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Investigation of factors affecting spontaneous ureteral stone excretion

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ABSTRACT

Introduction: Various factors such as structure of stone, size, location of stone and metabolic diseases affect stone excretion.**Objectives:** The aim of this study was to investigate factors related to spontaneous ureteral stone excretion.**Patients and Methods:** This descriptive-analytical observational study was conducted in the university urology centers of Yazd, Iran, during a 16-month period. All patients presenting with unilateral ureteral stone whose ureteral stone was confirmed by CT scan or ultrasound were included in the study. Pregnant patients, patients with uncontrolled hypertension, patients with multiple urinary stones, patients with more than four weeks of history of urinary stones, patients with severe hydronephrosis, and patients with malformations of ureter and kidney were excluded from the study. Computed tomography and ultrasound of the patients evaluated the size of the stone, the location of the stone and the degree of hydronephrosis and also perinephric stranding.**Results:** In this study, 146 patients with mean age of 45.3±15.1 years (ranging from 11 to 84 years) were enrolled. CT scan and ultrasound were diagnostic in 121 (82.9%) and 25 patients (17.1%) respectively. In logistic regression model analysis, size less than 5mm, stone location and male gender and diabetes were significant predictors of spontaneous stone excretion, while size less than 5 mm was the strongest predictor.**Conclusion:** The strongest predictor of spontaneous excretion is the size of the stone and the next step is the location of the stone. Male gender and diabetes are also contributing factors to the spontaneous excretion of ureteral stones.

Implication for health policy/practice/research/medical education:

The size and location of the stone is the most important predictor of spontaneous stone rejection. The results of our study showed unequal prevalence of urinary stones in men and women.

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Introduction

Urinary tract stones are one of the problems that about 15% of the world's population is affected. Men's rates of urinary stones are twice higher than women. Studies have also shown that its prevalence is increasing in the population (1). Various factors appear to be contributing to stone formation, including population aging, changes in eating habits, global warming, and the use of diagnostic tools (2, 3). At least one in every 11 Americans is exposed to urinary stones during their lifetime, with an annual economic burden of approximately \$ 4.5 billion (4).

A study in China also showed that one in every 17 Chinese adults in China is exposed to urinary stones during their lifetime. In addition to causing pain and

urinary tract infection (UTI), urinary stones can lead to chronic kidney disease and eventually kidney loss (5). Approximately 60% of ureteral stones can be excreted spontaneously. Various factors such as composition, size, location of stones and metabolic diseases affect stone disposal (6). Recent studies have shown that 68% and in some studies up to 98% of distal ureteral stones less than 5 mm in diameter and 47% of stones between 5 to 10 mm can be excreted spontaneously (7-9).

In a study in 2014, the most important factor affecting spontaneous excretion was stone size (10). Additionally, stone location, past history of spontaneous excretion, diabetes and C-reactive protein (CRP) can be effective factors (11). So far, no studies in Iran have investigated

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the factors affecting spontaneous ureteral stone removal. Urinary stone management is an economic burden in various countries. Deciding whether to intervene or wait for spontaneous removal of ureteral stones is one of the problems of urology, thereby identifying the factors associated with spontaneous ureteral stone removal **that** can help clinicians to make the appropriate decisions.

Objectives

The aim of this study was to investigate the factors associated with spontaneous ureteral stone excretion.

Patients and Methods

Study patients

This descriptive-analytical observational study was conducted in the urology centers of Shahid Sadoughi University of Medical Sciences, Yazd, Iran, during a 16-month period. The patients' demographic data were recorded by the researcher at the urology clinic. After obtaining **informed consent**, patients were examined by a urologist and an assistant.

