Gastrointestinal Involvement in Pediatric IgA Vasculitis: Clinical Features, Risk Factors, and Treatment Approach

ወ Şengül Çağlayan, ወ Sümeyra Başaran Çoban, ወ Kadir Ulu, ወ Betül Sözeri

Department of Pediatric Rheumatology, University of Health Sciences, Ümraniye Research and Training Hospital, İstanbul, Türkiye

ABSTRACT

Objective: This study aimed to evaluate the clinical and laboratory characteristics of gastrointestinal (GI) involvement in pediatric IgA vasculitis (IgAV) patients, with a particular focus on identifying risk factors for severe complications and exploring current management strategies.

Materials and Methods: This retrospective cohort study included pediatric patients diagnosed with IgAV who were followed at a tertiary medical center between January 2019 and March 2024. Patients were divided into two groups—severe and non-severe GI involvement—and data were analyzed comparatively.

Results: A total of 265 patients were included in the study, of whom 109 (41.1%) had GI involvement. Among these, 35 (32.1%) were classified as having severe GI involvement, while 74 (67.9%) were categorized as having non-severe involvement. All patients with GI symptoms reported abdominal pain, with 37 (33.9%) experiencing nausea and vomiting. Positive fecal occult blood tests were observed in 59 (54.1%) patients, melena in 4 (3.6%), and hematochezia in 14 (12.8%). Radiological findings showed intestinal wall edema in 28 (25.6%) patients, intussusception in 7 (6.4%), and intestinal perforation in 1 patient (0.9%). Laboratory markers such as NLR, MLR, SII, SIRI, SIAI, and CRP/albumin ratios were significantly elevated in the severe GI involvement group (p<0.05), while albumin levels were significantly lower (p<0.001).

Conclusion: NLR, MLR, SII, SIRI, SIAI, and CRP/albumin ratios were found to predict severe GI involvement, demonstrating their potential as useful clinical tools for early identification of high-risk patients.

Keywords: IgA vasculitis, gastrointestinal involvement, Henoch-Schönlein purpura, severe

How to cite this article: Çağlayan Ş, Başaran Çoban S, Ulu K, Sözeri B. Gastrointestinal Involvement in Pediatric IgA Vasculitis: Clinical Features, Risk Factors, and Treatment Approach. CM 2025;17(1):13-21

INTRODUCTION

Immunoglobulin A vasculitis (IgAV), formerly known as Henoch-Schönlein purpura (HSP), is the most common primary systemic vasculitis in childhood. The most common and characteristic feature of the disease is non-thrombocytopenic palpable purpura, typically observed on the lower extremities.^[1,2] Other common clinical manifestations include arthritis, arthralgia, gastrointestinal (GI) symptoms, and renal involvement.^[3,4] The disorder is typically self-limiting, but certain cases can develop complications, with GI involvement being one of the most significant and concerning.

Gastrointestinal symptoms occur in approximately twothirds of patients, typically appearing within one week after the onset of purpura.^[5] However, 20% of patients may present with GI involvement before the onset of the rash. ^[5] Abdominal pain is often the first symptom, and the severity of GI involvement can range from mild, including nausea, vomiting, and abdominal pain, to more severe manifestations.^[6] The small intestines are the most commonly affected areas due to their vulnerability to ischemic damage. Severe complications such as intussusception, gangrene, or perforation can result from edema, submucosal, and intramural hemorrhage in the intestinal wall. Less commonly, patients may develop bowel obstruction, stricture formation, protein-losing enteropathy, steatorrhea, hepatobiliary disease, acute pancreatitis, mesenteric vasculitis, or massive GI bleeding.^[6]



Address for Correspondence: Şengül Çağlayan, Department of Pediatric Rheumatology, University of Health Sciences, Ümraniye Research and Training Hospital, İstanbul, Türkiye **E-mail:** sengulturkercaglayan@gmail.com **ORCID ID:** 0000-0003-3014-5692

Received date: 18.10.2024 Revised date: 26.11.2024 Accepted date: 06.12.2024 Online date: 03.02.2025



In most cases, there are mild GI system symptoms such as abdominal pain, vomiting, and occult rectal bleeding. Since these cases are usually self-limiting, they do not typically require treatment. However, children with severe abdominal pain and/or rectal bleeding may require treatment with oral or intravenous (IV) corticosteroids.^[7] In steroid-resistant cases, second-line immunosuppressive therapies such as intravenous immunoglobulin (IVIG), mycophenolate mofetil (MMF), azathioprine (AZA), and cyclophosphamide can be used.^[7-10]

Although GI involvement has been well described, identifying patients at risk for severe GI complications remains a critical aspect of clinical management. Factors such as age, the presence of persistent purpura, and elevated inflammatory markers have been explored as potential risk indicators. ^[11–13] However, no definitive clinical or laboratory marker has been identified to reliably predict severe GI involvement thus far. Additionally, studies involving large pediatric cohorts of IgAV patients with GI manifestations are limited.

The aim of our study was to assess the clinical and laboratory characteristics of GI involvement, especially immune inflammatory indices, in IgAV patients and to provide a comprehensive overview, focusing on risk factors for severe complications and current management strategies.

