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Diagnostic value of selected hematological markers in differentiating acute appendicitis from reactive lymphoid hyperplasia in children: A retrospective single-center study

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ABSTRACT

Objective: This study aimed to evaluate the diagnostic performance of selected hematological markers for differentiating histopathologically confirmed acute appendicitis (AA) from reactive lymphoid hyperplasia (RLH) in children and to investigate their independent associations with AA.

Material and Methods: This retrospective, single-center study included 195 children with histopathologically confirmed AA (n=45) or RLH (n=150) following appendectomy. Preoperative leukocyte, neutrophil, lymphocyte, and platelet counts were recorded, and the systemic immune-inflammation index (SII) was calculated as platelet count × neutrophil count/lymphocyte count. The discriminatory performance of the hematological markers was evaluated using receiver operating characteristic (ROC) curve analysis, and optimal cutoff values were determined using the Youden index. Multivariable logistic regression analyses were performed to identify factors independently associated with AA.

Results: Leukocyte, neutrophil, platelet, and SII values were significantly higher in the AA group than in the RLH group, whereas the lymphocyte count was significantly lower (all $p<0.05$). ROC analysis showed the highest discriminatory performance for neutrophil count (AUC=0.724; 95% CI: 0.648–0.800), followed by SII (AUC=0.712; 95% CI: 0.634–0.791) and leukocyte count (AUC=0.690; 95% CI: 0.611–0.769). At the optimal cutoff values, neutrophil count had a sensitivity of 84.4% and a specificity of 56.7%, whereas SII had a sensitivity of 82.2% and a specificity of 56.0%. In multivariable analysis, SII remained independently associated with AA after adjustment for age, sex, and leukocyte count (adjusted OR=1.258 per 1,000-unit increase; 95% CI: 1.068–1.482; p=0.006). In the conventional hematological model excluding SII, neutrophil and platelet counts were independently and positively associated with AA, whereas lymphocyte count was inversely associated.

Conclusion: Selected hematological markers may provide supportive information for differentiating AA from RLH in children. Although SII was independently associated with AA, it did not demonstrate a diagnostic advantage over the absolute neutrophil count. Therefore, SII and other routine hematological markers should be considered adjuncts to, rather than standalone substitutes for, clinical assessment and imaging findings.

Keywords: Appendicitis; biomarkers; child; leukocyte count; lymphoid tissue.

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Çocuklarda akut apandisit ile reaktif lenfoid hiperplazinin ayırıcı tanısında seçilmiş hematolojik belirteçlerin tanısal değeri: Retrospektif tek merkezli bir çalışma

ÖZET

Amaç: Bu çalışmanın amacı, çocuklarda histopatolojik olarak doğrulanmış akut apandisit (AA) ile reaktif lenfoid hiperplazinin (RLH) ayırıcı tanısında seçilmiş hematolojik belirteçlerin tanısal performansını değerlendirmek ve bu belirteçlerin AA ile bağımsız ilişkilerini araştırmaktır.

Gereç ve Yöntemler: Bu retrospektif, tek merkezli çalışmaya, apendektomi sonrası histopatolojik olarak AA (n=45) veya RLH (n=150) tanısı doğrulanan toplam 195 çocuk dahil edildi. Ameliyat öncesi lökosit, nötrofil, lenfosit ve trombosit sayıları kaydedildi ve sistemik immün-inflamasyon indeksi (SII), trombosit × nötrofil/lenfosit formülü kullanılarak hesaplandı. Hematolojik belirteçlerin ayırt edici performansı, alıcı işletim karakteristiği (ROC) eğrisi analizi ile değerlendirildi ve optimal eşik değerleri Youden indeksi kullanılarak belirlendi. AA ile bağımsız olarak ilişkili faktörleri değerlendirmek amacıyla çok değişkenli lojistik regresyon analizleri gerçekleştirildi.

