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ORIGINAL ARTICLE

Can Serum C-Reactive Protein/Albumin Ratio be Used as a Marker of Chronic Helicobacter Pylori Infection?

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SUMMARY

Background: **Helicobacter pylori *(H. pylori)* is a Gram-negative bacterial agent that colonizes the gastric mucosa and leads to chronic infections. Various techniques are available for the detection of *H. pylori*; however, many of these methods are invasive, costly, and can only be performed in tertiary laboratories. It is necessary to find cost-effective and non-invasive novel indicators that can identify *H. pylori* infection and its activity.**
Objective: **The objective of this study was to investigate the correlation between the CRP/albumin ratio (CAR), which is frequently analyzed in laboratory settings, and the presence of *H. pylori*, as well as the activation of *H. pylori* infection.**
Methods: **The medical records of patients who had upper gastrointestinal endoscopy at our hospital were reviewed retrospectively. The data were analyzed using suitable tests with the IBM SPSS 27 software.**
Results: **The study included 613 patients, comprising 375 females (61.2%) and 238 males (38.8%). Among the participants, 327 (53.3%) tested positive for *H. Pylori*, while 286 (46.7%) tested negative. All patients presented with dyspeptic symptoms, and other indications for UGISE included anemia, gastroesophageal reflux, epigastric discomfort, dysphagia, nausea and vomiting, bleeding, and scanning.**
Upon comparing the laboratory results of *H. pylori*-positive and -negative patients, no significant change in CRP values was observed ($p > 0.05$). The albumin level was statistically considerably elevated in *H. pylori*-negative patients relative to -positive patients ($p = 0.009$). The CAR in *H. pylori*-positive patients was statistically substantially elevated compared to negative ones ($p = 0.04$).
Conclusions: **We assert that CAR may serve as a valuable biomarker for confirming the presence of *H. pylori* infection and for reflecting the systemic inflammatory status of patients.**
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INTRODUCTION

Helicobacter pylori (H. pylori) infection is the most prevalent chronic bacterial infection in humans. It is found in individuals across all age groups worldwide [1]. *H. pylori*, a Gram-negative, microaerophilic, spiral-shaped bacterium that infects the human stomach mucosa during early life, colonizes the mucosal gel layer and causes chronic infection [1]. More than 50% of the global population is colonized by *H. pylori*, with preva-

lence varying by geographic region and socioeconomic status [1]. *H. pylori* is significant, as it induces several gastrointestinal disorders over a patient's lifetime, including gastritis, gastric or duodenal ulcers, mucosa-associated lymphoid tissue lymphoma, and gastric adenocarcinoma [1,2]. There is a recognized correlation between the presence of *H. pylori* and the development of precancerous lesions in the stomach. *H. pylori* infection can lead to the onset of adenocarcinoma and has consequently been classified as a 'Group 1' carcinogen by the World Health Organization. Consequently, identifying the presence of this virus and understanding the mechanisms influencing its colonization and elimination is crucial [1,2].

Epidemiological studies have demonstrated that *H. pylori* infection is associated with various non-gastric diseases. Current research explains the associations among idiopathic thrombocytopenic purpura, iron deficiency anemia, chronic urticaria, metabolic disorders, neurological disorders, cardiovascular diseases, nonalcoholic hepatosteatosis, colorectal cancer, and *H. pylori* infection [3].

Multiple techniques are available to detect the presence and activity of *H. pylori.* Each of these methods has distinct advantages and disadvantages. None of these assessments can be considered the gold standard due to limitations in sensitivity or specificity. Nevertheless, the utilization of multiple tests, such as urease enzyme production tests, microscopy, bacterial isolation, and polymerase chain reaction (PCR), typically yields an acceptable diagnosis. Certain tests are conducted using biopsies obtained during the endoscopic process. However, these techniques are intrusive, costly, and can only be implemented by tertiary laboratories [4].