MATERIALS and METHODS

This retrospective cohort study included pediatric patients diagnosed with IgAV who were followed at the University of Health Sciences, Umraniye Research and Training Hospital, Department of Pediatric Rheumatology, between January 2019 and March 2024. A total of 265 IgAV patients were enrolled in the study, all of whom met the 2008 Ankara EULAR/PRIN-TO/PRES classification criteria.^[14] Clinical and laboratory features were retrospectively collected from the patients' medical charts and electronic records. GI involvement was defined by the presence of abdominal pain, nausea, vomiting, positive fecal occult blood test, melena, hematochezia, intestinal wall edema, intussusception, or intestinal perforation. However, fecal occult blood positivity alone, in the absence of other symptoms, was not considered indicative of GI involvement. Renal involvement, including hematuria, proteinuria, nephritic and nephrotic syndromes, and acute kidney injury, was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.^[15] Central nervous system involvement was defined as the presence of seizures, coma, hemorrhage, posterior reversible encephalopathy syndrome, or ataxia.^[6]

IgAV patients with GI involvement were categorized into two groups: the severe GI involvement group and the non-severe

GI involvement group. Severe GI involvement was defined by the presence of massive GI bleeding (excluding patients with only positive occult blood), severe abdominal complications such as intussusception, intestinal perforation, or intestinal obstruction, or the need for pulse methylprednisolone therapy due to GI involvement.^[12] Clinical and laboratory features were compared and analyzed between these two groups.

The study protocol was reviewed and approved by the Ethics Committee of the University of Health Sciences, Umraniye Research and Training Hospital (Approval Date: 07.11.2024, Approval No: B.10.1.TKH.4.34.H.GP.0.01/385), in accordance with the ethical principles laid down in the Declaration of Helsinki.

Statistical Analysis

The statistical analyses were conducted using SPSS version 25.0 software (SPSS Inc., Chicago, IL, USA). The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov test) to determine whether they were normally distributed. Descriptive analysis was presented using proportions, mean, standard deviation (SD), median, and interquartile range values, as appropriate. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. For comparisons between groups, the independent samples t-test and the Mann-Whitney U test were used, as appropriate.

Receiver operating characteristic (ROC) curves were used to assess the overall discriminatory ability of white blood cell count (WBC), absolute neutrophil count (ANC), absolute monocyte count (AMC), C-reactive protein (CRP), neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), systemic immune inflammation index (SII), systemic inflammation response index (SIRI), and systemic inflammation aggregate index (SIAI). This evaluation was performed to discriminate between severe and non-severe GI involvement patients. The Youden Index was calculated as Sensitivity + Specificity – 1. For all analyzed measures, two-tailed p-values less than 0.05 were considered significant.

RESULTS

Demographic and Clinical Characteristics of Patients

A total of 265 patients were evaluated in the study, of whom 134 (50.6%) were female. The median (IQR) age of the patients was 86 (63–117) months. According to the seasonal distribution of the cases, 76 patients (28.7%) presented in autumn, 72 patients (27.2%) in winter, 82 patients (30.9%) in spring, and 35 patients (13.2%) in summer. All patients pre-

sented with purpura. Of these, 109 patients (41.1%) had GI involvement, 94 patients (35.5%) had renal involvement, 58 patients (21.9%) had arthritis or arthralgia, and 11 patients (4.1%) had scrotal involvement.

Clinical Characteristics of Patients with Gastrointestinal Involvement

Gastrointestinal involvement was present in 109 patients. Of these, 35 patients (32.1%) were classified as having severe GI involvement, while 74 patients (67.9%) were classified as having non-severe GI involvement. Purpura was observed only on the lower extremities in 78 patients (71.5%), on both the lower and upper extremities in 28 patients (25.6%), and generalized, including the face, in three patients (2.7%). Bullous lesions developed in three patients (2.7%). Skin biopsies were performed on nine patients, all of which were consistent with leukocytoclastic vasculitis. Additionally, eight patients (7.3%) had arthritis, 25 patients (22.9%) had arthralgia, 37 patients (33.9%) presented with subcutaneous edema on the dorsum of the hands and feet, and six patients (5.5%) experienced scalp edema.

Abdominal pain was reported in all patients with GI involvement, while nausea and vomiting were reported in 37 patients (33.9%). Positive fecal occult blood tests were found in 59 patients (54.1%), melena in four patients (3.6%), and hematochezia in 14 patients (12.8%). Intestinal wall edema was observed in 28 patients (25.6%), intussusception in seven patients (6.4%), and intestinal perforation in one patient (0.9%).

Regarding renal involvement, nephritic proteinuria was observed in 39 patients (35.7%), microscopic hematuria in 32 patients (29.3%), macroscopic hematuria in three patients (2.7%), and hypertension in 10 patients (9.1%). Kidney biopsies were performed on three patients (2.7%) due to persistent nephritic proteinuria, revealing grade IIIa in two patients and grade IIIb in one patient.

