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Original Article

# C-reactive protein as a predictor of complication and hospital stay in pediatric appendicitis: Role of inflammatory biomarkers

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## ABSTRACT

**Objective:** Acute appendicitis (AA) is a leading cause of pediatric abdominal pain requiring surgical intervention. Differentiating simple appendicitis (SA) from complicated appendicitis (CA) preoperatively remains a clinical challenge. This study aimed to evaluate the diagnostic and prognostic utility of routinely available inflammatory markers—including C-reactive protein (CRP), fibrinogen, immature granulocyte (IG) count and percentage, neutrophil-to-lymphocyte ratio (NLR), and mean platelet volume (MPV)—in children with AA.

**Material and Methods:** This retrospective study included pediatric patients (<18 years) who underwent appendectomy for AA between January 2020 and December 2022. Patients were categorized as having SA or CA based on intraoperative and histopathological findings. Preoperative laboratory parameters were compared between groups. Spearman correlation and regression analyses were performed to assess associations with complication status and hospitalization duration.

**Results:** A total of 94 patients were included (mean age: 12.1±3.6 years; 63.8% male). CA was identified in 9 patients (9.6%). CRP levels were significantly higher in the CA group (p = 0.043) and independently predicted complications (OR: 1.018, 95% CI: 1.005–1.032, p =0.009). CRP was moderately correlated with both hospital stay (r =0.369, p <0.001) and fibrinogen levels (r =0.525, p <0.001). In multivariate linear regression, CRP remained a significant predictor of prolonged hospitalization (β =0.365, p =0.002), while fibrinogen did not. IG count, IG percentage, NLR, and MPV were not significantly associated with complication status or hospital stay.

**Conclusion:** CRP is a practical and reliable marker for predicting both complicated appendicitis and prolonged hospitalization in children. Fibrinogen is associated with disease burden but lacks independent predictive value. IG%, NLR, and MPV did not demonstrate clinical utility in this cohort. CRP may aid in preoperative risk stratification and postoperative care planning in pediatric AA.

**Keywords:** Appendicitis, C-reactive protein, fibrinogen, inflammatory markers

## INTRODUCTION

Acute appendicitis (AA) is one of the most common causes of abdominal pain and emergency surgical intervention in children (1–3). Although most cases present as simple appendicitis (SA), a significant proportion may progress to complicated appendicitis (CA), characterized by perforation, gangrene, or intra-abdominal abscess formation. Preoperative differentiation between SA and CA is critical for guiding timely surgical intervention, anticipating potential complications, and determining the length of hospital stay (4).

In pediatric patients, where the clinical presentation can often be atypical or nonspecific, reliance on laboratory parameters becomes especially important. Traditional inflammatory biomarkers—such as white blood cell (WBC) count, absolute neutrophil count (ANC), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP)—have been widely used to aid diagnosis and assess disease severity (5–7). Among these, CRP is often highlighted for its moderate predictive value in identifying CA, although its diagnostic accuracy may vary depending on the timing of measurement and patient age.

More recently, attention has turned to hematological markers that can be obtained automatically without requiring additional tests or blood draws. One such parameter is the immature granulocyte (IG) count and percentage, which reflects the early release of granulocytic precursors (promyelocytes,



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myelocytes, metamyelocytes) into the bloodstream during systemic inflammatory responses (8–10). Several studies have suggested that elevated IG values may have diagnostic and prognostic value in infectious and inflammatory diseases such as sepsis, urinary tract infections, and intra-abdominal infections, including appendicitis (9-11).

Despite promising findings in some reports, the diagnostic performance of IG percentage in distinguishing between SA and CA in children remains uncertain. Variation in sample size, patient age, and definition of complication severity may contribute to inconsistent results across studies (11-13). Therefore, there is still a need for further observational data, particularly from real-world, smaller-scale pediatric cohorts.

In this study, we aimed to evaluate the distribution and potential clinical relevance of several inflammatory markers—including CRP, WBC, ANC, NLR, MPV, IG count, and IG percentage—in pediatric patients with AA. In addition, we assessed length of hospital stay as a clinical outcome measure to further explore its association with disease severity. Although the number of complicated cases in our sample is limited, we sought to observe whether meaningful trends could be identified and compared to patterns described in the literature. We hypothesized that CRP and other inflammatory markers could serve as reliable predictors of complicated appendicitis and prolonged hospital stay in children.

