



Effectiveness of Laboratory Parameters in Predicting Complicated Acute Appendicitis in Pregnant Patients: A Retrospective Analysis

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ABSTRACT

Aim: Acute appendicitis during pregnancy presents a diagnostic challenge due to physiological and anatomical changes that can obscure classical symptoms. This study aimed to evaluate the predictive value of inflammatory markers—particularly C-reactive protein (CRP) and the CRP/albumin ratio (CAR)—for detecting complicated acute appendicitis in pregnant women.

Method: This retrospective study included 67 pregnant patients who underwent appendectomy for acute appendicitis between October 2019 and December 2024. Patients were categorized into complicated and non-complicated appendicitis groups based on histopathological findings. Laboratory parameters comprising the platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, neutrophil-to-lymphocyte ratio, systemic immune inflammation index, systemic inflammatory response index, receiver operating characteristic (ROC) curve, and decision curve analysis (DCA) were used to assess diagnostic and clinical performance.

Results: Complicated appendicitis was identified in 25.4% (n=17) of patients. Multivariate regression demonstrated that CRP [odds ratio (OR)=1.095; 95% confidence interval (CI)=1.042-1.151; p<0.001] and CAR (OR=23.863; 95% CI=4.223-134.830; p<0.001) were independent predictors. The ROC analysis demonstrated high diagnostic accuracy for CRP [area under the curve (AUC)=0.954] and CAR (AUC=0.946). The DeLong test revealed no significant difference between CRP and CAR (p=0.878), and DCA confirmed that both markers provided higher net clinical benefit than “treat-all” or “treat-none” strategies.

Conclusion: The results show that CRP and CAR may be promising, cost-effective biomarkers for early identification of complicated appendicitis in pregnancy, particularly where imaging is limited, but these single-center data require cautious interpretation and external validation before routine clinical use.

Keywords: Acute appendicitis, pregnancy, C-reactive protein, C-reactive protein/albumin ratio, inflammation markers

Introduction

Acute appendicitis is the most common non-obstetric surgical emergency during pregnancy, with an incidence reported in approximately 0.01-0.2% of all pregnancies.¹ Anatomical and physiological changes that occur during pregnancy make diagnosis difficult. The displacement of abdominal organs due to uterine enlargement, changes in pain localization, and pregnancy-related physiological leukocytosis are the main causes of these difficulties. In addition, symptoms such as

nausea, abdominal pain, or mild fever seen in pregnancy can mask the symptoms of appendicitis. Therefore, delays in diagnosis are common, increasing the risk of both maternal and fetal complications. Early diagnosis and surgical intervention are critical in preventing perforated appendicitis and associated fetal loss.^{1,2}

Clinical evaluation and imaging methods may have limited diagnostic value during pregnancy. Ultrasonography may be inadequate in the later stages of pregnancy due to uterine enlargement, but magnetic resonance imaging (MRI) is not



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available at every center. This situation leads clinicians to use laboratory markers as a diagnostic support tool. Inflammatory markers such as the platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), and systemic immune inflammatory index (SII) have been proposed as potential diagnostic and prognostic tools in the literature, including for appendicitis and predicting complications.^{3,4} C-reactive protein (CRP) is an inflammatory acute-phase reactant produced by the liver in response to inflammation or infection.⁴ However, a slight increase in CRP levels may be observed physiologically during pregnancy, which may reduce the specificity of the test.

The CRP/albumin ratio (CAR) is a parameter obtained by dividing the CRP level by the level of albumin, a protein in the blood, and has shown promise as a prognostic marker in several inflammatory conditions, where it helps predict the severity of the disease.⁴

Nevertheless, despite their potential, there is a notable absence of studies that validate the diagnostic and prognostic relevance of these clinical evaluation and imaging methods in forecasting complications associated with acute appendicitis during pregnancy.⁵

This study evaluated clinical characteristics, inflammatory markers, and outcomes in patients who underwent surgery for acute appendicitis during pregnancy. The study hypothesis was that CRP and CAR could be independent predictors of complicated acute appendicitis during pregnancy. Furthermore, the relationship between these parameters and other hematologic indices (NLR, PLR, SII, etc.) and the development of complications was investigated. Evaluating the diagnostic performance of these parameters may contribute to improving clinical outcomes for both the mother and fetus by supporting early diagnosis and appropriate treatment decisions.

