Original Article

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Comparison of the Diagnostic Value of the Neutrophil-to-Lymphocyte Ratio Versus the Pediatric Appendicitis Scoring System in Children with Suspected Acute Appendicitis

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ABSTRACT

Objective: This study aimed to evaluate and compare the diagnostic value of the neutrophil-to-lymphocyte ratio (NLR) and the pediatric appendicitis score (PAS) in pediatric patients with suspected acute appendicitis (AA).

Methods: This cross-sectional study included 300 children presenting with suspected AA who underwent appendectomy at Akbar Children's Hospital in Mashhad, Iran, between March 2022 and February 2024. Preoperative white blood cell count, neutrophil count, NLR, and PAS were assessed. Following appendectomy and histopathological confirmation, patients were stratified into three groups: negative appendicitis (normal appendix), uncomplicated appendicitis, and complicated appendicitis. Diagnostic parameters were then compared among these groups.

Results: A total of 300 children aged 6 to 18 years suspected of having AA were studied, including 175 boys (58.3%), with a mean age of 9.7±3.18 years. For the diagnosis of AA, an NLR cutoff of >2.82 yielded a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 97.15%, 92.59%, 98.35%, and 87.72%, respectively. Conversely, a PAS cutoff of >6.5 yielded a sensitivity, specificity, PPV, and NPV of 89.43%, 94.44%, 98.65%, and 66.23%, respectively.

Conclusion: Both NLR and the PAS were significantly elevated in children with AA. The NLR had higher sensitivity, whereas the PAS had greater specificity. Given its sensitivity, simplicity, and availability, the NLR could be effectively integrated into other clinical evaluations to enhance the diagnostic accuracy for AA in pediatric patients.

Keywords: Acute appendicitis; Pediatric appendicitis scoring; Neutrophil-to-Lymphocyte ratio; Children; Appendectomy.

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Introduction

Acute appendicitis (AA) in children often presents with atypical symptoms that mimic other conditions; however, it remains one of the most common causes of acute abdominal pain [1, 2]. The condition most frequently affects pediatric and adolescent populations, particularly those aged 10 to 19 years [3, 4]. Appendectomy is the definitive curative treatment, with an overall incidence rate of approximately 86 per 100,000 [5]. Despite advances in diagnostic modalities, including standard imaging such as computed tomography (CT) and ultrasonography, the negative appendectomy rate remains between 5% and 10% [6, 7]. Compared to adults, children experience higher rates of both complicated AA and negative appendectomies. This is largely attributed to anatomical factors, such as a thinner appendiceal wall, which compounds the diagnostic challenges [8]. In cases when there are no classic clinical signs, AA can be confused with other acute abdominal pathologies, and delayed diagnosis can lead to severe complications [9]. One of the most common differential diagnoses after a child is hospitalized for abdominal pain is "nonspecific abdominal pain" (NSAP)—a condition that, even after extensive clinical, laboratory, and imaging evaluations by a specialist, lacks a definitive etiology [10].

Various diagnostic tools have been developed to facilitate the early and accurate diagnosis of AA, minimize negative appendectomies, and reduce unnecessary emergency department revisits. These approaches encompass clinical scoring systems, inflammatory markers, imaging modalities, or a combination of these techniques [11]. Recent years have seen notable advancements in the diagnostic evaluation of pediatric patients with suspected AA [12]. Several studies have evaluated and compared the efficacy of standard scoring systems in children, including the pediatric appendicitis score (PAS), the Alvarado score, and the Appendicitis Inflammatory Response (AIR) score. The findings demonstrated that the use of scoring systems could aid physicians' decision-making, with the PAS emerging as the most useful tool [13]. Concurrently, while no single specific laboratory test is diagnostic for AA, numerous studies have investigated the use of inflammatory biomarkers for the early diagnosis, including the white blood cell (WBC) count, C-reactive protein (CRP), neutrophil count, and the neutrophil-to-lymphocyte ratio (NLR) [14]. The NLR is a cost-effective biomarker that reflects the balance between two distinct immune and inflammatory pathways, serving as a potential indicator of both the presence and severity of AA [15]. Furthermore, when combined with male sex, elevated leukocyte count, and right-sided abdominal pain, the NLR serves as an effective predictor and a reliable biomarker for ruling out, diagnosing, and grading the severity of AA [16].

