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Original Article

Diagnostic discrimination of C-reactive protein and blood count-derived indices for concurrent urinary tract infection in pediatric urolithiasis

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ABSTRACT

Objective: The aim of this study was to evaluate the diagnostic discrimination of CRP and CBC-derived inflammatory indices for identifying concurrent culture-confirmed UTI in children with urolithiasis during early clinical assessment.

Materials and Methods: This single-center retrospective observational study included 77 children with imaging-confirmed urolithiasis and 45 healthy controls. Concurrent UTI was defined by compatible symptoms together with urine culture growth of ≥10^5 colony-forming units/mL. Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), monocyte-to-platelet ratio (MPR), mean platelet volume (MPV), white blood cell count, and CRP were compared across study groups. Receiver operating characteristic analyses were used to assess diagnostic discrimination for culture-confirmed UTI.

Results: Among 77 children with urolithiasis, 46 (59.7%) had concurrent culture-confirmed UTI. Compared with both healthy controls and stone/UTI-negative patients, those with concurrent UTI had significantly higher NLR, MLR, MPR, white blood cell count, and CRP levels, whereas MPV showed poor discriminatory performance. CRP demonstrated the highest diagnostic discrimination for concurrent UTI (AUC 0.996), with a cutoff of ≥5 mg/L yielding 98.0% sensitivity and 100% specificity. Among the complete blood count–derived indices, NLR performed best (AUC 0.838), followed by MLR (AUC 0.827) and MPR (AUC 0.779). Secondary exploratory analyses suggested declining inflammatory markers after infection control and stone clearance in the surgical cohort, whereas a very small subgroup with culture-negative postoperative fever showed descriptive marker re-elevation in exploratory analyses.

Conclusion: In pediatric urolithiasis, CRP demonstrated the strongest diagnostic discrimination for concurrent culture-confirmed UTI, whereas NLR was the most informative supportive complete blood count–derived index. Secondary exploratory observations should be interpreted cautiously and require confirmation in larger cohorts. Overall, the present findings remain preliminary and require prospective validation before any routine clinical application.

Keywords: Biomarkers, child, C-Reactive Protein, inflammation, urolithiasis, urinary tract infections

Introduction

Pediatric urolithiasis has become an increasingly important clinical problem because of its rising incidence, high recurrence rates, and potential for long-term renal sequelae (1,2). Its prevalence varies according to geography, climate, genetic predisposition, hydration status, and dietary habits, and has increased in many regions in parallel with modern lifestyle changes (3). Beyond mechanical obstruction and urinary stasis, urinary stones may also provoke local and systemic inflammation through mucosal irritation and disruption of the epithelial barrier (4,5). When urinary tract infection (UTI) accompanies stone disease, clinical severity often increases, with higher rates of fever, hospitalization, and the need for invasive intervention (6).

Inflammation in urolithiasis is bidirectional: crystal deposition may initiate acute inflammatory responses, whereas persistent stone-related irritation may sustain chronic low-grade inflammation (5). Infection-related stones and recurrent UTIs further underscore the clinical relevance of inflammatory activity in stone disease (7,8). In routine practice, however, the more immediate challenge is to determine whether a child presenting with urolithiasis has concurrent bacterial infection

or sterile stone-related inflammation. This distinction is often difficult at initial presentation, when urine culture results are still pending but decisions regarding antibiotic therapy, hospitalization, and further intervention may already be required (6).

Accordingly, there is growing interest in routinely available inflammatory markers that may assist early assessment without additional cost or delay. Complete blood count (CBC)–derived indices have attracted attention as accessible markers of systemic inflammation. NLR and MLR have been evaluated across a range of infectious and inflammatory conditions, whereas evidence for MPR in pediatric urolithiasis remains limited (10-13). Mean platelet volume (MPV), although biologically linked to platelet activation and inflammation, has yielded inconsistent findings in pediatric stone disease (14,15). CRP is also widely used in the evaluation of bacterial infection, yet comparative data examining CRP together with multiple CBC-derived indices in children with urolithiasis remain limited.

