Original Article

ASSOCIATION OF RAISED WHITE BLOOD CELL AND NEUTROPHIL COUNTS WITH SPONTANEOUS STONE PASSAGE IN PATIENTS PRESENTING WITH ACUTE RENAL COLIC

Muhammad Seerwan*, Muhammad Muzammil Tahir**, Rana Ata Ur Rehman*
*PGR Urology, Shaikh Zayed Hospital, Lahore.
**Prof of Urology FPGMI/ Shaikh Zayed Hospital Lahore.

ABSTRACT

INTRODUCTION: Ureteric stones are a common urologic problem and presents usually with a severe colicky pain. There are a wide range of options available for the treatment of ureteric calculi ranging from conservative management to minimal invasive options such as ESWL and ureterorenoscopy to more invasive modalities e.g laproscopic ureterolithotomy and open ureterolithotomy.
Selection of patient who are best candidates for conservative management is a difficult decision. There are some known factors such as stone size and location, e.g small stone size and distal ureteric calculi have more chances of the spontaneous. But there are still some factors who are to be investigated. This study is carried out to investigate the association of raised WBCs and neutrophil counts with the spontaneous passage of ureteric calculi.

MATERIALS AND METHODS: 190 patients (95 in each group) with ureteric calculi fulfilling the inclusion criteria were registered through emergency and OPD of sheikh zayed hospital Lahore, Pakistan. They were allotted two groups. The patients with raised WBCs and neutropil counts at presentation were allocated Group A and patients without raised WBCs and neutropil counts were put in Group B. All the patients were managed on NSAIDs in case of pain and followed for 4 weeks for spontaneous passage of ureteric stones. For comparison, chi-square test was applied. P <0.05 was taken as significant.

RESULTS: A total of 190 cases of ureteric stones divided equally into two groups have average stone size of 7.45±1.16 mm (range 5.0-10.0 mm) Spontaneous passage of stone was noted in 147(77.4%) cases while it was not passed in 43(22.6%) cases. Spontaneous passage of stone was noted in 85(57.8%) cases in group A, who have raised WBCs and neutrophil counts, while in 62(42.2%) cases in group B, who are without raised WBCs and neutrophil counts and this difference was statistically significant (p-value=0.000)

CONCLUSION: We conclude that the raised WBCs and neutrophil counts can significantly contribute to the prediction of spontaneous passage of ureteric stones in patients presenting with acute ureteric colic. To maximize their predictive ability they should be combined with other factors such as the stone size and the location.

KEYWORDS: Ureter, stone, urolithiasis, renal colic

INTRODUCTION:

Urinary stone disease is the third most common disease of the urinary tract after urinary tract infection and pathologic conditions of the

Corresponding Author:
Muhammad Muzammil Tahir
Prof of Urology FPGMI/ Shaikh Zayed Hospital, Lahore
Email: dr-muzammil@yahoo.com

Ureteral stones affect approximately 12% of the world's population and comprise about 20% of urolithiasis cases. [3,4]Ureteric stones commonly presents with severe colicky pain.[1] there are multiple treatment options available i.e watchful waiting with or without medical expulsive therapy, ESWL, Ureterorenoscopy and uretherolithotomy. Minimal invasive techniques are safe and effective but still they have known complications and as significant ureteric stones can pass spontaneously their routine use causes unnecessary economic burden and morbidity to the patient.[5] Conversely conservative treatment is simple and cost effective but has several complications e.g recurrent colic UTI with fever and acute renal failure.[3,6]

For advising conservative treatment several factors are considered as potential predictors for spontaneous stone expulsion, however two most important factors for the prediction of spontaneous passage of ureteric stones are stone size and location. Stone size is the most significant parameter[7]. According to latest guidelines, stones sized <5 mm have on average 68% chances to pass spontaneously.[11] Another significant factor is the stone location. Patients with stones placed in the distal ureter have greater chances to be stone-free than the patients with stones in the proximal or mid-ureter.[7]

