The Diagnostic Value of Eosinophil Count And Platelet-To-Lymphocyte Ratio In Eosinophilic Gastroenteritis

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Research article

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Abstract

Objective: To evaluate the diagnostic value of eosinophil (EO) count and platelet-to-lymphocyte ratio (PLR) in eosinophilic gastroenteritis (EGE).

Methods: In total, 91 patients with EGE and 83 age–sex matched patients without EGE were selected as study subjects during January 2018 to December 2020. Data on blood cell count, and serum, C-reactive protein (CRP), and albumin levels were obtained from the Wuxi children's hospital electronic medical record system; the neutrophil-to-lymphocyte ratio (NLR), PLR, and CRP-to-albumin ratio (CAR) in the peripheral blood were recorded. Independent sample *t*-test, non-parametric test, or χ^2 test was used according the data type to compare the difference between two groups, and receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic value for EGE.

Results: The EO counts and PLR were significantly higher in the EGE group than those in the control group, whereas differences in the white blood cell, lymphocyte, neutrophil, and platelet counts, and the CRP level, NLR, and CAR were not significant. After treatment(Corticosteroids, 1mg/kg.d, lasting for 2 weeks), the EO counts and PLR in the EGE group decreased gradually and the difference was significant. The diagnostic value of EO counts and PLR was determined with an area under the ROC curve as 0.756 and 0.616, sensitivity was 75.00% and 34.29%, and specificity was 74.29% and 92.31%, respectively.

Conclusions EO and PLR represent potential predictive markers for diagnosing EGE.

Background

Eosinophilic gastroenteritis (EGE) is a rare digestive disorder that is characterized by eosinophilic infiltration in the digestive tract. Since the symptoms are very similar to those of other gastrointestinal diseases, the diagnostic rate of EGE is low. At present, there is no accurate information on the incidence of EGE. Previous population-based prevalence analysis has shown that EGE can occur at any age, men are more prone to developing EGE compared to women, and the prevalence rate is approximately 8.4–2.8/100,000. However, the etiology and pathogenesis of EGE have not been elucidated yet. At present, there is no unified standard for establishing diagnostic criteria for EGE; pathological tissue biopsy is generally performed for diagnosing the disease. Pathological biopsy is performed via multi-point sampling of digestive tract tissues via gastrointestinal endoscopy. Diagnosis is based on one or more eosinophil (EO) infiltration events observed in the pathological biopsy. Therefore, it is necessary to identify simple laboratory indicators that are easy to evaluate to improve the diagnosis of EGE. Blood cell count, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) have been considered as markers of the immune and inflammatory status in recent years. As these indicators are easy to detect, they are widely studied in diseases affecting the respiratory, digestive, and reproductive systems. Inflammation plays an important role in the initiation and progression of EGE, We speculate that the new inflammatory index from whole cell blood count may contribute to the diagnosis of EGE. At present, no study has evaluated the blood cell count, NLR, and PLR in relation to the diagnosis of EGE. The aim of

this study was to identify meaningful laboratory indexes for the diagnosis of EGE by analyzing the changes in blood routine and biochemical-related indexes.

Methods

Selection of participants

By using the electronic medical record query system of Wuxi children's Hospital in Jiangsu Province, 91 patients hospitalized in the Department of Gastroenterology and diagnosed with EGE from January 2018 to December 2020 were selected as the case group, and 83 patients without EGE during the same period were selected as the control group. The diagnostic criteria of EGE included [2,3]: 1) symptoms of gastrointestinal involvement including abdominal pain, abdominal distention, nausea and vomiting, change in defecation habits, and blood in stools; 2) pathological biopsy of the digestive tract showed that there were more than one areas with massive EO infiltration, and the hot spot area was ≥ 20 cells/high power field (HPF); 3) other diseases that may lead to the increase EO counts in the digestive tract, such as parasitic infection, inflammatory bowel disease, gastrointestinal malignant tumor, hematological system diseases, hypereosinophilic syndrome, and connective tissue diseases among others, were excluded.

Collection of research data

The clinical data of the selected subjects were obtained using the electronic medical record system, and the test data on routine blood indexes, albumin level, and C-reactive protein (CRP) level were collected.

