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Impact of chronic *Helicobacter pylori* infection on inflammatory markers and hematological parameters

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Abstract. – OBJECTIVE: Determining a non-invasive method for *Helicobacter pylori (H. pylori)* induced gastritis will be of great help especially in the field of pediatrics. In this study, we aimed to evaluate impact of chronic *H. pylori* infection on inflammatory markers and hematological parameters.

PATIENTS AND METHODS: 522 patients aged between 2 months and 18 years, with chronic dyspeptic complaints who underwent gastroduodenoscopy were included. Complete blood count, ferritin, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) tests were performed. Platelet to lymphocyte ratio (PLR) and neutrophil to lymphocyte ratio (NLR) values were calculated.

RESULTS: From 522 patients 54% had chronic gastritis and 28.6% had esophagitis, while 24.5% of their biopsy samples revealed *H. pylori.* The mean age of *H. pylori* positive patients was significantly higher ($p<0.05$). Females were in the majority in *H. pylori* positive and negative groups and in the group with esophagitis. The most common complaint in all groups was abdominal pain. In the *H. pylori* positive group, a significant increase in neutrophil and PLR values, a significant decrease in the NLR value were found. Ferritin and vitamin B12 values were significantly lower in the *H. pylori* positive group. No significant difference was found in the parameters we compared between the group with and without esophagitis, except for mean platelet volume (MPV). MPV values were significantly lower in the group with esophagitis.

CONCLUSIONS: Neutrophil and PLR values are practical and easily obtainable parameters related to inflammatory phases of *H. pylori* infection. They may become useful parameters in the follow-up. *H. pylori* infection is one of the important causes that trigger iron deficiency and vitamin B12 deficiency anemia. Further large-scale randomized controlled studies are needed to confirm our results.

Key Words:
H. Pylori, Noninvasive, Inflammatory markers, Hematological parameters.

Introduction

Chronic dyspeptic symptoms such as abdominal pain, nausea, vomiting or bloating are often suggestive for the diagnosis of gastritis and gastropathies in pediatric patients. The prompt diagnosis of these diseases might prevent life-threatening complications such as peptic ulcer disease or gastric cancer that develops after a long-term chronic gastric inflammation[1,2].

Helicobacter pylori (*H. pylori*) is the most common chronic bacterial infection in humans[3,4]. Studies[5] involving genetic sequence analysis show that humans have been infected with *H. pylori* since they migrated from Africa about 58,000 years ago. *H. pylori* has been demonstrated[4] worldwide and in individuals of all ages. *H. pylori*, a gram-negative, microaerophilic and spiral-shaped bacterium, infects human gastric mucosa at an early age, colonizes the mucosal gel layer and causes chronic inflammation in the stomach[6-8]. More than half of the world's population has *H. pylori* colonization[9]. Mostly, *H. pylori* infection in adults is the result of childhood infection[10]. Unless appropriate treatment is applied for natural infection, the infection continues for a lifetime[11,12]. *H. pylori* is important because it can cause various gastrointestinal diseases throughout the patient's lifetime, including gastritis, gastric or duodenal ulcer, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma[11,13].

The route of transmission of *H. pylori* infection is still unclear[3,14]. *H. pylori* has been isolated from human gastrointestinal tracts including saliva and stools. This suggests that oral-oral and fecal-oral routes constitute the main transmission pathway[14-16]. The infection is acquired through interpersonal and intrafamilial spread[17]. Diagnostic tests used for *H. pylori* can be divided into invasive and non-invasive techniques depending on

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the need for endoscopy[18]. Endoscopy is a relatively invasive method that can cause complications or put psychological burden on children and their parents. There are limitations for using endoscopy with control and follow-up purposes especially in children after *H. pylori* treatment. Therefore, the need for a non-invasive diagnostic method with high diagnostic accuracy has increased. As a result, some non-invasive methods have been developed. These include urea-breath test (UBT), *Helicobacter pylori* Stool Antigen (*Hp*SA) test and *H. pylori* antibody tests in serum, urine or saliva[13,19].