In this study, all patients with unilateral ureteral stone (less than 9 mm) which confirmed by CT scan or ultrasound were enrolled **in** the study. Patients who refused to participate in the study or were unable to participate in the study were excluded. Pregnant patients, patients with uncontrolled hypertension, patients with multiple urinary stones, patients with more than four weeks of history of urinary stones, patients with impacted stones, patients with severe hydronephrosis, patients with ureteral and renal abnormalities and patients **undergoing** urologic surgeries for the past six months, including transurethral lithotripsy (TUL), pyeloplasty, prostatectomy, retrograde intra-renal surgery, nephrectomy, percutaneous nephrolithotomy, nephrolithotomy, or single kidney patients, patients with ureteral and urethral stricture, severe and refractory pain, UTI, uremic patients and a bilateral ureteral stones were excluded. Other exclusion criteria included chronic diseases, history of stroke, neuropsychiatric disorders including cognitive and dementia disorders and physical disabilities. Additionally, if there were symptoms of UTI, septicemia, or drug-resistant pain before the 4-week interval, patients were excluded from the study and then underwent surgical intervention. To determine the sample size according to similar studies and based on the variance obtained at 95% confidence level and 80% power, the exact sample size was calculated (**146 patients**).

Computed tomography and ultrasound of these patients evaluated the size of the stone, the location of the stone and the degree of hydronephrosis. Urine analysis, CBC diff, blood urea, serum creatinine and CRP were measured. Accordingly, HbA1c, fasting blood sugar (FBS) and type of drugs were recorded for diabetic patients. Similarly, history of hypertension, type of drugs and history of dyslipidemia were also recorded for

hypertensive individuals. Patients were followed for four weeks. For most patients, tamsulosin 0.4 mg until stone excretion for up to four weeks and hydrochlorothiazide 25 mg daily and non-steroidal anti-inflammatory drugs (suppository or diclofenac 100 tablets) for pain relief were administered. Emergency cases were given ketorolac ampoule and for some patients corticosteroids in the absence of contraindication were prescribed.

Ethical issues

The study was conducted in accordance with the principles of Declaration of Helsinki, 1996 version and its later amendments and also Good Clinical Practice standards. Each subject signed a consent form before they were admitted into the study. Ethics approval was also received from Yazd University of Medical Sciences and ethics committee (#IR.SSU.MEDICINE.REC.1397.072). Additionally, during the study, patients would be excluded from research if they did not consent to continue their research. The results of this study were presented to the patients. This study was extracted from the residential thesis of Javid Gholami at the department of urology of this university.

Statistical analysis

After one month, due to low-radiation and low-cost, a kidney, ureter and bladder (KUB) X-ray was conducted for patients and if there was evidence of stones including hydronephrosis and no stone excretion, a CT scan was performed to check for spontaneous stone excretion. Our patients were divided into two groups of stone excretion and non-stone excretion. **To maintain the study blinding, another researcher entered the data into the SPSS software version 23 and analyzed.** The descriptive, chi-square, *t* test and logistic regression were used.

Results

In this study, 146 patients with mean age of 45.3±15.1 years (ranging from 11 to 84 years) were enrolled. Demographic information, patient history and interventions are summarized in [Table 1](#). Among all patients, 82 patients (56.2%) were male. Abdomen CT scan was diagnostic in 121 patients (82.9%) and KUB x-ray in 25 patients (17.1%).

The study of stone size showed that 68.5% of the stones were 5 to 9 mm. However, in almost half of the cases without intervention, these stones were passed spontaneously. Around 54.1% of stone cases were associated with mild hydronephrosis since in 28.1% a moderate hydronephrosis was detected. The most common location of the stone was the distal ureter. Approximately 1.3% of patients were treated with fluoroquinolone. In the case of interventional treatment, 84.3% of patients underwent **transurethral lithotripsy**.

According to [Table 2](#), almost half of all stones were

spontaneously passed. Stones less than 5 mm in size, especially when located in the distal of the ureter, had a very high chance of spontaneous excretion, therefore 90.9% of all stones less than 5 mm were excreted ($P=0.001$). The patients with higher CRP were less likely to have spontaneous stone excretion. In patients who had hydronephrosis, 57 were experienced the passage of stones at 4 weeks. With the higher degree of hydronephrosis, there

Table 1. Frequency of demographic characteristics, patient history and interventions

