Does elevated neutrophil-lymphocyte-ratio and platelet-lymphocyte-ratio indicate *Helicobacter pylori* infection among dyspeptic patients ? A cross-sectonal analytical study from Chitwan Medical College Teaching Hospital, Nepal

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ABSTRACT

INTRODUCTION

Acid peptic disease (APD) is a common gastrointestinal condition with a higher prevalence in populations of lower socioeconomic status. Various factors, including infections and specific medications, contribute to its development. This study investigated the relationship between simple, cost-effective inflammatory biomarkers - the Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) and *Helicobacter pylori* (HP) infection.

MATERIAL AND METHODS

Out of the 334 study participants with dyspeptic symptoms enrolled in this study, 167 were confirmed HP-positive through hematoxylin and eosin (H&E) staining of biopsy specimens obtained following upper gastrointestinal endoscopy. An equal number of age- and sex-matched HP-negative patients with dyspeptic symptoms were enrolled as controls. Venous blood samples were obtained and analyzed for complete blood count, and NLR and PLR were calculated post endoscopy.

RESULTS

We observed HP infection in 60% of female participants presenting with dyspeptic symptoms. A significant correlation was observed between dyspeptic symptoms categorized a postprandial epigastric discomfort, burning epigastric pain, and bloating with HP infection. Both NLR (<0.001) and PLR (<0.05) demonstrated statistically significant associations with HP infection status. Receiver operating characteristic (ROC) analysis suggested NLR to be a superior predictor of HP positivity compared to PLR.

CONCLUSION

This findings of the present study suggests NLR and PLR could serve as predictive inflammatory markers for HP infection in patients with dyspeptic symptoms. These findings may serve healthcare providers in resource-limited settings potentially helping in referral for specialist care and endoscopic evaluation. Specialist physicians and tertiary health centers could use these ratios in monitoring HP eradication therapy.

KEYWORDS

Helicobacter pylori, Lymphocyte, Neutrophil, Platelet, Dyspepsia

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INTRODUCTION

Acid peptic disease (APD), characterized by mucosal damage in the stomach or duodenum which usually manifests as peptic ulcers, GERD, or dyspepsia, is one of the most frequently encountered clinical condition.[1] In Nepal, physicians refer APD as the "national disease" due to its high prevalence (30–65%).[2] These findings however have a declining global trends which has been attributed to proper management and diagnosis of *H. pylori* (HP) and restricted NSAID use. HP is endemic in low-resource settings and has been proved to colonize gastric mucosa by urease mediated activity that induces inflammation and metaplasia in the stomach or duodenum.[3] In Nepal, where cost-effective and readily accessible blood tests like complete blood count (CBC)[4] is available, we can use its manually derived ratios: neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) to evaluate inflammation. NLR[5] and PLR[6] have recently been utilized as promising inflammatory markers since they offer specificity for chronic inflammation such as HP infection. This study evaluates NLR and PLR as predictors of HP-induced inflammation in dyspeptic patients.The findings of this study could be utilized as a valuable marker in resource constrained setting like Nepal. Such hematological indices could further help tackle this national disease through early detection and management.

MATERIAL AND METHODS

This study was conducted after receiving approval from the Institutional Review Committee of Chitwan Medical College (Reference: CMC-IRC/078/079-110). A total of 334 patients presenting with dyspeptic symptoms at the gastroenterology outpatient department of Chitwan Medical College Teaching Hospital between July 20 and December 19, 2023 were included as study participants. Patients with chronic diseases, co-existing inflammatory conditions, and chronic NSAIDs or steroids use were not included in the study. Patients with recent NSAID use were advised to discontinue the medication before enrolling in the study. Additionally, we excluded patients on proton pump inhibitors or HP eradication therapy or other medications that interfered with gastric acid production. All participants provided written informed consent, including acknowledgment of anonymized data publication.

An upper gastrointestinal endoscopy (UGI) was performed on all participants by specialist gastroenterologists and biopsy specimen was obtained from the gastroesophageal junction, antrum, or duodenum based on endoscopic findings. Specimens were preserved in 10% formaldehyde and submitted to the histopathology laboratory for evaluation by consultant pathologists.