The inflammatory profile of pediatric stone disease may also vary according to clinical context. Stone location may plausibly influence obstruction, urinary stasis, symptom burden, and the magnitude of the accompanying inflammatory response (9). In addition, postoperative febrile episodes with negative urine cultures may raise the possibility of sterile inflammatory activation rather than overt infection. These issues are clinically relevant, but they remain secondary to the central diagnostic question of whether routinely available inflammatory markers can help distinguish concurrent culture-confirmed UTI from noninfectious stone-related inflammation.

Comparative data evaluating CRP alongside multiple CBC-derived inflammatory indices in children with urolithiasis remain limited. Therefore, we aimed to assess the diagnostic discrimination of CBC-derived inflammatory indices and CRP for identifying concurrent culture-confirmed UTI in children with urolithiasis. Secondary exploratory analyses examined location-related variation in selected markers and described inflammatory marker trajectories in a small subgroup with culture-negative postoperative fever.

Materials and Methods

This single-center retrospective observational study was conducted at Gaziantep City Hospital after approval by the institutional ethics committee.'

Participants and eligibility criteria

Consecutive pediatric patients (0–18 years) evaluated for urolithiasis between October 2023 and January 2025 were screened. Urolithiasis was defined as the presence of a stone confirmed by imaging (ultrasonography, plain abdominal radiography, and/or non-contrast computed tomography). Patients were excluded if essential clinical or laboratory data were missing; if they had an acute infection unrelated to urolithiasis; chronic inflammatory/autoimmune disease; hematologic malignancy; immunosuppressive or systemic corticosteroid therapy; major surgery or trauma within the preceding three months; or a known metabolic stone disorder with distinct inflammatory profiles (e.g., primary hyperoxaluria or cystinuria). Individuals aged ≥18 years at the time of evaluation were not eligible.

A control group was retrospectively selected from healthy children without known urolithiasis and with no history of infection or surgical intervention within the preceding three months. Controls were recruited from routine outpatient assessments and were included only if they had no clinical evidence of acute illness at the time of blood sampling.

Clinical data and stone-related variables

Demographic variables (age and gender), prior UTI history, management strategy (surgical vs conservative), and laboratory values were abstracted from electronic medical records using a standardized data-extraction form.

Stone presence and location were initially assessed by ultrasonography (US) and, when feasible, corroborated by plain kidney–ureter–bladder radiography (KUB). Stone size was recorded as the largest diameter measured on imaging. To minimize modality-related measurement variability, a predefined hierarchy was applied for stone size: when non-contrast CT was available, the CT measurement was used; otherwise, the US measurement was used (KUB was employed for confirmation of stone presence rather than as the primary size measurement). According to institutional clinical practice, non-contrast CT was obtained for surgical planning when US demonstrated a stone diameter ≥15 mm. In addition, in patients with no visible stone on US but with hydronephrosis and costovertebral angle tenderness—particularly when ureteral stone was suspected—non-contrast CT was performed to confirm ureteral calculi. This approach was intended to address the limitations of US in detecting ureteral stones.

Because some stone-location subcategories had small sample sizes, stone location was collapsed into three clinical groups for analytic purposes: upper urinary tract (renal pelvis + lower pole), ureter, and lower urinary tract (bladder + urethra). The single case recorded as "ureter + renal pelvis" (n=1) was included in the ureter group. This approach was used to reduce the risk of spurious findings arising from small cell counts. For surgically treated patients, the index procedure was recorded (retrograde intrarenal surgery, percutaneous nephrolithotomy, extracorporeal shock wave lithotripsy, laser lithotripsy, or open surgery) in accordance with institutional practice.

Definition of UTI and related terms

Concurrent UTI was defined as compatible clinical findings (fever ≥38°C, dysuria, or pollakiuria) together with microbiological evidence of infection, specifically growth of $\geq 10^5$ colony-forming units/mL on urine culture obtained from a midstream clean-catch urine sample. Pyuria (e.g., ≥5 leukocytes/HPF or per institutional threshold) was recorded as a supportive finding but was not included in the primary UTI definition, because both irritative urinary symptoms and sterile pyuria may occur in children with urolithiasis in the absence of true bacterial infection. A culture-based definition was therefore preferred to improve diagnostic specificity for the primary analysis. Recurrent UTI was defined as ≥2 febrile episodes or ≥3 afebrile episodes documented in the medical record.