Materials and Methods

This study is a single-center, retrospective observational study conducted in the general surgery clinic of a tertiary care hospital between October 2019 and December 2024. To reduce bias, standardized diagnostic and pathological criteria were applied across all cases. The research was conducted in accordance with the Declaration of Helsinki, and ethical principles were observed. This study was approved by the local ethics committee of Ankara Bilkent City Hospital (decision number: 1-25-1008, date: 12.02.2025). Due to the retrospective nature of the study, individual informed consent was not obtained from patients; data were evaluated with identity information concealed.

Inclusion criteria for the study were cases of acute appendicitis during pregnancy that underwent surgery with a diagnosis of

acute appendicitis and histopathological confirmation. Exclusion criteria were active infection, autoimmune disease, malignancy, liver or kidney failure, hematologic diseases, and systemic steroid use. The study confirmed that there were no missing data. If missing observations were detected in the dataset, these cases were excluded from the analysis. Accordingly, 67 patients were included in the analysis (Figure 1).

Age, gestational age, pregnancy trimester, and laboratory results were evaluated in all patients. Laboratory samples were collected from all patients within the first 2 hours after presentation to the emergency department prior to surgery.

Specifically, albumin was included as a well-established negative, acute-phase reactant that decreases in the presence of major intra-abdominal inflammation and has been identified in previous studies as a marker of complicated appendicitis.⁶ Total bilirubin was evaluated because hyperbilirubinemia has been consistently associated with perforated or gangrenous appendicitis, largely through mechanisms involving hepatocellular dysfunction and endotoxin-mediated cholestasis.⁷ Electrolytes—particularly sodium—were assessed given evidence that hyponatremia frequently accompanies severe systemic inflammation and has been reported in patients with complicated appendicitis.⁸ Hemogram-derived inflammatory indices [NLR, PLR, LMR, SII, and the systemic immune response index (SIRI)] were incorporated based on robust studies demonstrating their predictive value for perforation, disease severity, and adverse clinical outcomes.^{3,4} Amylase was included because mild elevations have been reported in advanced intra-abdominal inflammation, particularly in cases of peritoneal irritation or localized enzymatic activation accompanying complicated appendicitis. Clinical series evaluating atypical biochemical

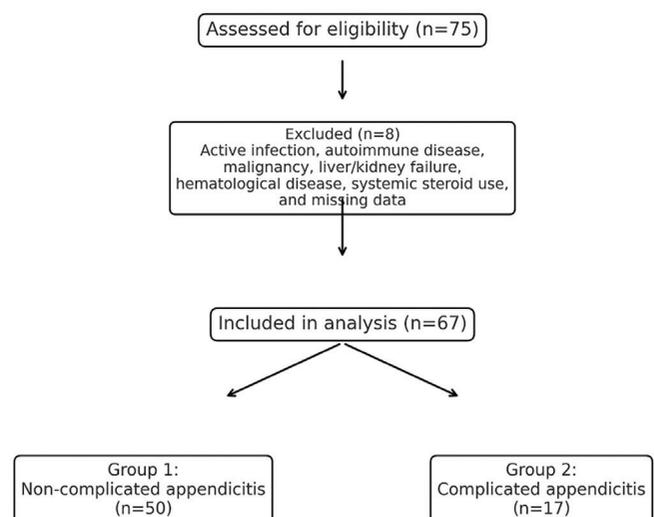


Figure 1. Flowchart of patient selection and grouping

profiles in perforated appendicitis have described transient increases in amylase, suggesting a secondary inflammatory or enzymatic response. Although not a standard marker of appendicitis, its assessment has been considered relevant in studies investigating broader biochemical changes in severe intra-abdominal infection. Accordingly, all biochemical and hematologic variables included in this study were selected a priori based on their literature-supported mechanistic relevance to inflammatory severity rather than simply being routinely collected laboratory measurements.

Laboratory markers included white blood cell count, neutrophil count, lymphocyte count, monocyte count, platelet count, CRP, albumin, sodium, and bilirubin.

Pregnancy periods were evaluated in three groups: first trimester ($\leq 13^{+6}$ weeks), second trimester (14^{+0} - 27^{+6} weeks), and third trimester (28^{+0} - 40^{+6} weeks). The relationship between the trimester and complications was evaluated in exploratory subgroup analyses. Inflammatory markers were also compared among trimesters (Supplementary Table 1).

Inflammatory markers were calculated as follows:

PLR: platelet/lymphocyte

LMR: lymphocyte/monocyte

NLR: neutrophil/lymphocyte

SII: neutrophil \times platelet/lymphocyte

SIRI: neutrophil \times monocyte /lymphocyte

CRP-to-albumin ratio: CRP/albumin.

