



Evaluation of the Systemic Immune Inflammatory Response in Cases Infected with *Helicobacter Pylori*

Helicobacter Pylori ile Enfekte Olguların Sistemik İmmün İnflamasyon Yanıtının Değerlendirilmesi

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ABSTRACT

Objectives: The effectiveness of systemic immune inflammation index (SII), which is a practical, new, and useful marker in indicating inflammation, in various malignant and non-malignant diseases has been shown. In the present study, it was aimed to examine the correlation between *Helicobacter pylori* (HP+), which causes chronic infection and inflammation, and SII.

Methods: A total of 88 HP+ cases and 154 HP– control cases were included our retrospective, randomized, and controlled study. HP± was assessed according to the endoscopic biopsy reports of cases. All secondary causes that may lead to inflammation were excluded from the study. The SI level of the case and control groups was calculated (absolute neutrophil × absolute platelet/absolute lymphocyte).

Results: In our study, no significant correlation between HP+, a chronic infection, and SII could not be shown (p>0.05). It was detected that HP+ was more common in young ages (p<0.05).

Conclusion: The results of our study suggest that SII may not be a useful marker in indicating HP+ as we could not find a significant correlation between SII and HP+.

Keywords: Endoscopy; *helicobacter pylori*; systemic immune inflammatory index.

ÖZET

Amaç: İnflamasyon göstermede pratik, yeni ve kullanışlı bir marker olan sistemik immün inflamasyon indeksinin (SII) çeşitli malign ve malign olmayan hastalıklarda etkinliği gösterilmiştir. Çalışmada, kronik bir enfeksiyon ve inflamasyona neden olan *Helicobacter pylori* pozitifliği ile SII ilişkisinin incelenmesi amaçlandı.

Yöntem: Retrospektif randomize kontrollü çalışmaya 88 *H. pylori* pozitif olgu ile 154 *H. pylori* negatif kontrol hastası dahil edildi. Olguların endoskopik biyopsi raporları doğrultusunda *H. pylori* pozitifliği ve *H. pylori* negatifliği değerlendirildi. İnflamasyona neden oluşturabilecek tüm sekonder nedenler dışlandı. Olgu ve kontrol grubunun SII düzeyi (mutlak nötrofil x mutlak trombosit/mutlak lenfosit) hesaplandı.

Bulgular: Çalışmamızda kronik bir enfeksiyon olan *H. pylori* pozitifliği ile SII arasında anlamlı bir ilişki gösterilemedi (p>0,05). *H. pylori* pozitifliğinin daha genç yaşlarda daha sık olduğu tespit edildi (p<0,05).

Sonuç: SII ile *H. pylori* pozitifliği arasında anlamlı bir ilişkinin gösterilemediği bu çalışmada, çalışmanın sonucu SII'nin *H. pylori* pozitifliğini göstermede kullanışlı bir marker olamayacağını düşündürmektedir.

Anahtar sözcükler: Endoskopi; *helicobacter pylori*; sistemik immün inflamatuvar indeks.

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Helicobacter pylori (HP) is a common bacterial infection and it is estimated that approximately 50% of the world's population is infected with HP. The prevalence of HP, whose main reservoir is human, shows great variation according to age, race, geographical region, and ethnicity. It is seen that in developing countries, most of the infections occur in childhood, the rate of being infected with HP is higher than in developed countries and it decreases with the developments in hygiene practices. HP has been associated with serious diseases of the gastrointestinal tract, including chronic gastritis, duodenal ulcer, and gastric cancer.^[1] Although infected cases are mostly asymptomatic, HP+ predisposes various diseases such as peptic ulcer, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma.^[2] It has been related to hypochlorhydria, multifocal atrophic gastritis, and increased gastrinemia at rates as low as 1–2%.^[3] Besides, HP+ has been also associated with various neurological, dermatological, hematological, ocular, cardiovascular, metabolic, allergic, and hepatobiliary diseases.^[4]

Today, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in particular as well as the combination of these systemic inflammation parameters, the systemic immune inflammation index (SII), are accepted as prognostic factors in malignant gastrointestinal system solid tumors such as colorectal cancer.^[5,6] It has also been shown that they are significantly higher in non-malignant diseases of the gastrointestinal tract, such as ulcerative colitis, than in healthy individuals and are closely related to disease activity.^[7]

