

FREQUENCY OF SPONTANEOUS EXPULSION OF LOWER URETERIC STONES IN PATIENTS WITH RAISED C-REACTIVE PROTEIN

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ABSTRACT

Background: Ureteric stone is a common condition a urologist has to deal with. Ureteric stones can be dealt conservatively as well as by surgical/endoscopic interventions. Prediction of spontaneous expulsion of ureteric stones early at the presentation by using inflammatory markers like C-reactive protein (CRP) would be extremely helpful in the management, as it could avoid unnecessary conservative management and elect for intervention at the outset

Objective: To determine the frequency of spontaneous expulsion of lower ureteric stones in patients with raised CRP

Methods: Descriptive cross sectional study was performed at the urology department of institute of kidney diseases Hayatabad medical complex patient. 195 patients were included in the study using non probability consecutive sampling. All patients had lower ureteric stone and raised CRP. Patients were followed till spontaneous expulsion or stone clearance. Data was analysed using SPSS 17.

Results: Out of 195 total patients 102(52%) were female and 93(48%) were male. Patients included in the study had age range from 18- 60yr, mean age was 33.21 ± 8.62 SD. Patients selected in the study had lower ureteric stones ranging from 5-9mm. mean stone size was $6.994 \text{ mm} \pm 1.09$ SD. Mean CRP was $3.34 \text{ mg/dl} \pm 2.49$ SD. CRP levels were also stratified into 2 groups. 75% of the patients had CRP 0.5-4.9 mg/dl levels where as 25% had CRP levels from 5-9.9 mg/dl. 32.19% (47/146) patients with CRP 0.5-4.9mg/dl passed stones spontaneously while 89.7% (44/49) patients with CRP 5-9.9 mg/dl passed stone spontaneously. After applying chi square, P value < 0.005.

Conclusion: CRP is an inflammatory serum marker which can help in the prediction of spontaneous expulsion of small lower ureteric stones and thus can avoid unnecessary conservative management. However clinical features of a patient should also be kept under consideration along with CRP levels before taking any decision for any intervention.

Keywords: C-reactive protein, spontaneous stone passage, urolithiasis

INTRODUCTION

Urolithiasis is a common disease all over the world with prevalence of about 4-15%, ureteric stones make about 20% of it¹. Acute renal colic secondary to urolithiasis being one of the most common emergencies a urologists has to deal with². Interventions commonly employed for the treatment include shock wave lithotripsy and ureteroscopy. These modalities are neither cost effective nor without complications³. On the other hand, several studies have shown spontaneous stone expulsion rates of about 98% for smaller lower ureteric stones⁴⁻⁶. However opting conservative management in every case is not always wise as it can result in sepsis and impaired renal functions as well⁷⁻⁹. Medical expulsive therapy is the facilitation of spontaneous stone

expulsion by using drugs like tamsulosin^{10,11}. Stone size is one of the most important factor which could predict stone passage^{4,12}. The incidence of spontaneous passage of distal ureteric stones 5mm or smaller can reach upto 71-98% in contrast to only 25-51% for larger stones^{5,13}. Other factors studied for prediction of spontaneous stone passage include significant pyuria, duration of pain, stone surface irregularity, and degree of obstruction¹⁴.

C-reactive protein (CRP) is an acute-phase protein, released into the bloodstream in response to inflammation. It is synthesized in the liver and activates complement system after binding with phosphocholine receptors^{15,16}. Role of CRP has been assessed in certain urological conditions, such as determination of degree of renal injury in pyelonephritis¹⁷, assessing the severity of urinary tract infection in children¹⁸, and in avoiding micturating cystourethrogram in paediatric patients with vesicoureteric reflux and fever¹⁹.

There is conflicting evidence on the role of raised inflammatory markers like CRP in acute ureteric colic²⁰. Some studies have shown increased chances of spontaneous stone expulsion with raising inflammatory markers²¹ while others have shown that higher the levels of inflammatory serum markers the less likely will be

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spontaneous expulsion and hence more likely will be the need for intervention^{22,23}

Our rationale is based on the fact that it is currently not clearly established whether inflammatory markers like CRP can be used as an independent factor in predicting spontaneous stone expulsion. Further, identifying such factors at initial presentation can help make us early decision regarding intervention and thus prevent unnecessary conservative treatment.

