Global Journal of Pharmacology 10 (4): 89-97, 2016
ISSN 1992-0075

DOI: 10.5829/idosi.gjp.2016.89.97

An Overview of Kidney Stone Disease in Lebanon

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Abstract: Nephrolithiasis is the most common urinary tract disorder. The purposes of this study were to identify the most common type of kidney stones in Lebanon and evaluate the life style and pharmacological measures followed by Lebanese patients who have kidney stones This descriptive study is a part of the clinical nutrition course at the School of Pharmacy in a Lebanese university. Each student had to contact 10 patients from different community pharmacies between October 2013 and May 2014. Inclusion criteria included adults with kidney stones aged above 18 and living in Lebanon for more than 10 years. A 20 minutes face-to-face interview using a questionnaire was conducted. Descriptive statistical analysis was done by a pharmacist specialized in epidemiology. 550 patients with self-reported stone disease were enrolled. Results showed that the most common stone type is oxalate (62.7%) and least is cysteine (5.3%). The most taken medications are non-steroidal anti-inflammatory drugs (58.2%) and paracetamol (34.9%). Patients' dietary habits included increased fluid intake (76.9%), decreased salt (38.4%) and meat consumption (34.7%) and avoidance of oxalate containing food (35.6%). In conclusion changing nutritional habits is one of the most accessible and inexpensive intervention to reduce kidney stones' risk. Educational and counseling efforts should be implicated in the management of nephrolithiasis.

Key words: Nephrolithiasis · Oxalate · Life Style · Nutritional Habits

INTRODUCTION

Nephrolithiasis is the most common urinary tract disorder [1]. Its prevalence rate has been increasing in many countries [2, 3]. It affects 1-5% of the societies in Asian countries, 5-10% in Europe and 13% in North America. This could be contributed to the dietary habits, climate and other geographical factors [4]. Nephrolithiasis incidence varies as a function of age; it is usually highest among adults aged 27-34 years [5]. According to estimates and surveys, men (~10%) are prone to form kidney stones, at some point in their lives, more than women (~7%). However, this gender gap is getting close as the prevalence of this disease is increasing in women [1, 6].

There are different etiologies for nephrolithiasis. Hereditary factors play a role which is clear in monogenic diseases such as cystinuria, Dent's disease and primary hyperoxaluria [5, 7]. Many evidences stress on the systemic nature of this disease where it has been shown that overweight/obesity, hypertension and diabetes are associated with an increased risk of stone formation [1, 8-11]. Environmental factors, especially diet and lifestyle, are also shown to play an important role in disease development [1, 6]. Different physiochemical factors enhance the formation of stones. One of these factors is the presence of renal pathology and abnormities in crystallization inhibitors (Such as citrate, phytate and phosphate). Another essential factor is the super saturation of urine with a stone constituent salt resulting in crystals growth and aggregation into a stone [5]. Thus the type of formed stone depends on urine compositions and super saturation; both of which are directly related to diet. Subsequently, stones could be made up of calcium oxalate, calcium phosphate, uric acid, cystine or struvite. Though it is usually asymptomatic, the characteristic cramping, intermittent pain and urinary tract blockage can occur during stone passage [12]. The pain is often accompanied with hematuria, nausea or vomiting and malaise. Fever and chills may also be present [13]. Moreover, this disease is a frequent cause of morbidity where it seems to be associated with an increased incidence of chronic kidney disease (CKD) and hypertension [1, 14,15].

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Recurrence is a main problem with this disease where almost 50% of individuals who develop stones are subjected to recurrent episodes within 10 years of the first occurrence especially if no preventive measures have been taken [6]. In fact, proper control and management of risk factors is the cornerstone in disease prevention. Diet and nutritional status are the modifiable risk factors that may represent targets for the prevention and treatment of the condition [9]. For this reason, tailored dietary recommendations (Incorporating or avoiding a variety of dietary measures) based on diet recalls are one of the most important measures, where increased fluid intake along with low sodium, low animal-protein and normal calcium diet have been the mainstays for the prevention of kidney stone recurrence [1, 6,16-18]. As the world's population evolves, so does the epidemiology of stone disease [19]. To date and according to our knowledge, there is no published literature in Lebanon that identifies the most common type of kidney stones and describes the nutritional habits associated with this disease in the Lebanese population. The primary objectives of the study is to identify the most common type of kidney stones in Lebanon and to evaluate the life style, dietary and pharmacological measures followed by a subset of Lebanese patients who have kidney stones. The secondary objective is to assess the association of comorbidities, symptoms and certain dietary measures with different stone types.

