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Original Article

Analysis of the influencing factors of abdominal Henoch-Schonlein purpura in children with gastrointestinal bleeding and the clinical value of PLR

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Abstract: Objective: To identify the influencing factors of gastrointestinal bleeding in children with abdominal-type Henoch-Schonlein purpura (HSP) and to assess the diagnostic value of PLR (platelet-to-lymphocyte ratio). Methods: We retrospectively analyzed the medical records of 112 children with abdominal HSP admitted to Northwest Women's and Children's Hospital from April 2021 to May 2023. Among them, 62 cases with gastrointestinal bleeding constituted the bleeding group, while the other 50 cases without gastrointestinal bleeding comprised the non-bleeding group. We compared PLR and related routine blood indicators between the two groups. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors for gastrointestinal bleeding. HSP children with gastrointestinal bleeding were further categorized based on treatment efficacy, and the predictive value of PLR for treatment efficacy was analyzed. Results: The observation group exhibited significantly higher levels of WBC, NEU, PLT, MPV, C-reactive protein, and PLR, along with lower lymphocyte levels compared to the control group (all $P < 0.05$). Univariate analysis revealed associations between symptom onset, abdominal pain, vomiting, levels of WBC, NEU, LYM, PLT, PLR, C-reactive protein and gastrointestinal bleeding (all $P < 0.05$). Multivariate logistic analysis identified onset with abdominal pain, high WBC values, and elevated PLR ratios as risk factors for gastrointestinal bleeding. The ROC curve demonstrated an AUC of 0.914 for PLR in predicting gastrointestinal bleeding. Additionally, PLR was significantly lower in the good efficacy group compared to the poor efficacy group. The AUC of PLR in predicting treatment efficacy was 0.804, indicating high predictive value. Conclusion: Elevated PLR may serve as a potential risk factor for gastrointestinal bleeding in children with abdominal-type allergic purpura. Monitoring changes in PLR could aid in diagnosis and improvements in treatment for this condition.

Keywords: PLR, abdominal type allergic purpura, gastrointestinal bleeding

Introduction

Henoch-Schönlein purpura (HSP) is characterized by the deposition of IgA-dominant immune complexes, leading to systemic small vessel vasculitis that manifests as leukocytoclastic vasculitis throughout the body. HSP is the most common multisystem small vessel vasculitis in children [1, 2], with an annual incidence of 13 to 20 cases per 100,000. Both the incidence and hospitalization rates are increasing annually [3]. Gastrointestinal involvement is the most serious short-term complication of HSP, with gastrointestinal bleeding being an early manifestation [4]. If not identified and treated in a timely manner, it can progress to intestinal intussusception, obstruction, or even perforation. Such development can lead to severe abdominal HSP and significantly worsen the prognosis of children [5]. Therefore, understanding the risk factors for gastrointestinal bleeding in children with HSP and identifying straightforward methods for its early detection are crucial for shortening the disease course and improving prognosis.

However, effective indicators for evaluating and predicting gastrointestinal involvement in HSP

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are still lacking in clinical practice. Studies have found that platelet surface molecule expression and the release of inflammatory mediators play important roles in inflammatory reactions [6]. The platelet-to-lymphocyte ratio (PLR), a commonly used blood index, has been widely utilized in the prediction and diagnosis of various diseases [6]. Recent evidence supports the efficacy of PLR in providing reliable prediction of disease conditions and prognosis in cardiovascular diseases, vasculitis, tumors, autoimmune diseases, and other conditions [7, 8]. It has emerged as a potential sensitive marker of inflammatory reactions [7, 8]. However, although some studies have investigated the utility of PLR, either alone or in combination, in the assessment of HSP [9], there is still limited research on its predictive value for gastrointestinal bleeding in children with HSP.

To further explore the influencing factors of gastrointestinal bleeding in children with abdominal HSP and the application value of PLR, we conducted a retrospective analysis of the medical records of 112 children with abdominal HSP.