## MATERIALS and METHODS

This retrospective study was conducted in the Pediatrics and Pediatric Surgery units of two tertiary care centers in Tokat, Türkiye. Pediatric patients under the age of 18 who underwent surgery with a preoperative diagnosis of acute appendicitis between January 2020 and December 2022 and were histopathologically confirmed to have acute appendicitis were evaluated using electronic medical records

Patients were included if they had undergone surgery for suspected acute appendicitis and had available preoperative laboratory parameters including complete blood count (CBC), C-reactive protein (CRP), fibrinogen, and immature granulocyte (IG) values. Patients were excluded if they had chronic inflammatory diseases (e.g., inflammatory bowel disease, autoimmune disorders), hematological malignancy, ongoing infection other than appendicitis, or if they had received antibiotics prior to hospital admission. Patients with normal appendix on histopathological examination were also excluded.

Patients were classified into two groups based on intraoperative findings and histopathology reports:

- Simple appendicitis (SA): including catarrhal and phlegmonous appendicitis
- Complicated appendicitis (CA): including perforation, abscess formation, gangrene, or the presence of intra-abdominal fecaliths

Demographic data including age, sex, and length of hospital stay (in days) were recorded. Preoperative laboratory parameters including white blood cell (WBC) count, neutrophil and lymphocyte counts, immature granulocyte (IG) count and percentage, CRP, fibrinogen, mean platelet volume (MPV), and neutrophil-to-lymphocyte ratio (NLR) were collected from hospital records. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

IG values were measured using an automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan), which detects promyelocytes, myelocytes, and metamyelocytes as part of the IG cluster.

### Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean and standard deviation or median (minumum-maximum), depending on the data distribution. Categorical variables were presented as frequency and percentage.

The Mann–Whitney U test was used to compare laboratory parameters between the simple and complicated appendicitis groups. Spearman correlation analysis was used to assess the relationship between inflammatory markers and length of hospital stay. Logistic regression was performed to identify predictors of complicated appendicitis, and linear regression analysis was used to evaluate factors associated with hospitalization duration. A $p < 0.050$ was considered statistically significant.

## RESULTS

A total of 94 pediatric patients who underwent surgery for acute appendicitis were included in the study. Of these, 85 patients (90.4%) were classified as having simple appendicitis, and 9 patients (9.6%) as complicated appendicitis. The mean age of the patients was 12.1±3.6 years, with a male predominance (63.8% male, 36.2% female).

When comparing laboratory parameters between the two groups using the Mann–Whitney U test, C-reactive protein (CRP) levels were significantly higher in the complicated appendicitis group ($p = 0.043$). Additionally, the length of hospital stay was significantly longer in the complicated group ($p = 0.001$).

No statistically significant differences were observed between the groups in terms of age ($p = 0.742$), WBC count ($p = 0.546$), absolute neutrophil count ($p = 0.507$), immature granulocyte count ($p = 0.682$), IG percentage ($p = 0.795$), NLR ($p = 0.708$), fibrinogen ($p = 0.419$), or MPV ($p = 0.289$). The median values and ranges of each parameter by group are presented in Table I.

Spearman correlation analysis showed a moderate positive correlation between CRP and both length of hospital stay ($r = 0.369$, $p < 0.001$) and fibrinogen levels ($r = 0.525$, $p < 0.001$). Similarly,

**Table I: Comparison of laboratory parameters between simple and complicated appendicitis groups**

| Parameter | Simple Appendicitis* | Complicated Appendicitis* | p† |
|---|---|---|---|
| Age (years) | 12.0 (4–18) | 12.0 (7–15) | 0.742 |
| WBC ($10^9$/L) | 15.3 (4.3–34.2) | 16.9 (10.3–21.7) | 0.546 |
| ANC ($10^9$/L) | 12.0 (2.65–29.6) | 14.6 (9.3–22.1) | 0.507 |
| IG | 0.07 (0–0.54) | 0.08 (0.01–0.22) | 0.682 |
| IG (%) | 0.50 (0.1–3.6) | 0.80 (0.2–1.9) | 0.795 |
| NLR | 7.34 (1.1–31.7) | 9.1 (2.7–16.2) | 0.708 |
| Fibrinogen (mg/dL) | 333.3 (33.3–586.2) | 390.7 (241.0–481.2) | 0.419 |
| MPV (fL) | 9.20 (7.4–12.8) | 8.9 (7.8–10.6) | 0.289 |
| CRP (mg/L) | 28.5 (0.1–149.0) | 115.7 (10.4–149.0) | 0.043 |
| Length of Stay (days) | 2.0 (1–12) | 3.0 (2–7) | 0.001 |