MATERIALS AND METHODS

This descriptive study is a part of the "Clinical Nutrition" course at the Lebanese International University, School of Pharmacy, in Beirut, Lebanon. The research project was approved by the university Institutional Review Board. Each student in the class was assigned to contact 10 patients with kidney stone disease from the community pharmacies. Patients who fit the eligibility criteria were enrolled in the study. The inclusion criteria included Lebanese adults with kidney stones disease older than eighteen years of age and living in Lebanon for more than 10 years. The pharmacy student obtained an informed consent from the enrolled participants then a 20 minutes face-to-face interview using a questionnaire was conducted. Data was collected from different regions of Lebanon between October 2013 and May 2014.

Detailed history was elicited from the patients regarding demographic information, education level, family history, type of stone, socio-economic status, urinalysis results, symptoms, pain location, associated medical conditions, average daily intake of fluid, dietary habits and medications that may predispose the patient to stone disease or that they use to treat or prevent this condition. Dietary history includes information regarding the consumption of leafy vegetables, coffee, citrus, grapes, beets, tea, beer, soy, peanuts, beans, eggplant, chocolate, berries and endive. Non-pharmacological treatment history includes hydration, dairy products, fruits and vegetables, avoiding oxalate, low meat and low salt diet, as well as surgery.

Statistical Analysis: Data were entered and analyzed using SPSS (Statistical Package for Social Sciences), version 21. A *P*-value of less than 0.05 was considered significant. Descriptive statistics were used to describe the patients' characteristics and outcomes. Results are shown as mean ± standard deviation (SD) for continuous variables and as percent (%) for categorical variables. The Chi-square test was used to compare nominal variables and Fisher exact test was used in case expected values within cells were inferior to five. The analysis was done by a separate pharmacist researcher who is specialized in epidemiology.

RESULTS

Descriptive Statistics of Kidney Stones Patients: The present analysis included 550 patients with self-reported stone disease, distributed equally between genders (51.5% males), with a mean age of about 43 years. Majority of patients are from the average socio-economic status (56.4%). The most common stone type in our population understudy appeared to be oxalate (62.7%) and least occurring was cysteine (5.3%). The Baseline characteristics of the enrolled patients are shown in Table 1.

Patients under study reported complaints from different symptoms with the most common being pain (84%). Others included blood in urine (48.9%), urine flow blockage (45.4%), fever (22.7%), nausea (45.6%), vomiting (34%) and swelling (11.8%). Treatment of kidney stones ranges between pharmacologic, non-pharmacologic and surgical interventions. These are summarized in figure 1 (A and b) where the most taken medications are non-steroidal anti-inflammatory drugs (58.2%) and paracetamol (34.9%). Regarding the non-pharmacologic treatment, most patients tend to increase their fluid intake (76.9%), decrease salt (38.4%) and meat consumption (34.7%) and avoid oxalate containing food (35.6%).

Table 1: Baseline characteristics of patients having kidney stones

		n (%)
Gender	Male	283 (51.5)
	Female	267 (48.5)
Education	< high school	164 (29.8)
	High school	163 (29.6)
	>high school	223 (40.5)
Socio-economic status	Poor	72 (13.1)
	Average	310 (56.4)
	Good	168 (30.5)
Type of stone	Oxalate	345 (62.7)
	Uric acid	130 (23.6)
	Cysteine	29 (5.3)
	Struvite	46 (8.4)
Family history of stone	Yes	296 (53.8)
	No	254 (46.2)
Kidney function checking	Cr Cl	55 (10)
	Urine analysis	495 (90)
Stone excreted in urine	Yes	317 (57.6)
	No	233 (42.4)

Abbreviation: Cr Cl, creatinine clearance

Table 2: Frequencies of most drugs and dietary habits related to kidney stones.