OBJECTIVES

To determine the frequency of spontaneous stone expulsion of small lower ureteric stones in patients with raised serum CRP

MATERIALS AND METHODS

Study design: Descriptive Cross Sectional

Setting: Institute of Kidney Diseases, Hayatabad Medical Complex Peshawar

Duration of study: 6 months from Jan 2018 to June 2018

Sample Size: Using W.H.O calculator, proportion of CRP level in spontaneous stone expulsion = 54.9%¹⁶, margin of error 7%, confidence interval 95%, sample size was 195

Sampling technique: Non- probability Consecutive

SAMPLE SELECTION

Inclusion criteria

- Patients with distal ureteric stone size 4mm to 9mm and with raised CRP
- All male and female patients from 18-60 yrs.

Exclusion criteria

Multiple ureteric calculi

- Pregnancy
- Solitary kidney
- Urinary tract infection
- Impaired renal functions
- Patients who do not want to undergo conservative treatment
- Patients suffering from any other inflammatory condition like infections, arthritis, , diabetes, hepatic failure

DATA COLLECTION PROCEDURE

This study was conducted after approval from College of Physicians and Surgeons, Karachi, Pakistan. Eligible candidate were selected from OPD and

emergency department after their screening through the inclusion and exclusion criteria. Informed written consent was obtained from the patients before their enrollment into the study. History taking and examination was done from all patients for suspected ureteric stone. Urine r/e, blood investigation, including serum urea and creatinine levels were carried out followed by x-ray KUB and ultrasound of the pelvis and abdomen. CRP was measured only at initial presentation. All investigations were performed in the hospital laboratory using the same protocol to avoid any conflict. Patients were followed till stone expulsion or stone clearance by ESWL or URS. This data was recorded on a separate proforma for each patient.

DATA ANALYSIS

The data was analyzed using SPSS 17. Mean $\pm$ S.D were calculated for numeric variables like age, stone size and CRP level. Frequency and percentage were calculated for qualitative variables like gender, stone size and spontaneous expulsion. Stone expulsion was stratified among age, gender and CRP levels and stone size to see effect modifier. Post stratification was applied using chi square test. P-value ≤ 0.05 was taken as significant. Data is presented in the form of tables and graphs

RESULTS

Total number of patients was 195. Out of these 102 were females representing 52% of the sample. Males were 93 which make 48% of the total sample. Female to male ratio was 1.08:1.

Patients included in the study had age range from 18- 60 yr. mean age was 33.21 ± 8.62 SD. Age was stratified into three groups. Age group 18-30yrs had 44.9 % of the patients, group 31-45 had 46.4% and group 46-60 had the lowest no. of patients 18.7%. Age distribution is shown in figure 1.

Patients selected in the study had lower ureteric stones ranging from 5-9mm. mean stone size was $6.994 \text{ mm} \pm 1.09 \text{ SD}$

Patients included in the study were those who had serum C reactive protein. Mean CRP levels was $3.34 \text{ mg/dl} \pm 2.49 \text{ SD}$. CRP levels were also stratified into 2 groups. 75% of the patients had CRP 0.5-4.9 mg/dl levels where as 25% had CRP levels from 5-9.9 mg/dl.

Patients were observed for spontaneous expulsion of lower ureteric stones. All patients had raised CRP levels. Out of 196, 91 patients had spontaneous stone expulsion while 105 patients had to undergo other interventions like ESWL, URS for stone clearance.

