

**Original Article****Serum C - Reactive Protein, White Cell Counts and Neutrophil Percentage are Predictors For Distal Ureteric Calculus Expulsion Rate: A Prospective Study****Ram Sagar Shah\* and Kaushal Sigdel**

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**DOI: <http://dx.doi.org/10.3126/jonmc.v8i1.24479>****Abstract****Background**

To determine the relationship between expulsion rate of distal ureteric calculus less than or equal to 10mm in size and C reactive protein (CRP) level, white cell count and neutrophil percentage.

**Materials and Methods**

A total of 186 patients with distal ureteric calculus of  $\leq 10$ mm were evaluated for stone expulsion rate and its correlation with serum CRP, white cell count and neutrophil percentage. All patients received tablet Tamsulosin 0.4mg for 4 weeks or till the expulsion of stone. Patients were called weekly till 4 weeks, or early if there was history of stone expulsion. Patients were divided in two groups according to normal and elevated CRP levels, white cell count and neutrophil percentage at baseline for statistical analysis.

**Results**

The patients had an average age of  $35.6 \pm 13.9$  years. 52.2% were male. Ratio of right to left was 1.58:1. Majority of the patients with distal ureteric calculus = 10mm passed their stone (74.7 %) with medical expulsion therapy. Expulsion of stone less than 5mm was statistically significant ( $p = 0.017$ ). Patients with normal neutrophil percentage and normal CRP level had higher stone expulsion rate than elevated neutrophil or CRP (85.2% vs. 40.9, 91.8% vs. 30.8% respectively). In patients with normal white cell count, 86.4% passed their stone while in elevated white cell count group 39.1% passed their stone.

**Conclusion**

This study showed patients with distal ureteric calculus of  $\leq 10$ mm with normal CRP level and normal neutrophil count had higher expulsion rate while WBC count showed no statistically significant association.

**Keywords:** *C-reactive protein, Neutrophil, Calculi*

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## Introduction

Urolithiasis is common problem which accounts for 8–15% of the world population [1]. Ureteric stones account for 20%, among this 70% of is distal ureteric stones [2]. There are many therapeutic options for ureteric stones, they are watchful waiting, medical expulsive therapy (MET), extracorporeal shockwave lithotripsy (ESWL) and Ureteroscopy with Intra-Corporeal Lithotripsy, besides these open, laparoscopic and robotic assisted techniques are available with limited indications. Most of the ureteric stones can pass spontaneously; application of minimally invasive techniques can be considered overtreatment adding unnecessary costs [3]. In study conducted in BPKIHS, Dharan, medical expulsive therapy (MET) was emphasized as first line treatment for distal ureteric stones without complications [4]. They found that neither watchful waiting nor MET has negative effect over the success rate of ureteroscopic stone removal in cases of failure of MET. MET is considered as the most simple and cost effective treatment then also it has complications like acute renal failure, febrile infections and recurrent ureteric colic. The conservative approach to treatment helps to control of pain, oedema, ureteric spasm, and infection, which favours stone expulsion [1].

Stone size and their location within the ureter decide that stones will pass through the ureter or not. Stones, of size <5 mm, are far more likely to pass spontaneously and required the management of symptoms only. They mentioned that 60% of ureteric stones passes spontaneously, of which 45% stones in the distal third of the ureter passed spontaneously, compared with the mid third of 22%, and the proximal third of 12% [5]. Plasma CRP predict the success rate of medical expulsive therapy for management of small distal ureteric calculi (4–9mm), Patients with CRP >18mg/L have low stone expulsion rate, and should undergo minimally invasive ureteroscopy, or noninvasive shock wave lithotripsy [6]. Passage rates of ureteric stone according to the level CRP i.e. low serum level group, the medium serum CRP level group, and the high serum CRP level group were 94.1%, 70%, and 50.0%, respectively. The passage rates of ureteric stones with a normal neutrophil percentage group and with a higher neutrophil percentage group were 94.5% and 83.1% respectively [7].

