

Inflammatory Biomarkers and Their Combinations for Early Identification of Complicated Appendicitis: A Prospective Observational Diagnostic Accuracy Study and Receiver Operating Characteristic Analysis.

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ABSTRACT

Background:

Distinguishing uncomplicated from complicated appendicitis is clinically important because delayed recognition of complicated disease may increase morbidity. This study evaluated the diagnostic performance of routine inflammatory biomarkers and selected combinations for identifying complicated appendicitis.

Methods:

A prospective observational diagnostic accuracy study was conducted at a tertiary care hospital in Idukki district, Kerala, India, during a one-year study period from January 2025 to December 2025. Patients undergoing appendectomy for clinically suspected acute appendicitis were evaluated. Complicated appendicitis was defined as perforation, gangrene, or acute peritonitis. Preoperative total leukocyte count (TLC), neutrophil percentage, lymphocyte percentage, and C-reactive protein (CRP) were analyzed. Group comparisons, binary diagnostic accuracy measures, and receiver operating characteristic (ROC) analysis were performed.

Results:

Among 191 patients, 74 (38.7%) had complicated appendicitis, and 117 (61.3%) had uncomplicated appendicitis. Complicated appendicitis was associated with older age and longer symptom duration. TLC, neutrophil percentage, and CRP were higher, whereas lymphocyte percentage was lower, in complicated cases (all $p < 0.001$). In binary analysis, CRP and lymphocyte percentage $< 13\%$ each had 64.8% sensitivity; CRP had the highest specificity (65.1%) and accuracy (65.0%) among individual markers. Combined markers increased specificity, reaching 86.7% for CRP plus neutrophil percentage plus TLC, but sensitivity decreased to 31.5%. ROC analysis showed the greatest discrimination for CRP (AUC 0.842, 95% CI 0.781–0.898), followed by TLC (AUC 0.706, 95% CI 0.626–0.780) and neutrophil percentage (AUC 0.674, 95% CI 0.595–0.750).

Conclusion:

CRP demonstrated the strongest discriminatory performance, while combined markers improved specificity at the cost of sensitivity. Routine inflammatory biomarkers may support clinical risk stratification but should not be used alone to screen for complicated appendicitis.

Recommendations

CRP, TLC, neutrophil percentage, and lymphocyte percentage may be considered adjunctive investigations alongside clinical assessment for early risk stratification of complicated appendicitis.

Keywords: Acute appendicitis; Complicated appendicitis; C-reactive protein; Total leukocyte count; Neutrophil percentage; Lymphocyte percentage; Diagnostic accuracy; Receiver operating characteristic; Inflammatory biomarkers.

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INTRODUCTION

Acute appendicitis is one of the most common surgical emergencies worldwide and remains a frequent cause of acute abdominal pain requiring hospital admission. Despite advances in diagnostic imaging and perioperative care, differentiating uncomplicated appendicitis from complicated appendicitis—which includes perforation, gangrene, and generalized peritonitis—continues to pose a clinical challenge. This distinction is clinically important because complicated appendicitis is associated with higher morbidity, longer hospital stay, increased risk of postoperative complications, and greater healthcare costs. Early identification of patients at risk for complicated disease can therefore influence clinical decision-making, timing of surgery, and prioritization of resources[1,2].

The progression of appendicitis from an uncomplicated inflammatory process to a complicated state is time-dependent and driven by increasing local and systemic inflammation. While imaging modalities such as ultrasonography and computed tomography have improved diagnostic accuracy, their availability, cost, and radiation exposure—particularly in younger patients—limit universal reliance on imaging alone. Consequently, clinicians continue to depend on a combination of clinical assessment and readily available laboratory investigations to guide early management, especially in resource-limited settings[3,4]. Among laboratory parameters, total leukocyte count (TLC) and neutrophil percentage are routinely used markers of acute inflammation and are often elevated in appendicitis. However, these markers may rise early in the disease course and are not specific to complicated disease. C-reactive protein (CRP), an acute-phase reactant synthesized by the liver, increases more gradually and is thought to reflect the severity and duration of inflammation[5]. Several studies have suggested that higher CRP levels are associated with perforation or gangrenous appendicitis, whereas others have reported overlapping values between uncomplicated and complicated cases. Similarly, lymphocyte count or percentage, which tends to decrease during severe inflammatory and stress responses, has been proposed as an additional marker of disease severity, but its clinical utility remains less clearly defined.

