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Diagnostic accuracy of increased C reactive protein levels in distal ureteric stone ejection prediction using a CT scan as the gold standard

Mudassar Saeed Pansota [a], Muhammad Shahzad Saleem [b], Asra Aleem [b], Burhan Barkat [b], Mumtaz Rasool [c]

[a] *Associate Professor, Department of Urology, Shahida Islam Medical & Dental College/Teaching Hospital, Lodhran.*
[b] *Assistant Professor, Department of Urology, BahaWal Victoria Hospital/Quaid-e-Azam Medical College, Bahawalpur.*
[c] *Professor, Department of Urology, BahaWal Victoria Hospital/Quaid-e-Azam Medical College, Bahawalpur.*
Correspondence: * *netygeulis749@hotmail.com*

ABSTRACT

BACKGROUND & OBJECTIVE: Numerous clinical urological diseases have been shown to benefit from CRP, such as the evaluation of renal injury in pyelonephritis, the determination of the severity of pediatric UTIs, and the prevention of voiding cystourethrography in cases of pediatric UTIs and vesicoureteral reflux. This study has been conducted to diagnose the accuracy of increased C reactive protein levels in distal ureteric stones.

METHODOLOGY: In total, 184 individuals with single distal ureteric stones were included. Patients with severe hydronephrosis, multiple ureteral stones, impaired renal function, pregnancy, single kidney, endoscopic procedures, or prior ureteric surgery history or concomitant ureteric anomalies were excluded. Each patient had a blood sample sent to the hospital laboratory to evaluate the serum levels of CRP (c-reactive protein). For four weeks, the researcher checked in with each patient once a week. After that, each patient had computed tomography, and the data was evaluated to determine whether or not ureteric stones were present.

RESULTS: The overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of elevated C reactive protein levels are 92.39%, 95.51%, 92.63%, and 94.02%, respectively, when using a CT scan as the gold standard to predict the ejection of a distal ureteric stone (p-value = 0.0001).

CONCLUSION: This study found that elevated C reactive protein levels have a fairly high diagnostic accuracy in predicting the ejection of distal ureteric stones.

KEYWORDS: Ureteric, Stone, Expulsion, C-reactive Protein, Sensitivity.

INTRODUCTION

Everywhere in the world, urolithiasis is prevalent; it affects 1–15% of the general population [1], 1%–5% in Asia, 5%–9% in Europe, and 20% in Saudi Arabia [2]. The Stone Belt region, which includes Pakistan, has a chronically high incidence of urolithiasis. The recurrence rate of urolithiasis is significant, ranging from 25% to 50% in 5 to 10 years and 75% after 20 years [3]. Urinary tract stones are a frequent issue in day-to-day emergency room operations. Acute ureteric colic occurs in about 1-2 instances per 1,000 persons annually, with a lifetime risk of 5–10% [1].

Ureteric stones account for twenty percent of urinary tract stones, and the distal portion of the ureter is where seventy percent of these stones are located [2]. The majority of ureteral calculi are usually self-passing and don't require treatment. Generally speaking, stones smaller than 4 mm can pass spontaneously; for stones larger than 5 mm, the rate of spontaneous passing is 68%, irrespective of the stone's location within the ureter [3]. Proximal ureteral calculi that are larger than 6 mm have a 5% or lower likelihood of stone passage, but distal ureteric stones have a 50% rate of expulsion with conservative management [4].

Urinary stones are usually diagnosed by clinical history and radiological imaging methods such as computed tomography (CT) scan, intravenous urography (IVU), and kidney-ureter-bladder (KUB) films. Among these, CT KUB is the most dependable approach for diagnosing ureteral stones due to its high sensitivity and specificity [5]. Roughly 70% of ureteral stones are distal ureter stones, sometimes referred to as lower ureteral stones. These stones are treated with a variety of techniques, including laparoscopic/open ureter lithotomy, extracorporeal shock wave lithotripsy, flexible Ureterorenoscopy, semi-rigid and cautious waiting for stone expulsion [4].

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When inflammation is present, a blood protein known as C-reactive protein (CRP), an acute-phase protein, is raised. By attaching to phosphocholine expressed on the surface of some bacteria and dead or dying cells, it performs the physiological function of stimulating the complement system [5]. The liver synthesizes CRP. High CRP levels cannot identify a particular disease because many other diseases might raise CRP production. It has been demonstrated that CRP is helpful in a number of clinical urological disorders, including pyelonephritis renal injury estimation.

Assessing the severity of pediatric UTIs and even refraining from voiding cystourethrography in cases where pediatric UTIs and vesicoureteral reflux are feverish [6,7]. In one trial, 54.9% of patients experienced spontaneous stone expulsion within 4 weeks, and elevated CRP had a 78.60% sensitivity and an 89.30% specificity in predicting stone ejection [8].