Laboratory measurements and inflammatory indices

Complete blood count (CBC) parameters and C-reactive protein (CRP) were obtained as part of routine care at presentation and, when applicable, during perioperative/postoperative follow-up. CBC measurements were performed using the same automated hematology analyzer throughout the study period, and CRP was processed in accredited laboratories according to institutional standards. To minimize analytical variability—particularly for platelet indices—samples were handled according to routine pre-analytical protocols and analyzed within the standard time window after venipuncture.

CBC-derived indices were calculated as follows:

- NLR = neutrophil count / lymphocyte count
- MLR = monocyte count / lymphocyte count
- MPR = monocyte count / platelet count

Mean platelet volume (MPV, fL) was recorded as reported by the laboratory. White blood cell count (WBC) and CRP (mg/L) were analyzed as reference inflammatory markers.

Timing of sampling and definition of time points

To preserve interpretability, analyses were restricted to clinically defined time points. The UTI-positive time point was defined as the laboratory measurement obtained within 24 hours of symptom onset during an episode fulfilling the study definition of UTI. In the surgical cohort, longitudinal comparisons were based on repeated measurements from the same patients at predefined time points. The preoperative time point was defined as the laboratory measurement obtained within 24 hours before surgery, whereas the postoperative stone-free/UTI-free time point was defined as the measurement obtained 4 weeks after surgery in the same patient, after confirmation of stone-free status and absence of UTI by clinical assessment, with urine culture considered when available. When multiple eligible measurements were available within the relevant time window, the value closest to the corresponding clinical event was selected to avoid duplication and standardize measurement selection. Paired analyses in the surgical cohort were restricted to patients with matched measurements available at the relevant predefined time points.

Culture-negative postoperative fever subgroup

A predefined subgroup analysis was performed in children who developed postoperative fever despite (i) radiologic confirmation of stone-free status and (ii) negative urine cultures. For this subgroup, hematologic and biochemical markers were compared across three clinically defined time points:

- preoperative UTI period (culture-confirmed UTI);
- intra-/perioperative period (stone present, urine culture negative); and
- postoperative febrile period (stone-free on imaging, urine culture negative, fever present).

This analysis was designed to descriptively characterize inflammatory trajectories in episodes suggestive of sterile postoperative inflammation.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics v25.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as numbers and percentages, while continuous variables are presented as mean and standard deviation or median with interquartile range (IQR), as appropriate. The normality of distribution was assessed using the Shapiro–Wilk test. Two-group comparisons were performed using Student's t-test or the Mann–Whitney U test, whereas comparisons across more than two groups were conducted using the Kruskal–Wallis test. When the overall comparison was significant, pairwise post hoc analyses were performed using Dunn's test (Bonferroni-adjusted). Paired comparisons were analyzed using the Wilcoxon signed-rank test, and categorical variables were compared using the chi-square or Fisher's exact test.

Diagnostic discrimination of NLR, MLR, MPR, MPV, and CRP for concurrent UTI was evaluated by receiver operating characteristic (ROC) analysis with calculation of the area under the curve (AUC) and 95% confidence intervals; optimal cutoffs were determined using the Youden index. ROC AUC comparisons were restricted to the prespecified comparison between the combined CRP+NLR logistic regression model and CRP alone, using the DeLong test. All tests were two-sided, and $p<0.05$ was considered statistically significant.

Given the retrospective design and modest sample size, ROC-based estimates were interpreted as exploratory measures of discrimination rather than definitive indicators of clinical diagnostic accuracy. To further examine whether inflammatory markers were independently associated with concurrent culture-confirmed UTI within the stone cohort, exploratory multivariable logistic regression analyses were performed using clinically relevant covariates available in the dataset, including age, sex, stone size, stone location, management strategy, and hydronephrosis. Because several inflammatory markers showed right-skewed distributions, ratio-based markers were log-transformed before modeling when appropriate. Analyses of stone location and culture-negative postoperative fever trajectories were predefined as secondary exploratory analyses and were interpreted cautiously.