Even when considering stone size and location, a significant number of patients with favorable characteristics are not stone-free by surveillance. Conversely on the other hand, large stones in the proximal ureter sometimes pass spontaneously and no intervention is needed. By considering this, we can say that there are some other parameters that effect spontaneous stones passage.[7]Some authors have found that there is increased chances of spontaneous passage of ureteric stones with increased White blood cells (WBCs) count. They showed spontaneous passage in 52.9% of patients with stone size ranging from 2.3 to 15 mm.[8] In another study they have found that predictability can be further increased by adding neutrophil counts to white blood cell count. They observed spontaneous stone passage in 65.1% of patients with raised WBCs and neutrophil counts and stone size <10 mm.[7] According to EAU guidelines on urolithiasis 2012 ureteric stones have only 47% chances to pass spontaneously in patients with normal WBCs and neutrophil counts.[11]

Other authors have shown contrary results. They have shown that there are less chances of spontaneous expulsion of ureteral stone in relation to raised C-reactive proteins (CRP) levels and neutrophil counts, rates decreased from 94% to 50% when CRP levels raises from 0-5 to >10. Similarly rate decreases from 94.5% to 83.1% when neutrophil count is increased.[9] In another study author also described that raised CRP levels decreases the chances of spontaneous expulsion of ureteric stones. He described that 54.9% patient out of 235 who passed stone spontaneously has significantly lower CRP levels than who required Ureteroscopy for stone extraction. He described the cut-off level of CRP >21.9 mg/dl.[10]

This study will be carried out to evaluate the association between raised inflammatory markers (increased WBCs and neutrophil counts) and spontaneous passage of ureteric stones in our population as no local data is available on this topic. This will help to avoid unnecessary intervention in patients with ureteric stones who have chances to pass spontaneously.

MATERIALS AND METHODS:

After obtaining Ethics committee approval from PGMI Sheikh Zayed Hospital Lahore, Pakistan, we performed a prospective analysis of 190 consecutive patients presented to the emergency or OPD department from Jan 2015 to June 2015 complaining of acute renal colic due to ureteral calculi.

190 patients fulfilling the inclusion criteria were registered through emergency and OPD of urology, sheikh zayed hospital Lahore. Detailed history including demographic details including age (in years) and sex (male or female) was taken. Informed consent was taken. The patients with raised WBCs and neutropil counts at presentation were allocated Group A and patients without raised WBCs and neutropil counts were put in Group B.

Exclusion criteria was the patients with fever >99°F at the time of presentation, a recently diagnosed infection on history/medical records, antibiotic therapy intake in the last 2 weeks or

an operation in the last 2 months, patients with positive urine culture or with pyuria on urine analysis > 5-6 pus cells per high power view at presentation and the patients with more than one calculus found in the same ureter on X-ray and/or USG and CT-Scan. Similarly if complications developed during follow up period and the insertion of a double-j ureteral stent or a percutaneous nephrostomy became necessary such patients were also excluded from the study.

All the patients were managed on NSAIDs in case of pain and followed for 4 weeks for spontaneous passage of ureteric stones. The patient was labeled for spontaneous passage of ureteric stone (yes or no) by having no stone found on follow up imaging at the completion of follow up.

All the collected data was entered into SPSS version 18 and analysed. The qualitative data like demographics (sex; male or female), spontaneous passage of ureteric stone (yes or no) was presented as frequency and percentages.

Quantitative data like age (in years) was presented as means and standard deviations.

Relative risk was calculated. Data was stratified for age, gender, size of stone and location to deal with effect modifiers. Post stratification chi-square test was applied.

P-value<0.05 was considered significant.

