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Helicobacter Pylori Eradikasyon Tedavisi Sonrasi HastaTakibinde Nöltrofil Lenfosit Oranının Duyarlılık ve Özgüllüğü

Specificity, Sensitivity and Usefulness of Neutrophil Lymphocyte Ratio in the Follow-up of Patients After Helicobacter Pylori Eradication Treatment

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Öz

Giriş ve Amaç: Endoskopik olarak H. Pilory pozitifliği tespit edilen ve eradikasyon tedavisi uygulanan hastaların takibinde tedavinin başarısını gözlemlemek için NRL oranının sensitivite ve spesifitesini ortaya koymayı amaçladık.
Gereç ve Yöntem: İstanbul Medipol Üniversitesi Pendik Hastanesi, Endoskopi Ünitesi'nde, üst gastrointestinal sistem endoskopisi yapılan 386 hasta değerlendirildi. HP pozitif ve negatif olan hastaların nötrofil, lenfosit sayıları, nötrofil lenfosit oranları (NLO) karşılaştırıldı. HP pozitif olan 205 hastaya 2 haftalık üçlü tedavi ile H. pylori eradikasyonu uygulandı. Tedavi bitiminden 4 hafta sonra gaitada H. Pilori antijen testi yapıldı ve negatif sonuç eradikasyon olarak tanımlandı. Eş zamanlı olarak tüm hastalara tam kan sayımı yapılarak. NLO hesaplandı ve değerler eradike edilen ve edilemeyen gruplar arasında karşılaştırıldı.
Bulgular: H. Pilory eradikasyonu 100 (%48,7) hastada sağlanabilmişken 105 (%51,3) hastanın gaitada antijen testi pozitif olarak geldi. Bu iki grup arasında nötrofil sayıları (P<0,0001), lenfosit sayıları(P<0,0001), ile nötrofil lenfosit oranı (P<0,0001) arasında istatistiksel olarak anlamlı fark mevcuttu. Nötrofil /Lenfosit oranının cutoff değeri 2,058 alındığında Helikobakter pilori eradikasyonunu tespit etmedeki duyarlılık ve özgüllüğü sırasıyla %90,5 ve %85 olarak tespit edildi
Sonuç: Çalışmamızda, tam kan sayımında bulunan parametrelerden elde edilen nötrofil/lenfosit oranı HP (+) olgularda daha yüksek bulunmuştur. Bu belirtecin tedavi süresince ve tedaviden sonra hastaları takip etmek için yararlı olabileceğini ancak başarılı HP eradikasyonu tedavisinden sonra, takip belirteci olarak nötrofil/ lenfosit oranındaki değişiklikleri değerlendirmek için daha geniş örneklem grubu ile yapılacak daha çok sayıda çalışmaya ihtiyaç olduğunu düşünmekteyiz.

Anahtar Kelimeler: Eradikasyon, Gastroskopi, Helikobakter Pilori, Nötrofil Lenfosit oranı, Tam kan sayımı

Abstract

Objective: The aim of this study is to determine the sensitivity and specificity of the NLR ratio in order to assess treatment effectiveness in the follow-up of patients who are endoscopic H. pylori-positive and administered eradication therapy.
Materials and Methods: The Endoscopy Unit at Istanbul Medipol University Pendik Hospital evaluated 386 individuals who underwent upper gastrointestinal endoscopy. Neutrophil and lymphocyte counts, as well as neutrophil-to-lymphocyte ratios (NLR), were compared in HP positive and negative patients. H. pylori eradication was performed on 205 HP-positive patients using a 2-week triple therapy. All patients had a complete blood count done at the same time, and NLR was computed and compared between the eradicated and non-eradicated groups.

Results: H. pylori eradication was accomplished in 100 (48.7%) of the patients, whereas the stool antigen test was positive in 105 (51.3%) of the patients. There was a statistically significant difference in neutrophil counts (P<0.0001), lymphocyte counts (P<0.0001), and neutrophil-to-lymphocyte ratio (P<0.0001). The sensitivity and specificity in identifying Helicobacter pylori eradication were determined to be 90.5% and 85%, respectively when the cutoff value for the Neutrophil-to-Lymphocyte ratio was set at 2.058.
Conclusion: The neutrophil-to-lymphocyte ratio was shown to be greater in HP (+) cases based on the parameters discovered in the complete blood count in our study. We believe that this measure might be used to monitor patients during and after therapy, but additional research with larger sample sizes is needed to assess changes in neutrophil-to-lymphocyte ratio as a follow-up indicator following successful HP eradication therapy.

