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ORIGINAL ARTICLE

The Clinical Significance of Neutrophil-Lymphocyte Ratio, Monocyte-Lymphocyte Ratio, and Platelet-Lymphocyte Ratio in Patients with Guillain–Barré Syndrome

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Abstract

Introduction: The purpose of this study was to determine the prognostic value of the pre-treatment neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and monocyte-lymphocyte ratio (MLR) in the diagnosis of Guillain–Barré syndrome (GBS).

Methods: This retrospective study enrolled a total of 98 GBS patients and 101 healthy control (HC).

Results: Our study showed that GBS patients had higher level of NLR, PLR, and MLR compared with HC ($p<0.001$, $p<0.001$, and $p<0.001$, respectively). We investigated the effectiveness of NLR, PLR, and MLR in prediction of GBS using receiver operating characteristic analysis. NLR had the highest area under curve (AUC) (0.912, 95% CI, 0.870–0.954) followed by MLR and PLR (AUC = 0.811 and 0.753, respectively).

Discussion and Conclusion: NLR, PLR, and MLR can be considered as a potential inflammatory biomarker for GBS patients.

Keywords: Guillain–Barré syndrome; monocyte-lymphocyte ratio; neutrophil-lymphocyte ratio; platelet-lymphocyte ratio.

Guillain–Barré syndrome (GBS) is the most common severe acute paralytic neuropathy and the immune system plays an important role in the development of this peripheral nerve disease[1]. The annual incidence is about 1–2/100.000 and has a mortality rate of 5–10%[2]. Patients usually presented with weakness and areflexia. Acute onset and rapid progressive symmetric weakness classically starts from the distal of the lower extremities[3].

The cause of GBS could not be established precisely, but the disease is based on a cellular and humoral immune mechanism. About more than half of GBS diseases, bacterial and viral infections such as campylobacter jejuni, cytomegalovirus, Epstein–Barr are considered to be responsible. Gangliosides and glycolipids are distributed throughout myelin in the peripheral nervous system, and viral and bacterial agents are presumed to cause production of antibody against them[4].

Recently, some researchers have suggested that white blood cell count (WBC) subtypes (platelet-lymphocyte ratio [PLR] and neutrophil-lymphocyte ratio [NLR]) can be used as predictors of prognosis in many diseases including immune system diseases[5-7]. Monocyte-lymphocyte ratio (MLR) was also considered as biomarker in many cases such as NLR and PLR[8,9]. In our study, we focused on these three systemic inflammatory markers (NLR, PLR, and MLR)

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Table 1. Comparison of laboratory values and clinical characteristics of patients with GBS and healthy controls

Parameter	GBS (n=98)	Healthy control (n=101)	p
Age (years)	55.02±17.38	54.68±19.89	0.899
Gender (female/male)	36/62	38/63	0.897
Clinical subtypes, n (%)			
AIDP	59 (60.2)		
AMAN	21 (21.4)		
AMSAN	18 (18.4)		
Laboratory findings			
White blood cell ($\times10^3/mm^3$)	9.29±3.39	7.42±1.85	<0.001
Neutrophils ($\times10^3/mm^3$)	5.97±2.85	3.70±1.26	<0.001
Lymphocytes ($\times10^3/mm^3$)	1.34±0.65	1.97±0.75	<0.001
Platelets ($\times10^3/mm^3$)	254.75±82.76	248.86±60.67	0.984
Monocyte ($\times10^3/mm^3$)	0.72±0.27	0.60±0.19	<0.001
MPV (fL)	9.03±1.26	8.78±1.5	0.094
PDW (fL)	15.56±2.07	15.57±2.21	0.759
RDW (%)	14.63±2.07	15.12±2.21	0.083
NLR	3.77±2.13	1.29±0.52	<0.001
MLR	169.36±74.42	112.85±40.13	<0.001
PLR	0.47±0.24	0.28±0.17	<0.001
CRP (mg/dl)	12.42±21.25	3.04±3.27	<0.001

GBS: Guillain–Barre syndrome; AIDP: Acute inflammatory demyelinating polyradiculoneuropathy; AMAN: Acute motor axonal neuropathy; AMSAN: Acute motor sensory axonal neuropathy; MPV: Mean platelet volume; PDW: Platelet distribution width; RDW: Red cell distribution width; NLR: Neutrophil-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; CRP: C-reactive protein.

because of the important role of inflammation in GBS formation. These parameters were previously discussed separately in GBS patients, but these three parameters were discussed together for the 1st time in our study.

