



Effect of eradication treatment for *Helicobacter pylori* on complete blood count and inflammatory parameters

Helicobacter pylori eradikasyon tedavisinin tam kan sayımı ve inflamatuvar parametrelere etkisi

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Background and Aims: Previously, *Helicobacter pylori* infection was held responsible for changes in complete blood count and inflammatory parameters. But changes in these parameters after eradication treatment was not entirely evaluated. This study was designed to evaluate the effect of eradication treatment for *Helicobacter pylori* infection on inflammatory markers and complete blood count parameters. **Materials and Method:** This single center, observational study enrolled participants who came to internal medicine outpatient clinics because of dyspeptic complaints and who were diagnosed to have *Helicobacter pylori* infection after endoscopic evaluation, between July 2021 and January 2022. Participants who were tested negative for *Helicobacter pylori* stool antigen test eight weeks after eradication treatment were included. Complete blood count and inflammatory parameters before and after eradication treatment were compared. **Results:** Mean participant age was 43.84 ± 12.59 years. There were significant decreases in erythrocyte sedimentation rate, C-reactive protein, platelet to lymphocyte ratio and neutrophile to lymphocyte ratio after eradication. Changes in platelet counts and mean platelet volumes were insignificant. **Conclusion:** Erythrocyte sedimentation rate, C-reactive protein, platelet to lymphocyte ratio and neutrophile to lymphocyte ratio were significantly lower after eradication for *Helicobacter pylori*. These parameters may be useful, simple, available and non-invasive tests that may be used in evaluation of eradication treatment for *Helicobacter pylori*.

Key words: Erythrocyte sedimentation rate, *Helicobacter pylori*, platelet count, C-reactive protein, blood cell count

Giriş ve Amaç: *Helicobacter pylori* enfeksiyonunun inflamatuvar ve tam kan sayımı parametrelerinde değişikliklere neden olduğu daha önce bildirilmiştir. Ancak eradikasyon tedavisi sonrasında bu parametrelerdeki değişiklikler yeterince incelenmemiştir. Bu çalışmanın amacı eradikasyonun, inflamatuvar belirteçler ve tam kan sayımı parametreleri üzerine etkisini belirlemektir. **Gereç ve Yöntem:** Bu tek merkezli gözlemsel çalışma, Temmuz 2021 ile Ocak 2022 tarihleri arasında iç hastalıkları polikliniğimize dispeptik yakınmaları nedeniyle başvuran ve üst gastrointestinal sistem endoskopisi uygulanan hastalardan *Helicobacter pylori* testi pozitif saptananlarla yapıldı. Tedaviden 8 hafta sonra yapılan kontrolde eradikasyonu başarılı olan hastalar çalışmaya alındı. Tedavi öncesi ve tedavi sonrası laboratuvar parametreleri kıyaslandı. **Bulgular:** Hastaların ortalama yaşı 43.84 ± 12.59 idi. Tedavi sonrası, eritrosit sedimantasyon hızı, C-reaktif protein, trombosit lenfosit oranı ve nötrofil lenfosit oranı değerlerinde anlamlı azalma olduğu saptandı. Trombosit sayısı ve ortalama trombosit hacmi değerlerinde tedavi öncesi ve sonrasında farklılık bulunmadı. **Sonuç:** *Helicobacter pylori* eradikasyonu yapılan hastalarda eritrosit sedimantasyon hızı, C-reaktif protein, trombosit lenfosit oranı ve nötrofil lenfosit oranı gibi inflamatuvar belirteçler tedavi öncesine göre anlamlı olarak azalmaktadır. Bunlar, *Helicobacter pylori* enfeksiyonunun değerlendirilmesinde kullanılabilecek, ucuz ve invaziv olmayan parametreler olabilir.

Anahtar kelimeler: Eritrosit sedimantasyon hızı, *Helicobacter pylori*, trombosit sayısı, C-reaktif protein, tam kan sayımı

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a bacteria that is the most frequent reason for chronic infection in human-beings. More than the half of the world

population is infected with this bacteria. *H. pylori* may long remain asymptomatic after colonization in the stomach (1). *H. pylori* may also affect other

organs and cause disorders (2). Chronic inflammation triggered by *H. pylori* was accused in pathogenesis of these disorders (3). *H. pylori* stimulates T-lymphocytes by heat shock protein production, urease activity and its lipopolysaccharide nature. *H. pylori* was previously reported to cause increases in interleukin-1, interleukin-6, interleukin-8 and tumor necrosis factor- α and thus inflammation exaggerates (4). Platelet counts were reported to be increased in inflammatory conditions. Especially in gastric mucosa, tissue injury resulting from *H. pylori* infection increases platelet activation and mean platelet volume (MPV) (5).