All patients underwent ultrasonography in the preoperative period. MRI was performed in patients whose appendix could not be visualized on ultrasound (US).

All patients underwent surgery for appendicitis. The specimens were examined pathologically and divided into two groups according to the histopathologic results.

Group 1: Non-complicated acute appendicitis. Phlegmonous and acute nonperforated appendicitis cases were included in the uncomplicated group.

Group 2: Complicated acute appendicitis. Complicated appendicitis was defined as cases in which intra-abdominal fecalitis, abscess, gangrene-necrotizing perforated appendicitis, or peritonitis were detected intraoperatively or histopathologically.

Due to the retrospective nature of the study, no prior sample size or power analysis was performed. All eligible patients accessible during the study period were included in the analysis.

Statistical Analyses

Statistical analyses were performed using SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Additionally, decision curve analysis (DCA) was conducted using the R software environment (R Foundation for Statistical

Computing, Vienna, Austria). The distribution of continuous variables was assessed using the Shapiro-Wilk test. Variables showing a normal distribution were presented as mean \pm standard deviation, and non-normally distributed variables were presented as median (minimum-maximum) values. Categorical variables were expressed as frequency (percentage). To evaluate differences between groups, the Student's t-test or Mann-Whitney U test was used for continuous variables, and the chi-square test or Fisher's exact test was used for categorical variables. The possibility of collinearity was assessed among the CRP, albumin, and CAR variables using Spearman correlation analysis and the variance inflation factor (VIF). Variables showing high correlation were not used together in the same model, and VIF analysis was performed to evaluate multicollinearity among independent variables.

To identify independent variables associated with the development of complicated appendicitis, univariate logistic regression analysis was first performed, followed by multivariate logistic regression analysis of variables with a p-value < 0.2 . The backward likelihood ratio method was used in multiple regression analysis. The VIF values for CRP and CAR were both above 100, indicating severe multicollinearity; therefore, CRP and CAR were not included together in the same regression model and were analyzed separately in two independent multivariate models to prevent collinearity bias. All other variables had VIF values below 2.0, indicating no significant collinearity.

Due to the limited number of events, only statistically significant variables were included in the model. Results were reported as odds ratios (ORs), 95% confidence intervals (CIs), and p-values. Receiver operating characteristic (ROC) curves were generated to evaluate diagnostic performance. For each marker, the area under the curve (AUC), 95% CIs, sensitivity, specificity, and positive and negative predictive values (PPV/NPV) were calculated. The optimal cut-off points in the ROC analyses were determined using the Youden index. Decision curve analysis was conducted to assess the net clinical benefit of the CRP and CAR models. Statistical significance was set at $p < 0.05$.

Results

A total of 67 out of 73 patients met the inclusion criteria and were included in the analysis. The mean age was 28.41 ± 5.48 years (19-41 years). Seventeen of the patients (25.4%) had complicated acute appendicitis. The mean gestational age was 18.13 ± 8.15 weeks, with a minimum of 4 weeks and a maximum of 36 weeks. MRI was performed in 20 patients (29.9%). Patient data are presented in Table 1.

According to univariate regression analysis, three parameters were associated with complicated acute appendicitis: CRP, LMR, and CAR ($p < 0.001$, $p = 0.028$, and $p < 0.001$, respectively)

Table 1. Data of complicated appendicitis and non-complicated appendicitis groups

