemiological characteristics of stone formers according to sex

	Males (%)	Females (%)	Total (%)
	727 (65.9%)	**377 (34.1%)**	**1104 (100%)**
Age ranges (years)			
18 – 30	93 (12.8)	60 (15.9)	153 (13.9)
30 – 39	202 (27.8)	75 (19.9)	277 (25.1)
40 – 49	154 (21.2)	86 (22.8)	240 (21.7)
50 – 59	147 (20.2)	84 (22.3)	231 (20.9)
≥ 60	131 (18.0)	72 (19.1)	203 (18.4)
BMI[1] ranges (kg/m^2)			
< 25	315 (43.3)	158 (41.9)	473 (42.8)
25 – 30	276 (38.0)	139 (36.9)	415 (37.6)
> 30	136 (18.7)	80 (21.2)	216 (19.6)
Consanguinity			
Yes	194 (26.7)	82 (21.8)	276 (25.0)
No	533 (73.3)	295 (78.2)	828 (75.0)
Family history of lithiasis			
Yes	242 (33.3)	132 (35.0)	374 (33.9)
No	485 (66.7)	245 (65.0)	730 (66.1)
Borough of residence*			
Urban	406 (55.8)	220 (58.4)	626 (56.7)
Rural	253 (34.8)	107 (28.4)	360 (32.6)
Mixed	68 (09.4)	50 (13.3)	118 (10.7)
Educationnal level**			
1-None	87 (12.0)	100 (26.5)	187 (16.9)
2-Primary	70 (09.6)	47 (12.5)	117 (10.6)
3-Middle (college)	201 (27.6)	81 (21.5)	282 (25.5)
Groupe A (1+2+3)	**358 (49.2)**	**228 (60.5)**	**587 (53.1)**
4-Secondary	170 (23.4)	74 (19.6)	244 (22.1)
5-University	199 (27.4)	75 (19.9)	274 (24.8)
Groupe B **(4+5)**	**369 (50.8)**	**149 (39.5)**	**517 (46.9)**

**; ** : respectively p <0.05; p <0.01 concerning the prevalence males vs. females for the Khi2 test; 1:BMI: body mass index = Weight (kg) / height (m2)*

Distribution according to body mass index (BMI), consanguinity and family history

The mean of BMI was 26.2 ± 4.6 kg/m^2 (15.7 to 45.7 kg/m^2); 57.2% of stone formers were overweight or obese (Table1), with 25.3% of obese patients in the 40-59 years range (p<0,0001) (Fig. 1). Patients had a consanguinity history in 25% and a family history of urolithiasis in 33.9% (Table 1).

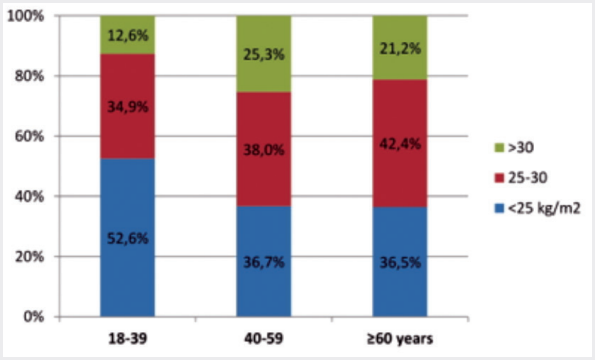

Figure 1. Distribution of stone formers by BMI ranges according to age ranges (p<0.0001)

Distribution according to borough of residence and educational level

There were 56.7% of stone formers living in urban boroughs (at least 5,000 inhabitants, a minimum of socio-educational facilities and agricultural activities in less than 25% of active persons), 32.6% in rural ones (less than 3,000 inhabitants and at least 50% of active persons working in agriculture) and 10.7% in intermediate ones.

Stone formers were without any formal education (group A) in 53.1% while 46.9% had secondary or university level (group B). There were more females among group A (Table 1).

Distribution according to medical history, stone location and stone removal

Stone formers have had ureteric colic (89.9%), painful urination (20.4%), urinary infections (21.6%) or other symptoms as hematuria, fever, vomiting, etc. (16.3%) (Table 2). There were 14.4% males and 23.1% females with high blood pressure (p<0.0001); 10.5% and 16.7% respectively with diabetes (p<0.01). There were 51.1% recurrences, with a male prevalence (Table 2).