Key words: Complete blood count, Eradication, Gastroscopy, Helicobacter Pylori, Neutrophil-to-Lymphocyte ratio.

1. Introduction

Helicocterpylori (H.pylori) is the microorganism that causes the greatest infections in people, with a prevalence of 20-50% in developed countries and around 80% in developing countries [1]. It can appear with a wide range of clinical symptoms and may be associated with a variety of endoscopic findings. It causes pathologies including chronic gastritis, peptic ulcers, stomach cancer, and MALToma (Mucosa Associated Lymphoid Tumor/Gastric Lymphoma). Furthermore, its etiological connection with major diseases such as anemia, arthritis, atherosclerosis, and immune thrombocytopenic purpura, has been discussed [2]. Serological tests in the diagnosis of Helicocterpylori (H.pylori) are quantitative methods with a sensitivity of more than 80% [3]. The H.pylori stool antigen test, which is a simple and practical ELISA-based test, has also been utilized in recent years. These tests have been found to be a sensitive and specific method in the evaluation of H.pylori eradication, although the findings obtained, as well as the sensitivity and specificity of the test, vary according to the kind of antibody employed in the test kit [3,4]. The current fast urease test has a sensitivity of more than 85% and a specificity of more than 95% [5]. Due to its high cost and challenging circumstances, PCR examination of mucosal biopsy samples is a technology that is primarily utilized in research-oriented investigations nowadays. PCR can identify H. pylorites in biopsy samples, gastric fluid, and stools. The procedure has a sensitivity and specificity of more than 95%. [6]. Culture, along with histology, is one of the most effective diagnostic procedures¬. The culture's sensitivity is estimated to be 70-95% and its specificity to be 100% [5].

We believe that a basic blood count may provide better guidance than culture, histology, ELISA, PCR, or Urease test in the follow-up of patients who were given eradication therapy due to H.pylori positivity. Many studies in the literature demonstrate that the neutrophil-to-lymphocyte ratio derived from a blood count can detect inflammation in the body in a sensitive way [7,8]. The neutrophil-to-lymphocyte ratio has been associated with H. pylori infection in the literature [9]. However, no study has been conducted in the follow-up of patients who have received eradication therapy to predict treatment effectiveness and demonstrate the sensitivity and specificity of the NLR ratio. The aim of this study is to determine the sensitivity and specificity of the NLR ratio in order to assess treatment effectiveness in the follow-up of patients who are endoscopic Helicobacter pylori-positive and administered eradication therapy.

2. Materials And Methods

In the study, 386 patients, aged between 18 and 65 years, who underwent upper gastrointestinal system endoscopy by a general surgeon with an endoscopy certificate approved by the Ministry of Health, were evaluated in the Endoscopy Unit of Istanbul Medipol University Pendik Hospital, between December 2019 and June 2021. The anesthesia and general surgery specialists informed the patients orally and in writing about the endoscopic procedure prior to the operation. Before the procedure, all patients had a complete blood count, coagulometric tests, and liver and kidney function tests. Endoscopies were performed under general anesthesia (PROPOFOL 1% 10gr/20 ml, Midazolam 50mg/10ml) given under the supervision of an anesthesiologist after 8-hour fasting. Patients who had dyspeptic symptoms and were diagnosed with antral gastritis after upper gastrointestinal endoscopy were enrolled in the study. All patients had a biopsy extracted from the antrum of the stomach using forceps for HP screening. All biopsies were histopathologically examined according to the Sydney classification [10]. Patients with Intestinal Metaplasia and Atrophy and patients who had additional pathological findings during upper gastrointestinal endoscopy besides antral gastritis were excluded from the study. Patients with uncontrolled diabetes, uncontrolled hypertension, malignancy, chronic liver diseases, chronic kidney failure, heart failure, chronic lung diseases, gastrointestinal system bleeding, and other diseases that may affect WBC and lymphocyte counts in the blood count were excluded from the study. Patients who had taken nonsteroidal anti-inflammatory medications or medicines that might alter white blood cell and lymphocyte counts, such as steroids, within the previous two weeks were excluded from the study. The Demographic data, pre-procedural complete blood count results, and pathology reports of 341 patients who met these criteria were evaluated. Neutrophil and lymphocyte counts, as well as neutrophil-to-lymphocyte ratios (NLR), were compared in HP positive and negative patients. H. pylori eradication was performed on 205 HP-positive patients using a 2-week triple therapy (60 mg lansoprazole, 1000 mg clarithromycin, 2000 mg amoxicillin). Medication counts were performed, and patients who ingested more than 90% of medicines were considered to have completed eradication therapy. An H.