The results of studies inspecting the association between *H. pylori* infection and platelet counts are conflicting. Studies about the patients who were diagnosed to have *H. pylori* infection, reported that the platelet counts were decreasing after eradication treatment (6,7). On the other hand, a study inspecting healthy people who underwent health check-ups, reported that there were no association between *H. pylori* infection and platelet counts (3).

Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are increasing in inflammation (8). After eradication of *H. pylori*, C-reactive protein (CRP), and fibrinogen levels were reported to be decreasing (9). When compared according to existence of *H. pylori* infection, there were significant differences in NLR and PLR between study groups (5,9,10). PLR was reported to be a marker of cardiovascular risk and it was demonstrating platelet activation (11).

Most of the studies researching the association between *H. pylori* and platelet counts and inflammatory markers, inspected the associations of time of diagnosis. But the association between *H. pylori* and inflammatory markers after eradication treatment was not elucidated. This study was designed to inspect the effect of eradication for *H. pylori* on inflammatory markers and platelet counts.

MATERIALS and METHODS

This single center, observational, prospective study was conducted in a university hospital with the participants who applied to internal medicine outpatient clinics with dyspeptic complaints and who were evaluated by upper gastrointestinal endoscopy, between July 2021 and January 2022. The patients participated in the study provided an informed written consent regarding the study. This study was approved by local ethic committee (App. No: 2021/057), and was conducted in concordance with Declaration of Helsinki and good clinical practices directives.

Patients who were diagnosed to have *H. pylori* infection, who accepted to enroll in the study, and who came to hospital 8 weeks after eradication treatment were included. Patients under 18 years of age, who had any symptoms and findings reminding a probable infection, who got medications like steroids, non-steroidal anti-inflammatory drugs and acetylsalicylic acid that could affect platelet counts, who had hematologic, hepatic and renal diseases were excluded. Patients who still had positive results for *H. pylori* in stool antigen test after eradication treatment were also excluded.

Upper gastrointestinal endoscopy was performed by same gastroenterologist with Olympus GIF Type Q150 videoendoscope (Olympus Medical Systems Corp., Tokyo, Japan). Biopsy specimens were obtained from mucosa of antrum, incisura angularis and corpus of stomach and were inspected under light microscopy after staining with hematoxylin-eosin and modified Giemsa methods by the same pathologist. All patients had *H. pylori* infection were treated with triple (clarithromycin 500 mg 2 \times 1, amoxicillin 1 gr 2 \times 1 and lansoprazole 30 mg 2 \times 1 per oral) eradication treatment regime.

Blood samples for complete blood counts, erythrocyte sedimentation rate (ESR) and CRP were

obtained from all participants before and 8 weeks after eradication treatment. Eradication for *H. pylori* was confirmed with *H. pylori* stool antigen test in all participants. Data of participants obtained before and after eradication treatment were compared.

Complete blood counts [neutrophil count, lymphocyte count, monocyte counts, platelet counts, mean platelet volume (MPV) and hemoglobin level] were analyzed by XN-1000 analyzer (USA). CRP levels were analyzed by Roche Hitachi Cobas 501 analyzer (Switzerland). Erythrocyte sedimentation rates were measured automatically using the Biosed 100 (Italy) device in blood sample tubes. NLR was calculated by division of neutrophil counts to lymphocyte counts. PLR was calculated by division of platelet counts to lymphocyte counts.

All data were evaluated using the statistical software SPSS for Windows (version 25, SPSS, Armonk, NY, USA). Data distributions were evaluated by Kolmogorov-Smirnov test. Quantitative data were presented as mean \pm standard deviation for normally distributed variables. Categorical data were presented as frequency and percentage. Paired samples t-test and independent samples

t-tests were used in appropriate conditions. A p value below 0.05 was considered significant.

RESULTS

ESR, CRP, PLR and NLR were significantly lower after eradication of *H. pylori*, but changes in platelet counts and mean platelet volumes (MPV) were insignificant.