This study was conducted to know the relationship between stone expulsion rate of distal ureteric stone with C-reactive protein, white cell count and neutrophil percentage. The result of the study may help us in framing a protocol for treatment of small distal ureteric stone in our institute and may fill the existing gap in literature.

## Materials and Methods

This prospective study was conducted at the Nobel Medical College Teaching Hospital, Biratnagar, Nepal, between February 2018 to March 2019 with approval by 'Institutional Review Committee.' A prior written informed and well understood consent was taken from all eligible patients. All patients above 18 years with distal ureteric stone less than or equal to 10mm were included. Patients with acute or chronic febrile infection, moderate to severe hydronephrosis, chronic renal insufficiency, pyonephrosis, Solitary kidney with stone, anatomical malformation of renal system, neoplasia, liver failure, multiple ureteric stone, pregnancy, hypersensitivity to Tamsulosin, Proximal or middle ureteric calculi and those who did not give consent were excluded. Spontaneous ureteric stone expulsion in patients with normal CRP was 90.9% whereas 58.8% had no spontaneous expulsion among high CRP group. The sample size was calculated with RR 1.5, power 80%,  $\alpha$ -error 5%; using 2-sided test, minimally 34 patients were required in each group. However, 185 patients included as the study considered multiple variables [7].

Investigations like complete and differential blood counts, C-reactive protein level, urine routine and microscopic test and urine culture sensitivity was done. Radiological examinations like X-ray Kidney-Ureter-Bladder (KUB), Ultrasonography (USG) of the urinary tract was done in all patients. CT Urography and Non-contrast enhanced computed tomography (NCCT) was done as and when indicated. The result of investigations was noted in the preset Proforma. Normal and elevated CRP was defined as <6mg/dL and >6mg/dL respectively. Normal and elevated white cell count was defined as 4000-11000 cells/cc and >11000 cells/cc respectively. Normal and elevated neutrophil percentage was defined as 50-75% and >75% respectively. Patients were divided in two groups according to normal and elevated CRP levels, white cell count and neutrophil percentage at baseline for statistical



analysis. Size of the stone was measured by USG or KUB or CT, as maximum transverse diameter in millimeters and was noted. Location of distal ureteric stone was defined from the lower border of the sacrum to the vesicoureteric junction. C-reactive protein level, white cell count and neutrophil percentage was estimated before administration of the anti-inflammatory drug. All patients were given tablet Tamsulosin for 4 weeks or till the expulsion of stone. Tablet Ketorolac was given thrice daily, till the pain subsided. In cases where the pain didn't subside with oral drug he/she was switched to injectable Ketorolac. In addition all patients were asked to drink at least 2 liters of water daily. Patients were advised to filter the urine to observe possible stone expulsion.

Patients were called weekly till 4 weeks, or early if there was history of stone expulsion. Detailed history about expulsion of stone was taken, and he/she underwent x-ray KUB and USG, CT urography for presence or absence of stone, and results were noted. Stone expulsion was defined as no stone seen on x-ray KUB, USG and CT. Duration for the expulsion of stone was also noted in the preset Proforma. The adverse effects of the drugs, if any, was recorded during follow up.

### Statistical Analysis

Statistical analysis was performed by using mean, standard deviation, number, percentage for descriptive analysis. Bivariate analysis was done by using student t-test and chi-square test for continuous variable and categorical variables respectively to compare between 2 groups of spontaneous expulsion of stone. Multivariate analysis was done using multiple logistic regressions. A value of  $p < 0.05$  was considered significant.

### Results

In NMCTH urology outpatient department, a total of 245 patients were presented with ureteric stones of which 186 patients fulfilled the inclusion criteria and included in the study. A detailed history, thorough general physical and systemic examination and investigations were carried out and the findings were noted in the preset proforma.

