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Research Article

Relationship of Prognostic Nutritional Index, HALP score and Inflammatory Markers with Clinical Outcomes in Children with Complicated Appendicitis

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Abstract

Aim: One of the most frequent diagnoses in children presenting with acute abdominal pain is acute appendicitis. This study aims to analyze the effectiveness of the biomarkers such as the Prognostic Nutrition Index (PNI), hemoglobin-albumin-lymphocyte-platelet (HALP) score, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) in predicting complicated appendicitis in children who undergo surgery for acute appendicitis.
Material and Method: A total of 253 children who underwent surgery for acute appendicitis in our clinic between January 1, 2022, and October 1, 2024, and underwent surgery for acute appendicitis were included in our study.
Results: Among the cases, 81% (n=205) were classified in the non-complicated, while 19% (n=48) were in the complicated group. In our analysis, we found that the PNI (p=0.027) and HALP score (p=0.007) were considerably lower in the complicated appendicitis group, whereas the neutrophil-to-lymphocyte ratio (NLR) (p=0.003) and platelet-to-lymphocyte ratio (PLR) (p=0.008) were significantly higher. Correlation analysis revealed a meaningful positive association between PNI and HALP score, a mild unfavorable association between PNI and both PLR and NLR, a strong positive correlation between HALP score and both PLR and NLR and a mild positive relationship between NLR and PLR.
Conclusion: PNI, HALP score, NLR, and PLR values measured at the time of admission to the emergency services may serve as potential predictors in differentiating between complicated and non-complicated appendicitis.

Keywords: Children, complicated appendicitis, prognostic nutritional index, hemoglobin-albumin-lymphocyte-platelet score, inflammatory markers

INTRODUCTION

Acute appendicitis (AcA) is one of the leading causes of acute abdominal pain in pediatric patients (1). If not promptly treated, increasing inflammation may lead to gangrene and necrosis of the appendix, ultimately resulting in perforation. This progression complicates AcA and may be accompanied by more severe complications such as abscess formation and generalized peritonitis (1,2).

The use of scoring systems in conjunction with diagnostic tools specifically ultrasonography (USG) and computed tomography (CT) helps reduce perforation rates, hospital stays, and unnecessary surgical interventions (3). However, studies continue to focus on developing more effective diagnostic methods to decrease the incidence of complicated appendicitis (CA) and to reduce mortality and morbidity rates, with particular emphasis on laboratory biomarkers (4).

Serum albumin is a well-known acute-phase protein that negatively correlates with conditions such as severe infection, systemic inflammation, malnutrition, and immunosuppression (5). In such clinical conditions, an elevation in platelet and neutrophil counts, a decline in lymphocyte levels, and the development of anemia are commonly observed (6). Based on these parameters, biomarkers such as the Prognostic Nutritional Index (PNI) (7,8), hemoglobin-albumin-lymphocyte-platelet (HALP) score (9,10), neutrophil-to-lymphocyte ratio (NLR), and

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platelet-to-lymphocyte ratio (PLR) (11) have been shown in various studies to be valuable in assessing an individual's immunological and nutritional status in processes associated with infection, inflammation, and malnutrition, and may be effective in predicting prognosis.

In this study, we aimed to determine whether there are significant differences and correlations between PNI, NLR, PLR, and HALP scores in pediatric CA and non-complicated appendicitis (NCA) cases, thereby evaluating the diagnostic efficacy of these biomarkers in predicting CA.

MATERIAL AND METHOD

Study Design

A retrospective descriptive cohort methodology was employed in this study. Children under the age of 18 who presented to the Aksaray University Department of Pediatric Surgery between January 1, 2022, and October 1, 2024, and who were prediagnosed with AcA based on history, physical examination, laboratory tests, USG, and, when necessary, CT, and subsequently underwent surgery, were incorporated into the study. Children who who had received antibiotic treatment prior to surgery had no recorded appendix diameter on USG or CT, had non-visualized appendices, or whose pathology reports indicated lymphoid hyperplasia, fibrous obliteration, carcinoid tumor, mucocele, or parasitic infestation, as well as those with a history of previous abdominal surgery, incomplete medical records, or chronic diseases, were omitted from the study.