Central nervous system involvement, characterized by seizures, was observed in two patients, both of whom were among those with severe GI involvement. Table 1 presents the demographic and clinical characteristics of patients with GI involvement, categorized by the severity of involvement.

Laboratory Characteristics of Patients with Gastrointestinal Involvement

When comparing the laboratory values of patients with severe and non-severe GI involvement, WBC, ANC, AMC, CRP, NLR, MLR, SII, SIRI, SIAI, and the CRP/albumin ratio were all found to be statistically significantly higher in the severe GI involvement group (p<0.001, p<0.001, p=0.008, p=0.043, p<0.001, p=0.046, p=0.011, p<0.001, p<0.001, p=0.024, respectively). In contrast, albumin levels were statistically significantly lower in the severe GI involvement group (p<0.001). The laboratory findings and inflammatory indices of the severe and non-severe GI involvement groups are presented in Table 2.

ROC analysis was conducted on various inflammatory indices to predict severe GI involvement. The results showed that the CRP/albumin ratio with values of 5.53 and above (Area Under Curve [AUC]: 0.635), NLR with values of 2.15 and above (AUC: 0.693), MLR with values of 0.20 and above (AUC: 0.619), SII with values of 1260 and above (AUC: 0.698), SIRI with values of 1.56 and above (AUC: 0.715), and SIAI with values of 648 and above (AUC: 0.704) all demonstrated moderate sensitivity and specificity in predicting severe GI involvement. The ROC curve analysis results and corresponding graphs are presented in Figure 1 and Table 3.

Treatment and Outcome of Patients with Gastrointestinal Involvement

In 17 patients (15.6%) with non-severe GI involvement, no medical treatment was initiated; they were managed with IV hydration and rest. The remaining 92 patients (84.4%) received medical treatment. Among those with non-severe GI involvement, 50 patients (66.6%) were started on low-dose oral corticosteroids (0.5 mg/kg/day), and 13 patients (17.3%) received nonsteroidal anti-inflammatory drugs (NSAIDs). Colchicine treatment was used in 20 patients (27%) in the non-severe GI involvement group and in 10 patients (28.5%) in the severe GI involvement group.

For the 34 patients with severe GI involvement, seven patients (20.5%) received 2 mg/kg IV corticosteroids, while the remaining 27 patients (79.5%) were treated with pulse methylprednisolone. Nine patients (26.4%) required second-line immunosuppressive therapy: AZA was administered to three patients, IVIG to three patients, MMF to one patient, IVIG and cyclosporine to one patient, and a combination of MMF, IVIG, cyclophosphamide, and plasmapheresis was used in one patient with renal infarction. Additionally, one patient required surgical intervention due to intestinal perforation. Intussusceptions resolved spontaneously without any sequelae in all patients.

During the six-month follow-up period after diagnosis, among patients with non-severe Gl involvement, two patients (2.6%) developed macroscopic hematuria, three patients (4%) developed microscopic hematuria, and three patients (4%) experienced a recurrence of purpura after a 1.5-month rash-free period. None of the patients with non-severe Gl in-

Table 1. Demographic, and clinical characteristics of patients with severe and non-severe gastrointestinal involvement

| | Severe GI involvement (n=34) | | Non-severe GI involvement (n=75) | | р |
|-------------------------------------|------------------------------------|------------|--|------|--------|
| | n | % | n | % | |
| Gender | | | | | |
| Female | 13 | | 32 | | 0.822 |
| Male | 21 | | 43 | | |
| Age, median IQR (months) | 103.5 (7 | 0.7–132.5) | 86 (62–126) | | 0.397 |
| Seasonal pattern | | | | | |
| Spring | 11 | 32.4 | 22 | 29.3 | 0.853 |
| Summer | 6 | 17.6 | 10 | 13.3 | |
| Autumn | 8 | 23.5 | 23 | 30.7 | |
| Winter | 9 | 26.5 | 20 | 26.7 | |
| Skin involvement | 34 | 100 | 75 | 100 | |
| Petechiae and purpura | 34 | 100 | 75 | 100 | 1.000 |
| Bullous lesion | 1 | 2.9 | 2 | 2.7 | 1.000 |
| Ulcer | 0 | 0 | 1 | 1.3 | 0.799 |
| Only lower extremities | 23 | 67.6 | 55 | 73.3 | 0.704 |
| Upper and lower extremities | 10 | 29.4 | 18 | 24 | 0.717 |
| Generalize involvement | 1 | 2.9 | 2 | 2.7 | 1.000 |
| Musculoskeletal involvement | | | | | |
| Arthritis | 3 | 8.8 | 5 | 6.7 | 0.703 |
| Arthralgia | 8 | 23.5 | 17 | 22.7 | 0.921 |
| Myalgia | 3 | 8.8 | 2 | 2.7 | 0.174 |
| Hand and foot edema | 12 | 35.3 | 25 | 33.3 | 0.841 |
| Scalp edema | 3 | 8.8 | 3 | 4 | 0.168 |
| Gastrointestinal system involvement | 34 | 100 | 75 | 100 | |
| Abdominal pain | 34 | 100 | 75 | 100 | 1.000 |
| Nausea-vomiting | 11 | 32.4 | 26 | 34.7 | 0.986 |
| Positive fecal occult blood test | 29 | 85.3 | 30 | 40 | <0.001 |
| Melena | 2 | 5.9 | 2 | 2.7 | 0.587 |
| Hematochezia | 14 | 41.2 | 0 | 0 | <0.001 |
| Intestinal wall edema | 16 | 47.1 | 12 | 16 | <0.001 |
| Intussusception | 7 | 20.6 | 0 | 0 | <0.001 |
| Intestinal perforation | 1 | 2.9 | 0 | 0 | 0.312 |
| Renal involvement | 23 | 67.6 | 26 | 34.7 | 0.003 |
| Nephritic proteinuria | 20 | 58.8 | 19 | 25.3 | 0.002 |
| Nephrotic proteinuria | 0 | 0 | 0 | 0 | 1.000 |
| Microscopic hematuria | 12 | 35.3 | 20 | 26.7 | 0.491 |
| Macroscopic hematuria | 2 | 5.9 | 1 | 1.3 | 0.229 |
| Hypertension | 9 | 26.5 | 1 | 1.3 | <0.001 |
| Scrotal involvement | 1 | 2.9 | 9 | 12 | 0.168 |
| Central nervous system involvement | 2 | 5.9 | 0 | 0 | 0.095 |