	Factor	n (%)	Factor	n (%)
Drugs	Indinavir	3 (0.5)	Vitamin D	100 (18.2)
	Topiramate	13 (2.4)	Vitamin C	86 (15.6)
	Cranberry	64 (11.6)	Calcium	108 (19.6)
	Ceftriaxone	30 (5.5)		
Diet	Leafy vegetables	240 (43.6)	Citrus	107 (19.5)
	Beets	46 (8.4)	Beer	92 (16.7)
	Peanuts	142 (25.8)	Eggplant	61 (11.1)
	Chocolate	205 (37.3)	Endive	32 (5.8)
	Coffee	286 (52)	Grapes	104 (18.9)
	Tea	283 (51.5)	Soy	72 (13.1)
	Beans	140 (25.5)	Meat	147 (26.7)
	Berries	69 (12.5)		
Hydration	<1 L	285 (51.8)		
	1-2 L	227 (41.3)		
	>2 L	38 (6.9)		

Patients affected by kidney stone disease were being counseled primarily by a physician (81%), with only 18 % being counseled by a pharmacist.

Factors Affecting Kidney Stones: Table 2 lists the common drugs and dietary habits found in nephrolithiasis patients. Calcium (19.6%), vitamins C & D (15.6 and 18.2% respectively) and cranberry (11.6%) are the most taken supplements. Regarding nutritional habits, it is important to mention hydration where only 6.9% of patients consume more than 2 liters of fluids per day, whereas 51.8% consume less than 1 liter per day. Diet in stone forming patients contains coffee (52%), tea (51.5%), leafy vegetables (43.6%), chocolate (37.3%), meat (26.7%), peanuts (25.8%) and beans (25.5%). Concerning comorbidities, figure 2a shows the common diseases co-occurring with nephrolithiasis. General urinary tract infection (UTI) is the major comorbidity (30%) followed by hypertension, diabetes, gout and bowel inflammation. But when taking every type of stone alone, figure 2b shows that UTI is the most common comorbidity in patients with oxalate (23.2%), cysteine (37.9%) and struvite (80.4%), while uric acid stone-forming patients have more gout (40%).

Comparison Between Types of Stones: Results of bivariate analysis done to compare different types of stones are summarized in table 3. A positive family history is associated with all stone types except for oxalate (p=0.026). The consumption of calcium supplements shows an association with oxalate stones but a decrease in other types (p=0.010). Although the hydration status shows no significant difference, it is noticed that the consumption of more than 2 liters per day is associated with lower stone formation.

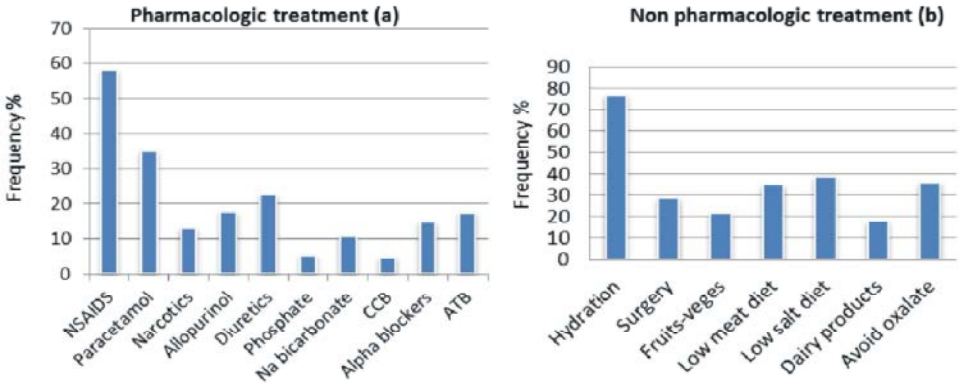

Fig. 1: Major pharmacologic (a) and non pharmacologic (b) treatments followed by kidney stones patients
Abbreviation: NSAIDS, non-steroidal anti-inflammatory drugs; CCB, calcium channel blockers; ATB, antibiotics.