pylori stool antigen test was conducted four weeks following the conclusion of therapy, and a negative result was diagnosed as eradication. Proton pump inhibitors, antibiotics, bismuth subsalicylate, and H2 blockers were not permitted to be used in the four weeks preceding the stool antigen test. The patients were split into two groups based on their eradication success: successful eradication (n = 100) and failed eradication (n = 105). All patients had a complete blood count done at the same time, and NLR was computed and compared between the eradicated and non-eradicated groups.

3. Results and Discussion

3.1.Results

In the study, 386 patients aged between 18 and 65 who had upper gastrointestinal system endoscopy between December 2019 and June 2021, were evaluated. Of these 386 patients, the study excluded 33 patients who had uncontrolled diabetes, uncontrolled hypertension, malignancy, chronic liver diseases, chronic renal failure, heart failure, chronic lung illnesses, or gastrointestinal system bleeding that might impact white blood cell and lymphocyte counts, 7 patients with intestinal metaplasia and atrophy in the biopsy result collected from the antrum, and 5 patients due to noncompliance with eradication therapy. The demographic data of the remaining 341 patients, as well as biopsy results, neutrophil and lymphocyte count and neutrophil-to-lymphocyte ratios are presented in Table 1. H. pylori was found to be positive in the antral biopsy results of 205 (60.1%) patients. Despite the endoscopic diagnosis of Antral Gastritis, H. Pylori was found to be negative in 136 (39.9%) patients. According to the Student's t-test, no statistically significant difference was found between the two patient groups in terms of sex and age. However, there was a significant difference in neutrophil counts (P<0.0001), lymphocyte counts (P<0.0001), and neutrophil-to-lymphocyte ratio (P<0.0001) in the H. Pylori positive group. (Figure 1)

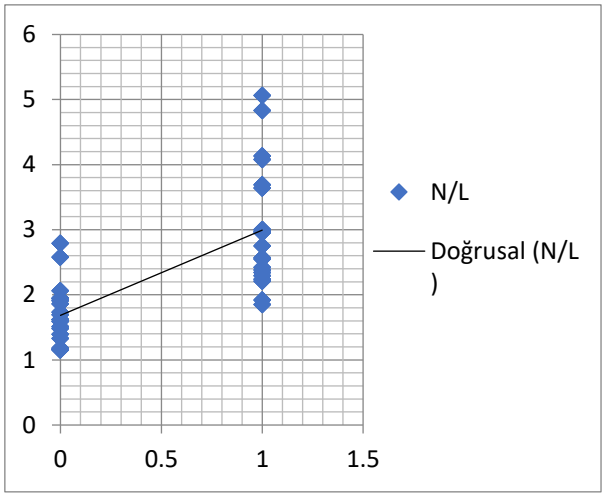

Figure 1. Relationship between Helicobacter positivity and neutrophil-to-lymphocyte ratio.

H. pylori eradication was performed on 205 HP-positive patients using a 2-week triple therapy. An H. pylori stool antigen test was conducted four weeks following the conclusion of therapy, and a negative result was diagnosed as eradication. Neutrophil counts, lymphocyte counts, and neutrophil-to-lymphocyte ratios were determined by the blood counts of the patients.

Table 1. Demographic characteristics and findings of the patients

	Helicobacter (+) n:205	**Helicobacter (-) n:136**	**p-value**
Mean age	46,39 ± 14,28	50,45 ± 17,55	**Insignificant**
Sex (F/M)	145/60	97/39	**Insignificant**
Neutrophil	5,19 ± 0,64	3,75 ± 0,83	**P<0.0001**
Lymphocyte	1,94 ± 0,51	2,40 ± 0,84	**P<0.0001**
Neutrophil-to-Lymphocyte	2,85 ± 0,79	1,69 ± 0,44	**P<0.0001**

H. pylori eradication was accomplished in 100 (48.7%) of the patients, whereas the stool antigen test was positive in 105 (51.3%) of the patients. The mean age of the patients who were eradicated was 50,45±17,55 years, while the mean age of the patients who could not be eradicated was 46,38±14,28 years, with no statistically significant difference in terms of mean age or sex (P<0.0001). However, there was a statistically significant difference in neutrophil counts (P<0.0001), lymphocyte counts (P<0.0001), and neutrophil-to-lymphocyte ratio (P<0.0001). (Table 2)(Figure 2). The sensitivity and specificity in identifying Helicobacter pylori eradication were determined to be 90.5% and 85%, respectively when the cutoff value for the Neutrophil-to-Lymphocyte ratio was set at 2.058 (Table 3).