Materials and methods

Clinical data

In this retrospective study, the medical records of 112 children with abdominal HSP admitted to Northwest Women's and Children's Hospital from April 2021 to May 2023 were collected. Among them, 62 cases with gastrointestinal bleeding were included in the bleeding group, while the remaining 50 cases without gastrointestinal bleeding were included in the non-bleeding group. This study was approved by the ethics committee of Northwest Women's and Children's Hospital and complied with the Helsinki Declaration.

Inclusion criteria: (1) children diagnosed with abdominal HSP according to diagnostic criteria [10]; (2) children aged < 14 years; (3) children with complete clinical data. Exclusion criteria: (1) children who had received steroid or immunosuppressive therapy within the past month; (2) children with significant organ dysfunction such as liver or kidney impairment; (3) children with severe infectious diseases or immune dysfunction; (4) children with malignant tumors; (5) children with mixed purpura.

Detection of laboratory indicators

Clinical data of all patients were retrieved from the medical record database of Northwest Women's and Children's Hospital, including age, gender, medical history, symptoms, signs, length of hospital stay, precipitating factors, rash distribution, and relevant examination results on the first day of admission. Routine blood tests were conducted using the Shenzhen Mindray BC-6800 fully automated blood cell analyzer. Parameters recorded and compared included white blood cell count (WBC), neutrophil count (NEU), lymphocyte count (LYM), platelet count (PLT), mean platelet volume (MPV), C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum albumin (ALB). PLR was also calculated (PLR = PLT/LYM).

Observation outcomes

1. Comparison of Laboratory Indicators: The laboratory indicators, including WBC, NEU, LYM, PLT, MPV, CRP, ALT, AST, ALB and PLR were recorded and compared between the two groups of patients. 2. Logistic Regression Analysis: A logistic regression analysis was performed to identify the risk factors for gastrointestinal bleeding in children with abdominal HSP. 3. Comparison of Serum Levels: Compare serum WBC levels and PLR before and after treatment in HSP children with gastrointestinal bleeding, categorized by different prognoses. 4. Receiver operating characteristic (ROC) Curve Analysis: ROC curve analysis was used to assess the predictive value of PLR for gastrointestinal bleeding in children with HSP and its prognostic value in HSP children with gastrointestinal bleeding.

Statistical analysis

The collected data were processed and analyzed using SPSS 20.0 software, and GraphPad Prism 8 software was used for visualization. Continuous variables conforming to normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and the comparison between two groups was performed using the independent samples t-test. Categorical variables were presented as n (%) and were analyzed using the chi-square test. ROC curve analysis was conducted to assess the predictive value of PLR for gastrointestinal bleeding. Logistic multivariate

Table 1. Comparison of baseline data between the two groups

	Bleeding group (n = 62)	Non-bleeding group (n = 50)	X^2	P
Gender			0.002	0.968
Male	30 (48.39)	24 (48.00)		
Female	32 (51.69)	26 (52.00)		
Age			0.015	0.902
≥ 7	28 (45.16)	22 (44.00)		
< 7	34 (54.84)	28 (56.00)		
BMI (kg/m^2)			0.002	0.968
≥ 21	30 (48.39)	24 (48.00)		
< 21	32 (51.69)	26 (52.00)		
Onset season			0.195	0.979
Spring	19 (30.65)	15 (30.00)		
Summer	11 (17.74)	8 (16.00)		
Autumn	12 (19.35)	9 (18.00)		
Winter	20 (32.26)	18 (36.00)		
Rash severity			0.073	0.964
Mild	20 (32.26)	15 (30.00)		
Moderate	22 (35.48)	18 (36.00)		
Severe	20 (32.26)	17 (34.00)		

Table 2. Comparison of general clinical characteristics between the two groups

	Bleeding group (n = 62)	Non-bleeding group (n = 50)	X^2	P
Length of stay (d)			10.69	0.001
≥ 7	45 (72.58)	21 (42.00)		
< 7	17 (27.42)	29 (58.00)		
Known causes of disease			5.025	0.025
Yes	38 (61.29)	20 (40.00)		
No	24 (38.71)	30 (60.00)		
Abdominal pain as the first symptom			11.75	0.001
Yes	50 (80.65)	25 (50.00)		
No	12 (19.35)	25 (50.00)		
Vomiting			5.658	0.017
Yes	40 (64.52)	21 (42.00)		
No	22 (35.48)	29 (58.00)		

regression analysis was used to analyze the independent influencing factors for gastrointestinal bleeding in children with abdominal HSP. Statistical significance was set at $P < 0.05$.