Bulgular: Akut apandisit grubunda lökosit, nötrofil, trombosit ve SII değerleri RLH grubuna göre anlamlı olarak daha yüksek, lenfosit sayısı ise daha düşüktü (tümü p<0,05). ROC analizinde en yüksek ayırt edici performans nötrofil sayısında saptandı (AUC=0,724; %95 GA: 0,648–0,800); bunu SII (AUC=0,712; %95 GA: 0,634–0,791) ve lökosit sayısı (AUC=0,690; %95 GA: 0,611–0,769) izledi. Optimal eşik değerlerinde nötrofil sayısının duyarlılığı %84,4, özgüllüğü %56,7; SII'nin duyarlılığı %82,2, özgüllüğü %56,0 idi. Çok değişkenli analizde SII, yaş, cinsiyet ve lökosit sayısı için düzeltme yapıldıktan sonra AA ile bağımsız olarak ilişkili bulundu (düzeltilmiş OR=1,258/her 1000 birimlik artış; %95 GA: 1,068–1,482; p=0,006). SII'nin yer almadığı konvansiyonel hematolojik modelde ise nötrofil ve trombosit sayıları AA ile bağımsız ve pozitif yönde, lenfosit sayısı ise ters yönde ilişkiliydi.

Tartışma: Seçilmiş hematolojik belirteçler, çocuklarda AA ile RLH'nin ayırt edilmesinde destekleyici bilgiler sağlayabilir. SII, AA ile bağımsız olarak ilişkili bulunmasına rağmen mutlak nötrofil sayısına göre tanısal bir üstünlük göstermemiştir. Bu nedenle SII ve diğer rutin hematolojik belirteçler, tek başına tanısal testler olarak değil, klinik değerlendirme ve görüntüleme bulgularını tamamlayan yardımcı parametreler olarak değerlendirilmelidir.

Anahtar Kelimeler: Apandisit; biyobelirteçler; çocuk; lenfoid doku; lökosit sayımı.

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INTRODUCTION

Acute appendicitis (AA) is the most common pediatric abdominal surgical emergency, with a lifetime risk of approximately 7–8% and a peak incidence during the second decade of life (1). Despite advances in laboratory testing and imaging, diagnosis remains challenging because clinical manifestations are often nonspecific, particularly in younger children, who frequently lack the classic triad of right lower quadrant pain, fever, and leukocytosis (2). Although clinical scoring systems such as the Pediatric Appendicitis Score (PAS) and modified Alvarado score facilitate risk stratification, neither provides sufficient diagnostic accuracy when used alone (3).

Negative appendectomy continues to occur in approximately 10–20% of pediatric cases (4, 5). Reactive lymphoid hyperplasia (RLH), a frequent but underrecognized pathological finding in these patients, is characterized by lymphoid follicular enlargement with preservation of normal appendiceal architecture and the absence of acute inflammatory changes (5). Because RLH commonly develops in response to viral or other antigenic stimulation during periods of active lymphoid tissue growth, it is encountered predominantly in children and adolescents (6, 7). Importantly, RLH may cause appendiceal wall thickening and luminal distension that closely resemble AA on ultrasonography, increasing the likelihood of unnecessary appendectomy (8, 9). As definitive diagnosis relies on postoperative histopathological examination, additional preoperative diagnostic tools are needed (4).

Routine complete blood count (CBC) parameters and CBC-derived inflammatory indices have attracted increasing interest because they are inexpensive, rapidly available, and readily incorporated into emergency evaluation (10, 11). Conventional hematological parameters, particularly leukocyte and neutrophil counts, remain widely used in the assessment of suspected AA, while composite indices such as the neutrophil-to-lymphocyte ratio (NLR) have also demonstrated diagnostic and prognostic value (12). More recently, the systemic immune-inflammation index (SII), calculated as platelet count×neutrophil count/lymphocyte count, has emerged as a composite marker integrating different components of the inflammatory and immune responses (13).

