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Evaluation of inflammatory markers and HALP score in childhood intussusceptions

Evaluation of inflammatory markers in childhood intussusception

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Abstract

Aim: Intussusception is the most common abdominal emergency in infancy. This study aims to determine whether HALP score and inflammatory markers scores, such as NLR and PLR, differ between cases requiring surgical reduction and those not requiring surgical reduction in patients diagnosed with intussusception who presented to the pediatric emergency department.

Methods: Our study included 78 children diagnosed with intussusception who presented to the Aksaray Training and Research Hospital Pediatric Emergency Department between January 1, 2018, and September 31, 2024. The cases were divided into two groups based on their treatment method: surgical and non-surgical.

Results: When comparing the groups, a significant difference was found for all three markers ($p<0.0001$) in terms of neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and HALP score. However, no statistically significant difference was detected for C-reactive protein levels ($p=0.095$).

Conclusion: NLR, PLR, and HALP scores can be utilized as useful markers in evaluating the prognosis of childhood intussusception. The effectiveness of these biomarkers should be validated by future studies.

Keywords

invagination, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, halp score

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Introduction

intussusception, a significant cause of acute abdominal emergencies in children, is defined as the telescoping of a proximal bowel segment into a distal one.[1] If left untreated, it disrupts the circulation to the bowel wall, leading to intestinal obstruction, venous congestion, and edema. This can further progress to necrosis, perforation, and shock.[2] While intussusception primarily affects children under three years of age, it is most commonly observed between five and nine months of age.[3]

While most cases of intussusception in children are idiopathic, approximately 5% of cases have a pathological lead point initiating the intussusception, such as a Meckel's diverticulum, duplication cyst, intestinal polyps, cystic fibrosis, lymphoma, or lymphadenopathy.[4]

While asymptomatic transient ileoileal or jejunal intussusceptions often resolve with conservative observation, symptomatic ileocolic intussusceptions in hemodynamically stable patients are primarily managed with pneumatic or hydrostatic reduction. Surgical manual reduction is reserved for cases where intussusception persists after these interventions or when there are signs of generalized peritonitis, perforation, or shock.[5]

In recent years, easily measurable markers like the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been shown to indicate the severity of systemic inflammation and correlate with prognosis in various infectious and inflammatory conditions.[6-9] Recent studies have indicated that the HALP score can serve as a prognostic factor in malignancies affected by inflammation and nutrition. This is attributed to anemia occurring in inflammatory processes, weakened immunity, and severe infections, alongside decreased albumin (a negative acute phase reactant), reduced lymphocyte count, and elevated platelet count.[9-11]

In our study, we aim to determine if there is a difference in NLR, PLR, and HALP scores between cases of childhood intussusception requiring surgical manual reduction and those not undergoing surgical treatment. By doing so, we intend to evaluate the effectiveness of these inflammatory markers in predicting the need for surgical manual reduction.

Materials and Methods

Study Design

Our study was conducted as a retrospective descriptive cohort study. We included 78 children under 18 years of age who presented to the Aksaray University Training and Research Hospital pediatric emergency department with a diagnosis of intussusception and were subsequently followed and treated between January 1, 2018, and September 31, 2024. Children who had previously presented with intussusception, those with an unclear radiological type of intussusception, and those with chronic diseases were excluded from the study.

Data Collection

Patient data were obtained from files. The included patients were divided into two distinct groups: a non-surgical group, comprising those treated with conservative observation or hydrostatic reduction, and a surgical group, consisting of patients who did not respond to hydrostatic reduction or presented with signs of generalized peritonitis, perforation, or shock, subsequently undergoing surgical manual reduction.

For each case, sex, age, prominent complaint at admission (abdominal pain, vomiting, bloody stools, diarrhea), season of admission, ultrasonographically measured length and type of the intussuscepted segment, and C-reactive protein (CRP) level at admission were recorded.

NLR (Neutrophil/Lymphocyte Ratio), PLR (Platelet/Lymphocyte Ratio), and the HALP score [(Hemoglobin (g/L) x Albumin (g/L) x Lymphocyte count (n/L) / Platelet count (n/L)] were evaluated at admission. Additionally, in the surgical group, these inflammatory markers were re-evaluated on postoperative day 3.[12]

Ethical Approval

This study was approved by the Ethics Committee of Aksaray University Health Sciences Scientific Research (Date: 05.09.2024, Decision No:2024/082).