Methods

A total of 242 cases who underwent an endoscopic procedure in our hospital in the past 2 years were included in our study, and we aimed to evaluate SII as a marker in indicating the presence of HP. Of these, there were 88 cases with HP+ and 154 cases with HP- (control group). In the study, a Karl Storz endoscopic device was used. The status of HP test positivity and negativity was assessed according to the endoscopic procedure biopsy taken from the antrum and corpus. The cases that were detected to be positive/negative according to the urea breath test and fecal HP antigen test response were not included in the study because standardization would not be achieved. In our study, which we retrospectively reviewed the data, the cases were randomly included in the study. The cases with the age of 18 years or above were evaluated by examining their entire medical history. The patients in the case

and control groups, who had the diagnosis of gastrointestinal system malignancies, other solid organ tumors, hematological malignancies, autoimmune diseases, rheumatic disease, active infection, chronic inflammation, anemia due to any etiological cause, reactive thrombocytosis, essential thrombocytosis, idiopathic thrombocytopenic purpura, celiac disease, inflammatory bowel diseases, those with antibiotic use in the past 2 months, steroid use, and those who underwent gastric bypass surgery were not included in the study. In addition, the cases with the CRP value of >3 mg/L and high sedimentation value with respect to age were excluded from the study. In our hospital, hemograms are analyzed in EDTA tubes using a symsysmax brand device. In the study, the hemograms of the cases were examined; the SII values were determined by dividing the multiplication of the neutrophil and platelet absolute values by the lymphocyte absolute value and the case and control groups were compared in terms of SII. Because the study was retrospective, informed consent was not obtained.

Ethical Committee approval was obtained for our study (Decision no: 2022/514/222/3).

The study was conducted in accordance with the Helsinki Declaration.

Statistical Analysis

The statistical analysis of the results obtained in the study was performed using the IBM SPSS Statistics 26 software (IBM SPSS, Türkiye). Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were used in the statistical evaluation of the study data. The Kolmogorov–Smirnov/Shapiro–Wilk test, Skewness–Kurtosis test, and graphical examinations were employed in testing whether the quantitative data conform with the normal distribution. In the comparison of two groups in terms of quantitative variables, the independent samples t-test was used in normally distributed data, and the Mann–Whitney U test was used in the data that did not show normal distribution. The Pearson Chi-square test was utilized to evaluate qualitative data. The statistical significance was assessed at the $p < 0.05$ level.

Results

A total of 242 cases, 146 (60.3% 9 females and 96 males [39.7%]), who underwent endoscopy in our hospital in 2022 were enrolled in the study. A statistically significant difference was detected between the ages of the cases according

Table 1. Evaluation of descriptive variables

	Total (n=442)		HP (-) (n=154)		HP (+) (n=88)		p
	n	%	n	%	n	%	
Age (year)							
Median (min-max)	50 (18-85)		51 (18-85)		46 (20-78)		0.025 ^a
Mean±SD	49.17±14.85		50.78±15.32		46.35±13.6		
Gender							
Female	146	60.3	90	58.4	56	63.6	0.427 ^b
Male	96	39.7	64	41.6	32	36.4	

*p<0.05; ^aIndependent t-test; ^bPearson Chi-square test. HP: Helicobacter pylori; SD: Standard deviation

Table 2. Evaluation of laboratory results

	HP (-) (n=154)	HP (+) (n=88)	p
Neutrophil (10 ³ /μL)			
Median (min-max)	4160 (980-14430)	4255 (1810-9670)	0.758 ^c
Mean±SD	4465.32±1724.20	4559.66±1759.84	
Lymphocyte (10 ³ /μL)			
Median (min-max)	2065 (680-4460)	2200 (790-4660)	0.386 ^a
Mean±SD	2196.95±755.42	2286.25±794.37	
Platelet (10 ³ /μL)			
Median (min-max)	262500 (101000-471000)	262000 (152000-475000)	0.405 ^a
Mean±SD	264077.92±64403.70	271488.64±69829.51	
SII			
Median (min-max)	524038.9 (165293.3-4953088.2)	481542.4 (156674.6-2323008.8)	0.852 ^c
Mean±SD	617346.10±505441.21	617307.21±414027.87	

^aIndependent t test; ^cMann-Whitney U Test. HP: Helicobacter pylori; SD: Standard deviation; SII: Systemic immune inflammation index

to the presence of HP incidence (p=0.025); the HP+ cases were younger than HP- cases. On the other hand, there were no significant differences between the gender distributions of cases in terms of the presence of HP (p>0.05).