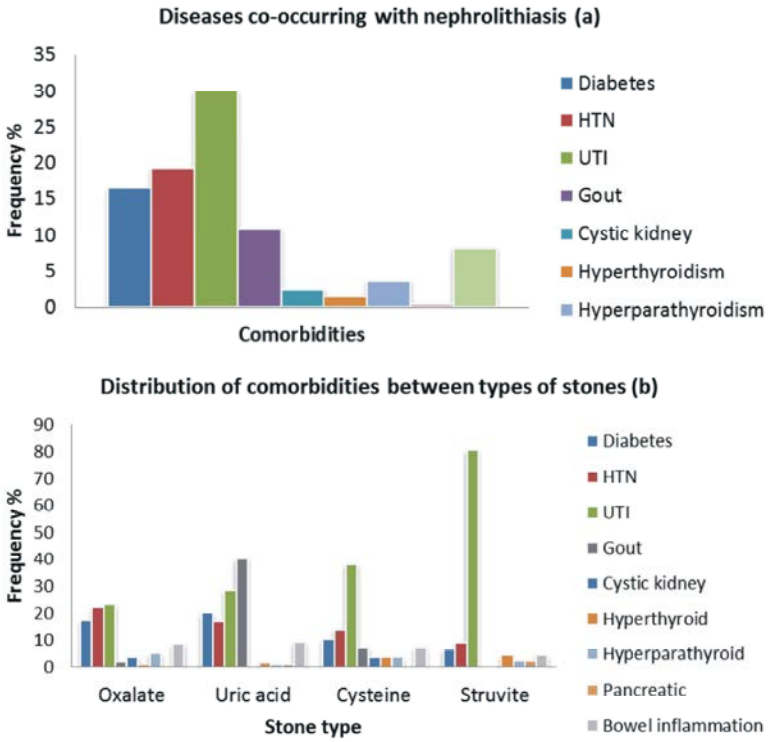

Fig. 2: Distribution of comorbidities in general population (a) and between types of stones (b). Comorbidities having a significant difference included UTI and Gout only ($p<0.001$).
Abbreviation: HTN, hypertension; UTI, urinary tract infection.

Table 3: Variation of multiple factors between the four different types of stones

	Oxalate	Uric acid	Cysteine	Struvite	
Factor	345 (62.7%)	130 (23.6%)	29 (5.3%)	46 (8.4%)	p-value
Family history					
Present	175 (59.1)	72 (24.3)	23 (7.8)	26 (8.8)	0.026
Absent	170 (66.9)	58 (22.8)	6 (2.4)	20 (7.9)	
Taking calcium					
Yes	82 (75.9)	19 (17.6)	4 (3.7)	3 (2.8)	0.010
No	263 (59.5)	111 (25.1)	25 (5.7)	43 (9.7)	
Hydration					
<1 L	185 (53.6)	64 (49.2)	12 (41.4)	24 (52.2)	0.357
1-2 L	140 (40.6)	57 (43.8)	12 (41.4)	18 (39.1)	
>2 L	20 (5.8)	9 (6.9)	5 (17.2)	4 (8.7)	
Vitamin C					
Yes	59 (68.6)	18 (20.9)	3 (3.5)	6 (7.0)	0.645
No	286 (61.6)	112 (24.1)	26 (5.6)	40 (8.6)	
Low salt diet					
Yes	151 (71.6)	41 (19.4)	11 (5.2)	8 (3.8)	0.002
No	194 (57.4)	88 (26.0)	18 (5.3)	38 (11.2)	
Fruits/vegetables					
Yes	74 (62.2)	27 (22.7)	6 (5.0)	12 (10.1)	0.904
No	271 (63.0)	102 (23.7)	23 (5.3)	34 (7.9)	
Dairy products					
Yes	72 (73.5)	17 (17.3)	2 (2.0)	7 (7.1)	0.078
No	273 (60.4)	113 (25.0)	27 (6.0)	39 (8.6)	

Symptoms reported by patients are significant on different types of stones regarding swelling (p=0.004), pain (p=0.008), fever (p<0.001) and chills (p=0.015). It is noticed that patients who suffer from pain (65.4%) have more oxalate stone type than those not complaining of pain (48%). Pain was distributed between back pain (58%), pain in the lower abdomen (52%) and pain in belly area (22.4%). Our results also found that uric acid stone is mostly associated with swelling and to a lesser extent with blood in urine, fever, chills and nausea. Cysteine stone is associated with most of the symptoms (Pain, blood in urine, fever, chills, nausea and vomiting). Struvite stones are more associated with blocking urine flow, fever and chills.