| | Total (n=67) | Non-complicated (n=50) | Complicated (n=17) | p-value |
|---|-----------------------------|-----------------------------|-----------------------------|---------|
| Age, years, (mean ± SD) | 28.41±5.48 | 28.22±5.83 | 29.0±4.35 | 0.564 |
| Gestational age, weeks, (mean ± SD) | 18.13±8.15 | 17.54±7.92 | 19.88±8.80 | 0.341 |
| Trimester, (%) | | | | |
| Trimester | 22 (32.8%) | 17 (77.3%) | 5 (22.7%) | 0.416* |
| Trimester | 36 (53.7%) | 28 (77.8%) | 8 (22.2%) | |
| Trimester | 9 (13.4%) | 5 (55.6%) | 4 (44.4%) | |
| Albumin, g/L, (mean ± SD) | 39.871±3.58 | 39.74±3.70 | 39.64±3.31 | 0.923 |
| Total bilirubin, mg/dL, median (min-max) | 0.5 (0.10-1.10) | 0.4 (0.1-1.10) | 0.5 (0.30-0.99) | 0.026 |
| Amylase, U/L, (mean ± SD) | 60.11±16.73 | 61.64±15.88 | 55.60±18.79 | 0.246 |
| Sodium, mEq/L, median (min-max) | 137 (132-141) | 137 (133-141) | 137 (132-141) | 0.489 |
| Calcium, mg/dL, (mean ± SD) | 8.74±0.48 | 8.75±0.49 | 8.72±0.53 | 0.764 |
| WBC, ×10 ⁹ /L, (mean ± SD) | 13.54±4.47 | 13.33±4.39 | 14.18±4.77 | 0.521 |
| Neutrophil, ×10 ⁹ /L, median (min-max) | 10.56 (2.41-27.18) | 10.54 (2.41-27.18) | 12.50 (4.80-21.09) | 0.280 |
| Neutrophil, %, median (min-max) | 83.0 (54.3-94.1) | 81.35 (54.3-94.1) | 85.70 (68.3-92.1) | 0.053 |
| Lymphocyte, ×10 ⁹ /L, median (min-max) | 1.37 (0.33-3.81) | 1.50 (0.33-3.81) | 1.34 (0.55-2.80) | 0.089 |
| Monocyte, ×10 ⁹ /L, median (min-max) | 0.54 (0.20-2.55) | 0.53 (0.220-1.23) | 0.54 (0.26-2.55) | 0.943 |
| MPV, fL, median (min-max) | 8.2 (6.5-16.2) | 8.2 (6.5-16.2) | 8.3 (6.8-10.4) | 0.624 |
| Platelet, ×10 ⁹ /L, median (min-max) | 257. (159.0-455.0) | 253 (165-447) | 261 (159-455) | 0.729 |
| RDW, %, median (min-max) | 14.2 (12.7-58.1) | 14.2 (12.7-21.4) | 14.2 (12.8-58.1) | 0.846 |
| LUC, %, (mean ± SD) | 0.13±0.05 | 0.13±0.04 | 0.12±0.06 | 0.751 |
| DNI, %, median (min-max) | 0.01 (0.00-12.70) | 0.10 (0-7.80) | 0.01 (0-12.7) | 0.652 |
| CRP, mg/L, median (min-max) | 14.0 (0.1-230) | 10.0 (0.1-70) | 57.0 (13.0-230.0) | <0.001 |
| PLR, median (min-max) | 170.64 (67.03-875.76) | 169.75 (67.03-875.76) | 187.32 (113.57-659.42) | 0.116 |
| LMR, median (min-max) | 2.89 (0.88-6.17) | 3.13 (0.97-6.17) | 2.25 (0.88-4.67) | 0.026 |
| NLR, median (min-max) | 6.71 (1.54-27.45) | 6.41 (1.54-27.45) | 8.92 (3.43-23.58) | 0.032 |
| SII, median (min-max) | 3.57 (0.39-17.50) | 3.49 (0.39-17.02) | 4.33 (1.03-17.50) | 0.048 |
| SIRI, median (min-max) | 1,724.58 (449.43-10,728.77) | 1,591.47 (449.43-10,515.09) | 2,341.54 (545.14-10,728.77) | 0.059 |
| CAR, median (min-max) | 0.34 (0.00-5.90) | 0.26 (0-2.0) | 1.39 (0.34-5.90) | <0.001 |
| Imaging | | | | |
| USG | 47 (70.1%) | 37 (78.7%) | 10 (21.3 %) | 0.237 |
| USG + MRI | 20 (29.9%) | 13 (65.0%) | 7 (35.0%) | |

*Fisher's exact test

WBC: White blood cell count, MPV: Mean platelet volume, RDW: Red blood cell distribution width, LUC: Large unstained cells, DNI: Delta neutrophil index, CRP: C-reactive protein, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic immune inflammatory index, SIRI: Systemic immune response index, CAR: CRP/albumin ratio

(Table 2). CRP and CAR were evaluated in two separate multivariate models due to significant collinearity (VIF>100). Multivariate analysis revealed that CRP (OR: 1.095, 95% CI: 1.042-1.151; p<0.001) and CAR (OR=23.863; 95% CI: 4.223-134.830; p<0.001) were independent predictors (Table 2, Figure 2). Total bilirubin initially appeared significant in univariate group comparison (p=0.026); however, it was not independently associated with complicated appendicitis in univariate logistic regression (p=0.139). As a result, bilirubin did not meet the criteria for multivariate inclusion and was removed during the backward elimination steps. Therefore, bilirubin was considered a negative finding in the adjusted analysis and was not retained as a clinically meaningful predictor.