Results

Comparison of baseline data between the two groups

There were no significant differences in gender, age, BMI, onset season, and rash severity between the two groups of children (all $P > 0.05$, **Table 1**).

Comparison of general clinical characteristics between the two groups

Patients in the bleeding group had a significantly longer hospital stay, a higher proportion of abdominal pain as the initial symptom, a higher incidence of vomiting, and more frequent precipitating factors compared to the non-bleeding group (all $P < 0.05$, **Table 2**).

Comparison of laboratory parameters between the two groups

We compared the laboratory parameters including WBC, NEU, LYM, PLT, MPV, CRP, and

Table 3. Comparison of laboratory parameters between the two groups

	Bleeding group (n = 62)	Non-bleeding group (n = 50)	t	P
WBC ($\times 10^9$/L)	12.56±1.16	8.61±0.88	19.89	< 0.001
NEU ($\times 10^9$/L)	7.65±0.88	4.85±1.01	15.67	< 0.001
LYM ($\times 10^9$/L)	2.2±0.23	2.63±0.28	8.924	< 0.001
PLT ($\times 10^9$/L)	316.31±12.58	306.2±10.94	4.478	< 0.001
MPV (fL)	9.57±0.82	9.54±0.77	0.843	0.198
CRP (mg/L)	7.22±0.99	3.76±0.73	20.60	< 0.001
ALT (U/L)	11.17±0.74	11.13±0.8	0.274	0.784
AST (U/L)	21.89±1.92	22.34±1.72	1.291	0.199
ALB (g/L)	41.32±4.38	42.14±3.78	1.046	0.298
PLR	145.49±16.07	117.93±14.45	9.434	< 0.001

WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; PLT: Platelet count; MPV: Mean Platelet Volume; CRP: C-reactive protein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALB: albumin; PLR: Physician Labeling Rule.

Table 4. Assignment of variables

Variables	Assignment
Predisposing factors	Yes = 1, no = 0
Abdominal pain as the first symptom	Yes = 1, no = 0
Vomiting	Yes = 1, no = 0
WBC	Normal = 1, abnormal = 0
NEU	Normal = 1, abnormal = 0
LYM	Normal = 1, abnormal = 0
PLT	Normal = 1, abnormal = 0
PLR	Normal = 1, abnormal = 0
CRP	Normal = 1, abnormal = 0

WBC: white blood cell; NEU: neutrophil; LYM: lymphocyte; PLT: Platelet count; CRP: C-reactive protein; PLR: Physician Labeling Rule.

PLR between the two groups. The results showed that there were no significant differences in MPV, ALT, AST, and ALB between the two groups (all P > 0.05); however, the bleeding group exhibited significantly higher levels of WBC, NEU, PLT, PLR, and CRP, while significantly lower LYM level than the non-bleeding group (all P < 0.05, **Table 3**).

Univariate and multivariate analysis of predictive factors for gastrointestinal bleeding in abdominal HSP patients

The univariate analysis suggested that the length of hospital stay, precipitating factors, initial symptoms of abdominal pain, occurrence of vomiting, and the expression levels of WBC, NEU, LYM, PLT, PLR, and CRP were notably associated with gastrointestinal bleeding in patients with abdominal HSP. Further, we performed a logistic multivariable regression analysis with the occurrence of gastrointestinal bleeding as the dependent variable (coded as 1 for "presence of gastrointestinal bleeding"). The variables and their corresponding assignments are detailed in **Table 4**. The multivariate analysis results indicated that initial symptoms of abdominal pain, elevated WBC levels, and an increased PLR ratio were independent risk factors for gastrointestinal bleeding in patients with abdominal HSP (all P < 0.05), as shown in **Table 5**.