Results

Study population and baseline characteristics

A total of 122 children were included in the analysis: 77 patients with imaging-confirmed urolithiasis and 45 healthy controls. Among stone-bearing patients, 62 (80.5%) underwent surgical intervention and 15 (19.5%) were managed conservatively. The control and urolithiasis groups differed significantly in age (5.6 ± 2.8 vs 7.6 ± 4.6 years; $p=0.038$) and sex distribution (male/female 40/5 vs 44/33; $p=0.001$).

Median stone size was significantly larger in surgically managed patients than in those followed conservatively (10.0 mm (IQR 8.0-13.0) vs 5.0 mm (IQR 4.5-7.0), $p<0.001$). The stone–UTI-positive group consisted of clinically compatible cases with culture-confirmed UTI ($\geq 10^5$ CFU/mL on urine culture); pyuria was not used as an inclusion criterion. Concurrent UTI was

Table I: Stone location, intervention type, and stone composition according to management strategy

Management strategy/ Stone location	n	Intervention(s) performed	Stone composition
Surgical (n=62)			
Renal pelvis	21	3 PCNL (staghorn), 18 RIRS	3 struvite (staghorn), 18 calcium oxalate (whewellite/weddellite)
Lower pole	20	RIRS	Calcium oxalate
Ureter	23	RIRS	Calcium oxalate
Ureter + renal pelvis	1	RIRS	Calcium oxalate
Bladder	4	2 open surgery, 2 laser lithotripsy	2 cystine, 2 calcium oxalate
Urethra	1	Laser lithotripsy	-
Non-surgical (n=15)			
Renal pelvis	2	1 ESWL, 1 medical therapy	-
Lower pole	10	7 ESWL, 1 spontaneous passage, 2 medical therapy	-
Ureter	3	3 spontaneous passage	-

***PCNL:** percutaneous nephrolithotomy, **RIRS:** retrograde intrarenal surgery, **ESWL:** extracorporeal shock wave lithotripsy. Dash indicates unavailable data.*

Table II: Hematological and biochemical parameters

Parameter	Control*	Stone-UTI negative*	Stone-UTI positive*	p†	p‡	p§	p‖
Total number of patients	45	31	46	-	-	-	-
NLR	0.9 (0.7-1.3)	1.3 (0.9-2.4)	2.7 (1.5-5.4)	<0.001	1.000	<0.001	<0.001
MLR	0.20 (0.16-0.26)	0.22 (0.17-0.28)	0.43 (0.28-0.67)	<0.001	1.000	<0.001	<0.001
MPR	0.0020 (0.0017-0.0024)	0.0016 (0.0013-0.0020)	0.0028 (0.0021-0.0035)	<0.001	0.058	0.002	<0.001
MPV, (fL)	9.7 (9.1–10.0)	8.1 (7.1–8.2)	8.2 (7.6–9.0)	<0.001	<0.001	<0.001	0.379
WBC, (10^3/μL)	7.2 (6.3–8.4)	7.5 (7.2–8.2)	12.6 (10.9–18.0)	<0.001	1.000	<0.001	<0.001
CRP, (mg/L)	1.7 (1.3–1.9)	1.7 (1.0–2.8)	12 (5–35)	<0.001	1.000	<0.001	<0.001

***: median (IQR), †: Kruskal–Wallis test, ‡: Control vs Stone-UTI negative, §: Control vs Stone-UTI positive, ‖: Stone-UTI negative vs positive (all post hoc tests Dunn's (Bonferroni-adjusted), **NLR:** neutrophil-to-lymphocyte ratio, **MLR:** monocyte-to-lymphocyte ratio, **MPR:** monocyte-to-platelet ratio, **MPV:** mean platelet volume, **WBC:** white blood cell count, **CRP:** C-reactive protein.*

Table III: Results of ROC analysis for distinguishing the presence of UTI in the stone cohort

Parameter	AUC (95% CI)	p	Optimal cutoff	Sensitivity (%)	Specificity (%)
CRP	0.996 (0.727-1.000)	<0.001	≥5 mg/L	98.0	100
NLR	0.838 (0.535-1.000)	<0.001	≥2	74.5	92.6
MLR	0.827 (0.526-1.000)	<0.001	≥0.333	61.7	100
MPR	0.779 (0.482-1.000)	<0.001	≥0.00237	66.7	92.6
MPV	0.642 (0.512–0.773)	0.043	≥8.7 fL	42.9	92.3
CRP + NLR	0.973 (0.693-1.000)	<0.001	Probability ≥0.555	95.7	100