Histopathological examination is the most reliable diagnostic tool for this infection. *H. pylori* tends to settle in the less acidic antrum and attract neutrophils and lymphocytes. Neutrophils and some substances released from mononuclear cells cause mucosal inflammation and thereafter gastritis. As a result, many cytokines, neutrophils, macrophages and lymphocytes leak into the gastric mucosa and subclinical low-grade systemic inflammation occurs[20,21]. *H. pylori* causes local inflammation in the stomach and a systemic humoral immune response. Most of the cases have asymptomatic chronic inflammation[20]. According to the Sydney Gastritis Classification System, an increase in neutrophil-predominant inflammatory cells represents acute gastritis, while an increase in chronic inflammatory cells (lymphocytes and plasmocytes) represents chronic gastritis[22].

Studies[23] have proved that because of systemic inflammation, *H. pylori* is associated with other conditions such as cardiovascular diseases, glaucoma, rosacea, eczema, chronic hives, stroke, Alzheimer's disease, Parkinson's disease, iron deficiency anemia, idiopathic thrombocytopenic purpura, diabetes, thyroid diseases and poor growth along with malnutrition in children. Also, other studies[24] have shown that high *H. pylori* antibody levels are significantly associated with coronary artery disease, atherosclerosis and high systolic blood pressure in diabetic subjects.

Several studies[25] have shown a correlation between inflammatory mediators and the presence of *H. pylori* infection. Especially C-reactive protein (CRP) levels have been observed to increase in *H. pylori*. Leukocyte activation occurs during any inflammatory reaction, and they have been also found to play a role in many chronic diseases, such as diabetes, hypertension, atherogenesis and thrombus formation and other inflammatory disorders. In addition to increased number of leukocytes, there is a significant relationship between the neutrophil/lymphocyte ratio (NLR) and the severity and prognosis of cardiovascular disease[26].

It is claimed[27] that as a result of the reaction of *H. pylori* antibodies with platelet glycoproteins, a decrease in platelets occurs, resulting in idiopathic thrombocytopenic purpura (ITP). In patients with ITP, it has been shown[27] that the number of platelets increases due to *H. pylori* eradication and autoantibodies disappear in most of the cases. Mean platelet volume (MPV) is an index that shows both the platelet and inflammatory activation. High MPV values indicate larger and very active platelets contributing to thrombotic events. Platelet volume and structural changes can help in the differential and early diagnosis of various diseases[28]. Some studies[29] show that patients with diabetes mellitus and coronary artery disease which lead to a low-grade inflammation have higher MPV values.

According to the recent studies, non-invasive biomarkers such as the NLR and the platelet to lymphocyte ratio (PLR) can predict inflammation in a variety of diseases, including gastritis. NLR and PLR are markers of acute inflammation obtained from a simple, safe, relatively non-invasive Complete Blood Count (CBC)[30,31]. Platelet count and MPV value can be examined during automatic CBC without any extra cost[28].

In this study, we aimed to evaluate the relationship between the groups of patients with *H. pylori* infection and hematological parameters such as leukocyte and neutrophil count, NLR, PLR, MPV and acute phase reactants such as CRP, erythrocyte sedimentation rate (ESR), ferritin, as well as the erythrocyte series. We also investigated how these parameters were affected in patients with esophagitis.

Patients and Methods

This study, approved by the Ethics Committee of Health Sciences University Bakırköy Dr. Sadi Konuk Training and Research Hospital, was carried out between April 2017 and December 2018.

522 of 556 patients with chronic dyspeptic complaints who were followed-up in the Pediatric Gastroenterology Clinic and underwent gastroduodenoscopy were included in the study. The ages of the patients ranged from 2 months to 18 years. Patients with chronic diseases including previously known hematological diseases (immune thrombocytopenic purpura, acute lymphoblastic or myeloblastic leukemia, lymphoma, au-

toimmune hemolytic anemia, minor and major thalassemia), systemic disease, chronic drug use that may alter hematological parameters and those with symptoms of parasitic and other infectious diseases were excluded from the study.