C-reactive protein (CRP) is an acute phase protein produced in the liver in response to cytokines, particularly interleukin-6 (IL-6), tumor necrosis factor (TNF) alpha, and interleukin-1 (IL-1). CRP, an indicator of systemic inflammation, increases in response to both acute and chronic disorders. The low-grade subclinical variations of CRP in chronic conditions carry significant pathophysiological implications [5]. Several studies have indicated a persistent low-grade elevation of circulating inflammatory markers, particularly CRP, in *H. pylori* infection [6,7]. Chronic inflammation can originate or aggravate several systemic diseases [8]. Serum albumin levels are inversely correlated with the severity of the inflammatory response, a phenomenon attributed to the hypercatabolic state observed in inflammatory conditions. This is further influenced by the downregulation of cytokines such as TNF-alpha and IL-6, which reduce albumin synthesis in the liver. Additionally, albumin levels are associated with the nutritional status of individuals. Elevated CRP and diminished albumin levels were correlated with an intensified inflammatory response. Persistent and elevated inflammation may signify hypercytokinemia, potentially resulting in weight loss and malnutrition [9]. The CRP-albumin ratio (CAR) indicates the interplay between systemic inflammation and nutritional status. It has been demonstrated that it can predict patient prognosis in several conditions, including sepsis, acute pancreatitis, hepatocellular carcinoma, small cell lung cancer, pancreatic cancer, esophageal cancer, and biliary tract cancer [10-12]. Recent investigations have linked higher CAR values with increased inflammatory burden, poor prognosis, and higher mortality [12]. One study identified CAR as a robust prognostic factor for predicting the outcomes of gastric cancer [13].

This study aimed to examine the relationship between CAR, which is frequently analyzed in laboratory settings, and both the presence and density of *H. pylori.*

MATERIALS AND METHODS

The project obtained permission from Uşak University Non-Interventional Clinical Research Ethics Committee on April 4, 2024, with decision number 360-360-18. Records of patients over 18 years of age who presented with dyspeptic complaints to the general surgery and gastroenterology outpatient clinics of our hospital from January 2020 through December 2023 were reviewed retrospectively. All patients underwent upper gastrointestinal endoscopy (UGISE). Patient records are stored and accessed from electronic medical records and file archives. Our hospital serves a population of approximately 500,000 and accepts patients in all medical branches of emergency and outpatient clinics. The hospital features a specialized gastroenterology unit, and patients may also come from a general outpatient setting. Multiple clinicians were involved in performing the procedures. The exclusion criteria encompass the following conditions: age under 18, pregnancy, referrals from other hospitals, incomplete electronic medical records, prior diagnosis of autoimmune illness, active infections (such as pulmonary or urinary tract), and acute conditions. Patients with transient ischemic attack (TIA) or stroke, albuminuria, a history of albumin replacement therapy within the past six months, malignancy, connective tissue disorders, vasculitis, celiac disease, chronic liver disease, chronic kidney disease, or heart failure at the time of diagnosis or hospital admission, as well as patients with a history of systemic infection within the last four weeks or those receiving steroid treatment, were excluded.

Endoscopic and histologic examination

Patients presented to the endoscopy unit following a 10-hour fast (8:30 - 9:30 am). They obtained a routine upper gastrointestinal endoscopy (UGIE) performed by a gastroenterologist or surgeon with a Fujinon endoscope. Biopsies were obtained from the antrum to evaluate *H. pylori* colonization, and histopathology and slides were reviewed by more than one specialized pathologist. The quality control measures for histopathological evaluation of biopsies were provided as standardized biopsy collection, consistent histological techniques (staining

protocols, quality reagents), experienced pathological review (expert evaluation, interobserver calibration), integration with other diagnostic methods (rapid urease test, microbial culture), and regular proficiency testing (external quality assessment, internal audits).

Biopsy samples were preserved in 10% formaldehyde and embedded in paraffin. Cross-sections (4 µm) were stained with hematoxylin-eosin (HE), alcian blue (AB; pH 2.5), periodic acid-Schiff (PAS), and toluidine blue. The cross-sections were classified according to the Sydney system, which relies on five histological variables: neutrophil activity, chronic inflammation, glandular atrophy, intestinal metaplasia, and *H. pylori* concentration [14]. Endoscopic examination results, *H. pylori* presence (positive), *H. pylori* absence (negative), and laboratory test outcomes were documented.

