CAN MEAN PLATELET VOLUME INDICATE *HELICOBACTER* POSITIVITY AND SEVERITY OF GASTRIC INFLAMMATION? AN ORIGINAL STUDY AND REVIEW OF THE LITERATURE

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SUMMARY – *Helicobacter pylori* (*H. pylori*) is a common problem and a significant cause of chronic gastric inflammation. *H. pylori*, ongoing gastric inflammation and its severity are the most critical component of precursors of gastric cancer. Hypothetically, every chronic tissue injury activates platelets, and the mean platelet volume (MPV) reflects this action well. The potential relationship between *H. pylori* and platelet count has been shown before. However, there are few and conflicting papers about the relationship between MPV and *H. pylori* related chronic gastric inflammation and its severity. The study aimed to assess any potential relationship between MPV and presence of *H. pylori*, as well as the severity of chronic gastric inflammation. A total of 6890 endoscopic reports were initially evaluated, and a total of 218 dyspeptic patients having undergone upper endoscopy were included. Of these, 118 (54.2%) were *H. pylori* positive and 100 (45.8%) were *H. pylori* negative. At least four gastric biopsies were obtained and evaluated according to Sydney classification. Age, gender, hemoglobin, mean corpuscular volume, ferritin, serum iron and C-reactive protein, as well as endoscopic findings were also recorded. A $p<0.05$ was accepted as significant. The MPV and platelet count did not differ between *H. pylori* positive and *H. pylori* negative groups of patients ($p>0.05$). There were no differences and correlation between MPV and gastric inflammation severity according to Sydney classification ($p>0.05$). When stratifying MPV as <9.15 fL and >9.15 fL, there was no difference between *H. pylori* positive and *H. pylori* negative groups either ($p>0.05$). In this study, we found no relationship between MPV and presence of *H. pylori* or severity of gastric inflammation. Although there are still conflicting publications on this issue, in our opinion and according to the results of this study, MPV is not a suitable marker for evaluation of gastric inflammation severity, being *H. pylori* either positive or negative.

Key words: *Mean platelet volume; Helicobacter pylori; Gastritis; Inflammation*

Introduction

Helicobacter pylori (*H. pylori*) infection and related clinical conditions such as chronic gastric inflammation, gastric cancer, and immune thrombocytopenia are still growing clinical problems all over the world be-cause of some well-known difficulties in their treatment, diagnosis, and management[1-4]. Moreover, it may not be possible to be recognized by patient or clinicians unless presented with a noisy clinical picture as peptic ulcer bleeding because it often leads to slow chronic infection without manifesting itself[5]. It is possible to diagnose *H. pylori* infection by noninvasive tests, as recommended by well-known guidelines[6]. However, the degree of chronic gastric inflammation that is commonly evaluated by Sydney classification and the con-

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ditions that increase susceptibility to stomach cancer can almost only be understood by upper endoscopic biopsies, not yet with noninvasive tests[6]. Nevertheless, even nowadays, the possibility of upper endoscopy is still not available everywhere and is not suitable for every patient, while histologic examinations of endoscopic biopsies are expensive and time-consuming[7]. Consequently, a new, simple, reliable and straightforward indicator of chronic inflammation of the stomach such as a blood marker is needed to overcome such difficulties[8].

It is well-known that acute or chronic inflammation occurring in any part of human tissues activates platelets *via* some specific cytokines, chemokines and immune mediators stimulated by various cells[8]. The mean platelet volume (MPV) is a part unit of complete blood count analysis that represents mainly platelet induction and aggravation, and that can easily be obtained in daily routine. It has recently been studied as an inflammatory marker, a disease severity index and a predictor of prognosis in a variety of acquired diseases including localized psoriasis, rheumatoid arthritis, cardiovascular diseases, stroke, Graves' disease and intrahepatic cholestasis[9-13]. Because of these remarkable studies, it is claimed that MPV can be a promising and potential blood marker of inflammation. However, although serum MPV is found to be statistically different in control groups in most of the clinical trials, some results of the studies, particularly those investigating local inflammations such as Graves' disease, psoriasis and rheumatoid arthritis, are conflicting and unsatisfactory[13-15].