Comparison of WBC and PLR between children with different treatment efficacy

Subsequently, we collected treatment data from HSP patients with gastrointestinal bleeding and divided them into a good efficacy group (40 cases) and a poor efficacy group (22 cases) based on their final treatment outcomes (Recovery of laboratory indicators and recurrence of gastrointestinal bleeding within six months). The serum WBC levels and PLR before and after treatment were compared between the two groups. The results indicated that the pre-treatment PLR in the good efficacy group was significantly lower than that in the poor efficacy group (P < 0.05), whereas there was no significant difference in the pre-treatment WBC levels (P > 0.05). After treatment, both groups exhibited a significant decrease in WBC levels and PLR compared to their pre-treatment values. However, the post-treatment PLR in the good efficacy group were significantly lower than those in the poor efficacy group (all P < 0.05) (**Figure 1**).

Table 5. Multivariate analysis

Factor	B	S.E.	Wals	P	OR	95% C.I.	
						Lower limit	Upper limit
Abdominal pain as the first symptom	1.104	0.556	4.213	0.023	3.145	1.076	8.993
WBC	0.151	0.055	6.923	0.019	1.156	1.021	1.423
PLR	0.071	0.036	4.523	0.034	1.265	1.071	1.158

WBC: white blood cell; PLR: Physician Labeling Rule.

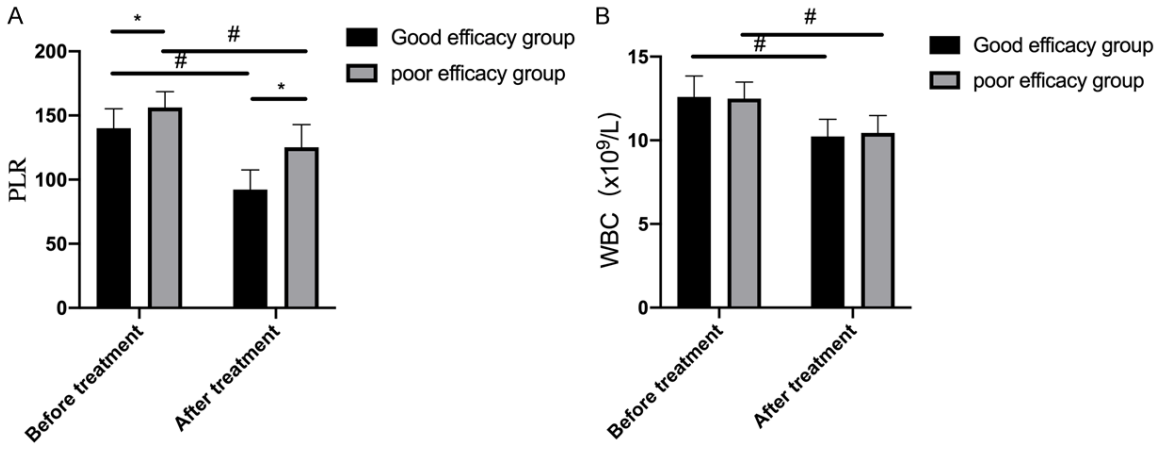

Figure 1. Comparison of PLR and WBC in children with good and poor treatment efficacy. A: Comparison of PLR in children with different treatment effects. B: Comparison of WBC in children with different treatment effects. * indicates $P < 0.05$ for comparison between groups; # indicates $P < 0.05$ for comparison before and after treatment within the group. WBC: white blood cell; PLR: platelet-to-lymphocyte ratio.

Assessing PLR as a predictor and prognostic tool for gastrointestinal bleeding in pediatric HSP patients

Elevated PLR is an independent risk factor for gastrointestinal bleeding in children with abdominal HSP. We analyzed the predictive value of PLR for gastrointestinal bleeding in abdominal HSP. The area under the ROC curve (AUC) was 0.914 ($P < 0.001$, 95% CI 0.860-0.968) with a cutoff value of 137.5, yielding a sensitivity of 92.00% and specificity of 70.97%. This indicates that a PLR value > 137.5 is associated with an increased risk of gastrointestinal bleeding in children with abdominal HSP. Further, we also analyzed the prognostic value of PLR in predicting therapeutic outcomes for HSP children with gastrointestinal bleeding. The AUC for PLR in this context was 0.804 ($P < 0.001$) with a sensitivity of 92.00% and specificity of 70.97%, highlighting its significant prognostic value (**Figure 2**).