The presence of *H. pylori* was deemed positive (+), whereas its absence was regarded as negative (-). The concentration of *H. pylori* was categorized into three degrees: +1, +2, and +3.

Biochemical analysis

Venous blood samples were collected from antecubital veins following an overnight fast. Hemoglobin, glucose, creatinine, albumin, and C-reactive protein levels were evaluated in our institution's laboratory. At our hospital, CRP levels varied from 0 to 5 mg/dL, while albumin levels ranged from 3.5 to 5.2 mg/dL. The CAR value is calculated by dividing the CRP level by the albumin level.

The clinical demographic data of patients, laboratory findings at admission (CBC, C-reactive protein, albumin, CAR, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR)), endoscopic findings, endoscopic biopsy results, and the presence, intensity, and activity of *H. pylori* positivity and inflammation were evaluated.

Statistical analysis

Statistical analysis was conducted utilizing the Statistical Package for the Social Sciences (SPSS), version 27.0, from IBM Corp., Armonk, NY, USA. Shapiro-Wilk and Kolmogorov-Smirnov tests, together with box plots, histograms, and Q-Q plots, were generated for normality assessment. Descriptive statistics are expressed as the mean ± standard deviation (SD). CAR values for *H. pylori (-)* and *H. pylori (+)* were compared using an independent samples *t*-test. Statistical significance for all tests was established at a p-value of < 0.05.

For evaluating the association between two independent groups lacking normal distribution, the Mann-Whitney U test was utilized; for three or more categories, the Kruskal-Wallis test was employed. Chi-squared analysis and Fisher's exact test were used to investigate the correlations between categorical variables. Sperman's rho correlation analysis was employed to examine the link between continuous variables. The analysis findings are displayed in tables, with a significance level accepted at $p < 0.05$.

The CAR, NLR, and PLR values were evaluated by ROC (receiver operating characteristic) curve analysis to determine the presence of *H. pylori*. The sensitivity and specificity values at the threshold are presented. The study evaluated the diagnostic utility of the CRP/albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), CRP, and albumin levels in predicting the presence of *H. pylori*. The AUC value for CAR was calculated as 0.547 (95% CI: 0.502 - 0.593, $p = 0.044$), indicating a statistically significant predictive value. However, since the AUC value is below 0.6, CAR cannot be considered a strong diagnostic marker, which likely explains its exclusion from the discussion section. For albumin, the AUC value was 0.561 (95% CI: 0.515 - 0.606, $p = 0.009$), also statistically significant, suggesting that albumin levels may be influenced by *H. pylori* infection. In contrast, the other parameters did not demonstrate statistically significant predictive power, with NLR having an AUC of 0.515 ($p = 0.510$), PLR an AUC of 0.491 ($p = 0.689$), and CRP one of 0.541 ($p = 0.078$).

RESULTS

The study included 613 patients, comprising 375 females (61.2%) and 238 males (38.8%). Out of the patients, 327 (53.3%) tested positive for *H. Pylori,* while 286 (46.7%) tested negative. The average age of all patients was 54.04 (± 14.86). The mean age of *H. Pylori*-positive patients was 52.35 (± 14.73), while the mean age of *H. Pylori*-negative patients was 55.98 (± 14.8). The mean age of *H. pylori*-positive patients (52.35 ± 14.73 years) was significantly lower than that of *H. pylori*-negative patients (55.98 ± 14.8 years, $p = 0.002$). In a comparison of *H. pylori*-positive and *H. pylori*-negative patients by gender, *H. pylori* positivity was found to be significantly higher in males. A statistically significant correlation was identified between gender and *H. pylori* positivity ($p = 0.03$). All patients exhibited dyspeptic symptoms, and additional indications for UGISE included anemia, gastroesophageal reflux, epigastric pain, dysphagia, nausea and vomiting, bleeding, and scanning.

Upon comparison of the laboratory results between *H. pylori*-positive and -negative patients, no significant differences were observed in hemoglobin, lymphocyte, platelet, and CRP values ($p > 0.05$). However, white blood cell, neutrophil, and monocyte counts were statistically significantly higher in *H. pylori*-positive patients compared to *H. pylori*-negative individuals ($p < 0.05$). The albumin level was statistically significantly higher in *H. pylori*-negative patients compared to -positive patients ($p = 0.009$). The CAR values of *H. pylori*-positive patients were statistically significantly higher compared to those of -negative patients ($p = 0.04$). No statistical significance was found between *H. pylori*-positive and -negative patients for the distributions of platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio

Table 1. Demographic characteristics of patients, symptoms in *H. pylori*-positive and *H. pylori*-negative patients.