Concerning dietary habits, the ones having a statistically significant difference included leafy vegetables (p=0.010), tea (p=0.039), beer (p=0.023) and meat (p<0.001). Diet mostly associated with oxalate stones included leafy vegetables, peanuts, chocolate, coffee, tea, beans, grapes and soy. Whereas those associated with uric acid stones included beets, beer, eggplant, grapes and meat. Cysteine was mostly associated with beets, citrus, beer, eggplant, endive and meat and finally struvite was associated with beets, chocolate, berries and citrus.

DISCUSSIONS

Discussion was focused mainly on calcium oxalate and uric acid stones as they constitute 86% of stone types in the sample population studied. Our study revealed that calcium oxalate appears to be the most common stone type among the Lebanese population. Most data showed that approximately 80% of patients with nephrolithiasis form calcium stones, the majority of which are composed primarily of calcium oxalate [20-22]. Lebanese patients under study reported low fluid intake and high consumption of oxalate containing food both of which lead to hypercalciuria which could be a main cause of calcium oxalate stone formation [4]. The percentage of females reporting kidney stone disease was almost near to that reported by males. The increased incidence of stone disease in women is obviously observed in the new studies [19].This is hypothesized to be related to obesity where it is shown that calcium oxalate stones are directly associated with body mass index [23]. Individuals of lower socioeconomic status are prone more than others to develop chronic diseases. This has been related to environmental and dietary factors. A significant association between nephrolithiasis and low annual household incomewas shown [24]. However, our study described that most patients are from average socioeconomic status. This could be contributed to the fact that most of the students have contacted pharmacies located in areas where people are of average socioeconomic incomes.

There are different nutritional factors associated with stone disease that varies according to stone type and risk factors. The main measure for preventing and/or reducing kidney stones is altering improper habitual dietary patterns [25]. Appropriate fluid and potassium intake are associated with a reduced risk of nephrolithiasis, whereas diets rich in sodium, animal protein and sugars might increase this risk [16]. Adequate liquid intake is a key measure that will not only prevent the concentration of substances in the urine, but also the frequency with which solid micro particles are expelled from the urinary tract [26]. Patients are also counseled to avoid leafy green vegetables, such as spinach and small leaf vegetables, because of their high oxalate contents although studies by Liu and Monga [27] and Taylor and Curhan [28] did not support the assumption that high dietary oxalate intake poses a risk for increased incidence of urinary stone disease. This incidence is also increased by protein consumption since it will decrease the pH creating an acid load that may increase urinary calcium, uric acid and oxalate excretion [5]. Similarly, Ferraro *et al*. [29] assured that consumption of sugar-sweetened soda and punch increases the risk of stone formation in which fructose has been shown to be associated with increased urinary excretion of calcium, oxalate and uric acid. A study by Curhan et al.[29] showed that consumption of 8-oz of caffeinated coffee and tea decreased the risk of stone formation in women by 10% and 8%, respectively. However, our study showed an association between tea intake and oxalate stone formation. This could be due to the fact that caffeine increases diuresis moderately together with the excretion of magnesium, potassium, calcium and sodium [30]. Additionally, it was noted that dietary phytate, present in bran and seeds, decreases the risk of stone formation, forms insoluble complexes in the intestinal tract with calcium and inhibits crystal formation in the urinary tract [19, 31-33]. A decreased risk of stone formation was also associated with diets rich in fruits and vegetables that are not rich in oxalate [34]. In addition to increasing urinary volume, potassium and magnesium, this diet provides an alkali medium that help in increasing urinary citrate and phytate. Therefore inhibit stone formation and decrease the super saturation of calcium and uric acid [34-38]. Furthermore, they help decrease the

