

A Study of Relationship between Spontaneous Passage Rates of Ureteral Stones Less than 10 mm and Serum C-Reactive Protein Levels and Neutrophil Percentages

MOHAMED M. YASSIN, M.D.; HANY M. ABDALLA, M.D. and MINA E. AZMY, M.Sc.

The Department of Urology, Faculty of Medicine, Ain Shams University

Abstract

Background: Ureteric stones is relatively a common condition in urological practice to which several treatment options are available for ureteric stones, these include conservative management and medical expulsive therapy, endoscopic removal, extracorporeal shock wave lithotripsy, percutaneous, laparoscopic and open surgical approaches.

Stone size and location in ureter are well-studied predictors for spontaneous passage of ureteric stones, but more predictors are needed to be evaluated to make patients, in which medical expulsive therapy is probably beneficial, more accurately chosen.

Aim of Study: In this study we aim to evaluate serum CRP levels and neutrophil percentage as predictors for spontaneous passage of lower ureteric stones less than 10mm, both are used as indicators of inflammatory changes in ureter that may oppose stone passage.

Patients and Methods: A total of 52 patients who were diagnosed with distal ureteric stones less than 10mm in the duration from October 2021 to March 2022 were tested for CRP level and neutrophil percentage at time of presentation and followed-up for 4weeks for stone passage.

Results: Of the 52 patients, 34 patients (65.38%) passed their stones while 18 patients (34.61%) needed ureteroscopy. The mean of serum CRP was statistically lower in patients who passed their stones (3.91 ± 1.53 SD compared to 8.28 ± 4.89 SD in patients whose stones didn't pass with p -value 0.000), similarly neutrophil percentage was statistically lower in this group (63.89 ± 9.68 compared to 73.22 ± 11.34 with p -value 0.003). However, in multivariate regression analysis CRP levels only show statistically significant with stone size and not neutrophil percentage (p -values were 0.007, 0.004 and 0.25 respectively).

Conclusion: CRP level can be used with stone size and location in ureter as a predictor for spontaneous passage of ureteric stones, but neutrophil percentage may need more studies to evaluate its value.

Key Words: Ureter – Calculi – C-reactive protein – Neutrophil percentage – Prognosis.

Correspondence to: Dr. Mina E. Azmy,
[E-Mail: mina.azmy@gmail.com](mailto:mina.azmy@gmail.com)

Introduction

URETERIC calculi is a very common urologic condition which represent one of the leading causes of urological emergency due to ureteric colic or subsequent urinary obstruction or infection [1]. It's crucial to precisely choose patients who will benefit from conservative management and medical expulsive therapy for ureteric stones and those whose stones aren't likely to pass spontaneously to avoid undue delay of intervention in them. Stone size and location are proven to be a good predictors for SSP, smaller stones and distal are more likely to pass spontaneously [2].

Many other factors were suggested to increase the ability to predict SSP such as degree of hydronephrosis [3] and different inflammatory markers; the latter included WBCs count, serum CRP levels, neutrophil percentage and neutrophil to lymphocytes ratio which are thought to be indicators for degree of ureteral inflammation and edema which make SSP less likely [4-6].

Abbreviations:

SSP : Spontaneous stone passage.
WBCs : White blood cells.
NP : Neutrophil percentage.
CRP : C-reactive protein.
UTI : Urinary tract infection.
CTUT : Computed tomography urinary tract.
CBC : Complete blood count.
KUB : Kidney, ureter and bladder X-ray.
mm : Millimeter.
SD : Standard deviation.
COVID-19 : Corona virus disease of 2019.
NSAID: Non-steroidal anti-inflammatory drugs.
ROC : Receiver operating characteristic.
AUC : Area under curve.
ESWL : Extra-corporeal shock wave lithotripsy.
URS : Ureteroscopy.

The aim of this study:

Is to evaluate the value of CRP and NP as predictors of SSP.

Patients and Methods

This study was a prospective study which included 56 patients who have visited the urology outpatient clinic of Ain Shams University Hospitals and Om-Elmasryen General Hospital, this work was approved by the research ethics committee at the Faculty of Medicine, Ain Shams University FMASU MS 603/2021. The study included 56 patients who were diagnosed in the outpatient clinic with single distal ureteral stone less than 10mm. Pregnant women, patients with severe hydronephrosis, febrile UTI, renal impairment and those with inflammatory diseases including suspected COVID-19 patients all were excluded from the study.