***AUC:** area under the curve, **CI:** confidence interval, **CRP:** C-reactive protein, **NLR:** neutrophil-to-lymphocyte ratio, **MLR**: monocyte-to-lymphocyte ratio, **MPR:** monocyte-to-platelet ratio, **MPV:** mean platelet volume, **UTI:** urinary tract infection, *: For MPV, higher values were considered indicative of UTI; AUC and the optimal cutoff were derived accordingly. For the combined CRP+NLR model, the cutoff corresponds to the predicted-probability threshold from logistic regression. p values: DeLong test, AUC vs 0.50.'*

identified in 46 of 77 stone-bearing patients (59.7%) and was more frequent in the surgical group than in the conservative group (74.2% vs 13.3%, p<0.001); management-related stone characteristics are shown in Table I.

Between-group differences in inflammatory markers

Hematological and biochemical parameters differed across the study groups. For the primary clinically relevant comparison within the stone cohort, children with concurrent UTI had higher median NLR, MLR, and MPR values and higher WBC and CRP levels than stone/UTI-negative patients (all p<0.001). Comparisons with healthy controls were retained as secondary analyses to provide biological context. In post hoc pairwise analyses, adjusted using Bonferroni or Dunn correction according to data distribution, the overall between-group differences were attributable mainly to the contrast between stone/UTI-positive and stone/UTI-negative patients (MPR, control vs. stone/UTI-positive, p=0.002, all other p<0.001). By contrast, MPV was the only parameter that differed significantly between stone/UTI-negative patients and healthy controls (Table II). MPV values were lower in the stone cohort than in controls and showed poor discriminatory performance in ROC analysis (Table III).

Diagnostic discrimination for concurrent UTI

ROC analysis used culture-confirmed UTI as the reference standard. CRP showed the highest discrimination (AUC 0.996; 95% CI 0.727–1.000); confidence intervals were wide, likely reflecting sample size and case mix. A cutoff of ≥5 mg/L yielded 98.0% sensitivity and 100% specificity (Table III). Among CBC-derived indices, NLR performed best (AUC 0.838; cutoff ≥2.0), followed by MLR (AUC 0.827; cutoff ≥0.333) and MPR (AUC 0.779; cutoff ≥0.00237). MPV showed poor discrimination (AUC 0.642; 95% CI 0.512–0.773; cutoff ≥8.7 fL) (Table III). A CRP+NLR logistic model did not improve discrimination versus CRP alone (AUC 0.973 vs 0.996; DeLong p=0.628). Stone size was not correlated with inflammatory indices (NLR: r=0.198, p=0.215).

Table IV: Inflammatory markers by collapsed stone location during culture-confirmed UTI episodes

Parameter	Upper urinary tract (renal pelvis + lower pole)*	Ureter*	Lower urinary tract (bladder + urethra) *
Total number of patients	22	23	4
WBC (×10^3/μL)	12.0 (10.9-14.1)	15.0 (9.9-18.6)	22.1 (17.8-24.2)
CRP (mg/L)	10.3 (7.9-17.5)	13.0 (10.0-82.5)	27.5 (21.8-34.8)
NLR	2.07 (0.91-3.00)	2.91 (2.31-4.56)	4.31 (3.19-4.86)
MLR	0.26 (0.15-0.33)	0.48 (0.43-0.61)	0.49 (0.49-0.50)
MPR	0.00222 (0.00137-0.00281)	0.00463 (0.00276-0.00648)	0.01017 (0.00822-0.01169)
MPV (fL)	7.95 (7.60-8.65)	8.20 (7.55-9.00)	9.10 (9.00-9.20)

**: median (IQR)*

Table V: Longitudinal inflammatory marker changes in the surgical cohort and the culture-negative postoperative fever subgroup