Materials and Methods

In this retrospective study, the ethics review committee approved the study protocol. Between January 2013 and June 2018, we carried out hospital records of patients with GBS. Our study included 98 patients with GBS and 101 healthy controls (HCs). The diagnosis of GBS was determined according to accepted diagnostic criteria[10,11]. HC admitted to the emergency department for routine control. These people had no solid tumors, any signs of infection, peripheral neuropathy, or chronic disease. HC was randomly determined and was similar in age and gender to GBS patients. Patients were excluded if they had local or systemic infections (n=3), chronic diseases (autoimmune, renal, cardiovascular... etc.) (n=12), steroid use (n=1), malignancy (n=4), chronic inflammatory demyelinating polyradiculoneuropathy (n=6), and age <18 years old (n=2). Demographic characteristics of patients (age and sex), electrophysiological studies, and laboratory results were noted. The complete blood count test was performed at the time of ED admission (pre-treatment) and laboratory values were recorded. WBC subgroups were calculated.

The definition of NLR, PLR, and MLR was neutrophil, platelet, and monocyte count divided by the lymphocyte count one by one. Electromyography was performed by neurologists for the first 2 days of hospitalization. The patients were classified as axonal and demyelinating subtypes according to electrodiagnostic criteria[12]. Patients were divided into three subgroups based on electrophysiological findings: (a) Acute inflammatory demyelinating polyradiculoneuropathy (AIDP); (b) acute motor axonal neuropathy (AMAN); and (c) acute motor sensory axonal neuropathy (AMSAN)[13]. Patients were divided into two subtypes: (a) Demyelinating forms (AIDP) and (b) axonal forms (AMAN and AMSAN). Intravenous immunoglobulin was administered to all the patients.

Statistical Analysis

In the comparisons between GBS and HC and patients subtypes, the mean±standard deviation for numerical variables, number and percentage for categorical variables was given. In continuous variables, t-test or Mann–Whitney U test was used according to normality in distribution. In our study, Chi-square and Fisher's exact tests

Table 2. Comparisons of laboratory and clinical parameters between AIDP and axonal subgroups

Parameter	AIDP (n=59)	Axonal (n=39)	p
Age (years)	55.05±17.16	54.97±17.93	0.954
Gender (female/male)	19/40	17/22	0.289
Hospitalization days	12.18±15.81	15.43±21.99	0.087
Laboratory findings			
White blood cell ($\times10^3$/mm^3)	9.52±3.69	8.93±2.86	0.557
Neutrophils ($\times10^3$/mm^3)	6.22±3.14	5.61±2.32	0.368
Lymphocytes ($\times10^3$/mm^3)	1.3±0.65	1.41±0.67	0.528
Platelets ($\times10^3$/mm^3)	247.24±83.48	266.82±80.31	0.209
Monocyte ($\times10^3$/mm^3)	0.73±0.3	0.71±0.24	0.994
MPV (fL)	8.96±1.17	9.25±1.41	0.490
PDW (fL)	15.58±2.15	15.66±1.78	0.330
RDW (%)	14.82±2.29	14.35±1.68	0.361
NLR	3.94±2.27	3.51±1.89	0.423
MLR	0.47±0.24	0.48±0.25	0.609
PLR	166.2±83.4	174.14±59.02	0.195
CRP (mg/dl)	13.67±22.73	10.43±19.09	0.376

GBS: Guillain–Barre syndrome; AIDP: Acute inflammatory demyelinating polyradiculoneuropathy; MPV: Mean platelet volume; PDW: Platelet distribution width; RDW: Red cell distribution width; NLR: Neutrophil-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; CRP: C-reactive protein.

