Clinics of Oncology

Review Article ISSN: 2640-1037 | Volume 6

Diagnostic Accuracy of Raised Platelet to Lymphocyte Ratio in Predicting Helicobacter Pylori Infection in Patients with Dyspepsia

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Received: 25 Jun 2022
Accepted: 07 Jul 2022
Published: 13 Jul 2022
J Short Name: COO

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Citation:

Khan RTY. Diagnostic Accuracy of Raised Platelet to Lymphocyte Ratio in Predicting Helicobacter Pylori Infection in Patients with Dyspepsia. Clin Onco. 2022; 6(9): 1-5

Keywords:

Helicobacter Pylori; Platelet to Lymphocytes Ratio; H.P Noninvasive Marker

1. Abstract

1.1. Introduction

Helicobacter Pylori (HP) infection is prevalent among patients with dyspepsia in developing countries with low socioeconomic status. The gold standard investigation is invasive method gastric biopsy through upper GI endoscopy, however non-invasive methods (stool for HP antigen) are not reliable up to the mark also need to wait for two weeks without symptomatic treatment. It is important to have a reliable, cost effective and easily accessible non-invasive marker to diagnose patients with H. pylori infection. Several non-invasive laboratory have been predicted in having the role in diagnosis of H.pylori infection. Therefore, the aim of our study was to determine the diagnostic accuracy of platelet to lymphocyte ratio in predicting H.Pylori infection in patients with dyspepsia.

1.2. Methods

This was a cross sectional study which was conducted at Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi from December 2019 to May 2020.Patients of either gender aged between 18 to 65 years with symptoms of dyspepsia for more than two weeks were included in the study. All baseline investigations were performed, including complete blood count, absolute lymphocyte count and platelet count. All patients then underwent endoscopy and gastric mucosal biopsy. The biopsy was reviewed by histopathologist with expertise in gastrointestinal pathology for presence of H. pylori. PLR was derived using predesignated formula. A cutoff of PLR was obtained using ROC and the sensitivity, specificity, PPV, NPV and diagnostic accuracy was obtained for PLR in predicting H.Pylori infection.

1.3. Results

Total number of patients included in the study was 167, among which 90(53.9%) were females Mean age was 35.9±12.2 years. The baseline characteristics showed mean White Blood Cell (WBC) count of 8.4±2.4 x 109/L, absolute lymphocyte count of 2.9±1.7 x 109/L, platelet count (PLT) of 306 ±110 x 109/L .The mean PLR was 135.9±98.4. The neutrophils, platelet count, alanine transaminase and PLR were significantly higher in patients with H.Pylori infection compared to those without H.pylori infection; while TLC and lymphocyte count were significantly lower in the former.Female gender (p-value-0.12) was also significantly associated with H.Pylori infection. Area under ROC of PLR was 0.87 (p-value ≤ 0.001). At a cutoff of ≥118, the sensitivity, specificity, NPV and PPV were 87.36 %, 91.25%, 91.57% and 86.90% respectively for PLR in predicting H.Pylori infection in patients with dyspepsia with diagnostic accuracy of 89.22%.

1.4. Conclusion

In conclusion, this study revealed that raised PLR was significantly associated with H.Pylori infection with an excellent diagnostic accuracy. However, further studies comprising of larger sample size are required to validate this score.

2. Introduction

Helicobacter pylori is a gram-negative bacterium that colonizes the human stomach and can lead to chronic gastritis, peptic ul-

cer, gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma [1]. The route of transmission of infection remains unknown although person-to-person transmission through feco-oral or oral-oral exposure seems most likely [2, 3]. HP is associated with peptic ulcer disease, gastric ulcers, mucosa-associated lymphoid tissue lymphoma, gastric cancer and NAFLD [4, 5]. Although nearly 50% of the population is infected with HP worldwide, the prevalence, incidence, age distribution and sequelae of infection are significantly different in different parts of the world [6]. High prevalence of H. pylori infection in Pakistani population is comparable to the data of other countries that is 73.5% in males and 75.4% in females and increased with increasing age [7].

Helicobacter pylori infection can be diagnosed with the help of tests, which can be divided into non-invasive and invasive. Among the non-invasive tests are the serology for HP infection, stool for HP antigen and urea breath test (UBT). Several biomarkers such as C reactive protein (CRP), neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have also been studied in the past as non-invasive tests for detection of gastric mucosal injury secondary to HP infection and can also be helpful in assessing the severity of HP infection [8] The invasive test consists of upper gastrointestinal endoscopy (UGIE) through which a biopsy specimen is taken for histopathology, culture of HP organism and detection of nucleic acid of HP through polymerase chain reaction (PCR) [9].