Originally introduced as a prognostic marker for hepatocellular carcinoma, SII has subsequently been investigated in various inflammatory and surgical conditions (13).

Previous studies have investigated SII and other hematological markers in pediatric AA and have reported their potential diagnostic value and associations with disease severity (14–17). However, most studies have compared patients with AA with heterogeneous control populations, including those with negative appendectomy specimens or mesenteric lymphadenitis and elective surgical patients, rather than focusing specifically on histopathologically confirmed RLH (18, 19). This distinction is clinically relevant because RLH may mimic AA both clinically and radiologically and may itself be accompanied by alterations in inflammatory parameters.

Therefore, this study aimed to evaluate the diagnostic performance of selected hematological markers, including leukocyte, neutrophil, lymphocyte, and platelet counts and SII, for differentiating histopathologically confirmed AA from RLH in children undergoing appendectomy. We also sought to determine clinically relevant cutoff values for these markers and to assess their associations with AA after adjustment for potential confounding factors.

MATERIAL AND METHODS

Study Design

A retrospective diagnostic accuracy study was conducted at a tertiary pediatric surgery center in Türkiye between January 2020 and December 2024. The study was approved by the University of Health Sciences, UÜmraniye Training and Research Hospital Ethics Committee (approval no. 216; September 11, 2025) and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective design.

Patient Selection

Approximately 1,400 pediatric appendectomies were performed during the study period. Reactive lymphoid hyperplasia (RLH) was identified in 150 specimens. A randomly selected cohort of 45 children with acute appendicitis (AA) served as the comparison group. Therefore, the proportions of AA and RLH in this analysis were not intended to represent the institutional incidence of AA or the overall negative appendectomy rate.

The final diagnosis was established by histopathological evaluation of the resected appendix. Based on these findings, patients were assigned to either the AA group (n=45) or the RLH group (n=150). Only patients with histopathologically confirmed AA or RLH were included.

The exclusion criteria were incomplete preoperative complete blood count (CBC) data, concurrent systemic infection, chronic inflammatory, hematological, or immunological disease, malignancy, or preoperative treatment with corticosteroids or immunosuppressive agents.

Clinical Management

Children presenting with suspected AA underwent routine clinical evaluation supported by laboratory and imaging findings. The indication for appendectomy was determined according to the overall clinical assessment. Perioperative antibiotic therapy followed institutional treatment protocols, whereas postoperative management was individualized according to operative findings and clinical recovery.

Data Collection and Laboratory Measurements

Age and sex were recorded for all participants. Peripheral venous blood samples obtained before surgery were analyzed for white blood cell (WBC), neutrophil, lymphocyte, and platelet counts using automated hematology analyzers in the central laboratory under standardized quality-control procedures.

The systemic immune-inflammation index (SII) was calculated according to the method described by Hu et al. (13) SII=[platelet count ($\times10^3/\mu L$) × neutrophil count ($\times10^3/\mu L$)]/lymphocyte count ($\times10^3/\mu L$).

Individual CBC parameters and calculated SII values were subsequently compared between the two study groups.

Outcome Measures

The primary objective was to evaluate the diagnostic performance of selected hematological markers, including WBC, neutrophil, lymphocyte, and platelet counts and SII, for differentiating histopathologically confirmed AA from RLH. Receiver operating characteristic (ROC) curve analysis was used to assess the discriminatory performance of each marker by determining the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) at the optimal cutoff values.

A secondary objective was to evaluate whether the investigated hematological markers were independently associated with AA after adjustment for age and sex using multivariable logistic regression analysis.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean±standard deviation (SD) and median, and categorical variables as number (n) and percentage (%). The distribution of continuous variables was assessed using the Shapiro–Wilk test together with visual inspection of histograms and Q–Q plots. Because continuous variables were not normally distributed, between-group comparisons were performed using the Mann–Whitney U test. Categorical variables were compared using the chi-square test.