Fisher's exact test was applied. p<0.05 was considered statistically significant. GI: Gastrointestinalt

| | Severe GI involvement (n=34) | Non-severe GI involvement (n=75) | р | |
|---------------------------|---------------------------------|-------------------------------------|--------|--|
| WBC, mm ³ | 13850 (10770–19520) | 9540 (7980–12670) | <0.001 | |
| ANC, mm ³ | 9580 (7335–13982) | 5690 (4150–9080) | <0.001 | |
| ALC, mm ³ | 2400 (1892–3800) | 2770 (2140–3800) | 0.434 | |
| AMC, mm ³ | 755 (597–1077) | 570 (460–730) | 0.008 | |
| Hemoglobin, g/dL | 12.6 (11.7–13.4) | 12.4 (11.4–13.1) | 0.353 | |
| Platelet, mm ³ | 422000 (327000–472000) | 377000 (322000–455000) | 0.379 | |
| CRP, mg/L | 24.5 (5.1–43.1) | 9 (2–27.8) | 0.043 | |
| Albumin, g/dL | 4.1 (3.6–4.4) | 4.4 (4.1–4.6) | <0.001 | |
| NLR | 4.1 (2.3–7.4) | 1.9 (1.4–3.9) | <0.001 | |
| PLR | 150.2 (106.6–226.1) | 135.9 (104.5–181.1) | 0.374 | |
| MLR | 0.27 (0.16–0.40) | 0.19 (0.14–0.29) | 0.046 | |
| SII | 1686 (831.3–2639.8) | 732.8 (480.6–1424.3) | 0.011 | |
| SIRI | 2.8 (1.6–4.8) | 1.1 (0.6–2.7) | <0.001 | |
| SIAI | 1345 (530–1818) | 428 (240–974) | <0.001 | |
| CRP/Albumin ratio | 6.5 (1.2–11.3) | 2.2 (0.4–6.4) | 0.024 | |

Mann Whitney U test was applied. p<0.05 was considered statistically significant. Data is expressed as Median (IQR). WBC: White blood cell count; ANC: Absolute neutrophil count; AMC: Absolute monocyte count; CRP: C-reactive protein; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet- lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; SIAI: Systemic inflammation aggregate index

volvement required a renal biopsy. In the severe GI involvement group, two patients (5.8%) developed microscopic hematuria, two patients (5.8%) developed proteinuria, and one patient (2.9%) had both proteinuria and hematuria. Renal biopsies were performed on three of these patients.

DISCUSSION

In this retrospective cohort study, we analyzed the clinical and laboratory characteristics of GI involvement in pediatric IgAV patients, focusing on identifying risk factors for severe complications. The study revealed several significant findings that contribute to the understanding of GI involvement in IgAV. To the best of our knowledge, this is the first study to evaluate SII, SIRI, SIAI, and the CRP/albumin ratio in IgAV.

Our findings confirm the significant prevalence of GI symptoms in IgAV and support the observation that approximately one-third of these patients may experience a severe disease course. In this study, GI involvement was observed in 41.1% of the total patient cohort, consistent with the literature.^[16,17] In our cohort, severe GI involvement accounted for 32.1% of children with IgAV and GI involvement. This rate varies across studies in the literature. For instance, in the study by Li et al.,^[12] the rate was 48.9%, while in the study by Ekinci et al.,^[16] it was 36.7%, similar to our findings. In contrast, Sestan et al.^[13] reported a lower rate of 14.9%. These differences in severe GI involvement may be attribut-

