

ORIGINAL ARTICLE

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Diagnostic utility of simple hematologic markers in acute gastroenteritis patients admitted to the emergency department**Okcan Bardakci¹, Murat Das¹, Gokhan Akdur¹, Okhan Akdur¹, Yavuz Beyazit²**¹Canakkale Onsekiz Mart University, Department of Emergency Medicine, Canakkale, Turkey²Canakkale Onsekiz Mart University, Department of Internal Medicine, Canakkale, TurkeyReceived 15 November 2019; Accepted 27 February 2020
Available online 16.05.2020 with doi: 10.5455/medscience.2019.08.9213**Abstract**

The contributions of hematologic parameters to the inflammatory response via different leukocyte and platelet pathways are well known. However, the diagnostic yield of these parameters in acute gastroenteritis (AGE) is not yet well understood. This study was planned to investigate the diagnostic value of simple hematological markers, including mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), red cell distribution width (RDW), platelet distribution width (PDW), and platelet-to-lymphocyte ratio (PLR), in patients with AGE admitted to the emergency department. A total of 57 patients with AGE of either viral or bacterial origin and 69 age and sex-matched control subjects were studied. NLR, PLR, MPV, PDW, and RDW values in all patients were calculated and recorded from complete blood cell counts. A total of 126 patients (57 men [45.2%] and 69 women [54.8%]) were included in the study. The mean NLR and PLR values of AGE patients were significantly higher than those of health controls (NLR = 4.44 ± 4.1 for AGE patients and 2.22 ± 1.2 for controls [$P < 0.001$]; PLR = 160.4 ± 102.4 for AGE patients and 113.8 ± 42.6 for controls [$P = 0.02$]). ROC curve analysis suggested that the optimum NLR cut-off point for AGE was 2.08, with a sensitivity, specificity, PPV, and NPV of 70%, 65%, 62%, and 72%, respectively (AUC = 0.704). The optimum PLR cut-off point for AGE was 105.55, with sensitivity, specificity, PPV, and NPV of 71%, 50%, 54%, and 68%, respectively (AUC = 0.648). We demonstrated that NLR and PLR levels are elevated in AGE patients. Thus, NLR and PLR levels can be considered a valuable tool to differentiate acute gastroenteritis from other non-inflammatory emergent conditions.

Keywords: Acute gastroenteritis, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio**Introduction**

Acute gastroenteritis (AGE) is a common and costly clinical problem in both children and adults with various etiologies. AGE can be defined as the inflammation of the gastrointestinal system and is usually characterized by diarrhea, fever, nausea, and vomiting [1]. AGE affects 3 to 5 billion children each year, with 1.5 million visits to primary care providers each year and 220000 hospital admissions for children under 5 years of age. Moreover, hospital admissions in adult AGE patients appear to be increasing in recent years [2]. Although there is no single specific test to diagnose AGE, history and physical examination have paramount importance. Unfortunately, these findings and complaints usually resolve within several days of the initial complaint, and diarrhea and abdominal tenderness may not be present [3]. This could confuse the differential diagnosis, which includes acute appendicitis, diverticulitis, ovarian cyst rupture, and adnexitis [4]. Moreover, it should be noted that no symptoms may be present in

the early phases of AGE apart from abdominal tenderness or pain. For this reason, in emergency medicine settings, the diagnosis and follow-up of these patients must be performed with caution using a multidisciplinary approach.

Recently, different hematological parameters have been proposed to evaluate the inflammatory status of distinct disease states. [5-7]. In this context, mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), red cell distribution width (RDW), platelet distribution width (PDW), and platelet-to-lymphocyte ratio (PLR) have been found to be effective as a reflection of inflammatory burden and disease activity in several disorders, including hyperemesis gravidarum, acute appendicitis, ulcerative colitis, chronic viral hepatitis, hepatocellular carcinoma, and cardiovascular diseases [5,8-13]. Unfortunately, there is scarce evidence that demonstrates the value of these hematologic markers in patients with AGE. Moreover, these studies have shown conflicting results; thus, no definitive conclusions can be made [13, 14]. With this background, in this study we aimed to analyze the diagnostic value of MPV, PDW, PLR, NLR, and RDW in AGE patients.