Statistical Analysis

IBM SPSS (Statistical Package for the Social Sciences) 23 for Windows was used for the statistical analysis of the research data. The Kolmogorov-Smirnov test and skewness and kurtosis values, which are other assumptions of normal distribution, were used for normality tests of numerical variables. Comparisons between two independent groups were analyzed using the Mann-Whitney U test, and comparisons between two dependent groups were analyzed using the Wilcoxon signed-rank test. For descriptive statistics, the median (25-75 Interquartile Range) was used for non-normally distributed data, and numbers and percentages were used for categorical variables. Chi-square and Fisher's Exact tests were used to analyze categorical data. Significance was evaluated based on $p<0.05$ for each variable.

Reporting Guidelines

This study was reported according to the STROBE guidelines.

Results

Results

The study included 78 patients, of whom 37.2% (n = 29) were female and 62.8% (n = 49) were male, with no significant difference observed between the groups in terms of gender (p=0.684). The median age (25–75 IQR) of the patients at admission was 19.0 (13.0–39.75) months, which was 35.0 (13.75–58.50) in the surgical group and 16.5 (12.25–31.0) in the non-surgical group. Age was significantly higher in the surgical group (p=0.01) (Table 1). While 71.7% of cases aged ≤3 years were treated non-surgically, 60.2% of cases aged >3 years underwent surgical reduction, a statistically significant difference (p=0.012).

It was observed that 33.3% (n = 26) of cases presented in winter, 30.8% (n = 24) in autumn, 24.4% (n = 19) in spring, and 11.5% (n = 9) in summer. No significant difference was found between groups based on season (p=0.349).

When evaluating prominent complaints at admission, 25% (n = 6) of cases with abdominal pain, 90% (n = 9) with bloody stools, 47.8% (n = 11) with vomiting, and 21.1% (n = 4) with diarrhea underwent surgical reduction. A statistically significant difference was observed between groups (p=0.001) (Table 1).

Based on ultrasound-detected intussusception type, colocolic and jejunojejunal intussusceptions were not observed in the surgical group. However, 10.3% (n = 3) of ileoileal intussusceptions and 60% (n = 27) of ileocolic intussusceptions required surgical intervention, with a significant difference between groups (p<0.001) (Table 1). The median (25–75 IQR) intussuscepted segment length was 48 (40–61.25) mm in the surgical group and 20 (15–30) mm in the non-surgical group, a statistically significant difference (p<0.001) (Table 1).

The median (25–75 IQR) CRP level was 9.88 (2.41–21.39) in the surgical group and 3.55 (0.60–14.55) in the non-surgical group,

with no significant difference (p=0.095). The median NLR was 5.50 (4.33–7) in the surgical group and 2.01 (1.35–2.52) in the non-surgical group. The median PLR was 203.37 (168.75–250.79) in the surgical group and 101.72 (72.95–131.69) in the non-surgical group. The median HALP score was 2.44 (1.85–3.23) in the surgical group and 5.58 (4.28–7.37) in the non-surgical group. Statistically significant differences were found for NLR, PLR, and HALP score between groups (p<0.001) (Table 1).

Table 1. *Comparison of demographic, clinical characteristics and inflammatory markers of the two groups*