However, little work has been done in our country regarding the diagnostic accuracy and the use this relatively simple tool in predicting H.Pylori infection in our population. Therefore, the aim of our study was to determine the diagnostic accuracy of platelet to lymphocyte ratio in predicting H.Pylori infection in patients with dyspepsia.

3. Operational Definitions

3.1. Histopathological diagnosis of H pylori

H. pylori infection was considered positive on gastric biopsy in the presence of thin, curved bacilli staining bluish in color on Giemsa staining, on the surface of gastric mucosa or in the gastric pits.

3.2. Platelet to lymphocyte ratio (PLR):

The ratio was calculated by following formula.It is the ratio of platelet count (n X 103/mm3) to absolute lymphocyte count (n X 103/mm3). The cut off value of >120 would be considered to have HP infection.

$$PNR = \frac{\text{platelet count (n X 103/mm3)}}{\text{Absolute Lymphocyte count}}$$

4. Methodology

This was a cross sectional study which was conducted at Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation Karachi from December 2019 to May 2020.Patients of either gender aged between 18 to 65 years with symptoms of dyspepsia for more than two weeks were included in the study. The patients with present or past history of peptic ulcer disease or gastrointestinal bleed, known coagulation disorder, hematological disorder, celiac disease, chronic kidney disease, malignancy or ongoing intake of immunosuppression and NSAIDs usage for more than 2 weeks and females with heavy menstural blood loss were excluded from the study.

This study was conducted after approval from the Ethical Review Committee (ERC) of the institution. Written informed consent was taken from all patients. A thorough history was taken and complete physical examination of all patients was performed, and the findings were recorded in the structured proforma. All baseline investigations were performed, including complete blood count, absolute lymphocyte count and platelet count. All patients then underwent endoscopy and gastric mucosal biopsy. The biopsy was reviewed by histopathologic with expertise in gastrointestinal pathology for presence of H. Pylori.

The data analysis was performed using SPSS version 22. Quantitative variables such as age, lymphocyte count and platelet count were expressed as mean ± standard deviation. Categorical variables such as gender, presence of H.Pylori on gastric mucosal biopsy were presented as frequency and percentages. Continuous variables were analyzed using the t-test or the Mann Whitney test, while categorical variables were analyzed using the Chi-square or the Fisher exact test. A p value of <0.05 was considered as statistically significant. PLR was derived using the above mentioned formula. A cutoff of PLR was obtained using ROC and the sensitivity, specificity, PPV, NPV and diagnostic accuracy was obtained for PLR in predicting H.Pylori infection.

5. Results

Total number of patients included in the study was 167, among which 90(53.9%) were females while 77(46.1%) were males. Mean age was 35.9±12.2 years. At the time of presentation, forty-one (24.6%) patients were hypertensive while 33(19.8%) had diabetes. Ninety-four (56.3%) had history of dyspeptic symptoms for more than one month. The gross appearance of gastric mucosa on upper GI endoscopy findings was absolutely normal in 124(74.3%) patients while erosions and ulcers were noticed in 29(17.4%) and 14(8.4%) patients respectively. On gastric mucosal biopsy, H.Pylori was noted in 87(52.1%) patients. The baseline characteristics showed mean Hemoglobin (Hb) of 12.2±2.3 g/dL; White blood cell (WBC) count of 8.4±2.4 x 109/L, absolute lymphocyte count of 2.9±1.7 x 109/L, platelet count (PLT) of 306 ±110 x 109/L, serum creatinine of 0.48±0.46 mg/dL and alanine transaminase(ALT) of 26.8±16 U/L. The mean PLR was 135.9±98.4. The neutrophils, platelet count, alanine transaminase and PLR were significantly higher in patients with H.pylori infection compared to those without H.pylori infection; while TLC and lymphocyte count were significantly lower in the former (Table 1). Female gender (p-val-

ue-0.12) was significantly associated with H.pylori infection (Table 2). Area under ROC of PLR was 0.87 (p-value ≤ 0.001) (Figure 1). At a cutoff of ≥118, the sensitivity, specificity, NPV and PPV were 87.36 %, 91.25%, 91.57% and 86.90% respectively for PLR in predicting H.Pylori infection in patients with dyspepsia with diagnostic accuracy of 89.22% (Table 3).