Data Collection

Patient details were obtained from electronically stored medical records. After applying the exclusion criteria, 253 cases were ultimately included in the study. Based on pathological or intraoperative findings, the patients were categorized as either non-complicated appendicitis (NCA; acute suppurative, acute phlegmonous) or complicated appendicitis (CA; perforated, gangrenous, or with phlegmon formation).

Gender, age at presentation, hemogram, electrolytes, renal and liver function tests, hemostasis parameters including C-reactive protein (CRP), coagulation tests (INR, PT, PTT) , appendix diameter reported by USG or CT and appendix pathology report were recorded. In addition, PNI [Albumin (g/L) + 0.005x Total Lymphocyte count (mm^3)], NLR (Neutrophil-to-Lymphocyte ratio), PLR (Platelet-to-Lymphocyte ratio), HALP score [(Hemoglobin (g/L) x Albumin (g/L) x Lymphocyte count (n/L)/Platelet count (n/L)] at admission were calculated and recorded.

Ethics Approval

The research was ethically approved by Aksaray University Scientific Research Ethics Committee on November 21, 2024 with decision number 2024/135.

Statistical Analysis

Data from the study were analyzed using version 23 of IBM SPSS Statistics software for Windows. To assess the normality of numerical variables, the Shapiro-Wilk test and skewness and kurtosis values were used. For continuous variables, basic statistical analyses were reported as median and interquartile range (25th–75th percentile), while categorical variables were expressed as frequencies and percentages.

The Spearman correlation analysis test was used to evaluate the relationships between two continuous variables. The Mann–Whitney U test served to evaluate differences in continuous variables across two independent groups, as the Fisher's Exact Test was used for categorical variables. Results with p-values under 0.05 were considered significant.

RESULTS

A total of 253 patients, including 165 boys and 88 females with a median age of 12 years (IQR: 9–15) at the time of admission, were analyzed in our study. Of the cases, 81% (n=205) were classified in the NCA group, while 19% (n=48) were in the CA group. Among the NCA cases, 72.7% (n=149) were diagnosed with acute suppurative appendicitis, and 27.3% (n=56) with acute phlegmonous appendicitis. In the CA group, 85.4% (n=41) had perforated appendicitis, 10.4% (n=5) had gangrenous appendicitis, and 4.2% (n=2) had plastron appendicitis.

Regarding age and sex variables, no statistically marked variation was found between the two groups. The median (IQR) appendix diameter measured via ultrasonography or CT was 10 mm (8.85–11.00) in the CA group and 8.5 mm (7.0–10.0) in the NCA group, with a meaningful statistical importance between the groups (p<0.001) (Table 1).

The overall median (IQR) PNI value was 54.4 (46.77–60.40), whereas it was lower in the CA group at 50.17 (42.85–58.21), with a meaningful statistical disparity between the groups (p=0.027). The HALP score median (IQR) was 4.05 (2.21–7.08) overall and 3.25 (1.28–5.46) in the CA group, again showing a statistically meaningful significance between the groups (p=0.007) (Table 1).

The median (IQR) NLR and PLR values were 6.53 (3.81–12.78) and 182.41 (105.34–350.46), respectively, in the CA group, and 4.55 (2.53–8.44) and 138.42 (85.17–224.59) in the NCA group. Both NRL and PLR were to a considerable extent higher in the CA group compared to the NCA group (p=0.003 and p=0.008) (Table 1).

The median (IQR) neutrophil and platelet counts were higher in the CA group [12,385.0/mm^3 (9,852.5–14,165.0) and 330,000/mm^3 (261,000–371,000), respectively] than in the NCA group [10,560/mm^3 (7,285–13,490) and 281,000/mm^3 (221,000–364,000), respectively]. In the analysis, both neutrophil and platelet counts were found to be statistically significantly higher in the CA group (p=0.022 and p=0.024) (Table 1).

