

## Original Research Article

# Evaluation of the relationship of disease activity with neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients with peptic ulcer and gastritis

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### ABSTRACT

**Background:** Dyspepsia is a confusing complaint in terms of patient approach and management. Since the most important clinical diagnoses that occur with dyspeptic complaints are gastroduodenitis, peptic ulcer disease and gastric-esophageal cancers, endoscopic evaluation method is often preferred in the diagnosis. It has been shown that NLR (neutrophil to lymphocyte ratio) can be an important marker in many chronic systemic diseases, especially malignancies. Since upper gastrointestinal endoscopy is an invasive and costly procedure, NLR and PLR (Platelet to lymphocyte ratio) may be useful as a new marker to help in the diagnosis of gastritis and peptic ulcer. In our study, we aimed to investigate how NLR and PLR changes seen in patients with gastritis and peptic ulcer diseases.

**Methods:** A total of 906 patients who applied to the internal medicine clinic of our hospital between January 2016 and September 2017 were included in the study. The demographic data, drugs, endoscopy and biopsy results and hemogram parameters of the patients were obtained from the outpatient clinic records. NLR and PLR values were calculated and statistically interpreted.

**Results:** According to the endoscopy results, a total of 906 patients with 311 (34.3%) gastritis, 288 (31.8%) peptic ulcer and 307 (33.9%) normal findings were included in to the study. Male to female ratios were 55% to 45% in gastritis patients, 55,6% to 44,4% in peptic ulcer patients and 53,4% to 46,6% in normal subjects. The median age of the patients was 50 years (18-82 years). The median NLR and PLR ratios were 1.82 (0.54-8.35) and 107.8 (46.27-446.43) in the gastritis group, 1.9 (0.61-9.86) in the peptic ulcer group and 110.95 (44.03-340.65) and 1.71 (0.56-12.89) and 106.02 (40.41-397.62) in the normal group. While a significant difference was obtained between the groups in terms of NLR ( $p=0.048$ ), no significant difference was found for PLR ( $p=0.422$ ).

**Conclusions:** In our study, a statistical significant difference was found between patients with gastritis and peptic ulcer and normal subjects in terms of NLR, but this difference was not at a level that could be used in clinical practice.

**Keywords:** Gastritis, Peptic ulcer, Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio

### INTRODUCTION

Dyspepsia is a set of symptoms that includes complaints such as discomfort and pain in the epigastric region, indigestion, fullness, bloating, early satiety, burning,

nausea, and belching. The prevalence of dyspepsia is between 25-40 %.<sup>1</sup> The causes of dyspepsia are mainly functional (60%) and organic (40%). Major organic causes are gastroesophageal reflux disease (GORD) gastroduodenitis, peptic ulcer disease (PUD), upper

gastrointestinal system malignancies, hepatobiliary disorders; drug use and dietary reasons. In a study performed with upper gastrointestinal endoscopy in 3926 dyspeptic patients; 2,664 (67.3%) of them had normal endoscopic findings; however gastroduodenitis or peptic ulcer was found in 1,202 (30.6%) and upper gastrointestinal malignancy in 82 (2.1%) of the patients.<sup>2</sup> The fact that they present with the same complaints as patients with malignancy shows the importance of accurate and early diagnosis. Although many new disease-specific biomarkers have been identified in recent years, most of these markers are time-consuming and expensive. Peripheral blood cells undergo numerical and functional changes in response to inflammation.<sup>3</sup> Based on these changes, a number of inflammatory biological markers such as monocyte to lymphocyte ratio (MLR), neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been investigated in order to predict the activity and prognosis in various inflammatory gastrointestinal diseases and cancers.<sup>4</sup> These markers can be easily available from the peripheral blood count and also cheap.

Most patients with dyspeptic complaints are endoscopically normal. However, the fact that treatable causes such as gastritis and PUD are seen in approximately one third of the patients and the risk of malignancy necessitates the cheap, easy, practical and less invasive procedure for patients. The effectiveness of NLR and PLR as an indicator of inflammation in many malignancies and chronic diseases has been proven. In our study we aimed to investigate whether the NLR and PLR values of the patients are associated with gastritis and peptic ulcer activity that detected endoscopically.

