

Relationship between the Level of *Helicobacter pylori* and Number of Platelets in Non-ITP Patients Who Underwent Gastroscopy

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Abstract

Purpose: To investigate both the presence of *H. pylori* in non-ITP patients who had not undergone *H. pylori* eradication, and also its relationship (if any) with the number of platelets. **Methods:** This retrospective study was performed with a total of 220 cases aged between 18 and 65 years who had undergone gastroscopy. *H. pylori* levels of the participants were investigated, and concurrently their hemograms were analyzed, and their platelet counts were performed. At the same time, cases in the *H. pylori* positive arm were compared with subgroups categorized based on their degree of positivity. **Results:** A statistically significant difference was not detected between platelet counts of the cases based on their *H. pylori* levels ($p = 0.583$). A statistically significant difference was detected between *H. pylori* levels, and distribution of histopathological diagnosis of the cases ($p = 0.001$; $p < 0.01$). **Conclusion:** Our study results revealed that in cases where any primary or secondary factor which might affect platelets is absent, the presence of *H. pylori* has not any effect on platelet counts.

Keywords

Helicobacter pylori, Immune Thrombocytopenia, Platelets

1. Introduction

Helicobacter pylori (*H. pylori*), a gram-negative spiral bacterium that colonizes the human stomach, is globally known as a causative agent of many gastrointestinal diseases and a risk factor for the development of gastric cancer and lymphoma. *H. pylori* causes one of the most common human chronic infections, being present in the gastric mucosa of more than 50% of the world population

[1]. Infection has also been associated to non-digestive diseases such as coronary heart disease, acne rosacea, chronic idiopathic urticaria, hematological disorders, and immune thrombocytopenia (ITP) [2]. The prevalence of *H. pylori* is variable in the population, reaching up to 80% [2].

Platelets have important roles in hemostasis. The normal platelet count ranges between $100 \times 10^9/L$ and $450 \times 10^9/L$ [3]. Circulating lifetime of platelets is ten days and almost 1/3 of platelets are seized in the spleen [3]. Consequently, a continuous balance between production and consumption is essential. Generally defined as a platelet count less than $150 \times 10^9/L$, thrombocytopenia is caused by increased destruction or consumption, splenomegaly, and decreased production due to bone marrow suppression or failure [4]. Besides the contribution of age, gender and genetic factors are known to affect the platelet count.

Successful eradication against *H. pylori* had been increasingly demonstrated to recover platelet counts in patients with ITP [5], and reports on the long-term outcome of this established treatment have been published [6] [7]. In contrast, Matsukawa *et al.* reported a reduction in platelet counts 8 weeks after the successful eradication therapy for the pathogen in non-ITP patients [8].

The aim of the present study was to investigate both the presence of *H. pylori* in patients without primary and secondary disease which will affect the number of platelets who had not undergone *H. pylori* eradication, and also its relationship (if any) with the number of platelets.

2. Material and Method

Study Design: This retrospective study was performed with a total of 220 cases aged between 18 and 65 years who had undergone gastroscopy. The cases were grouped according to age, gender, histopathological diagnosis (*H. pylori* positive, and negative), and platelet counts. *H. pylori* positive patients were sub-grouped within themselves as cases with low, moderate, and higher bacterial densities.

Patients with previously known hematologic malignancy, and/or received radiotherapy or chemotherapy for the treatment of these malignancies, cases with disease which primarily and secondarily related to *H. pylori* infection, patients using drugs which will possibly effect platelet counts, and participants who had used drugs with the intention to eradicate *H. pylori* were excluded from the study.

Outcome Measures: *H. pylori* levels of the participants were investigated, and concurrently their hemograms were analyzed, and their platelet counts were performed. At the same time, cases in the *H. pylori* positive arm were compared with subgroups categorized based on their degree of positivity.

Statistical Analysis: Data were analyzed using the NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. The distribution of categorical variables in both groups was compared using Pearson chi-square, Continuity Correction,

and Fisher's Freeman Halton tests. Data are expressed as mean \pm standard deviation (SD) or median (interquartile range), as appropriate. Statistical significance was assumed for $p < 0.05$.

3. Results

A total of 220 patients met the eligibility criteria for the study. Of the 220 patients (147 females, 73 males) whose charts were reviewed, the mean age was 42.93 ± 12.52 (range 18 to 65) years.