In comparison to the NCA group, the CA group exhibited significantly higher CRP levels and slightly lower sodium levels [median (IQR) CRP: 119.0 mg/L (79.75–182.75) vs. 10.75 mg/L (2.31–40.75); Sodium: 136.0 mmol/L

(134.25–138.00) vs. 137.0 mmol/L (135.0–139.0)]. Statistically meaningful disparities were found between the two groups for both CRP and sodium (p<0.001 and p=0.047). The median (IQR) PT and INR values in the CA group were 12.90 seconds (12.23–15.17) and 1.11 (1.07–1.22), respectively, while in the NCA group, they were 12.51 seconds (12.13–13.50) and 1.07 (1.02–1.14), respectively. There was a statistically meaningful significance between the CA and NCA in terms of INR but not for PT (p=0.001 and p=0.39) (Table 1).

Table 1. Comparison of demographic, laboratory and pathological findings of the two groups

	Complicated (n=48)	Non-complicated (n=205)	
	MD (25-75 IQR)	MD (25-75 IQR)	p
Age (year)	12.0 (9.00–14.75)	12.0 (9.0–15.0)	0.90*
Appendix diameter (mm)	10 (8.85–11.00)	8.5 (7.0–10.0)	**<0.001***
Hemoglobin (g/L)	12.95 (12.10–13.77)	13.50 (12.40–14.50)	0.054*
Leukocyte (/mm³)	15315.0 (13065.0–17122.5)	13900 (10225–16975)	0.061*
Neutrophil (/mm³)	12385.0 (9852.5–14165.0)	10560 (7285–13490)	**0.022***
Lymphocyte (/mm³)	1850.0 (987.0–2937.5)	2160.0 (1380.0–3035.0)	0.05*
Platelet (/mm³)	330000 (261000–371000)	281000 (221000–364000)	**0.024***
C-Reactive protein (mg/L)	119.0 (79.75–182.75)	10.75 (2.31–40.75)	**<0.001***
Albumin (g/L)	40.00 (36.12–45.67)	43.1 (38.95–46.75)	0.05*
Sodium (mmol/L)	136.0 (134.25–138.00)	137.0 (135.0–139.0)	**0.47***
Potassium (mmol/L)	4.1 (4.0–4.5)	4.1 (3.9–4.35)	0.766
AST (u/L)	14.5 (11.25–20.00)	16.0 (11.0–20.0)	0.893*
ALT (u/L)	14.5 (11.25–18.00)	16.0 (11.8–20.0)	0.301*
Creatinine (mg/dl)	0.55 (0.47–0.68)	0.57 (0.47–0.68)	0.738*
Urea (mg/dl)	23.0 (17.25–30.75)	23.0 (18.0–28.0)	0.659*
PT (sec)	12.90 (12.23–15.17)	12.51 (12.13–13.50)	**0.39***
INR	1.11 (1.07–1.22)	1.07 (1.02–1.14)	**0.001***
PTT (sec)	24.51 (21.52–28.37)	24.80 (22.00–28.41)	0.990*
NLR	6.53 (3.81–12.78)	4.55 (2.53–8.44)	**0.003***
PLR	182.41 (105.34–350.46)	138.42 (85.17–224.59)	**0.008***
HALP score	3.25 (1.28–5.46)	4.43 (2.42–7.25)	**0.007***
PNI	50.17 (42.85–58.21)	55.10 (47.40–60.87)	**0.027***
	Complicated n (%)	**Non– Complicated n (%)**	
Gender			
Female	19 (39.6)	69 (33.7)	0.518**
Male	29 (60.4)	136 (63.3)	
Pathology			
Suppurative appendicitis	-	149 (72.7)	
Phlegmoneus appendicitis	-	56 (27.3)	
Gangrenous appendicitis	5 (10.4)	-	
Perforated appendicitis	41 (85.4)	-	
Plastron appendicitis	2 (4.2)	-	

*Mann Whitney U test, **Fisher exact test, MD: median, AST: aspartate aminotransferase, ALT: alanine aminotransferase, PT: prothrombin time, INR: international normalized ratio, PTT: partial thromboplastin time, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, HALP: hemoglobin, albumin, lymphocyte, and platelet, PNI: prognostic nutritional index

Table 2 displays the correlation analysis among the variables. A considerable positive correlation exists between NLR and PLR (r=0.786, p<0.001). NLR displayed a mild inverse association with PNI (r=-0.698, p<0.001) and a strong inverse association with HALP score (r=-0.762, p<0.001). PLR showed a strong negative association with PNI (r=-0.788, p<0.001) and a very strong negative association with HALP score (r=-0.967, p<0.001). The HALP score had a strong positive association with PNI (r=0.875, p<0.001).