Table 3. Diagnostic accuracy of parameters for prediction Guillain–Barre syndrome

Parameters	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	95% CI	p
NLR	0.912	2.5	91.6	99.7	0.870 to 0.954	<0.001
MLR	0.811	0.35	72.6	79.2	0.750 to 0.872	<0.001
PLR	0.753	125	70.5	73.3	0.683 to 0.823	<0.001
CRP	0.739	3.5	55.8	76.2	0.670 to 0.808	<0.001

AUC: Area under the curve; NLR: Neutrophil-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; CRP: C-reactive protein; CI: Confidence interval.

were used in categorical data. Receiver operating characteristic (ROC) curves were used to predict GBS. Statistical analysis was performed using SPSS for Windows version 18.0 and $p<0.05$ was considered statistically significant.

Results

A total of 98 GBS patients were enrolled in this study, including 36 female (36.7%) and 62 male (63.3%) with a mean age of 55.02±17.38 years (21–88). The control group consisted of a total of 101 healthy individuals (38 females and 63 males) with a mean age of 54.68±19.89 years (21–90). Basic laboratory and clinical features of patients with GBS and HC are shown in Table 1. Briefly, there was no difference between the two groups in terms of the age and gender. As shown in Table 1, significantly higher WBC, the neutrophil, monocyte count, and CRP levels were detected in GBS patient compared with HC. In addition, lymphocyte count of GBS patients was significantly lower than HC ($p<0.001$). We found that NLR, PLR, and MLR were significantly higher in GBS patients than HC ($p<0.001$).

The subtypes of classification of GBS patients were as follows: AIDP (n=59), AMAN (n=21), and AMSAN (n=18). The mean hospitalization days to the confirmed diagnosis of GBS were 13.47±18.48 days (2–132). The comparisons of the demographic features and laboratory findings among the subgroups are shown in Table 2. There were no marked differences between the subgroups with regard to all laboratory and demographic parameters (Table 2).

We investigated the effectiveness of NLR, PLR, MLR, and CRP in prediction of GBS using ROC analysis. It was found that the area under curve (AUC) values of these variables were statistically significant to predict GBS (Fig. 1). NLR had the highest AUC (0.912, 95% CI, 0.870–0.954), followed by MLR, PLR, and CRP (AUC = 0.811, 0.753, and 0.739, respectively). Moreover, with NLR >2.5, the highest sensitivity