Gastric biopsies (at least two samples from the antrum and at least two samples from the corpus) were taken from each patient by performing gastroduodenoscopy. CBC and biochemical tests were performed before.

Gastroduodenoscopy

Each patient was administered with Midazolam approximately 20 minutes before the procedure, providing a mild sedation. All upper gastrointestinal endoscopies were performed and reported by the same gastroenterologist. Microscopic examination was carried out with Giemsa staining, which was used to identify *H. pylori*.

H. pylori positive patients were included in the study group and *H. pylori* negatives as the control group. In addition, a comparison was made between patients with and without esophagitis regarding the same parameters.

Biochemical Measurements

For CBC, samples were taken from the antecubital vein into vacuum tubes containing ethylene diamine tetra acetic acid (EDTA). The samples taken were tested within one hour by an automated hematology analyzer. CBC contained absolute values of platelets, erythrocytes, leukocytes, and the entire leukocyte formula, including MPV, hemoglobin (Hb), hematocrit (Htc), mean corpuscular volume (MCV) and red blood cell distribution width (RDW), which are platelet and erythrocyte indices. PLR and NLR values were calculated by dividing the absolute number of platelets and neutrophils by the absolute number of lymphocytes. Biochemically tested ferritin, vitamin B12, CRP, and ESR values were recorded.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) for Windows v. 26.0 program (IBM Corp., Armonk, NY, USA) was used for statistical study and data analysis. Mean, standard deviation, median lowest, highest, frequency, and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured with the Kolmogorov Simirnov test. Mann-Whitney U test was used to analyze quantitative independent data. Chi-square test was used in the analysis of qualitative independent data, and Fisher's test was used when Chi-square test conditions were not met. Continuous variables were defined as mean ± standard deviation (SD), and categorical variables were given as percentages. $p<0.05$ value was considered statistically significant.

Results

522 of 556 patients who applied to the Pediatric Gastroenterology outpatient clinic with dyspeptic complaints and underwent gastroduodenoscopy were included in our study. 22 patients because of cerebral palsy, 3 patients because of Wilson's cirrhosis, 2 patients because of celiac disease, 7 patients because of other chronic disease were excluded from the study.

The mean age of 136 *H. pylori* positive patients included in the study group was 11.6±4.2 years and 38.2% of them were male. The mean age of 420 *H. pylori* negative patients was 10.0±5.8 years and 46.2% of them were male (Table I). The mean age of *H. pylori* positive patients was significantly higher than that of negative patients ($p<0.05$). There was no significant ($p>0.05$) difference between two groups in terms of gender distribution, and female patients were the majority in both groups (Table II).

Table I. Demographic characteristics of patients, distribution of complaints and endoscopy findings.

		Mean ± SD/n-%	
Age (year)		10.4 ± 5.5	
Gender	Male	246	44.2%
	Female	310	55.8%
Complaints			
Abdominal pain		388	69.8%
Nausea		141	25.4%
Vomiting		89	16.0%
Bitter water in mouth		11	2.0%
Bad breath		7	1.3%
Early satiety		3	0.5%
Melena		2	0.4%
Hematemesis		9	1.6%
Anorexia		30	5.4%
Chronic gastritis	(-)	256	46.0%
	(+)	300	54.0%
Esophagitis	(-)	397	71.4%
	(+)	159	28.6%
H. pylori	(-)	420	75.5%
	(+)	136	24.5%

Table II. Findings in patients with and without *H. pylori*.