Receiver operating characteristic (ROC) curve analysis was used to assess the discriminatory performance of each hematological marker. Areas under the curve (AUCs) with 95% confidence intervals (CIs) were calculated, and optimal cutoff values were determined using the Youden index, with corresponding sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Table 1. Comparison of demographic characteristics between the acute appendicitis and reactive lymphoid hyperplasia groups

Gender, n (%)			0.793[a]
Male	**23 (51.1)**	**80 (53.3)**	
Female	22 (48.9)	70 (46.7)	
Age (years) mean±SD / median	11.7±4.3 / 12.0	10.7±5.2 / 11.0	0.308[b]

a: Chi-Kare (Chi-Square) test; b: Mann–Whitney U test; SD: Standard deviation.

Multivariable logistic regression analysis was performed to identify factors independently associated with acute appendicitis (AA) using three Enter models. Model 1 included age, sex, and SII; Model 2 additionally included WBC count. Because SII is derived from neutrophil, lymphocyte, and platelet counts, these components were evaluated separately in Model 3 together with age, sex, and WBC count. SII was scaled per 1,000-unit increase. Results are reported as adjusted odds ratios (aORs) with 95% CIs. Multicollinearity was assessed using variance inflation factors (VIFs), and model performance was summarized using Nagelkerke R^2. All tests were two-sided, with $p<0.05$ considered statistically significant.

RESULTS

Patient Demographics

The study included 195 children, comprising 45 patients with acute appendicitis (AA) and 150 with reactive lymphoid hyperplasia (RLH). Sex distribution was similar between the groups (51.1% vs. 53.3% male, respectively; p=0.793), as was age (median, 12.0 vs. 11.0 years, respectively; p=0.308) (Table 1). Because the AA cohort was randomly selected, the proportions of AA and RLH in the study population were not intended to represent the institutional incidence of AA or the overall negative appendectomy rate.

Laboratory Parameters

All evaluated complete blood count (CBC) parameters differed significantly between the two groups (Table 2). Leukocyte count was higher in the AA group than in the RLH group (mean±SD: 15.4±7.9 vs. 13.0±12.1 ×10³/μL; median: 14.2 vs. 10.5 ×10³/μL; p<0.001). Similar findings were observed for neutrophil count (11.50±4.06 vs. 8.22±4.77 ×10³/μL; median: 10.72 vs. 6.71 ×10³/μL; p<0.001) and platelet count (306.0±64.1 vs. 284.1±74.5 ×10³/μL; median: 301.0 vs. 281.0 ×10³/μL; p=0.034). In contrast, lymphocyte count was lower in the AA group (1.84±0.91 vs. 2.16±0.99 ×10³/μL; median: 1.61 vs. 2.06 ×10³/μL; p=0.039). SII values were also significantly higher in the AA group than in the RLH group (mean±SD: 2.625±2.119 vs. 1.634±2.139; median: 1.897 vs. 963; p<0.001).

Diagnostic Performance

Receiver operating characteristic (ROC) analysis demonstrated the highest AUC for neutrophil count (AUC=0.724; 95% CI: 0.648–0.800), followed by SII (AUC=0.712; 95% CI: 0.634–0.791) and leukocyte count (AUC=0.690; 95% CI: 0.611–0.769) (Table 3; Fig. 1). Platelet and lymphocyte counts showed lower discriminatory ability, with AUC values below 0.65. Thus, although SII demonstrated moderate discriminatory ability, its AUC did not exceed that of the absolute neutrophil count.

According to the Youden index, the optimal cutoff value was 7.715 ×10³/μL for neutrophil count and 1.081 for SII. At these thresholds, neutrophil count yielded a sensitivity of 84.4%, specificity of 56.7%, positive predictive value (PPV) of 36.9%, and negative predictive value (NPV) of 92.4%. For SII, the corresponding sensitivity, specificity, PPV, and NPV were 82.2%, 56.0%, 35.9%, and 91.3%, respectively (Table 3).