The stones were located in the upper urinary tract in 89% and in the bladder in 8.4%. Bladder stones were more prevalent among males (p<0.0001) in whom they increased after 50 years (p<0.0001).

Calculi were spontaneously passed in 51.9%, whereas 19.7% required conventional surgery and 15.5% endourology or extracorporeal shock wave lithotripsy (ESWL). In 3.6%, the stone remained in situ (Table 2).

Table 2. Anamnesis and characteristics of urinary stones according to sex

	Males (%)	Females (%)	Total (%)
	727 (65.9%)	377 (34.1%)	1104 (100%)
Presenting symptoms [1]			
Ureteric colic	648 (89.1)	345 (91.5)	993 (89.9)
Painful urination**	169 (23.2)	56 (14.9)	225 (20.4)
Urinary tract infection**	124 (17.1)	115 (30.5)	239 (21.6)
Others	118 (16.2)	62 (16.4)	180 (16.3)
Medical history			
Hypertension**	105(14.4)	87 (23.1)	192 (17.4)
Diabetes**	76 (10.5)	63 (16.7)	139 (12.6)
Recurrence**			
Yes	399 (54.9)	165 (43.8)	564 (51.1)
No	328 (45.1)	212 (56.2)	540 (48.9)
Number of episodes**			
One	327 (45.0)	211 (56.0)	538 (48.7)
Two	182(25.0)	83 (22.0)	265 (24.0)
Three or more	218 (30.0)	83 (22.0)	301 (27.3)
Anatomical location**			
Kidney	567 (78.0)	330 (87.5)	897 (81.2)
Ureter	57 (07.8)	28 (07.4)	85 (07.7)
UUT[2]	**624 (85.8)**	**358 (94.9)**	**982 (88.9)**
LUT[3]	**83 (11.4)**	**10 (02.7)**	**93 (08.4)**
Multiple	20 (02.8)	09 (02.4)	29 (02.6)
Stone removal*			
Spontaneous expulsion	386 (53.1)	187 (49.6)	573 (51.9)
Open surgery	149 (20.5)	69 (18.3)	218 (19.7)
ESWL/Endourology	95 (13.1)	76 (20.2)	171 (15.5)
In situ	26 (03.6)	14 (03.7)	40 (03.6)
Multiple	71 (09.8)	31 (08.2)	102 (09.2)

*, ** : respectively p<0.05 and p<0.01 concerning the prevalence males vs. females for the Khi2 test; [1]: Patients could have more than one symptom; [2] : UUT: Upper urinary tract; [3]: LUT: Lower urinary tract (Bladder)

Stone composition

Calcium oxalate was the main component in 75% of calculi, calcium phosphates in 8.9%, uric acid in 10.2%, struvite (magnesium ammonium phosphate hexahydrate) in 3.4% and cystine in 1% (Table 3). The rate of consanguinity among patients with cystinuria was 27.3% (p=0.063).

Calcium oxalate dihydrate was more prevalent in males than in females, while calcium phosphates and uric acid were more prevalent in females (p<0.0001). The proportion of calcium oxalate monohydrate was decreasing after 50 years, while uric acid increased continuously from 2.1% in the age 18-30 years, to 30.3% in those aged 60 years or more (p<0.0001) (Fig. 2). Among obese stone formers, there were less calcium oxalate and more uric acid stones than in patients with a normal BMI (p<0.0001) (Fig. 3).

There were 16.9% of stones containing struvite (Table 3), more frequent in the bladder (Fig. 4) and mainly in women (p<0.01). Patients with cystine stones had 27.3% of consanguinity (Table 4). The ratio (recurrent stones/first

stones) was 2.7 in cystine, 1.7 in uric acid, 1.3 in calcium phosphates and 1.3 in calcium oxalate dihydrate.