		H. pylori (-)			*H. pylori* (+)			
		Mean ± SD/n-%		Median	Mean ± SD/n-%		Median	*p*
Age (year)		10.0±5.8		10.0	11.6 ±4.2		13.0	0.000[m]
Gender	Male	194	46.2%		52	38.2%		0.104[X2]
	Female	226	53.8%		84	61.8%		
Complaints								
Abdominal pain		284	67.6%		104	76.5%		0.051[X2]
Nausea		106	25.2%		35	25.7%		0.908[X2]
Vomiting		71	16.9		18	13.2%		0.310[X2]
Bitter water in mouth		9	2.1%		2	1.5%		0.625[X2]
Bad breath		7	1.7%		0	0.0%		0.203[X2]
Early satiety		3	0.7%		0	0.0%		1.000[X2]
Melena		2	0.5%		0	0.0%		1.000[X2]
Hematemesis		8	1.9%		1	0.7%		0.348[X2]
Anorexia		25	6.0%		5	3.7%		0.307[X2]
Chronic gastritis	(-)	256	61.0%		0	0.0%		0.000[X2]
	(+)	164	39.0%		136	100.0%		
Esophagitis	(-)	302	71.9%		95	69.9%		0.645[X2]
	(+)	118	28.1%		41	30.1%		

[m]Mann-Whitney U test; [X2]Chi-square test.

From 522 patients who underwent upper gastrointestinal endoscopy, 54% had chronic gastritis and 28.6% had esophagitis, while 24.5% of their biopsy samples revealed *H. pylori* (Table I).

The distribution of complaints in *H. pylori* positive and negative groups was similar. The most common complaint in both groups was abdominal pain (76.5-67.6%). The rate of chronic gastritis was significantly higher in the *H. pylori* positive group ($p<0.05$). The rate of esophagitis between the two groups did not differ significantly ($p>0.05$) (Table II).

The mean age in the esophagitis positive group was 9.9±6.2 years and 54.7% of them were males whereas in the negative group the mean age was 10.6±5.2 years and 40.1% of them were males. The mean age did not differ significantly ($p>0.05$) between these two groups. The rate of female patients in the group with esophagitis was significantly higher than the group without esophagitis ($p<0.05$). When the complaints were compared in the group with and without esophagitis, the most common complaint was abdominal pain, while only vomiting and early satiety complaints were significantly higher in the group with esophagitis ($p<0.05$). (Table III).

Hb, MCV, RDW, thrombocyte, white blood cell count (WBC), lymphocyte, MPV, CRP and ESR values did not differ significantly ($p>0.05$) in the *H. pylori* positive and negative groups. However, a significant ($p<0.05$) increase in neutrophil values and an insignificant ($p>0.05$) decrease in lymphocyte values were found in the *H. pylori* positive group. In the *H. pylori* positive group, the NLR value was significantly lower ($p<0.05$) than that of the *H. pylori* negative group. PLR value was significantly higher in *H. pylori* positive patients ($p<0.05$). Ferritin and vitamin B12 values were significantly lower ($p<0.05$) in the *H. pylori* positive group. (Table IV)

Hb, MCV, RDW, thrombocyte, WBC, neutrophil, lymphocyte, NLR, PLR, CRP, ferritin, vitamin B12 and ESR values did not differ significantly between groups with esophagitis positive and negative cases ($p>0.05$). In the group with positive esophagitis, the MPV value was significantly lower ($p<0.05$) than that of the group with esophagitis negative (Table V).

Table III. Findings in patients with and without esophagitis.

		Esophagitis (-)			Esophagitis (+)			
		Mean ± SD/n-%		Median	Mean ± SD/n-%		Median	*p*
Age (year)		10.6±5.2		12.0	9.96±6.2		11.0	0.127[m]
Gender	Male	159	40.1%		87	54.7%		**0.002**[X2]
	Female	238	59.9%		72	45.3%		
Complaints								
Abdominal pain		283	71.3%		105	66.5%		0.223[X2]
Nausea		104	26.2%		37	23.3%		0.474[X2]
Vomiting		50	12.6%		39	24.5%	0.310	**0.001**[X2]
Bitter water in mouth		10	2.5%		1	0.6%	0.625	0.148[X2]
Bad breath		6	1.5%		1	0.6%	0.203	0.399[X2]
Early satiety		0	0.0%		3	1.9%	1.000	**0.023**[X2]
Melena		2	0.5%		0	0.0%	1.000	1.000[X2]
Hematemesis		6	1.5%		3	1.9%	0.348	0.751[X2]
Anorexia		17	4.3%		13	8.2%	0.307	0.066[X2]
Chronic gastritis	(-)	183	46.1%		73	0.0%	45.9%	0.969[X2]
	(+)	214	53.9%		86	54.1%	54.1%	

[m]Mann-Whitney U test; [X2]Chi-square test.

