ORIGINAL RESEARCH

Assessment of Radiological and Inflammatory Markers as Predictors of Spontaneous Transit of Mid and Lower Ureteric Stones: A Prospective Observational Study

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ABSTRACT

Background: Ureteric stones, a common condition affecting individuals across the world, often lead to significant morbidity due to symptoms such as severe pain, hematuria, and urinary tract infections. The aim of this study was to evaluate the role of radiological and inflammatory markers in predicting the spontaneous passage of mid and lower ureteric stones.

Material and Methods: This prospective observational study was conducted at a tertiary care hospital with 110 patients diagnosed with unilateral mid or lower ureteric stones. The inclusion criteria comprised adults aged 18-65 years, with a single radio-opaque ureteric stone, confirmed by non-contrast computed tomography (NCCT) or ultrasonography (USG). The primary outcome was spontaneous stone passage within 4-6 weeks, confirmed by follow-up NCCT or USG. Secondary outcomes included the association of inflammatory markers (CRP, ESR, WBC count) and radiological factors with spontaneous passage.

Results: Among the 110 patients, 72.73% experienced spontaneous stone passage, while 27.27% required surgical intervention. The majority of stones were <5 mm in size (54.55%). Elevated CRP, ESR, and WBC count were observed in a significant proportion of patients. A strong correlation was found between stone size, hydronephrosis, and the spontaneous passage of stones. Follow-up revealed a progressive increase in stone expulsion rates from 60% at 2 weeks to 85% at 6 weeks.

Conclusion: This study demonstrates that smaller stone size, absence of hydronephrosis, and elevated inflammatory markers like CRP, ESR, and WBC count significantly predict the spontaneous passage of mid and lower ureteric stones. These findings assist clinicians in predicting stone expulsion and determining the need for surgical intervention.

Keywords: Ureteric stones, Spontaneous passage, CRP, Hydronephrosis, Inflammatory markers

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INTRODUCTION

Ureteric stones, a common condition affecting individuals across the world, often lead to significant morbidity due to symptoms such as severe pain, hematuria, and urinary tract infections. The kidneys produce urine, which flows through the ureters and into the bladder. When stones, made of minerals such as calcium oxalate, form in the kidneys, they can travel into the ureters, causing obstruction. These obstructions can result in acute pain, a condition

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known as renal colic, and lead to complications such as hydronephrosis, infection, and permanent kidney damage if left untreated. While some stones pass spontaneously through the urinary tract, others may require medical or surgical intervention. The spontaneous passage of ureteric stones is an unpredictable process, and it is crucial to identify patients who are likely to experience spontaneous transit to prevent unnecessary interventions.[1]A growing body of research has focused on the prediction of spontaneous stone passage, particularly for mid and lower ureteric stones. Ureteric stones are classified based on their location in the ureter: proximal (upper), mid, and distal (lower). Mid and lower ureteric stones, in particular, present a unique challenge. These stones are typically smaller in size and located closer to the bladder, which might improve their chances of spontaneous passage. However, various factors, including the stone's size, composition, the degree of obstruction, and associated inflammatory or radiological markers, can influence the likelihood of spontaneous passage. Recent studies suggest that radiological imaging and inflammatory biomarkers can provide valuable insights into predicting whether a stone will pass without surgical intervention. These markers, in combination with clinical assessment, may aid in forming treatment strategies for affected patients, potentially reducing the need for invasive procedures.[2]Radiological imaging plays a critical role in diagnosing and monitoring the progression of ureteric stones. Traditional imaging techniques, such as X-ray, ultrasound, and computed tomography (CT) scans, are commonly used to determine the size, location, and characteristics of the stones. Among these, CT imaging is often considered the gold standard due to its high sensitivity and accuracy in detecting stones, particularly small ones, and in assessing the degree of obstruction. A study of radiological findings can provide valuable insights into the condition of the ureter and its ability to accommodate the stone. For instance, the degree of obstruction, as indicated by the size of the stone and the dilation of the renal pelvis or the ureter, can predict the likelihood of spontaneous passage. Smaller stones and those causing minimal obstruction are more likely to pass spontaneously, whereas larger stones with severe obstruction are less likely to do so.[3]Alongside radiological markers, the role of inflammatory biomarkers has gained attention in the prediction of spontaneous stone passage. Ureteric stones can cause an inflammatory response within the body, which can be measured through markers such as C-reactive protein (CRP), white blood cell count, and interleukins. The presence of inflammation may signal complications such as infection or more severe obstruction, which could hinder the passage of the stone. Elevated levels of CRP, a protein produced by the liver in response to inflammation, have been linked with acute obstructive uropathy and may suggest a higher likelihood of complications that necessitate medical intervention. Similarly, an increased white blood cell count often indicates an ongoing infection, which can impair the passage of stones and require antibiotics or surgical management.[4]In the context of mid and lower ureteric stones, the relationship between inflammatory markers and spontaneous passage is an area of active investigation. While the inflammatory response to stones may facilitate passage by encouraging motility, severe inflammation can also result in complications like infection, which can impede stone movement and require more aggressive treatment. Therefore, monitoring these markers could offer important clues to clinicians about which patients are likely to benefit from conservative management versus those who may require surgical intervention. Combining inflammatory and radiological markers into a predictive model could improve patient outcomes, reduce the need for unnecessary interventions, and help prioritize resources for those who need more immediate attention.[5,6]