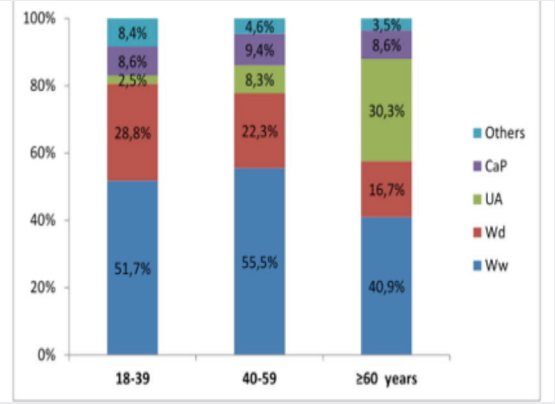

Figure 2. Composition of stones according to age ranges (p<0.0001)

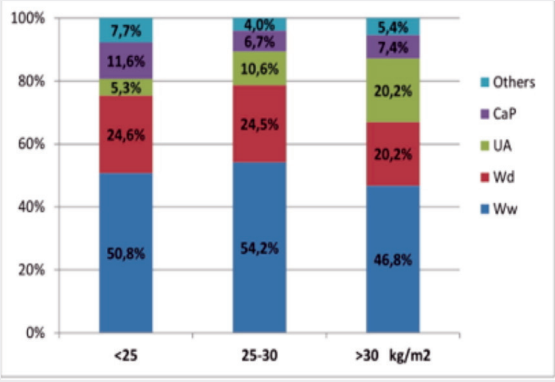

Figure 3. Composition of stones according to BMI ranges (p<0.0001)

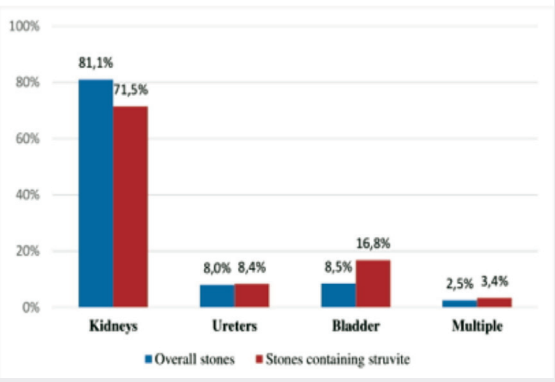

Figure 4. Location of stones containing struvite versus overall stones (p<0.0001)

Table 3. Stone composition according to sex

	Males (%)	Females (%)	Total (%)
	700 (65.9%)	**362 (35,5%)**	**1062 (100%)**
Main stone component **			
Ww[1]	350 (50.0)	195 (53.9)	545 (51.3)
Wd [2]	202 (28.9)	50 (13.8)	252 (23.7)
CaOx [3] (Ww+Wd)	**552 (78.9)**	**245 (67.7)**	**797 (75.0)**
CaP[4]	44 (06.3)	51 (14.1)	95 (08.9)
UA[5]	68 (09.7)	40 (11.0)	108 (10.2)
Struvite[6]	24 (03.4)	12 (03.3)	36 (03.4)
Cystine	07 (1.0)	04 (1.1)	11 (01.0)
Others[7]	05 (0.7)	10 (02.8)	15 (01.4)
Struvite in the stone**			
(in different proportions)	99 (14.1)	80 (22.2)	179 (16.9)

** : p <0.01 concerning the prevalence males vs. females for the Khi2 test; 1 :Whewellite : calcium oxalate monohydrate ; 2 :Weddellite : calcium oxalate dihydrate; 3 : Total calcium oxalate (Ww+Wd); 4 : Calcium phosphates; 5 : Uric acid; 6: Hexahydrate magnesium ammonium phosphate; 7: Others: urates, proteins or mucopolysaccharids

Table 4. Stone composition according to consanguinity

Main stone component	Consanguinity (%)	No Consanguinity (%)
Ww	117 (21.5)	428 (78.5)
Wd	71 (28.2)	181 (71.8)
CaOx[1]	188 **(23.6)**	609 (**76.4**)
CaP	28 (29.5)	67 (70.5)
UA	30 (27.8)	78 (72.2)
Struvite	15 (41.7)	21 (58.3)
Cystine	03 (27.3)	08 (72.7)
Others[7]	3 (20.0)	12 (80.0)

p =0.063 concerning the prevalence of consanguinity vs. no consanguinity for the Khi2 test.