Parameter	Preoperative	Perioperative/Intraoperative	Postoperative	p*
Panel A. Changes across predefined time points in the surgical cohort				
WBC (×10^3/μL)*	12.1 (n=48)	7.9 (n=55)	7.2 (n=62)	<0.001
NLR*	2.67 (n=45)	1.21 (n=58)	1.40 (n=62)	<0.001
MLR*	0.43 (n=47)	0.20 (n=59)	0.22 (n=62)	<0.001
MPR*	0.00282 (n=46)	0.00175 (n=59)	0.00159 (n=62)	<0.001
MPV (fL)*	8.20 (n=47)	7.95 (n=58)	7.60 (n=62)	0.042
CRP (mg/L)*	12.0 (n=47)	1.8 (n=58)	1.7 (n=61)	<0.001
Panel B. Inflammatory marker trajectories in the culture-negative postoperative fever subgroup				
WBC (×10^3/μL)†	17.8 (13.8-18.4) (n=8)	9.9 (8.2-11.2) (n=7)	14.5 (12.0-15.1) (n=8)	-
CRP (mg/L)†	21.0 (14.5-34.5) (n=7)	1.8 (1.2-3.0) (n=7)	17.5 (11.8-24.2) (n=8)	-
NLR†	3.23 (2.36-9.5) (n=7)	1.30 (0.73-2.9) (n=7)	3.46 (3.25-5.47) (n=8)	-
MLR†	0.33 (0.30-0.46) (n=7)	0.19 (0.15-0.26) (n=7)	0.40 (0.36-0.48) (n=8)	-
MPR†	0.0028 (0.002-0.007) (n=7)	0.0017 (0.0016-0.0023) (n=7)	0.0034 (0.0022-0.0046) (n=8)	-

****: median (Wilcoxon signed-rank test), †: median (Q1-Q3)***

Adjusted analyses within the stone cohort

In exploratory multivariable logistic regression analyses adjusted for age, gender, stone size, stone location, management strategy, and hydronephrosis, log-transformed NLR remained independently associated with concurrent UTI (OR 72.14, 95% CI 3.40–1530.34; p=0.006). However, the wide confidence interval suggests substantial imprecision and possible model instability. Hydronephrosis was also independently associated with concurrent UTI (OR 3.61, 95% CI 1.38–9.40; p=0.009). By contrast, a conventional adjusted logistic model including CRP was unstable because of quasi-complete separation, precluding reliable estimation of an adjusted effect size. These findings suggest that NLR may retain an independent signal, whereas the apparent strength of CRP should be interpreted cautiously despite its high discriminatory performance in ROC analysis.

Stone location–related differences

During UTI episodes, monocyte-based indices were evaluated according to stone location (Table IV). Because some location subcategories had small sample sizes, stones were collapsed into three clinical groups for analysis: upper urinary tract (renal pelvis + lower pole), ureter (ureter + renal pelvis), and lower urinary tract (bladder + urethra). In this classification, MLR and MPR values tended to be higher in ureteral and lower urinary tract stones than in upper urinary tract stones. Only limited differences were observed across groups for MPV, and no clear location-related differences were detected for CRP or NLR. Given the small size of the lower urinary tract group, these findings were interpreted as exploratory and inferential conclusions were avoided.

Temporal changes in the surgical cohort

In the surgical cohort, temporal comparisons were based on matched repeated measurements obtained from the same patients at predefined time points. Inflammatory markers declined consistently over time (Table V, Panel A). From the preoperative UTI period, defined as within 24 hours before surgery, to the perioperative period, significant reductions were observed in WBC, NLR, MLR, MPR, and CRP (all p<0.001), whereas the change in MPV did not reach significance (p=0.065). From the perioperative period to the postoperative stone-free/UTI-free assessment performed 4 weeks after surgery, WBC showed a further significant decline, whereas the other parameters remained stable. Comparisons between preoperative UTI values and postoperative stone-free/UTI-free values also demonstrated significant decreases across all markers.

Culture-negative postoperative febrile episodes

Eight patients developed postoperative fever despite radiologic confirmation of stone-free status and negative urine cultures. In this subgroup, inflammatory markers declined from the preoperative UTI period to the intraoperative period but increased again during the postoperative febrile episode (Table V, Panel B). This pattern was consistent across WBC, CRP, and CBC-derived indices.