		H. pylori (+) n (%)	*H. pylori* (-) n (%)	Total n (%)	p
Gender	male	140 (42.8)	98 (34.3)	238 (36.3)	0.03 [x2]
	female	187 (57.2)	188 (65.7)	375 (61.2)	
Age	mean (SD)	52.35 (± 14.73)	55.98 (± 14.8)	54.04 (± 14.86)	0.002 [m]
Additional symptoms to dyspepsia	anemia	62 (19)	10 (3.5)	72 (11.74)	< 0.001 [x2]
	scan/control	26 (8)	3 (1)	29 (4.7)	< 0.001 [x2]
	GERD	19 (5.8)	0	19 (3.1)	< 0.001 [x2]
	epigastric pain	22 (6.7)	1 (0.3)	23 (3.8)	< 0.001 [x2]
	dysphagia	5 (1.5)	0	5 (0.8)	0.06 [fe]
	nausea/vomiting	5 (1.5)	1 (0.3)	6 (1)	0.22 [fe]
	bleeding	4 (1.2)	0	4 (0.7)	0.12 [fe]

[m] Mann-Whitney U test, [x2] chi-squared test, [fe] Fisher´s exact test, p < 0,05 is statistically significant.
SD standard deviation, GERD gastroesophageal reflux disease.

Table 2. *H. pylori* laboratory findings in H. pylori-positive and -negative patients.

		H. pylori (+)	H. pylori (-)	Total	p
Hgb	mean (SD)	13.33 (± 2.03)	13.37 (± 1.87)	13.35 (± 1.96)	0.79 [t]
Wbc	mean (SD)	7.65 (± 2.02)	7.19 (± 2.18)	7.43 (± 2.11)	< 0.001 [m]
Neutrophil	mean (SD)	4.7 (± 1.78)	4.45 (± 1.99)	4.58 (± 1.88)	0.02 [m]
Lymphocyte	mean (SD)	2.33 (± 0.9)	2.26 (± 0.86)	2.3 (± 0.88)	0.19 [m]
Monocyte	mean (SD)	0.47 (± 0.16)	0.45 (± 0.2)	0.46 (± 0.18)	0.01 [m]
Platelet	mean (SD)	274.75 (± 71.23)	271.86 (± 80.97)	273.4 (± 75.88)	0.13 [m]
CRP	mean (SD)	5.59 (± 11.86)	3.16 (± 4.75)	4.46 (± 9.32)	0.07 [m]

SD standard deviation, Hgb hemoglobin, Wbc white blood cell, CRP C-reactive protein.
[t] t-test, [m] Mann-Whitney U test.

Table 3. Comparison of biopsy results with laboratory values in *H. Pylori*-positive patients.

Biopsy	GRADE	n/%	CAR	NLR			PLR			*H. pylori* positivity	
			p [kw]	r	p [s]	p [kw]	r	p [s]	p [kw]	r	p [s]
H. pylori (+)	1	130/39.8	0.37	0.00	0.92	0.6	0.03	0.48	0.24	-	-
	2	179/54.7									
	3	18/5.5									
H. pylori density	0	29/8.9	0.38	-0.02	0.72	0.07	0.07	0.19	0.54	0.29	<0.01
	1	271/82.9									
	2	27/8.3									
Neutrophil activity	0	16/4.9	0.60	-0.03	0.49	0.03	-0.5	0.33	0.62	0.11	0.03
	1	231/70.6									
	2	76/23.2									
	3	4/1.2									

[kw] Kruskal-Wallis H test, [s] Spearman's rho correlation test, p < 0,05 is statistically significant.

CAR C-reactive protein/albumin ratio, NLR neutrophil-to-lymphocyte ratio, PLR platelet-to-lymphocyte ratio.

Table 4. Logistic regression analysis for H. pylori-positive and -negative patients.