Variable	Frequency	Percent
Gender		
Male	82	56.2
Female	64	43.8
Diagnosis		
CT scan	121	82.9
Sonography	25	17.1
Medication for diabetes		
Metformin	12	37.5
Glibenclamide + metformin	6	18.8
Insulin	11	34.4
Acarbose + metformin	3	9.4
History of urology surgery		
Dyslipidemia	30	20.5
Hypertension	27	18.5
Diabetes	31	21.2

Table 2. Clinical findings of stone passage by dyslipidemia, corticosteroids, size and location of the stone, CRP and hydronephrosis

Variable		Stone excretion at week 4		P value
		Positive	Negative	
Dyslipidemia	Positive	17	13	0.573
	Negative	59	57	
Corticosteroids use	Positive	13	5	0.091
	Negative	63	60	
Size				
<5 mm	Proximal	6	11	0.029
	Medial	2	5	
	Distal	2	20	
5-9 mm	Proximal	18	6	
	Medial	17	12	
	Distal	25	22	
CRP (mg/L)	Negative	20	12	0.063
	+1	21	17	
	+2	2	7	
Hydronephrosis	No	19	7	0.032
	Mild	40	39	
	Moderate	17	24	

was a lower likelihood of spontaneous stone excretion ($P=0.03$). Table 3 shows that serum creatinine levels are significantly associated with spontaneous stone excretion while higher serum creatinine levels decrease the chance of spontaneous stone excretion at four weeks ($P<0.05$). According to Table 4, there was a significant relationship between stone excretion time and stone size.

The logistic regression model analysis after adjusting for other variables showed that size less than 5 mm, stone location and male gender and diabetes were significant predictors of spontaneous stone excretion while mean size less than 5 mm was the strongest predictor. In stones less than 5 mm, a higher chance of spontaneous passage was seen. Regarding stone location, less than one-third of cases of upper ureteral stones had spontaneous excretion, and based on adjustment for other variables, stone excretion was 0.3% in people with a history of diabetes. We also found a correlation between spontaneous stone excretion and diabetes. According to the logistic regression, male gender also reduces the likelihood of stone excretion (Table 5).

Discussion

In our study, the majority of patients (56.2%) were male. Historically, the incidence of urinary stones in men has been reported to be two to three times that of women; however the results of several studies also indicated that the proportion is decreasing and the incidence of nephrolithiasis in women is faster than in men. The cause of this increase is not exactly known, but lifestyle changes that appear to increase the prevalence of obesity in women, a known risk factor for kidney stones, appear to be involved (12-14).

In our study, approximately 5% of patients had at least one of the metabolic syndrome disorders, namely hypertension, diabetes, or dyslipidemia. Numerous studies, including studies by Jeong et al and Obligado and Goldfarb, and several other studies have proven that diabetes, obesity, and hypertension increase the

Table 3. The relationship of stone excretion at week 4 with renal function

Variable	Stone excretion at week 4				P value
	Negative		Positive		
	Mean	SD	Mean	SD	
BUN (mg/dL)	34.2	14.3	30.6	17.8	0.185
Serum creatinine (mg/dL)	1.18	0.22	1.05	0.25	0.001

Table 4. The relationship between stone excretion time and stone size

Variable	Stone excretion time				P value
	Mean	SD	Min	Max	
Less than 5 mm (N=35)	7.06	4.7	1	19	0.040
5-9 mm (N=40)	9.45	4.99	1	21	

Table 5. Predictive value of variables by adjusting for other factors in spontaneous ureteral stone excretion

Variable		B	Std. Error	P value	Odds Ratio	95% CI	
						Lower	Upper
Gender	Male	-0.799	0.3940	0.043	0.450	0.208	0.973
	Female	0 ^a	-	-	1	-	-
Stone location	Proximal	-1.227	0.4803	0.011	0.293	0.114	0.751
	Medial	-0.474	0.4635	0.306	0.622	0.251	1.544
	Distal	0 ^a	-	-	1	-	-
Hydronephrosis	No	0.622	0.6380	0.329	1.863	0.534	6.507
	Mild	0.215	0.4321	0.618	1.240	0.532	2.893
	Moderate	0 ^a	-	-	1	-	-
History of diabetes	Positive	-1.093	0.5045	0.030	0.335	0.125	0.901
	Negative	0 ^a	-	-	1	-	-
History of hypertension	Positive	0.096	0.5141	0.852	1.101	0.402	3.015
	Negative	0 ^a	-	-	1	-	-
Stone size (mm)	<5	1.810	0.5005	<0.001	6.111	2.291	16.298
	5-9	0 ^a	-	-	1	-	-

incidence of urinary tract stones independently and lead to an increase in the medical costs. Therefore, one aspect of prevention and recurrence of renal stones may be attention to metabolic syndrome (15-18).