Discussion

Primary diagnostic message: Early identification of concurrent UTI

In this retrospective cohort of children with urolithiasis, our primary objective was to determine whether routinely available inflammatory markers could support the early identification of concurrent urinary tract infection. The main finding was that CRP showed the strongest discrimination for concurrent culture-confirmed UTI, while NLR was the most informative adjunctive complete blood count–derived index. Within the stone cohort, children with concurrent UTI exhibited a distinct systemic inflammatory profile characterized by higher WBC, CRP, and leukocyte-derived ratios than stone/UTI-negative patients, whereas MPV showed limited discriminatory utility. Importantly, adding NLR to CRP did not improve diagnostic performance beyond CRP alone. Overall, these findings support the use of CRP, with NLR as a supportive adjunct, in the early clinical assessment of suspected infection in pediatric urolithiasis.

Inflammatory profile of infection in pediatric stone disease

Pediatric urolithiasis is increasingly encountered in clinical practice and is associated with substantial recurrence risk and potential long-term morbidity (1,2). Stones may induce inflammation through urothelial irritation and epithelial barrier disruption, while superimposed infection may further amplify this response (4,5). In our cohort, children with urolithiasis and concurrent UTI had higher NLR, MLR, MPR, WBC, and CRP levels than both stone/UTI-negative patients and healthy controls, supporting the presence of a systemic inflammatory response beyond stone-related local irritation alone. This finding is consistent with the broader clinical observation that UTI accompanying stone disease is associated with greater illness severity and increased healthcare utilization (6). Comparisons with healthy controls were retained to provide biological context, but the clinically relevant contrast in this study was the distinction between stone/UTI-positive and stone/UTI-negative patients.

Discriminatory performance of CRP and CBC-derived indices

CRP provided the strongest discrimination for concurrent UTI (AUC 0.996; cutoff ≥5 mg/L), consistent with its established role as an acute-phase reactant in bacterial infection. Nevertheless, this near-perfect performance should be interpreted with caution. In a retrospective single-center cohort of modest size, ROC-based estimates may be overly optimistic because of spectrum effects, case selection, timing of sampling, and the absence of internal validation. Accordingly, CRP should be regarded as an adjunctive marker rather than a stand-alone diagnostic test, and the observed cutoff and performance estimates require prospective confirmation in broader clinical settings.

Among the CBC-derived indices, NLR showed the most useful supportive performance (AUC 0.838; cutoff ≥2.0). NLR has been widely studied as a rapid marker of systemic inflammation and physiologic stress and has also been evaluated in pediatric urolithiasis with UTI (10-12,16). Our findings suggest that NLR may provide supportive information when interpreted together with clinical and microbiological data. MLR and MPR also demonstrated moderate discriminatory performance. These monocyte-based indices may reflect monocyte activation and broader inflammatory signaling, while MPR may additionally capture aspects of platelet–immune interaction, although evidence in pediatric urolithiasis remains limited (13,17). In practical terms, these indices may provide supportive information but are unlikely to outperform CRP in routine clinical presentations.

The combined CRP+NLR model did not improve discrimination beyond CRP alone, which is clinically plausible given that both markers likely reflect overlapping aspects of infection-driven systemic inflammation rather than independent diagnostic dimensions. By contrast, MPV showed poor discriminatory performance and was not considered clinically informative in this cohort, particularly in light of its recognized pre-analytical sensitivity and inconsistent findings in the literature (14,15,18,19).

Because several clinical variables differed across the cohort, we additionally performed exploratory multivariable analyses within the stone cohort. After adjustment for age, sex, stone size, stone location, management strategy, and hydronephrosis, NLR remained independently associated with concurrent UTI, whereas hydronephrosis also remained independently associated. In contrast, CRP could not be modeled reliably in a conventional multivariable logistic framework because of quasi-complete separation, underscoring both its strong apparent signal in this dataset and the need for caution when interpreting near-perfect discrimination in a modest retrospective cohort.

The width of several confidence intervals around ROC estimates further indicates limited precision and underscores the constraints imposed by sample size.