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Materials and Methods

Patient selection

This is a case-control study conducted in patients who had been diagnosed with AGE, either bacterial or viral, in the Adult Emergency Department at Canakkale Onsekiz Mart University Hospital, Çanakkale, Turkey, between January 1, 2017 and December 31, 2017. After the approval from the ethics committee of Canakkale Onsekiz Mart University (2011-KAEK-27/2019-1900040923) a total of 57 patients with AGE and 69 age-matched healthy controls without any complaints were recruited for this study. The power of the study was 80% associated with 95% confidence interval. The AGE group included 57 patients who presented to the emergency department with complaints of abdominal pain, vomiting, and diarrhea, on whom a complete blood cell (CBC) count was performed, and who were discharged from emergency department with a final diagnosis of AGE (International Classification of Diseases, 10th revision, code A08.4-A08.5) after exclusion of acute abdomen diagnosis. Patients who were younger than 18 years of age, had incomplete hospital data, had used previous medications, or had chronic inflammatory bowel diseases, malabsorption syndromes, immunodeficiency and malnutrition, or chronic hematologic and malignant disease were not included in the present study. The control subjects were people who presented to the same emergency department with nonspecific complaints and met the exclusion criteria, with normal physical and laboratory examination. The study was approved by the ethics committee of Canakkale Onsekiz Mart University (Ethical approval no:2011-KAEK-27/2019-1900040923) and was conducted in accordance with the guidelines of the Helsinki Declaration.

Laboratory analysis

All blood samples were collected from the AGE patients and control group from the antecubital vein and without the use of any anticoagulant. Blood samples were taken in 2 ml tubes containing EDTA and analyzed in the central biochemistry laboratory of the hospital, using the same Beckman Coulter (High Wycombe, UK) Gen-S automated analyzer for all samples. The analyzed blood samples were: white blood cell count ($4-10 \times 10^3/\mu\text{L}$), neutrophil count ($2-12 \times 10^3/\mu\text{L}$), lymphocyte count ($1-4.9 \times 10^3/14.3\%$), MPV (6.9 to 10.8 fl), platelet count ($156 \text{ to } 373 \times 10^3/\mu\text{L}$), RDW (pg), and PDW (%). The NLR was calculated from the differential count by dividing the absolute neutrophil count by the absolute lymphocyte count; the PLR was calculated by dividing the platelet count by the lymphocyte count.

Statistical analysis

Data were evaluated using SPSS Statistics for Windows, Version 22.0 statistical software (IBM Corporation, Armonk, NY, USA). The independent-samples T-test with bootstrap results was used to compare two independent groups. For categorical variables, the chi-square test was used to compare independent groups. Normally distributed continuous variables were expressed as mean $\pm$ SD and compared using independent samples T-tests. Mann-Whitney's U-tests were used for non-normally distributed continuous

variables. The correlation between classification of the patient groups separated by cutoff values was calculated according to the variables, and real classification was expressed by examination of sensitivity and specificity

Results

A total of 126 patients (57 men [45.2%] and 69 women [54.8%]) were included in the study. Table 1 summarizes the demographic and laboratory characteristics of the AGE patients and control group. The mean age of the AGE patients and control group were 49.9 ± 18.5 years and 47.2 ± 16.4 years, respectively. The two groups were not significantly different with regard to age or distribution of gender.

Table 1. Comparison of clinical and laboratory parameters between patients and controls

	Gastroenteritis (n:57)	Healthy Controls (n:69)	P
	Mean $\pm$ SD	Mean $\pm$ SD	
Age(year)	49.9 $\pm$ 18.5	47.2 $\pm$ 16.4	0.398
Gender			
Female(%)	33 (57.8)	36 (52.1)	
Male(%)	24 (42.2)	33 (47.9)	
WBC (mm 3 $\times$ 10 3)	9.5 $\pm$ 3.1	7.5 $\pm$ 1.7	<0.001
Neutrophil (mm 3 $\times$ 10 3)	4.4 $\pm$ 4.1	2.2 $\pm$ 1.2	<0.001
Lymphocyte (mm 3 $\times$ 10 3)	2.07 $\pm$ 1.01	2.2 $\pm$ 0.66	0.252
Hgb (g/dl)	12.8 $\pm$ 1.9	13.9 $\pm$ 1.6	0.001
NLR	4.44($\pm$ 4.1)	2.22 $\pm$ 1.2	<0.001
PLR	160.4 $\pm$ 102.4	113.8 $\pm$ 42.6	0.02
MPV (fL)	8.3 $\pm$ 0.95	8.8 $\pm$ 1.06	0.06
RDW (%)	14.6 $\pm$ 3.1	14.1 $\pm$ 1.7	0.237
PDW (%)	16.7 $\pm$ 0.63	16.2 $\pm$ 0.69	0.26

The mean NLR and PLR values of AGE patients were significantly higher than those of health controls (NLR = 4.44 ± 4.1 for AGE patients and 2.22 ± 1.2 for controls [$P < 0.001$]; PLR = 160.4 ± 102.4 for AGE patients and 113.8 ± 42.6 for controls [$P = 0.02$] (Figure 1-2).