Despite extensive literature on laboratory markers in appendicitis, there is no universal agreement on which markers—or combinations of markers—provide reliable discrimination between uncomplicated and complicated appendicitis. Many studies focus on single parameters or use different cut-off values, making comparisons difficult. Furthermore, while individual markers may show modest

diagnostic performance, combining markers may improve specificity or predictive value, although often at the expense of sensitivity. A systematic evaluation of both individual and combined inflammatory markers, along with assessment of their overall discriminatory ability using receiver operating characteristic (ROC) analysis, is therefore warranted[6,7].

The present study evaluated the role of commonly available inflammatory markers—TLC, neutrophil percentage, lymphocyte percentage, and CRP—in distinguishing complicated appendicitis from uncomplicated appendicitis. The objectives were to compare the distribution of these markers between outcome groups, assess diagnostic accuracy using binary cut-off analysis, examine the performance of selected marker combinations, and evaluate overall discriminative ability using receiver operating characteristic analysis. By focusing on routine laboratory tests obtained at admission, the study sought to provide practical evidence for early risk stratification of appendicitis and support informed clinical decision-making.

MATERIALS AND METHODS

Study design and setting

This was a prospective observational diagnostic accuracy study conducted at a tertiary care hospital in Idukki district, Kerala, India, under the Department of Pathology. Participants were recruited using a convenience sampling approach. The study period was January 2025 to December 2025. The study was not a randomized controlled trial.

Study population and eligibility criteria

The study population comprised patients who underwent appendicectomy for a clinical diagnosis of acute appendicitis, with subsequent confirmation of the diagnosis on histopathological examination.

Data were collected prospectively at hospital admission before surgical intervention. Recorded variables included age, sex, duration of symptoms, total leukocyte count (TLC), neutrophil percentage, lymphocyte percentage, and C-reactive protein (CRP) levels. Laboratory results were obtained from the hospital's central laboratory database.

Inclusion criteria: All patients who underwent appendicectomy with a preoperative clinical diagnosis of appendicitis and whose diagnosis was confirmed by histopathology were included.

Exclusion criteria: Patients undergoing interval, elective, or incidental appendicectomy were excluded. Patients with conditions known to influence inflammatory markers, including Crohn's disease, pelvic inflammatory disease,

gastroenteritis, systemic infection, or pregnancy, were also excluded.

Study procedure and outcome definition

Blood samples were collected at hospital admission before surgical intervention. The primary outcome was complicated appendicitis, defined as appendicitis associated with perforation, gangrene, or acute peritonitis. Final classification was based on histopathological examination of the resected appendix. When perforation was suspected intraoperatively, macroscopic findings documented by the operating surgeon were considered in conjunction with histopathological findings.

Sample size estimation

The minimum sample size was estimated using the sensitivity-based formula for a diagnostic accuracy study: $n = Z^2 \times Se \times (1 - Se) / (d^2 \times P)$ $= 1.96^2 \times 0.84 \times 0.16 / (0.15^2 \times 0.18) = 127.48$; rounded up to 128 participants.

The calculation assumed an anticipated sensitivity of 84%, specificity of 89%, disease prevalence of 18%, and absolute precision of 15%. The sensitivity-based calculation determined the required sample size because it yielded the larger estimate. A total of 191 patients were included in the final analysis.

Measures to address potential bias

Potential selection bias was recognized because convenience sampling was used. To reduce information and classification bias, predefined eligibility criteria were applied prospectively, laboratory measurements were obtained before surgery from the central laboratory database, and the same outcome definition and reference-standard approach were applied across outcome groups. Missing laboratory observations were not treated as abnormal values; marker-specific analyses used the available observations, and the binary diagnostic analysis used the complete-case subset for which all variables required for the four-marker comparison were available. The single-centre design and convenience sampling remain important sources of potential selection bias.

Statistical analysis

Statistical analyses were performed using SPSS version 26 and EZR statistical software. Categorical variables were summarized as frequencies and percentages. Continuous variables were assessed for distribution using the Shapiro–Wilk test (with the Kolmogorov–Smirnov test also used

during preliminary assessment). Approximately normally distributed continuous variables were summarized as mean $\pm$ standard deviation (SD), while non-normally distributed variables were summarized as median with interquartile range (IQR).