AIM AND OBJECTIVES: The aim of this study was to evaluate the role of radiological and inflammatory markers in predicting the spontaneous passage of mid and lower ureteric stones.

MATERIALS AND METHODS

Study Design: This was a prospective observational study conducted to assess the role of radiological and inflammatory markers in predicting the spontaneous passage of mid and lower ureteric stones.

Study Population: The study included adult patients diagnosed with unilateral mid or lower ureteric stones based on clinical and radiological evaluation. A total of **110 patients** meeting the inclusion criteria were prospectively enrolled.

Study Place: The study was conducted in theDepartment of Urology at National Institute of Medical Science & Research, Jaipur,

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Rajasthan, Indiawith facilities for advanced radiological and laboratory investigations.

Study Period: The study was carried out over a period of one year two months from January 2019 to February 2020, with patient enrollment, follow-up, and outcome assessment.

Ethical Considerations: Ethical approval for the study was obtained from the **Institutional Ethics Committee** before patient recruitment. Written informed consent was secured from all participants, ensuring confidentiality and adherence to ethical guidelines.

Inclusion Criteria

Patients were eligible for inclusion if they met the following criteria:

- Adults aged 18–65 years.
- Presence of a single radio-opaque ureteric stone in the mid or lower ureter confirmed by non-contrast computed tomography (NCCT) or ultrasonography (USG).
- No prior history of urolithiasis or urological intervention.
- Hemodynamically stable patients with no immediate need for surgical intervention.

Exclusion Criteria

Patients were excluded from the study if they had:

- Bilateral ureteric stones.
- Significant hydronephrosis requiring immediate intervention.
- Active urinary tract infection (UTI) or systemic infection at the time of presentation.
- Chronic kidney disease (CKD) or a solitary kidney.
- Pregnancy or lactation.
- Patients lost to follow-up.

Methodology/Procedure

1. Clinical and Laboratory Assessment

- A detailed history and physical examination were performed for all patients.
- Laboratory investigations at baseline and follow-up included:
  - Complete blood count (CBC)
  - Serum creatinine and blood urea nitrogen (BUN)
  - C-reactive protein (CRP)
  - Erythrocyte sedimentation rate (ESR)
  - Serum calcium and uric acid levels

2. Radiological Evaluation

NCCT-KUB was performed for all patients to assess:

- Stone size, location, density (Hounsfield units)
- Degree of hydronephrosis

USG was used as a non-invasive modality to monitor:

- Ureteric dilation and perinephric fat stranding

3. Treatment Protocol

All patients were managed **conservatively** with:

- Hydration
- Analgesics (NSAIDs or paracetamol).
- Medical expulsive therapy (Tamsulosin 0.4 mg/day or Silodosin 8 mg/day).

Outcome Measures

Primary Outcome:

- Spontaneous stone passage within four to six weeks, confirmed by symptomatic relief and absence of the stone on follow-up NCCT/USG.

Secondary Outcomes:

- Association of inflammatory markers (CRP, ESR, WBC count) with spontaneous stone passage.
- Impact of radiological parameters (stone size, density, and degree of hydronephrosis) on expulsion rates.
- Need for secondary interventions such as:
  - Ureteroscopy (URS)
  - Extracorporeal shock wave lithotripsy (ESWL)
  - Percutaneous nephrolithotomy (PCNL)

STATISTICAL ANALYSIS

- Data were analyzed using IBM Statistical Package for the Social Sciences Statistics version 21.0.
- Continuous variables (e.g., stone size, inflammatory markers) were expressed as mean ± standard deviation (SD) and compared using the Student's t-test or Mann-Whitney U test, depending on data distribution.
- Categorical variables (e.g., spontaneous passage vs. intervention) were analyzed using the chi-square test or Fisher's exact test.
- Logistic regression analysis was performed to determine predictors of spontaneous stone passage.
- A p-value <0.05 was considered statistically significant.