## METHODS

This study was conducted in the Internal Medicine Clinic of Health Sciences University Istanbul Training and Research Hospital. Patients who applied to the internal medicine outpatient clinic with various dyspeptic complaints and were evaluated with upper gastrointestinal (GIS) endoscopy for further examination were included in the study. The data of the patients were found by scanning the patient files. Endoscopy procedures were performed in the internal medicine endoscopy unit and biopsy materials evaluated in the pathology clinic. A total of 906 patients who applied to our outpatient clinic between January 2016 and September 2017 and met the inclusion criteria were included in the study. Inclusion criterias are; being over 18 years old, patients whose complete blood count is determined within one month before upper GIS endoscopy and finding the accessible pathology result of the endoscopy procedure. The exclusion criterias are; patients who have had upper GIS endoscopy due to gastrointestinal bleeding. Patients with active infection, drug use (steroids, chemotherapeutics, etc.), active malignancy, connective tissue disease, end-stage renal failure and chronic liver disease and patients who have

passed more than a month after their complete blood count obtained and children and pregnant women.

Demographic data, endoscopic results, presence chronic inflammation and helicobacter pylori infection in pathology, use of aspirin, NSAID and other drugs and hemogram parameters were recorded.

NLR parameter was calculated by proportioning the neutrophil and lymphocyte counts and PLR parameter was calculated by proportioning thrombocyte and lymphocyte counts.

SPSS (Statistical Package for Social Sciences) 24.0 for Windows program was used for the statistical analysis of the data. Descriptive statistics were made. Median (min-max) and ratio values were used in descriptive statistics. Kruskal-Wallis, Mann Whitney U test were used in the analysis of quantitative independent data, Chi-square test was used in the analysis of qualitative independent data, and Fischer test was used when Chi-square test conditions were not met. P value <0.05 was used as the significance value.

## RESULTS

A total of 906 patients with 311 (34.3%) gastritis, 288 (31.8%) peptic ulcer and 307 (33.9%) normal findings were included in the study. Four hundred and ninety five (54.6%) of the patients were male and 411 (45.4%) were female. The male / female ratio was 55% / 45% in gastritis patients, 55.6% / 44.4% in peptic ulcer patients and 53.4% / 46.6% in subjects with normal endoscopic findings. The mean age of the gastritis and peptic ulcer patient group was 50 years (min-max; 18-82 years) and subjects with normal endoscopy was 51 years (18-82 years). No significant difference was found in terms of age and gender between the groups ( $p = 0.862$  and  $p=0.942$  respectively). Of the peptic ulcer patients, 147 (51.4%) had ulcers localized in the stomach, 129 (45.1%) in the duodenum, and 10 (3.5%) both in the stomach and duodenum. There were accompanying duodenitis in 52 (16.7%) of the gastritis patients. Helicobacter Pylori positivity in 206 (66.2%) of gastritis patients; It was detected in 213 (74.5%) of the peptic ulcer patients and a statistically significant difference was observed between the two groups ( $p=0.028$ ). Inflammation was mild-moderate in 287 (93.2%) of gastritis patients and severe in 21 (6.8%); It was mild-moderate in 261 (91.6%) of ulcer patients, and severe in 24 (8.4%) ( $p=0.461$ ) (Table 1).

Details of the hemogram parameters of patients with peptic ulcer gastritis and normal endoscopic findings are given in Table 2.

Median NLR was 1.82 (min-max; 0.54-8.35) in the gastritis group, 1.9 (min-max; 0.61-9.86) in the ulcer group and 1.71 in patients with normal endoscopic

findings (min-max; 0.56-12.89) ( $p=0.048$ ). When the groups were compared in terms of NLR, there was a significant difference between the gastritis and peptic ulcer patient group and the normal group ( $p=0.084$  and  $0.018$ ), while there was no significant difference between the two patient groups ( $p=0.455$ ).

The median PLR in the gastritis group was 107.8 (46.27-446.43), in the ulcer group 110.95 (44.03-340.65), and in patients with normal endoscopic findings 106.02 (40.41-397.62) ( $p=0.422$ ). When gastritis, peptic ulcer, and normal groups were compared in terms of PLR, no statistically significant difference was found between the three groups ( $p=0.993$ ,  $p=0.260$  and  $p=0.246$  respectively) (Table 2).