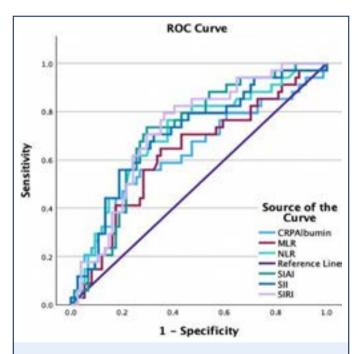


Figure 1. Receiver operating characteristic (ROC) curves of the inflammatory indices for IgA vasculitis with severe gastrointestinal involvement

CRP: C-reactive protein; MLR: Monocyte-lymphocyte ratio; NLR:Neutrophil-lymphocyteratio;SIAI:Systemic inflammation aggregate index; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index

| Table 3. ROC analysis to evaluate the cut-off value for predicting severe gastrointestinal involvement | | | | | | | | | |
|--|---------|-------|-------------|---------|---------|------|------|-------|--|
| | Cut-off | AUC | 95% CI | Sen (%) | Spe (%) | PPV | NPV | р | |
| CRP/albumin ratio | 5.53 | 0.635 | 0.516-0.755 | 55.9 | 73 | 48.7 | 78.6 | 0.027 | |
| MLR | 0.20 | 0.619 | 0.505–0.734 | 70.6 | 66 | 40 | 79.6 | 0.041 | |
| NLR | 2.15 | 0.693 | 0.585–0.801 | 79.4 | 66 | 44.3 | 88.4 | 0.000 | |
| SII | 1260.2 | 0.698 | 0.592-0.805 | 64.7 | 72 | 51.2 | 81.8 | 0.000 | |
| SIRI | 1.56 | 0.715 | 0.616-0.814 | 79.4 | 62.7 | 49.1 | 87 | 0.000 | |
| SIAI | 648.3 | 0.704 | 0.603-0.804 | 73.5 | 69.7 | 52.1 | 85.2 | 0.000 | |

ROC: Receiver operating characteristic; AUC: Area under curve; CI: Confidence interval; Sen: Sensitivity; Spe: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; CRP: C-reactive protein; MLR: Monocyte-lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; SIAI: Systemic inflammation aggregate index

able to differing admission standards across countries and regions. Studies reporting higher rates were generally conducted in tertiary referral centers.

In the present study, abdominal pain was the most common symptom, occurring in 100% of patients with GI involvement. The second most common symptoms were a positive fecal occult blood test and nausea/vomiting, consistent with the literature.^[16-18]

It has been noted in the literature that with increasing age, both clinical deterioration in IgAV and the need for more aggressive treatment tend to rise.^[11–13,19] In our study, although the median age of patients with severe GI involvement was higher, we did not observe a statistically significant difference. Several studies have reported a relationship between the spread of the rash to the upper extremities or the presence of a generalized rash and increased disease severity. ^[12,20,21] However, in our study, no association was found between the distribution of skin lesions and the occurrence of severe GI involvement. Therefore, further studies are needed to determine these relationships.

In our study, renal involvement was observed in 35.5% of pediatric patients with IgAV. Renal involvement and biopsy-proven IgA nephritis were more frequent in the severe GI involvement group, consistent with findings from previous studies.^[12,13,22,23] Therefore, we believe that patients with severe GI involvement should be closely monitored for potential renal complications.

One of the most critical challenges in managing IgAV with GI involvement is identifying patients at high risk for life-threatening complications. Although no single marker for predicting severe GI involvement has been identified in studies to date, several inexpensive and practical biomarkers have been investigated for their potential to predict the risk of severe GI involvement. In our study, commonly used, cost-effective, and easily accessible laboratory parameters and indices were evaluated, and values for WBC, ANC, AMC, CRP, NLR, MLR, SII, SIRI, SIAI, and the CRP/albumin ratio were found to be significantly higher in patients with severe GI involvement.

In the literature, NLR is one of the most frequently recommended parameters for predicting severe GI involvement. Multiple studies, including meta-analyses, have demonstrated that elevated NLR is associated with a higher risk of GI bleeding and severe GI complications, with specific cut-off values (ranging from approximately 2.05 to 2.48) showing high sensitivity and specificity.^[23-30] In our study, similar to the findings in the literature, the optimal NLR threshold for predicting severe GI involvement was determined to be 2.15, with 79.4% sensitivity and 66.0% specificity. Overall, NLR can be considered a reliable and cost-effective marker for assessing inflammation and guiding early intervention in IgAV patients with possible GI complications. In a recent study by Rigante et al.,^[31] high neutrophil count and low lymphocyte count were associated with GI involvement. Additionally, lower levels of 25-hydroxyvitamin D were identified as a high-risk factor for severe GI involvement.

A new hematological parameter, MLR, has recently been shown to be an effective marker of disease activity in patients with systemic lupus erythematosus, Takayasu arteritis, and rheumatoid arthritis.^[32-34] The only study evaluating MLR in IgAV was conducted by Yuan et al.^[35] Like our findings, their study identified a cut-off MLR value of 0.245, which distinguished children with IgA vasculitis and GI involvement from those without GI involvement, with an AUC of 0.694, 52.9% sensitivity, and 77.8% specificity.