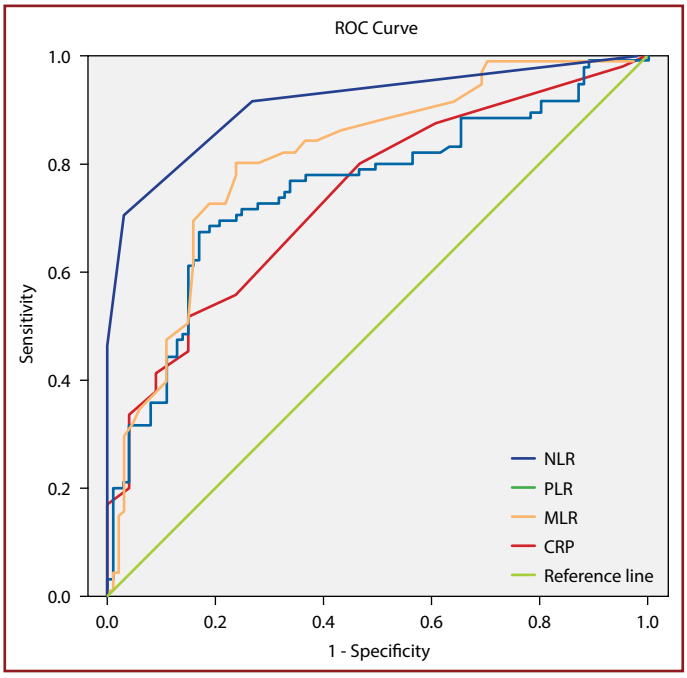

Figure 1. Area under the receiver operating characteristic curve (area under the curve [AUC]) for laboratory parameters in the diagnosis of GBS. NLR had the highest AUC in predicting AC (AUC=0.912), MLR, PLR, and CRP (AUC=0.811, 0.753, and 0.739, respectively).

ROC: Receiver operating characteristic; NLR: Neutrophil-lymphocyte ratio; MLR: Monocyte-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; CRP: C-reactive protein.

(91.6%) and specificity (99.7%) were achieved for prediction of GBS cases (Table 3).

Discussion

In this study, NLR, MLR, and PLR values were significantly higher in GBS patients than HC group. In addition, higher CRP values were detected in these patients, but its diagnostic value was low. All these diagnostic parameters once again showed the relationship between the inflammatory factors and GBS disease.

At present, abnormally activated monocytes may play a role in the pathogenesis of inflammation. As commonly known, the role of monocytes in the immune system is cytokine expression, antigen presentation, or phagocytosis[14]. Studies have shown the relationship between increased number of monocytes and disease and disease severity. For example, Shahid et al.[15 reported that elevated monocyte count was associated with cardiovascular diseases. Another study, Wang et al.[16] showed that monocyte counts were higher in autoimmune disorders such as systemic lupus erythematosus. Similarly, the blood–brain barrier is permeable to monocytes and monocytes can be differentiate into microglia cells pass through this structure and this can be demonstrate the important role of monocytes in the neuroinflammatory process[17]. A study published in 2018 demonstrated that monocytes can be a useful biomarker in the early period of Parkinson's disease[18]. In addition, Peng et al.[19] also found that monocyte count was significantly higher in migraine patients. Like monocytes, MLR is an indicator of inflammation as an immune marker and its function on diseases has been investigated. Xiang et al.[20] reported that MLR was associated with solid tumors. A recent study found that MLR was significantly higher in GBS patients compared to controls[3]. Similar to the literature, we found that both the number of monocytes and the MLR in GBS patients were higher than in the HC group. However, there was no significant difference between GBS subgroups.

Many of biomarkers have been elucidated about the presence of inflammation and immune response, however, in recent years, the most popular of these are NLR and PLR[21,22]. In a study conducted in multiple sclerosis (MS) patients in 2016, NLR was found to be significantly higher in MS disease and relapse period[23]. It has been reported that higher levels of NLR and PLR may be a prognostic factor in the late stages of ovarian cancer[24]. A recent study showed that higher NLR values were detected in patients with cerebral ischemic stroke compared with controls[25]. There are few studies in the diagnostic value of WBC subtypes in GBS patients, in one of them, NLR and PLR are reported to be a useful in subtypes of adult GBS patients[7]. In our study, we demonstrated the availability of NLR and PLR in GBS patients. Our data showed that with the high specificity and sensitivity (91.6% and 99.7%, respectively) predicted the presence of GBS when NLR 2.5 was above. In PLR, we found lower specificity and sensitivity (70.5% and 73.3%, respectively) rates with a cutoff value of 125.

Study Limitation

The limitations of study: (1) This is a retrospective study, (2) small sample size and the results are only from one center, (3) post-treatment blood samples were not collected, and (4) larger prospective studies are needed in the future.

Conclusion

As a result, WBC subtypes such as NLR, PLR, and MLR can be considered as a potential inflammatory biomarker for GBS patients, due it being inexpensive and easy calculated.

Ethics Committee Approval: The Antalya Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 28.02.2019, number: 7/21).

Peer-review: Externally peer-reviewed.

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Conflict of Interest: None declared.

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