Post-endoscopy blood samples were collected from the antecubital vein and analyzed within 3-6 hours using an automatic hematology analyzer (Horiba 9-part). Internal quality controls were performed before sample analysis.

We recorded absolute neutrophil count, absolute lymphocyte count, platelet count, and HP infection status (positive or negative) in a preformed proforma. The study population comprised 167 HP-positive patients and an equal number of age- and sex-matched HP-negative controls. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive statistics included frequency, ratio, mean, minimum, maximum, and standard deviation for continuous variables. Student's t-test was employed for comparing independent, normally distributed variables. Mann-Whitney U test was used for non-normally distributed variables. Categorical variables were compared using Pearson's chi-square test and Fisher's exact test. Receiver Operating Characteristic (ROC) curve analysis was performed to determine optimal threshold values, accuracy, specificity, sensitivity, and positive and negative predictive values. Statistical significance was set at $p<0.05$.

RESULTS

The study included 334 participants (167 HP-positive and their 167 age- and sex-matched controls), with ages ranging from 18 to 73 years (mean: 43.50±13.61 years). HP infection was most prevalent in adults aged 25-65 years and least common among participants over 65 years. Female participants showed a significantly higher association with HP infection ($p<0.001$). Dyspeptic symptoms, including postprandial epigastric discomfort, burning epigastric pain, and bloating demonstrated significant associations with HP infection in different level. ($p<0.05$). Detailed demographic and clinical characteristics are presented in table 1.

Table 1. Demographic and symptomatic characteristics of study participants according to presence of HP (n=334)

Variables	Number (%)	HP infection		χ^2	*p*-value
		Positive (%)	Negative (%)		
Age group				0.000	
Youth(<=24)	38 (11.3)	19 (50)	19 (50)		
Adult(25-65)	266 (79.6)	133 (50)	133 (50)		1.00
Seniors(>65)	30 (8.9)	15 (50)	15 (50)		
Gender				11.509	
Male	167 (50)	68 (40.7)	99 (59.3)		
Female	167 (50)	99 (59.3)	68 (40.7)		**0.001****
Marital status				1.981	
Married	272 (81.5)	131 (48.2)	141 (51.8)		0.159
Unmarried	62 (18.5)	36 (58.1)	26 (41.9)		
Dyspeptic Symptoms					
Post-prandial epigastric discomfort				20.893	
Yes	70 (20.9)	52(74.3)	18 (25.7)		**<0.001****

No	264 (79.1)	115(43.6)	149 (56.4)		
Burning Epigastric pain				9.431	
Yes	315 (94.3)	151 (47.9)	164 (52.1)		**<0.002****
No	19 (5.6)	16 (84.2)	3(15.8)		
Bloating				7.271	
Yes	294 (88.1)	139 (47.3)	155 (52.7)		**<0.007****
No	40 (11.90	28 (70)	12 (30)		
Early satiety				1.069	
Yes	38 (11.3)	16 (42.2)	22 (57.8)		0.301
No	296 (88.6)	151 (51)	145 (49)		

** denotes significant association (By applying the Pearson chi-square test at 5% level of significance)

Significant differences were observed in neutrophil counts, platelet counts, and creatinine levels between HP-positive and HP-negative patients (p<0.001). No significant differences were found in lymphocyte counts, hemoglobin levels, random blood sugar (RBS), or liver enzymes (AST and ALT) between the two groups. Complete laboratory parameters are detailed in table 2.