Chronic gastric inflammation is an example of local chronic inflammation. *H. pylori* is one of the most important reasons for this. Hypothetically, every chronic tissue injury activates platelets, and MPV reflects this action well. The potential relationship between *H. pylori* and platelet count has been shown before. However, there are few and conflicting papers about the relationship between MPV and *H. pylori* related chronic gastric inflammation and its severity. There are only two studies in the field, and confusing results are presented as well. Topal *et al.*[9] found that no statistically significant difference was obtained and there was no correlation and relationship between MPV and *H. pylori* intensity or gastric inflammation severity, whereas Umit and Ümit[16] report that the mean platelet count was lower in *H. pylori* positive patients than in *H. pylori* negative patients, whereas the

mean MPV was higher in *H. pylori* positive group than in *H. pylori* negative group.

In this study, we aimed to evaluate the relationship between the mean MPV and gastric inflammation severity, being *H. pylori* positive or negative. With this study, we hope to make an important contribution to the literature by clarifying the topic that has been presented with controversial results so far.

Material and Method

This study was conducted at the Gastroenterology Department, Zonguldak Bülent Ecevit University Medical Faculty, a tertiary reference center for all endoscopic procedures. A total of 6890 endoscopic reports and case files from January 2013 to June 2017 were reviewed meticulously. The main criteria for inclusion in the study were as follows: dyspeptic patients aged 18-85 who had no cancer history and gastric surgery in the past; patients with upper gastrointestinal endoscopy and at least four biopsies taken from the antrum and corpus or small curvature of stomach; patients with gastric biopsy specimens stained with hematoxylin-eosin and assessed in accordance with Sydney classification; and patients that had complete blood count within the normal range before upper endoscopy and standard ferritin, iron, and C-reactive protein (CRP) levels. The main exclusion criteria were as follows: patients with gastric or colon dysplasia or polyps and any malignancy; patients with acute phase responses such as high level of CRP and ferritin and leukocytosis; patients with any chronic disease such as chronic hepatitis B or C, cirrhosis, rheumatologic diseases; patients with any hematologic disease; patients with malabsorption syndrome; and patients using special medication that could change platelet count. All laboratory blood tests were accepted if they were taken before upper endoscopy by international guidelines. Histopathological reports were accepted if the investigation was made according to Sydney classification. *H. pylori* infection and other parameters were recorded as the degree of intensification and severity as none, mild (+), moderate (++) and severe (+++). This study was conducted in accordance with the International Helsinki Declaration. The local ethics committee approved this work (code 2017-07-13). A written informed consent was obtained from all patients having participated in the study.

Table 1. Basic study demography

	H. pylori (+)	H. pylori (-)	p
Patients (n, %)	118 (54.2%)	100 (45.8%)	0.799
Age (yrs)	52.8±13.6	52.3±15.5	0.724
Gender (male/female)	64/54	55/45	0.910
Platelet x10⁶ μ/mL (NR: 140-400)	250±58.8	243±49.7	0.724
MPV (fL) (NR:7-10.5)	8.67±1.02	8.68±0,81	0.998
Hemoglobin (mg/dL) (NR: 12-16.5)	14.1±1.23	14.2±1.15	0.495
MCV (fL) (NR:80-99)	87.2±3.31	87.7±3.79	0.330
Ferritin (mg/dL) (NR:11-308.6)	46.2(9.5-253)	43.2(11-323)	0.903
Serum iron (μg/dL) (NR: 60-180)	77±27.9	76,62±30.07	0.923
CRP (mg/dL) (NR: 0-8)	2.54±1.46	3.06±1.12	0.854
Endoscopic findings:			
ESG	45	69	NS
lower esophageal sphincter dysfunction + ESG	65	56	
ESG + ulcer or erosion of bulbs	8	5	

H. pylori = *Helicobacter pylori*; NR = normal range; NS = nonsignificant; MPV = mean platelet volume; MCV = mean corpuscular volume; CRP = C-reactive protein; ESG = erythematous superficial gastritis; MPV was not different between *H. pylori* positive and *H. pylori* negative groups (p>0.05).

