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RESEARCH ARTICLE

Clinical Characteristics and Stone Types of Patients with Kidney Staghorn Stone in a Tertiary Referral Center in Iran

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Abstract:

Objective:

In the past, infectious agents were assumed to be the leading cause of staghorn stones. The metabolic factors were thought to be a secondary cause. However, recent research has shown that any stone can fill the pelvis and calyces in the same manner as a staghorn stone. This retrospective study investigated the relationship between the staghorn stone's chemical composition and patients' demographic characteristics by analyzing the stone samples.

Methods:

The medical records of 170 patients with staghorn stones were studied from a tertiary referral center in central Iran. Then, the specimens of their stones were sent to the laboratory for infrared spectroscopy and x-ray powder diffraction analyses.

Results:

The mean age and body mass index were 49.66 years and 29.1 kg/m^2, respectively. Men comprised the majority of patients. Of the entire cohort, 13.6% had diabetes, and 28.6% had hypertension. Sixty-eight of the stones were pure stones. Calcium oxalate and uric acid constituted the majority of the pure stones. Only 1.7% of the pure stones were composed of struvite. Most of the non-pure or mixed stones were composed of uric acid plus a small composition of calcium oxalate or phosphate.

Discussion:

However, 16.% of the mixed stones were struvites, confirming a metabolic background. In the adjusted model (age, BMI, presence of hypertension), patients with diabetes have a 14-fold higher chance of developing a mixed stone (P= 0.018; OR:14.113; CI=1.582-125.924).

Conclusion:

The complete staghorn stone forms for the same reasons as other kidney stones. It appears that infectious background is not the predominant cause in the current era. Alterations in living conditions and nutrition might also be a reason which requires further investigation.

Keywords: Staghorn stone, Kidney stone, Infrared spectroscopy, X-ray powder diffraction, Metabolic disorders, Uric acid.

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1. INTRODUCTION

The stones that occupy almost the entire upper tract collecting system are known as staghorn stones, often involving the renal pelvis, infundibulum, and calyces [1]. Based on the occupied pyelocalyceal system space, they are categorized as either complete or incomplete [2]. The underlying causes are frequent urinary tract infections and anatomical problems, such as ureteropelvic junction stenosis, neurogenic bladder, and metabolic disorders [3].

Staghorn stones are associated with metabolic disorders in 70% of patients. Hypercalciuria is the most prevalent metabolic disorder (64.2%), followed by hypocitraturia (53.3%),

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hyperuricosuria (21.4%), hypomagnesemia (14.2%), hyperoxaluria (7.1%), primary hyperparathyroidism (7.1%), and renal tubular acidosis type I (7.1%) [3]. Before the early 1970s, some believed that patients with staghorn stones did not require metabolic preventive treatment. However, Blandy and Singh found that 28% of staghorn stone patients who do not receive preventive metabolic therapy die due to kidney failure [4].

This retrospective study investigated the relationship between the staghorn stone's chemical composition and patients' demographic characteristics by analyzing the stone samples.

2. MATERIALS AND METHODS

A total of 170 patients with staghorn stones were referred to our center in two years (2017 and 2018) to undergo percutaneous nephrolithotomy or open surgery. The inclusion criteria included a complete staghorn stone.

The exclusion criteria were having: 1) risk of anatomical factors predisposed to medullary cystic kidney disease (tubular ectasia), 2) ureteral stenosis, 3) calyceal diverticulosis, 4) ureteral stricture, 5) horseshoe kidney, and 6) ureterocele. The data were extracted from the patient's medical records, including age, sex, weight, height, the reason for admission to our center, history of diabetes, blood pressure, serum creatinine, urine analysis and culture, stone size and location, kidney side (left or right), and previous treatments (open surgery, percutaneous nephrolithotomy or extracorporeal shock wave lithotripsy).

The stone samples of the patients were then sent to the laboratory to be studied by infrared spectroscopy and x-ray powder diffraction. The Statistical Package for Social Sciences IBM (SPSS-IBM), version 25 (SPSS Inc., Chicago, Illinois, USA), was used to perform the analysis. Moreover, T-test and Fisher's exact test were used to analyze the data.