Multivariable Logistic Regression Analysis

The results of the multivariable logistic regression analyses are presented in Table 4. In Model 1, which included age, sex, and SII, SII remained independently associated with AA (aOR=1.264 per 1,000-unit increase; 95% CI: 1.072–1.490; p=0.005), whereas age and sex were not independently associated with AA.

In Model 2, after additional adjustment for leukocyte count, SII remained independently associated with AA (aOR=1.258 per 1,000-unit increase; 95% CI: 1.068–1.482; p=0.006). Leukocyte count was not independently associated with AA in this model (aOR=1.018; 95% CI: 0.991–1.046; p=0.200).

Table 2. Comparison of preoperative laboratory parameters between patients with acute appendicitis and those with reactive lymphoid hyperplasia

Parameters	Acute appendicitis (n=45) Mean±SD / Median	Reactive lymphoid hyperplasia (n=150) Mean±SD / Median	p
Leukocyte (×10³/μL)	15.4±7.9 / 14.2	13.0±12.1 / 10.5	<0.001
Neutrophil (×10³/μL)	11.50±4.06 / 10.72	8.22±4.77 / 6.71	<0.001
Platelet (×10³/μL)	306.0±64.1 / 301.0	284.1±74.5 / 281.0	0.034
Lymphocyte (×10³/μL)	1.84±0.91 / 1.61	2.16±0.99 / 2.06	0.039
SII	2.625±2.119 / 1.897	1.634±2.139 / 0.963	<0.001

*: Mann–Whitney U test. SII: Systemic Immune-Inflammation Index = (Platelet count×Neutrophil count) / Lymphocyte count.

Table 3. ROC curve analysis: discriminatory performance of preoperative laboratory parameters in differentiating acute appendicitis from reactive lymphoid hyperplasia

Neutrophil (×10³/µL)	7.715	0.724 (0.648–0.800)	84.4	56.7	36.9	92.4
SII	1.081	0.712 (0.634–0.791)	82.2	56.0	35.9	91.3
Leukocyte (×10³/µL)	10.985	0.690 (0.611–0.769)	84.4	53.3	34.9	91.9
Platelet (×10³/µL)	275.5	0.604 (0.516–0.693)	71.0	48.0	29.1	84.7
Lymphocyte (×10³/µL)	1.695	0.602 (0.510–0.693)	55.6	64.0	32.9	83.2

Cutoff values determined by the Youden index (maximum of sensitivity + specificity − 1). Top two performers (neutrophil count and SII) are highlighted. SII: Systemic Immune-Inflammation Index = (Platelet×Neutrophil) / Lymphocyte; AUC: Area under the ROC curve; CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value.

Table 4. Multivariable logistic regression analysis of factors associated with acute appendicitis

Model	Variables	aOR	95% CI	p
Model 1	Age at surgery (years)	1.075	0.993–1.164	0.074
	Sex (Ref: Male)	0.815	0.399–1.664	0.574
	SII (per 1,000-unit increase)	1.264	1.072–1.490	0.005
Model 2	Age at surgery (years)	1.083	0.999–1.174	0.054
	Sex (Ref: Male)	0.799	0.390–1.635	0.539
	SII (per 1,000-unit increase)	1.258	1.068–1.482	0.006
	WBC count (×10³/µL)	1.018	0.991–1.046	0.200
Model 3	Age at surgery (years)	1.119	1.021–1.227	0.017
	Sex (Ref: Male)	0.726	0.337–1.564	0.413
	WBC count (×10³/µL)	1.007	0.972–1.043	0.700
	Neutrophil count (×10³/µL)	1.162	1.065–1.267	<0.001
	Platelet count (×10³/µL)	1.006	1.001–1.012	0.039
	Lymphocyte count (×10³/µL)	0.653	0.437–0.976	0.038

The Enter method was used for all models. VIF ranges were 1.026–1.082 for Model 1, 1.027–1.100 for Model 2, and 1.063–1.230 for Model 3. Nagelkerke R^2 values were 0.084, 0.096, and 0.226 for Models 1, 2, and 3, respectively. aOR: Adjusted odds ratio; CI: Confidence interval; SII: Systemic immune-inflammation index; WBC: White blood cell; VIF: Variance inflation factor.