The ROC curve was performed for CRP and CAR. For CRP, the cut-off value was found to be 23 mg/L (AUC=0.954, 95% CI=0.903-1.000, p<0.001, sensitivity=94.1%, specificity 86.0%). For CAR, the cut-off value was found to be 0.55 (AUC=0.946, 95% CI=0.893-0.999, p<0.001, sensitivity=94.1%, specificity 86.0%) (Figure 3). When the CRP cut-off value was 23 mg/L

and the CAR cut-off value was 0.55, the PPV was 69.9% and the NPV was 97.7% (Table 3). Comparison of the ROC curves using the DeLong method revealed no statistically significant difference between CRP and CAR (AUC 0.954 vs. 0.946, p=0.878), indicating comparable discriminatory performance. Decision curve analysis demonstrated that both the CRP and CAR models provided a higher net clinical benefit across most threshold probabilities (0.10-0.45) than the “treat-all” and “treat-none” strategies, indicating good clinical usefulness (Figure 4).

In exploratory subgroup analyses, no statistically significant differences were observed in CRP, CAR, or other inflammatory indices among the first, second, and third trimesters (p>0.05). However, a numerically higher rate of complicated appendicitis was observed in the third trimester (44.4%) than in the first and second trimesters (22.7% and 22.2%, respectively) (Supplementary Table 1).

Table 2. Univariate and multivariate logistic regression analyses

| Variables | OR (95% CI) | p-value |
|--|----------------------|---------|
| Univariate logistic regression analyses | | |
| Age, years | 1.027 (0.928-1.136) | 0.610 |
| Gestational age, weeks | 1.037 (0.967-1.111) | 0.306 |
| Trimester | | 0.388 |
| 1.Trimester | Reference | |
| 2.Trimester | 0.971 (0.273-3.451) | 0.964 |
| 3.Trimester | 2.720 (0.522-14.16) | 0.235 |
| Albumin, g/L | 0.993 (0.851-1.159) | 0.926 |
| Total bilirubin, mg/dL | 6.637 (0.541-81.375) | 0.139 |
| Amylase, U/L | 0.977 (0.942-1.013) | 0.201 |
| Sodium, mEq/L | 1.118 (0.800-1.562) | 0.513 |
| Calcium, mg/dL | 0.828 (0.266-2.575) | 0.745 |
| WBC, ×10 ⁹ /L | 1.043 (0.923-1.179) | 0.495 |
| Neutrophil, ×10 ⁹ /L | 1.062 (0.936-1.205) | 0.349 |
| Neutrophil, % | 1.071 (0.984-1.166) | 0.111 |
| Lymphocyte, ×10 ⁹ /L | 0.401 (0.146-1.103) | 0.077 |
| Monocyte, ×10 ⁹ /L | 2.524 (0.483-13.201) | 0.273 |
| MPV, fL | 1.012 (0.692-1.480) | 0.952 |
| Platelet, ×10 ⁹ /L | 0.999 (0.991-1.008) | 0.896 |
| RDW, % | 1.077 (0.944-1.229) | 0.271 |
| LUC, % | 0.174 (0-7,195.203) | 0.747 |

Table 2. Continued

| Variables | OR (95% CI) | p-value |
|---|------------------------|---------|
| DNI, % | 1.060 (0.845-1.330) | 0.613 |
| CRP, mg/L | 1.095 (1.042-1.151) | <0.001 |
| PLR | 1.003 (0.998-1.007) | 0.232 |
| LMR | 0.553 (0.327-0.98) | 0.028 |
| NLR | 1.110 (0.997-1.235) | 0.057 |
| SII | 1.154 (0.999-1.334) | 0.052 |
| SIRI | 1.000 (1.000-1.000) | 0.151 |
| CAR | 23.863 (4.223-134.830) | <0.001 |
| Multivariate logistic regression analyses for CRP* | | |
| CRP, mg/L | 1.095 (1.042-1.151) | <0.001 |
| Multivariate logistic regression analyses for CAR* | | |
| CAR | 23.863 (4.223-134.830) | <0.001 |

OR: Odds ratio, CI: Confidence interval, WBC: White blood cell count, MPV: Mean platelet volume, RDW: Red blood cell distribution width, LUC: Large unstained cells, DNI: Delta neutrophil index, CRP: C-reactive protein, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, SII: Systemic immune inflammatory index, SIRI: Systemic immune response index, CAR: CRP/albumin ratio