	Beta	OR	95% CI (lower - upper)	p
Gender	0.332	1.393	0.990 - 1.961	0.057
Age	-0.021	0.979	0.968 - 0.990	< 0.001
CRP/Albumin	2.237	9.366	2.097 - 41.834	0.003
PLR	-0.002	0.998	0.994 - 1.002	0.280
NLR	0.090	1.094	0.950 - 1.260	0.210
Constant	1.017	2.765		0.008

OR odds ratio, CI confidence intervals, p < 0.05 is statistically significant.
NLR neutrophil-to-lymphocyte ratio, PLR platelet-to-lymphocyte ratio, CRP C-reactive protein.

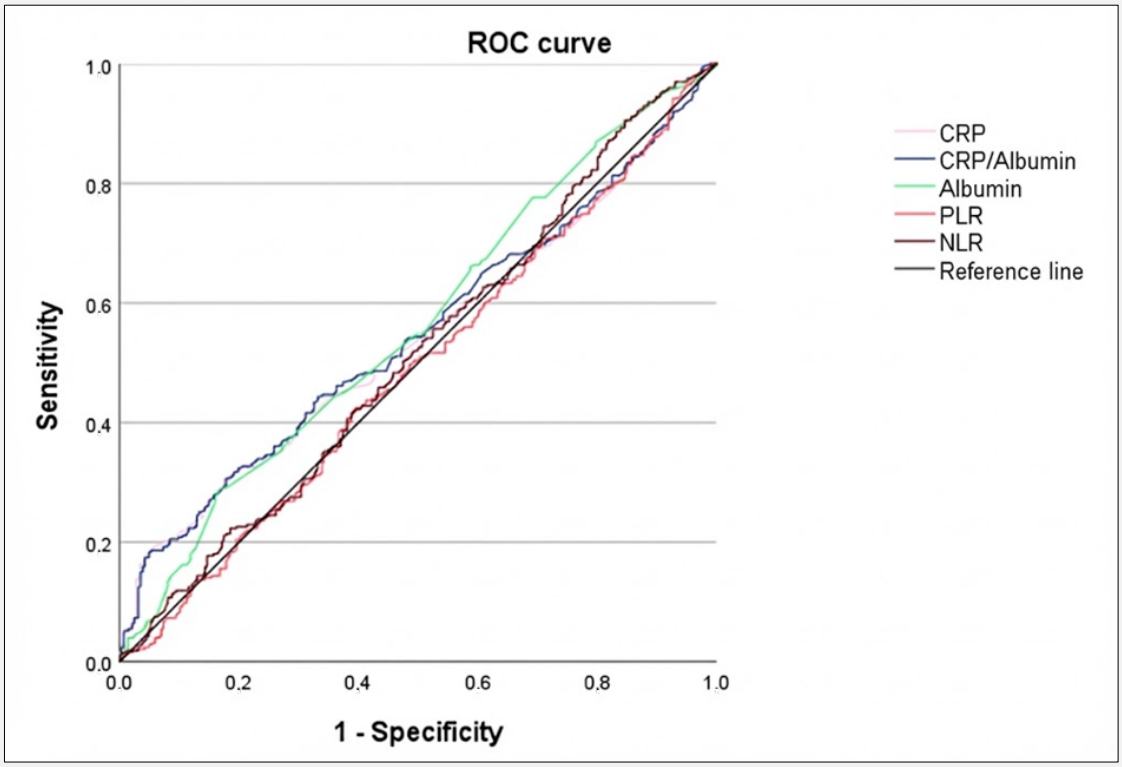

Figure 1. ROC curves of CRP, CAR, albumin, PLR, and NLR values.

NLR neutrophil-to-lymphocyte ratio, PLR platelet-to-lymphocyte ratio, CRP C-reactive protein.

(NLR). No statistically significant correlation was seen between *H. pylori* positivity, *H. pylori* activity, and CAR, NLR, PLR. As shown in Table 1, a statistically significant relationship was found between *H. pylori* inflammation and NLR (p = 0.03).