Discussion

H. pylori is a stomach pathogen that infects more than half of the people in the world[32]. The consequences of *H. pylori* infection appear to be due to some factors such as gene editing factors, patient genetic predisposition, receptor gene polymorphisms, specific cytokine constituents and environmental influences[33,34]. Most infected children will not develop any complications; however, immunological events that develop in the gastric mucosa of children play a decisive role in the outcome of the infection. Colonization of the stomach by this pathogenic bacterium causes an

Table IV. Distribution of laboratory findings in *H. pylori* positive and negative groups.

	H. pylori (-)		*H. pylori* (+)		
	Mean ± SD/n-%	Median	Mean ± SD/n-%	Median	*p*
Iron	71.6±44.1	64.0	68.6±35.8	62.7	0.949[m]
Vitamin B12	470.2±304.3	384.8	382.9±245.5	306.7	0.023[m]
Hb	12.6±1.3	12.6	12.7±1.7	12.9	0.147[m]
MCV	82.9±34.3	81.0	80.7±5.7	81.4	0.957[m]
RDW	13.5±1.8	13.1	13.6±1.6	13.3	0.400[m]
Thrombocyte x10³	313.3±102.9	296.0	332.0±97.4	316.0	0.071[m]
WBC	8.56±3.03	8.18	8.49±2.32	8.44	0.565[m]
Neutrophile	4.52±3.23	3.81	4.62±2.02	4.33	0.028[m]
Lymphocyte	3.27±1.79	3.01	2.94±1.09	2.73	0.165[m]
NLR	1.84±2.16	1.28	1.82±1.18	1.53	0.023[m]
PLR	115.9±79.5	100.0	123.6±54.3	112.5	0.023[m]
MPV	10,0±5.7	9.9	9.8±1.8	9.9	0.923[m]
CRP	0.6±1.5	0.1	0.4±0.7	0.1	0.637[m]
Ferritin	33.2±32.5	23.0	21.9±17.1	19.2	0.019[m]
ESR	18.0±13.2	16.3	12.1±8.0	10.0	0.211[m]

[m]Mann-Whitney U test.

Table V. Distribution of laboratory findings in the group with and without esophagitis.

	Esophagitis (-)		Esophagitis (+)		
	Mean ± SD/n-%	Median	Mean ± SD/n-%	Median	*p*
Iron	67.3±36.1	63.0	79.4±53.4	68.3	0.123[m]
Vitamin B12	447.6±303.7	354.7	456.0±265.7	395.0	0.362[m]
Hb	12.5±1.4	12.6	12.8±1.3	12.8	0.125[m]
MCV	83.1±36.3	81.4	80.8±5.0	80.5	0.318[m]
RDW	13.6±1.7	13.2	13.4±1.7	13.0	0.182[m]
Thrombocyte x10³	313.5±100.7	294.5	326.4±104.2	322.0	0.086[m]
WBC	8.5±2.9	8.2	8.7±3.0	8.2	0.619[m]
Neutrophile	4.5±2.6	3.9	4.5±3.8	3.8	0.611[m]
Lymphocyte	3.0±1.2	2.9	3.5±2.3	3.1	0.077[m]
NLR	1.9±2.1	1.4	1.7±1.6	1.3	0.131[m]
PLR	119.7±77.3	103.5	113.1±68.2	100.5	0.237[m]
MPV	10.2±6.0	10.0	9.6±1.5	9.6	0.026[m]
CRP	0.6±1.5	0.1	0.5±0.9	0.1	0.804[m]
Ferritin	30.2±28.6	22.1	32.2±33.9	21.3	0.915[m]
ESR	18.1±12.6	17.0	12.1±10.9	8.5	0.068[m]

[m]Mann-Whitney U test.

inflammatory response which consists of epithelial cell damage as well as the collection of neutrophils, then T and B lymphocytes, plasma cells, and macrophages[35,36]. *H. pylori* causes a persistent gastric inflammation in nearly all infected people[37].