All patients recruited in the study were evaluated primarily with full history taking, general and local examination, pelvi-abdominal ultrasound, CTUT without contrast, CBC with differential and serum CRP level.

The patients were followed-up for 4 weeks only to see if the stones will pass out spontaneously or not, during which 4 patients were lost. For patients whose stones didn't pass, KUB was done for patients with radiodense stones and CTUT for those with radiolucent stones after 4 weeks to diagnose if the stones have passed or not. The only treatment all patients received during the follow-up time was once daily α -blockers capsule and NSAIDs on demand.

After finishing the study patients were classified into 2 groups:

Group A: Patients in whom the stones passed spontaneously within 4 weeks and Group B: Patients in whom the stones did not pass spontaneously within 4 weeks and they needed intervention, this is shown in Fig. (1).

Patient characteristics were investigated by the use of Independent *t*-test, and Chi-square test. The association between CRP levels and Neutrophil percentage and the ureteral stone removal rates was investigated. Multivariate logistic regression analysis was conducted.

Results

From the 56 patients 4 were excluded from the study because they were lost during follow-up,

thus 52 patients with ureteral stones fulfilling the inclusion criteria and completed the study protocol were included in our study. All patients ranged from 24 to 65 years old with mean age \pm SD 42.56 ± 13.51 . Twenty-nine patients were males (55.8%) and twenty-three were females (44.2%). Side location was distributed as sixty-seven with left ureteral stones (67.3%) and thirty-two patients with right ones (32.69%). Calculi size ranged between 4-8mm, and their mean size \pm SD was $5.86 \text{mm} \pm 1.53$. The range of neutrophil percentage was 51-88% with mean \pm SD $67.11\% \pm 11.12$. CRP range was from 1.9-21mg/dl with mean \pm SD 5.42 ± 3.73 . Spontaneous passage of stone occurred in thirty-four patients (65.4%) and failure of spontaneous stone passage was in eighteen patients (34.6%).

Univariate analysis is shown in (Table 1); stone size, serum CRP level and neutrophil percentage all found to be statistically significant ($p=0.005$, 0.000 and 0.003 respectively).

Whoever, in multivariate regression analysis (Table 2) stone size and serum CRP only showed to be independent predictors for SSP ($p=0.004$ and 0.007 respectively), while NP didn't show such significance as shown in (Table 2).

Receiver operator characteristic curve was used to determine CRP and stone size cut-off point for prediction of spontaneous ureteric stone expulsion. According to ROC curve, the area under the curve (AUC) for CRP was 74%. Using ROC, a cut-off point of 4mg/L for CRP achieves sensitivity of 83% and specificity of 65% (Fig. 2). Similarly, the area under the curve (AUC) for stone size was 72%. Using ROC, a cut-off point of 5mm for stone size achieves sensitivity of 49 % and specificity of 76%.

Table (1): Relation between stone size, NP and serum CRP level and SSP.

	Spontaneous passage No.=34	Failure of spontaneous passage No.=18	<i>p</i> -value	Sig.
<i>Stone size:</i>				
Mean \pm SD	5.44 \pm 1.39	6.67 \pm 1.49	0.005•	HS
<i>Neutrophil %:</i>				
Mean \pm SD	63.89 \pm 9.68	73.22 \pm 11.34	0.003•	HS
<i>CRP mg/dl:</i>				
Mean \pm SD	3.91 \pm 1.53	8.28 \pm 4.89	0.000	HS

•: Independent *t*-test.

Table (2): Multivariate logistic regression analysis for predictors of spontaneous passage.

	Standard Error	t Stat	p-value	Lower 95%	Upper 95%
Size	0.036155	-2.95643	0.004855	-0.17963	-0.03416
Age	0.004068	-0.33442	0.739551	-0.00954	0.006823
Neutrophil%	0.006236	-1.16435	0.250157	-0.0198	0.005284
CRP	0.018887	-2.82023	0.007006	-0.09126	-0.01527

HS: Highly significant. NS: Non-significant. S: Significant.