A comparison of the laboratory results of positive and negative patients for *H. pylori* revealed no significant differences in hemoglobin, lymphocyte, platelet, and CRP values (p > 0.05). White blood cell, neutrophil, and monocyte counts were statistically significantly

higher in *H. pylori*-positive patients compared to *H. pylori*-negative individuals ($p < 0.05$). The albumin level was statistically considerably lower in *H. pylori*-positive patients compared to those who were negative ($p = 0.009$). A statistically significant difference was observed between the CAR values of *H. pylori*-positive and -negative patients. The CAR value in *H. pylori*-positive individuals was statistically significantly elevated compared to that in -negative patients ($p = 0.04$). No statistical significance was observed between the two groups regarding PLR and NLR levels ($p > 0.05$) (Table 2).

A correlation analysis between CAR and the age of *H. pylori*-positive patients revealed a low-level, positive significant connection ($r = 0.25$, $p < 0.001$). No association was observed among the other metrics.

In the comparison of *H. pylori* positivity, neutrophil activity, and *H. pylori* density in biopsy results of *H. pylori*-positive individuals, a positive correlation was observed between *H. pylori* density and neutrophil activity (correlation coefficient $r = 0.29$, $p < 0.01$). However, no statistically significant relationship was found between *H. pylori* positivity, neutrophil activity, and CRP/albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), or platelet-to-lymphocyte ratio (PLR). A statistically significant relationship was identified only between neutrophil activity and NLR ($p = 0.03$). Additionally, no statistically significant correlation was observed between *H. pylori* density and neutrophil activity with CAR, NLR, or PLR.

A statistically significant relationship was found between the level of inflammation and the neutrophil-to-lymphocyte ratio (NLR) ($p = 0.03$) (Table 3).

In the ROC analysis conducted to predict the presence of *H. pylori*, statistical significance was observed in the CAR value; however, no statistical significance was found in the NLR and PLR values. At the threshold of the CAR value of 0.0475, sensitivity was 53.8% and specificity was 52.1% (Figure 1).

DISCUSSION

This study reveals a significant correlation between *H. pylori* infection and CAR. *H. pylori* infection occurs at varied rates (28 - 84%) throughout various global populations. Its frequency is higher in societies with poor socioeconomic status [15]. Infection is typically contracted throughout childhood and, if left untreated, it can persist for the duration of the host's life. Determinants such as age, ethnicity, and socio-economic position influence the prevalence of infection [15,16]. The prevalence of *H. pylori* positivity increases with age [17]. Our study revealed that *H. pylori*-positive patients were actually younger than *H. pylori*-negative patients. The existing literature on the subject indicates that *H. pylori* colonization is more prevalent in older age groups. In this study, although the age difference was minimal, the high rate of *H. pylori* positivity in the younger group may be attributable to the relatively small population size of the study. This observation may also be attributed to the fact that the study was conducted in a limited group, such as patients admitted to a tertiary hospital with dyspeptic complaints. The literature also indicates that spontaneous clearance of *H. pylori* infection can be observed in certain periods, particularly in children. *H. pylori* colonization may decrease in relation to antibiotic use, and the small number of patients in our study may have been affected by these conditions [18.19]. The literature indicates that *H. pylori* is predominant in males [20]. Our results revealed that *H. pylori* positivity was more prevalent in men. This has been attributed to hormonal influences that enhance the immune system and women's reduced exposure to environmental variables like smoking.

Several studies have indicated a persistent mild increase in serum inflammatory markers, particularly CRP, in *H. pylori* infection [7,21]. In the literature, some acute phase reactants and ratios, such as NLR and PLR, have been studied in *H. pylori* infection. These ratios have been obtained using routine hemogram parameters in recent years and increased inflammation states. In a study by Saglam et al., no difference was found between *H. pylori* (+) and *H. pylori* (-) patients in Hgb, CRP, erythrocyte sedimentation rate (ESR), ferritin, and leukocyte levels. However, NLR was found to be lower and PLR higher in the *H. pylori*-positive group [22]. Conversely, Melito et al. observed that childhood and adolescent gastritis did not have a significant effect on platelet count, MPV, PLR, or NLR. However, lymphocyte levels were significantly higher in children with non-*H. pylori* pediatric gastritis compared to *H. pylori*-positive and -negative patients [23]. A meta-analysis study revealed no association between *H. pylori* infection and WBC or CRP [24].