In 70% of patients at presentation, the stones were 5 to 9 mm in size. Overall, 52% of all stones less than 5 mm had spontaneous excretion. Additionally, 47.3% of the stones were distal to the ureter when referred. The distal ureteral stones had a high chance of spontaneous excretion; like 60% of all distal ureteral stones less than 9 mm in diameter and 90% of distal ureteral stones less than 5 mm in our study. Similar studies show that 70% of stones are distal when the patient is referred, and in general, 70% of distal ureteral stones are spontaneously excreted (19–21).

In this study, a significant relationship between spontaneous stone excretion and hydronephrosis was found. The results of most studies in this area were inconsistent with our study. In the study by Ahmed et al (10), those who did not have hydronephrosis had a higher chance of successful excretion, while our results indicated that the chance of spontaneous excretion in mild to moderate hydronephrosis is higher than in those without hydronephrosis. However, in a study by Jendeborg et al, stones associated with moderate-to-severe hydronephrosis were more likely to have spontaneous excretion than mild hydronephrosis, which was only observed for lower ureteral stones.

In our study, no significant relationship between spontaneous stone excretion and levels of blood urea nitrogen (BUN) was detected. However, a significant relationship between serum creatinine level and spontaneous stone excretion at 4 weeks was seen too. It seems that lower serum creatinine levels can lead to spontaneous stone excretion. Further studies are needed in future studies.

In this study, no significant relationship between levels of CRP and spontaneous stone excretion at 4 weeks was seen, however it was shown that the higher the serum CRP concentration, the lower the likelihood of spontaneous stone excretion. Park et al found that measuring serum CRP levels in patients with small urinary tract stones (less than 8 mm) would be useful in predicting spontaneous stone excretion (22).

In our study, by analyzing the logistic regression model, the strongest predictor of spontaneous excretion of stone was size and the next was its location. The success rate of spontaneous stone excretion has been reported in stones less than 5 mm by 71% to 98% and for stones between 5 to 10 mm, it was 25% to 35% (23). The results of recent studies indicated that size and the location of the stone have a crucial role in its spontaneous excretion. These results were in line with most previous comparisons (24-26). In our study, male gender and diabetes were also predictors of spontaneous stone excretion. In the studies of Tthey et al (27) and Mohammad et al (11), no relationship between genders as a predictor was found. In the study by Mohammad et al, serum CRP, stone size, and previous history of stone passage were significant and independent predictors. In general, previous studies have not considered or examined the predictors of gender and diabetes; hence the results of this study may be useful in future studies.

Conclusion

The most important predictor of spontaneous stone passage is the size and location of the stone; thereby these two cases are very helpful in making the choice between expected treatment and medication or interventional measures. According to the present study, the prevalence of urinary stones in men and women is equal. High

prevalence of metabolic syndrome including diabetes, hypertension and dyslipidemia in patients with renal stone can be noticeable. History of diabetes is also an effective factor in stone excretion and needs more sample size for decision making. Finally, the average time for spontaneous stone excretion, especially in cases less than 5 mm, was 7 days and it takes longer for larger stones.

Limitations of the study

Our investigation is restricted by its cross-sectional design and therefore, the causal associations could not be established. Hence, we suggest longitudinal studies in a larger population.

Authors' contribution

MA, HK and JG conceived the idea of this publication. HM and JG performed the data collection. MA and HK contributed to the literature review, data analysis, and review of the article for final publication.

Conflicts of interest

The authors declare that there is no conflict of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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