Table 2. Patients recovering and not recovering following a two-week treatment

	Recovering patients n=100	**Non-recovering patients n=105**	**P-value**
Mean age	50,45 ± 17,55	46,38 ± 14,28	**0,071 (Insignificant)**
Male/Female	70/30	75/30	**Insignificant**
Mean neutrophil count/mm^3	3,75 ± 0,83	5,19 ± 0,64	**<0.0001**
Mean lymphocyte count/mm^3	2,40 ± 0,84	1,94 ± 0,51	**<0.0001**
Mean neutrophil-to-lymphocyte ratio	**1,69 ± 0,44**	**2,85 ± 0,79**	**<0.0001**

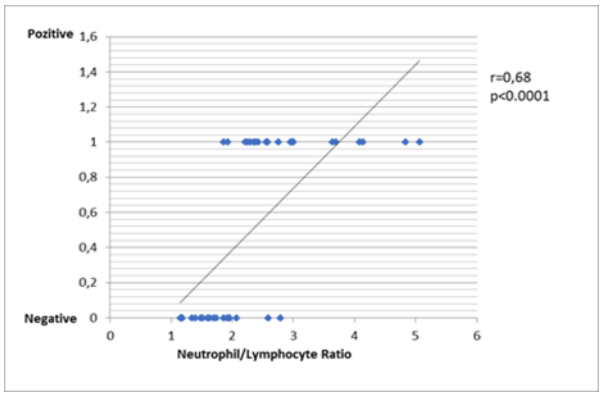

Figure 2. Relationship between helicobacter positivity and neutrophil-to-lymphocyte ratio after three weeks

3.2. Discussion

H. *pylori* infection is associated with severe gastrointestinal diseases such as peptic ulcer (15%), ulcer complications (2 -10%), gastric cancer (1-3%), and B-cell lymphoma, the primary gastric lymphoma at the rate of 0.1% [11]. It has been demonstrated in the literature that indicators such as sedimentation, fibrinogen, acute phase reactants, and CRP are elevated in H. pylori-positive patients due to the presence of a systemic inflammatory response [12]. The aim of our study was to determine if there were any changes in the hemogram test, which is a basic blood test, of H. pylori, the most prevalent infectious agent in the world and a known carcinogen. Furthermore, NLR is a number obtained by dividing the absolute neutrophil count by the absolute lymphocyte count, and research has shown that it is a sensitive indicator that can reveal the systemic response [9,13]. As a result of our study, we discovered a statistically significant difference in NLR between the groups who received H. Pylori eradication and those who did not after the treatment of the patients administered with pylori eradication (P<0.0001).

Epidemiological studies have revealed that H. Pylori prevalence is directly connected to occupational health, lifestyle, and socioeconomic status and that it differs among nations and within the different regions of the same community. In fact, H. Pylori was shown to be present in 78.4% of industrial workers and 64.3% of other workers in a study conducted in the United Arab Emirates [14]. The prevalence of H. Pylori infection in asymptomatic patients was investigated in a study conducted in Tunisia in 2000, and the frequency of H. Pylori was found to be 82.7% [15].

In a study conducted in Sivas, Helicobacter infection (+) was found in 70.1% of the cases [16]. The prevalence of H. pylori was found to be 50.8% in a regional evaluation conducted by Cerrahpaşa Medical Faculty Family Medicine Department [17]. In our study, we found the frequency of H. Pylori to be 60.1% in the Pendik district. Additionally, we discovered that the Neutrophil count and NLR were statistically significantly higher in H. Pylori-positive patients. Along with being an indicator of an inflammatory response, there are studies demonstrating NLR connection with Helicobacter Pylori positivity. Farah et al. revealed the correlation between H. Pylori positivity and NLR in their study. They also highlighted that the severity of gastritis may be related to NLR and stated that NLR is statistically significantly high (p=0,007) in patients with grade 4 symptomatic gastritis [18]. We did not evaluate the statistical correlation between the severity of gastritis or gastritis-related symptoms and NLR in our study. However, Patients who were H. Pylori positive were given a 2-week eradication therapy (60 mg lansoprazole, 1000 mg clarithromycin, and 2000 mg amoxicillin) as recommended by Thai consensus. An H. pylori stool antigen test was conducted in all individuals four weeks following the treatment to evaluate H. pylori eradication. Simultaneously, neutrophil counts, lymphocyte counts, and NLR were evaluated using the patients' hemograms. At this point, we believe we have obtained two significant results in the statistical analysis of our study.

