

The correlation between tissue *Helicobacter pylori* severity and the increase in serum neutrophil/lymphocyte ratio in patients with active chronic gastritis.

Yahya Atayan^{1*}, Payam Hacisalihoglu²

¹Department of Gastroenterology, Gümüşhane State Hospital, 29100 Gümüşhane, Turkey

²Department of Pathology, Medical Faculty, Yeni Yüzyıl University, Gaziosmanpaşa Hospital, Turkey

Abstract

Introduction: *Helicobacter pylori* are a microaerophile gram-negative bacteria and the most frequent factor of chronic gastritis. Recently, there has been an inclination to various non-invasive tests to determine the severity of *H. pylori* infection in the gastric tissue. The serum neutrophils/lymphocytes rate (NLR) is a simple, safe, non-invasive and active inflammation reagent. The purpose of this study is examining the correlation between the increase in the positivity/severity of *H. pylori* infection and the increase in the NLR.

Material and method: 149 patients were included into the study by considering the Sydney criteria in accordance with *H. pylori* severity degrees in 3 groups; Mild (n=49), Moderate-Severe (n=67) and Severe (n=33). A Control Group was also formed (n=22) with negative *H. pylori* by three experienced pathologists.

Result: It has been determined that the severity has increased among the groups with *H. pylori* positive as regard to the increase in serum NLR (r: 0.295, p: 0.017), there has been a significant correlation has been determined between the Control Group and the Moderate-Severe patients (p:0.014), the Severe patients (p:0.002).

Conclusion: It is suggested that the serum NLR, which can be used in order to predict the severity of the *H. pylori* Infection in patients with chronic gastritis, can be a practical, inexpensive and non-invasive test.

Keywords: *Helicobacter pylori*, Serum neutrophils/lymphocytes rate, Chronic gastritis.

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Introduction

Currently *H. pylori* infection is prevalent in 50% of the world's population [1]. Chronic gastritis associated with *H. pylori* infection is characterized histologically by the presence of lymphoid follicle hyperplasia, intestinal metaplasia and neutrophil infiltration to the lamina propria in varying degrees [2]. According to the Sydney Gastritis Classification System, the increase in neutrophil predominant inflammatory cells represents acute gastritis, while the increase in chronic inflammatory cells (lymphocytes and plasmacytes) represents chronic gastritis [3]. Due to the fact that Sydney Gastritis Classification System requires an invasive procedure, there is an inclination to various non-invasive tests in order to predict the severity of *H. pylori* infection. Serum neutrophil/lymphocyte ratio (NLR) is a simple, safe, relatively non-invasive acute inflammation marker [4]. The aim of our study is to determine the correlation between the severity of *H. pylori* infection and active and chronic gastritis, and the increase in serum NLR in patients with chronic *H. pylori* gastritis.

Materials and Methods

We retrospectively reevaluated the histories, the complete blood count (CBC) test results and the pathology reports of 450 patients who had undergone gastroscopic examination due to dyspeptic complaints in our gastroenterology unit between 2014 and 2015. The endoscopic biopsies were taken from the gastric antrum by an experienced gastroenterologist and were interpreted by an experienced pathologist. Severity of active and chronic gastritis and *H. pylori* infection were scored using a 3 scale scoring system as "mild, moderate and severe" according to the Sydney Gastritis Classification System. Glandular atrophy and intestinal metaplasia were also noted in the pathology reports. 149 patients with active, chronic *H. pylori* gastritis without any other concomitant inflammatory disorders were included in our study. A control group consisting of 22 subjects with dyspeptic complaints who had undergone gastroscopic biopsy was also included. The subjects in the control group had no histopathologically determined *H. pylori* infection or gastritis nor did they have any other known inflammatory disorders. The serum NLRs of the 171 patients enrolled in our study were calculated according to the results of

the CBC tests performed prior to the gastroscopic biopsy procedures. Using the SPSS 17 program, the Pearson Correlation Rates were performed and the statistical analysis of the patient and control groups was compared.

Results

Eighty (47.6%) of the 171 patients were male, and 91 (53.3%) were female. The average age of the male patients was 58, the female patients was 50. According to the histopathological examination, the gastritis activity score of 50 patients (33.6%) was determined to be mild, whereas that of 63 patients (42.3%) were moderate, and of 36 patients (24.2%) were severe. The severity of the *H. pylori* infection was determined to be mild in 49 patients (32.9%), whereas 67 patients (45%) were moderately, 33 patients (22.1%) were severely infected by *H. pylori*. Forty patients (26.8%) had mild, 75 patients (50.3%) had moderate and 34 patients (22.8%) had severe chronic gastritis.