Statistical analysis

On statistical analysis, the Windows compatible SPSS 18 (Chicago, Illinois, USA) program was used. First, it was searched whether all data distributions were normal or not with at least three tests including Kolmogorov Smirnov test; then appropriate statistical methods were selected. Normally distributed data were presented as mean ± standard deviation, whereas the data without normal distribution were introduced as median with minimum-maximum levels. The Mann Whitney U, one way ANOVA, independent samples test, Student's T-test and χ²-test were used to compare data groups. The level of statistical significance was set at p<0.05.

Results

A total of 218 patients were enrolled in this study. The main evaluation was initiated by dividing the group into *H. pylori* positive and *H. pylori* negative patients. There were 118 (54.2%) *H. pylori* positive and 100 (45.8%) *H. pylori* negative patients. Age, gender, hemoglobin, mean corpuscular volume, ferritin, CRP, serum iron, endoscopic findings, and platelet count were similar in both groups (p>0.05 all) (Table 1). The MPV and platelet count did not differ between *H. pylori* positive and *H. pylori* negative groups (p>0.05). There was no difference in the mean MPV levels between the subgroups of inflammation according to Sydney classification (p>0.05 all). There was no correlation between the mean MPV levels and the severity of inflammation either (Table 2). When evaluating the mean MPV as <9.15 fL and >9.15 fL with gender matching (according to the study by Icli *et al.*[12]), there were no differences between *H. pylori* positive and *H. pylori* negative groups either (p>0.05 all) (Table 3).

Discussion

In this study, we evaluated the relationship between the mean MPV and chronic gastric inflammation severity, with *H. pylori* positive and negative. Our main findings showed that the mean MPV was not different between *H. pylori* positive and *H. pylori* negative groups (p>0.05), and no statistical correlation and differences were found among the gastric inflammation subgroups, or in the severity of inflammation according to Sydney classification. We analyzed MPV measurement by stratifying <9.15 fL and >9.15 fL groups,

but we found no differences between *H. pylori* positive and *H. pylori* negative groups. The most powerful parts of our work were as follows: we analyzed all patient files very carefully and selected the cases among special

Table 2. Mean platelet volume (MPV) values were not different among inflammation groups, so there was no correlation between MPV and severity of gastric inflammation (p>0.05 all)

Sydney classification (n)	Mean platelet volume (fL) (mean ± standard deviation)	p
Helicobacter pylori (n):		
none (100)	8.68±0.81	
mild (75)	8.75±0.99	NS
modarate (29)	8.46±1.06	
severe (14)	8.71±1.1	
Inflammation (n):		
none (3)	8.46±0.72	
mild (54)	8.6±0.84	NS
moderate (104)	8.71±0.92	
severe (57)	8.69±1.04	
Activation (n):		
none (131)	8.66±0.9	
mild (44)	8.67±0.94	NS
moderate (39)	8.69±1.04	
severe (3)	9.3±0.51	
Intestinal metaplasia (n):		
none (166)	8.67±0.94	
mild (42)	8.65±0.88	NS
moderate (10)	8.85±0.99	
severe (0)	0	
Atrophy (n):		
none (190)	8.67±0.89	NS
existing (28)	8.71±1.18	

NS = nonsignificant

patient groups who had no serious chronic disease except for dyspepsia, and therefore we kept such patients out of the study if it was the smallest factor that could affect the results such as a drug, chronic inflammatory disease, etc.; unlike previous studies, we measured CRP levels in all patients to exclude any acute or chronic inflammation that could affect platelet function. Therefore, even a patient with the smallest CRP elevation was not included in the study; and all endoscopic procedures and histologic examinations were done by the same clinicians having at least ten years of experience in the field. So, the diagnosis of *H. pylori* and gastric inflammation scores were very reliable. The most important limitation of our work was its retrospective design.