First of all, we discovered a statistically significant difference in NLR between the groups who received H. Pylori eradication and those who did not after the treatment of the patients administered with pylori eradication (P<0.0001). Murat et al. found NLR in HP + patients to be statistically significantly higher in their study. They also stated that it can also be utilized in the follow-up of treatment in patients receiving eradication therapy [10]. There are other studies in the literature indicating the relationship between H. pylori infection and NLR [18]. Distinctively in our study, when the cutoff value of the Neutrophil-to-Lymphocyte ratio was set at 2.058, the sensitivity and specificity in identifying Helicobacter pylori eradication were determined to be 90.5% and 85%, respectively. (Table 3). Culture is widely regarded as the gold standard for detecting H. pylori. It is not an appropriate procedure for follow-up since it necessitates endoscopy and biopsy. Aktepe et al. recognized histology as the gold standard and reported that the culture method had a sensitivity and specificity rate of 61% and 91%, respectively [19]. When Kalem et al. used the culture method as the gold standard, they discovered the urease test and histological examination method to have a sensitivity and specificity of 97.5% and 20.7%, 72.5%, and 100%, respectively [20]. Although culture is alone is considered as the gold standard method for diagnosing H. pylori, it is recommended to use more than one method, such as urease test and/or histology and/or stool antigen tests and/or molecular methods, in conjunction with culture to increase the accuracy of the diagnosis. As a result, we believe that NLR can be used as a simple, inexpensive, and easily accessible parameter in the evaluation of H. pylori eradication, not alone, but in conjunction with other methods, for follow-up purposes, and that more comprehensive studies on the subject are required in this regard.

Table 3. Sensitivity and specificity of the neutrophil-to-lymphocyte ratio when the cutoff value was set at ≤2,058

	Non-recovering patients	**Recovering patients**	**Total**
N-to-L ratio >2,058	95	15	**110**
N-to-L ratio ≤2,058	10	85	**95**
	105	100	**205**

Secondly, we discovered that H. Pylori turned negative in 48.7% (n=100) of the patients to whom we administered eradication therapy, while eradication therapy failed in 51.3 % (n=105). Antibiotic resistance has arisen as a major issue in recent years. According to a study conducted in Thailand, H. pylori eradication with standard triple therapy was ineffective (<80%) due to increasing antibiotic resistance [21]. It is underlined that more effective regimens are required to enhance the treatment of this significant bacterium [22]. Demir et al. reported a 58.6% H. pylori eradication rate in a study conducted in our country [23]. Kadayıfcı et al. reported an 84% success rate with lansoprazole + amoxicillin + clarithromycin in a meta-analysis they conducted in our country in 1997, and now this rate is observed to have decreased significantly [24]. The success rate of eradication therapy was found to be as low as 48.7% in our study. It has been observed that a triple therapy of 60 mg lansoprazole, 1000 mg clarithromycin, and 2000 mg amoxicillin alone does not offer enough eradication, particularly in our country's circumstances. Despite the fact that there are several studies in the literature demonstrating the efficacy of these treatments, we believe that additional treatment modalities such as probiotics and bismuth should be investigated in addition to anti-biotherapy [25,26].

4. Conclusion

A complete blood count is a low-cost, easily accessible test that may be conducted at any medical facility. In our study, the neutrophil-to-lymphocyte ratio was shown to be greater in HP (+) cases based on the parameters observed in the total blood count. We believe that this measure might be used to monitor patients during and after therapy, but additional research with larger sample sizes is needed to assess changes in neutrophil-to-lymphocyte ratio as a follow-up indicator following successful HP eradication therapy. Furthermore, we would like to point out that antibiotic resistance may be a significant issue in the eradication of HP (+) patients, and that extensive and prospective studies are required in this respect.

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