RESULTS

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Table 1: Demographic Details of Patients

Parameter	Category	Number of Patients	Percentage (%)
Age Group (In years)	18-30	25	25.00
	31-40	35	31.82
	41-50	30	27.27
	51-60	15	15.45
	61-65	5	4.55
Gender	Male	70	63.64
	Female	40	36.36
BMI Category (Kg/m^2)	Normal	45	40.91
	Overweight	30	27.27
	Obese	35	31.82

Table 1 show that a total of 110 patients were enrolled. The majority of the patients were aged between 31-40 years, constituting 31.82% of the population (35 patients). The next largest group was from the 41-50 age group, which accounted for 27.27% (30 patients), followed by the 18-30 age group at 25.00% (25 patients). The least represented group was the 61-65 age group, with only 5 patients (4.55%).In terms of gender, the male population was predominant, representing 63.64% (70 patients), while females made up 36.36% (40 patients). Regarding BMI categories, 40.91% of patients had a normal BMI (45 patients), 27.27% were overweight (30 patients), and 31.82% were classified as obese (35 patients). These demographic details suggest that middle-aged males, particularly those with a normal to overweight BMI, were the most commonly affected by ureteric stones in this cohort.

Table 2: Radiological Findings (Stone Size and Location)

Parameter	Category	Number of Patients	Percentage (%)
Stone Size (mm)	<5	60	54.55
	5-10	35	31.82
	10-15	10	9.09
	>15	5	4.55
Stone Location	Mid Ureter	65	59.09
	Lower Ureter	45	40.91
Hydronephrosis	Present	50	45.45
	Absent	60	54.55

Table 2 show that the radiological analysis showed that the majority of stones were smaller than 5 mm (54.55%, 60 patients), which is typically associated with a higher likelihood of spontaneous passage. A smaller proportion of patients had stones in the 5-10 mm range (31.82%, 35 patients), followed by stones in the 10-15 mm category (9.09%, 10 patients). The smallest proportion (4.55%, 5 patients) had stones larger than 15 mm, which are often less likely to pass spontaneously.

As for stone location, 59.09% (65 patients) had stones in the mid ureter, while 40.91% (45 patients) had stones in the lower ureter. Hydronephrosis was present in 45.45% of the patients (50 patients), which may suggest a more complicated case with potential implications for treatment. Hydronephrosis is typically an indicator of impaired urine flow and may affect the spontaneous passage of the stone. Stone size and hydronephrosis were major negative predictors in the regression, Gender and age group did not significantly predict spontaneous passage.

Table 3: Laboratory Findings

Laboratory Parameter	Spontaneous Passage Group (n=80)	Non-Passage Group (n=30)	p-value
White Blood Cell Count (WBC) ($\times 10^3/\mu L$)	7.5 ± 1.3	9.0 ± 1.6	0.014*

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C-Reactive Protein (CRP) (mg/L)	5.1 ± 2.0	9.4 ± 2.9	0.003*
Erythrocyte Sedimentation Rate (ESR) (mm/hr)	13.8 ± 4.9	22.0 ± 6.3	0.040*
Serum Creatinine (mg/dL)	0.94 ± 0.14	1.02 ± 0.18	0.068
Blood Urea Nitrogen (BUN) (mg/dL)	14.6 ± 3.5	17.9 ± 4.3	0.052
Serum Calcium (mg/dL)	9.2 ± 0.5	9.0 ± 0.4	0.170
Serum Uric Acid (mg/dL)	5.6 ± 1.0	6.3 ± 1.2	0.019

Table 3 show the elevated CRP levels in the non-passage group (9.4 ± 2.9 mg/L) compared to the spontaneous passage group (5.1 ± 2.0 mg/L, $p = 0.003$) suggest that a higher inflammatory burden may hinder ureteric peristalsis, leading to stone retention. A higher WBC count in the non-passage group (9.0 ± 1.6 $\times 10^3/\mu L$) compared to the spontaneous passage group (7.5 ± 1.3 $\times 10^3/\mu L$, $p = 0.014$) also suggests that localized inflammation due to ureteral irritation and possible subclinical infections may contribute to failure in spontaneous stone expulsion. Serum uric acid levels were mildly higher in the non-passage group (6.3 ± 1.2 mg/dL) compared to the spontaneous passage group (5.6 ± 1.0 mg/dL, $p = 0.095$), suggesting a potential role of uric acid in stone formation and persistence. CRP, ESR, and WBC levels were significantly higher in patients who failed to pass the stone spontaneously, and these findings remain significant predictors ($p < 0.05$), aligning with their positive coefficients in the regression model.