For comparisons between complicated and uncomplicated appendicitis, the Mann–Whitney U test was used for non-normally distributed continuous variables, and Welch's independent-samples t-test was used for continuous variables compatible with approximate normality. Categorical variables were compared using the Pearson chi-square test; Fisher's exact test was used when expected cell counts were insufficient for chi-square assumptions.

For binary diagnostic accuracy, each marker was classified using a predefined positive-test threshold and a 2 $\times$ 2 contingency table was used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive likelihood ratio (LR+), and negative likelihood ratio (LR–), with 95% confidence intervals (CI) where available.

For binary diagnostic accuracy analysis, TLC, neutrophil percentage, and CRP were categorized using prespecified cut-off values of $>12 \times 10^3/\mu\text{L}$, $>75\%$, and $>30 \text{ mg/L}$, respectively. Lymphocyte percentage was categorized as $<13\%$. A positive test was defined as a value above the specified cut-off for TLC, neutrophil percentage, or CRP, or a lymphocyte percentage $<13\%$.

Lymphocyte percentage was classified as positive when $<13\%$. Combined-marker tests were considered positive when all component markers met their respective binary positive-test criteria.

Receiver operating characteristic (ROC) analysis was performed for TLC, neutrophil percentage, and CRP to evaluate discrimination between complicated and uncomplicated appendicitis. Complicated appendicitis was treated as the positive outcome. The area under the curve (AUC) was calculated with a 95% CI. AUC significance was assessed against the null hypothesis of 0.5. The Youden-optimal threshold was reported for descriptive interpretation. Lymphocyte percentage was included in the group-wise and binary analyses but was not included in the ROC analysis; therefore, no lymphocyte AUC is reported in the present manuscript.

Ethical considerations

Ethical approval was obtained from the Institutional Ethics Committee of Al-Azhar Medical College and Super Specialty Hospital, Ezhallor, Thodupuzha, Idukki, Kerala, India (IEC approval number: AAMC/IEC/103; approval

date: 24 September 2024). A waiver of informed consent was granted because the study involved analysis of hospital records without direct patient contact and without intervention beyond routine clinical care.

distribution of patients according to outcome group is presented in Table 1.

Baseline demographic and clinical characteristics

Table 1 presents the demographic and clinical characteristics of the study population. Patients with complicated appendicitis were older and had a longer duration of symptoms than patients with uncomplicated appendicitis. Sex distribution did not differ significantly between the groups.

RESULTS

Participant flow

A total of 191 patients who fulfilled the eligibility criteria were included in the final analysis. Of these, 74 (38.7%) had complicated appendicitis and 117 (61.3%) had uncomplicated appendicitis. Complicated appendicitis was defined as perforation, gangrene, or acute peritonitis. The

Table 1. Baseline demographic and clinical characteristics of the study population (overall and by outcome).

Characteristic	Overall (N=191)	Complicated (n=74)	Uncomplicated (n=117)	p value
Outcome group, n (%)	—	74 (38.7)	117 (61.3)	—
Age (years)	36.6±14.3; 36.0 (25.0–45.0); 18–79	40.7±16.6; 39.0 (28.5–50.0); 18–79	34.1±12.1; 33.0 (24.0–43.0); 18–67	0.012†
Sex, n (%)	114 (59.7) male; 77 (40.3) female	48 (64.9) male; 26 (35.1) female	66 (56.4) male; 51 (43.6) female	0.313‡
Age group, n (%)	≤20: 33 (17.3); 21–40: 89 (46.6); 41–60: 56 (29.3); >60: 13 (6.8)	≤20: 11 (14.9); 21–40: 29 (39.2); 41–60: 23 (31.1); >60: 11 (14.9)	≤20: 22 (18.8); 21–40: 60 (51.3); 41–60: 33 (28.2); >60: 2 (1.7)	0.004‡
Duration of symptoms (hours)	31.4±18.7; 28.0 (18.5–41.0); 4–92	46.2±19.4; 46.5 (34.2–57.8); 6–92	22.0±10.2; 22.0 (15.0–29.0); 4–44	<0.001†
Duration category, n (%)	<24: 74 (38.7); 24–48: 84 (44.0); >48: 33 (17.3)	<24: 9 (12.2); 24–48: 32 (43.2); >48: 33 (44.6)	<24: 65 (55.6); 24–48: 52 (44.4); >48: 0 (0.0)	<0.001‡

† Welch's independent-samples t-test for continuous variables compatible with approximate normality or Mann–Whitney U test for non-normal variables, as applicable. ‡ Pearson chi-square test. Continuous variables are shown as mean±SD; median (IQR); range where reported. Categorical variables are shown as n (%). Complicated appendicitis includes acute peritonitis, perforated appendicitis, and gangrenous appendicitis. Final classification was based on histopathology, with intraoperative macroscopic assessment considered when perforation was suspected.

