



Association Between C-reactive Protein/Albumin Ratio and Histopathological Severity of Gastritis in Children with *Helicobacter pylori* Infection

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Abstract

Aim: Considering that systemic inflammatory indicators may insufficiently represent localized gastric inflammation in juvenile populations, chronic *Helicobacter pylori* (*H. pylori*) infection is associated with persistent gastric inflammation, which may influence systemic inflammatory parameters in children. This study aimed to investigate whether the C-reactive protein/albumin ratio (CAR) was associated with the severity of histopathological gastritis and *H. pylori* colonization density in *H. pylori*-positive children.

Methods: This retrospective cross-sectional study included 121 children aged 1-18 years who underwent upper gastrointestinal endoscopy for dyspeptic symptoms and were diagnosed with *H. pylori* infection. Gastritis severity, activity, and *H. pylori* colonization density were graded according to the modified Sydney classification system. The association between the CAR and histopathological parameters was analyzed.

Results: The study included 121 pediatric patients (mean age \pm standard deviation: 14.49 \pm 2.83 years), of whom 66% were female. No statistically significant association was observed between the CAR and chronic gastric inflammation grade, gastric inflammatory activity grade, or *H. pylori* colonization density grade ($p=0.735$, $p=0.287$, and $p=0.318$, respectively). Although the median CAR was higher in patients with severe *H. pylori* colonization than in those with mild or moderate colonization, this difference did not reach statistical significance ($p=0.744$).

Conclusion: The findings indicate that the CAR is not associated with histopathological severity or colonization density of *H. pylori* in children and does not reflect the histopathological severity in pediatric *H. pylori* gastritis.

Keywords: C-reactive protein, child, gastritis, *Helicobacter pylori*, inflammation

Introduction

Helicobacter pylori (*H. pylori*) infection remains a significant global health problem and is typically acquired during early childhood, often persisting throughout life in the absence of eradication therapy. Although the overall prevalence of *H. pylori* infection has declined in recent years, it continues to affect a substantial proportion of

the pediatric population worldwide. In children, *H. pylori* infection is usually asymptomatic but is consistently associated with chronic gastric inflammation, whereas severe complications such as peptic ulcer disease or premalignant lesions are considerably less common than in adults (1). The prevalence of *H. pylori* infection varies according to geographical and socioeconomic factors, and previous studies from Türkiye have reported high

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prevalence rates in children, ranging from approximately 50% to over 60%, with prevalence increasing with age (2,3).

C-reactive protein (CRP) is a positive acute-phase reactant synthesized by the liver that increases in response to systemic inflammation, whereas albumin is a negative acute-phase reactant that decreases during inflammatory states (4,5). Recent studies in the literature on these two inflammatory markers have shown that the CRP/albumin ratio (CAR) is closely associated with the prognosis and mortality in inflammatory diseases related to inflammation, such as acute pancreatitis, Crohn's disease, rheumatoid arthritis, and ulcerative colitis (6-9). *H. pylori* gastritis is associated with chronic inflammatory stress (10). It is therefore reasonable to investigate CAR in *H. pylori* gastritis. However, a comprehensive review of the literature did not identify any previous studies evaluating the relationship between CAR and histopathological features of gastritis or *H. pylori* colonization in children. We hypothesized that CAR might be associated with histopathological features of gastritis and the severity of *H. pylori* colonization in children.

The aim of the present study was to evaluate the association between the CAR and clinical, endoscopic, and histopathological features of gastritis, as well as *H. pylori* colonization density, in children with *H. pylori* infection. By elucidating this relationship, we aimed to determine whether readily available systemic inflammatory parameters reflect the severity of localized gastric histopathological changes in pediatric *H. pylori* gastritis, rather than to assess their diagnostic performance.

Materials and Methods

Compliance with Ethical Standards

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the University of Health Science Türkiye, Gulhane Scientific Research Ethics Committee (approval number: 2022-207, date: 26.05.2022).

Study Design and Patient Selection

This study was designed as a retrospective cross-sectional observational study including pediatric patients who underwent upper gastrointestinal endoscopy for dyspeptic complaints and were diagnosed with *H. pylori* gastritis based on histopathological examination. Patients with previous *H. pylori* eradication therapy, recent antibiotic or proton pump inhibitor use, chronic systemic inflammatory diseases, or incomplete clinical or laboratory data were excluded from the study. A total of 121 pediatric patients aged 1-18 years who met the inclusion criteria were enrolled. The patient selection process and study flow are summarized in Figure 1.