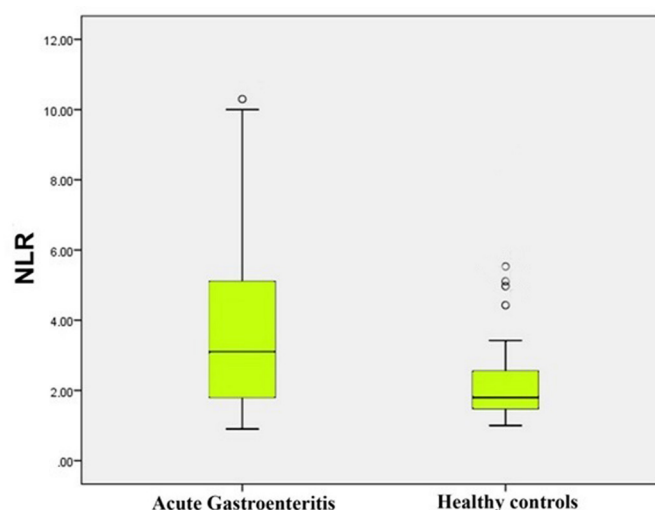


Figure 1. NLR levels of acute gastroenteritis patients and healthy controls

The ROC curve analysis was performed to evaluate the predictive ability of hemogram parameters to diagnose AGE. Sensitivity, specificity, and area under the curve values for hemogram parameters were estimated based on cutoff values determined by ROC analyses.

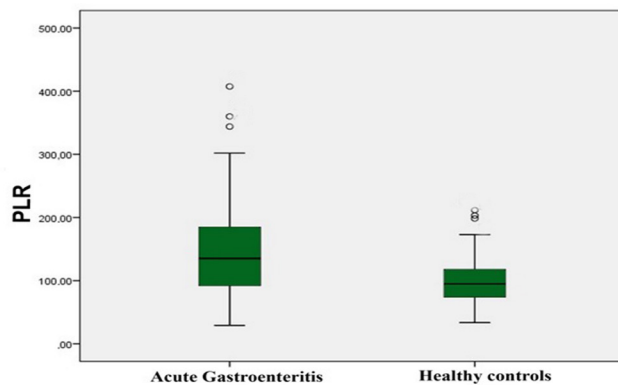


Figure 2. PLR levels of acute gastroenteritis patients and healthy controls

The ROC curve analysis suggested that the optimum NLR cut-off point for AGE was 2.08, with a sensitivity, specificity, PPV, and NPV of 70%, 65%, 62%, and 72%, respectively (AUC = 0.704; Fig. 3). The optimum PLR cut-off point for AGE was 105.55, with a sensitivity, specificity, PPV, and NPV of 71%, 50%, 54%, and 68%, respectively (AUC = 0.648; Fig. 3). The results of the same analysis for the other hematologic parameters are summarized in Table 2.

Table 2. ROC analyses of NLR and PLR with other hematologic indices to differentiate acute gastroenteritis from healthy controls.

	Cutoff	AUC	Sensitivity (%)	Specificity (%)	PPV(%)	NPV(%)
NLR	2.08	0.704	70	65	62	72
PLR	105.55	0.648	71	50	54	68
MPV	8.35	0.376	49	66	54	60
PDW	16.4	0.571	66	48	53	64
RDW	13.6	0.550	68	46	50	60

NLR. neutrophil-to-lymphocyte ratio; **PLR:** platelet to lymphocyte ratio; **MPV:** mean platelet volume; **PDW:** platelet distribution width; **RDW:** red cell distribution width; **AUC:** area under curve; **PPV:** positive predictive value; **NPV:** negative predictive value

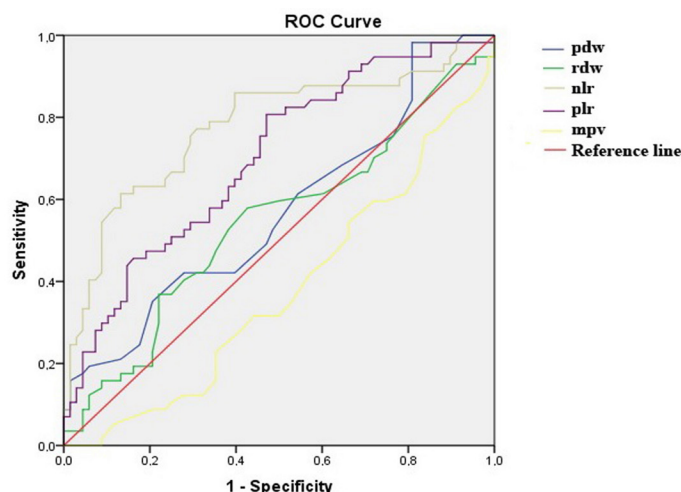


Figure 3. Receiver operating characteristic (ROC) curves of NLR and PLR with other hematologic indices

There were no statistically significant differences in MPV, PDW, and RDW between the two groups (Table 1).