In their work examining NLR and MPV in relation to *H. pylori* infection, Güclü et al. observed that NLR was dramatically reduced in the *H. pylori*-positive group, but platelet and lymphocyte levels were significantly increased [25]. Asil et al. observed a reduction in NLR among *H. pylori*-positive individuals, indicating that *H. pylori* eradication resulted in a decreased NLR [26,27].

Upon comparison of the laboratory results between *H. pylori*-positive and -negative individuals, no significant differences were seen in Hgb, lymphocyte, platelet, CRP, NLR, and PLR measures ($p > 0.05$). However, white blood cell, neutrophil, and monocyte levels were statistically significantly higher in *H. Pylori*-positive patients compared to *H. Pylori*-negative patients. The inconsistencies in results may stem from variations in sample sizes among studies, as well as differences in the socio-demographic characteristics of the patient groups. A persistent, mild elevation of circulating inflammatory markers, particularly CRP, is noted in *H. pylori* infection. In a study conducted by Jackson et al. involving 2,361 individuals, elevated levels of sedimentation, fibrinogen, and CRP, both acute phase reactants, were observed in *H. pylori*-positive patients, indicating a substantial correlation between *H. pylori* and systemic in-

flammatory response [28]. A study indicates that CRP levels significantly contribute to the development of gastritis caused by *H. pylori* infection [29]. Nevertheless, several research in the literature indicate that *H. pylori* infection and CRP are unrelated. A study conducted in Korea revealed that *H. pylori* infection was not correlated with inflammatory markers (CRP, NLR, and PLR) [30]. This indicates that CRP does not consistently elevate in chronic inflammation solely attributable to *H. pylori*, thereby contradicting the notion that chronic *H. pylori* infection induces significant systemic inflammation. However, further research is required on this topic. These differences observed in the results of the studies in the literature may be due to socioeconomic status, geographical region, sample size, and characteristics of the subjects or laboratory differences, because CRP levels may vary depending on the sociodemographic characteristics of the subjects, smoking, genetic factors, and comorbidities (cardiovascular disease, diabetes).

The relationship between chronic *H. pylori* infection and its potential to promote systemic inflammation and elevate standard CRP levels remains unclear. In addition, some authors have examined the relationship between high-sensitivity CRP (hsCRP), which is more sensitive than standard CRP, and *H. pylori* (+). Standard CRP tests are less sensitive, meaning they are designed to detect higher levels of inflammation, usually from acute conditions like infections or injuries. Hs-CRP measures C-reactive protein at much lower levels than the standard CRP test. This sensitivity makes it useful for detecting low-grade chronic inflammation that may be associated with cardiovascular disease and other long-term health conditions.

Jafarzadeh et al. discovered that levels of high-sensitivity CRP (hsCRP) increased with the occurrence and severity of *H. pylori* gastritis. Serum hs-CPR levels were higher in *H. pylori*-infected patients. It was found that serum hs-CRP levels in H. pylori-infected patients were significantly higher than those in healthy controls [31, 32].

This study observed no difference in standard CRP levels between patients with *H. pylori* positivity and those with negative CRP levels. We routinely use standard CRP in the laboratory. This is a more economical test and is widely used. However, it should be kept in mind that the results with hs-CRP may be different.

In our study, the albumin level was statistically significantly lower in individuals who tested positive for *H. pylori* compared to those who tested negative ($p = 0.009$).

Research on *H. pylori* and serum albumin levels indicates a substantial correlation between infection and decreased serum albumin levels, increased globulin levels, and a decreased albumin/globulin ratio, which may be associated with the patient's nutritional status and microprotein synthesis [33,34]. In their work examining the correlation between *H. pylori* infection and disulfide, thiol ischemia-modified albumin, Yüksel et al. observed that albumin levels in the positive group were low, but not significantly so [35]. Brenner et al. showed that *H. pylori* infection had no correlation with C-reactive protein and leukocyte count but an inverse correlation with serum albumin level [36].