In Model 3, which evaluated conventional hematological parameters without SII, age (aOR=1.119; 95% CI: 1.021–1.227; p=0.017), neutrophil count (aOR=1.162; 95% CI: 1.065–1.267; p<0.001), and platelet count (aOR=1.006; 95% CI: 1.001–1.012; p=0.039) were independently and positively associated with AA, whereas lymphocyte count was inversely associated with AA (aOR=0.653; 95% CI: 0.437–0.976; p=0.038). Sex (p=0.413) and leukocyte count (p=0.700) were not independently associated with AA in this model. No evidence of relevant multicollinearity was observed, with VIF values ranging from 1.026 to 1.082 in Model 1, from 1.027 to 1.100 in Model 2, and from 1.063 to 1.230 in Model 3. Nagelkerke R^2 values were 0.084, 0.096, and 0.226 for Models 1, 2, and 3, respectively.

DISCUSSION

The present study evaluated selected hematological markers for differentiating histopathologically confirmed reactive lymphoid hyperplasia (RLH) from acute appendicitis (AA) in children undergoing appendectomy. Patients with AA had significantly higher leukocyte, neutrophil, platelet, and SII values and lower lymphocyte counts than those with RLH. Among the evaluated markers, neutrophil count had the highest discriminatory performance (AUC=0.724), followed by SII (AUC=0.712) and leukocyte count (AUC=0.690). In multivariable analysis, SII remained independently associated with AA after adjustment for age, sex, and leukocyte count. However, in a separate model evaluating conventional hematological parameters, neutrophil and platelet counts were independently and positively associated with AA, whereas lymphocyte count showed an inverse association. Taken together, these findings suggest that SII may provide supportive information in differentiating AA from RLH but does not demonstrate a clear diagnostic advantage over routinely available hematological parameters, particularly the absolute neutrophil count.

Differentiating AA from RLH before surgery remains challenging because both conditions may share overlapping clinical and

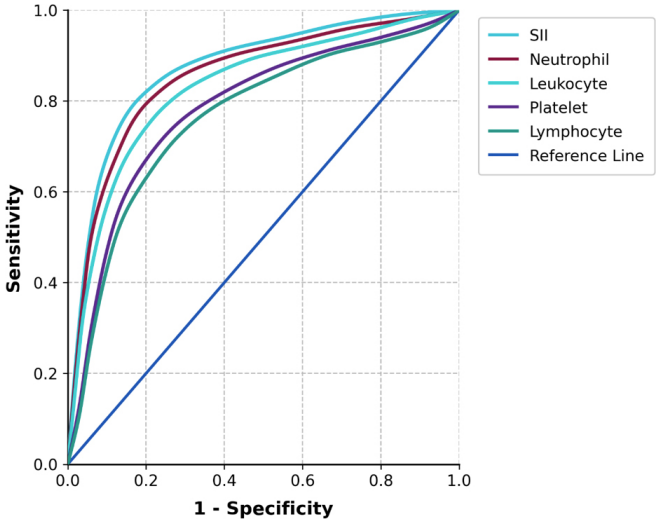

Figure 1. Receiver operating characteristic (ROC) curves showing the discriminatory performance of selected hematological markers for differentiating acute appendicitis from reactive lymphoid hyperplasia in children. Neutrophil count showed the highest area under the curve (AUC=0.724), followed by the systemic immune-inflammation index (SII; AUC=0.712), leukocyte count (AUC=0.690), platelet count (AUC=0.604), and lymphocyte count (AUC=0.602).