The CRP/albumin ratio is considered a more valuable and reliable marker than CRP or albumin alone for predicting in-flammatory status and prognosis in various diseases. Sever-

al studies have demonstrated its association with prognosis in patients with conditions such as colorectal cancer, coronary artery disease, inflammatory bowel disease, Takayasu arteritis, rheumatoid arthritis, and sepsis.^[36–38] However, no study has been conducted to date to evaluate the CRP/albumin ratio in IgAV patients. In our study, CRP levels were higher in patients with severe GI involvement, reflecting the increased hyperinflammation. Albumin levels were lower in these patients, likely due to its role as a negative acute phase reactant and the absorption defects caused by severe GI involvement (4.1 vs. 4.4, p<0.001). Therefore, the CRP/albumin ratio may be more useful than either parameter alone.

SII, SIRI, and SIAI are newly defined indices used as markers of both local and systemic inflammation. In the literature, these indices have been evaluated in several vasculitides, including Kawasaki disease, Behcet disease, and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. ^[39-42] In Behcet disease, these indices were found to be associated with increased disease activity.^[39] In Kawasaki disease, they were linked to IVIG resistance and the development of coronary artery lesions.^[40,41] In ANCA-associated vasculitis, higher values of these indices were associated with a more severe disease course and poor outcomes.^[42] In our study, SII, SIRI, and SIAI parameters were evaluated for the first time in patients with IgAV. These indices were significantly elevated in patients with GI involvement. While they demonstrated moderate sensitivity and specificity in predicting severe GI involvement, their high negative predictive values suggest that the likelihood of severe GI involvement is low in cases where these indices are below the established cut-off values. This may aid clinicians in monitoring patients and identifying those at lower risk for severe complications.

In cases of non-severe GI involvement, the condition is typically mild and self-limiting, requiring only supportive treatment. However, patients presenting with severe abdominal pain, rectal bleeding, or intussusception require intervention, and steroid treatment should be considered, as it can reduce the intensity and duration of abdominal pain.^[7] The management of IgAV patients with steroid-resistant severe GI involvement remains controversial, and various second-line therapies have been proposed.^[7-10] Consistent with other cohorts, all our patients with severe GI involvement received steroids during the initial episode of IgAV, and second-line immunosuppressive agents were employed in those with a refractory course. In one patient who developed renal infarction, plasmapheresis was performed in addition to immunosuppressive therapy.

While our study provides valuable information about the clinical course of GI involvement in pediatric IgAV, it also has some limitations. The retrospective design and single-center nature of the study may limit the generalizability of the findings. In addition, the lack of a standardized definition for severe GI involvement across studies may contribute to the variability in reported rates of severe cases. Future multicenter, prospective studies are needed to confirm our results and to better define risk factors for severe GI complications in IgAV.

CONCLUSION

In conclusion, this study highlights the significant prevalence of GI involvement in pediatric patients with IgAV, with severe complications occurring in approximately one-third of affected patients. NLR, MLR, SII, SIRI, SIAI, and CRP/albumin ratios have been found to predict severe GI involvement, demonstrating their potential as useful clinical tools for early identification of high-risk patients. Despite advances in understanding the clinical course and laboratory features of GI involvement in IgAV, standardized criteria are needed to define severe GI involvement. The findings also highlight the importance of careful monitoring for renal complications in patients with severe GI involvement, as well as the need for timely and appropriate intervention to reduce potentially life-threatening outcomes.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Umraniye Research and Training Hospital Clinical Research Ethics Committee (No: B.10.1.TKH.4.34.H.GP.0.01/385, Date: 07/11/2024).

Authorship Contributions: Concept: Ş.Ç., B.S.; Design: Ş.Ç., B.S.; Supervision: B.S.; Funding: B.S.; Materials: K.U., S.B.Ç., Ş.Ç.; Data Collection or Processing: K.U., S.B.Ç., Ş.Ç.; Analysis or Interpretation: K.U., Ş.Ç.; Literature Search: S.B.Ç., Ş.Ç.; Writing: S.Ç., B.S.; Critical review: B.S., K.U., S.B.Ç., Ş.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Informed Consent: Written informed consent was obtained from all patients.

Use of AI for Writing Assistance: No AI technologies utilized.

Financial Disclosure: The authors declared that this study received no financial support.

Peer-review: Externally peer reviewed.