Laboratory variables by outcome

As shown in Table 2, complicated appendicitis was associated with higher TLC, higher neutrophil percentage, lower lymphocyte percentage, and substantially higher CRP. These differences were statistically significant for all four markers (p<0.001).

Table 2. Distribution and group-wise comparison of laboratory variables by outcome.

Variable	Overall	Complicated	Uncomplicated	Statistical test	p value
TLC ($\times 10^3/\mu\text{L}$)	11.83 $\pm$ 3.63 (n=178)	13.47 $\pm$ 3.65 (n=68)	10.81 $\pm$ 3.24 (n=110)	Welch t-test	<0.001
Neutrophils (%)	72.67 $\pm$ 10.29 (n=181)	76.82 $\pm$ 9.30 (n=69)	70.12 $\pm$ 10.06 (n=112)	Welch t-test	<0.001
Lymphocytes (%)	26.9 (19.3–34.1) (n=191)	23.17 $\pm$ 9.20 (n=74)	29.72 $\pm$ 10.87 (n=117)	Welch t-test	<0.001
CRP (mg/L)	25.6 (13.6–57.9) (n=185)	57.9 (34.2–100.9) (n=73)	16.4 (9.3–29.1) (n=112)	Mann–Whitney U	<0.001

Data are presented as mean $\pm$ SD for approximately normally distributed group data and as median (IQR) for non-normally distributed data. n varies across variables because of missing laboratory observations. TLC, total leukocyte count; CRP, C-reactive protein; IQR, interquartile range; SD, standard deviation.

complicated and 83 uncomplicated cases. CRP and lymphocyte percentage <13% had the highest sensitivity among individual markers (64.8% each). CRP had the highest specificity (65.1%) and accuracy (65.0%) among the individual tests.

Diagnostic accuracy of individual markers

Table 3 summarizes binary diagnostic performance among the complete-case subset (n=137), comprising 54

Table 3. Diagnostic accuracy of individual inflammatory markers using binary cut-off analysis.

Marker	Positive-test definition	TP	FP	FN	TN	Sensitivity %, (95% CI)	Specificity %, (95% CI)	PPV %, (95% CI)	NPV %, (95% CI)	Accuracy %, (95% CI)	LR+ (95% CI)	LR– (95% CI)
TLC	$>12 \times 10^3/\mu\text{L}$	32	34	22	49	59.3 (45.0–72.4)	59.0 (47.7–69.7)	48.5 (36.0–61.1)	69.0 (56.9–79.5)	59.1 (50.4–67.4)	1.45 (1.03–2.03)	0.69 (0.48–1.00)
Neutrophil %	$>75\%$	33	30	21	53	61.1 (46.9–74.1)	63.9 (52.6–74.1)	52.4 (39.4–65.1)	71.6 (59.9–81.5)	62.8 (54.1–70.9)	1.69 (1.18–2.42)	0.61 (0.42–0.88)
Lymphocyte %	$<13\%$	35	31	19	52	64.8 (50.6–77.3)	62.7 (51.3–73.0)	53.0 (40.3–65.4)	73.2 (61.4–83.1)	63.5 (54.9–71.6)	1.74 (1.23–2.44)	0.56 (0.38–0.84)
CRP	$>30 \text{ mg/L}$	35	29	19	54	64.8 (50.6–77.3)	65.1 (53.8–75.2)	54.7 (41.7–67.2)	74.0 (62.4–83.5)	65.0 (56.4–72.9)	1.85 (1.30–2.64)	0.54 (0.36–0.80)

TP=true positive; FP=false positive; FN=false negative; TN=true negative; PPV=positive predictive value; NPV=negative predictive value; LR+=positive likelihood

ratio; LR–=negative likelihood ratio. Disease positive was defined as complicated appendicitis.