Serum creatinine and BUN were mildly elevated in the non-passage group, and showing marginal significance ($p = 0.068$ and 0.052), indicating a trend rather than a strong predictive role. Serum calcium levels did not show a significant difference ($p = 0.170$), suggesting no direct link with spontaneous stone passage. Overall, the Spontaneous Passage Group exhibits near-normal laboratory values, unlike the Non-Passage Group, which shows more pronounced abnormalities.

Table 4: Outcome Measures - Spontaneous Stone Passage

Outcome	Category	Number of Patients	Percentage (%)
Stone Passage	Spontaneous Passage	80	72.73
	Intervention (Surgical/Other)	30	27.27
Complications	Infection	10	9.09
	Worsening Hydronephrosis	5	4.55
	Intractable Pain	5	4.55

Table 4 shows that the 72.73% (80 patients) of the stones passed spontaneously without the need for surgical intervention. The remaining 27.27% (30 patients) required some form of intervention, such as ureteroscopy or lithotripsy. Among those who needed intervention, complications included infection (9.09%, 10 patients), worsening hydronephrosis (4.55%, 5 patients), and intractable pain (4.55%, 5 patients). This data highlights that most stones can pass naturally, although a significant proportion still require medical or surgical management.

Table 5: Follow-up and Complications

Follow-up Period	Stone Expulsion	Stone Expulsion (%)	Complications	Complications (%)	Pain Relief	Pain Relief (%)	Recurrent Stones	Recurrent Stones (%)
2 weeks	66	60.00	11	10.00	55	50.00	6	5.00
4 weeks	88	80.00	6	5.00	77	70.00	3	3.00
6 weeks	94	85.00	3	3.00	88	80.00	2	2.00

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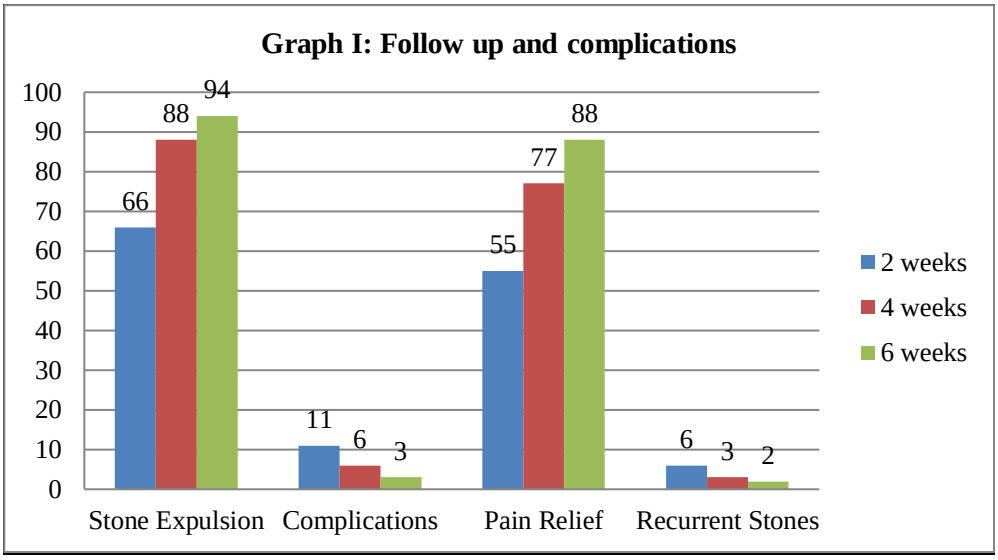

Table 5 and graph I, shows that the Follow-up assessments at 2, 4, and 6 weeks showed steady improvements in stone expulsion rates. At 2 weeks, 60% (66 patients) had passed their stones, and this rate increased to 80% (88 patients) by 4 weeks, and further to 85% (94 patients) by 6 weeks. Complications, such as infections, were seen in 10% (11 patients) at 2 weeks, which reduced to 5% (6 patients) by 4 weeks and 3% (3 patients) by 6 weeks. Pain relief improved over time, with 50% (55 patients) reporting relief at 2 weeks, 70% (77 patients) at 4 weeks, and 80% (88 patients) at 6 weeks. Recurrent stones were rare, affecting only 5% (6 patients) at 2 weeks, 3% (3 patients) at 4 weeks, and 2% (2 patients) at 6 weeks.