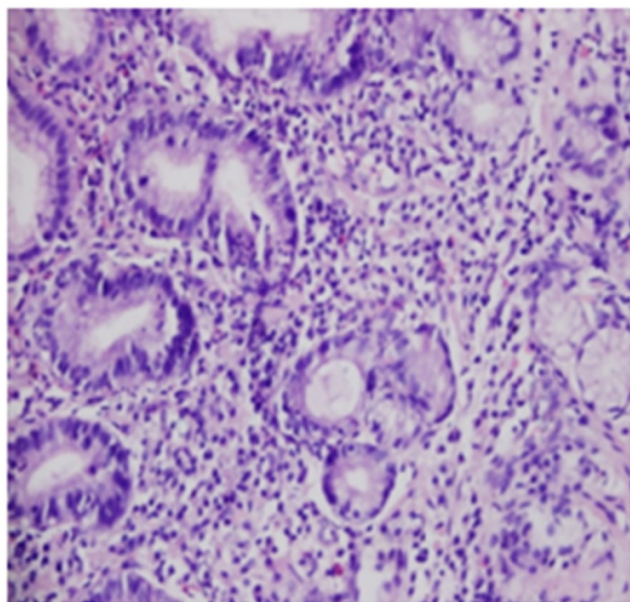


Figure 1. Haematoxylin & eosin 400X photomicrograph image of a case with severely active chronic gastritis shows greater than 2/3 of the gastric glands to be infiltrated by neutrophils.

The control group consisted of 22 subjects with dyspeptic symptoms who had undergone gastroscopic examination and biopsy and revealed no active, chronic gastritis or *H. pylori* infection according to the histopathological interpretation. The mean serum NLR value of the patients who were mildly infected by *H. pylori* was 1.55. This rate was 2.04 in moderately infected patients, 2.15 in severely infected patients and 1.52 in the control group (Table 1). Our study determined a correlation between the increase in the severity of tissue *H. pylori* positivity (mild, moderate and severe) and the increase in serum NLRs of the patients ($r:0.295$, $p:0.017$, Table 2). There was no significant correlation between the increase in the serum NLRs of the control group and the mildly infected patients ($p:0.3$) however, we determined a statistically significant correlation between the increase in serum NLRs of

the control group and the patients who were moderately and severely infected by *H. pylori* ($p:0.014$, $p:0.002$, respectively). We also determined a statistically significant correlation between the severity of *H. pylori* infection and gastritis activity and the chronicity scores of the patients in our study ($r:0.309$, $r:0.226$, $p:0.0005$, $p:0.006$, respectively) (Table 2).

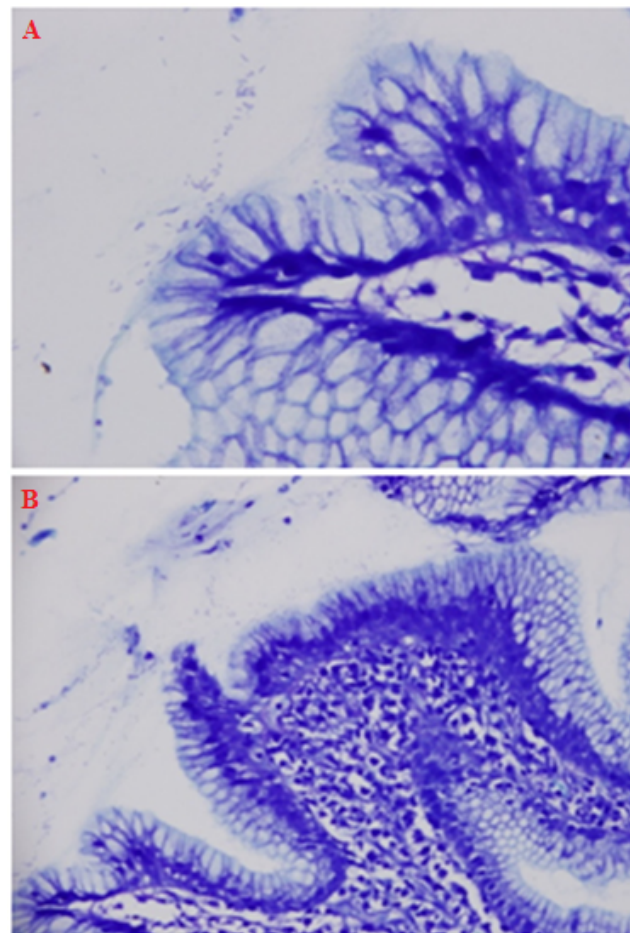


Figure 2. a, b. Giemsa 400X (a) and giemsa 1000X (b) photomicrograph images of a case with severe *H. pylori* infection show *H. pylori* microorganisms cluster over >2/3 of the foveolar epithelium.

Discussion

H. pylori is a microaerophilic gram-negative bacteria and the most common human pathogen in our century. It has been determined to be colonized in almost half of the world's population [1]. *H. pylori* is the most common etiologic factor of chronic gastritis [5]. The bacteria have a predilection for the gastric antral mucosa because it can reproduce more easily in the mucus secreting areas of the stomach. *H. pylori* has virulence factors which play a role in the pathogenesis of the infection, such as kinase inhibitors, which also take part in the loss of polarity and elongation in the gastric epithelial cells. Additionally, proinflammatory cytokines are released, resulting the activation of neutrophils which play a major role in the active inflammation [6,7]. While neutrophils play a role in the active inflammation in acute gastritis; lymphocytes and plasma cells accompany the inflammatory process in chronic gastritis

[8]. According to the Sydney Gastritis Classification and Rating System, the severity of the inflammatory activity in acute gastritis is assessed by the infiltration of neutrophils into the gastric crypts, and the severity of chronic inflammation is determined by the infiltration of lymphocytes into the lamina propria.