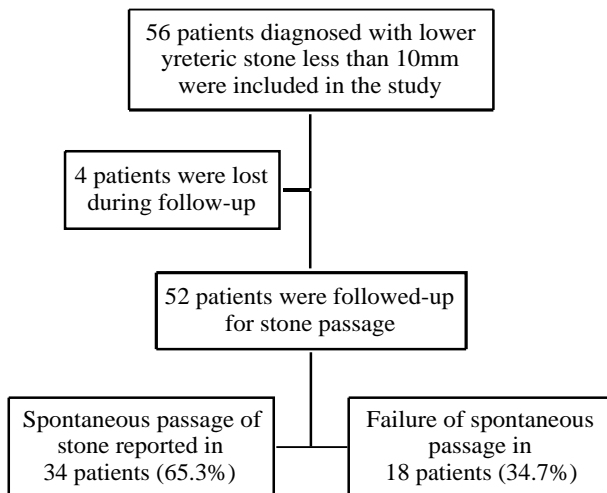


Fig. (1): Consort flow chart of the study.

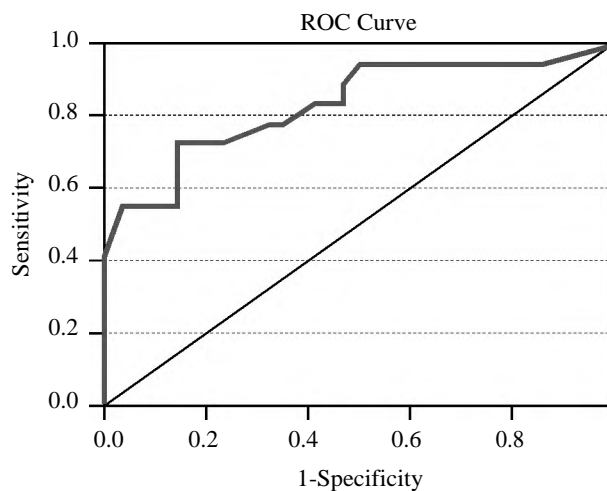


Fig. (2): ROC curve for CRP as a predictor of SP of ureteric stones.

Discussion

Ureteric colic is a common complaint for people diagnosed in the emergency room or the urology outpatient clinics having a ureteric stone. After management of the episode of ureteric colic there are many ways for treating ureteric stones varying from watchful waiting, minimal invasive, to open or laparoscopic management [7].

ESWL and URS have high success rates in the treatment of ureteral stones, but they aren't free of complication and may not be afforded by some patients. On the other hand, active surveillance may be cheaper and has no operation stress, but it may be accompanied with UTI, episodes of renal colic, deterioration in kidney function. Also, spontaneous stone passage may not be reached and the intervention after this waiting may increase the risk of complications due to stone impaction and the subsequent local inflammation of the ureter [4].

Some physicians may face a difficulty in taking a decision whether this patient needs immediate intervention or active surveillance and watchful waiting. Therefore, predicting the probability of spontaneous stone passage will be so helpful.

In this study, we evaluated serum CRP levels and neutrophil percentage as a predictor for the spontaneous passage of ureteral stones.

Stone size and stone location are the most widely studied factors by the researchers. Several studies reported that stone size is very important in prediction of spontaneous stone passage proving that the smaller the stones the higher the probability to pass spontaneously.

Ahmed, Abul-fotouh, et al., Medina, J. Sáenz, et al., and Buldu, Ibrahim, et al., all confirmed the role of stone size as a predictor for stone passage with results show that a percentage ranging from 68% to up to 100%, in some studies, of ureteral stones less than 5mm can pass spontaneously [3,8,9].

In our study stone size was statistically significant ($p=0.004$) with a sensitivity 94% and specificity 76% of passing spontaneously with a cut off value ≤ 5 mm.

Angulu et al., suggested serum CRP level of 2.8mg/dl as the cutoff point above which interventional treatment must be initiated for patients presented with ureteral colic on top of ureteral stone [10]. Park et al, stated that when CRP levels range from 0-4.9mg/dl, spontaneous passage rates of the stone were high, which suggests that conservative management may be preferred when CRP levels are low [7].