Variable	Surgery (n = 30)	Non-Surgery (n = 48)	*P* value
	MD (25-75 IQR)	MD (25-75 IQR)	
Age, mo	35.0 (13.75-58.50)	16.5 (12.25-31.0)	.01*
Invaginated segment, mm	48 (40-61.25)	20 (15-30)	<0.001*
CRP	9.88 (2.41-21.39)	3.55 (0.60-14.55)	.095*
NLR	5.50 (4.33-7)	2.01 (1.35-2.52)	<0.001*
HALP score	2.44 (1.85-3.23)	5.58 (4.28-7.37)	<0.001*
PLR	203.37 (168.75-250.79)	101.72 (72.95-131.69)	<0.001*
	Surgery	Non-Surgery	
	n (%)	n (%)	
Gender			
Female	12 (41.4)	17 (58.6)	0.684**
Male	18 (36.7)	31 (63.3)	
Type			
Ileoileal	3 (10.3)	26 (89.7)	<0.001***
Ileocolic	27 (60.0)	18 (40.0)	
Colocolic	0 (0.0)	2 (100.0)	
Jejunojejunal	0 (0.0)	2 (100.0)	
Season			
Spring	8 (42.1)	11 (57.9)	.349**
Summer	2 (22.2)	7 (77.8)	
Fall	7 (29.2)	17 (70.8)	
Winter	13 (50)	13 (50)	
Clinical symptoms			
Abdominal pain	6 (25)	18 (75)	.001***
Bloody stool	9 (90)	1 (1)	
Vomiting	11 (47.8)	12 (52.2)	
Diarrhea	4 (21.1)	15 (78.9)	
Fever	0 (0)	2 (100)	
Age, y			
≤3	15 (28.3)	38 (71.7)	.012**
>3	15 (60.0)	10 (40.0)	

**Mann-Whitney U test **Pearson Chi-square ***Fisher exact test MD: Median CRP: C-reactive protein, NLR: neutrophil–lymphocyte ratio, PLR: platelet–lymphocyte ratio, HALP: hemoglobin, albumin, lymphocyte, and platelet*

Table 1. *Comparison of pre-op and post-op day 3 inflammatory markers in surgical treatment group*

(n = 30)	MD (25-75 IQR)	z	*P* value
NLR-day 1	5.50 (4.33-7.00)	-4.78	<0.001*
NLR-day 3	1.79 (1.63-1.89)		
PLR-day 1	203.37 (168.75-250.79)	-4.78	<0.001*
PLR-day 3	109.71 (91.53-121.50)		
HALP-score day 1	2.44 (1.85-3.25)	-4.78	<0.001*
HALP-score day 3	4.01 (3.34-5.15)		

** Wilcoxon signed-rank test*

Furthermore, in the surgical group, the median (25–75 IQR) NLR on postoperative day 3 was 1.79 (1.63–1.89), PLR was 109.71 (91.53–121.50), and HALP score was 4.01 (3.34–5.15). Statistically significant differences were observed for all three markers when comparing admission and postoperative day 3 values (p<0.001) (Table 2).

Discussion

In our study, we found that children diagnosed with intussusception who underwent surgical manual reduction had significantly lower NLR and PLR values and a significantly higher HALP score at admission (p<0.001). Furthermore, we observed that CRP levels, which are commonly used for monitoring and prognosis in numerous inflammatory, infectious, and tissue damage conditions,[13-14] were ineffective in predicting the need for surgical manual reduction (p=0.095).

It is generally reported that hematological parameter combinations such as NLR and PLR, calculated from a complete blood count, can be used as biomarkers to predict prognosis in many infectious and inflammatory conditions. This is due to the increase in neutrophil count in the blood and the rise in platelets, which are effective in regulating various inflammatory states in the presence of a systemic infection or inflammatory response.[6-8,12] In a study of 115 patients who underwent surgical operations for intussusception, with 47 of these cases involving resection, a comparison between the resection and non-resection groups revealed significantly higher NLR and PLR values in the group that underwent resection, a statistically significant difference.[15] A retrospective study evaluating the accuracy of NLR in predicting the differentiation between complicated and non-complicated appendicitis, which assessed 81 adult appendicitis cases, reported that an NLR > 7 served as a specific and predictive marker for complicated appendicitis.[6] Another study that evaluated 61 mild and 26 moderate pancreatitis cases found that PLR and NLR values were higher in moderate pancreatitis cases, with statistical analysis revealing a significant difference between the two groups.[7] In another study that included 291 appendicitis and 101 control pediatric cases, analysis between the appendicitis and control groups revealed that the NLR value was significantly higher in the appendicitis group. Furthermore, it was reported that the NLR value was significantly higher in children with gangrenous appendicitis compared to those with acute appendicitis.[16] In our study, we found that both PLR and NLR values were significantly higher in the surgical group. We attribute this to more intense ischemia in the intussuscepted segment, leading to the release of more inflammatory factors into the bloodstream. Additionally, we observed a significant decrease in PLR and NLR values on postoperative day 3 in the surgical group compared to their preoperative values (p<0.001).