Our results were similar to the study by Topal *et al.*[9], but different from the study by Umit and Ümit[16]. In the former involving 114 patients, there was no correlation or difference between the mean MPV and *H. pylori* presence, as well as gastric inflammation severity (p>0.05). Our study had a higher number of patients than the study by Topal *et al.*[9] (218 *vs.* 114), so our results could be more reliable than those reported by these authors. Moreover, they did not consider all factors that might affect MPV and platelet function in their study; unlike them, we did take in consideration important parameters such as CRP and iron storage status. The study by Umit and Ümit[16] that included 4823 patients found the mean MPV and platelet count to be statistically different between *H. pylori* positive and *H. pylori* negative groups (p<0.001). They also report that 20.5% of *H. pylori* positive patients had a higher MPV value (>10 fL), while 2.8% of *H. pylori* negative patients had high MPV (>10 fL), and this finding was statistically significant (p<0.001). These results are completely different from the results of our study and the study by Topal *et al.*[9]. Therefore, we considered this result as conflicting and

Table 3. MPV evaluation as <9.15 fL and >9.15 fL with gender-matched subjects (according to the study by Icli et al.[12]) yielded no statistical difference between H. pylori positive and negative groups (p>0.05)

	Female (n=99)		p	Male (n=119)		p
	MPV(fL) <9.15 (n=72)	MPV(fL) >9.15 (n=27)		MPV(fL) <9.15 (n=82)	MPV(fL) >9.15 (n=37)	
H. pylori (+)	38 (52.8%)	16 (56.3%)	0.726	40 (48.8%)	24 (64.9%)	0.153
H. pylori (–)	34 (47.2%)	11 (40.7%)		42 (51.2%)	13 (35.1%)	
Total (218%100)	72 (100%)	27 (100%)		82 (100%)	37 (100%)	

H. pylori = *Helicobacter pylori*; MPV = mean platelet volume; fL = femtolitre

Table 4. Summary of studies investigating the relationship between MPV and H. pylori related gastric inflammation severity

Author	Patients (n) (f/m)	Year	Age (yrs) (mean)	MPV(fL) (mean)	Plt	p	Result/Conclusion
Topal *et al.*	114 (73/41	2010	38.5±13.12	8.8±1.4	–	>0.05	MPV level cannot be used as a simple marker to reflect *H. pylori* intensity and severity of inflammation
Umit and Ümit	4823 (2233/2600)	2015	60(18-80)	8.79±1	247±82	<0.001	Higher MPV values were observed in *H. pylori* positive patients
Güçlü *et al.*[21]	199 (111/88)	2017	46.5±14	10.1±0.7	270±79	>0.05	There were no differences between MPV and total *H. pylori*-negative patients and *H. pylori* positive patients
Akar (present study)	218 (99/119)	2018	52.8±13.6	8.67±1.02	250 ±58	>0.05	There were no differences in mean MPV between *H. pylori* positive and negative patients or among chronic gastric inflammation subgroups

H. pylori = Helicobacter pylori; MPV = mean platelet volume; fL = femtolitre; Plt = platelet; f = female; m = male
Topal *et al.*[9] found that there was no relationship between mean MPV and chronic gastric inflammation severity being *H. pylori* positive or negative, whereas Umit and Ümit[16] claimed that higher MPV values were observed in *H. pylori* positive patients

discordant information due to some reasons. In their study, Umit and Ümit[16] included 4823 patients who had undergone upper endoscopy, but no endoscopic findings are reported. According to that study, it is doubtful how the *H. pylori* diagnosis was obtained. Another problem associated with that study was that it was carried out between 2004 and 2014 (ten years), so this long working time could have caused data loss or changes, thus the data could not be homogeneous. Consequently, we did not find the results reported by Umit and Ümit[16] as reliable. In Table 4, we summarized the studies of MPV and *H. pylori* presence, as well as gastric inflammation severity.