Statistical analysis

Data were processed using Excel (Microsoft, Redmond, WA, USA) and imported into SPSS version 22.0 (IBM, Armonk, NY, USA) for statistical analysis. Categorical variable data were statistically described by calculating the percentage. If the measurement data followed normal distribution, then the mean and standard deviation were calculated; for abnormal distribution, the median along with upper and lower quartiles [M (Q25–Q75)] were determined. The inter-group comparison of measurement data was performed via *t*-tests, and inter-group comparisons of classified variable data were performed via chi-square tests. Receiver operating characteristic (ROC) curve analysis was performed to analyze the optimal cutoff value of EO and PLR for predicting EGE, demonstrating the maximum sensitivity and specificity. The predictive validities were quantified as areas under the curve (AUC). Values of $p < 0.05$ were considered significant, and the confidence interval (CI) was 95%.

Results

Comparison of general data

A total of 174 subjects were included in this study, including 91 cases in the EGE group and 83 cases in the control group. The average age of patients in the EGE group was 8.91 ± 3.58 years and that of the

control group was 7.99 ± 3.10 years. There was no significant difference between the two groups ($t = -1.813$, $P = 0.072$); the male-to-female ratio in the EGE group was 1.46:1 and that in the control group was 1.52:1. There was no significant difference in gender composition between the two groups ($\chi^2 = 0.048$, $P = 0.826$).

Analysis of blood routine and biochemical indexes

The number of peripheral blood EOs in the EGE group was significantly increased and was 2.95-fold higher than that in the control group ($t = 5.474$, $P < 0.001$). Although the peripheral blood leukocyte and platelet counts decreased slightly in the EGE group compared to those in the control group, there was no significant difference between the counts of both groups, whereas there was almost no difference in neutrophil count, lymphocyte count, hemoglobin content, serum CRP, and albumin levels (Table 1.1). In addition, we found that there were significant differences in EO count, and hemoglobin and albumin levels before and after treatment (Corticosteroids, 1mg/kg.d, lasting for 2 weeks) in the EGE group (Table 1).

Table 1.1
Comparison of routine blood and biochemical indexes between the EGE and control group.

	EGE	CON	t	p
WBC($\times 10^9/L$)	7.38(6.36-9.13)	7.31(6.06-8.78)	0.682	0.495
NE($\times 10^9/L$)	3.05(2.21-4.62)	3.05(2.46-3.77)	0.194	0.846
L($\times 10^9/L$)	3.55(3.1-4.35)	3.53(2.46-5.17)	0.692	0.489
EO($\times 10^9/L$)	0.56(0.53-0.60)	0.29(0.08-0.53)	5.474	<0.001
HB(g/L)	125(118-132)	126(118-133)	-0.154	0.878
PLT($\times 10^9/L$)	282(238-339)	309(254-361)	-1.858	0.063
CRP(mg/L)	1.5(0-3.1)	1.6(0-2.5)	0.790	0.430

EGE, eosinophilic gastroenteritis group; CON, control group; WBC, white blood cell; NE, neutrophils; L, lymphocyte; HB, hemoglobin; EO, eosinophils; PLT, platelet; CRP, C-reactive protein; ALB, albumin.

Table 1.2
Comparison of routine blood and biochemical indexes before and after treatment in EGE group

	Pre-T	Post-T	t	p
WBC($\times 10^9/L$)	7.38(6.36-9.13)	7.37(4.19-9.92)	0.033	0.974
NE($\times 10^9/L$)	3.05(2.21-4.62)	3.07(2.11-4.10)	0.350	0.726
L($\times 10^9/L$)	3.55(3.1-4.35)	3.59(3.12-4.82)	1.460	0.142
EO($\times 10^9/L$)	0.56(0.53-0.60)	0.26(0.12-0.43)	32.63	<0.001
HB(g/L)	125(118-132)	129(122-142)	6.864	<0.001
PLT($\times 10^9/L$)	282(238-339)	279(145-389)	0.407	0.684
CRP(mg/L)	1.5(0-3.1)	1.4(0-2.0)	0.760	0.570
ALB(g/L)	42.6(40.2-45.1)	43.9(40.6-50.7)	7.076	<0.001

Pre-T, pre-treatment; Post-T, post-treatment; EGE, eosinophilic gastroenteritis group; CON, control group; WBC, white blood cell; NE, neutrophils; L, lymphocyte; HB, hemoglobin; EO, eosinophils; PLT, platelet; CRP, C-reactive protein; ALB, albumin.