Discussion

Henoch-Schönlein purpura (HSP) is the most prevalent type of vasculitis in children, with its exact etiology and pathogenesis remaining incompletely understood. It is often attributed to factors such as infection, dietary triggers, medications, insect bites, and vaccinations, particularly in individuals with a genetic predisposition, leading to immune dysfunction and activation of helper T cells (Th) [11]. Gastrointestinal bleeding poses a significant risk, affecting the overall disease condition and prognosis. Studies indicate a rising incidence of gastrointestinal bleeding among children with HSP. Approximately 28.6% of patients experience gastrointestinal bleeding before seeking medical attention, and 50.0% develop it after consultation [12]. Moreover, gastrointestinal bleeding often presents with subtle symptoms, making diagnosis challenging. Therefore, identifying laboratory markers to evaluate gastrointestinal bleeding is crucial. Even in the absence of initial symptoms or signs, early administration of corticosteroids can prevent disease progression, which is a key area of interest for clinicians [13]. Additionally, actively identifying risk factors for gastrointestinal bleeding in children with abdominal HSP can provide valuable insights for clinical prevention and treatment strategies.

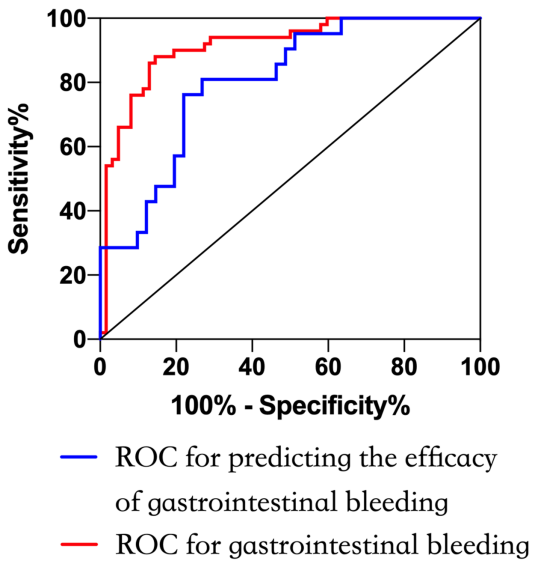

Figure 2. Assessing PLR as a predictor and prognostic tool for gastrointestinal bleeding in pediatric HSP patients. ROC: Receiver Operation Characteristic.

This study indicates that children in the bleeding group had a higher incidence of predisposing factors, abdominal pain as the initial symptom, and vomiting compared to the non-bleeding group. Notably, abdominal pain as the initial symptom was identified as an independent risk factor for gastrointestinal bleeding. The underlying mechanism is speculated to involve adverse gastrointestinal stimuli, such as local chemical substances, which trigger the release of serotonin from the stomach and small intestine during HSP, leading to abdominal pain. This can subsequently provoke vomiting reflexes, further increasing the permeability and fragility of gastric and intestinal arterioles or capillaries in HSP patients, exacerbating exudative bleeding and ultimately resulting in gastrointestinal hemorrhage [14]. Moreover, infections, particularly upper respiratory tract infections, are common precipitating factors for HSP onset [15]. Subsequent comparisons of laboratory indicators between the two groups revealed that WBC, NEU, PLT, PLR, and C-reactive protein levels were significantly higher in the bleeding group than in the non-bleeding group, while LYM levels were significantly lower. These findings suggest marked differences in inflammatory cells and derived inflammatory factors, indicating distinct inflammatory states between the groups. It is well established that an increase in PLT is often associated with inflammatory diseases, likely due to increased platelet production rather than prolonged survival [16]. Activated platelets during inflammatory responses can release inflammatory mediators and express surface molecules, mediating inflammatory cascades. HSP, being a form of vasculitis, has been associated with significantly increased PLT counts in affected children, consistent with our observations [16]. The decreased number of LYM reflects disruption in the body's immune response. Children with HSP often exhibit immune dysfunction and disturbances, including suppressed T lymphocyte function and reduced immune response [17]. In various infectious or non-infectious conditions causing systemic inflammatory responses, an increase in NEU often accompanies a decrease in LYM, with NEU playing a predominant role. In HSP, vasculitis is characterized by NEU infiltration around blood vessels [18].