Discussion

In this study, the diagnostic value of MPV, NLR, PLR, RDW, and PDW was investigated in AGE patients. The findings of the present study revealed that only NLR and PLR were higher in AGE patients compared with controls. NLR values were found to have high sensitivity, specificity, and predictive value in differentiating AGE patients from controls.

AGE is the inflammation of gastrointestinal system, usually triggered by a bacterial or viral infection and causing abdominal cramps, diarrhea, and vomiting. Although the role of inflammation in AGE is unclear, pathophysiology usually differs depending the underlying condition. In response to the presence of an irritant or infectious agent, it is not surprising to encounter systemic hematologic responses in peripheral blood data.

The unique role of platelets in inflammatory conditions has been outlined in a number of studies in which the link between platelet activation and the pathophysiology of the diseases with inflammation was detected [15]. In this context, preliminary evidence suggests that MPV levels are significantly affected in patients with gastroenteritis [13,14]. Although a majority of these studies were performed in children, all of them demonstrated a significant decrease in MPV levels. Mete et al [13] recently showed that MPV levels were lower in children with rotavirus gastroenteritis compared with healthy children. Similarly, a study by Matowicka-Karna et al. [16] demonstrated that that MPV levels in patients infected with *Entamoeba histolytica* were lower than in controls. Interestingly, Çelik et al. [17] showed that MPV levels were increased in amebiasis patients with gastroenteritis. Authors speculated that the discrepancies between studies was likely associated with the severity of the systemic inflammation. In this study, we found no significant difference in MPV levels between AGE patients and controls. This might be due to several reasons, including the severity of systemic inflammation and the relatively small number of study participants.

The other platelet indices, such as PDW, may present valuable clinical data in inflammatory diseases. A number of studies correlated blood PDW values to many diseases including appendicitis, pre-eclampsia, recurrent miscarriages, and dementia [18-22]. PDW is an index that reflects the heterogeneity of platelets. In inflammatory conditions, activation of platelets causes platelet shape alterations, with anisocytosis leading to an increase in PDW values [23-24]. Similar to MPV levels, we observed no alterations in PDW values between study groups.

NLR is another parameter investigated in the present study. NLR is a simple, widely used, and inexpensive index of systemic inflammatory burden that correlates with prognosis in distinct disease conditions [11]. Although there are no studies that have specifically investigated NLR in AGE patients, there are a number of studies that investigated NLR in inflammatory and neoplastic conditions including ulcerative colitis, acute appendicitis, colorectal cancer, hepatocellular, nasopharyngeal, and metastatic renal cell carcinoma [11,25-28]. Considering that the primary agent in gastroenteritis is infectious microorganisms, it can be predicted that neutrophil count, which is highly sensitive for the detection of infectious conditions, and its ratio to lymphocyte count would provide more valuable information.

The elevated PLR and NLR levels that have been demonstrated in the current study could also be a result of a physiological immune response of circulating leucocytes and platelets to gastroenteritis-associated inflammatory conditions, which results in amplification of neutrophils and platelets and a decrease in lymphocyte counts. Similar to NLR, PLR is another hematologic parameter that is suggested to have a key value in the diagnosis of systemic inflammation [29]. Although PLR alterations in gastroenteritis patients have not been demonstrated previously, literature data suggests elevated PLR levels in distinct disease conditions. In a recent study by Çınar et al. [30], PLR values were found to be significantly higher in acute appendicitis during pregnancy. Similarly, Akpınar et al. [31] demonstrated the predictive value of PLR in ulcerative colitis patients. In this context, the finding of elevated NLR and PLR in gastroenteritis patients adds significant value to the diagnostic evaluation of AGE patients in emergency clinical settings.

We recognize some limitations inherent to our study. The first limitation is the negligence of other well-demonstrated inflammatory markers such as TNF- α , and IL-6 and IL-1 β . It would be noteworthy to evaluate serum levels of these pro-inflammatory cytokines and correlate these cytokine levels with our test results. Secondly, despite the findings of the present study, our results should be interpreted cautiously because of the relatively moderate sample size which limited the power of the study. And third, it would have been useful to evaluate the same AGE patients after clinical and laboratory remission was achieved was achieved.

Conclusion

Clinicians may find it difficult to distinguish AGE from a number of acute inflammatory disease conditions despite appropriate medical evaluations in emergency clinics. Therefore, easy-to-use hematologic markers, especially NLR and PLR, can be considered as a valuable tool to differentiate acute gastroenteritis from other non-inflammatory emergent conditions.

Competing interests

We declare that we have no conflict of interest.

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethical approval

Ethical approval was received from the ethics committee of Canakkale Onsekiz Mart University (2011-KAEK-27/2019-1900040923)

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