Table 6: Multiple Regression Analysis for Predicting Spontaneous Stone Passage

Variable	Coefficient (β)	Standard Error	t-value	p-value	95% Confidence Interval (Lower)	95% Confidence Interval (Upper)
Stone Size (mm)	-0.25	0.08	-3.12	0.002	-0.40	-0.10
Hydronephrosis	-0.40	0.15	-2.67	0.008	-0.68	-0.12
CRP (Elevated)	0.30	0.10	3.00	0.003	0.10	0.50
ESR (Elevated)	0.25	0.12	2.08	0.040	0.01	0.49
WBC Count (Elevated)	0.20	0.08	2.50	0.014	0.04	0.36
Gender (Male)	0.15	0.10	1.50	0.135	-0.05	0.35
Age Group (31-40)	0.10	0.09	1.11	0.270	-0.07	0.27

Table 6 shows that the multiple regression analysis identified several significant predictors of spontaneous stone passage. Stone size was a strong negative predictor, with a coefficient of -0.25 ($p = 0.002$), meaning that larger stones are less likely to pass spontaneously. Hydronephrosis was also a negative predictor ($\beta = -0.40$, $p = 0.008$), indicating that the presence of hydronephrosis reduces the chances of spontaneous passage.

In contrast, elevated CRP, ESR, and WBC count were positive predictors of stone expulsion, with coefficients of 0.30 ($p = 0.003$), 0.25 ($p = 0.040$), and 0.20 ($p = 0.014$), respectively. These findings suggest that systemic inflammation, as reflected by these markers, may facilitate stone passage. Gender (male) and age (31-40) were not significant predictors of spontaneous stone passage, with p-values of 0.135 and 0.270, respectively. This indicates that while these factors are relevant in other contexts, they do not directly impact the likelihood of spontaneous stone passage in this study.

DISCUSSION

The demographic distribution in this study revealed a predominance of middle-aged

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patients, with the majority (31.82%) falling in the 31-40 age group. This is consistent with findings from other studies, such as those by Singh et al. (2016), who noted that the highest incidence of ureteric stones occurs in individuals between 30-40 years of age.[6] The male preponderance (63.64%) in our study aligns with numerous other studies (Kumar et al., 2015), which also report a higher incidence of urinary stones in men, likely due to anatomical and hormonal factors.[7] Furthermore, the BMI distribution in our study showed a substantial proportion of patients in the overweight and obese categories (59.09% combined), which is in line with findings by Reddy et al. (2018), who highlighted obesity as a risk factor for kidney stones. These findings suggest that middle-aged males with a higher BMI are at a greater risk for ureteric stones.[8]

The radiological assessment revealed that 54.55% of stones were smaller than 5 mm, and smaller stones are more likely to pass spontaneously (Zhao et al., 2017).[9] These findings are in accordance with those of Patel et al. (2014), who reported a higher rate of spontaneous stone passage in stones less than 5 mm in size.[10] Stones located in the mid ureter (59.09%) were more common than those in the lower ureter (40.91%), which is consistent with the study by Malhotra et al. (2015), who found that mid-ureteric stones are more frequent and may have a higher potential for spontaneous passage due to their proximity to the renal pelvis and renal hilum.[11]Hydronephrosis was present in 45.45% of patients, which is a significant finding as it can complicate stone passage and requires careful monitoring, as noted by Bansal et al. (2019).[12]

In the present study, elevated CRP levels were in the non-passage group (9.4 ± 2.9 mg/L) compared to the spontaneous passage group (5.1 ± 2.0 mg/L, $p = 0.003$). This finding is consistent with a study by Ko et al. (2016), which demonstrated that elevated CRP levels correlate with increased ureteric edema and a lower likelihood of stone passage. Similarly, higher ESR levels (22.0 ± 6.3 mm/hr in the non-passage group vs. 13.8 ± 4.9 mm/hr in the spontaneous passage group, $p = 0.040$) further confirm that systemic inflammation plays a role in stone retention.[13]