Table 2. Comparison of lab parameters with HP infection status among APD patients (n=334)

Variables	HP infection		Mean rank difference	Z-value	*p*-value
	Positive	Negative			
	Median (IQR)				
Neutrophil	54 (15)	50 (12)	60.28	**-5.721**	**< 0.001****
Lymphocytes	34.0 (9)	35 (8)	13.62	-1.295	0.19
Hemoglobin	12.3 (2.3)	12 (2)	2.49	-0.240	0.810
Platelets	194 (106)	220 (100)	41.74	**-3.595**	**< 0.001****
RBS	102 (27)	102 (16)	12.12	-1.150	0.25
Creatine	0.69 (0.28)	0.5 (0.28)	85.36	**-8.100**	**< 0.001****
AST	30 (13)	32 (10)	7.79	-0.744	0.45
ALT	32 (16)	30 (7)	19.03	-1.825	0.06
NLR	1.54 (0.88)	1.32 (0.54)	45.84	**-4.339**	**< 0.001****
PLR	5.62 (3.64)	6.38 (3.45)	20.06	**-1.899**	**< 0.05****

** denotes significant difference (By applying the Mann -Whitney U test at a 5% level of significance)

Inflammatory Markers and HP Status: Both the NLR (<0.001) and PLR (<0.05) showed statistically significant correlations with HP infection status. (figure 1)

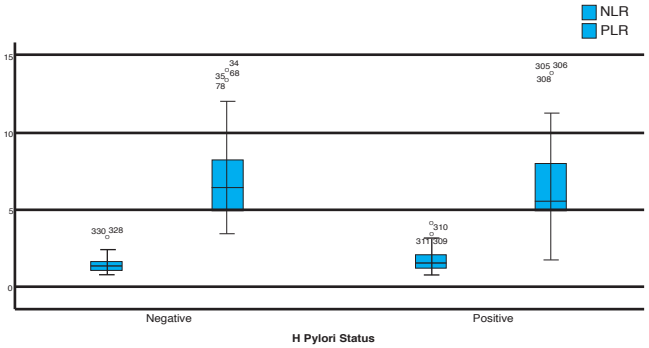

Figure 1. Comparison of NLR and PLR according to HP infection status among APD patients attending Gastro OPD of CMCTH (n=334)

ROC curve analysis was performed to evaluate the predictive capability of these inflammatory markers. The NLR demonstrated superior predictive value with an area under the curve (AUC) of 0.644 (95% confidence interval: 0.535-0.753) compared to PLR. The optimal cut-off points for predicting HP positivity were determined to be ≥1.18 for NLR and ≥5.39 for PLR, providing the best balance between sensitivity and specificity (Figure 2).

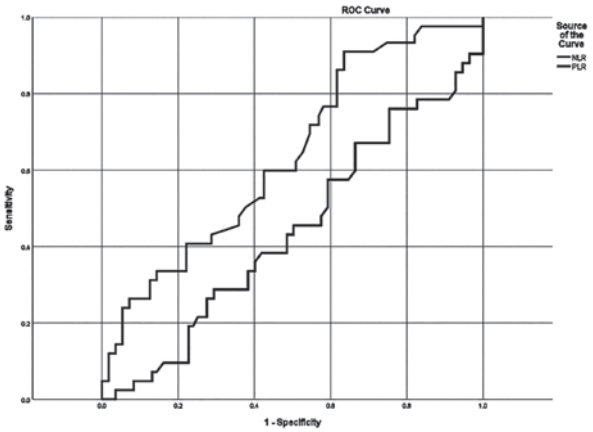

Figure 2. ROC showing prediction of positive HP according to NLR and PLR among APD patients attending Gastro OPD of CMCTH (n=334)

DISCUSSION

Various diagnostic tools are available for HP infection detection, including tissue biopsy, stool antigen, and urea breath tests. However, definitive guidelines exist only for children and patients over 55 years.[4] While both non-invasive and invasive techniques are utilized, no single method has demonstrated clear superiority. In this study, we employed tissue biopsy with H&E staining following upper gastrointestinal endoscopy, which remains the gold standard for HP diagnosis.[7]

Our findings demonstrate significant associations between HP infection and simple yet reliable inflammatory markers (NLR and PLR) in patients with dyspeptic symptoms. Global estimates suggest that 50% of the world's population is infected with HP, with higher prevalence rates in low- and middle-income countries.[8,9] Our previous research in a similar setting reported a prevalence of approximately 42%.[10]

HP infection is usually acquired at an earlier age and may persist for an indefinite period with or without symptoms, nonetheless, it has been proved to cause GI diseases.[11,12] We observed that most dyspeptic patients presented with statistically significant epigastric pain (p<0.002) and bloating (p<0.007), likely secondary to HP infection.[11,13] While previous studies have reported correlations between infection and symptom severity,[14] we did not assess symptom severity in our study population.