Secondary exploratory observations: Stone size and stone location

Beyond the primary diagnostic question, we explored whether inflammatory indices varied according to stone burden and anatomical location. We did not identify a significant correlation between stone size and inflammatory markers, suggesting that the systemic inflammatory signal at presentation was driven more by infection status than by stone burden in this cohort. We also observed an exploratory tendency toward higher monocyte-based indices in ureteral and lower urinary tract stones than in upper urinary tract stones. Anatomical location may plausibly influence obstruction dynamics, mucosal irritation, and urinary stasis, thereby modulating inflammatory responses; it is also clinically relevant to symptom profile and spontaneous passage potential (9). However, because some location-specific subgroups were small, particularly the lower urinary tract group, these observations should be interpreted cautiously and regarded as hypothesis-generating rather than definitive.

Exploratory postoperative fever subgroup

We additionally described inflammatory marker trajectories in a small subgroup of children who developed postoperative fever despite radiologic stone-free status and negative urine cultures. In the broader surgical cohort, inflammatory markers declined from the preoperative UTI period to

the perioperative and postoperative stone-free/UTI-free periods, consistent with reduced inflammatory burden after infection control and stone clearance; similar peri-procedural declines in leukocyte-derived parameters have been reported in related contexts (20). In the subgroup with culture-negative postoperative fever, marker levels again increased during the febrile episode after an initial perioperative decline. Nevertheless, this subgroup was very small, and alternative explanations—including antibiotic exposure, timing of sampling, low-level infection, or other postoperative inflammatory processes—could not be excluded. Accordingly, these findings should be interpreted strictly as descriptive and hypothesis-generating. Although postoperative fever after endourological procedures has been recognized previously, the present subgroup does not support clinical inference and requires confirmation in larger, prospectively characterized cohorts (21).

Clinical implications

From a clinical perspective, one of the main challenges in children presenting with urolithiasis is deciding whether empiric antibiotic therapy is warranted while urine culture results are pending. In this cohort, CRP and, to a lesser extent, NLR were associated with concurrent culture-confirmed UTI and may offer supportive information during early assessment. However, these markers should not replace urine culture or comprehensive clinical evaluation, and the very high discriminatory estimates observed here should be interpreted cautiously given the retrospective design, limited sample size, and lack of internal validation.

Limitations

This study has several strengths, including the concurrent evaluation of multiple complete blood count–derived indices together with CRP and its focus on a clinically relevant diagnostic question within the stone cohort. Several limitations should also be acknowledged. The retrospective single-center design limits generalizability and introduces the potential for selection bias and unmeasured confounding. The control and stone groups also differed in age and gender; although the multivariable model was adjusted for these covariates, residual confounding cannot be excluded. Although key sampling windows were predefined, the study remained based on routine-care retrospective data. Although the UTI definition was intentionally culture-based to improve diagnostic specificity in a setting where stone-related irritation may mimic infection, some misclassification remains possible; however, the use of midstream urine specimens and the absence of pyuria in culture-negative cases reduce the likelihood of substantial classification error. The culture-negative postoperative fever subgroup was very small and exploratory, precluding exclusion of alternative explanations for marker re-elevation. Moreover, given the number of comparisons performed across biomarkers, groups, and exploratory subanalyses, findings beyond the primary diagnostic question should be interpreted cautiously. Finally, the very high AUC observed for CRP may reflect spectrum effects, and without internal validation the reported discriminatory estimates may be optimistic; the wide confidence intervals around several ROC estimates further indicate limited precision. Prospective multicenter studies are needed before these findings can be confirmed..

Conclusion

In pediatric urolithiasis, CRP demonstrated the strongest diagnostic discrimination for concurrent culture-confirmed UTI, whereas NLR was the most informative supportive complete blood count–derived index. Secondary exploratory observations, including those related to stone location and culture-negative postoperative fever, should be interpreted cautiously and confirmed in larger cohorts. Overall, the present findings are preliminary and require prospective validation before informing routine clinical application.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Gaziantep City Hospital (March 19, 2025, reference number: 145/2025).

Contribution of the authors

DY: Study conception and design, data collection, data analysis and interpretation, literature review, manuscript drafting. HTT: Supervision, critical revision of the manuscript. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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