***:** *median (min–max),* **†:** *Mann–Whitney U test.* ***WBC:** white blood cell count,* ***ANC:** absolute neutrophil count,* ***IG:** immature granulocyte,* ***NLR:** neutrophil-to-lymphocyte ratio,* ***MPV:** mean platelet volume,* ***CRP:** C-reactive protein*

**Table II: Spearman correlation coefficients between laboratory parameters and hospital stay / complication status**

| Variable | Hospital Stay | | Complication Status | |
|---|---|---|---|---|
| | r | p* | r | p* |
| CRP | 0.369 | < 0.001 | 0.215 | 0.042 |
| Fibrinogen | 0.358 | 0.001 | 0.087 | 0.422 |
| IG | –0.046 | 0.669 | –0.044 | 0.684 |
| IG% | –0.059 | 0.585 | 0.028 | 0.797 |
| NLR | 0.083 | 0.432 | 0.039 | 0.710 |
| MPV | –0.063 | 0.548 | –0.111 | 0.292 |

***:** *Spearman's rho correlation coefficients,* ***IG:** immature granulocyte,* ***NLR:** neutrophil-to-lymphocyte ratio,* ***MPV:** mean platelet volume,* ***CRP:** C-reactive protein.*

**Table III: Logistic regression for complicated appendicitis**

| Predictor | OR (Exp(B)) | 95% CI | p |
|---|---|---|---|
| CRP | 1.018 | 1.005–1.032 | 0.009 |
| Fibrinogen | 1.005 | 0.997–1.013 | 0.219 |

***CRP:** C-reactive protein*

**Table IV: Linear regression for hospital stay**

| Predictor | β (Standardized) | B (Unstd.) | p | Model Type |
|---|---|---|---|---|
| CRP | 0.470 | 0.018 | <0.001 | Univariate |
| Fibrinogen | 0.360 | 0.007 | 0.001 | Univariate |
| CRP | 0.365 | 0.014 | 0.002 | Multivariate |
| Fibrinogen | 0.161 | 0.003 | 0.168 | Multivariate |

***CRP:** C-reactive protein, Model $R^2$ (multivariate) = 0.222, Adjusted $R^2$ = 0.203*

fibrinogen was moderately correlated with hospitalization duration (r =0.358, p =0.001). A strong positive correlation was also observed between IG percentage and IG count (r =0.897, p <0.001); however, neither showed any significant association with hospital stay or complication status. Other parameters, including NLR and MPV, were also not significantly correlated with clinical outcomes (p >0.050 for all) (Table II).

Univariate logistic regression revealed that CRP was a significant predictor of complicated appendicitis (OR: 1.018, 95% CI: 1.005–1.032, p =0.009), whereas fibrinogen was not (p =0.219) (Table III). Regarding hospitalization duration, both CRP (β =0.470, p <0.001) and fibrinogen (β =0.360, p = 0.001) were found to be positively associated in univariate linear regression. In multivariate analysis including both markers, only CRP remained statistically significant (β =0.365, p =0.002), while fibrinogen did not (p =0.168) (Table IV).

## DISCUSSION

Acute appendicitis is the most common surgical emergency in children and can progress from a benign inflammatory process to a severe, complicated condition involving perforation, abscess, or gangrene. Identifying markers that accurately predict disease severity is essential for optimizing management and improving outcomes.

In this study, CRP emerged as both the most reliable diagnostic and prognostic biomarker. CRP levels were significantly higher in complicated cases and independently predicted complication status in univariate logistic regression (OR =1.018; 95% CI:1.005–1.032; p =0.009). CRP also showed a moderate positive correlation with hospital stay (r =0.369; p <0.001) and remained an independent predictor of prolonged hospitalization in multivariate linear regression (β = 0.365; p = 0.002). These results are consistent with Beltran et al. (14), who reported that CRP >80 mg/L predicted perforation with high sensitivity (82%) in children , and Xharra et al. (15), who found CRP >50 mg/L significantly correlated with abscess formation.

The biological context for CRP's predictive power lies in its acute-phase regulation by interleukin6 (IL6), which elevates rapidly after tissue injury or bacterial invasion (16). IL6, along

with interleukin1β (IL1β) and tumor necrosis factorα (TNFα), induces hepatocyte synthesis of CRP, which then facilitates complement activation and opsonization (17). In complicated appendicitis, transmural inflammation, neutrophil infiltration, and bacterial translocation accentuate cytokine release, leading to sharply elevated CRP and fibrinogen levels (16,17).