Mean platelet count of the patients was $253,050.00 \pm 56,586.56 \times 10^3/\text{mm}^3$ (range, $122 \times 10^3/\text{mm}^3$ to $400 \times 10^3/\text{mm}^3$). *H. pylori* was not observed in 35.9% ($n = 79$) of the study participants. Low (26.4%, $n = 58$), moderate (21.8%; $n = 48$), high (15.9%; $n = 35$) *H. pylori* densities were seen in respective number of patients. Histopathological diagnoses of the study participants were chronic active gastritis (46.4%; $n = 102$), chronic inactive gastritis (19.1%; $n = 42$), chronic panmucosal gastritis (11.4%; $n = 25$), and chronic superficial gastritis (23.2%; $n = 51$).

A statistically significant difference was not detected among cases as for distribution of mean ages, and genders categorized according to levels of *H. pylori* ($p = 0.098$; $p = 0.398$).

A statistically significant difference was not detected between platelet counts of the cases based on their *H. pylori* levels ($p = 0.583$). Mean platelet counts of *H. pylori*-negative ($258.25 \pm 65.80/\text{mm}^3$), low-positive ($251.74 \pm 49.90/\text{mm}^3$), moderately positive ($253.69 \pm 52.44/\text{mm}^3$) and highly-positive ($242.60 \pm 50.38/\text{mm}^3$) cases were also estimated.

A statistically significant difference was detected between *H. pylori* levels, and distribution of histopathological diagnosis of the cases ($p = 0.001$; $p < 0.01$). Chronic active gastritis was most frequently observed in cases with high *H. pylori* levels relative to those without ($p = 0.001$; $p < 0.01$). Chronic inactive gastritis was observed at significantly higher rates in whom *H. pylori* was not observed when compared with cases with low, moderate, and high *H. pylori* levels ($p = 0.001$; $p = 0.001$; $p = 0.001$; $p < 0.01$). Similarly, in patients who had low *H. pylori* densities, chronic inactive gastritis was detected at statistically significantly higher rates when compared with patients with moderate, and high levels of *H. pylori* ($p = 0.008$; $p = 0.023$; $p < 0.05$). Chronic superficial gastritis was observed at a significantly lower rate in cases without *H. pylori* when relative to those with low, and moderate levels of *H. pylori* ($p = 0.015$; $p = 0.018$; $p < 0.05$). Similarly, chronic superficial gastritis was observed at a remarkably, though not significantly lower when compared with low, and moderate levels of *H. pylori* ($p = 0.084$; $p = 0.086$; $p > 0.05$) (Table 1) (Figure 1).

A statistically significant difference was not detected between *H. pylori*-negative cases, and cases with lower *H. pylori*-positivity ($p = 0.511$; $p > 0.05$). A statistically significant difference was not found between *H. pylori*-negative, and moderately positive cases ($p = 0.667$; $p > 0.05$). Platelet counts were $16,000/\text{mm}^3$ higher in *H. pylori*-negative cases when compared with highly positive-cases

Table 1. Evaluation of platelet counts and histopathological diagnoses based on levels of *Helicobacter pylori*.

	Levels of <i>Helicobacter pylori</i>				p Value
	Negative (n = 79) n (%)	Low (n = 58) n (%)	Moderate (n = 48) n (%)	High (n = 35) n (%)	
Chronic active gastritis	26 (32.9%)	28 (48.3%)	24 (50.0%)	24 (68.6%)	*0.001**
Chronic inactive gastritis	34 (43.0%)	8 (13.8%)	0 (0.0%)	0 (0.0%)	
Chronic panmucosal gastritis	8 (10.1%)	3 (5.2%)	8 (16.7%)	6 (17.1%)	
Chronic superficial gastritis	11 (13.9%)	19 (32.8%)	16 (33.3%)	5 (14.3%)	