Our findings of elevated neutrophil counts in HP-positive patients align with previous research,[14,15] reflecting the

inflammatory response to gastric mucosal infection. As neutrophils are the first line of defense, the increase in its number can be expected. We observed lower lymphocyte counts in HP-infected patients, consistent with previous studies.[13] The combination of increased neutrophils and decreased lymphocytes resulted in significantly higher NLR values among HP-positive patients (p<0.001), corroborating earlier findings.[13-17] This similarity may be explained by our study population being limited to patients with dyspeptic symptoms. Some researchers suggest using NLR as a screening tool for UGI endoscopy referral in dyspeptic patients.[18] Similar recommendations could be made based on the present findings among adult population though studies in pediatric populations have reported contrasting results.[19,20]

We observed decreased platelet counts (p<0.001) in HP-positive patients over HP-negative patients, consistent with previous reports.[21,22] While the mechanism remains unclear, studies suggest platelet count improvement following HP eradication therapy.[22] Lower PLR values in HP-infected patients (p<0.05) align with previous adult studies,[11,16] though pediatric studies report contrary findings.[20-22] It could as well be true that the ratio reverses in the older population, however, this age-related difference is beyond the scope of the present study and warrants further investigation in larger cohort studies.

In this study we report NLR to be a superior predictor of HP positive similar to previous studies.[13,17] Also, PLR was found to be statistically significant with HP status aligning with the existing literature.[11,16] The statistical significance of both ratios supports their potential utility in predicting HP status.[21] Hence, we recommend the use of both NLR and PLR in predicting the HP status. This could as well be used as a tool in deciding eradication of HP infection with more such future studies.

Other clinical parameters, including hemoglobin and RBS, showed no significant differences between groups.These parameters have been found to decrease in severe cases of APD probably owing to peptic ulcer bleed. In the present study, no severity grading was done.

HP infection has been linked to development of several liver diseases and its eradication has been suggested to play a role in reducing of several fatty liver disease.[23] In the present study, neither we observed any rise in liver enzymes (ALT, AST), nor, it was statistically significant between HP status which was in accordance with several published literatures.[23] We observed elevated serum creatinine in HP-positive patients (p<0.001). Recent studies from China and Japan suggest a relationship between HP infection and chronic renal failure,[24] though our study design precludes definitive conclusions about this association.

Several limitations of the study warrants mention here. We did not account for potential confounders such as dietary habits, smoking, alcohol use, and family history of gastrointestinal disease. Also, a selection bias may exist due to recruitment from a gastroenterology clinic. Additionally, we did not establish cut-off values for NLR and PLR based on age, gender or other sociodemographic factors and the cross-sectional nature of the study limits casual inference between inflammatory markers and HP status. Nonetheless,we recommend utilizing NLR and PLR as cost-effective screening tools in resource-limited settings to guide specialist referrals and endoscopic evaluation. While these ratios may aid in treatment decisions and monitoring HP eradication, confirmatory diagnostic testing remains essential. Future large-scale, multicenter longitudinal studies should establish population-specific cutoff values and investigate the temporal relationship between inflammatory markers and HP infection.

CONCLUSION

This study demonstrates the potential utility of NLR and PLR as reliable, non-invasive biomarkers for HP infection in patients with APD. Both ratios showed significant associations with HP status, with NLR shown as the stronger predictor. As these hematological variable are derived from routine CBC and require no additional testing, while being cost-effective provide diagnostic edge in resource constrained setting. In specialist tertiary settings, these markers could complement existing diagnostic strategies and enhance clinical decision-making, however, larger multicenter studies are needed to validate these findings across diverse populations and establish population-specific reference ranges.

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CONFLICTS OF INTEREST

None

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