Mean participant age was 43.84 ± 12.59 (42.25 ± 14.23 in males, 44.82 ± 11.55 in females). Total of 63 participants, 24 (38%) were male and 39 (62%) were female. Study parameters of participants before and after eradication treatment for *H. pylori* were shown in Table 1.

When compared to beginning of the study, there was 1.44 ± 38.58 decrease in platelet counts, 1.87 ± 6.5 in CRP, -0.67 ± 2.3 in ESR and 0.12 ± 0.75 increase in MPV values. Comparison of parameters according to gender of participants who were eradicated of *H. pylori* infection were shown in Table 2. While hemoglobin levels before treatment were lower in females compared to males; platelet and ESR levels were higher than males. There were no significant changes in platelet count, MPV and CRP levels between males and females.

Table 1 Study parameters of participants before and after eradication treatment for *H. pylori*

Parameter	Before Eradication	After Eradication	P value
Leukocyte counts ($\times 10^9/L$)	7.77 ± 2.55	7.60 ± 2.39	0.540
Neutrophil counts ($\times 10^9/L$)	4.85 ± 2.30	4.33 ± 1.98	0.059
Lymphocyte counts ($\times 10^9/L$)	2.21 ± 0.79	2.40 ± 0.74	0.023
Platelet counts ($\times 10^9/L$)	279.63 ± 71.86	278.19 ± 66.64	0.767
Monocyte counts ($\times 10^9/L$)	0.57 ± 0.21	0.59 ± 0.19	0.376
Hemoglobin (g/dL)	13.69 ± 1.80	13.77 ± 1.73	0.673
Mean platelet volume (fL)	9.85 ± 1.14	9.95 ± 0.89	0.276
C-reactive protein (mg/dL)	5.27 ± 8.20	2.57 ± 2.75	0.021
Erythrocyte sedimentation rate (mm/h)	13.84 ± 8.21	12.91 ± 7.04	0.024
Neutrophil to lymphocyte ratio	2.70 ± 2.73	1.84 ± 0.84	0.013
Platelet to lymphocyte ratio	145.83 ± 79.07	123.54 ± 45.96	0.015

Table 2 Comparison of parameters according to gender of participants who were eradicated for *H. pylori* infection

Parameter	Male (n = 24)	Female (n = 39)	P value
Age (years)	42.25 ± 14.23	44.82 ± 11.55	0.436
Leukocyte counts (×10 ⁹ /L)	7.58 ± 2.82	7.89 ± 2.40	0.650
Neutrophil counts (×10 ⁹ /L)	4.51 ± 2.34	5.05 ± 2.28	0.369
Lymphocyte counts (×10 ⁹ /L)	2.27 ± 0.83	2.17 ± 0.78	0.654
Platelet counts (×10 ⁹ /L)	256.54 ± 73.07	293.85 ± 68.19	0.044
Monocyte counts (×10 ⁹ /L)	0.61 ± 0.24	0.54 ± 0.19	0.193
Hemoglobin (g/dL)	14.83 ± 2.05	12.99 ± 1.19	<0.001
Mean platelet volume (fL)	9.50 ± 1.44	10.06 ± 0.86	0.053
C-reactive protein (mg/dL)	3.37 ± 4.37	5.75 ± 8.93	0.294
Erythrocyte sedimentation rate (mm/h)	9.67 ± 8.44	16.63 ± 6.88	0.004
Neutrophil to lymphocyte ratio (before)	2.22 ± 1.42	3.0 ± 3.27	0.276
Neutrophil to lymphocyte ratio (after)	1.71 ± 0.78	1.91 ± 0.87	0.361
Platelet to lymphocyte ratio (before)	124.59 ± 52.22	158.90 ± 89.95	0.095
Platelet to lymphocyte ratio (after)	109.23 ± 32.31	132.34 ± 51.05	0.052
Change in platelet counts	-2.83 ± 30.95	-0.59 ± 42.98	0.825
Change in mean platelet volume	0.23 ± 1.09	0.05 ± 0.42	0.351
Change in C-reactive protein	-1.16 ± 4.02	-2.31 ± 7.66	0.498
Change in sedimentation rate	-0.25 ± 2.27	-0.92 ± 2.18	0.263

DISCUSSION

This present study evaluate the effect of eradication treatment for *H. pylori* on inflammatory markers and complete blood count parameters documented that ESR, CRP, PLR and NLR values were decreasing. But changes in platelet counts and MPV values were insignificant after treatment.