DISCUSSION

This study has revealed important epidemiological characteristics of urolithiasis in adults. The sex-ratio M/F was 1.9, decreasing with respect to the last study in the same region, where it was 2.2 [14]. This suggests an increase in the number of female stone formers as reported in other studies [1, 11, 15]. Indeed, the sex-ratio M/F is weaker than in previous years, whereas the prevalence of urolithiasis in the world has increased [2]. All studies reported clearly a higher prevalence among male stone formers, in the Maghreb [17-19], Africa [20], Europe [1, 21, 22], Asia [23-25] and USA [11]. Androgens seem to increase the urinary excretion of oxalates, as well as the crystallization of calcium oxalates, whereas the estrogens tend to decrease them [26, 27].

Age is a relevant parameter, because the lithogenic factors and the pathologies linked to this disease do not

express in the same way at different ages [10]. The mean age of the present series was 45.3 years (age range 18 to 85 years). It was 38 years ten years ago in the same region (age range 4 to 91 years) [14]. In Maghreb, the mean age of stone formers was 46 [19] to 49 years [17], and in Saudi Arabia the patients were younger (33 years) [24]. In developed countries, those in the fifth decade were most affected [1, 21]. This indicates that there is little difference between our stone formers population and that of industrialized countries with regard to age.

Patients aged between 40 and 59 years had the highest proportion of obese, then this rate decreased significantly. The prevalence of urolithiasis among overweight or obese subjects is well documented [2, 8, 10, 23, 27] and may be higher among females [28], as we have found: 58.1% of females were overweight or obese. The relationship between overweight and urolithiasis can be explained by a decrease in urinary pH and an increase in the excretion of calcium, oxalate, sodium and uric acid [28, 29].

Stone formers from urban areas were 56.7%, similar to findings in some reports [7, 30] which said that urolithiasis is an illness of city dwellers. Western diet habits in many developing countries seem to contribute to increase this disease [4]. It is likely that the diet of subjects living in cities, rich in calories, such as refined sugars, animal protein, saturated fats, as well as salt, calcium and oxalates is at the cause of this disease [1]. In addition, city dwellers often have stressful jobs, which promote urinary lithiasis [31]. Stress induces the excretion of oxalate, calcium and uric acid, whilst also reducing magnesium, an inhibitor of urinary crystallization [3]. The availability and proximity of health centers in urban areas could also explain this finding.

There were 53.2% of stone formers with a very low standard of education as reported in the literature [2, 7, 23], especially in women. Therefore, a better education of girls and women is suitable.

Consanguinity has been observed in 25%, a higher rate than the one of the studied region (18.5%) (www.forem.dz). Interestingly, a high incidence of kidney stones has been reported in the population of isolated areas (eg. islands) with a high rate of consanguinity [32].

Among the risk factors, there is a family history of stone disease [23, 33, 34]. In our series, 33.9% had such a risk. The parents in the first degree of stone formers are twice as likely to having urolithiasis [3]. The existence of ancestors with urolithiasis is often the result of a disorder being hereditary [5].

Ureteric colic is the most presenting symptom revealing a presence of calculi, often nocturnal, when urine concentration is at a maximum [35]. This symptom has been reported in our study by 89.9% of patients.

The recurrence occurred in 51.1% of our series, predominantly amongst men, who had also more episodes than females, as reported by Daudon et al [1]. Almost 50-53% of stone formers relapse in about 7-10 years after the first episode [34, 36] and after 25 years, all relapse if preventative measures are not taken [3]. Specific preventative measures should be adapted to each specific type of urolithiasis [1, 37].

It has been estimated that around 70 to 80% of stones are spontaneously expelled [1]. In our series, 51.9% were expelled, 19.7% were treated by open surgery, which is still widespread in Algeria, but clearly decreasing from 2006, where it represented 79.7% [14]. Open surgery is at present rare in developed countries, where the stones are treated by ESWL or endoscopic techniques, according to size, location and hardness of stones, internal anatomy, patient symptoms and choice [35]. Endourological procedures and ESWL have been carried out on only 15.5% of subjects of our series, because it is an expensive treatment.