Endoscopic and Histopathological Evaluation

Esophagogastroduodenoscopy was performed by a single pediatric gastroenterologist using an Olympus X260 endoscope (Olympus, Japan) under deep sedation administered by an anesthesiologist. *H. pylori* diagnosis was based on five biopsy samples—two from the antrum, two from the corpus, and one for rapid urease testing (campylobacter-like organism test). The biopsy samples were processed, stained with hematoxylin-eosin, and examined via light microscopy. The severity of gastritis and *H. pylori* colonization density were graded according to the modified Sydney system (11).

Laboratory Parameters

Laboratory findings, including serum CRP and albumin levels obtained at the time of diagnosis, were retrieved from the hospital database. The reference ranges in our laboratory are 0-5 mg/L for CRP and 3.0-5.5 g/dL for albumin.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corporation, Armonk, NY, USA). Normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean \pm standard deviation or median (minimum-maximum), as appropriate. Non-parametric tests were used for group comparisons, including the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for comparisons involving more than

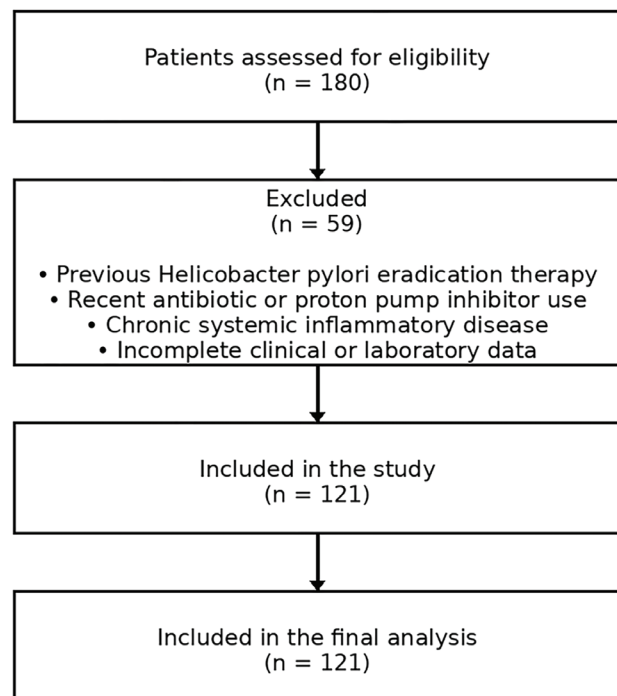


Figure 1. Flow diagram of patient selection and study population

two groups, with Bonferroni-adjusted post hoc analyses when applicable. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test. Diagnostic performance analyses, including receiver operating characteristic analysis, were not performed. A p-value <0.05 was considered statistically significant.

Results

Descriptive analyses

A total of 121 pediatric patients were included (mean age: 14.49±2.83 years). The mean CRP level was 2.94±9.53 mg/L, the mean albumin was 4.46±0.47 g/dL, and the mean CAR was 0.72±2.26 (Table 1). Of the patients, 62.0% were aged ≥15 years and 66.6% were female. Endoscopic evaluation revealed antral gastritis in 43.8% of patients and pangastritis in 56.2%. Histopathologically, gastritis severity was classified as mild in 19.0%, moderate in 64.5%, and severe in 16.5% of patients. Similarly, *H. pylori* colonization density was mild in 31.4%, moderate in 46.3%, and severe in 22.3% of cases. Neither intestinal metaplasia nor atrophy was observed in any patient.

Relationship Between CAR and Clinical and Histopathological Parameters

No significant associations were identified between CAR and demographic, clinical, endoscopic, or histopathological parameters, including gastric inflammation grade, inflammatory activity, and *H. pylori* colonization density (all p>0.05) (Table 2). Although median CAR values tended to be higher in patients with severe *H. pylori* colonization compared with those with mild or moderate colonization, this difference did not reach statistical significance (p=0.74).