ultrasonographic features. RLH is characterized by lymphoid follicular enlargement within the appendiceal wall, usually related to viral infection or antigenic stimulation, and may produce mural thickening that resembles inflammatory appendicitis (8, 20). Previous studies have reported RLH in approximately 10–20% of pediatric appendectomy specimens, although this proportion varies according to patient selection and pathological criteria (7, 21). Because definitive differentiation between AA and RLH relies on histopathological examination of the resected appendix, the identification of preoperative parameters that may contribute to this distinction remains clinically relevant (8, 9).

The systemic immune-inflammation index integrates platelet, neutrophil, and lymphocyte counts into a single parameter and therefore reflects several components of the inflammatory and immune responses (13). The higher SII values observed in AA in the present study are consistent with the neutrophilia, relative lymphopenia, and platelet response that may accompany acute inflammation. RLH, in contrast, represents lymphoid proliferation associated with antigen-driven immune stimulation rather than the neutrophil-predominant inflammatory response characteristic of AA (5, 8). Nevertheless, these hematological changes are not specific to appendicitis and may occur in a variety of inflammatory conditions. Accordingly, SII should be regarded as a supportive inflammatory marker rather than a disease-specific biomarker.

The ROC findings provide important context for interpreting the potential role of SII. Neutrophil count showed the highest AUC (0.724), followed closely by SII (0.712), whereas leukocyte count had an AUC of 0.690. Therefore, although SII demonstrated moderate discriminatory ability, it did not outperform the absolute neutrophil count. Previous pediatric studies have also reported diagnostic or prognostic associations between SII and acute appendicitis. Firinci et al. (17) reported high diagnostic performance for SII when children with appendicitis were compared with elective surgical controls. Feier et al. (15) demonstrated associations between systemic inflammatory indices and appendicitis severity across different age groups. Siki et al. (16) also reported diagnostic value for SII in children with AA. Differences in diagnostic performance across studies may partly reflect differences in comparator populations. In the present study, the control group consisted exclusively of patients with histopathologically confirmed RLH, which represents a clinically relevant mimic of AA and may itself be associated with alterations in inflammatory parameters.

The multivariable analyses further clarify the relationship between SII and conventional hematological markers. SII remained independently associated with AA after adjustment for age and sex and retained this association after leukocyte count was added to the model. However, because SII is mathematically derived from neutrophil, lymphocyte, and platelet counts, its individual components were evaluated in a separate model to avoid simultaneously entering mathematically dependent variables. In this conventional hematological model, neutrophil and platelet counts were independently and positively associated with AA, whereas lymphocyte count was inversely associated; leukocyte count was not independently significant. These findings indicate that the association observed for SII likely reflects the combined contribution of its constituent hematological components and should not be interpreted as evidence of superiority over simpler CBC parameters. In particular, the strong independent association of neutrophil count, together with its numerically higher AUC, supports the continued clinical relevance of this readily available conventional marker.

At their optimal cutoff values, both neutrophil count and SII demonstrated sensitivities above 80% and NPVs above 90% in the present cohort, whereas specificity and PPV were comparatively modest. These findings suggest that lower values of these markers may provide supportive information when AA is considered less likely; however, they should not be used in isolation to exclude the diagnosis or determine management. Importantly, predictive values are influenced by disease prevalence, and the deliberately unequal composition of our study population (45 AA and 150 RLH cases) does not represent the prevalence of these diagnoses in routine clinical practice. Therefore, the PPV and NPV observed in this cohort should not be directly extrapolated to unselected pediatric populations. Rather than serving as standalone decision thresholds, these hematological markers may be most appropriately interpreted alongside clinical examination, established scoring systems, and imaging findings. Consistent with this approach, Guo et al. (22) reported improved diagnostic performance when SII was combined with the Pediatric Appendicitis Score, supporting the integration of laboratory markers with clinical assessment rather than their use in isolation.

