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Research Article

Association of *Helicobacter Pylori* Infection with Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Neutrophil-to-Monocyte Ratio

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Abstract

Aim: In our study, we aimed to show the relationship between neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, neutrophil-monocyte ratio and mean platelet volume, and *Helicobacter pylori* positivity and severity.

Material and Methods: In this study, we included 596 patients without active and/or chronic disease who underwent upper gastrointestinal system endoscopy due to dyspeptic complaints in a state hospital between July 2021 and July 2022. Demographic and laboratory data were obtained retrospectively from electronic patient records. The patients were divided into two groups as positive and negative for *Helicobacter pylori* according to the pathology report. *Helicobacter pylori* presence was defined as none, mild, moderate and severe. Hemogram parameters were compared between the groups.

Results: Mean age of the patients (n=596) was 41.8±13.57 years, 374 (62.8%) were female, and 331 (55.5%) were H*elicobacter pylori* positive. There was no statistically significant difference between *Helicobacter pylori* positive and negative patient groups in terms of age, gender, leukocytes, lymphocytes, monocytes, platelets, hemoglobin, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, neutrophil-monocyte ratio and mean platelet volume values. When the hemogram parameters were evaluated according to the severity of *Helicobacter pylori*, a statistically significant difference was found between the groups only in terms of lymphocyte levels (p=0.028). However, this difference was not considered clinically significant.

Conclusion: Neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, neutrophil-monocyte ratio and mean platelet volume are thought to be popular recently and easy, accessible and inexpensive parameters for diagnosis and degree of inflammation in many systemic diseases, but in our study, no statistically significant relationship was found between *Helicobacter pylori* positivity and severity and hemogram parameters. Prospective studies with larger numbers of cases are needed to accept these parameters as predictors for *Helicobacter pylori* infection.

Keywords: Helicobacter pylori, neutrophil-lymphocyte ratio, thrombocyte-lymphocyte ratio, neutrophil-monocyte ratio

INTRODUCTION

Helicobacter pylori (HP) is a gram-negative, spiral, flagellated, and microaerophilic bacterium (1). More than half the world's population is infected by HP. Person-to-person transmission usually occurs by either the oral–oral or fecal–oral route (2). After colonizing the gastric mucosa, HP plays a role in the development of chronic active gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and gastric adenocarcinoma (3). Furthermore, some epidemiological studies have associated HP infection with extragastric diseases such as idiopathic thrombocytopenic purpura, iron deficiency anemia, cardiovascular diseases, and non-alcoholic fatty liver disease. Given that HP infection affects a vast proportion of the world's population, the diagnosis and treatment have become increasingly important (4). HP induces local inflammation in the stomach and systemic humoral

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immune responses. Most patients have an asymptomatic but chronic inflammation (5). Previous studies have investigated several parameters such as leukocytes, C-reactive protein, and procalcitonin as markers of inflammation in HP-associated gastritis (6). Components of complete blood count (CBC), a simple and inexpensive test, such as leukocytes, neutrophils, lymphocytes, platelets, mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) can help differentiate the causes of hematological diseases and predict some inflammatory events. NLR and PLR are two of the most important parameters among all these components (7-10).

This study sought to investigate whether the presence and severity of HP infection are associated with parameters of CBC in patients undergoing upper gastrointestinal (GI) endoscopy for dyspeptic complaints.

MATERIAL AND METHOD

In this study, the authors scanned the results of upper GI endoscopy procedures performed on 3865 patients in a state hospital's endoscopy unit between July 2021 and July 2022. Among all these patients, 596 patients who underwent endoscopy only for dyspeptic complaints, who received a CBC test, and who had no active and/or chronic diseases were retrospectively analyzed. Upper GI endoscopy data of the patients included in the study were obtained from the hospital's endoscopy unit database. Age, sex, and reason for endoscopy were recorded from upper GI endoscopy reports. Data on the presence, severity, and site of HP infection according to the Sydney System for Classification were obtained from the pathology reports in the hospital's electronic database. Electronic health records were reviewed for the presence of chronic kidney disease, diabetes mellitus, ischemic heart disease, pregnancy, chronic liver disease, celiac disease, and active infection. Furthermore, components of CBC including leukocytes, neutrophils, lymphocytes, monocytes, platelets, hemoglobin, and MPV tested within the last one month were accessed and used to calculate NLR, PLR, and neutrophil-to-monocyte (NMR) ratio.

All patients scheduled for upper GI endoscopy were advised to fast for 8 hours before the procedure. Written informed consent was obtained from all patients. Endoscopic examinations were performed by a gastroenterologist and an endoscopy nurse using EG 530WR; Fujinon device (Tokyo, Japan). During gastroscopy, at least two biopsy specimens were collected from the gastric antrum and corpus to investigate HP. The presence of HP was determined by using light microscopic examination of gastric mucosal biopsy slides stained with hemotoxylin eosin and giemsa. The Sydney System for Classification was routinely used. HP infection was classified into absent, mild, moderate, and severe.