Even though the infection is acquired early in life, the associated diseases develop mainly in adulthood. Probably the nature of the immune response and the diverse inflammatory mediators present in the gastric mucosa in childhood can be determinant factors for the final outcome of infection in adulthood. Therefore, it is important to evaluate each case of infection in children carefully to prevent the development of severe gastric diseases associated with *H. pylori* infection in adults[38]. In our study, inflammatory indicators were evaluated in the pediatric patient group who underwent gastroduodenoscopy. A significant (p<0.05) increase in neutrophil and PLR values were found in the *H. pylori* positive group. Thus, we considered that neutrophil and PLR values are practical parameters related to inflammatory phases of *H. pylori* infection. They may become useful parameters in the follow-up.

A study[39] conducted in Japan showed the relationship between increased serum anti-Haptoglobin Antibody (anti-HP) levels and interleukin-6 (IL-6) secreted by monocytes, lymphocytes, endothelial cells, and mesangial cells. Moreover, *H. pylori* has also been recognized[40] to cause a systemic inflammatory reaction due to both its association with IL-6 and its ability to promote chronic inflammation.

Another study focused on evaluating systemic inflammatory markers associated with *H. pylori* infection to distinguish between individuals requiring treatment and asymptomatic carriers. In a study[41] conducted for this purpose, it was proven that acute phase reactants (CRP) increased significantly in *H. pylori* positive patients.

The proportion of infected children increases with age. By the age of 10 most children in developing countries are infected by *H. pylori*[42]. In our study, the average age of *H. pylori* positive patients was significantly higher than negative patients (p<0.05). Female/male ratio was in favor of female patients in both groups (p>0.05). The mean age of 420 *H. pylori* negative patients was 10.0±5.8 years. From these data, we can conclude that *H. pylori* infection is more common in females and older age groups. In addition, a recent review shows that females were the dominated gender in *H. pylori* positive group. However, there was no significant difference by age and gender between both groups (*H. pylori* positive and negative)[43].

According to the reported symptoms, post-prandial fullness and epigastric pain were significantly more frequent in infected patients[43]. Recurrent abdominal pain in the epigastric region is the main gastrointestinal symptom in children with or without gastro esophageal reflux sensation, nausea and emesis[44,45]. In our experience, the distribution of complaints in *H. pylori* positive and negative groups was similar. The most common complaint in both groups was abdominal pain which

was followed by nausea, vomiting, bitter water in mouth, bad breath, and early satiety, respectively. A study[46] from a public hospital in Venezuela reported a high prevalence (73%) of *H. pylori* infection in symptomatic children with recurrent abdominal pain. In the study of Sasaran et al[47], in pediatric patients who underwent upper gastrointestinal endoscopy, the most common presentation symptom was found to be abdominal pain. In the same study, nausea was found significantly more frequently in patients with gastritis. When we compared the complaints between groups with and without esophagitis, the most common complaint was abdominal pain too, while only vomiting and early satiety complaints were significantly higher in the group with esophagitis ($p<0.05$).

Among the acute phase reactants, we reviewed in our study, no significant difference was found between *H. pylori* positive and negative patients in terms of CRP, ESR, and ferritin levels. Likewise, there was no significant difference in these parameters between patients with and without esophagitis.

In the study conducted by Melit et al[30], the effect of *H. pylori* positive and negative pediatric gastritis on parameters including erythrocytes, thrombocytes, MPV, NLR, and PLR was evaluated. In this study, it was observed that childhood and adolescent gastritis did not have a significant effect on platelet count, MPV, PLR, or NLR. It has been concluded that a significant increase in lymphocyte count may be a sign of non-*H. pylori* pediatric gastritis, and severe gastritis may cause a significant decrease in Hb and Htc levels.