In our study when serum CRP increases spontaneous stone passage decreases and vice versa ($p=0.007$). When the CRP level is <4 mg/dl the probability of stone passage increased with sensitivity 83% and specificity 65%.

It's worth to be mentioned that McSorley et al., suggested that CRP is more useful as a tool to monitor the progress of those admitted with acute ureteral colic helping in making a decision at what point and for whom surgical intervention is considered; In this study 50 patients presented with ureteral colic were evaluated by series of serum CRP level which were taken at first presentation and during admission in the urology department. The results of the study showed that there is no significant difference in CRP levels at the first presentation between those who were managed conservatively and those who needed intervention. While they have found a statistical and clinical significant difference in the highest recorded CRP during admission between the intervention and conservative groups [11].

Considering neutrophil percentage, park et al., studied 187 patients prospectively with ureteral stone < 8mm and concluded that as the neutrophil percentage increases the probability of spontaneous passage decreases and immediate intervention should be considered. They have divided the patients into 2 groups according to the neutrophil percentage. Group (A) patients with normal neutrophil percentage and found that the percentage of patients with spontaneous stone passage were 94.5%, Group (B) patients with high (>74%) have passed the stones spontaneously [7]. While Puntub et al, did not give the same conclusions and the NP did not seem to be a significant factor in the multivariate analysis [12].

In our study, although being associated with lower rates of stone expulsion in univariate analysis, higher neutrophil percentages wasn't statistically significant factor in predicting spontaneous stone passage in the multivariate logistic regression analysis.

Conclusion:

Serum CRP can be used as a predictive factor for spontaneous passage of ureteric stones together with stone size and location.

References

- 1- DELLABELLA M., MILANESE G. and MUZZONIGRO G.: Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *The Journal of Urology*, 170 (6): 2202-5, 2003.
- 2- JENDEBERG J., GEIJER H., ALSHAMARI M., CIERZNIAK B. and LIDÉN M.: Size matters: The width and location of a ureteral stone accurately predict the chance of spontaneous passage. *European Radiology*, 27 (11): 4775-85, 2017.
- 3- AHMED A-F., GABR A.H., EMARA A-A., ALI M., ABDEL-AZIZ A-S. and ALSHAHRANI S.: Factors predicting the spontaneous passage of a ureteric calculus of > 10mm. *Arab Journal of Urology*, 13 (2): 84-90, 2015.
- 4- SFOUNGARISTOS S., KAVOURAS A., KATAFIGI-OTIS I. and PERIMENIS P.: Role of white blood cell and neutrophil counts in predicting spontaneous stone passage in patients with renal colic. *BJU International*, 110 (8b): E339-E45, 2012.
- 5- LEE K.S., HA J.S. and KOO K.C.: Significance of neutrophil-to-lymphocyte ratio as a novel indicator of spontaneous ureter stone passage. *Yonsei Medical Journal*, 58 (5): 988-93, 2017.
- 6- ÖZCAN C., AYDOĞDU O., SENOCAK C., DAMAR E., ERASLAN A., OZTUNA D., et al.: Predictive factors for spontaneous stone passage and the potential role of serum C-reactive protein in patients with 4 to 10mm distal ureteral stones: A prospective clinical study. *The Journal of Urology*, 194 (4):1009-13, 2015.
- 7- PARK C.H., HA J.Y., PARK C.H., KIM C.I., KIM K.S. and KIM B.H.: Relationship between spontaneous passage rates of ureteral stones less than 8 mm and serum C-reactive protein levels and neutrophil percentages. *Korean Journal of Urology*, 54 (9): 615-8, 2013.
- 8- MEDINA J.S., PARRA R.A., GONZÁLEZ E.R., GONZÁLEZ L.L., MARTÍNEZ L.C., MONTARROSO LF, et al.: Prognostic factors of spontaneous expulsion in ureteral lithiasis. *Actas Urológicas Españolas (English Edition)*, 34 (10): 882-7, 2010.
- 9- COLL D.M., VARANELLI M.J. and SMITH R.C.: Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. *American Journal of Roentgenology*, 178 (1): 101-3, 2002.
- 10- ANGULO J.C., GASPAR M.J., RODRÍGUEZ N., GARCÍA-TELLO A., TORRES G. and NÚÑEZ C.: The value of C-reactive protein determination in patients with renal colic to decide urgent urinary diversion. *Urology*, 76 (2): 301-6, 2010.
- 11- MCSORLEY S., DRURY M., MAJUMDAR P., HALLSALL A. and NALAGATLA S.: C-reactive protein to predict the need for surgical intervention in acute renal colic. *Journal of Clinical Urology*, 7 (6): 380-3, 2014.
- 12- PUNTUB A. and LERDPRAIWAN W.: Relationship between the spontaneous passage rates of ureteral stones less than 10mm and serum C-reactive protein levels, white blood cell count and neutrophil percentages. *The Insight Urology*, 39 (2): 42-9, 2018.