Table 2. Correlations between variables

Spearman			1	2	3	4	5	6	7
1	Appendix diameter (mm)	r	1						
		p	.						
2	CRP (mg/L)	r	.193**	1					
		p	0.002	.					
3	Na (mmol/L)	r	-.148*	-.302**	1				
		p	0.018	0.000	.				
4	INR	r	0.04	.299**	-.272**	1			
		p	0.526	0.000	0.000	.			
5	NLR	r	.222**	.230**	-.200**	.186**	1		
		p	0.000	0.000	0.001	0.003	.		
6	PLR	r	0.056	.225**	-.155*	.145*	.786**	1	
		p	0.376	0.000	0.014	0.022	0.000	.	
7	HALP	r	-0.046	-.265**	.215**	-.202**	-.762**	-.967**	1
		p	0.467	0.000	0.001	0.001	0.000	0.000	.
8	PNI	r	-0.09	-.262**	.239**	-.255**	-.698**	-.788**	.875**
		p	0.155	0.000	0.000	0.000	0.000	0.000	0.000

CRP: C-reactive protein, Na: sodium, INR: international normalized ratio, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, HALP: hemoglobin, albumin, lymphocyte, and platelet, PNI: prognostic nutritional index, **p<0.01, *p<0.05

DISCUSSION

Among the studies conducted so far, no prior research has specifically evaluated the prognostic value of PNI and HALP scores in pediatric appendicitis cases. In our study, we found that both the PNI (p=0.027) and HALP (p=0.007) scores were to a considerable extent lower in the CA compared to the NCA. Conversely, NLR and PLR values were to a considerable extent higher in the CA group than NCA (p=0.003 and p=0.008). Furthermore, PNI demonstrated a strong positive relationship with the HALP score, a strong negative correlation with PLR, and a moderate negative correlation with NLR. The HALP score was very strongly negatively correlated with PLR and strongly negatively correlated with NLR. Additionally, we observed a strong positive relationship between NLR and PLR.

PNI is a composite score calculated based on serum albumin and lymphocyte levels, reflecting an individual's nutritional, immunologic, and inflammatory status. Initially developed to assess prognosis and mortality risk in malnourished cancer patients (7), subsequent studies have shown its relevance in various inflammatory processes. PNI has been found to reflect immune status, inflammation, and nutrition and has also been reported to predict overall survival in several malignancies (8,12). In a study involving 514 patients undergoing abdominal surgery, it was observed that the preoperative PNI values of patients with wound infection were markedly lower than the other patients (13). Similarly, in a study of 45 patients who underwent surgery for strangulated ileus, preoperative PNI values were significantly lower in those who developed postoperative complications compared to those who did not. Moreover, a strong negative correlation was reported between PNI and NLR (8). In another study including 699 adult patients with AcA, PNI values were markedly lower in the CA group compared to the NCA group. Regression analysis identified PNI as an important risk factor in distinguishing between CA and NCA (12). Consistent with the literature, our study found that PNI values were markedly lower in the CA cases compared to NCA (p=0.027). What's more, we observed a strong positive relationship between PNI and HALP score (r=-0.875, p<0.001), a strong negative correlation with PLR (r=-0.788, p<0.001), and a moderate opposite association with NLR (r=-0.698, p<0.001).