RESULTS:

There were total 190 cases enrolled in this study that have ureteric stone. The mean age of the patients was 42.63±10.41. In our study majority of the cases were male 149(78.4%) and 41(21.6%) were female cases. Spontaneous passage of stone was noted in 147(77.4%) cases while it was not passed in 43(22.6%) cases. Average stone size was 7.45±1.16mm. In our study 31 (17.4%) stones were located at the proximal ureter, 71(37.4%) at the mid ureter and 86(45.3%) at the distal ureter.

Spontaneous passage of stone was noted in 85(57.8%) cases in group A, who have raised WBCs and neutrophil counts, while in 62(42.2%) cases in group B, who are without raised WBCs and neutrophil counts and this difference was statistically significant (p-value=0.000)(Table 1)

When data was stratified for gender it was noted that passage of stone was high in male 114(77.6%) while lower in female 33(23.4%) with a p-value of 0.677 showing insignificant difference. There was insignificant difference with respect to passage of stone in various age groups as p-value was 0.513.

Passage of stone was noted in 28(19.0%) at proximal ureter, 55(37.4%) in mid ureter and 64(43.5%) in the distal ureter and this difference was statistically significant as the p-value was noted as 0.040. (Table 2)

There was passage of stone in 93(63.3%) of size range 5 to 7 mm while in 54(36.7%) with size more than 7 mm and this was statistically significant difference. p-value= 0.000 (Table 3)

Table# 1

Association between WBC and neutrophil counts and Spontaneous Passage of StoneSpontaneous passage of stone * Group of patients Cross tabulation

		Group of		
		Raised WBC's	Normal WBC's	Total
Spontaneous passage of stone	YES	85 57.8%	62 42.2%	147 100.0%
	No	10 23.2%	33 76.8%	43 100.0%
Total		95 50.0%	95 50.0%	190 100.0%

p-value=0.000

Table # 2

Stratification for location of stone
Spontaneous passage of stone * Location of stone Cross tabulation

		Location of stone			
		Proximal ureter	Mid ureter	Distal ureter	Total
Spontaneous passage of stone	Yes	28 19.0%	55 37.4%	64 43.5%	147 100.0%
	No	5 11.6%	16 37.2%	22 51.2%	43 100.0%
Total		33 17.4%	71 37.4%	86 45.3%	190 100.0%

p-value=0.040

Table # 3

Stratification for Stone size
Spontaneous passage of stone * Group of stone size Cross tabulation

		Group of stone size		
		5-7	>7	Total
Spontaneous passage of stone	Yes	93	54	147
		63.3%	36.7%	100.0%
	No	8	35	43
		18.6%	81.4%	100.0%
Total		101	89	190
		53.2%	46.8%	100.0%

p-value= 0.000

DISCUSSION:

Ureteric stones are a common urologic problem and presents usually as a ureteric colic episode. Initial management of a ureteral colic episode is the relief of pain with painkillers. After the relief of pain there is a wide range of options available for the treatment of ureteric calculi ranging from conservative management to minimal invasive options such as ESWL and URS to more invasive modalities e.g laproscopic ureterolithotomy and open ureterolithotomy.

Watchful waiting is a simple and cost effective treatment as most the ureteral stones pass spontaneously.[6,13] However different complications can develop during conservative management and they may include recurrent colic episodes, urinary tract infection leading to urosepsis with permanent loss of renal function.[3,4,13]

On the other hand extracorporeal shock wave lithotripsy (ESWL) and ureterorenoscopy (URS) have high stone free rates ranging from 63%–86% and 57%–92% respectively.[5,12] However these procedures are costly and have known complications.[3,5,6,13]

The proper selection of patients who can be offered active surveillance depends on different factors such as stone size and location with the help of which we can predict that a stone will be able to pass spontaneously or not.[4,5,14] The stone size is very important in predicting spontaneous passage of ureteric stone and is confirmed by several studies which prove that smaller stones have a higher chance to pass spontaneously than the larger ones. It has been shown that stones less than 5 mm have up to 68% chance to pass spontaneously.[5] Some other studies have shown still higher rate of spontaneous clearance of 76–100% for stones smaller than 5 mm while on the other hand only 0–60% of stones can pass spontaneously who are larger than 5 mm.[14,15]In our study average stone size is 7.45±1.16 mm. The spontaneous clearance rate in our control group is 42.2 % which is comparable to other studies.