**Table 1: General characteristics of patient groups.**

Patient characteristics	Gastritis	Peptic ulcer	Normal	P value
<b>Patient number (N)</b>	311	288	307	
<b>Median age (min-max) (year)</b>	50 (18-82)	50 (18-82)	51 (18-82)	0,942
<b>Gender N (%)</b>				
Male	171 (55%)	160 (55.6%)	164 (53.4%)	
Female	140 (45%)	128 (44.4%)	143 (46.6%)	0,862
<b>Endoscopic localisation N (%)</b>				
Gastric	259 (83.3%)	147 (51.4%)		0,000
Duodenum	52 (16.7%)	129 (45.1%)		
Gastric+duodenum	-	10 (3.5%)		
<b>H. Pylori positivity N (%)</b>				
Positive	206 (66.2%)	213 (74.5%)		0,028
Negative	105 (33.8%)	73 (25.5%)		
<b>Chronic inflammation level N (%)</b>				
Mild	287 (93.2%)	261 (91.6%)		0,461
Severe	21 (6.8%)	24 (8.4%)		

**Table 2: Hemogram parameters of the groups.**

Hemogram parameters median (min-max)	Gastritis (n=311)	Peptic ulcer (n=288)	Normal (n=307)	P value
<b>Wbc (<math>10^9/l</math>)</b>	7.0 (3.61-12.62)	7.21 (2.86-14.07)	7.0 (3.29-13.72)	0,182
<b>Hemoglobin (gr/dl)</b>	13.7 (6.9-18.2)	13.4 (5.9-18.0)	13.2 (6.2-17.9)	0,002
<b>Platelet (<math>10^9/l</math>)</b>	246 (118-478)	247 (113-479)	244 (107-457)	0,697
<b>Neutrophile (<math>10^9/l</math>)</b>	4.07 (1.62-9.24)	4.18 (1.52-9.34)	3.84 (1.53-10.7)	0,038
<b>Lymphocyte (<math>10^9/l</math>)</b>	2.25 (0.56-4.65)	2.19 (0.78-5.98)	2.21 (0.8-5.33)	0,857
<b>MPV (fl)</b>	10.4 (7.4-14.4)	10.4 (7.8-13.1)	10.4 (8.3-13.9)	0,814
<b>Neutrophil to lymphocyte ratio</b>	1.82 (0.54-8.35)	1.90 (0.61-9.86)	1.71 (0.56-12.89)	0,048
<b>Platelet to lymphocyte ratio</b>	107.8 (46.27-446.43)	110.95 (44.03-340.65)	106.02 (40.41-397.62)	0,422

For the NLR value; 1.7 is determined as the threshold value according to the current literature.<sup>5-7</sup> One hundred and twenty nine (32.4%) of 398 patients had gastritis, 115 (28.9%) had gastric ulcers and 154 (38.7%) had normal findings with  $NLR \leq 1.7$ . However; of the 508 patients with  $NLR > 1.7$ , 182 (35.8%) had gastritis, 173 (34.1%) had ulcers, and 153 (30.1%) had normal findings

( $p=0.024$ ) (Table 3). When the groups were compared in pairs, a statistically significant difference was found between the two patient groups and the normal group while there was no significant difference between the two patient groups ( $p=0,030$  between the normal and gastritic group  $p=0.012$  between the normal and ulcer groups;  $p=0.700$  was found between the gastritis and ulcer

group). When the cut-off value was taken as 2; of 556 patients with  $NLR \leq 2$ ; 190 (34.2%) had gastritis, 161 (29%) had ulcers, and 205 (36.9%) had normal findings and of 350 patients with  $NLR > 2$ , 121 (34.6%) had gastritis, 127 (36.3%) had ulcers, and 102 (29.1%) had normal findings ( $p = 0.024$ ) (Table 3). When the groups were compared according to this threshold value, a significant change was found only in peptic ulcer patients ( $p=0,006$ ) When the cut-off value was taken as 3; 274 (33.9%) of 809 patients had gastritis, 250 (30.9%) had ulcers and 285 (35.2%) had normal findings. Of 97 patients with  $NLR > 3$ ; 37 (38.1%) had gastritis, 38 (39.2%) had ulcers, and 22 (22.7%) had normal findings ( $p=0.042$ ) (Table 3). When the groups were compared in pairs over this threshold value, a significant difference

was found between both patient groups and normals, while no significant difference was found between the peptic ulcer and gastritis groups ( $p=0,045$ ,  $p=0,015$ , and  $p=0,632$  respectively).

The patient groups were compared, taking 106 as the PLR threshold value. Of 433 patients with  $PLR < 106$ , 152 (35.1%) had gastritis, 129 (29.8%) had ulcers and 152 (35.1%) had normal endoscopic findings; of 471 patients with  $PLR \geq 106$ , 159 (33.8%) had gastritis, 159 (33.8%) had ulcers, and 153 (32.5%) had normal findings ( $p=0.429$ ). When the groups were compared in terms of PLR value, there was no significant difference between all three groups ( $p=0,811$ ,  $p=0,219$  and  $p=0,317$  respectively) (Table 3).

