

ORIGINAL ARTICLE

The predictive value of serum C-reactive protein for spontaneous stone passage in patients with distal ureteric stones – an analytical cross sectional study.

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ABSTRACT... Objective: To determine and compare the frequency of spontaneous stone passage within 4 weeks in patients with 4-8 mm distal ureteric stones with normal baseline serum CRP ≤ 6 mg/L and raised baseline serum CRP >6 mg/L. **Study Design:** Analytical Cross-sectional. **Setting:** Department of Urology and Renal Transplantation, Faisalabad Medical University, Allied Hospital-I, Faisalabad Pakistan. **Period:** November 2025 to April 2026. **Methods:** 110 individuals between the ages of 18 and 50 who had a single distal ureteric stone measuring 4 to 8 mm participated in the analytical cross-sectional study. Consecutive non-probability sampling was the method employed. Based on baseline serum CRP values, two patient groups were created: those with CRP ≤ 6 mg/L and those with CRP >6 mg/L at presentation. Standardised medical expulsive therapy, which includes tamsulosin 0.4 mg once daily, diclofenac as needed, and sufficient water intake, was prescribed to each patient. Together with a KUB X-ray and ultrasound KUB verified SSP at the four-week follow-up assessment. The frequencies of SSP and non-SSP were compared between the two groups using the chi-square test and the ideal CRP cut-off value was determined using receiver operating characteristic (ROC) curve analysis. **Results:** The average stone size was 6.06 ± 1.26 mm, and the average patient age was 35.27 ± 8.66 years. In all, 81 patients (73.6%) experienced spontaneous stone expulsion. Patients with a CRP level of ≤ 6 mg/L had a significantly greater SSP than those with a level of >6 mg/L (95.4% vs. 42.2%, $p < 0.001$). The ROC analysis's area under the curve (AUC) of 0.945 (95% CI: 0.904-0.986, $p < 0.001$) demonstrated a high degree of prediction for the serum level of CRP. The ideal cut-off value for CRP levels for SSP prediction was determined to be ≤ 9.53 mg/L, with an 87.7% sensitivity and an 86.2% specificity. **Conclusion:** In individuals with 4–8 mm distal ureteric stones, the serum CRP level is a significant predictor of spontaneous stone passage. Lower CRP levels result in a much higher spontaneous passing rate. When incorporated into routine clinical examination, serum CRP levels may be helpful for improving patient stratification and assisting in the choice between conservative and interventional treatment choices.

Key words: C-Reactive Protein, Distal Ureter, Medical Expulsive Therapy, Spontaneous Stone Passage, Urolithiasis, Ureteral Calculi.

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INTRODUCTION

The prevalence of urolithiasis is high in the world, at 3-5%, and in all cases of urolithiasis, 20% are due to stones in the ureters.¹ The most frequent site of occurrence of the ureteric stones is the distal part of the ureter (68 % of all the ureteric stones).² It is important to begin management as early as possible as ureteric stones can be very painful, and may cause renal function to deteriorate as well. Treatment involves a wait and watch approach, medical expulsion therapy, intra-corporeal lithotripsy using a ureteroscope, extracorporeal shockwave

lithotripsy and open or laparoscopic surgery.³

For individuals with distal ureteric stones smaller than 10 mm that are both clinically stable and symptomatically controlled, alpha blockers are advised.⁴ The size and site of the stones are excellent indicators of spontaneous stone passage (SSP). Other predictors of spontaneous ureteric stone expulsion have also been proposed, including the degree of hydronephrosis and inflammatory markers such WBC count, serum C-Reactive protein level, neutrophil percentage, and neutrophil-

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to-lymphocyte ratio.⁵

C-reactive protein was discovered in 1930 by Tillett and Francis.⁶ Smooth muscles, macrophages, endothelial cells, and lymphocytes all synthesize CRP, which is raised in inflammatory circumstances and is most concentrated in the serum as in ureteric stone patients as well.⁷

While a number of factors influence spontaneous stone passage, serum CRP's prognostic value is debatable. The current scientific investigation is warranted due to a recent prospective study that found SSP rate of 76% of distal ureteric stones (5–10 mm) with a CRP level of less than 6 mg/L.⁸ Nevertheless, no significant connection between CRP and SSP was found by multivariate analysis in the other recent prospective scientific paper.⁹ The current study is warranted to determine whether serum CRP can accurately predict spontaneous passage in 4–8 mm distal ureteric stones, thereby guiding the decision between conservative management and early intervention at the very first presentation of such patients, given the uncertainty surrounding CRP as a biomarker.