Diagnostic accuracy of combined markers

Table 4 shows the performance of predefined composite tests. The combined criteria increased specificity compared

with individual markers but reduced sensitivity. The three-marker combination had the highest specificity (86.7%) and the lowest sensitivity (31.5%).

Table 4. Diagnostic accuracy of combined inflammatory-marker criteria using binary cut-off analysis.

Combined marker(s)	Definition of test positive	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)	LR+ (95% CI)	LR- (95% CI)
TLC + neutrophil %	Positive when both component markers meet their binary positive criteria	25	21	29	62	0.463 (0.326–0.604)	0.747 (0.640–0.836)	0.543 (0.390–0.691)	0.681 (0.575–0.775)	0.635 (0.549–0.716)	1.830 (1.146–2.922)	0.719 (0.545–0.949)
CRP + neutrophil %	Positive when both component markers meet their binary positive criteria	21	15	33	68	0.389 (0.259–0.531)	0.819 (0.720–0.895)	0.583 (0.408–0.745)	0.673 (0.573–0.763)	0.650 (0.564–0.729)	2.152 (1.220–3.794)	0.746 (0.589–0.944)
CRP + neutrophil % + TLC	Positive when all three component markers meet their binary positive criteria	17	11	37	72	0.315 (0.195–0.456)	0.867 (0.775–0.932)	0.607 (0.406–0.785)	0.661 (0.564–0.749)	0.650 (0.564–0.729)	2.375 (1.208–4.673)	0.790 (0.647–0.964)

Abbreviations: TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.

Receiver operating characteristic analysis

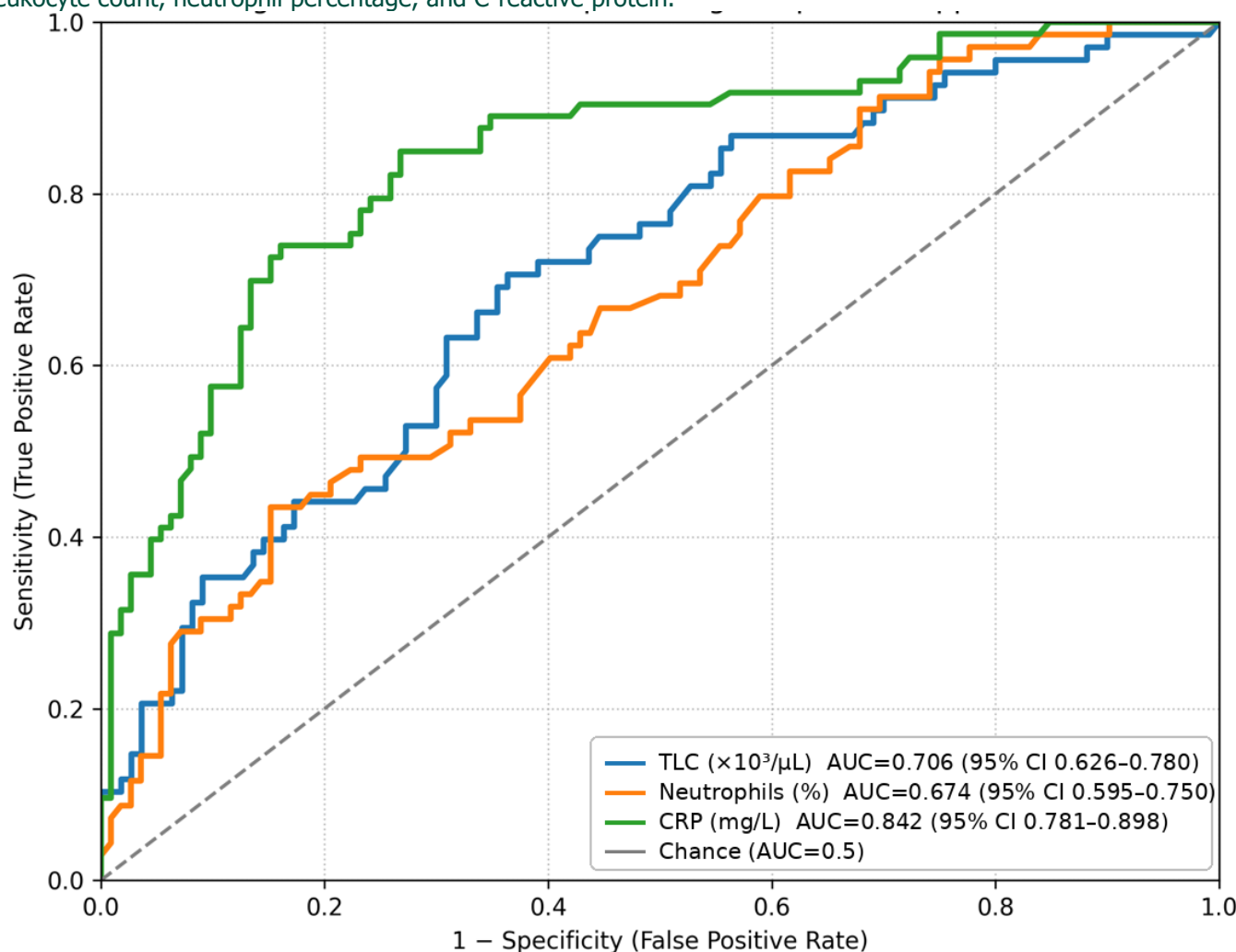
Table 5 presents ROC performance for TLC, neutrophil percentage, and CRP. CRP demonstrated the strongest discrimination (AUC 0.842), while TLC and neutrophil percentage demonstrated moderate discrimination. Lymphocyte percentage was not included in this ROC analysis and is therefore not represented in Table 5.