In patients with *H. pylori* infection, low serum albumin may indicate potential nutritional inadequacy or result from other underlying causes, such as inhibited albumin synthesis. In the literature, several theories have been proposed to explain the relationship between *H. pylori* infection and low serum albumin levels. These include malabsorption of amino acids due to gastric dysfunction caused by H. pylori, during infection hepatocyte resources are diverted to produce other proteins such as IgG, and albumin synthesis in the liver decreases, inhibition of albumin production as a negative acute phase reactant in subclinical disease states caused by H. pylori (such as chronic gastritis or subclinical peptic ulcer), and increased albumin degradation associated with inflammation. However, the mechanisms underlying the inverse relationship between serum albumin levels and *H. pylori* infection have not yet been fully clarified [36]. Identifying low albumin levels in *H. pylori*-positive patients may offer clinical advantages during diagnosis and treatment.

Despite the absence of alterations in CRP levels among *H. pylori*-positive individuals, CAR in these patients was statistically substantially elevated compared to in those who were negative, accompanied by a reduced albumin level ($p = 0.04$). No prior research exists in the literature examining the link between *H. pylori* and CAR. CAR may be a more significant metric than CRP alone, as it reflects both inflammatory response and nutritional status.

CAR has also been the focus of extensive research in the context of numerous inflammatory and neoplastic conditions. These studies suggest that CAR may serve as a crucial indicator of the inflammatory response and could potentially influence clinical decision-making processes. Some studies have reported that CAR is a superior indicator of inflammatory response in patients with sepsis compared to CRP or albumin alone. Furthermore, CAR has been found to be more effective than other inflammatory indicators in evaluating the presence and severity of coronary artery disease [37].

CAR and CRP-to-lymphocyte ratio (CLR) have been shown to have high sensitivity and specificity in detecting the activity of ulcerative colitis, while PLR and NLR have low diagnostic values [38].

Feng et al. examined the levels of various cytokines, including CAR, as well as other markers such as platelet, erythrocyte sedimentation rate (ESR), and interleukin-6 (IL-6) in ulcerative colitis patients. The study indicated that CAR and IL-6 may serve as potential biomarkers for evaluating the activity of ulcerative colitis [39]. However, it should be noted that markers such as IL-6 and other cytokines are often more expensive and not part of the standard repertoire of laboratory tests. Conversely, CAR has emerged as a potentially superior

alternative due to its wide availability and cost-effectiveness in clinical settings.

The correlation between CAR levels and *H. pylori* has not been previously examined; however, it has been established as significant in the pathogenesis of *H. pylori*. Research by Alkurt et al. in gastric cancer has demonstrated that CAR serves as a robust prognostic marker for predicting outcomes in gastric cancer patients [13]. In their 2021 meta-analysis of 3,346 patients, Yu et al. concluded that CAR may serve as a predictive factor in the treatment of gastric cancer patients [40].

Considering the relationship between chronic *H. pylori* colonization and gastric precancerous lesions, similar to the abovementioned studies, the finding of high CAR in *H. pylori*-positive patients in our study may have clinical significance.

Our study has several limitations. First, the retrospective design may have introduced selection bias. Second, the study population was relatively small. A significant limitation is the absence of a control group consisting of healthy individuals, which restricts the ability to evaluate the impact of potential risk factors on the outcomes. Additionally, the lack of assessment of factors such as the influence of medical treatment on CRP/albumin levels (CRP/ALB), the presence of comorbidities, and confounding variables like nutritional status further complicates the interpretation of the findings. The use of multiple clinicians for endoscopic procedures and multiple specialists for histopathologic evaluation may have introduced variability, potentially affecting the results. Lastly, the single-center design limits the generalizability of the findings to a broader population.

CONCLUSION

Numerous prior research has established the correlation between *H. pylori* infection and gastric cancer. The correlation between *H. pylori* infection and CAR has been examined, revealing a substantial association between CAR and the presence of *H. pylori* infection. Despite its limited sensitivity and specificity, we see that CAR is considered a valuable biomarker for indicating *H. pylori* infection and assessing the systemic inflammatory status of patients. Additional prospective studies with larger populations involving multiple centers and comparisons with other markers of inflammation are necessary to accurately evaluate the potential role of CAR in the diagnosis of *H. pylori.*

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