Comparison of inflammation-related indexes including NLR, PLR, and CRP-to-albumin ratio (CAR)

In this study, the NLR, PLR, and CAR were calculated using blood cell count data, and serum CRP and albumin concentrations. We found that the PLR in the EGE group was significantly lower than that in the control group ($t = -2.273$, $P = 0.023$). However, there was no significant difference in NLR and CAR between the two groups (Table 2.1). Moreover, we found that there was a significant difference in PLR before and after treatment in the EGE group.

Table 2.1
Comparison of NLR, PLR, and CAR between EGE and CON groups

	NLR	PLR	CAR
EGE	0.85 (0.63–1.17)	89.23 (63.56–109.7)	0.041 (0–0.07)
CON	0.88 (0.49–1.35)	76.05 (63.36–90.45)	0.036 (0–0.06)
t value	0.056	-2.273	1.300
P value	0.956	0.023	0.194

EGE, eosinophilic gastroenteritis group; CON, control group; PLR, platelet-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio.

Table 2.2
Comparison of NLR, PLR, and CAR before and after treatment in EGE group

	NLR	PLR	CAR
Pre-T	0.85 (0.63–1.17)	89.23 (63.56–109.70)	0.041 (0–0.07)
Post-T	0.87 (0.52–1.32)	78.77 (43.56–118.93)	0.039 (0–0.08)
<i>t</i> value	0.245	5.061	1.243
P value	0.806	<0.001	0.205

Pre-T, pre-treatment; Post-T, post-treatment; PLR, platelet-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; CAR, C-reactive protein-to-albumin ratio.

Application of EO and NLR values in the diagnosis of EGE

An ROC curve was generated to analyze the value of EO and PLR for diagnosing EGE. The AUC was determined as 0.756 and 0.616, the sensitivity was 75.00% and 34.29%, and the specificity was 74.29% and 92.31% for EO and PLR, respectively; the differences were significant (Fig. 1 and Table 3).

Table 3
Analysis of AUC and evaluation indexes of EO counts and PLR in the diagnosis of eosinophilic gastroenteritis

	AUC	95% CI	Youden	Cut-off	Sensitivity (%)	Specificity (%)	Z value	P value
EO	0.756	0.685~0.870	0.49	>0.51	75.00	74.29	6.502	□ 0.001
PLR	0.616	0.540~0.689	0.27	>60.85	34.29	94.31	2.601	0.009

EO, eosinophil count; PLR, platelet-to-lymphocyte ratio; AUC, area under the curve; CI, confidence interval.

Discussion

EGE is a rare subtype of eosinophilic gastrointestinal diseases. It is characterized by EO infiltration into gastrointestinal tissues, resulting in gastrointestinal wall inflammation, edema, and granulation tissue proliferation. A study found that the incidence rate of EGE in the United States was 8.4–28.0/10 million in the previous 50 years, and the highest incidence of the disease was observed in the previous 30–50 years. Kinoshita et al. found that the incidence rate of EGE in Asia is approximately 13.75/10 million, which is 5.5-fold higher than that in the United States, and the ratio of male-to-female patients is 1.2:1 [4–7]. In China, there is a lack of reliable epidemiological data on EGE. It is estimated that the incidence rate of EGE in China is similar to that in Japan. However, no reliable investigation on EGE prevalence has been performed in China; the exact incidence rate has not been established. Therefore, our study analyzed the

age and gender composition of patients with EGE diagnosed in Wuxi children's Hospital from 2018 to 2020. We found that the average age of children with EGE was 8.91 ± 3.58 years, and the gender ratio of men-to-women was 1.46:1. Zhengyang et al. studied 88 patients with EG and found that the male-to-female ratio is 1.2:1, with an average age of 45.1 years, and also found that abdominal pain is the most common symptom, and 73.3% of patients tested were positive for allergen screening [8]. This indicates that a large-scale epidemiological investigation is required to determine the actual incidence rate and epidemiological characteristics of EGE in China.