Table 5. Summary of receiver operating characteristic performance for inflammatory biomarkers.

Marker	Direction for ROC	n (Comp / Uncomp)	Missing	AUC (95% CI)	SE (bootstrap)	p-value (vs 0.5)	Youden - optimal cut-off	Sensitivity	Specificity	Youden J
TLC ($\times 10^3/\mu\text{L}$)	Higher = more likely complicated	178 (68 / 110)	13	0.706 (0.626 – 0.780)	0.040	<0.001	11.67	0.706	0.636	0.342
Neutrophil (%)	Higher = more likely to be complicated	181 (69 / 112)	10	0.674 (0.595 – 0.750)	0.040	<0.001	79.80	0.435	0.848	0.283
CRP (mg/L)	Higher = more likely complicated	185 (73 / 112)	6	0.842 (0.781 – 0.898)	0.030	<0.001	25.80	0.849	0.732	0.581

The Youden-optimal cut-off maximizes sensitivity + specificity – 1 and is reported for descriptive interpretation; it should not be interpreted as a validated clinical threshold. The binary diagnostic cut-offs in Table 3 are separate from these ROC-derived thresholds.

Figure 1. Receiver operating characteristic curves for predicting complicated appendicitis using total leukocyte count, neutrophil percentage, and C-reactive protein.



The positive class was defined as complicated appendicitis. ROC curves are plotted as sensitivity versus 1-specificity. The figure displays TLC, neutrophil percentage, and CRP only, consistent with the ROC analysis described in the Methods and Table 5.

DISCUSSION

In this prospective observational diagnostic accuracy study of 191 patients, complicated appendicitis accounted for 38.7% of cases. In relation to the study objective of

identifying routinely available markers associated with complicated disease, older age and longer symptom duration were more frequent among complicated cases (Table 1), with nearly half of complicated cases presenting after more than 48 hours. These findings support the importance of symptom duration as a clinical context variable when interpreting inflammatory biomarkers.

Consistent with the objective of comparing inflammatory profiles between outcome groups, complicated appendicitis was associated with higher TLC and neutrophil percentage,

lower lymphocyte percentage, and substantially higher CRP (Table 2). The larger separation observed for CRP is biologically plausible because CRP rises with sustained inflammation and tissue injury, whereas leukocytosis and neutrophilia may occur earlier and are less specific to complicated disease[8-13].

The binary diagnostic analysis addressed the objective of evaluating individual marker thresholds. Among the complete-case subset, CRP and lymphocyte percentage <13% showed the highest sensitivity among individual markers, while CRP showed the highest specificity and accuracy (Table 3). Nevertheless, the sensitivity and specificity of individual markers remained in the moderate range, indicating that none of the evaluated thresholds should be considered a definitive rule-in or rule-out test when used alone[14,15].

The combined-marker analysis further addressed the objective of assessing whether combinations improve diagnostic performance. Specificity increased from the individual-marker range to 86.7% with the three-marker combination of CRP, neutrophil percentage, and TLC, but sensitivity decreased to 31.5% (Table 4). This trade-off indicates that composite criteria may be more useful for supporting a higher-specificity rule-in strategy than for screening, because a substantial proportion of complicated cases would be missed if the composite were used alone[16–19].