*VIF analysis showed high collinearity between CRP and CAR (VIF>100); therefore, they were analyzed in separate multivariate models

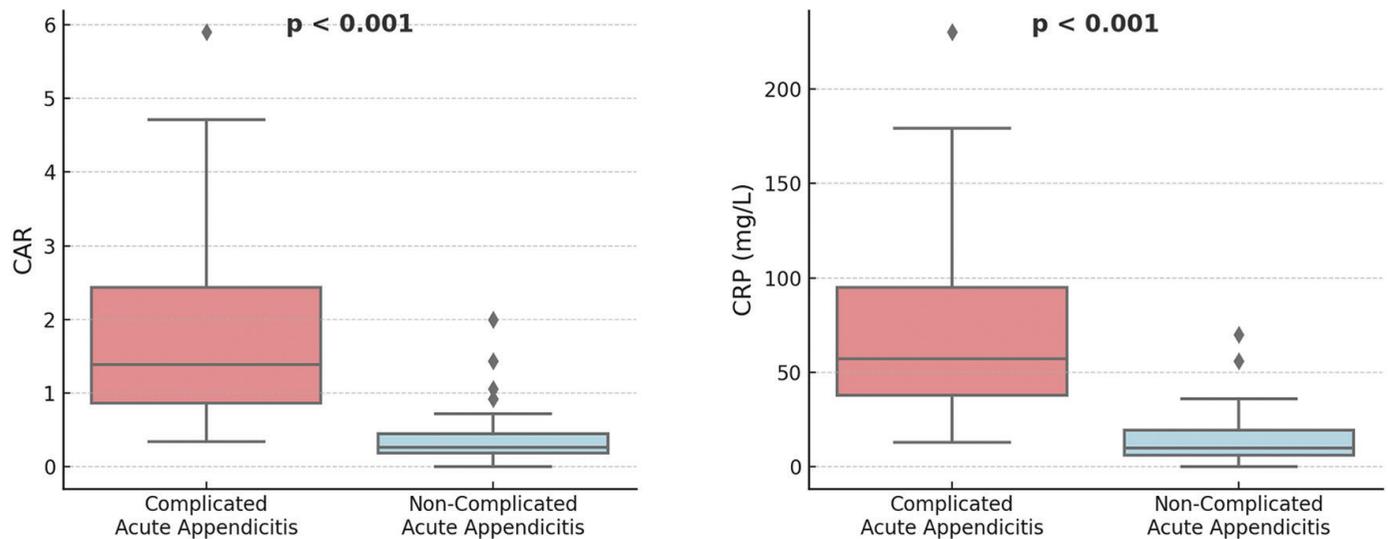


Figure 2. Comparison of CRP and CAR levels between complicated and non-complicated acute appendicitis in pregnant women (CRP: C-reactive protein, CAR: CRP/albumin ratio)

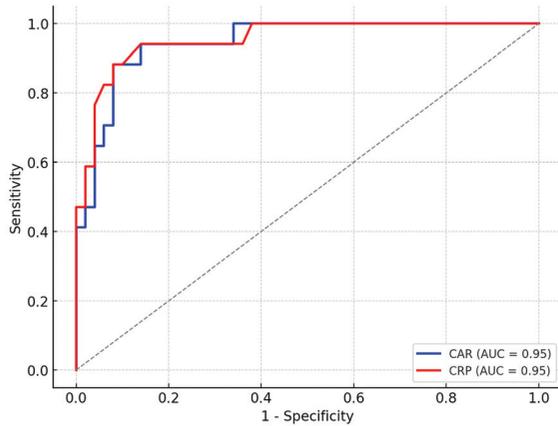


Figure 3. Receiver operating characteristic curve analysis for CRP and CAR

*No significant difference was observed between the areas under the curve of CRP and CAR (DeLong test, $p=0.878$)
(CRP: C-reactive protein, CAR: CRP/albumin ratio)