intake of dietary sodium, animal proteins and total calories [34]. Thus decrease the nutritional risk factors that contribute to the formation of kidney calculi. A reduced risk of calcium stones in individuals who consumed higher amounts of wine and beer was also observed [29, 39,40]. This could be due to the diuretic effects of alcohol where it was shown that antidiuretic hormone level is decreased with alcohol intake leading to urine dilution [41, 42]. However, our study revealed significant association between uric acid stones and beer consumption. Beer seems to increase the risk of urate stone disease due to the uricosuric effect caused by its high purine-guanosine content [15, 43]. There is growing evidence that calcium intake has a protective effect [44, 45]. This may be due to the binding of calcium with intestinal oxalate leading to a decrease in both oxalate absorption and its subsequent urinary excretion [46, 47]. Evidences showed that the incidence of nephrolithiasis is reduced by the consumption of dairy-rich diets (800–1200 mg/d of dietary calcium), whereas it is increased with the intake of calcium supplements especially when taken away from meals [18, 32, 44, 45]. This inconsistent finding could be related to the fact that the absorption of calcium supplements is increased when taken without food leading to increased calcium urinary excretion with little or no effect on the absorption and excretion of oxalate. Therefore, calcium supplements should be administered as calcium citrate and preferentially taken with, or shortly after, meals by stone-forming individuals [48]. A randomized, controlled trial showed that after 5 years on low-salt, low-protein, normal-calcium diets, stone recurrence in these patients was significantly lower than among those on the low-calcium diet [5]. Consequently, dietary calcium restriction is no longer considered appropriate therapy for hypercalciuria because there is no evidence that lower calcium intake prevents stones and because of the threat of bone demineralization [48, 49]. In Curhan *et al.* [50] prospective study, vitamin C supplementation, which may be metabolized into oxalate, was not associated with an increased risk of stone formation in women. One of the risk factors for uric acid stone formation is urine acidity where beer, tea and meat are dietary components that can decrease urinary pH. Another risk is a diet rich in purines. These associations contribute to the need for counseling against high consumption of purine rich food. Grapes, beets and eggplants were seen in our data to be associated with uric acid stones this could be due to their fructose content that elevates uric acid and helps driving up the rates of kidney disease [51, 52].

Although renal calculus can be cured, the subsequent disorder causes painful and recurrent episodes that lead to costly medical visits and procedures [53]. In addition to hydration, pain management is part of the acute treatment of all stone types. Majority of patients reported taking NSAIDs, paracetamol or narcotics to alleviate the pain associated with stone passage. Some patients use calcium channel blockers or Alfa blockers since they are able to relax the smooth muscles of the ureters and facilitate stone passage. Along with the embedding of the bacteria in the stones, kidney stones result in blocking urine flow which enhance the residence and growth of bacteria for longer times in the urinary tract; these lead to a wide percentage of patients suffering from UTI that is obviously associated with all stone types. Empiric antibiotics treatment was the action taken for the signs and symptoms of the infection [13]. Different studies revealed an association between kidney stone disease and different comorbidities, especially metabolic syndrome [24]. There is evidences of support existence of a link between nephrolithiasis and both diabetes and hypertension [11, 54-56].

Limitation and Strength: Limitation of the study: missing data regarding the body mass index (BMI) of the patients. A high BMI is greatly linked to a significant and progressive increase in the risk of stone formation [5]. Compared to those with a BMI of 20-22.5 kg/m2, those with a BMI =27.5 kg/m2 had an approximate two-fold higher risk of having a hospitalization for kidney stones [57]. Obesity increases urine acidity, risk of dehydration and the renal excretion of calcium, uric acid and oxalate [9, 58-64].

Strength of the study: it is a descriptive study that can be used to build on future epidemiological and interventional studies to test whether an effective nutritional counseling would be effective in avoiding the modifiable risk factors and thus result in decline of this disease.

CONCLUSION

It has been hypothesized that the cumulative effects of transient renal obstruction during stone passage, renal mineral deposition and collateral renal injury from urolithiasis treatments (Extracorporeal shock wave lithotripsy, ureteroscopy, laser lithotripsy) may result in damage to nephrons and impairment of kidney function [65, 66]. Therefore, we are in great need for increased efforts in the primary prevention of nephrolithiasis as a

means of reducing mortality, morbidity and cost secondary to CKD and expensive treatments. Measures to prevent kidney stones include dietary modifications, nutritional supplements and medications, depending on the specific type of kidney stone and urine characteristics [13]. Changing the nutritional habits is one of the most accessible, appealing and inexpensive interventions to potentially decrease the risk of kidney stones. Educational and counseling efforts should be greatly implicated in the management of stone disease as lifestyle modification plays an important role in protecting against chronic diseases (As diabetes, hypertension and obesity) which have been associated with renal calculus formation.

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