At present, the diagnostic standard of EGE proposed by Talley in 1990 is used; the typing standard was proposed by Klein in 1970. These criteria require pathological biopsies; therefore, endoscopic tissue biopsy is the key sample required in the diagnosis of EGE [3, 9, 10]. However, the cut-off point of EO levels in the diagnosis of EGE is controversial. Tally has stated that EO counts ≥ 20 /HPF in at least one site should be used as the diagnostic standard, whereas Collins has suggested that the relevant pathological changes in the lesion site, such as EO degranulation, EO gland or crypt abscesses, and small intestinal microvilli atrophy, should be evaluated instead of quantifying EO infiltration [11]. Therefore, it is necessary to perform multi-point and multiple endoscopic biopsies in the clinic for diagnosing suspected patients with EGE to improve the accuracy of diagnosis. In addition, there is a demand for alternative simple and effective screening methods.

White blood cells and their subtypes play a key role in the process of inflammatory response in EGE, and peripheral blood EOs may play a role in the diagnosis of EGE. Yun et al. found that the absolute number of EOs in the peripheral blood increases in approximately 54.6% of children with EGE, and EO counts increase significantly in children with serosal-type EGE [2, 12] which is consistent with the results reported by Tally et al. [3]. Another study reported that the EO count in peripheral blood can be used as the classification basis for the severity of EGE [13]. Our study found that the peripheral blood EO count could be used as a diagnostic indicator of EGE; based on ROC analysis of EO in EGE, the AUC was 0.756, and the diagnostic sensitivity and specificity were 75.00% and 74.29%, respectively. However, the increase in peripheral blood EO count can also be found in allergic diseases such as asthma. Therefore, peripheral blood EO counts still need to be further investigated as a valuable indicator for the diagnosis of EGE [14, 15].

Serum CRP is an inflammatory index used to evaluate infection and inflammation in the clinic [16, 17]. However, Jing et al. analyzed 23 children with EGE and found that only 3 cases showed elevated serum CRP levels [18]. Our study showed that there was no significant difference in the average CRP level between the EGE and control groups. NLR, PLR, and CAR indirectly reflect the inflammatory status in the body and are related to the diagnosis and prognosis of various diseases [19–22]. The PLR is an emerging inflammatory marker that, in combination with NLR and other hematologic indices, can help in the diagnosis and assessment of the activity and severity of several rheumatic diseases, in early detection of various comorbidities at a subclinical stage, and in monitoring the response to anti-inflammatory therapies [23]. Among the aforementioned indicators, we found that the average PLR in the EGE group was higher than that in the control group, which suggests its use as a potential indicator for the diagnosis

of EGE. ROC analysis of PLR in EGE showed that the AUC was 0.616, and the sensitivity and specificity were 34.29% and 92.31% respectively.

Conclusion

EGE is a rare chronic digestive disease that is not associated with any specific symptoms and is often misdiagnosed and not reported. At present, EGE is mainly diagnosed via pathological biopsies of the gastrointestinal tract. Our study revealed that patients with EGE showed higher EO counts and PLR than those in the control group. Therefore, EO and PLR may be considered as novel and simple predictive markers for assessing the risk of developing EGE. Further studies with a large sample size should be performed to confirm the diagnostic utility of EO and PLR in patients with EGE.

List Of Abbreviations

EO, eosinophil; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-leukocyte ratio; EGE, eosinophilic gastroenteritis; CRP, C-reactive protein; CAR, CRP-to-albumin ratio; ROC, receiver operating characteristic; AUC, area under the curve.

Declarations

Authors' contributions

Q L collected data, interpreted the results, and wrote the initial draft and final version of the paper. RMZ drafted the work critically for important intellectual content and contributed to the final version of the paper. XZL contributed to the conception of the work and participated in the critical drafting of the academic content of the work. WJH was analyzed and calculated. ZMN contributed to the conception of the work and took part in the data collection. All authors read and approved the final manuscript.

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Ethics approval and consent to participate

Study approval was obtained from the Medical Research Council Scientific and Research Ethics Committee. Parents/legal guardians signed the informed consent form before any study-related procedures occurred.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Consent has been given by the patients and parents, via the written informed consent.

Competing interests

The authors declares that they have no competing interests.

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Figures

Figure 1

Receiver operating characteristic curve of EO counts and PLR in the diagnosis of eosinophilic gastroenteritis. PLR, platelet-to-lymphocyte ratio; EO, eosinophil.