REFERENCES

- Saulsbury FT. Clinical update: Henoch-Schönlein purpura. Lancet 2007;369:976–8. [CrossRef]
- Piram M, Mahr A. Epidemiology of immunoglobulin A vasculitis (Henoch-Schonlein): current state of knowledge. Curr Opin Rheumatol 2013;25:171–8. [CrossRef]
- 3. Xu L, Li Y, Wu X. IgA vasculitis update: Epidemiology, pathogenesis, and biomarkers. Front Immunol 2022;13:921864. [CrossRef]
- Jelusic M, Sestan M, Giani T, Cimaz R. New insights and challenges associated with iga vasculitis and IgA vasculitis with nephritis-is it time to change the paradigm of the most common systemic vasculitis in childhood? Front Pediatr 2022;10:853724. [CrossRef]
- Jauhola O, Ronkainen J, Koskimies O, et al. Clinical course of extrarenal symptoms in Henoch-Schonlein purpura: a 6-month prospective study. Arch Dis Child 2010;95:871–6. [CrossRef]
- Brogan P, Nott KA. Immune Complex Small-Vessel Vasculitis: IgA Vasculitis (Henoch–Schönlein) and Hypersensitivity Vasculitis. In Petty RE (editor). Textbook of Pediatric Rheumatology. USA: Elsevier; 2020.
- Ozen S, Marks SD, Brogan P, Groot N, de Graeff N, Avcin T, et al. European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis-the SHARE initiative. Rheumatology (Oxford). 2019;58:1607–16. [CrossRef]
- Wang H, Zhang B, Li S, Ou R, Liu Y, Tan W. Clinical outcome in pediatric refractory gastrointestinal Henoch-Schönlein purpura treated with mycophenolate mofetil. Eur J Pediatr 2020;179:1361–6. [CrossRef]
- Cherqaoui B, Chausset A, Stephan JL, Merlin E. Intravenous immunoglobulins for severe gastrointestinal involvement in pediatric Henoch-Schönlein purpura: A French retrospective study. Arch Pediatr 2016;23:584–90. [CrossRef]
- Crayne CB, Eloseily E, Mannion ML, Azerf SP, Weiser P, Beukelman T, et al. Rituximab treatment for chronic steroid-dependent Henoch-Schonlein purpura: 8 cases and a review of the literature. Pediatr Rheumatol Online J 2018;16:71. [CrossRef]
- Coşkun S, Güngörer V, Ekici Tekin Z, Çelikel E, Kurt T, Tekgöz N, et al. Preadolescent-versus adolescent-onset immunoglobulin A vasculitis: The impact of age on prognosis. Pediatr Int 2023;65:e15426. [CrossRef]
- 12. Li Y, Zhang X, Liu H, Li G, Guan W, Zhang T, et al. Severe gastrointestinal involvement in pediatric IgA vasculitis: a retrospective single-center cohort study in China. Front Pediatr 2023;11:1194214. [CrossRef]
- Sestan M, Kifer N, Frkovic M, Sapina M, Srsen S, Batnozic Varga M, et al. Gastrointestinal involvement and its association with the risk for nephritis in IgA vasculitis. Ther Adv Musculoskelet Dis 2021;13:1759720X211024828. [CrossRef]
- Ozen S, Pistorio A, Iusan SM, Bakkaloglu A, Herlin T, Brik R, et al; Paediatric Rheumatology International Trials Organisation (PRINTO). EU-LAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis 2010;69:798–806. [CrossRef]
- Rovin BH, Adler SG, Barratt J, Bridoux F, Burdge KA, Chan TM, et al. Executive summary of the KDIGO 2021 Guideline for the Management of Glomerular Diseases. Kidney Int 2021;100:753–79. [CrossRef]
- Ekinci RMK, Balci S, Melek E, Karabay Bayazit A, Dogruel D, Altintas DU, Yilmaz M. Clinical manifestations and outcomes of 420 children with Henoch Schönlein Purpura from a single referral center from Turkey: A three-year experience. Mod Rheumatol 2020;30:1039–46. [CrossRef]
- Karadağ ŞG, Tanatar A, Sönmez HE, Çakmak F, Kıyak A, Yavuz S, et al. The clinical spectrum of Henoch-Schönlein purpura in children: a single-center study. Clin Rheumatol 2019;38:1707–14. [CrossRef]