32.19% (47/146) patients with CRP 0.5-4.9mg/dl passed stones spontaneously while 89.7% (44/49) patients with CRP 5-9.9 mg/dl passed stone sponta-

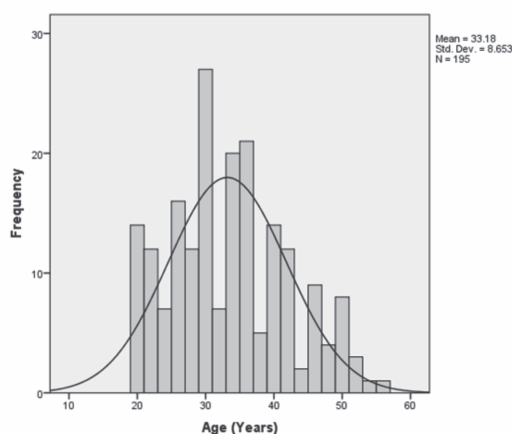


Figure 1: Age Distribution

Table 1

Spontaneous Stone Expulsion	CRP stratification		P value
	0.5-4.9mg/dl	5-9.9mg/dl	
no	99	5	<0.005
yes	47	44	
Total	146	49	

neously. After applying chi square P value < 0.005 table 1.

DISCUSSION

Ureteric stone prevalence is about 15% of the population and acute ureteric colic is one of the most frequent emergency, a urologist has to deal with². There are different treatment options including conservative management, shock wave lithotripsy (SWL) and ureteroscopy (URS). Advancement in minimally invasive surgery has resulted in widespread acceptance of ESWL and URS as very efficient modalities with success rates ranging from 63-86% and 57-92% respectively^{7,24,25}. Nevertheless both these interventions are associated with complications and are expensive. On the other hand conservative management can be very successful and cost effective in favorable candidates with spontaneous expulsion of up to 98% for stones 5mm or less according to American Urological Association meta-analysis^{9,26}. However this approach can also lead to morbidity in the form of recurrent colic, infections, loss of work, uncertainty and derangement of renal functions as well⁷⁻⁹.

The decision to elect between conservative therapy and minimally invasive treatment for small ureteric stones is challenging for a urologist. Urgent surgical decompression is required only in cases where there is evidence of sepsis, deranging renal function, ongoing severe pain despite medical treatment. Different factors

have been studied which could predict spontaneous expulsion of stones, the most significant being the stone size and location. Increasing evidence is now showing role of inflammatory markers in this regard. Use of such marker would be extremely helpful in improving the management of distal ureteric stones by not only predicting the spontaneous expulsion but also in deciding early to undergo intervention and hence prevent complications.

Inflammatory markers most studied are white blood cell count and CRP. There is conflicting data about their usefulness²⁷. Sfoungaristos has shown statistically significant increased chances of spontaneous stone expulsion with raised WBC count and neutrophil count. Reason being as stone passes along the ureter it provokes inflammatory response and those passing through the entire length of ureter would result in higher levels of these counts²¹.

However park et al have shown increased rates of spontaneous stone expulsion with normal neutrophil count as compared to raised counts. Furthermore they proved statistically significant decreased spontaneous expulsion rates with raised CRP levels. They reasoned that greater degree of inflammation would result in more edema and higher CRP levels and hence less chances of spontaneous expulsion^{23,27}. Angulo et al have found CRP levels of 2.8mg/dl to be cut off for intervention²⁸.

The results of our study showed significant association between spontaneous stone expulsion and CRP levels. Patients with higher CRP levels had more spontaneous expulsion while patients with lower CRP levels were more likely to have undergone intervention. Similar results were shown by Sfoungaristos et al for stone passage in terms of WBC and neutrophil count. Theoretically stones passing through the entire length of ureter would result in greater degree of inflammation and hence higher CRP in contrast to those stones who fail to pass the entire length. However inflammation persisting for longer time can also lead to impedence of stone passage as well²⁹. So this should be kept in consideration that markers like CRP and WBC count are only laboratory values and any decision for intervention or conservative management should be taken after assessing all relevant clinical factors.

CONCLUSION

Serum CRP is a relatively newer marker now increasingly being used for the purpose of predicting spontaneous stone expulsion of small lower ureteric stones. However current evidence still does not support CRP levels alone to be recommended for this purpose. Clinical assessment of every individual patient is still the mainstay of decision for intervention.

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