Recent studies have demonstrated that the HALP score can serve as an indicator of prognosis in various conditions involving inflammation and malignancy (9,10,14). In a retrospective study of 436 adult appendicitis cases, in the CA group, the HALP score was markedly reduced in comparison to the NCA group (15). Similarly, in another study evaluating adult AcA patients categorized by high and low HALP scores based on a cutoff value, abscess formation, perforation, and postoperative morbidity were significantly higher among those with low HALP scores (14). Consistent with these findings, our study also found a significantly lower HALP score in the CA group (p=0.007), along with strong negative correlations between the HALP score and both PLR (r=-0.967, p<0.001) and NLR (r=-0.762, p<0.001).

It has been widely shown that both NLR and PLR are important biomarkers reflecting systemic inflammation, not only in cancer but also in various systemic diseases (16,17). The ease with which these indices can be calculated from routine complete blood counts offers a significant practical advantage. In a study assessing inflammatory markers in adult AcA patients with CA and NCA classification, PLR and NLR were significantly elevated in the CA group, indicating their potential role in predicting CA (12). Likewise, in a study including 504 pediatric patients admitted with abdominal pain, NLR and PLR values were significantly higher among children who required surgery, suggesting these markers may serve as practical tools in identifying surgical abdominal pain in children (18). In another study involving 1265 children operated on with a prediagnosis of AcA, NLR and PLR values were found to be significantly higher in the AcA group than in the pathologically appendicitis negative group and also in the CA group than in the NCA group (19). In the course of this study, both NLR (p=0.003) and PLR (p=0.008) values were markedly elevated in the CA group, and a strong positive association was observed between these two markers (r=0.786, p<0.001). These findings may reflect increased systemic inflammation in the CA group.

Currently, imaging modalities allow for direct visualization and measurement of the appendix, and a diameter of <6 mm is generally accepted as normal, while an appendiceal diameter of ≥6 mm is considered a valuable diagnostic finding for appendicitis (3). In a study involving 574 adult patients diagnosed with AcA, increased appendiceal diameter on ultrasound or CT was found to be significantly associated with higher rates of CA (11). Similarly, in a study evaluating 171 pediatric cases of gangrenous and non-gangrenous appendicitis, the diameter of the appendix was considerably greater in gangrenous cases (20). In our study, we also found that the appendiceal diameter was markedly larger in the CA group (p<0.001). We believe that increased inflammation leads to more pronounced edema in the appendiceal wall, and the resulting obstruction of the lumen increases intraluminal pressure, contributing to this finding.

CRP is an acute phase protein, and higher CRP values have been shown to aid in the diagnosis of CA in various studies on AcA (11,21). Consistent with the literature, in our analysis, a considerable rise in CRP levels was observed in the CA (p<0.001).

During intense inflammatory responses, the rapid consumption of coagulation factors can lead to disseminated intravascular coagulation, a condition associated with an increased risk of bleeding (22). PT is used to assess the extrinsic hemostatic cascade, and the INR is a standardized value derived from PT that allows for consistent reporting across laboratories. Recent studies have suggested that elevated PT and INR levels may serve as predictive markers for CA (23,24). In our study, we found that both PT (p=0.039) and INR (p=0.001) levels were substantially higher in the CA group. Given the role of inflammation in surgical conditions, we recommend evaluating these parameters preoperatively to predict the severity of inflammation better and take necessary precautions.

This study has some limitations. First, its retrospective design carries the risk of information and selection bias. Second, the single-center nature of the study may limit the generalizability of the findings. Despite these limitations, the study also has some strengths. The inclusion of a relatively large cohort of patients increases the statistical power and reliability of the findings. Moreover, the combined assessment of multiple inflammatory indices such as NLR, PLR, PNI and HALP score allowed a more comprehensive analysis of the systemic inflammatory response and strengthened the robustness of prognostic assessments.

CONCLUSION

In pediatric patients, acute appendicitis is among the leading causes requiring emergency surgical intervention, and early diagnosis is crucial. In addition to routine evaluations, blood-based biomarkers derived from complete blood counts and biochemical analyses may help predict the presence of complicated appendicitis in pediatric patients presenting with abdominal pain. These biomarkers can help the surgeon select the most appropriate treatment approach.

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