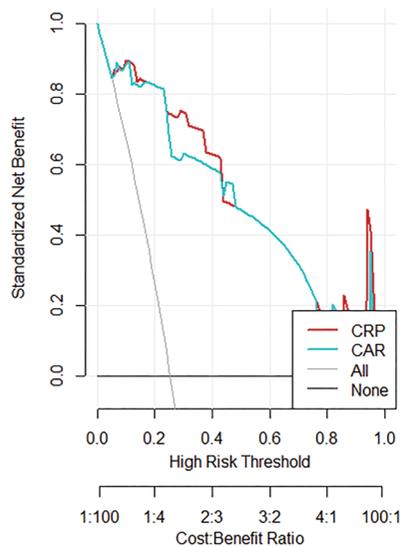


Figure 4. Decision curve analysis comparing the clinical net benefit of the CRP and CAR models

*Decision curve analysis showing that both the CRP and CAR models provided higher standardized net benefit than the “treat-all” and “treat-none” strategies between threshold probabilities of 0.10 and 0.45; CAR demonstrated slightly greater net benefit than CRP within this range.
CRP: C-reactive protein, CAR: CRP/albumin ratio

Discussion

In this study, the cases of 67 patients undergoing surgery for acute appendicitis during pregnancy were retrospectively reviewed. The rate of complicated appendicitis was found to be 25.4%. The main finding of the study was that CRP and CAR levels appeared to be significant independent predictors of complicated appendicitis, although these results should be interpreted cautiously due to the limited sample size. In the ROC analysis, both CRP and CAR showed high diagnostic accuracy (AUC 0.954 and 0.946, respectively) in this dataset; however, these values may be subject to optimism given the limited number of events. The DeLong test revealed no significant difference between the two markers ($p=0.878$). Decision curve analysis confirmed the clinical usefulness of both models, showing greater net benefit compared to the “treat-all” and “treat-none” strategies.

These findings suggest that CRP and CAR may serve as promising laboratory markers for predicting complicated appendicitis in pregnant women. In particular, CAR may provide diagnostic balance despite the physiological increase in CRP during pregnancy, as it reflects both the inflammatory response (CRP) and changes in albumin levels. Nevertheless, the small sample size and low number of events require these findings to be interpreted cautiously, as the high AUC values may reflect optimism or overfitting.

In the literature, the number of studies focusing on the prognostic evaluation of acute appendicitis during pregnancy is limited. There are few studies investigating the prognostic value of CRP and CAR in this specific patient group, and the present study contributes to this limited body of evidence. Similarly, Bozbiyık et al.⁹ reported that negative appendectomy rates were higher due to the limited use of imaging methods in the diagnosis of acute appendicitis in pregnant women but that the clinical course and postoperative outcomes were similar to those in non-pregnant patients. This finding supports the diagnostic difficulties highlighted in our study. Assessing the prognosis of acute appendicitis during pregnancy is a complex issue; due to the potential risks for both the mother and the fetus, the development of accurate prediction systems in this area is of great importance. Surgical intervention remains

Table 3. Diagnosis of complicated appendicitis with a CRP cut-off of 23 mg/L and a CAR cut-off of 0.55

| | | Non-complicated appendicitis | Complicated appendicitis | p-value |
|-----|----------|------------------------------|--------------------------|---------|
| CRP | <23 mg/L | 43 (97.7%) | 1 (2.3%) | <0.001* |
| | ≥23 mg/L | 7 (30.4%) | 16 (69.6%) | |
| CAR | <0.55 | 43 (97.7%) | 1 (2.3%) | <0.001* |
| | ≥0.55 | 7 (30.4%) | 16 (69.6%) | |

*Fisher’s exact test

CRP: C-reactive protein, CAR: CRP/albumin ratio

the gold standard, but conservative management may be considered in selected cases.¹⁰ In this context, the use of simple and accessible laboratory parameters that predict the risk of complications can provide important support in determining the optimal timing of surgery.

The potential use of CRP and CAR in predicting complicated acute appendicitis in pregnant women represents a promising area of research. CRP is a well-established marker of inflammation, and high levels have been shown to be associated with complicated acute appendicitis,¹¹ and CAR is a parameter that reflects both inflammation and nutritional status, allowing for a more comprehensive assessment of the inflammatory response.¹² A CRP level ≥ 34.82 mg/L significantly increases the risk of complications (OR=6.24) and provides high diagnostic accuracy (AUC=0.95, sensitivity 85.7%, specificity 90.9%).¹³ CRP levels are significantly higher in patients with complicated acute appendicitis. For example, mean CRP levels have been reported as high as 154.17 mg/L in patients with perforated appendicitis compared with 2.95 mg/L in uncomplicated cases.¹⁴ This strong relationship can be explained by CRP's direct correlation with the severity of inflammation in the appendix wall.^{15,16}