The MPV has recently become a favorite topic of many researchers as a simple, easy-going and inexpensive marker of chronic inflammation-related diseases[14,17,18]. In many studies involving systemic diseases such as diabetes mellitus or Behçet disease, the mean MPV was statistically different between patient group and control group[19,20]. However, this difference was not shown in localized inflammatory diseases such as Graves' disease or rheumatoid arthritis[13,15].

Up to now, *H. pylori* is still a hot topic, and it continues to be the subject of many studies. Nowadays, MPV has been presented as a new, promising and straightforward marker of inflammation. However, there are only a few studies demonstrating a relationship between MPV and *H. pylori*. Conflicting results have been presented so far. These studies are briefly summarized in Table 4 with essential demographic data and results/conclusions. Our study is the fourth paper evaluating MPV and gastric inflammation severity, being *H. pylori* positive or negative. Our work contributes to the literature by clarifying this issue, which has a small number of contradictory information, as clearly seen in the literature summary. To us, when the inflammation is located at a highly limited site such stomach and anterior part of the eye, there is not enough cytokine and immunomodulator release, thus platelet activation from bone marrow is not so prominent to activate MPV[8].

In conclusion, although MPV has recently emerged as a marker of inflammation in many systemic diseases, there is still an ongoing debate about its diagnostic usefulness and benefit in daily clinical practice. This paper is the fourth study to investigate the relationship between MPV and *H. pylori* related chronic gastric inflammation severity. Our results show that MPV is not a useful marker of chronic gastric inflammation severity, being *H. pylori* positive or negative.

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Sažetak

MOŽE LI VOLUMEN TROMBOCITA UKAZIVATI NA POZITIVAN STATUS NA *HELICOBACTER* I TEŽINU UPALE ŽELUCA? IZVORNO ISTRAŽIVANJE I PREGLED LITERATURE

T. Akar

Helicobacter pylori (*H. pylori*) je čest problem i značajan uzrok kronične upale želuca. *H. pylori*, trajna upala želuca i njezina težina su najkritičnija komponenta prekursora raka želuca. Hipotetski, svaka kronična ozljeda tkiva aktivira trombocite, a srednji volumen trombocita (*mean platelet volume*, MPV) dobro odražava njihovo djelovanje. Potencijalni odnos između *H. pylori* i broja trombocita je prikazan ranije. Međutim, postoji i nekoliko suprotnih članaka o odnosu između MPV i kroničnih upala želuca povezanih s *H. pylori* i njihove težine. Istraživanje je imalo za cilj procjenjivati bilo koji potencijalni odnos između MPV i postojanja *H. pylori*, kao i težine kronične upale želuca. U početku je evaluirano 6890 endoskopskih izvješća, a uključeno je ukupno 218 dispeptičnih bolesnika koji su podvrgnuti gornjoj endoskopiji. Od njih je 118 (54,2%) bolesnika bilo pozitivno na *H. pylori*, dok ih je 100 (45,8%) bilo negativno na *H. pylori*. Najmanje četiri želučane biopsije su uzete i ocjenjivane prema klasifikaciji Sydney. Zabilježeni su i dob, spol, hemoglobin, srednji korpuskularni volumen, feritin, serumsko željezo i C-reaktivni protein te endoskopski nalazi. Vrijednost p<0,05 je prihvaćena kao značajna. MPV i broj trombocita nisu se razlikovali između skupina bolesnika pozitivnih i negativnih na *H. pylori* (p>0,05). Također nije bilo razlike i korelacije između MPV i težine upale želuca prema klasifikaciji Sydney (p>0,05). Kada je MPV stratificiran kao <9,15 fL i >9,15 fL, također nije nađena nikakva razlika između skupina bolesnika pozitivnih i negativnih na *H. pylori* (p>0,05). U ovom istraživanju nismo pronašli nikakav odnos između MPV i postojanja *H. pylori*, kao i težine upale želuca. Iako u ovom pogledu još postoje sukobljene publikacije, za nas i ovu studiju MPV nije prikladan biljeg za procjenu jačine želučanih upala, bez obzira je li *H. pylori* pozitivan ili negativan.

Ključne riječi: *Srednji volumen trombocita; Helicobacter pylori; Gastritis; Upala*