A major strength of the present study is the use of histopathologically confirmed RLH as the comparison group. Previous investigations have often compared AA with heterogeneous populations, including normal appendices, negative appendectomy specimens, mesenteric lymphadenitis, or elective surgical controls (18, 19). Such comparator groups may not fully represent the specific diagnostic challenge posed by RLH, which can closely mimic AA. Similar to the studies by Kaya et al. (14) and Ucar Karabulut et al., (5) which evaluated hematological parameters in AA and lymphoid hyperplasia, the present study considered RLH as a distinct pathological entity. This approach provides a focused assessment of routinely available hematological markers in a clinically relevant differential diagnostic setting.

Limitations

This study has several limitations. First, its retrospective, single-center design introduces the possibility of selection bias. Only children who underwent appendectomy and had histopathologically confirmed AA or RLH were included; therefore, children with suspected RLH who were managed nonoperatively were not represented. Second, the AA cohort was randomly selected from the institutional appendectomy population, and the resulting distribution of AA and RLH was determined by the study design rather than by their prevalence in clinical practice. Consequently, PPV and NPV estimates should be interpreted within the context of this selected cohort and may not be directly generalizable to unselected populations. Third, laboratory parameters were evaluated only at admission, and potentially relevant variables such as C-reactive protein, clinical scoring systems, symptom duration, and imaging findings were not incorporated into the multivariable models. The relatively limited number of AA cases also restricted the number of variables that could be included in the regression analyses. Finally, the proposed cutoff values were derived from the same cohort in which diagnostic performance was assessed and were not externally validated.

Further prospective, multicenter studies incorporating clinical scores, inflammatory biomarkers, and imaging findings are needed to externally validate these results and determine whether combining routinely available hematological markers provides incremental diagnostic value in distinguishing pediatric AA from RLH.

CONCLUSION

Selected hematological markers may provide supportive information for differentiating acute appendicitis from reactive lymphoid hyperplasia in children. SII demonstrated moderate discriminatory performance and remained independently associated with acute appendicitis after adjustment for age, sex, and leukocyte count; however, it did not show a diagnostic advantage over the absolute neutrophil count. Conventional CBC parameters, particularly neutrophil count, also showed clinically relevant associations with acute appendicitis. Therefore, these readily available hematological markers should be considered adjuncts to, rather than substitutes for, clinical assessment and imaging findings. Prospective multicenter studies with external validation are needed to determine their incremental value in preoperative diagnostic assessment.

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Health Sciences, Umraniye Training and Research Hospital (Date: Sep 11, 2025, Decision No. 216).

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Hasta Onamı: Çalışmanın geriye dönük tasarımı nedeniyle bilgilendirilmiş onam şartından feragat edildi.

Çıkar Çatışması: Yazar, herhangi bir çıkar çatışması bulunmadığını beyan eder.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

Yazma Yardımı için Yapay Zeka Kullanımı: Çalışma verilerinin oluşturulması, yorumlanması, analiz edilmesi veya raporlanmasında yapay zeka (AI) destekli hiçbir teknoloji kullanılmamıştır. AI destekli dil araçları, yalnızca makalenin anlaşılırlığını ve dilbilgisi kalitesini artırmak amacıyla kullanılmıştır. Yazarlar, nihai makaleyi gözden geçirip onaylamışlardır ve içeriği konusunda tüm sorumluluğu üstlenmektedirler.

Yazarlık Katkıları: Fikir – NG, CŞ; Tasarım – NG, CŞ, CG; Denetlemeler – NG, CŞ; Veri toplanması ve/veya işleme – NG, CŞ, MSD, MA,CG; Analiz ve/veya yorumlama – NG, CŞ, MSD, CG; Literatür araştırması – NG, CŞ, MSD, SLM, CG; Yazım – NG; Eleştirel incelemeler – NG, CŞ, AK.

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