Therefore, it is hypothesized that luminal inflammation and obstruction may contribute to high CRP in ureteric inflammatory disorders. The measurement of CRP has the extra benefit of being readily available in all medical facilities, rapid, affordable, and non-invasive. Therefore, the purpose of this study was to ascertain if elevated levels of C reactive protein might accurately predict the ejection of a distal ureteric stone.

METHODOLOGY

After approval from the ethical review committee (SIMC/H.R./7722/23), 184 patients with solitary distal ureteric stones with a size of ≤10 mm and ages ranging from 20 to 50 who presented to the urology departments of Shahida Islam Teaching Hospital, Lodhran, and Bahawal Victoria Hospital, Bahawalpur, from February 2023 to July 2023 were chosen for this cross-sectional validation study. The sample was selected through a non-probability consecutive sampling technique. The study determined the sample size with a 95% confidence interval, an 8% margin of error, and a prevalence of 54.9% for spontaneous stone expulsion within 4 weeks. Additionally, the study found that increased CRP had a 78.60% sensitivity and an 89.30% specificity in predicting stone expulsion [8].

Participants with a history of endoscopic procedures or ureteric surgery, a single kidney, severe hydronephrosis, multiple ureteral stones, pregnancy, impaired renal function, associated ureteric anomaly, diabetes, liver failure, or any inflammatory disease (enteritis, hepatitis, respiratory infections, arthritis, or viral infections (as assessed on history and medical record) were excluded from the study.

Patients were asked for their informed consent. Each patient had a blood sample sent to the hospital laboratory to evaluate the serum levels of CRP (c-reactive protein), and the effect of stone expulsion on CRP levels was recorded. Every patient received 0.4 mg of tamsulosin daily at bedtime, 12 hourly tabs of ciprofloxacin 500 mg and 50 mg of diclofenac sodium, one tab every 8 hours for pain management when needed, and 4 weeks of syp potassium citrate TDS. The subjective evaluation indicated that medication compliance was present. The researcher followed up with each patient once a week for four weeks.

Following this, computed tomography was performed on each patient, and the results were assessed for the presence or absence of ureteric stones by a consultant radiologist with at least five years of post-fellowship experience. The CT scan report and stone expulsion on CRP levels were Corelated.

The data that was gathered was examined using SPSS version 25.0. The mean and standard deviation were used to represent quantitative variables. The quantitative variables were measured using proportion and frequency calculations. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of high C reactive protein levels in predicting the ejection of a distal ureteric stone were assessed using a 2x2 contingency table, with a CT scan serving as the gold standard. A chi-square test was applied , and a p-value ≤0.05 was taken as significant.

RESULTS

The study's ages ranged from 20 to 50 years old, with a mean age of 32.73 ± 8.77 years. The age range of the majority of the 108 patients (58.70%) was between 31 to 50 years old. With a female-to-male ratio of 1.4:1, 106 (57.61%) of the 184 patients were female and 78 (42.39%) were male. Ureteric colic lasts, on average, 28.55 ± 9.01 hours. The stone's average size is 6.42 ± 1.34 mm. The average BMI is 3.39 ± 2.70 kg/m2. The distribution of patients according to demographic features is shown in Table I. Stone passage with relation to CRP levels (raised or low) is shown in Table- II.

There were 85 true positives and four false positives in situations where the CRP level was positive. Table III shows that out of the patients with negative CRP levels, 88 were true negatives ,and 07 were false negatives. Raised C reactive protein levels' overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy in predicting the following percentages, using a CT scan as the gold standard for distal ureteric stone expulsion: 92.39, 95.65, 95.51, 92.63, and 94.02% , respectively.

Table-I:Demographic features of selected patients.

Variables	Categories	No. of Patients n(%)
Age (years)	20-35	76(41.30)
	36-50	108(58.70)
Gender	Male	106(57.61)
	Female	78(42.39)
Duration of ureteric colic (hours)	≤24	77(41.85)
	>24	107(58.15)
Size of stone (mm)	≤5	49(26.63)
	6-10	135(75.37)
Side Affected	Right	117(63.59)
	Left	67(36.41)
Residence	Rural	78(42.39)
	Urban	106(57.61)

Table-II:Stone passage with relation to CRP levels (raised or low).

CRP levels	Stone Passage
	No. of Patients (n%)
Raised (>6 mg/dl)	85(46.20)
Low (≤6 mg/dl)	07(3.80)

Table-III:Stone passage with relation to CRP levels (raised or low).