Exclusion criteria: age under 18 years, having chronic kidney disease, diabetes mellitus, hypertension, ischemic heart disease, heart failure, pregnancy, chronic liver disease, celiac disease, gastric adenocarcinoma, gastric or bulbar ulcer, active infection, and using proton pump inhibitors.

The study was approved by the Medical Research Ethics Committee (Ethics committee decision date/no: 06.10.22/22-10T/26). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis and calculations were performed using SPSS Statistics software Ver. 22.0. Variables were checked for normal distribution using visual (histogram) and analytical methods (Kolmogorov–Smirnov test). Continuous data was expressed in mean and standard deviation, whereas categorical data was expressed in rate and percentage. Analyses for HP infection status of the patients were performed using Mann–Whitney U test for the comparison of continuous variables between groups and Chi-squared test for the comparison of categorical variables. HP severity and CBC parameters between groups were compared using the Kruskal–Wallis test, and post-hoc analyses were performed using Mann–Whitney U test and Bonferroni correction. Statistical significance was set at $p<0.05$.

RESULTS

The 596 patients included in the study were assessed retrospectively. The mean age of the patients was 41.8±13.57 years. Positive HP test was observed for 331 (55.5%) patients. There was no statistically significant difference between HP-positive and HP-negative patients in terms of age, sex distribution, leukocyte, lymphocyte, monocyte, platelet, hemoglobin, NLR, PLR, NMR and MPV values (Table 1).

Of 331 HP-positive patients, infection was severe in 134 (40.5%), moderate in 117 (35.3%), and mild in 80 (24.2%). Based on biopsy specimens, the most common site of HP infection in the stomach was in the antrum and corpus in 297 (89.7%) patients, only in the corpus in 23 (6.9%) patients and only in the antrum in 11 (3.4%) patients.

Analysis of CBC parameters for HP severity showed a statistically significant difference between the groups in terms of lymphocyte counts (p=0.028) (Table 2). The difference between the groups arose from the difference between patients with moderate and severe HP. The lymphocyte count was 2266.8±733.3 µL in patients with moderate HP and 2538.5±776.6 µL in patients with severe HP.

Table 1. Comparison of demographic characteristics and CBC parameters of patients by HP status

	HP (+)	HP (-)	Total	P
Age (years)[a]	40.35±13.25	41.98±13.94	41.8±13.57	0.164
Sex, n (%)				
Female	203 (61.3)	171 (64.5)	374 (62.8)	0.422
Male	128 (38.7)	94 (35.5)	222 (37.2)	
CBC Parameters[a]				
Leukocytes (/µL)	7581.8±1850.7	7517±1804.2	7553±1828.9	0.888
Neutrophils (/µL)	4358.9±1442.6	4336.4±1485.7	4348.9±1460.7	0.970
Lymphocytes (/µL)	2412.6±764.7	2366.9±709.1	2392.3±740.2	0.367
Monocytes (/µL)	546.1±159.5	557.5±162.2	551.2±160.7	0.305
Platelets (/µL)	251418.1±56744.9	256097.7±65719	253498.8±60890.2	0.708
Hb (g/dL)	14.5±1.9	14.5±1.75	14.5±1.83	0.866
NLR	1.98±1.1	1.99±1.1	1.98±1.1	0.792
PLR	114.1±46.6	116.3±43.2	115.1±45.1	0.208
NMR	8.39±3.3	8.1±2.73	8.25±3.1	0.309
MPV (fL)	8.12±1.56	8.02±1.4	8.1±1.5	0.621

[a]Values are given as mean ± standard deviation. Hb, hemoglobin; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; NMR, neutrophil to monocyte ratio

Table 2. Association between HP severity and CBC parameters

CBC Parameters[a]	HP Severity			
	Mild	Moderate	Severe	P
Leukocytes (/µL)	7502 ±2008	7343.6±1730.6	7837.6±1836.3	0.086
Neutrophils (/µL)	4293.5±1512.9	4278.9±1440.1	4467.9±1405.3	0.411
Lymphocytes (/µL)	2414.9±761.3	2266.8±733.3	2538.5±776.6	0.028*
Monocytes (/µL)	514.5±155.7	544.7±153.4	566.1±164.9	0.068
Platelets (/µL)	249476.3±52665.3	249299±57440.4	254427.6±58727.7	0.762
Hb (g/dL)	14.5±1.84	14.57±1.99	14.45±1.87	0.811
NLR	1.9±0.94	2.14±1.37	1.89±0.81	0.432
PLR	112.92±43.6	121.26±52.39	108.59±42.24	0.102
NMR	8.9±4.55	8.26±3.01	8.2±2.66	0.439
MPV (fL)	8.3±1.62	8.13±1.52	8±1.56	0.252

[a]Values are given as mean ± standard deviation. *p < 0,05
Hb, hemoglobin; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; NMR, neutrophil to monocyte ratio

DISCUSSION

Considering that HP infects more than half the world's population, this study investigated the effect of HP and its severity on components of CBC, NLR, PLR, and NMR, which are simple, inexpensive, and easily accessible tests. Literature offers conflicting data on NLR and PLR. Of the 596 patients included in our study, 331 (55.5%) had a positive HP test. HP-positive and HP-negative groups had no significant difference in terms of CBC parameters. The strengths of our study were the exclusion of patients with chronic inflammatory conditions, chronic disease, and active infection that may affect CBC parameters and ratios and the inclusion of patients with dyspeptic complaints.