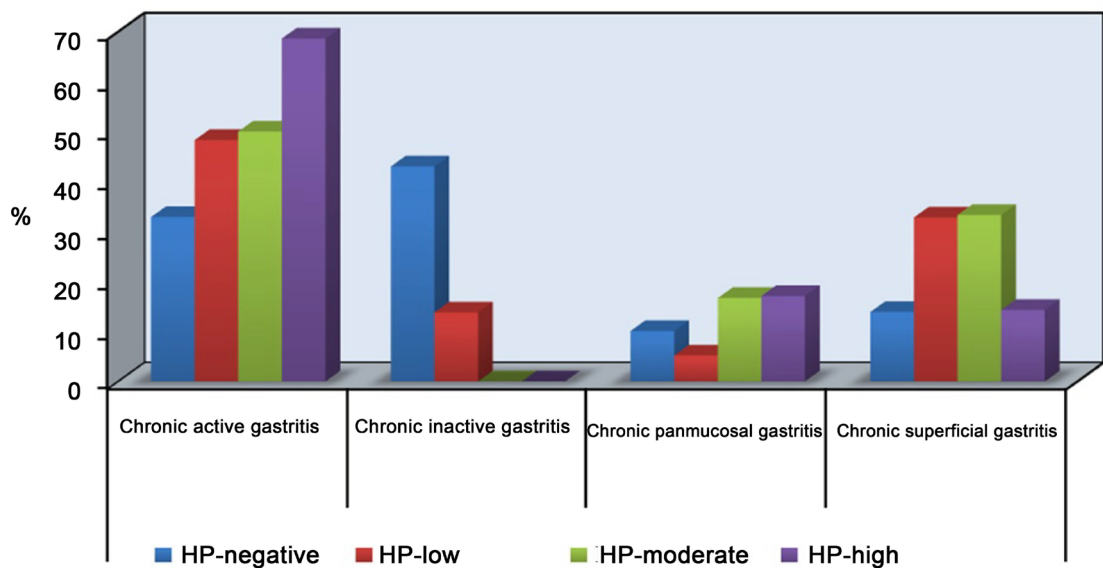


Figure 1. Distribution of histopathological diagnoses based on levels of *Helicobacter pylori*.

without any statistically significant intergroup difference ($p = 0.169$; $p > 0.05$).

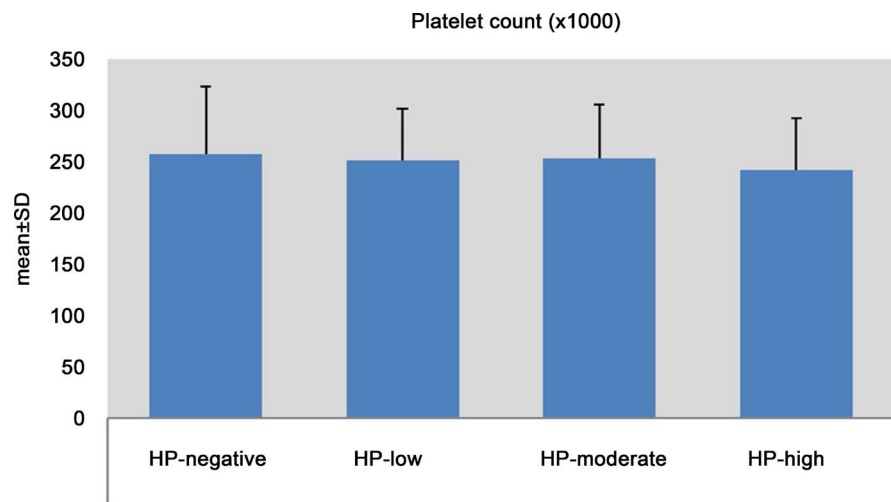
A statistically significant difference was not detected between cases with low, and moderate levels of *H. pylori* positivity regarding platelet counts ($p = 0.846$; $p > 0.05$). Still platelet counts in cases with low, and high levels of *H. pylori*-positivity did not differ statistically significantly ($p = 0.396$; $p > 0.05$). Also, platelet counts in cases with moderately, and highly-positive *H. pylori* did not differ statistically significantly ($p = 0.336$; $p > 0.05$) (Table 2) (Figure 2).

4. Discussion

The aim of our study was to investigate if any correlation exists between *H. pylori* level, and platelet counts in patients who had undergone gastroscopy, and hadn't any disease which might affect platelet counts. In the literature, many studies have investigated the impact of *H. pylori* eradication on platelet counts, however any study which evaluated the relationship between platelet counts and *H. pylori* levels has not been encountered. In the present study, we have found that presence of *H. pylori*, and degree of positivity were independent from age, and gender. In accordance with the literature, *H. pylori* was detected most fre-

Table 2. Evaluation of platelet counts based on levels of *Helicobacter pylori*.

	<i>p</i> Value
HP-negative vs. HP-low	0.511
HP-negative vs. HP-moderate	0.667
HP-negative vs. HP-high	0.169
HP-low vs. HP-moderate	0.846
HP-low vs. HP-high	0.396
HP-moderate vs. HP-high	0.336

**Figure 2.** Distribution of platelet counts according to levels of *Helicobacter pylori*.

quently in patients in whom we detected *H. pylori*-positivity. *H. pylori* density was at its lowest level in patients with chronic inactive gastritis.