Given the high prevalence of AA and the persistent diagnostic challenges, further research is required to improve diagnostic accuracy, assess disease severity for surgical prioritization, and reduce negative appendectomy rates. Therefore, our primary objective was to evaluate the predictive value of the NLR and PAS for diagnosing AA, differentiating uncomplicated from complicated appendicitis, and establishing optimal cutoff values for both metrics.

Materials and Methods

This cross-sectional study included 300 pediatric patients aged 6 to 18 years with a clinical suspicion of AA based on their history and physical examination. All participants underwent appendectomy at Akbar Children's Hospital in Mashhad, Iran, between March 2022 and February 2024.

Inclusion criteria were age 6 to 18 years with suspected AA requiring appendectomy. The exclusion criteria were known hematological disorders, chronic disease, active viral, bacterial, or parasitic infections, asthma, malignancies, autoimmune disorders, a history of abdominal trauma within the past 7 days, and pregnancy.

Data were collected using a checklist that included demographic characteristics, PAS criteria, admission complete blood count (CBC) results, and histopathological reports. The PAS scoring system evaluates eight clinical and laboratory parameters: migration of pain to the right iliac fossa (1 point), anorexia (1 point), nausea or vomiting (1 point), right iliac fossa tenderness (2 points), tenderness elicited by coughing, percussion, or hopping (2 points), elevated temperature (1 point), leukocytosis (1 point), and neutrophilia (1 point) yielding a total score ranging from 0 to 10. Following surgery, all appendiceal specimens underwent histopathological examination. Based on the pathological findings, patients were stratified into three groups: complicated appendicitis (defined by the presence of abscess, perforation, and gangrene), uncomplicated appendicitis (subacute, acute, or lymphoid hyperplasia), and negative appendicitis (normal appendix).

Descriptive statistics were utilized to summarize the data, with continuous variables presented as means and standard deviations or medians. The Kolmogorov–Smirnov test was used to assess the normality of data distribution. For normally distributed variables, parametric tests were used, including the Student's t-test for two-group comparisons and analysis of variance (ANOVA) with Tukey's post hoc test for multiple comparisons. The receiver operating characteristic (ROC) curve analysis and Youden's index were used to determine the optimal cutoff values for NLR and PAS. All statistical analyses were performed using SPSS software (version 26). A p-value <0.05 was considered statistically significant.

Results

In this cross-sectional analytical study, we examined 300 children aged 6-18 years suspected of AA and candidates for appendectomy, including 175 (58.3%) boys and 125 (41.7%) girls (boy-to-girl ratio 1.4:1), with a mean age of 9.7±3.18 years. The frequency distribution of PAS scores is shown in Figure 1. The mean leukocyte count, neutrophil percentage, lymphocyte percentage, and NLR were 13.56±4.99 (10^3/µL), 74.69±12.35%, 16.57±10.14%, and 7.02±5.34, respectively. Based on histopathological findings, 54 (18%) patients, with a mean age of 11.2 years, had negative appendicitis (normal appendix), and 246 (82%) children had confirmed appendicitis. Of these, 153 (51%) children, with a mean age of 9.5 years, were diagnosed with uncomplicated appendicitis (subacute, acute, lymphoid hyperplasia), and 93 (31%) children, with a mean age of 9.4 years, had complicated appendicitis (abscess, perforation, or gangrene).