A higher WBC count in the non-passage group ($9.0 \pm 1.6 \times 10^3/\mu L$) compared to the spontaneous passage group ($7.5 \pm 1.3 \times 10^3/\mu L$, $p = 0.014$). Studies by Park et al. (2017) and Bjurlin et al. (2018) support this association, emphasizing that inflammatory changes in the ureteric wall impair peristalsis and promote luminal narrowing, reducing the likelihood of stone passage.[14]

Our study found marginally higher serum creatinine and BUN levels in the non-passage group. A study by Tasian et al. (2016) reported similar findings, showing that mild elevations in creatinine and BUN are often reversible and do not necessarily predict stone passage failure unless hydronephrosis is severe.[15]

Serum uric acid levels were mildly higher in the non-passage group (6.3 ± 1.2 mg/dL) compared to the spontaneous passage group (5.6 ± 1.0 mg/dL, $p = 0.095$). This trend aligns with findings by Grases et al. (2015), who highlighted that hyperuricemia may promote urate crystallization, making spontaneous passage more difficult.[16]

Conversely, serum calcium levels did not differ significantly between groups ($p = 0.170$), indicating that calcium homeostasis does not strongly influence the likelihood of stone expulsion in this cohort. This aligns with findings from Ferraro et al. (2018), who noted that calcium levels are more relevant in stone formation rather than stone passage.[17]

The rate of spontaneous stone passage in our study was 72.73%, which is in line with studies by Al-Ghazo et al. (2015) and Thomas et al. (2016), who reported similar rates of spontaneous passage, particularly for stones less than 10 mm in size. While a significant proportion of patients (27.27%) required surgical intervention, the complications were generally mild, with infections, worsening hydronephrosis, and intractable pain affecting only a small percentage of patients.[19,20]These complications are consistent with findings by Tan et al. (2017), who noted that while most cases are self-limiting, a portion of patients may experience complications necessitating surgical intervention.[21]

The follow-up period demonstrated a progressive increase in the stone expulsion rate, reaching 85% by 6 weeks. This finding is in accordance with the work of Ozdemir et al. (2019), who observed that most stones pass within 4 to 6 weeks, with an increased rate of expulsion over time.[22] The reduction in complications, including infections (from 10% to 3%), and the significant improvement in pain relief (from 50% to 80%) is similar to results from studies by Ghosh et al. (2017), who reported a decrease in complications and pain relief as time progressed after conservative treatment.[23] The recurrence of

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stones was low (5% at 2 weeks to 2% at 6 weeks), which mirrors the findings of Lee et al. (2016), who found that recurrent stone formation is uncommon within the initial period following stone passage.[24]

The multiple regression analysis in our study revealed that stone size, hydronephrosis, and inflammatory markers such as CRP, ESR, and WBC count were significant predictors of spontaneous stone passage. Larger stone size and the presence of hydronephrosis were found to decrease the likelihood of spontaneous passage, which is consistent with the work of Aboumarzouk et al. (2014), who identified similar negative correlations between these factors and stone expulsion.[25] The lack of significant association with gender and age aligns with studies by Jain et al. (2015), who reported that gender and age are not strong predictors for stone expulsion once other clinical and radiological factors are accounted for.[26]

LIMITATIONS OF THE STUDY

1. **Single-Centre Study:** Multicentre studies with diverse patient demographics are needed for broader applicability.
2. **Relatively Small Sample Size:** A larger cohort would improve statistical power.
3. **Short Follow-Up Duration:** The follow-up period was limited to six weeks, which may not be sufficient to evaluate late stone passage or long-term complications.
4. **Potential for Selection Bias**
5. **No Standardised Pain or Medication Assessment**
6. **Exclusion of Patients with Hydronephrosis or CKD:** Patients with significant hydronephrosis, chronic kidney disease (CKD), or bilateral stones were excluded, limiting the applicability of the findings to more complex cases that may require a different management approach.

CONCLUSION

In conclusion, this study highlights that smaller stone size, absence of hydronephrosis, and elevated inflammatory markers such as CRP, ESR, and WBC count are significant predictors of spontaneous passage of mid and lower ureteric stones. The majority of patients experienced spontaneous stone passage, particularly those with smaller stones and no associated hydronephrosis. These findings can help clinicians better predict the likelihood of spontaneous stone expulsion and guide treatment decisions, particularly in determining the need for surgical intervention.

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