Furthermore, our multifactorial analysis revealed that elevated WBC and PLR were independent risk factors for gastrointestinal bleeding in children with HSP. The increased WBC likely reflects underlying infections, suggesting that children with significant infections may be more susceptible to gastrointestinal bleeding. HSP is characterized by immune abnormalities, with lymphocytes playing a crucial role in the immune system and reflecting the body's immune status. Dysregulation of lymphocytes can lead to disturbances in suppressive T cells, activation of polyclonal B cells, and production of autoantibodies, collectively contributing to the development of HSP [19, 20]. During the acute phase of HSP, inflammatory cells can promote reactive thrombocytosis, which enhances platelet activation. Activated platelets release inflammatory mediators and surface molecules, such as P-selectin and E-selectin, influencing their interactions with other cells and playing a significant role in the disease process. PLR, a relatively new inflammatory predictor, reflects the degree of inflammatory response and is convenient to measure. An increase in PLR, indicative of acute inflammation and prethrombotic states [21, 22], was noted in the gastrointestinal bleeding group compared to non-bleeding group, suggesting an active role for platelets in the disease process. However, the specific mechanisms and roles require further investigation.

We further analyzed the predictive performance of PLR for gastrointestinal bleeding in

children with HSP using ROC analysis. The results showed that the AUC for PLR in predicting gastrointestinal bleeding in children with HSP was 0.829, with a 95% CI of 0.739 to 0.918, and $P < 0.001$. The optimal predictive cutoff value for PLR was 1.96, with a sensitivity of 73.17% and specificity of 78.0%, indicating that PLR has significant predictive value in assessing gastrointestinal bleeding in children with HSP. Previous study [23] investigated the relationship between NLR or PLR and gastrointestinal bleeding in HSP patients, and the results showed that although NLR was significantly elevated in HSP patients, PLR was more markedly elevated in those with gastrointestinal bleeding. This suggests that PLR can also serve as an inflammatory marker in children with HSP and gastrointestinal bleeding, which is consistent with our observations. To further validate the clinical value of PLR in HSP patients with gastrointestinal bleeding, we classified them into a good efficacy group and a poor efficacy group. Comparison of PLR revealed that the PLR in the good efficacy group was significantly lower than that in the poor efficacy group. Additionally, ROC curve analysis demonstrated that PLR had promising predictive value for treatment efficacy in HSP patients with gastrointestinal bleeding, with an AUC of 0.804.

In summary, this study identified abdominal pain as the initial symptom, elevated WBC, and increased PLR as independent risk factors for gastrointestinal bleeding in children with HSP. Clinical vigilance is warranted when these conditions occur. Furthermore, PLR has significant clinical value in predicting gastrointestinal bleeding in children with HSP. As an effective predictive indicator, PLR can be obtained through routine blood cell analysis, offering economic, practical, and repeatable advantages, thereby facilitating repeated testing and dynamic observation. However, this study has certain limitations. First, as a retrospective study, the sample size is relatively small and is constrained by regional factors. There is a need for multi-center, large-scale studies and more prospective research to further validate its predictive efficacy. Second, the retrospective nature of the data may introduce selection bias, potentially affecting the external validity of our findings. Lastly, we only analyzed the clinical value of PLR alone in HSP children with gastrointestinal bleeding. Whether combining PLR with other indicators could provide greater clinical value remains to be further confirmed.

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Disclosure of conflict of interest

None.

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