**Table 3: Comparison of the groups according to various NLR and PLR cut off values.**

Cut off value	Gastritis N (%)	Peptic ulcer N (%)	Normal N (%)	P value
<b>NLR (<math>\leq 1.7</math>) (n:398)</b>	129 (32.4%)	115 (28.9%)	154 (38.7%)	P:0.024
<b>NLR (<math>&gt; 1.7</math>) (n=508)</b>	182 (35.8%)	173 (34.1%)	153 (30.1%)	
<b>NLR (<math>\leq 2</math>) (n=556)</b>	190 (34.2%)	161 (29%)	205 (36.9%)	P:0.024
<b>NLR (<math>&gt; 2</math>) (n=350)</b>	121 (34.6%)	127 (36.3%)	102 (29.1%)	
<b>NLR (<math>\leq 3</math>) (n=809)</b>	274 (33.9%)	250 (30.9%)	285 (35.2%)	P:0.042
<b>NLR (<math>&gt; 3</math>) (n=97)</b>	37 (38.1%)	38 (39.2%)	22 (22.7%)	
<b>PLR (<math>\leq 106</math>) (n=433)</b>	152 (35.1%)	129 (29.8%)	152 (35.1%)	P:0.429
<b>PLR (<math>&gt; 106</math>) (n=471)</b>	159 (33.8%)	159 (33.8%)	153 (32.5%)	

## DISCUSSION

Since the most important clinical diagnoses emerging as dyspepsia are gastric-esophageal cancers and peptic ulcer disease, the first consideration in approaching these patients is whether they have or not the alarm symptoms. Onset of complaints over 55 years old, unexplained weight loss, progressive dysphagia, presence of a family history of gastric cancer should be considered as alarm symptoms.<sup>1,8</sup> While the primary approach is to evaluate with upper GIS endoscopy in patients with alarm symptoms, upper GIS endoscopy is frequently preferred in the management of dyspepsia in patients without alarm symptoms and in cases of H. Pylori positivity.<sup>9</sup> Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are the parameters with proven efficacy as a simple, cheap and reliable indicator of inflammation that can be obtained from complete blood count.<sup>10</sup> The prognostic and predictive value of NLR and PLR in many malignancies such as pancreas, colon, stomach, breast, hepatocellular carcinoma has been demonstrated.<sup>11-13</sup> It has also been shown that NLR can be an important marker in showing the exacerbation and progression of systemic diseases such as restless legs syndrome, subacute thyroiditis, Behçet's disease.<sup>14-16</sup>

In a study in which NLR was evaluated as a non-invasive marker to predict advanced stage disease in patients with chronic hepatitis B, no difference was found between the patients and the healthy control group. However a

negative and significant difference was found with the Histological Activity Index (HAI) obtained from the biopsy.<sup>17</sup>

In many studies in patients with stomach cancer, it has been shown that the pre-operative NLR is both correlated with the disease activity and stage. The NLR median values of the patients in these studies were 2.58, 2.95 and 2.7, and these values have been shown to be significant in terms of determining prognosis.<sup>18-20</sup> These values are higher than patients with gastritis and peptic ulcer with normal endoscopy included in our study. Although we did not include the gastric cancer patients in our study and because of it we don't know the negative predictive value of NLR; calculation of the NLR value and especially high detection in elderly patients who cannot tolerate endoscopy but are symptomatic can be evaluated carefully in terms of malignancy.

The platelet to lymphocyte value also has been shown as a simple, inexpensive and easily available inflammation indicator in many types of cancer and in chronic diseases.<sup>11,21-23</sup> There are also studies in which the prognostic significance cannot be demonstrated.<sup>22-24</sup> In our study, when the patient groups were compared in terms of PLR threshold value as 106; no significant difference was found between the groups and the NLR value was found to be more significant than PLR. In the study conducted by Gao et al.; the NLR value was found to be more significant, as in our study.<sup>25</sup>

The other complete blood count parameters such as total leukocyte count, thrombocyte count were not found statistically significant. In a study similar to our study, Güçlü et al. found these hemogram parameters nonsignificant in patients with helicobacter pylori positive and negative gastritis.<sup>26</sup> Changes with inflammation in parameters other than NLR and PLR are contradictory, and new large randomised controlled studies are needed to be used as a noninvasive marker.

## CONCLUSION

In our current study; a significant difference was found between the NLR values of patients with gastritis and peptic ulcer and patients with normal endoscopic findings, but this difference was not at a level that could be used in clinical practice. For PLR, no statistically significant difference was found between those with peptic ulcer and gastritis and endoscopically normal subjects. The prognostic importance of NLR in patients with gastric cancer has been shown in many studies, and a more comprehensive study by including patients with gastric cancer will be more useful for clinical practice.

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