Similarly, elevated CAR values have been linked to the systemic inflammatory response accompanied by increased CRP and decreased albumin.¹⁷⁻¹⁹ Although some studies in the general population have reported that CAR is not an independent predictor of complicated appendicitis,²⁰ its potential role in pregnant women has not yet been investigated. In pediatric populations, CAR has been found to be a significant predictor of complicated appendicitis; when CAR ≥ 1.39 , the likelihood of complications increases markedly, with a sensitivity of 86.61% and specificity of 84.62%.²¹ Zhao et al.²² found the CAR ≥ 1.04 threshold to be diagnostically significant in adults (AUC=0.871), whereas Zengin et al.²⁰ reported that CAR was not an independent predictor in multivariate analysis. This discrepancy may stem from physiological hemodilution and altered protein synthesis during pregnancy, which may modify CAR behavior. From this perspective, the present study is one of the first to directly compare CRP and CAR in a pregnant population.

The World Society of Emergency Surgery recommends MRI when available, given its lack of radiation and high diagnostic accuracy.²³ However, in our study, the MRI utilization rate was 29.9%, which may reflect limited resources, access difficulties, or a preference for US as the first-line imaging modality. Considering the limited contribution of imaging in predicting complications, laboratory markers such as CRP and CAR may play an important complementary role in clinical decision-making.

The lack of significance of hematological indices such as PLR, LMR, NLR, SII, and SIRI in predicting complications can be explained by pregnancy-specific hematological and hormonal changes. Physiological increases in neutrophil counts, altered LMRs, and expanded plasma volume during pregnancy can affect baseline values, reducing the diagnostic reliability of these indices.²⁴⁻²⁷ Furthermore, trimester-specific variations in immune and hormonal activity may contribute to the instability of these ratios as consistent predictive markers. This finding was consistent across our exploratory trimester subgroup analyses.

Although total bilirubin showed a significant difference between groups at baseline in the univariate comparison, it did not show independent predictive value in the univariate logistic regression and was excluded in the backward elimination process. This indicates that bilirubin did not contribute meaningfully to the adjusted model and should be considered a negative finding rather than an omitted or selectively reported result. The absence of an independent association is consistent with previous reports showing that bilirubin may be elevated in inflammatory abdominal conditions due to non-specific hepatocellular or cholestatic responses but rarely remains significant after multivariate adjustment.⁷ This suggests that bilirubin may reflect nonspecific physiological variation in pregnancy rather than functioning as a clinically meaningful predictor of complication severity.

Study Limitations

This study has certain limitations. The single-center, retrospective design increases the risk of selection bias and limits external validity. The number of patients was determined by including all eligible cases without performing a specific power analysis. Limited access to MRI (29.9%) may have restricted the radiological confirmation of complicated cases. Furthermore, physiological changes during pregnancy complicate the interpretation of biomarkers such as CRP and CAR. Nevertheless, this study is one of the first analyses to demonstrate the high diagnostic performance of CRP and CAR for predicting complicated appendicitis in pregnant women. Larger multicenter, prospective studies are warranted to validate and expand these findings.

Conclusion

This study suggests that CRP and CAR may be promising and easily accessible biomarkers for the early identification of complicated appendicitis in pregnancy; however, these findings should be interpreted cautiously given the small, single-center nature of the study. External validation in larger, multicenter cohorts is required before these markers can be integrated into routine clinical practice. Physiological

and biochemical changes during pregnancy may influence inflammatory biomarkers; therefore, CRP and CAR should be used as complementary—rather than standalone—diagnostic tools within a combined clinical, laboratory, and imaging-based assessment strategy.

Ethics

Ethics Committee Approval: This study was approved by the local ethics committee of Ankara Bilkent City Hospital (decision number: 1-25-1008, date: 12.02.2025).

Informed Consent: Due to the retrospective nature of the study, individual informed consent was not obtained from patients; data were evaluated with identity information concealed.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: H.P.Ö., H.F.M., A.G., Ş.M.B., M.A.P., Ö.A., Concept: H.P.Ö., Ö.A., Design: H.P.Ö., H.F.M., A.G., Ş.M.B., M.A.P., Ö.A., Data Collection or Processing: H.F.M., A.G., Ş.M.B., M.A.P., Ö.A., Analysis or Interpretation: H.P.Ö., H.F.M., Ö.A., Literature Search: H.P.Ö., H.F.M., Ö.A., Writing: H.P.Ö., H.F.M., A.G., Ş.M.B., M.A.P., Ö.A.

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