H. pylori may cause chronic active gastritis, atrophic gastritis, peptic ulcer, gastric adenocarcinoma and gastric lymphoma in human-beings. For this reason, eradication of *H. pylori* is strongly advised to prevent development of complications (12). *H. pylori* infection results in gastric injury mediated by inflammatory mediators triggered by activated immune system components and activated platelets (13). Complete blood count parameters such as platelet counts, MPV and calculated ratios such as PLR and NLR may readily be used to evaluate

existence of inflammation. To assess the treatment success for *H. pylori*, these parameters may be useful in medical institutions where invasive diagnostic tests for *H. pylori* are unavailable (7).

A study revealed that eradication of *H. pylori* resulted in significant decrease in CRP levels (14). In a study reported from Italy, ESR were reported to decrease after *H. pylori* eradication (15). Another study stated that PLR, as a marker of inflammation, and since it was found to be higher in symptomatic patients, might be useful in differentiating symptomatic and asymptomatic patients who were infected with *H. pylori*. PLR was significantly higher in patients who had positive results for *H. pylori*. In addition, levels of PLR were found to be correlated with the severity of *H. pylori* infection. But changes after eradication treatment in PLR was not evaluated in this study (9).

It was reported that chronic inflammation caused by *H. pylori* in gastric mucosa results in increases in neutrophil counts and decreases in lymphocyte counts (16). In concordance with the mentioned study above; in present study, neutrophil counts and NLR were found to be decreased and lymphocyte counts were found to be increased after *H. pylori* eradication. In a study with 1289 patient who underwent gastric endoscopy, NLR were significantly higher in *H. pylori* positive patients compared with *H. pylori* negative patients (5). Differentiating from aforementioned studies, our study revealed that ESR, CRP, PLR, and NLR values representing the inflammation were significantly decreased especially after eradication treatment.

Matsukawa et al. reported 294 patients who received *H. pylori* eradication treatment; 243 (82.7%) were tested negative for *H. pylori* after treatment. In follow-up of these patients, platelet levels at eighth weeks, sixth months, first, second, and third years were all lower than the basal platelet levels (17). In another study, Matsukawa et al. reported that 88% of enrolled 178 patients were eradicated of *H. pylori* and platelet levels were significantly lower only in female participants eight weeks after treatment. This was explained by increased sensitiveness of females to infections compared with males (6). A study with 17 thousand patients revealed no association between *H. pylori* infection and platelet counts (3). Present study, congruently, reveals no association between platelet counts and *H. pylori* infection.

Topal et al. reported no association between *H. pylori* and MPV (18). Another study reported by Altın et al, revealed that changes in MPV values were insignificant after *H. pylori* eradication (7). There are some affecting factors to be taken into consideration for measurement of MPV; delaying of blood sample may result in increased platelet contact with the anticoagulant, which will make platelets to enlarge in size, temperature of medium

in which blood samples wait and factors regarding measurement device may change MPV results (19). Compatible with the studies above, our study reports that there is no association between *H. pylori* and MPV.

There are some limitations of our study. Sample size was relatively low, increasing study period could be useful to enroll more participants and increase sample size. Another point is; clarithromycin used in eradication treatment of *H. pylori* has anti-inflammatory effects, besides its antibacterial effects. It was reported that clarithromycin depressed interleukin-6 production, and this may explain its anti-inflammatory effects (20). Unfortunately, all patients in this presented study got treatment regimes that contained clarithromycin, thus we could not inspect anti-inflammatory effects of clarithromycin. Data of participants who were eradicated for *H. pylori* could not be compared to data of patients who were not eradicated, because there were no cases who rejected to have eradication treatment for *H. pylori* or who could not complete the eradication treatment, during the study period.

In conclusion; this study documented that ESR, CRP, PLR and NLR were significantly lower after eradication for *H. pylori*. Changes in platelet counts and MPV were insignificant. These significant parameters may be useful, simple, available and non-invasive tests that may be used in evaluation of eradication treatment for *H. pylori*, especially in medical centers where specific *H. pylori* tests are unavailable.

Ethics: This study was approved by the Lokman Hekim University, Ethics Committee on May 27, 2021, number 2021/057.

Conflict of interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Acknowledgments: Authors of this study thank to Mr. Fatih AÇIKGÖZ for statistical advices, Dr. Emre AKARSU for pathologic evaluation and Dr.

Fahri YAKARYILMAZ for endoscopic procedures and Dr. Metin YILDIRIMKAYA for laboratory analyzes

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