In literature, in chronic ITP patients, increase in the platelet count was observed by the eradication of *H. pylori* [9] [10] [11] [12] [13]. Because of this increase seen in the platelet counts, *H. pylori* eradication has been debated as a first-line treatment. Suvajdzić *et al.* performed *H. pylori* eradication in 23 patients among 39 *H. pylori*-positive cases with diagnosis of chronic ITP, and revealed statistically significant increase in platelet counts in these patients. Increase in platelet counts was not observed in untreated *H. pylori*-positive patients or *H. pylori*-positive patients who had not undergone eradication therapy [9]. Noonavath *et al.* measured peripheral platelet counts of 16 patients with diagnosis of chronic ITP at 6. weeks, 3., and 6. months, and significant increases in platelet counts were detected when compared with baseline values [10]. Rostami *et al.* administered eradication treatment to 79 patients with diagnosis of chronic ITP, and *H. pylori* infection, and followed up platelet counts in peripheral blood for 48 weeks. In 62 patients among patients who had completed treatment, *H. pylori* was eradicated. Platelet counts of 48% (30/62) of these patients increased with treatment, while any increase in platelet counts of *H. pylori* negative patients. Increase in platelet counts of the patients who responded to eradication treatment continued for 48 weeks, while in cases unresponsive to eradication

treatment duration of disease decreased significantly [11].

In a randomized controlled study performed by Suzuki *et al.* on 36 patients diagnosed as chronic ITP, potential mechanisms involving the impact of eradication of *H. pylori* in increasing number of platelets was investigated. *H. pylori* positive patients were randomized into eradication, and non-eradication groups. The patients in the eradication group received standard antibiotherapy for *H. pylori* infection. Platelet counts in treated patients increased $50 \times 10^3/\text{microL}$ over pre-treatment values. Virulence factors were analyzed with PCR, and Anti-CagA IgG antibodies were analyzed using ELISA test. Platelet response rates were 46.2%, and 0% in the *H. pylori* eradication, and non-eradication groups, respectively. Platelet response was not found to be related to the presence of *H. pylori* virulence factors, and urease. Anti-CagA antibody titers were significantly higher in responders to treatment relative to nonresponders ($p = 0.04$) [12]. In a study by Kuwana *et al.*, the authors detected that *H. pylori* eradication treatment increased platelet counts in patients with chronic ITP, and response rates to eradication treatment in Japan were higher than those obtained in European countries (*excl.* Italy). Even though pathogenesis of ITP associated with *H. pylori* is still not known, as is known many factors play a role in its mechanism. In their study, Kuwana *et al.* have demonstrated that components of *H. pylori* may imitate molecular structures of platelet antigens. So, they indicated dramatic increase in platelet counts with eradication of *H. pylori* [13]. Many interpretations have been suggested for the pathogenic mechanism, but the phenomenon is still poorly understood [14] [15]. Studies show that the outcome of bacterial eradication may depend on genetic factors of the host, on environmental factors or even on the *H. pylori* strain [15].

In non-ITP patients, eradication of *H. pylori* caused a decrease in platelet counts [8] [16]. These diverse results between patients with and without ITP directed investigators to investigate the mechanism of this phenomenon. In a study performed by Matsukawa *et al.*, gastroscopy was performed in a group of patients with only dyspeptic symptoms, and among them those with *H. pylori* positivity received eradication therapy. At 8th week of the therapy a statistically significant drop in peripheral blood platelet counts was observed ($p = 0.020$) [8]. In another study by Matsukawa *et al.* on 294 patients, 243 patients had undergone successful *H. pylori* eradication, and platelet counts were observed for 3 years after eradication. A significant drop in peripheral blood platelet counts was observed in non-ITP patients [16]. Our patient group had not any primary or secondary disease which might affect platelet counts, and they had not received *H. pylori* eradication therapy. In the comparison between *H. pylori*-positive, and -negative groups, a statistically significant intergroup difference was not detected ($p > 0.05$). Among *H. pylori*-positive cases a statistically significant difference between *H. pylori* levels, and platelet counts was not found ($p > 0.05$).

Limitations of our study include the retrospective design and relatively small number of our series. In addition, some details of history and factors that may influence the outcome may not be completely documented. Due to these restric-

tions, associations should be interpreted with caution.

Our study results revealed that in cases where any primary or secondary factor which might affect platelets is absent, the presence of *H. pylori* has not any effect on platelet counts. In our study a statistically significant difference was not observed between presence, and density of *H. pylori* and platelet counts which supports the assumption suggesting that eradication of *H. pylori*, and variations in platelet counts might be mediated via another mechanism. Re-evaluation of the relationship between *H. pylori* infection, and platelet counts, in the light of more detailed parameters, and larger scale studies will provide a reference value which will be required during treatment planning process.

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