Categories	A positive result on CT	A negative result on CT	P-value
Positive on raised CRP levels	85 (TP)*	04 (FP)***	0.0001
Negative on raised CRP levels	07 (FN)**	88 (TN)****	

-TP=True positive **-FP=False positive ***-FN=False negative *-TN=True negative**
Sensitivity: 92.39%, Specificity: 95.65%, Positive Predictive Value (PPV): 95.51%
Negative Predictive Value (NPV): 92.63%,Diagnostic Accuracy: 94.02%

DISCUSSION

The serum of patients experiencing acute inflammation was initially identified as serum C-reactive protein (CRP), which reacted with the C- (capsular) polysaccharide of pneumococcus [9,10]. When CRP was first identified in 1930 by Tillett and Francis, it was believed to be a harmful secretion because it was raised in patients suffering from a number of diseases, including cancer [11,12]. However, the fact that hepatic production was found proved it is a native protein. Clinically, CRP values range from 13 to 15 and are utilized as indicators of the severity of inflammation. A ureteral stone that obstructs the ureter causes an inflammatory shift in the proximal submucosal layer, which stops the stone from passing through [13-16].

In order to evaluate the diagnostic accuracy of high C reactive protein levels in predicting the ejection of a distal ureteric stone, it was used after a CT scan as the gold standard in this study. The overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of elevated C reactive protein levels are 92.39%, 95.51%, 92.63%, and 94.02%, respectively, when using a CT scan as the gold standard to predict the ejection of a distal ureteric stone. 54.9% of patients in one experiment had spontaneous stone expulsion within 4 weeks, and increased CRP was a strong predictor of stone ejection with a 78.60% sensitivity and an 89.30% specificity [8]. In another study, CRP levels >1.35 mg/dl have shown a sensitivity of 97.6% and specificity of 70.2% [1].

Park et al. determined the correlation between the neutrophil count and CRP level and the spontaneous passing rate of ureteric stones < 8 mm [16].A retrospective analysis was performed on 187 patients with ureteral stones ≤8 mm treated consecutively. The definition of ureteral stone removal was the absence of any ureteral stones on imaging tests for eight weeks following diagnosis and therapy. The patients were split into two groups based on the proportion of neutrophils and three groups based on the serum CRP levels [8].

The relationships between these variables and the rates of ureteral stone passage were determined. The groups with low blood CRP levels (94.1%; 159/169), medium serum CRP levels (7/10), and high serum levels (4/8) had ureteral stone passing rates, accordingly. Urinary stone passing rates were 94.5% (121/128) and 83.1% (49/59) in the group with a higher neutrophil percentage and a normal neutrophil percentage, respectively (p=0.011). To determine if a patient with a tiny ureteral stone (less than 8 mm) would pass the stone spontaneously, measurements of serum CRP and neutrophil percentages are helpful. Aggressive treatment should be taken into consideration when a patient's neutrophil percentage and serum CRP level are elevated [16].

Angulo et al., study found that patients with lower CRP had a higher likelihood of ureteric calculus passing through on its own [17].There is no specific cut-off level of CRP to predict the spontaneous passage of a ureteric stone, according to a study measuring CRP in patients with ureteral colic caused by urolithiasis. However, a cut-off point of 28 mg/L for CRP achieved an optimal sensitivity of 75.8% and a specificity of 88.9% when deciding whether to drain the stone [18].

In a different study by Park et al., 90.9% of patients showed spontaneous evacuation of the calculus in those with negative CRP levels [16]. Furthermore, it was shown that only 58.8% of patients with elevated CRP had spontaneous ejection of the calculus; of the 56 patients in the research, only nine showed this phenomenon. They, therefore, concluded that the calculus's spontaneous transit rate decreased with increasing CRP.

In contrast to individuals who did expel the calculus, those who experienced spontaneous expulsion of the calculus had normal CRP levels, according to a study by Sagar and Kaushal [19]. According to a study by Jain et al., patients with zero CRP had a higher rate of calculus ejection that occurs on their own [20].

According to certain studies that investigate the role of CRP as a diagnostic marker in some urological diseases, we assess serum CRP levels in patients with ureteric stones based on the ureteric wall inflammation caused by ureteric stones in a trial to use CRP as a factor that aids in the management of ureteric stones in addition to other factors like stone size, site, and degree of hydronephrosis [21-23].

Our study established a significant correlation between the serum CRP level and spontaneous ureteric stone expulsion, suggesting that the stone's associated submucosal edema and inflammatory changes in the ureteric wall may be the cause of the failure of medical expulsive therapy for ureteric stones [2].

CONCLUSION

According to the study's findings, elevated C reactive protein levels have a fairly high diagnostic accuracy when it comes to predicting the ejection of distal ureteric stones. Therefore, to minimize needless treatments in these specific

individuals, we advise that this inexpensive and readily accessible diagnostic tool be performed regularly to forecast distal ureteric stone removal. So, we recommend that in patients with raised CRP levels, medical treatment can be given for 4 weeks in patients with distal ureteric stones before undergoing any intervention.

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Authors' Contribution:

Mudassar Saeed Pansota : Substantial contributions to the conception and design of the work.
Muhammad Shahzad Saleem : The acquisition and analysis of data for the work.
Asra Aleem : Drafting the work and reviewing it critically for important intellectual content.
Burhan Barkat : Interpretation of data for the work.
Mumtaz Rasool : Final approval of the version to be published.