Jafarzadeh et al[48] conducted a study to determine the total leukocyte count and NLR in adult patients with *H. pylori* infected peptic ulcer and asymptomatic patients and to evaluate whether there is a relationship between them. In this study, the leukocyte, neutrophil count, and NLR were found to be significantly higher in *H. pylori* infected peptic ulcer patients and asymptomatic patients compared to the control group. At the same time, the differences of these parameters were also significantly different between the peptic ulcer and asymptomatic patients.

In the study of Şahin et al[49], no relationship was found between NLR and MPV values and childhood *H. pylori* infection, severity classification, or pre- and post-treatment status.

In our study, while there was no significant difference in the leukocyte count between *H. pylori* positive and negative patients, a significant ($p<0.05$) increase in neutrophil values and a non-significant ($p>0.05$) decrease in lymphocyte values were found in the *H. pylori* positive group. In the *H. pylori* positive group, the NLR value was significantly lower ($p<0.05$) than that in the *H. pylori* negative group. On the other hand, PLR value was significantly higher in the *H. pylori* positive group than that in the *H. pylori* negative group ($p<0.05$). With these results, it was thought that neutrophil count and PLR value might be a good inflammatory indicator for chronic gastritis and *H. pylori*.

A significant increase in leukocyte and NLR values was found in a study[48] on this subject in adults, and a significant increase in lymphocyte level was found in patients with severe chronic gastritis in another study[30]. In addition, the absence of a difference in these parameters in our study on children can be explained by the fact that this infection becomes more severe as they get older, leads to chronic inflammation and perhaps increases the risk of carcinogenesis. It may be useful to use these parameters in the future follow-up of children with *H. pylori.*

In contrast to adults, *H. pylori* induced inflammation in children has received little investigative attention; however, the biology of the pediatric response to infection may reveal cellular events that promote tolerance to the bacteria and persistence of the associated inflammation. Understanding the immunobiological basis for the reduced inflammatory response in *H. pylori* infected children, particularly in comparison to that of infected adults, is critical for identifying mechanisms by which the host suppresses the neoplastic potential of *H. pylori* infection in children[38].

Recent studies[41] have focused on evaluating systemic inflammatory status markers associated with *H. pylori* infection to distinguish between individuals requiring treatment and asymptomatic carriers. Thereby, it has been proven[41] that acute phase reactants are significantly increased in *H. pylori* positive patients. Another study[50] showed that leukocytes and NLR come out as reliable markers of systemic inflammation. A recent study[26] in adults with gastritis with and without *H. pylori* infection highlighted a significant increase in the number of leukocytes, neutrophils, and lymphocytes in *H. pylori* positive patients compared to those in negative ones. The same authors stated that there is a positive relationship between neutrophil count, NLR and severity of symptoms. These findings are also supported by the work of Atayan and Hacısalihoğlu[51]. In the study of Melit et al[30], while leukocyte

and neutrophil counts were significantly higher in children with gastritis caused by *H. pylori*, they could not prove the same relationship for lymphocytes and NLR. However, higher mean NLR values, which were not statistically significant, were found in *H. pylori* positive patients. A more recent study involving adults found no difference in NLR, neutrophils, or leukocytes in *H. pylori* positive patients, while demonstrating a significant increase in lymphocytes associated with the severity of this infection[41].

Many studies[47,52,53] have shown that *H. pylori* infection is associated with iron deficiency and vitamin B12 deficiency anemia[52]. According to a Palestinian study[52], *H. pylori* infection causes a decrease in mean erythrocytes, Hb and Hct levels. It has also been found[53] that treating the infection provides a significant improvement in serum iron and vitamin B12 levels, even without supplementation. Sasaran et al[47] revealed in their study that there is a relationship between *H. pylori* gastritis and lower erythrocyte values. In our study, however, iron, Hb, MCV and RDW values did not differ significantly ($p>0.05$) between *H. pylori* positive and negative groups, but MCV values were found to be lower in the *H. pylori* positive group and the group with esophagitis. In addition, ferritin and vitamin B12 values were significantly lower ($p<0.05$) in the *H. pylori* positive group than that in the *H. pylori* negative group. This result supports the thesis that *H. pylori* infection is associated with iron and vitamin B12 deficiency. In addition, iron, Hb, MCV, RDW, ferritin, and vitamin B12 values did not differ significantly ($p>0.05$) between the groups with and without esophagitis in our study. The guidelines of both ESPGHAN and NASPGHAN in 2011 on management of *H. pylori* infection in children recommended that children with iron deficiency anemia should be tested for *H. pylori* infection[54].