METHODS

The objective of this analytical cross-sectional study was “to determine and compare the frequency of spontaneous stone passage within 4 weeks in patients with 4-8 mm distal ureteric stones with normal baseline serum CRP ≤ 6 mg/L and raised baseline serum CRP > 6 mg/L.” The sample size was determined using the WHO sample size calculator.⁸ This study was conducted at the Department of Urology and Renal Transplantation, Faisalabad Medical University from November, 2025 to April, 2026.

This study used non-probability consecutive sampling as its sampling method. Patients between the ages of 18 and 50 who had a single distal ureteric stone measuring 4 to 8 mm were included in this study. Patients with a history of open or endoscopic ureteral surgery, liver failure, chronic inflammatory illnesses, active cancer, infectious diseases, acute and chronic renal failure, and pregnancy were not included in the study.

Ethical approval (ERC Certificate No. 48.ERC/

FMU/2024-25-24 dated 13-02-2025) was obtained and after approval, 110 patients were recruited in Urology outpatient department of Allied Hospital-I, Faisalabad. All patients enrolled in this study were examined by relevant history and physical examination with verbal and written informed consent from each patient. On 1st presentation, laboratory tests such as renal function tests and serum C reactive protein (CRP) level by particle enhanced immunoturbidimetric assay (PETIA) were done along with imaging tests to confirm a distal ureteric stone i.e., abdominal-pelvic ultrasound and Digital X-ray KUB.

Patients were split into two groups: those whose baseline blood CRP levels were elevated (> 6 mg/L) and those whose baseline serum CRP levels were normal (≤ 6 mg/L). Every patient received 2.5 litres of water each day, a non-steroidal anti-inflammatory medicine (NSAID) (diclofenac 50 mg), and an alpha-blocker (tamsulosin 0.4 mg) every night. Follow up was suggested at 28 days with USG KUB and digital X-ray KUB to check for the expulsion of stone. In each group, the number of patients who passed stone spontaneously after 28 days follow up were recorded. The study proforma included information on all the variables, including age, sex, stone size and location, and blood C-Reactive protein level. The predictive significance of baseline serum C-reactive protein for spontaneous stone passing within four weeks was assessed for stones in the distal ureter (4–8 mm) in both groups.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp. Armonk, NY, USA) was used to analyze the data. The mean and standard deviation were used to express the quantitative variables, including age, stone size, and serum CRP level. Frequencies and percentages were used to report categorical characteristics, such as gender and SSP. In patients with 4–8 mm distal ureteric stones, the probability of spontaneous stone passage within 4 weeks was compared using the Chi-Square test between patients with normal baseline serum CRP (≤ 6 mg/L) and elevated baseline serum CRP (> 6 mg/L). Chi-square analysis was used to adjust effect modifiers (stone size and age) following stratification. Receiver operating characteristic (ROC) curve analysis was

used to determine the best cut-off value for SSP prediction and the diagnostic precision of serum CRP. If a P-value was less than 0.05, it was deemed significant.

RESULTS

This study included 110 individuals with a single 4-8 mm distal ureteric stone. The mean age in years was 35.27 ± 8.66, including males 68.2% (75) and females 31.8% (35). The mean stone size was reported to be 6.06 ± 1.26 with a mean serum CRP of 8.65 ± 6.99 (Range 1.57-38.4 mg/L). After four weeks of conservative management, 81 patients (73.6%) reported SSP, while 29 patients (26.4%) reported Non-SSP.

Baseline characteristics are shown in Table-I. All patients with baseline serum CRP ≤ 6 mg/L had significantly greater rates of spontaneous stone passage (62/65, 95.4%) than those with baseline serum CRP > 6 mg/L (19/45, 42.2% with p < 0.001, Chi-square test), Table-II.

TABLE-I

Baseline demographic and clinical characteristics (N=110)

Characteristics	Value
Mean Age (Years) ± SD	35.27 ± 8.66
Male, n (%)	75 (68.2%)
Female, n (%)	35 (31.8%)
Mean Stone Size (mm) ± SD	6.06 ± 1.26
Stone Size 4-5 mm, n (%)	39 (35.5%)
Stone Size 6-8 mm, n (%)	71 (64.5%)
Mean Serum CRP (mg/L) ± SD	8.65 ± 6.99
CRP ≤ 6mg/L, n (%)	65 (59.1%)
CRP > 6mg/L, n (%)	45 (40.9%)
Spontaneous Stone Passage, n (%)	81(73.6%)
Non-Spontaneous Stone Passage, n (%)	29 (26.4%)
Right Sided Ureteric Stone, n (%)	60 (54.5%)
Left Sided Ureteric Stone, n (%)	50 (45.5%)