Research indicates that hematological markers such as albumin, hemoglobin, lymphocytes, and platelets are associated with inflammation or nutritional status. These markers can effectively predict prognosis in inflammatory, infectious, and malignant conditions.[9-11,17] A study including 684 cases diagnosed with acute appendicitis reported that the incidence of gangrene, perforation, periappendicular abscess, and postoperative complications was significantly increased in the group with a low HALP score compared to the group with a high HALP score.[11] In a study evaluating 213 cases in the emergency department, although no statistical significance was found when comparing groups based on albumin, hemoglobin, lymphocyte, and platelet levels, it was reported that patients who underwent surgery due to ileus had significantly lower HALP scores.[18] In another study that evaluated

a total of 436 appendicitis cases, comprising 126 complicated and 310 non-complicated instances, it was reported that the HALP score was significantly lower in the complicated appendicitis group and that the preoperative HALP score could be used to predict the diagnosis.[9] In our study, the median (25–75 IQR) HALP score was found to be 2.44 (1.85–3.23) in the surgical group, while it was 5.58 (4.28–7.37) in the non-surgical group, indicating a significantly lower score in the surgical group (p<0.001). This finding suggests its effectiveness in predicting the need for treatment. We believe this difference is a result of the metabolic response to severe inflammation caused by the compression of the intussuscepted segment in cases requiring surgery.

Studies conducted on children diagnosed with intussusception have identified a positive correlation between the increasing age of the cases and the need for surgical treatment.[19-20] A study including 153 intussusception cases in children under 12 years of age reported that the probability of a pathological lead point is very high in children over 5 years old, and early surgical intervention should be considered in these children.[21] In our study, we also found that age was significantly higher in cases in the surgical group compared to the non-surgical group (p=0.01). We observed that 71.7% of cases aged ≤3 years were treated non-surgically, whereas 60.2% of cases aged > 3 years underwent surgical reduction (p=0.012). We believe this is related to the increased incidence of pathologies initiating intussusception with advancing age.

It has been reported that the length of the intussusception segment and the presence of currant jelly stools are effective factors that increase the likelihood of surgical reduction in children with intussusception.[19-20,22] In a study investigating successful factors for non-surgical reduction in 99 children diagnosed with intussusception, the average length of the intussuscepted segment in cases requiring surgical treatment was found to be 7.9 cm. In contrast, it was 3.5 cm in cases that underwent non-surgical reduction. A significant difference was observed between these two groups, and in univariate analysis, bloody stool was identified as an effective predictor for surgical intervention.[20] In a study investigating factors associated with surgical treatment in 106 children with ileoileal and ileocolonic intussusception, it was reported that the length of the intussuscepted segment > 3.5 mm (p=0.042) and strawberry jelly stool were effective in predicting surgery in the surgical treatment group.[19] In our study, we also found that 9 out of 10 patients presenting with bloody stools required surgical treatment. Furthermore, the median (25–75 IQR) length of the intussuscepted segment was 48 (40–61.25) mm in the surgical group compared to 20 (15–30) mm in the non-surgical group, a statistically significant difference (p<0.001). We attribute this to the more intense ischemia resulting from obstruction within the longer intussuscepted segment in the surgical group.

Limitations

The main limitations of our study are the retrospective study design and the limited number of cases.

Conclusion

In the treatment of intussusception, early diagnosis and appropriate treatment are vitally important in reducing mortality and morbidity. Alongside ultrasonography, a thorough evaluation of physical examination and clinical findings continues to play a significant role in guiding treatment. Furthermore, NLR, PLR, and HALP scores may contribute to clinical and ultrasonography findings in predicting intussusception cases that require surgical intervention.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were 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.

Informed Consent

Informed consent was not required due to the retrospective design of the study and the use of anonymized patient data.

Data Availability

The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there is no conflict of interest.

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None.

Abbreviations

CRP: C-reactive protein
HALP: Hemoglobin, albumin, lymphocyte, and platelet
IQR: Interquartile range
NLR: Neutrophil-to-lymphocyte ratio
PLR: Platelet-to-lymphocyte ratio

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