Location is the second important factor that is related to spontaneous clearance of ureteric calculi. Hubner *et al*[16] showed that the rate of spontaneous passage was 45% for distal ureteric stones as compared to mid uretric and proximal ureteric stones which were 22% and 12% respectively. Some other studies have shown the rate of spontaneous passage of stones of 71%, 46% and 22% for the stones that are located in the distal, mid and proximal ureter, respectively.[17] Apart from the stone size and location, there are some other factors that have been investigated as a predictor for the spontaneous passage of ureteric calculi.

The results of our study are comparable to other studies. The mean age of the patients is 42.63±10.41 years in our study and it is comparable to the study by Sfoungaristos S et al who showed the median age of their patients as 39 years. There are 21.6 % female patients in our study as compared to 53.8 % in the study described above. The stone location in our study was distributed between upper, middle and lower ureter as 17.4, 37.4 and 45.7 % respectively as compared to the above mentioned study in which there was a more proportion of distal ureteric stones i.e 9.6% at UPJ, 10.3% located at the proximal ureter, 14.7% at the mid ureter, 20.5% at the distal ureter and 44.9% at the VUJ. Average stone size in our study is 7.45 mm as compared to 7.1 mm in the compared study. In our study we have found that the increased WBCs and neutrophil counts are statistically significant predictors for the spontaneous passage of ureteric calculi as compared to control group, (P=0.000). The rate of spontaneous passage of

ureteric calculi in our study is 57.8 % as compared to 65.1% shown by Sfoungaristos S et al in their study.[7]

Sfoungaristos S and associates in another study in 2012 showed the rate of spontaneous passage of ureteric stones with raised WBCs counts as 52.7 %.[8]

The WBCs and neutrophil counts are usually increased in acute inflammation. A possible explanation of these findings may be that the increase in WBCs and neutrophil counts show the inflammation that is caused by the interaction of the moving stone with the ureteral mucosa during its passage down the ureter, as it is shown that the inflammation is produced by the interaction between the stone and ureteral mucosa at the site of stone.[18]

On the other hand the stones that are static in the ureter produce very little inflammation during renal colic as compared to the stones which are moving down the ureter. But it still remains a theory, as the pathophysiologic processes at the ureteral level during an acute attack of colic is not extensively studied and explained. Other studies have also advocated some other factors such as submucosal oedema, ureteral peristalsis and ureteral wall spasm at the site of stone affect spontaneous passage of ureteric stone.[19,20] Similarly it is important to consider that severe and prolonged inflammation may decrease the luminal diameter of ureter and the ureteral compliance and will result in hindrance to stone passage.[18] So when considering these inflammatory markers for the prediction of spontaneous passage there should be an upper cut off limit after which potential complications can be produced. If these inflammatory markers are significantly raised, the conservative treatment should be immediately stopped and the alternative standard modality of treatment should be offered.

CONCLUSION:

Summarizing the results of our study we conclude that the raised WBCs and neutrophil counts can significantly contribute to the prediction of spontaneous passage of ureteric stones in patients presenting with acute ureteric colic. These tests are simple, easy and cost effective, and can be performed quickly in the emergency department. To maximize their predictive ability they should be combined with other factors such as the stone size and the location.

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Submitted for publication: 01.01.2016
Accepted for publication: 10.02.2016

O son of Adam, when you see that your Lord, the Glorified, bestows His Favors on you while you disobey Him, you should fear Him (take warning that His Wrath may not turn those very blessings into misfortunes).

Hazrat Ali (Karmulha Wajhay)