TABLE-II

Spontaneous stone passage by CRP category

CRP Category	Total Patients	SSP, n (%)	Non SSP, n (%)	P-Value
≤ 6 mg/L	65	62 (95.4)	3 (4.6)	< 0.001
> 6 mg/L	45	19 (42.2)	26 (57.8)	
Total	110	81 (73.6)	29 (26.4)	

Using ROC curve analysis, the predictive accuracy of baseline serum CRP for SSP was evaluated. With an area under the curve (AUC) of 0.945 (95% CI: 0.904–0.986, p < 0.001), the serum CRP appears to have a high diagnostic value for predicting stone passage. With 87.7% sensitivity and 86.2% specificity, the optimal cut-off point for CRP to predict spontaneous passing was ≤ 9.53 mg/L, according to Youden’s index. At this cut-off, the positive predictive value (PPV) was 94.7% and the negative predictive value (NPV) was 71.4% (Table-III, Figure-1)

FIGURE-1

ROC curve of serum CRP for predicting spontaneous stone passage (AUC = 0.945, 95% CI: 0.904-0.986, p < 0.001).

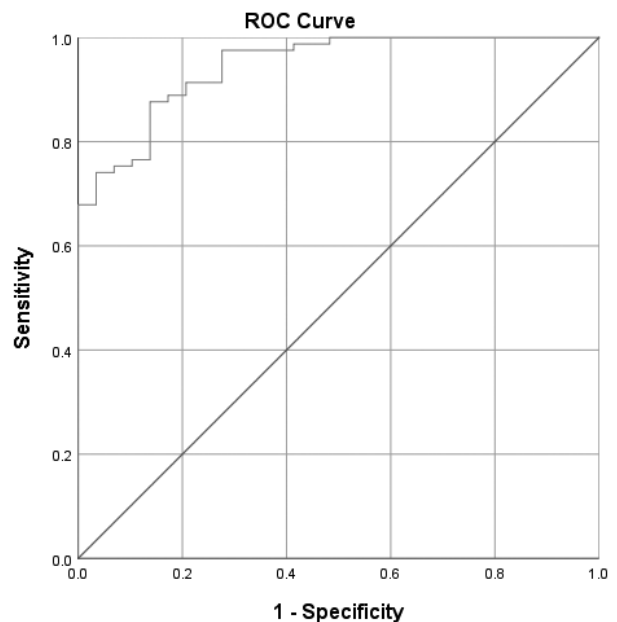


TABLE-III

ROC curve analysis of serum CRP for predicting spontaneous stone passage

Parameter	Value
AUC (95% CI)	0.945 (0.904 - 0.986)
P-value	< 0.001
Optimal CRP cut-off (Youden's index)	≤ 9.53 mg/L
Sensitivity	87.7%
Specificity	86.2%
Positive Predictive Value	94.7%
Negative Predictive Value	71.4%

For potential effect modifiers like age and stone size, subgroup analyses were carried out. Serum CRP continued to be a statistically significant predictor of spontaneous stone passage across all categories ($p < 0.05$ for all), according to the post-stratification Chi-square test (TABLE-IV).

TABLE-IV

Subgroup analysis of spontaneous stone passage by serum CRP category

Subgroup	CRP \leq 6 mg/L (SSP%)	CRP $>$ 6 mg/L (SSP%)	P-Value*
Age			
< 34 years	25/26 (96.2)	9/22 (40.9)	< 0.001
\geq 34 years	37/39 (94.9)	10/23 (43.5)	< 0.001
Stone size			
4-5 mm	30/30 (100)	6/9 (66.7%)	0.001
6-8 mm	32/35 (91.4)	13/36 (36.1)	< 0.001

*Post-stratification Chi-square test

Fisher's Exact Test was used for the stone size 4-5 mm subgroup due to the expected cell count $<$ 5.

DISCUSSION

Medical expulsion therapy (MET) remains a crucial component of treatment for distal ureteric stones of appropriate size ($<$ 10mm), which are a major cause of acute urological hospitalization.¹⁰ According to the American Urological Association, up to 98% of stones in the distal portion of the ureter that are 5 mm or less spontaneously expel.¹¹ For ureteric stones measuring 5-7 mm, 7-9 mm, and $>$ 9 mm, respectively, Coll et al. found spontaneous stone passage (SSP) rates of 60%, 48%, and 25%.¹²

Edema develops both at and distal to the level of stone impaction due to inflammation leading to spasm and ureteric swelling that obstructs the stone expulsion. However, if stone left in position for an extended period, fibrosis can develop as a result of the prolonged mechanical pressure and loss of circulation to the area.¹³ It is left as a clinical conundrum in this context, who might benefit most from MET and who may not. Thus, different inflammatory and biochemical markers including serum CRP levels have been employed for predicting SSP and Non-SSP of distal ureteric stones.¹⁴