Previous studies around the world, on patients with dyspeptic complaints, reported different HP infection rates, including rates between 11%–48.8% for European

countries and 7.1%–30% for the United States (11,12). However, infection rates have been reported to be between 31.2% and 95% in developing countries and Asian countries (13-20). The HP Prevalence study conducted in Turkey in 2003 (TURHEP) reported the prevalence of HP to be 83% based on urea breath test. The TURHEP study classified the country into five regions; HP infection was found to be higher in those living in Central and Eastern Anatolia regions than in those living in Western and Southern regions (21). Recent studies conducted in Turkey reported HP infection rates between 36.6% and 66% (22-26). Peculiarly, patients who underwent endoscopy due to dyspeptic complaints were found to have HP infection rates between 28.8% and 62.6% (27-30). In our study, the rate of HP infection in patients with dyspeptic complaints was found to be 55.5%, which is in line with previous studies from Turkey. This supports the fact that Turkey, a country of transition between Asia and Europe, has a prevalence rate between that of developing and developed countries.

In this study, the rate of HP infection in both the antrum and corpus was found in 89.7% of the patients and in antrum or corpus only was found in 10.3% of the patients, which supports the recommendation that biopsy specimens should be collected from both the antrum and corpus and examined in two separate dishes (according to Sydney or Kimura protocols) as stated in the Maastricht VI/Florence consensus report (31).

Leukocytes and their subgroups and NLR have been shown to be markers of systemic inflammation (7-9,32). Recently, a limited number of studies have investigated the association between HP and CBC parameters, including NLR and PLR and have yielded conflicting results. Yalın et al. (2022) found no statistically significant difference between HP-positive and HP-negative groups in terms of leukocytes, neutrophils, lymphocytes, platelets, hemoglobin, NLR, and PLR (10). Similarly, Koç et al. (2022) also reported no statistically significant difference between HP-positive and HP-negative groups in terms of leukocytes, neutrophils, platelets, NLR, and PLR (25). In contrast to these two studies, Farah et al. reported HP-positive patients to have significantly higher levels of leukocytes, neutrophils, lymphocytes, and NLR (33). Ferhatoğlu et al. reported no significant difference between HP-positive and HP-negative patients in terms of leukocytes, neutrophils and lymphocytes, but found NLR to be significantly higher in HP-positive patients (34). Nalbant et al., on the other hand, found no statistically significant difference between the groups in terms of lymphocytes, monocytes, hemoglobin, NLR, and PLR, but unlike other studies, they found neutrophil count to be significantly lower in HP-positive patients (28). Such higher levels of leukocytes, neutrophils, and NLR reported in some studies may be attributed to subclinical microinflammatory reactions caused by HP. However, our study found no statistically significant difference between HP-positive and HP-negative groups in any component of CBC.

MPV, which has recently been shown to be an inflammatory marker for some local and systemic diseases, has been associated with disease severity and prognosis. Previous studies have reported that acute and chronic inflammation activates platelets, resulting in increased MPV (35-39). Chronic gastritis is an example of local chronic inflammation, and HP is one of the most common causes. Out of the studies that have investigated the association between HP and MPV, one has found a statistically significant difference between HP-positive and HP-negative groups in terms of MPV (40), while others have found no statistically significant difference between the groups in terms of MPV (10,27,30). Our study found no statistically significant difference between HP-positive and HP-negative groups in terms of MPV. A possible explanation of this result is that HP infection does not cause as much inflammation as in other systemic diseases, resulting in inadequate secretion of cytokines and immunomodulators and inadequate activation of platelets.

Two studies reported that as HP infection increased in severity, NLR and PLR decreased significantly (25,33). Our study, on the other hand, found that HP severity had a statistically significant correlation with only lymphocyte count. However, this association was not considered to be clinically significant since lymphocyte count did not increase with increasing severity of HP infection.

The limitations of this study include its retrospective design and lack of data about smoking and alcohol use among patients.

CONCLUSION

NLR, PLR, NMR, and MPV have recently become increasingly popular and are considered to be easy, accessible, and inexpensive markers for diagnosing numerous systemic diseases and for predicting the severity of inflammation. However, further prospective studies with a larger sample size are needed in order for these parameters to be recognized as markers of HP infection.

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