Various studies[55] have reported an association between *H. pylori* and immune thrombocytopenia in both adults and pediatric patients. In the study conducted by Umit and Umit[56], an increase of MPV was demonstrated in adults' patients infected with *H. Pylori*. In our study, no significant difference was found in the platelet count and MPV values between *H. pylori* positive and negative groups. In addition, there was no significant difference in thrombocyte count between groups with and without esophagitis, but the MPV value was significantly lower in the group with esophagitis than that in the group without esophagitis ($p<0.05$). There is little data on a possible association between *H. pylori* and thrombocytopenia in children. These studies[57,58] have been performed on a small number of patients, and only a partial or significant increase in platelet count has been identified in selected cases after *H. pylori* eradication. In addition, although one of the few studies[28] in the literature comparing MPV and platelet values in pediatric patients did not detect an association between the presence and severity of gastritis and MPV, it found a weak association between gastritis or *H. pylori* infection and platelet count as a slight decrease. MPV value did not show a significant change in any of the groups studied[28]. In a similar study[47], no significant change was found in MPV values of children with gastritis regardless of the etiology and no correlation between this parameter and gastritis severity was detected. However, the same study revealed that the presence of mild to moderate gastritis may cause a slight increase in the platelet count. The lack of difference in the count and parameters of thrombocytes in our study may be related to the severity of gastritis. Unfortunately, since gastritis was not graded in our study, a comparison could not be made in this respect.

Farah et al[31] found that PLR level in the *H. pylori* positive group was higher than that in the *H. pylori* negative group in their study on adults. In the same study, the level of PLR was found to be proportional to symptoms associated with *H. pylori*. The study of Kaplan et al[59] highlighted that the combination between NLR and PLR may be a better predictor of *H. pylori* infection and associated gastrointestinal complications than NLR alone. In our study, PLR and also neutrophil values were found significantly higher in the *H. pylori* positive group compared to the negative group. Based on this result, it was concluded that PLR and neutrophil levels might be an easily obtainable parameter in the detection and follow-up of systemic inflammation due to *H. pylori*.

Limitations

The most important limitations are that biopsies taken by upper gastrointestinal endoscopy could not be graded, and that inflammatory parameters could not be evaluated after treatment and in long-term follow-ups.

Conclusions

H. pylori is a chronic bacterial infectious agent that causes systemic inflammation. Systemic in-

flammation is a risk factor for the development of gastric pathologies and other diseases. Therefore, it is important to monitor *H. pylori* with noninvasive indicators in children. Neutrophil and PLR values are practical and easily obtainable parameters related to inflammatory phases of *H. pylori* infection. They may become useful parameters in the follow-up. In addition, *H. pylori* infection is one of the important causes that trigger iron deficiency and vitamin B12 deficiency anemia. Further large-scale randomized controlled studies are needed to confirm our results. These studies must include the effect of *H. pylori* eradication on inflammatory parameters and long-term case follow-ups.

Conflict of Interest
The Authors declare that they have no conflict of interests.

Availability of Data and Materials
Data sharing is not applicable to this article.

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Informed Consent
Written informed consent was provided by parents of patients for each endoscopic procedure and study.

Authors' Contribution
Conception and design: NÖS, HAC; Acquisition of data: HAC; Analysis and interpretation of data: NÖS; Drafting the article: NÖS; Supervision: HAC; Validation and final approval: NÖS.

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Ethics Approval
This study was approved by the Ethics Committee of Health Sciences University Bakırköy Dr. Sadi Konuk Training and Research Hospital.

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