This study sought to ascertain and compare the incidence of SSP within 4 weeks in patients with

distal ureter stones measuring 4–8 mm and baseline blood CRP levels that were either normal (\leq 6 mg/L) or increased ($>$ 6 mg/L). The overall SSP rate in the current trial was 73.6% (81/110 patients) after four weeks of medical expulsion therapy. Similar to our results, a previous prospective research by Ahmad et al. found an SSP rate of 76% in 5–10 mm distal ureteric stones treated with MET.⁸ Ramasamy et al. reported that 78% of patients with distal ureteric stones who had conservative treatment had SSP.¹⁵

The second aspect of our study that revealed a significant negative correlation was the link between serum CRP and SSP. The SSP ratio was 95.4% (62/65) for patients with CRP \leq 6 mg/L and 42.2% (19/45) for those with CRP $>$ 6 mg/L ($p <$ 0.001). Ahmad et al.'s prospective study, however, found a significant correlation between CRP levels and stone passage (\leq 6 mg/L, 76% vs. 11%, $p <$ 0.001). On the other hand, higher CRP ($>$ 6 mg/L) was present in 89% of the non-spontaneous passage group, indicating a substantial inverse connection between CRP levels and stone passage.⁸ Our research and that of these authors showed an inverse relationship between serum CRP and SSP.

One of the study's findings is that a cut-off level of less than or equal to 9.53 mg/L was shown to be optimal for the CRP for prediction of SSP, with sensitivity of 87.7% and specificity of 86.2%. This cut-off level's PPV and NPV were 94.7% and 71.4%, respectively. Aldaqadossi (2013) discovered that the CRP threshold is 21.9 mg/L, indicating that individuals with CRP $>$ 21.9 mg/L do not have high SSP and should have minimally invasive surgery planned earlier.¹⁶ However, Özcan et al. established a cut-off value for serum CRP of 5.06 mg/L using ROC analysis.¹⁴

The size of the stone can already be used to forecast spontaneous stone expulsion. 4-5 mm stones in the low CRP group (\leq 6 mg/L) showed 100% SSP. The percentage of SSP in 6-8 mm distal ureteric stones was 91.4% in the low CRP group and 36.1% in the high CRP group. In this regard, a prospective cohort examination of 251 patients with distal ureteric stones (4–10 mm) by Özcan et al. found that stone size and serum C-reactive protein were independent predictors of spontaneous stone

passage. They reported that the mean stone size differed significantly between the non-SSP group (6.15 ± 1.77 mm, $p < 0.001$) and the spontaneous passage group (5.0 ± 1.38 mm). Serum CRP levels also differed significantly (3.4 mg/L in the SSP group, 9.2 mg/L in the Non-SSP group, $p < 0.001$).¹⁴ The results confirm our observation of the incremental predictive value of CRP beyond stone size especially in borderline stones (stone size 4-8 mm).

Contrary to several other studies that suggested this would be a potential predictor, Jendeborg et al. discovered that C-reactive protein (CRP) was not an independent factor for predicting spontaneous expulsion of ureteral stone. Their final predictive model did not include CRP because it was not statistically significant for either short-term (OR 1.0, 95% CI 0.98-1.1; $p = 0.21$) or long-term (OR 0.99, 95% CI 0.99-1.0; $p = 0.27$) outcomes. Stone size and location continued to be the most significant determinants of spontaneous passage. We discovered that CRP was a major predictor of SSP, but in this study it was not.¹⁷

CONCLUSION

With an AUC of 0.945, serum C-reactive protein (CRP) appears to be a very significant and clinically excellent predictive marker. A helpful indicator of spontaneous stone passage in patients undergoing medical expulsion therapy, who have distal ureteric stones that are 4–8 mm in size. There was a strong correlation between lower CRP and higher stone expulsion rates, and elevated CRP was seen consistently with lower stone expulsion rates. A CRP threshold of ≤ 9.53 mg/L had a high diagnostic accuracy and could be used as a practical ancillary tool to stone size for guiding management decisions. The use of CRP in routine assessment can aid in patient stratification, help to select the right conservative treatment approach and help to avoid unnecessary surgery for the right patients.

LIMITATIONS

Generalizability is impossible because this was a single-center study with a short follow-up period. Larger multicenter investigations are required to validate the findings.

RECOMMENDATIONS

Serum CRP may be used as an adjunct to risk-stratify 4–8 mm distal ureteric stones and guide decisions regarding conservative versus early intervention.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	Muhammad Irfan Munir: Data acquisition.
3	Ghulam Abbas: Data analysis.
4	Muhammad Tahir Bashir Malik: Proof reading.
5	Moin Anwar: Data analysis.
6	Aamir Imtiaz Khan: Critical revisions.