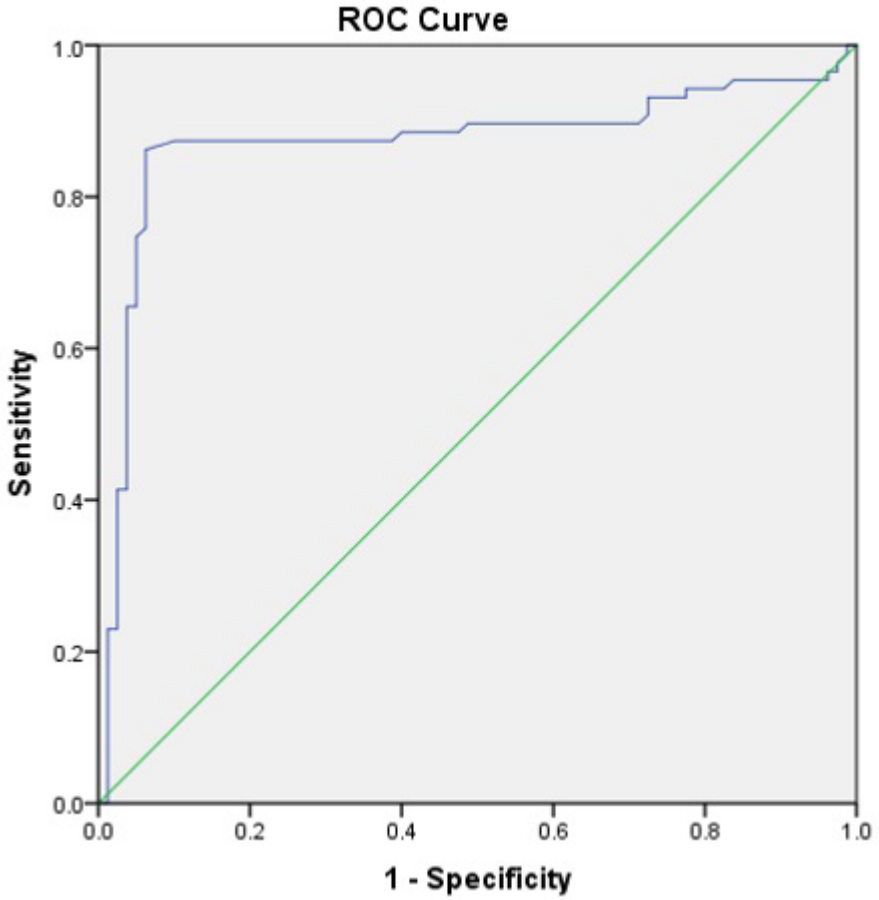

Figure 1: Area under ROC curve for PLR is 0.87(p-value≤0.001)

Table 1: The baseline characteristics in H.pylori positive vs H.Pylori negative group for continuous variables

Variable	H.Pylori Positive (n=87) Mean ± SD	H.Pylori Negative(n=80) Mean ± SD	p-value
Age(years)	34.5 ± 11.2	37.4 ±13.1	0.14
Hemoglobin (Hb)(g/dL)	11.9 ±2.1	12.5 ± 2.5	0.12
TLC(109/L)	7.9 ± 2.29	8.9 ± 2.5	0.009
Absolute Neutrophil count(109/L)	63.6±13.3	53.1±13	≤0.001
Absolute Lymphocyte count(109/L)	12.7±1.4	14.1±1.5	≤0.001
Platelets(109/L)	328.6 ± 119.5	282.2 ± 94	0.006
Serum Creatinine(mg/dl)	0.5 ± 0.4	0.45± 0.49	0.47
Alanine Transaminase(IU/L)	29.4 ± 16.9	24.1 ±14.5	0.03
PLR	175.9± 105.1	92.5 ±68.3	≤0.001

Table 2: Comparison of baseline categorical variables in terms of H.Pylori infection

Variable		H.Pylori Positive(n=87) n(%)	H.Pylori Negative(n=80) n(%)	p-value
Gender	Male	32(36.7)	45(56.3)	0.009
	Female	55(63.3)	35(43.7)	
Diabetes	Present	16(18.4)	17(21.3)	0.77
	Absent	71(81.6)	60(78.7)	
Hypertension	Present	19(21.8)	22(27.5)	0.39
	Absent	68((78.2)	58(72.5)	
Duration of symptoms	< 1month	31(35.6)	42(52.5)	0.652
	≥1 month	56(64.4)	38(47.5)	
PLR	<118	11(12.6)	73(91.3)	≤0.001
	≥118	76(87.4)	7(8.7)	

Table 3: Showing sensitivity, specificity, Positive Predictive Value, Negative Predictive value and Diagnostic accuracy of PLR in predicting H.Pylori infection