Patients were divided in two groups according to CRP, white cell count and neutrophils levels at baseline. All patients were given medical expulsion therapy. They were called weekly till 4 weeks, or early if there was history of stone expulsion.

**Table 1: Spontaneous expulsion of the stone according to its size**

Size of stone	Spontaneous expulsion + (%)	Spontaneous expulsion - (%)	X2 value	P-value
<5 mm	39(88.6)	5(11.4)	5.901	0.017
5-10 mm	100(70.4)	42(29.6)		

Expulsion of stone less than 5mm was statistically significant (p value 0.017).

**Table 2: Spontaneous expulsion of the stone with medical expulsive therapy**

Stone passed	Stone size (mm)				
	<5	5-6	6-7	7-9	9-10
Yes	40 (88.9%)	25 (75.8%)	23 (71.9%)	26 (70.3%)	25 (64.1%)
No	5 (11.1%)	8 (24.2%)	9 (28.1%)	11 (29.7%)	14 (35.9%)
Total	45	33	32	37	39

**Table 3: Relationship of spontaneous expulsion of stone with white cell count**

WBC (cells/cc)	Spontaneous expulsion (+) (%)	Spontaneous expulsion - (%)	X2 value	P-value
Normal (4000-11000)	121(86.4)	19 (13.6)	41.018	<0.001
High (>11000)	18(39.1)	28 (60.9)		

**Table 4: Relationship of passage of stone with neutrophil percentage**

Neutrophil percentage (%)	Spontaneous expulsion (+) (%)	Spontaneous expulsion - (%)	X2 value	P-value
Normal (50-75)	121 (85.2)	21 (14.8)	34.913	<0.001
High (>75)	18 (40.9)	26(59.1)		

**Table 5: Relationship of passage of stone with CRP level**

CRP (mg/L)	Spontaneous expulsion (+) (%)	Spontaneous expulsion - (%)	X2 value	P-value
Normal ( $\leq 6$ )	123 (91.8)	11 (8.2)	73.872	<0.001
High (>6)	16(30.8)	36 (69.2)		

### Discussion

Ureteric stones are common problems accounts for 10 to 15% of the population [7]. Different



**Table 6: Comparison of patient characteristics according to success of spontaneous expulsion of stone**

Characteristics	Spontaneous expulsion (+)	Spontaneous expulsion (-)	p-value
Number of patients (n)	139	47	
Age (y)	37.64±12.676	37.34±13.180	0.890
Male/Female	69/70	28/19	0.311
Left/Right	53/86	19/28	0.863
CRP (mg/L)			
Normal (≤6)	123	11	<0.001
High (>6)	16	36	
White cell count (cells/cc)			
Normal (4000-11000)	121	19	<0.001
High (>11000)	18	28	
Neutrophil percentage (%)			
Normal(50-75)	121	21	<0.001
High(>75)	18	26	

treatment options are used according to the size, location, and clinical aspects of the stone. These treatments include watch full waiting, medical expulsive therapy, extracorporeal shock wave lithotripsy; ureteroscopy; and ureteric stone removal through laparoscopic and open surgery. The advances of minimal invasive techniques and their high success rate have resulted in its wide adoption for treatment of ureteric stone [8]. However they are costly and have complications. Conservative management is cheap but not complication free. Making the decision of whether to use either of treatment methods is difficult. Identification of factors that could help in the prediction of treatment success would be conducive to treatment selection therefore this prospective study was conducted to determine the relationship between the stone expulsion rates of distal ureteric stones less than or equal to 10mm with CRP level, white cell count and neutrophil percentage. One hundred and eighty six patients were included. Patients underwent baseline investigations and prescribed with medical expulsive therapy. Follow up was done weekly or till expulsion of the stone. One hundred and thirty nine patients (74.7%) passed their stone with medical expulsion therapy.