The ethical committee of the Urology and Nephrology Research Center of Shahid Beheshti University of Medical Sciences approved the protocol of study with an ethical code as IR.SBMU.UNRC.REC.1397.37.

3. RESULTS

The clinical characteristics and stone types of 117 men and 53 women were investigated in this study. The highest incidence rate was between the 30-40 and 50-60 years old age groups. The mean age and body mass index were 49.66 years old and 29.1 kg/m^2, respectively. Moreover, 13.6% of patients had diabetes, and 28.6% had hypertension. The mean stone size and serum creatinine level were 36.33 mm and 1.37 mg/dl, respectively (Table **1**).

Overall, 68% of the stones were pure, and 32% had a mixed composition. Most of the pure stones were composed of calcium oxalate and uric acid, with an equal proportion of 42.6% for each. Most mixed stones (55.6%) were made of uric acid with either calcium phosphate or calcium oxalate. Only 1.7% of pure stones and 16.7% of mixed stones were infectious (struvite). Moreover, 94% of the stones were metabolic, and 6% were infectious (Table **2**).

Most of the pure stones (50.6%) were composed of calcium oxalate in men and uric acid in women (52.2%). The difference was significant (P = 0.027; Table **2**). In nondiabetic patients, most of the stones were pure (70.3%), while in diabetic patients, most of the stones were mixed (56.3%). The difference was significant (p = 0.036). In nondiabetic patients, most of the pure stones were composed of calcium oxalate, while in diabetic patients, most stones were composed of uric acid. The difference was significant (p = 0.015). Most of the stones were composed of uric acid with calcium phosphate and calcium oxalate in both diabetic and non-diabetic people, but the difference was not significant. There was no significant relationship between hypertension and stone type (Table **3**).

Among individuals with a body mass index of less than 25 kg/m2, most stones (83.3%) were composed of calcium oxalate. Moreover, in those with a 25–30 kg/m2 body mass index, most stones (61.9%) were composed of calcium oxalate. In individuals with more than 30 kg/m^2 body mass index, most stones (72.2%) were composed of uric acid. This difference was significant (p = 0.023; Table **4**).

Based on multiple logistic regression and considering the clinical characteristics of patients and their stones, it was determined that having diabetes is significantly related to stone type (P= 0.018; OR:14.113; CI=1.582-125.924). In other words, people with diabetes have a 14-fold higher chance of developing a mixed stone (Table **5**).

4. DISCUSSION

To our knowledge, this is the first study that uses infrared spectroscopy and x-ray powder diffraction to study staghorn stones in our country. Most previous studies used qualitative wet chemical analysis to investigate stone types [5, 6]. This method has the following disadvantages: 1) it is time-consuming; 2) it cannot be done on small kidney stones; 3) it cannot evaluate very small particles within the main stone; and 4) it might have false negative and positive results [7, 8].

Table 1. Clinical characteristics of the studied patients.

-	Mean	Standard Deviation
Age (years)	46.99	14.89
Stone diameter (mm)	36.33	23.65
Serum creatinine (mg/dl)	1.37	1.18
Body mass index (kg/m^2)	29.16	3.76

Table 2. The stone composition of the studied patients based on sex.

-		Total Stones		Women		Men		P-value
		N	%	N	%	N	%	
Pure or mixed	Mixed	54	32	14	37.8	35	30.2	0.384
	Pure	115	68	23	62.2	81	69.8	
Pure	Ca. Ox	49	42.6	5	21.7	41	50.6	0.027
	Cystine	13	11.3	4	17.4	6	7.4	
	Uric acid	49	42.6	12	52.2	32	39.5	
	Apatite	1	0.9	1	4.3	0	0	
	Brushite	1	0.9	0	0	1	1.2	
	Struvite	2	1.7	1	4.3	1	1.2	
Mixed	Ca.Ox + Ca.P	12	22.2	5	35.7	6	17.1	0.369
	Ca.Ox / Ca.P + uric acid	30	55.6	6	42.9	21	60.0	
	Ca.Ox / Ca.P + cystine	0	0	0	0	0	0	
	Ca.ox / Ca.P + struvite	6	11.1	2	14.3	3	8.6	
	Uric acid + cystine	1	1.9	1	7.1	0	0	
	Ca.Ox + uric acid + struvite	2	3.7	0	0	2	5.7	
	Uric acid + struvite	1	1.9	0	0	1	2.0	
	Ca.Ox + ammonium urate	2	3.7	0	0	2	5.7	

Abbreviations: Ca.Ox; calcium oxalate, Ca. P; calcium phosphate.