Table 1. The correlation between the severity of *H. pylori* infection and serum NLRs of the active, chronic gastritis patients and the control group.

Patient groups	The number of patients	Mean NLR	Minimum	Maximum
Mild <i>H. pylori</i> infection	49	1.5578	0.60	2.38
Moderate <i>H. pylori</i> infection	67	2.0458	0.70	4.9
Severe <i>H. pylori</i> infection	33	2.1512	1.00	5.6
Control group (not infected with <i>H. pylori</i>)	22	1.5202	0.7	2.24

H. pylori: *Helicobacter pylori*
 NLR: Neutrophil/lymphocyte ratio

The severity of *H. pylori* infection is assessed by the infiltration of the microorganisms in the gastric foveolar

Table 2. The correlation between gastritis activity, chronicity scores, the severity of *H. pylori* infection and the increase in serum NLRs of the patients.

Patient groups		Severity of <i>H. pylori</i> infection	Severity of active gastritis	Severity of chronic gastritis	Increase in serum NLR values
<i>H. pylori</i> infection n: 149	P. Correlation (r)	-	0.309	0.226	0.295
	p value	-	0.0005	0.006	0.017
Active gastritis n: 149	P. Correlation(r)	0.309	-	0.385	-0.154
	p value	0.0005	-	0.0005	0.061
Chronic gastritis n:149	P. Correlation(r)	0.226	0.386	-	-0.037
	p value	0.006	0.0005	-	0.653

P. Correlation: Pearson correlation
 NLR: Neutrophil/lymphocyte ratio

Due to the fact that Sydney Gastritis Classification System is associated with an invasive procedure, in recent studies, relatively non-invasive tests have started to be used to determine the severity of *H. pylori* infection in gastritis patients. In previous years, Karttunen et al. [14], stated that mucosal inflammation due to *H. pylori* infection is reflected in the amount of peripheral blood leucocytes. In 2004, serum NLR is determined to be an economic, relatively non-invasive acute inflammation marker by Avanzas et al. for the first time, in acute myocardial infarction patients [4]. Later on, in 2014, in a study conducted by Farah et al. [15], it was determined that there was a statistically significant difference between the serum NLRs of the patients with chronic *H. pylori* gastritis detected by urea breath test and the gastritis patients without *H.*

epithelium [3]. In our study, the severity of *H. pylori* infection is scored by a triple scale as “mild, moderate and severe”, according to the Sydney Gastritis Classification System (Figures 1 and 2). In a study of Stolte et al. [9], conducted with 240 patients with chronic *H. pylori* gastritis, a statistically significant correlation is determined between the increase in the tissue *H. pylori* colonization and activity of gastritis. In a study of Duarte et al. [10], including 261 patients with chronic gastritis, it was determined that there was a significant correlation between the severity of *H. pylori* colonization and chronic inflammation. Additionally, in another study, Faigel et al. [11], stated that the presence of acute and/or chronic gastritis is correlated with the presence of *H. pylori* in gastric antral mucosal tissue. Similarly, in a study conducted by Fared et al. [12], among 150 patients with chronic gastritis, it was reported that there was a significant correlation between the tissue *H. pylori* intensity and neutrophil activity. In another study, Tanka et al. [13], determined that the intensity of *H. pylori* colonization is significantly correlated with the neutrophil activity and chronic inflammation. In our study, consistent with the literature, we determined that there is a statistically significant correlation between the severity of *H. pylori* infection and the severity of active and chronic gastritis (r: 0.309, 0.226; p: 0.0005, 0.006, respectively) (Table 2).

pylori infection. Jafarzadeh et al. [16], stated that elevated serum leucocyte counts and NLR can be a marker of inflammation and infection among *H. pylori* infected peptic ulcer patients. The authors found a significant difference between the mean serum neutrophil count and serum NLRs of the peptic ulcer patients infected by *H. pylori* and the *H. pylori* negative control group.

In our study, in consistence with the literature, we determined a statistically significant correlation between the severity of *H. pylori* infection in mild and moderately scored patient groups, and the increase in their serum NLRs (r:0.295, p:0.017, Table 1) however, we did not find a significant difference in the increase in serum NLRs between the patients who had moderate and severe *H. pylori* infection. Similarly, in terms of

increase in serum NLR, we found no significant difference between the mildly infected patients and the control group but we determined a significant difference between that of the patients with moderate and severe *H. pylori* infection and the control group. (p:0.3, p:0.014, p:0.002 respectively). As a conclusion of our study, we suggest that serum NLR may be used to predict the severity of *H. pylori* infection in patients with chronic gastritis during and at the end of the therapy periods and it can be a practical, safe, inexpensive and a relatively non-invasive method.

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*Correspondence to

Yahya Atayan
 Department of Gastroenterology
 Gümüşhane State Hospital
 Turkey