We have noted that the stones in the lower urinary tract moved from 22.6% in 2006 [14] to 8.4% % in this study. This reflects a clear improvement of the socio-economical level because bladder calculi are observed much more in weak socio-economic conditions [12, 27]. In this study, male is more affected by bladder stones than female, mainly after 50 years. An explanation could be that bladder stones are linked to urine stasis because of prostatic obstacle, bladder diverticulum or neurological malfunctioning [35].

The aim of stone analysis is to collect all pertinent information enabling the doctor to establish the causes of stone formation. It should then be carried out for all stone formers [38]. Our study has shown that calcium oxalate is the major component of stones (75%) as in Algeria [13-15], in Africa [17-19, 30] and throughout the world [11, 21, 22, 29, 38]. We found 51.3% of whewellite and 23.7% of weddellite. Whewellite is known as an oxalo-dependent crystalline species and weddellite as calcium dependent

[39]. Calcium oxalate stone is shown to be related to genetic [6], or acquired causes, generally linked with environmental factors, in particular nutritional ones [10, 40]. The food survey carried out on our patients showed that they had nutrition imbalance (elevated levels of sugar, salt, dry vegetables, oxalates) and above all, 50% of them drank less than one liter water per day. To prevent the crystallization risk, patients must have high water intake to achieve a daily urine output of 2 l/day [40].

Struvite has been found in 16.9% of stones. Of these, 16.8% were located in the bladder. Struvite was dominant in 3.4% of cases, as reported by Bouslama et *al* in the East of Algeria [15]. This species is decreasing in our region from 2006, where 28.08% of stones contained struvite [14]. This can be explained by an improvement in the treatment of urinary tract infections and better health care of patients. Indeed, struvite stones are markers of urinary tract infections, and/or poor care, induced by ureasic germs such as Proteus, Klebsiella, Pseudomonas in an alkaline environment [1, 3]. Stones mainly composed of calcium phosphates accounted for 8.9% of cases by comparison to 16.7% in 2006 [14]. This decrease could be also the consequence of the diminution of urinary tract infections (non ureasic germs).

Cystine, which is the most frequent monogenic hereditary urolithiasic diseases, represents around 1% of stones [6, 41], as found in our series. In 2006, it was the main component of 0.7% calculi in this region [14], closest to that found in Morocco (0.6%) [17]. Cystine was the most recurrent stone in our series and patients with this type had a 27.3% rate of consanguinity. Weddellite and calcium phosphates who showed a rate of recurrence of 1.3, are often related to hypercalciuria [39]. This could be a result of genetic polymorphism [42].

Uric acid was the main component of 10.2% of our series, similar to that of industrialized countries (9-10%) [21, 22], but is much frequent in the Maghreb (19 to 21%) [17, 18]. These stones are often linked to a protein-rich diet resulting in elevated concentrations of uric acid and low urine pH [41] as well as a low diuresis [3]. Studies suggested a correlation between the metabolic syndrome and hyperuricemia, associated to a defect in ammoniogenesis and an increased urine acidity, which favors the formation of uric acid stones [43].

We found that the rate of stone formers with arterial hypertension was greater than that found in the general population, and females were significantly more affected than males. This should therefore encourage looking for a metabolic syndrome in all stone formers with uric urolithiasis, especially in those with arterial hypertension and/or overweight [22, 33].

The stones had a significantly different distribution according to sex, age, BMI ranges and location. Man had more calcium oxalate dehydrated stones and women more uric acid and calcium phosphates. The production of estrogens in women results in higher urinary phosphaturia [44]. Calcium phosphates and struvite (in different proportions) were more frequent in the bladder. While calcium oxalate stones decrease with age and BMI, uric acid stones increase.

Therefore, in view of the relationship between obesity and urolithiasis disease, the clinicians should recommend stone formers prone to being overweight, to lose weight, under the guidance of a dietitian.

CONCLUSION

The epidemiological profile coming out from this study is similar to the one described in Maghreb and close to the one in industrialized countries. Calcium oxalate is the most frequent component of stones and cystine the most recurrent ones. Uric acid increases among the elderly and overweight/obese patients. Stones related to infection are decreasing. There is a clear improvement of the socio-economical level of our population, but modern techniques of stone removal should be more used. A multidisciplinary approach should be taken to assist change in dietary habits, good hydration and health education as preventative measures in overcoming this disease.

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