Table 3. The stone composition of the studied patients according to underlying diabetes mellitus and hypertension.

-		Diabetes mellitus					Hypertension				
		No		Yes		P-value	No		Yes		P-value
		N	%	N	%		N	%	N	%	
Pure or mixed	Mixed	54	32	9	56.3	0.036	27	32.1	13	38.2	0.527
	Pure	115	68	7	43.8		57	67.9	21	61.8	
Pure	Ca.Ox	49	42.6	0	0	0.015	28	49.1	9	42.9	0.611
	Cystine	13	11.3	0	0		6	10.5	2	9.5	
	Uric acid	49	42.6	7	100		22	38.6	9	42.9	
	Apatite	1	0.9	0	0		0	0	1	4.8	
	Brushite	1	0.9	0	0		0	0	0	0	
	Struvite	2	1.7	0	0		1	1.8	0	0	
Mixed	Ca.Ox + Ca.P	12	22.2	2	22.2	1.000	6	22.2	3	23.1	1.000
	Ca.Ox / Ca.P + uric acid	30	55.6	6	66.7		15	55.6	7	53.8	
	Ca.Ox / Ca.P + cystine	0	0	0	0		0	0	0	0	
	Ca.ox / Ca.P + Struvite	6	11.1	1	11.1		3	11.1	2	15.4	
	Uric acid + cystine	1	1.9	0	0		1	3.7	0	0	
	Ca.Ox + uric acid + struvite	2	3.7	0	0		1	3.7	1	7	
	Uric acid + struvite	1	1.9	0	0		0	0	0	0	
	Ca.Ox + ammonium urate	2	3.7	0	0		1	3.7	0	0	

Note: Ca.Ox; calcium oxalate, Ca.P; calcium phosphate.

Table 4. Stone composition based on body mass index.

-		Body Mass Index						P value
		< 25		25 ≤ x < 30		30 ≤		
		N	%	N	%	N	%	
Pure or mixed	Mixed	1	14.3	7	25	7	28.0	0.76
	Pure	6	85.7	21	75	18	72.0	

(Table 4) contd.....

-		Body Mass Index						
		< 25		25 ≤ x < 30		30 ≤		P value
		N	%	N	%	N	%	
Pure	Ca.Ox	5	83.3	13	61.9	4	22.2	0.023
	Cystine	0	0	1	4.8	1	5.6	
	Uric acid	1	16.7	7	33.3	13	72.2	
	Apatite	0	0	0	0	0	0	
	Brushite	0	0	0	0	0	0	
	Struvite	0	0	0	0	0	0	
Mixed	Ca.Ox + Ca.P	0	0	1	14.3	1	14.3	1.000
	Ca.Ox / Ca.P + uric acid	1	100	3	42.9	4	57.1	
	Ca.Ox / Ca.P + cystine	0	0	0	0	0	0	
	Ca.Ox / Ca.P + struvite	0	0	1	14.3	0	0	
	Uric acid + cystine	0	0	1	14.3	0	0	
	Ca.Ox + uric acid + struvite	0	0	0	0	1	14.3	
	Uric acid + struvite	0	0	0	0	0	0	
	Ca.Ox + ammonium urate	0	0	1	14.3	1	14.3	

Note: Ca.Ox; calcium oxalate, Ca.P; calcium phosphate.

Table 5. The effect of the patient's factors on mixed stone composition.