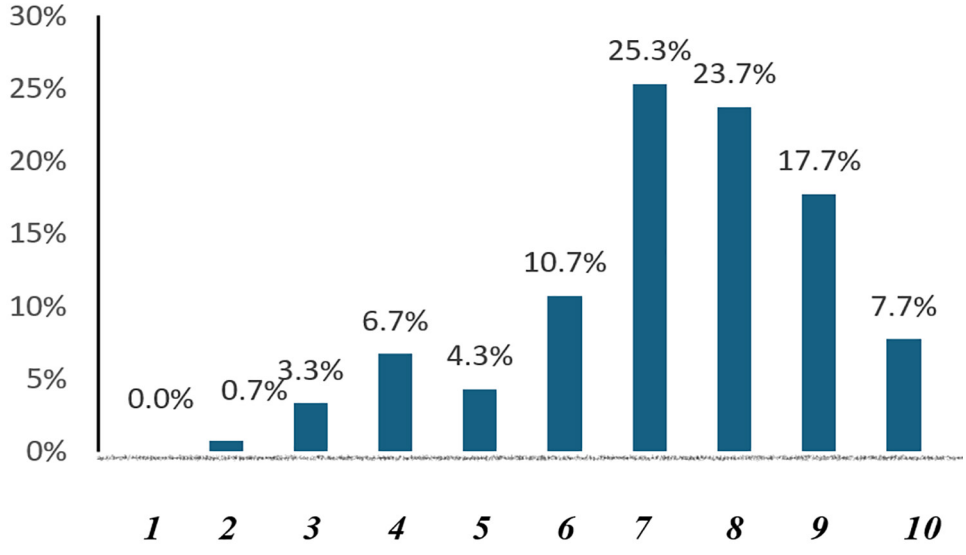


Fig. 1. Frequency distribution of pediatric appendicitis score (PAS) in children with suspected acute appendicitis.

Table 1. Distribution of histopathological outcomes in children with suspected acute appendicitis

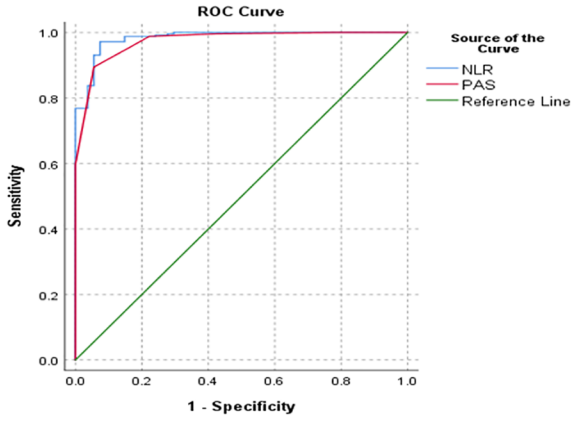
Pathology results	Uncomplicated[a]	Complicated[b]	Normal[c]	
Frequency n (%)	153 (51.0)	93 (31.0)	54 (18.0)	
Pathology based on Sex				
Girls n (%)	64 (51.2)	37 (29.6)	24 (19.2)	p=0.85
Boys n (%)	89(50.9)	56 (32.0)	30 (17.1)	
Pathology based on Age				
Mean±SD	9.5±3.1	9.4±2.8	11.2±3.7	F(ANOVA)=6.86 p=0.001** p^{ac} and p^{bc}<0.05*

For quantitative variables, the mean±SD, and for qualitative data, the frequency and percentage are reported. *p<0.05, **p<0.01

Table 2. Distribution of measured indices according to histopathological results in patients with suspected appendicitis.

Variable	Uncomplicated[a]		Complicated[b]		Normal[c]		*p value*
	mean	SD	mean	SD	mean	SD	
WBC (×10^3/µL)	13.28	4.01	17.02	4.72	8.40	2.71	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05
Neutrophil %	76.02	7.00	84.14	5.82	54.65	9.47	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05
Lymphocytes %	15.82	5.34	8.10	3.18	33.26	8.37	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05
NLR	5.62	2.70	12.36	5.69	1.81	0.76	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05
CRP	43.11	42.68	86.12	70.56	20.12	44.12	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05
PAS	7.40	1.02	8.67	0.98	4.44	1.24	0.0001 P^{ab}, P^{ac}, P^{bc}<0.05

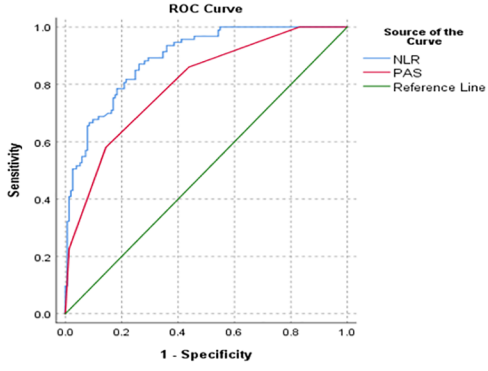
WBC: White blood cell count; NLR: Neutrophil-to-lymphocyte ratio; CRP: C-reactive protein; PAS: Pediatric appendicitis score; For quantitative variables, mean±SD was reported.