The ROC analysis provided a complementary assessment using continuous measurements. CRP showed the strongest discrimination (AUC 0.842), whereas TLC (AUC 0.706) and neutrophil percentage (AUC 0.674) showed moderate discrimination (Table 5 and Figure 1). Thus, the ROC findings support the principal objective that CRP provides greater overall discriminatory information than the other markers evaluated in the ROC analysis.

Lymphocyte percentage was included in the group-wise and binary diagnostic analyses but was not included in the ROC analysis. This distinction is now stated explicitly in the Methods, Results, and Discussion to avoid implying that a lymphocyte ROC analysis was performed. Consequently, no AUC or ROC-derived threshold for lymphocyte percentage is reported.

Several limitations should be considered. Missing laboratory values reduced the effective sample size for marker-specific analyses. Dichotomizing continuous biomarkers reduces information and may produce thresholds that perform differently across settings. The binary diagnostic analysis was based on 137 complete cases, whereas marker-specific ROC analyses used 178, 181, and

185 observations for TLC, neutrophil percentage, and CRP, respectively; these differences reflect missing laboratory observations rather than different disease definitions. Convenience sampling and the single-centre design may introduce selection bias and limit generalizability.

Generalizability

The findings are primarily applicable to patients with acute appendicitis evaluated in tertiary-care hospital settings with access to routine inflammatory laboratory investigations. The results may be relevant to similar resource-limited settings in which readily available biomarkers are used for early risk stratification. Extrapolation to other healthcare settings and broader populations should be undertaken cautiously because the study was conducted at a single tertiary-care centre, used convenience sampling, and included patients undergoing appendectomy. Multicentre studies involving diverse patient populations are required to validate the diagnostic performance and clinical applicability of these inflammatory markers and their combinations.

CONCLUSION

Routine inflammatory markers demonstrate meaningful differences between uncomplicated and complicated appendicitis but have limited standalone diagnostic power when applied as binary tests. CRP provides the strongest overall discrimination among the biomarkers evaluated by ROC analysis. Combined markers increase specificity but reduce sensitivity, limiting their use as standalone screening tools. These findings support a multimodal approach integrating laboratory markers with clinical assessment and symptom duration for early risk stratification of complicated appendicitis.

Limitations

The study was conducted at a single tertiary-care centre and used convenience sampling, which may limit generalizability and introduce selection bias. Some laboratory variables had missing values, resulting in different sample sizes across analyses. The binary diagnostic cut-offs may not be universally applicable and require validation in independent populations. Lymphocyte percentage was not evaluated by ROC analysis, limiting direct comparison of its continuous discriminatory performance with the other biomarkers. The combined-marker criteria also require validation before clinical implementation.

Recommendations

CRP, TLC, neutrophil percentage, and lymphocyte percentage may be considered adjunctive investigations alongside clinical assessment for early risk stratification of complicated appendicitis. Combined inflammatory markers may be useful when greater specificity is required; however, they should not be used as standalone screening tests because of limited sensitivity. Further prospective, multicentre studies are recommended to validate diagnostic cut-offs and determine the clinical utility of these marker combinations.

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Ethics Committee of Al-Azhar Medical College and Super Specialty Hospital, Ezhalloor, Thodupuzha, Idukki, Kerala, India (IEC approval number: AAMC/IEC/103; approval date: 24 September 2024). A waiver of informed consent was granted because the study involved analysis of hospital records without direct patient contact and without intervention beyond routine clinical care.

Consent for publication

Not applicable. The study does not contain any individual person's data in an identifiable form.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional regulations and ethical approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the conception and design of the study. Data collection and analysis were performed by the authors. All authors participated in interpretation of the data, drafting and revising the manuscript, and approved the final version for submission.

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Abbreviations

AUC: Area Under the Curve; CI: Confidence Interval; CRP: C-reactive Protein; FN: False Negative; FP: False Positive; IQR: Interquartile Range; LR⁻: Negative Likelihood Ratio; LR⁺: Positive Likelihood Ratio; NPV: Negative Predictive Value; PPV: Positive Predictive Value; ROC: Receiver Operating Characteristic; SD: Standard Deviation; TN: True Negative; TP: True Positive; TLC: Total Leukocyte Count.

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