Variables	P-value	Odds Ratio	95% Confidence Interval	
			Lower	Upper
Diabetes mellitus	0.018	14.113	1.582	125.924
Age	0.535	1.021	0.957	1.088
Body mass index	0.306	0.884	0.698	1.119
Hypertension	0.406	0.425	0.057	3.195
Constant	0.676	6.214		

The qualitative wet chemical analysis method cannot detect stones with the same biochemical composition but different crystal types [9]. For instance, it cannot distinguish between calcium oxalate monohydrate and calcium oxalate dehydrate [9, 10]. Therefore, chemical analysis is a semi-qualitative method with insufficient results. Hence, we used infrared spectroscopy and X-ray powder diffraction.

Infrared spectroscopy is a reliable, fast evaluating method that can be done on small samples. It is appropriate for clinical laboratories due to its low cost [11, 12]. It can detect non-crystal components of the stone. Therefore, it is effective in detecting organic components, particularly drug and purine metabolites [12]. X-ray powder diffraction is easy and can be done on small stone samples. It can accurately analyze the crystal components of the stone and differentiate between them [13, 14].

A study in Japan on 82 patients (44 men and 38 women) with staghorn stones showed that magnesium ammonium phosphate is the most prevalent stone type [15]. In 2005, the American Urological Association reported that most staghorn stones are of the non-metabolic type in the United States [16]. In 2011, a study conducted by the same association on staghorn stone types revealed that 56% were metabolic and 44% were infectious. Furthermore, 55% of the metabolic staghorn stones were composed of calcium phosphate [6]. The findings of the second report on this association are inconsistent with its previous findings.

Moreover, the outcomes of 72 patients who underwent PNL for staghorn calculi between 2010 and 2015 were reported by Haden and colleagues. Twenty-eight patients (39%) had infection stones, while 44 (61%) had metabolic stones. Within the metabolic group, the compositions of the stones were CaP (52%), CaOx (18%), UA (18%), and cystine (12%) [17].

Some studies have shown that the staghorn stone types have changed over time, especially in the last two decades. For example, in some studies, the stone type changed from calcium oxalate to calcium phosphate [9]. These changes seem to be the result of alterations in people's environment, lifestyle, nutrition, and possibly urine pH and damage to the kidney due to extracorporeal shock wave lithotripsy [18 - 20].

Although renal stones are a prevalent urological problem in our country, there are few published studies on the subject. In our study population, our findings indicate that the formation process of staghorn stones is identical to that of other types of kidney stones. Despite the previous assumption that staghorn stones are mainly due to infection [15, 16], our research suggests that they are due to metabolic factors, including environmental and lifestyle factors. Consequently, it appears that all stone prevention recommendations for other kidney stones are also applicable to staghorn stones.

Timely diagnosis of the stone type and necessary preventive and therapeutic measures can be effective for many patients and for preserving kidney function [19, 20].

CONCLUSION

It seems that infectious agents are not the main cause of staghorn stone formation in the kidney. Our study provides new insight into the role of metabolic disorders in patients with staghorn stones. Therefore, large-scale studies with more patients are recommended.

LIMITATIONS

A limitation of our work is that we have taken all our data from a single referral center with a heterogenous regional referral pattern. This means that patients are referred to it from all over the country, and to some extent, this can be a reason to generalize the results and lack of access to first urine analysis results and 24-hour urine collections. The other limitation is that, in many cases, we could not access patients whose medical records had missing data, resulting in insufficient metabolic evaluation.

AUTHORS' CONTRIBUTION

Farzaneh Sharifiaghdas contributed to project development, data collection, and management.

Maryam Taheri participated in project development, manuscript writing, and editing.

Nadia Nikravesh, Mohadese Ahmadzade, and Mehdi Dadpour participated in data collection and management. Behzad Narouie contributed to data analysis, manuscript writing, and editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The ethical committee of the Urology and Nephrology Research Center of Shahid Beheshti University of Medical Sciences approved the study protocol with an ethical code as IR.SBMU.UNRC.REC.1397.37.

HUMAN AND ANIMAL RIGHTS

No animals were used in the studies that are the basis of this research. This research was conducted on humans in accordance with the Helsinki Declaration of 1975, as revised in 2013 (http://ethics.iit.edu/ecodes/node/3931).

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article are available within the article.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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