دراسة عن العلاقة بين المرور التلقائي لحصوات الحالب الأقل من ١٠ مم ومستويات بروتين C التفاعلي والنسبة المئوية للخلايا المتعادلة

تعد حصوات الحالب نسبياً مشكلة شائعة يعاني منها ٨٪ من السكان، وتتراوح نسبة انتشارها بين ٣٪ إلى ٥٪.

هناك طرق عدة لعلاج حصوات الحالب، من بينها العلاج التحفظي، استخراج الحصوات عن طريق مناظير الحالب، تفتيت الحصوات بالموجات التصادمية، استخراج الحصوات عن طريق المنظار عبر الجلد، استخراج الحصوات عن طريق مناظير البطن والفتح الجراحي لاستخراج الحصوات.

أثناء اختيار طريقة العلاج المناسبة التي تحقق نجاحاً في العلاج يجب أخذ عدة عوامل في الاعتبار من بينها خصائص وصفات الحصوة، المضاعفات المتوقعة من العلاج، تفضيل المريض لأحد وسائل العلاج ومدة العلاج. من الهام تقييم كل حالة على حدى بعناية لتعظيم الفائدة وتقليل المخاطر والمضاعفات الناتجة عن الحصوات أو العلاج.

فيما يخص العلاج التحفظي باستخدام العلاج الدوائي الطارد الذي يهدف للمرور التلقائي لحصوات الحالب، تم دراسة عدة عوامل للتنبؤ بفاعلية هذا الأسلوب العلاجي. عدة عوامل تم اقرارها كمتنبئات جيدة للمرور التلقائي لحصوات الحالب باستخدام العلاج الدوائي ولكن حجم الحصوة ومكانها هما العاملان اللذين يتم أخذهما في الاعتبار في الممارسة الإكلينيكية. لذلك، هناك احتياج لتحديد أدق وتنبؤ بشكل أفضل لتقسيم المرضى إلى هؤلاء الذين من المتوقع أن يجنوا فائدة من العلاج الدوائي، وأولئك اللذين من المتوقع أن يوفر لهم التدخل وقتاً ومالاً.

كلا من مستويات بروتين C التفاعلي والنسبة المئوية للخلايا المتعادلة يستخدم كدليل للاستجابة الالتهابية للجسم ومستوياتهم تتناسب مع العلامات الإكلينيكية للإلتهاب. حصوات الحالب التي تسبب انسداد بالحالب تسبب التهاباً بالطبقة تحت المخاطية بالجزء الأدنى بالحالب، وهذا بدوره يجعل من الصعوبة بمكان مرور الحصوة بشكل تلقائي.

في هذه الدراسة تم تقييم مستويات بروتين C التفاعلي والنسبة المئوية للخلايا المتعادلة على احتمالية المرور التلقائي لحصوات بأسفل الحالب، تدعم نتائج هذه الدراسة أهمية مستوى بروتين C التفاعلي في التنبؤ بمرور الحصوات موضع الدراسة التلقائي بقيمة فاصلة ≥ 4 ملجم /ديسيليتز بحيث أن المرضى نوى مستويات بروتين C التفاعلي التي تتخطى ذلك يكون من الأنسب التدخل الفوري لتحقيق نتائج أفضل من المراقبة اليقظة. في حين لم تظهر نتائج دراسة مستويات الخلايا المتعددة تأثيراً مماثلاً على مرور الحصوات التلقائي.