Fibrinogen, another acute-phase reactant, was moderately correlated with both CRP ($r = 0.525$; $p < 0.001$) and hospital stay ($r = 0.358$; $p = 0.001$), reflecting its role in clotting and inflammation. Although it failed to be an independent predictor in logistic regression, its elevation likely represents a response to endothelial activation and systemic inflammation driven by IL6 and IL1β (18). Alvarez et al .(19) similarly reported increased fibrinogen in perforated appendicitis, though its predictive value diminished when adjusted for CRP.

We assessed immature granulocyte (IG) count and percentage as early hematologic markers. IGs surge in the marrow during systemic inflammation and are measurable by modern hematology analyzers (20). Güngör et al. (21) previously demonstrated that elevated IG% could predict complicated appendicitis in children (AUC = 0.78). However, in our cohort neither IG nor IG% correlated with complications or hospital stay—despite their strong internal correlation ($r = 0.897$; $p < 0.001$). This discrepancy may be due to differing analyzer thresholds, sample timing relative to symptom onset, or the small number of complicated cases limiting statistical power.

Neutrophil-to-lymphocyte ratio (NLR) has been studied widely in both adult and pediatric AA, with some series demonstrating NLR >5 as a predictor of perforation (22,23). Mechanistically, stress-induced neutrophilia and lymphopenia produce a high NLR, reflecting systemic inflammation. However, our study did not support NLR as a reliable marker, perhaps due to variability in immune response among children or early presentation before peak leukocyte changes. This lack of correlation may also be explained by the relatively small number of complicated cases, reducing statistical power and masking potential associations.

Similarly, mean platelet volume (MPV) has been proposed as a marker of platelet activation in inflammation (24). High MPV may indicate heightened cytokine-mediated platelet production. Yet, we found no association between MPV and complication status or hospital stay, reinforcing the inconsistent reliability of this marker in AA.

From a pathophysiological standpoint, complicated appendicitis follows a sequence: mucosal ulceration→transmural necrosis→wall perforation → peritoneal contamination. Neutrophil infiltration and bacterial translocation trigger a cytokine cascade dominated by IL1β, TNFα, and IL6 (16,17). IL6 stimulates acute-phase protein synthesis (CRP, fibrinogen), while IL1β/TNFα contribute to local capillary dilation and tissue injury (17). Lysozyme and protease release by neutrophils may also facilitate abscess formation. As such, CRP and fibrinogen rise rapidly and correlate with both clinical severity and systemic recovery time.

Importantly, our findings highlight that CRP's prognostic utility extends beyond diagnostic discrimination to clinical management. Its correlation with hospital stay duration suggests that this routinely available marker may guide expectations for postoperative recovery, antibiotic duration, and discharge planning—a potential benefit corroborated by Yüksel et al. (25), who found elevated CRP predicted prolonged recovery in pediatric AA .

Strengths of our study include its focus on a pediatric population with preoperative laboratory data and validated outcomes, comprehensive analysis of multiple biomarkers, and use of robust statistical methods including multivariate modeling. Nonetheless, limitations must be acknowledged: the retrospective, single-center design carries inherent bias; the number of complicated cases was small; and laboratory sampling timing was variable. Additionally, while IL1β and TNFα were not measured directly, their known role in the inflammatory cascade provides a pathophysiologic basis for our findings.

In conclusion, CRP remains the most practical and reliable indicator of both complicated appendicitis and hospital stay duration in children. Fibrinogen correlates with disease burden but lacks independent predictive strength, and emerging markers such as IG%, NLR, and MPV were not significant in our cohort. Importantly, the clinical implications of these findings suggest that CRP could be incorporated into perioperative decision-making: higher CRP levels may help identify children at greater risk of complications, guide the urgency of surgical intervention, inform the intensity and duration of antibiotic therapy, and aid in planning discharge timing. Future prospective multi-center studies should seek to determine optimal CRP thresholds and explore integrated biomarker panels that might include cytokines or IG metrics, to enhance early risk stratification and tailor pediatric appendicitis management.

## Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Tokat Gaziosmanpasa University (03.06.2021, reference number: 83116987-506 ).

## Contribution of the authors

Study conception and design: ***AİÇ, SC;*** data collection: ***SC***; analysis and interpretation of results: ***AİÇ, SC***; draft manuscript preparation: ***AİÇ, SC***. 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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