NLR AUC: 0.984	PAS
P <0.0001	AUC: 0.974
Youden index J 89.74	P <0.0001
Sensitivity: 97.15%	Youden index J 83.87
Specificity: 92.59	Sensitivity: 89.43%
	Specificity: 94.44%

Test Result / Variable(s)	Area	Std. Error	*p* value
NLR	0.98	0.007	0.0001
PAS	0.97	0.009	0.0001

Fig. 2. Receiver operating characteristic (ROC) curves for neutrophil-to-lymphocyte Ratio (NLR) and pediatric appendicitis score (PAS) in the diagnosis of acute appendicitis. NLR: Neutrophil-to-lymphocyte ratio; PAS: Pediatric appendicitis score



NLR	PAS
AUC: 0.892	AUC: 0.801
P <0.0001	P <0.0001
Youden index J 60.96	Youden index J 43.68
Sensitivity: 87.1%	Sensitivity: 58.06%
Specificity: 73.86%	Specificity: 85.62%
PPV: 66.94 NPV: 90.40	PPV: 71.05 NPV: 77.06

Test Result / Variable(s)	Area	Std. Error	*p* value
NLR	0.89	0.20	0.0001
PAS	0.80	0.27	0.0001

Fig. 3. Receiver operating characteristic (ROC) curves for neutrophil-to-lymphocyte ratio (NLR) and pediatric appendicitis score (PAS) in differentiating uncomplicated from complicated acute appendicitis. NLR: Neutrophil-to-lymphocyte ratio; PAS: Pediatric appendicitis score

According to Table 1, there was no significant difference in histopathological results between male and female patients (p=0.85). However, age analysis revealed that both uncomplicated and complicated appendicitis occurred more frequently in younger children, with pathological results differing significantly across the 3 age groups (p<0.05).

Table 2 details the distribution of laboratory parameters across the histopathological groups. Significant differences were observed among the three groups for WBC count, NLR, CRP, and PAS (all p=0.001).

ROC curve analysis for the diagnosis of appendicitis (Figure 2) revealed optimal cutoff points of 2.82 for NLR and 6.5 for PAS. The area under the ROC curve (AUC) was 0.98 for NLR and 0.97 for PAS, indicating that NLR had a marginally higher diagnostic accuracy than PAS for this purpose (0.98 vs. 0.97).

Furthermore, ROC curve analysis to differentiate between uncomplicated and complicated appendicitis (Figure 3) identified cutoff values of 6.56 for NLR and 8.5 for PAS. The corresponding AUCs were 0.89 and 0.80, respectively.

Discussion

In this cross-sectional study of 300 pediatric patients aged 6 to 18 years with suspected AA who underwent appendectomy, we found that the NLR showed higher sensitivity, whereas PAS demonstrated higher specificity for diagnosing AA. Consequently, a negative NLR result was more reliable for ruling out AA, while a positive PAS result was more reliable for confirming the diagnosis.

The PAS remains a valuable diagnostic tool for pediatric appendicitis. Chuluun *et al.* reported that a PAS of ≥6 strongly correlated with appendicitis, achieving 92.9% sensitivity and 99.3% specificity at a cutoff of 7.5, underscoring its utility in distinguishing appendicitis from other causes of abdominal pain and reducing negative appendectomy rates [4]. Similarly, Derakhshanfar *et al.* identified a cutoff

of 5.5, yielding 91% diagnostic accuracy in patients under 18 years of age [17]. In the present study, an optimal cutoff of 6.5 provided greater specificity while lower sensitivity, a discrepancy potentially attributable to differences in sample size and interobserver variability in PAS assessments.