In patients with stone size less than 5mm, thirty nine (88.6%) passed their stone while in patients with stone size of 5-10mm, one hundred (70.4%) passed their stone, ( $p < 0.017$ ). Results of studies mentioned below are in accordance with our

result. Tchev et al, [5] reported stone expulsion rate as 71% for lower ureteric stones. Stones smaller than 6mm had 88.7% chance of spontaneous passage while stone 6mm or larger had 57.5% expulsion chances. In meta-analysis of different studies done by Segura et al, [9], showed that 98% of stone less than 5mm are passed spontaneously with conservative management, Hussein, [6] reported incidence of spontaneous expulsion of distal ureteric stones as high as 71-98% for stone =5mm and only 25-51% for stone more than 5mm. Park et al, [7] reported expulsion rate of 90.9% for ureteric stone less than 8mm.

One hundred and twenty one patients (86.4%) with normal white cell count passed their stone with medical expulsion therapy while 19 (13.6%) did not pass. Eighteen patients (39.1%) with high white cell count passed stone but 28 (60.9%) did not pass the stone. In bivariate analysis, higher spontaneous expulsion of stone with normal white cell count was statistically significant ( $p$  value  $< 0.001$ ). Sfoungaristos et al, [3] reported a statistically significant higher expulsion rate with elevated white cell count. They gave a hypothesis that probably stones that are impacted and immobile in the ureter produce minimal inflammation during renal colic, or at least a less significant reaction than that produced by a stone which is travelling down the ureter.

One hundred and twenty one patients (85.2%) with normal neutrophil percentage passed their stone while 21 (14.8%) did not pass. Eighteen patients (40.9%) with high neutrophil percentage passed stone but 26 (59.1%) did not pass their stone. Relationship of passage of stone with medical expulsion therapy and neutrophil percentage was statistically significant, ( $p$  value  $< 0.001$ ) i.e. patients with distal ureteric calculus and high neutrophil percentage have less chance of spontaneous expulsion of their stone. Park, et al, [7] reported higher stone expulsion rate (94.5%) in normal neutrophil group. Spontaneous passage rates were lower in the higher neutrophil percentage group than in the normal neutrophil percentage group ( $p = 0.011$ ), which correlates with our study. In contrast, Sfoungaristos et al, [3] reported a statistically significant higher stone expulsion rate in patients with high neutrophil percentage. But they also emphasized that prolonged inflammation in the lumen decrease the ureteral compliance and



luminal diameter hindering stone passage. In patients with normal CRP level, 123 (91.8%) patients passed their stone with medical expulsion therapy while 11 (8.2%) did not pass their stone. Sixteen patients (30.8%) with high CRP level passed their stone while 36 (69.2%) did not pass their stone, which was statistically significant, ( $p$  value  $<0.001$ ). Patients of distal ureteric calculus with normal CRP level have high chances of spontaneous expulsion of stone with medical expulsion therapy. Angulo et al, [10] reported that patients of ureteric stone with low CRP level had higher expulsion rate when compared to high CRP level ( $p < 0.001$ ). Park et al, [7] reported that the number of patients whose ureteric stones were naturally passed was 159 (94.1%) out of 169 with serum CRP levels of 0–4.9 mg/dL, 7 (70%) out of 10 with CRP levels of 5.0–9.9 mg/dL, and 4 (50%) out of 8 with CRP levels of 10 mg/dL or higher. The higher the CRP levels, the lower the spontaneous passage rates ( $p < 0.001$ ). Hussein, [6] reported that patients with spontaneous stone expulsion had significantly lower serum CRP level than those who failed to pass the stone. Their study results matches with our results.

### Conclusion

Normal C-reactive protein level and normal neutrophil percentage were significantly associated to spontaneous expulsion of distal ureteric stone of  $\leq 10$  mm with medical expulsive therapy. So, MET can be considered in patients with distal ureteric calculus (10 mm) without hydro-ureteronephrosis or with mild hydrouretero nephrosis with normal CRP levels and neutrophil percentages.

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