The difference between H+ cases and H- cases in terms of neutrophil, lymphocyte, and platelet counts was found to be statistically insignificant (p>0.05). No statistically significant difference was detected in the SII index of the cases with respect to the presence of HP as well (p>0.05).

Discussion

In our study, the effectiveness of SII in showing HP+, which is a common disease, was investigated, and determined that the mean age of HP+ cases was lower than that of HP- control group (HP+: 46; HP-: 51 years) (Table 1). The mean age of the cases with HP+ was reported as 54 years in the study by Poonyam et al.^[8] In a Japanese co-

hort,^[9] it has been shown that the prevalence of HP positivity is 80-90% in those born before 1950, 10% in those born in the 1990s, whereas <2% in those born after 2000. These results have been considered to be attributed to the change in the understanding of cleaning along with changing hygiene conditions. However, in our study in which the endoscopy reports were randomly evaluated, the age of the cases with HP+ was observed to be lower, unlike the results reported in other studies. The literature data examining the relationship between HP+ and age are not adequate and there is a need for epidemiological studies conducted in different populations.

SII, a powerful marker in predicting survival outcome of cases diagnosed with colorectal cancer, is considered to be helpful to identify high-risk patients among patients with similar TNM stage.^[10] It is thought that SII, NLR, and PLR would be promising prognostic predictors for metastatic

non-small cell lung cancer cases.^[11] In a meta-analysis including 11 studies and 2724 cases, it has been indicated that high SII can be a promising marker for the prediction of poor prognosis in cases with gynecological and breast cancer, especially ovarian cancer and triple-negative breast cancer.^[12] High SII is an independent adverse prognostic factor in resectable gastroesophageal adenocarcinoma patients with and without neoadjuvant therapy.^[13] Its reliability as a marker has been tested in non-malign diseases. Guven et al.^[14] found that the SII level of the case group was statistically significantly higher than that of the control group in their studies conducted with 214 (107 cases and 107 controls) participants.

Farah et al.^[15] detected significantly higher NLR and PLR in HP+ cases than in HP- cases and showed that there is also a significant positive correlation between the NLR and PLR levels and the severity of symptoms.^[16] In the study by Kaplan et al.,^[17] including 1289 cases, it was reported that the combination of PLR-NLR was a good marker of gastrointestinal complications associated with HP+ and HP-. However, in their study conducted with the inclusion of 448 cases, Boyuk et al.^[18] showed that NLR and PLR in HP+ cases were not significantly higher than in the control group. Although our study is the first study assessing the correlation between HP and SII, the NLR and PLR values, the subcomponents of this index, were evaluated in HP positivity (Table 2). It was found in our study that there was no significant correlation between HP+ and SII; hence, our results were similar to the results reported by Boyuk et al.,^[18] but different from the results of Farah et al.^[15,16] and Kaplan et al.^[17] While it has been shown that SII can be a reliable marker in inflammation in all the said studies, in which malignant and non-malignant inflammatory response is induced, no significant results could be obtained in our study in which strong exclusion criteria were implemented. We think that it is necessary to continue the search on new markers to be used in showing HP and that the negative predictive value of SII in HP positivity may be significant. To generalize the results obtained, our study needs to be supported by studies conducted with different HP+ patient groups.

Study Limitations

As our study included retrospective data, symptom evaluation of HP+ cases could not be performed. In addition, the absence of information regarding the use of proton pump inhibitors and whether the cases received previous HP eradication treatment as well as the small number of patients created limitations for our study.

Conclusion

In our study, we investigated the correlation between HP+ and SII, since no significant correlation between HP+ and SII was shown, we do not think that SII is suitable as a predictor or a marker for prognosis follow-up in such cases. There is no study in the literature similar to our study examining the relationship between HP and SII. We are of the opinion that the effectiveness of SII should be evaluated more clearly, in the case that studies investigating the relationship between HP and SII increase.

Disclosures

Ethics Committee Approval: The study was approved by Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee, Date: 30.03.2022, decision number: 2022/514/222/3.

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