The sensitivity and specificity observed in our study exceeded those reported by Schneider *et al.* [18], who reported values of 77% and 65%, respectively, in a cohort of 588 children under 10 years of age. Bhatt *et al.* [19] reported a sensitivity of 92.8% and a specificity of 69.3%, whereas Goldman *et al.*, [20] documented 94% and 98%, respectively, at a cutoff of 7. These variations might be attributed to differences in the study population. Notably, Goldman *et al.,* evaluated all children presenting with abdominal pain, rather than restricting the cohort to those with suspected AA. Furthermore, Fujii *et al.,* conducted a retrospective study of 72 children in Japan who underwent surgery for AA and found a significant difference in PAS values between uncomplicated and complicated cases [21]. A PAS cutoff ≥8 yielded a sensitivity of 73%, a specificity of 89%, a positive predictive value (PPV) of 91%, and a negative predictive value (NPV) of 68%, with higher scores correlating with prolonged hospital stays and increased postoperative complications. While our findings aligned with their observations regarding severity stratification, higher sensitivity and specificity were observed in our cohort.

Regarding the NLR, Haji Bandeh *et al.,* conducted a systematic review and meta-analysis evaluating its role in predicting AA and distinguishing between complicated and uncomplicated cases [22]. They reported that an NLR cutoff of 4.7 for diagnosing AA yielded a sensitivity of 88.9% and a specificity of 90.9%. For differentiating complicated from uncomplicated appendicitis, an NLR cutoff of 8.8 achieved a sensitivity of 76.9% and a specificity of 100%. Their findings showed significantly higher NLR values in patients with AA, particularly in complicated cases, supporting an elevated NLR as a predictive marker for complicated appendicitis. These results aligned with our observations. Similarly, Nicola *et al.,* evaluated the diagnostic value of NLR and PAS in three patient groups, reporting an NLR cutoff of 6.14 with a sensitivity of 75.5% and a specificity of 82.6%, demonstrating robust diagnostic accuracy for AA. In their study, the PAS, with a cutoff point of 6, demonstrated inferior performance, suggesting that NLR was superior for distinguishing negative from positive AA [23]. Our findings corroborated these conclusions, demonstrating the higher sensitivity and specificity of NLR for both diagnosing and stratifying AA.

In a separate systematic review, Yoon and colleagues reported that NLR had a sensitivity of 82% and a specificity of 76% for diagnosing AA [24]. For comparison, the WBC count achieved a sensitivity of 79% and a specificity of 66%, while CRP demonstrated a sensitivity of 73% and a specificity of 68%. The analysis concluded that NLR provided moderate diagnostic power for pediatric appendicitis. In contrast, our study demonstrated greater diagnostic accuracy for the NLR. Such discrepancies might reflect variations in study populations, clinical settings, laboratory assay methodologies, and histopathological reference standards.

This study had several limitations. First, the relatively limited sample size and single-center design might restrict the generalizability of our findings. Second, the inclusion of only patients who ultimately underwent appendectomy introduced a potential selection bias, as it excluded those managed conservatively or discharged without surgery. Future research should prioritize larger-scale, multicenter prospective studies that encompass all children presenting with suspected AA, regardless of whether surgical intervention is performed.

In conclusion, our findings indicated that both the NLR and the PAS were significantly elevated in children with AA. While the NLR offered superior sensitivity, making it an excellent tool for ruling out the diagnosis of AA, the PAS provided greater specificity, rendering it highly reliable for confirming the diagnosis. The concurrent use of both metrics might represent an optimal diagnostic strategy to confirm appendicitis and minimize negative appendectomy rates. Given its high sensitivity, simplicity, and widespread availability, the NLR could be seamlessly integrated into routine clinical evaluations to enhance the diagnostic accuracy for AA in pediatric patients.

Declaration

Ethics Approval and Consent to participate: The present study received ethical approval under the code of ethics with the ID number (IR.IAU.MSHD.REC.1401.173). Written informed consent was obtained from the parents or legal guardians of all participants included in the study. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for Publication: All authors have read and approved the final version of the manuscript and consent to its publication.

Conflict of Interest: The authors declare that they have no conflicts of interest.

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Data Availability Statement: The data that support

the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contributions: MM: Conceptualization, investigation, data curation, and writing-original draft; TZ: Conceptualization, data curation, and writing-review and editing; JY: Writing-original draft; AK: Data curation and writing-original draft; FO: Data curation and writing-original draft; SMAR: Writing-original draft.

Declaration of generative AI in scientific writing: The authors used Grammarly to enhance the manuscript's readability and language.

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