- Rubino C, Monacelli C, Marrani E, Paci M, Indolfi G, Simonini G, et al. Gastrointestinal involvement in IgA vasculitis: a single-center 11-year study on a cohort of 118 children. Clin Rheumatol 2021;40:5041–6. [CrossRef]
- Liao CH, Tsai M, Yang YH, Chiang BL, Wang LC. Onset age is a risk factor for refractory pediatric IgA vasculitis: a retrospective cohort study. Pediatr Rheumatol Online J 2020;18:86. [CrossRef]
- St John J, Vedak P, Garza-Mayers AC, Hoang MP, Nigwekar SU, Kroshinsky D. Location of skin lesions in Henoch-Schönlein purpura and its association with significant renal involvement. J Am Acad Dermatol 2018;78:115-20. [CrossRef]
- 21. Hočevar A, Tomšič M, Jurčić V, Perdan Pirkmajer K, Rotar Ž. Predicting gastrointestinal and renal involvement in adult IgA vasculitis. Arthritis Res Ther 2019;21:302. [CrossRef]
- 22. Wang K, Sun X, Jing S, Lin L, Cao Y, Peng X, et al. Development and validation of nomogram prediction model for severe kidney disease in children with Henoch-Schönlein purpura: A prospective analysis of two independent cohorts-forecast severe kidney disease outcome in 2,480 hospitalized Henoch-Schönlein purpura children. Front Immunol 2022;13:999491. [CrossRef]
- 23. Ekinci RMK, Balci S, Sari Gokay S, Yilmaz HL, Dogruel D, Altintas DU, et al. Do practical laboratory indices predict the outcomes of children with Henoch-Schönlein purpura? Postgrad Med 2019;131:295–8. [CrossRef]
- Gayret OB, Erol M, Tekin Nacaroglu H. The relationship of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio with gastrointestinal bleeding in Henoch-Schonlein purpura. Iran J Pediatr 2016;26:e8191.
- 25. Makay B, Gücenmez ÖA, Duman M, Ünsal E. The relationship of neutrophil-to- lymphocyte ratio with gastrointestinal bleeding in Henoch-Schonlein purpura. Rheumatol Int 2014;34:1323–7. [CrossRef]
- Yakut HI, Kurt T, Uncu N, Semsa Cayci F, Celikel Acar B. Predictive role of neutrophil to lymphocyte ratio and mean platelet volume in Henoch-Schönlein purpura related gastrointestinal and renal involvement. Arch Argen Pediatr 2020;118:139–42. [CrossRef]
- 27. Hong SH, Kim CJ, Yang EM. Neutrophil-to-lymphocyte ratio to predict gastrointestinal bleeding in Henoch: Schönlein purpura. Pediatr Int 2018;60:791–5. [CrossRef]
- Li B, Ren Q, Ling J, Tao Z, Yang X, Li Y. Clinical relevance of neutrophil-to-lymphocyte ratio and mean platelet volume in pediatric Henoch-Schonlein Purpura: a meta-analysis. Bioengineered 2021;12:286– 95. [CrossRef]
- Fu W, Ye W, Liu X, Zhu S, Fu H, Zhu R, et al. Meta-analysis of the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in Henoch-Schonlein purpura and its complications. Int Immunopharmacol 2021;94:107454. [CrossRef]
- Lei W, Yun-Yun S, Ai-E X. Neutrophil-to-lymphocyte ratio: A biomarker for predicting systemic involvement in Henoch-Schonlein purpura. Indian J Dermatol Venereol Leprol 2021;88:132. [CrossRef]
- 31. Rigante D, Guerriero C, Silvaroli S, Paradiso FV, Sodero G, Laferrera F, et al. Predictors of gastrointestinal involvement in children with IgA vasculitis: Results from a single-center cohort observational study. Children (Basel) 2024;11:215. [CrossRef]
- 32. Suszek D, Gorak A, Majdan M. Differential approach to peripher-al blood cell ratios in patients with systemic lupus erythematosus and various manifestations. Rheumatol Int 2020;40:1625–9. [CrossRef]
- Seringec AN, Yildirim CG, Gogebakan H, Acipayam C. The C-reactive protein/albumin ratio and complete blood count parameters as indica-tors of disease activity in patients with Takayasu arteritis. Med Sci Monit 2019;25:1401-9. [CrossRef]
- Du J, Chen S, Shi J, Zhu X, Ying H, Zhang Y, et al. The association between the lymphocyte-mono-cyte ratio and disease activity in rheumatoid arthritis. Clin Rheumatol 2017;36:2689–95. [CrossRef]

- 35. Yuan Y, Liu J, Zhou Y, Du X, Chen Q, Zhou J, et al. The relationship between monocyte-to-lymphocyte ratio and the risk of gastrointestinal system involvement in children with IgA vasculitis: A preliminary report. Adv Clin Exp Med 2021;30:999–1005. [CrossRef]
- Cui J, Li X, Zhang Z, Gao H, Li J. Common laboratory blood test immune panel markers are useful for grading ulcerative colitis endoscopic severity. BMC Gastroenterol 2022;22:540. [CrossRef]
- Afifi N, M Medhat B, Abdel Ghani AM, Mohamed Ali Hassan HGE, Behiry ME. Value of albumin-fibrinogen ratio and CRP-albumin ratio as predictor marker of disease activity in Egyptian RA patients, correlated with musculoskeletal sonography. Open Access Rheumatol 2020;12:241–8. [CrossRef]
- Sabanoglu C, Inanc IH. C-reactive protein to albumin ratio predicts for severity of coronary artery disease and ischemia. Eur Rev Med Pharmacol Sci 2022;26:7623–31.

- Mentesoglu D, Atakan N. The association between Behçet disease activity and elevated systemic immune-inflammation index: A retrospective observational study in a tertiary care hospital. Natl Med J India 2024;37:74–8. [CrossRef]
- Yi C, Zhou YN, Guo J, Chen J, She X. Novel predictors of intravenous immunoglobulin resistance in patients with Kawasaki disease: a retrospective study. Front Immunol 2024;15:1399150. [CrossRef]
- 41. Huang T, Peng Q, Zhang Y, Zhu Z, Fan X. The Systemic Immune-Inflammation Index (SII) and coronary artery lesions in Kawasaki disease. Clin Exp Med 2024;24:4. [CrossRef]
- 42. Kim Y, Choi H, Jung SM, Song JJ, Park YB, Lee SW. Systemic immune-inflammation index could estimate the cross-sectional high activity and the poor outcomes in immunosuppressive drug-naïve patients with antineutrophil cytoplasmic antibody-associated vasculitis. Nephrology (Carlton) 2019;24:711-7. [CrossRef]