Statistics	Percentage
Sensitivity	87.36%
Specificity	91.25%
Positive Predictive Value	91.57%
Negative Predictive Value	86.90%
Diagnostic Accuracy	89.22%

6. Discussion

Helicobacter pylori is a common human pathogen implicated in certain gastrointestinal diseases. About half of the world's population is estimated to be infected with this pathogen.1 unless treated, colonization usually persists lifelong. H. pylori infection represents a key factor in the etiology of various gastrointestinal diseases, ranging from chronic active gastritis without clinical symptoms to peptic ulceration, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue lymphoma. The number of peer-reviewed publications on Helicobacter has rapidly increased, from less than 200 in 1990 to approximately 1,500 per year over the last few years7. Despite this wide attention important issues, such as the transmission route of H. pylori, are still poorly understood. Although the prevalence of H. pylori in the Western world is decreasing, gastric colonization by H. pylori remains widespread in the developing world. Infection with H. pylori can be diagnosed by a variety of tests and can often be successfully treated with antibiotics. Unfortunately, the increase in antibiotic resistance is starting to affect the efficacy of treatment, and, in spite of the impact of H. pylori, preventive vaccination strategies still do not exist. A better understanding of H. pylori persistence and pathogenesis is thus mandatory to aid the development of novel intervention and prevention strategies.

Farah et al., [10] indicated a significant association between HP infection and inflammation on the basis of PLR, a simple and reliable indicator of inflammation. Totally, 200 patients with HP were included in the study as patient and control groups respectively. Numbers of white blood cells (WBC), neutrophils, platelet but not lymphocytes in the patients with HP were higher than those without HP, hemoglobin levels were comparable. Patients with HP had significantly higher PLR compared to those without HP. Using a cut-off level of 140, PLR predicted severe symptoms with a sensitivity of 92% and specificity of 70% (area under ROC curve=0.645, 95% CI: 0.587-0.703; P<.001.

Another study [11], evaluated a total of 234 patients. The control group, HP-negative gastritis group and HP-positive gastritis group consisted of 79 (33.9%), 73 (31.3%) and 82 (35.1%) patients respectively. No statistical significance were found between groups for age, gender, WBC, PLT, and MPV levels. The HP-positive gastritis group had a markedly higher neutrophil level and a lower lymphocyte and HB levels compared to the other groups ($P < 0.001$, $P < 0.001$, $P = 0.014$, respectively). The platelet levels were increased in whole groups, but this increase was lowest in the HP-positive gastritis group. Furthermore, there was no significant differences for platelet levels between study groups. The PLR were remarkably higher in the HP-positive gas-tritis group compared to the other groups ($P < 0.001$) with an area under the ROC curve of 0.88. The cut-off value of PLR for the differential diagnosis between H.pylori (-) and H.pylori (+) gastritis was 121.6, sensitivity was 97% (95%

CI: 90.5% to 99.7%), and specificity was 70% (95% CI: 58.0% to 80.1%) [11].

We hypothesized that since HP can cause chronic inflammation, it should be associated with an increase in the levels of systemic inflammatory markers, including the PLR. Some studies have indicated the effectiveness of the PLR and NLR in predicting the prognosis and survival of patients with malignant or chronic disorders. Thus, we consider that these parame¬ters may be used as diagnostic biomarkers for HP-positive gastritis [11].

However, our results also revealed that H. pylori infection was significantly associated with the increased platelet to lymphocyte ratio (PLR) with an excellent sensitivity of 87.36 % and a far better specificity of 91.25% as compared to the previous studies along with diagnostic accuracy of 89.22% with an AUROC, which is also higher as compared to the previous studies.

The hypothesis that systemic inflammation is induced by chronic H. pylori infection remains controversial. These inconsistent results may be due to the variation in each study's limited sample sizes, heterogeneous participant groups, and often-incomplete control of confounding factors which can have a significant influence on both H. pylori infection and systemic inflammation, as H. pylori infection is related to living in crowded conditions with poor hygiene and low socioeconomic status while systemic inflammation and are also related to socioeconomic status.

The present study has strength of its diagnostic method of tissue biopsy that is gold standard and secondly a comparatively better AUROC values as compared to the former studies. However, there are also several limitations that should be considered when interpreting our findings. First, small sample size, secondly, it is a single center study and lastly we cannot exclude the possibility of residual or unmeasured confounding factors that may have an influence on PLR.

7. Conclusion

In conclusion, this study revealed that raised PLR was significantly associated with H.Pylori infection with an excellent diagnostic accuracy. However, further studies comprising of larger sample size are required to validate this score.

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