Table 1. Socio-demographic and clinical characteristics of the patients

Variable	Median (min-max)
Age (years)	15 (5-18)
CRP (mg/L)	0.64 (0.05-102)
Albumin (g/dL)	4.48 (1.5-5.5)
CRP/albumin	0.15 (0.01-23.08)

CRP: C-reactive protein

Table 2. Association between the C-reactive protein/albumin ratio and demographic, clinical, endoscopic, and histopathological characteristics

		CRP/albumin Median (min-max)	p
Gender	Female (n=77)	0.14 (0.01-23.08)	0.459*
	Male (n=44)	0.23 (0.02-3.47)	
Age (year)	<15 (n=46)	0.12 (0.02-23.08)	0.928*
	≥15 (n=75)	0.16 (0.01-4.81)	
Stomach pain	No (n=17)	0.25 (0.02-5.63)	0.153*
	Yes (n=104)	0.15 (0.01-23.08)	
Nausea/vomiting	No (n=78)	0.15 (0.01-23.08)	0.820*
	Yes (n=43)	0.14 (0.01-5.63)	
Retrosternal burning	No (n=82)	0.15 (0.01-23.08)	0.794*
	Yes (n=39)	0.15 (0.01-4.81)	
Regurgitation	No (n=114)	0.14 (0.01-23.08)	0.172*
	Yes (n=7)	0.2 (0.09-2.07)	
Endoscopic finding	Antral gastritis (n=53)	0.09 (0.02-23.08)	0.408*
	Pangastritis (n=68)	0.19 (0.01-4.68)	
Gastric inflammation grade	Mild (n=23)	0.15 (0.02-3.11)	0.735**
	Moderate (n=78)	0.14 (0.01-5.63)	
	Severe (n=20)	0.14 (0.01-23.08)	
Gastric inflammatory activity grade	Mild (n=36)	0.12 (0.02-3.11)	0.287**
	Moderate (n=56)	0.12 (0.01-5.63)	
	Severe (n=22)	0.16 (0.04-23.08)	
	Negative (n=7)	0.1 (0.04-1.82)	
Gastric <i>H. pylori</i> colonization density grade	Mild (n=38)	0.07 (0.02-5.63)	0.318**
	Moderate (n=56)	0.13 (0.01-3.47)	
	Severe (n=27)	0.22 (0.01-23.08)	

*Mann-Whitney U test

**Kruskal-Wallis test post-hoc: Bonferroni Mann-Whitney U test

Discussion

Helicobacter pylori infection remains the most common chronic bacterial infection worldwide and represents a significant public health burden, particularly in developing countries (1). A Turkish epidemiological study by Ertem et al. reported that the prevalence of *H. pylori* infection in children under 4 years old was 18.2%, increasing to 65% in adolescents (3). Consistent with previous epidemiological data, the majority of patients in the present cohort were adolescents, with a higher prevalence observed among individuals aged 15 years and older. Similar to prior reports, no significant gender-related differences were observed, supporting the notion that *H. pylori* infection affects male and female children equally.

Previous studies have demonstrated a close association between *H. pylori* colonization density and both chronic gastric inflammation and gastric inflammatory activity, with increasing bacterial burden being linked to more pronounced mucosal inflammation (12). Consistent with these reports, our findings indicate that gastric inflammatory activity increases in parallel with rising *H. pylori* colonization density, supporting the concept that bacterial load plays a key role in the severity of the local gastric inflammatory response in pediatric patients. The absence of gastric atrophy or intestinal metaplasia in this cohort is in line with existing pediatric literature, which indicates that *H. pylori* infection in childhood is more commonly associated with chronic gastritis and peptic ulcer disease rather than premalignant gastric lesions (13).

The primary aim of this study was to determine whether the CRP/CAR reflects histopathological severity in pediatric *H. pylori* gastritis. Despite clear histopathological evidence of gastric inflammation and inflammatory activity, no significant association was observed between the CAR and any of the following: chronic gastric inflammation grade, gastric inflammatory activity grade, or *H. pylori* colonization density grade. These findings suggest that this systemic inflammatory marker does not adequately reflect the degree of localized gastric inflammation in children with *H. pylori* infection.

The CRP/CAR is an inflammation-based prognostic marker linked to the severity of inflammatory conditions. The CAR has been widely investigated as an inflammation-based marker in pediatric and adult populations, particularly in conditions characterized by systemic and high-grade inflammatory responses. Previous studies have demonstrated its clinical utility in diseases such as complicated appendicitis, sepsis, inflammatory bowel disease, and advanced liver disease, where inflammation is diffuse, persistent, and associated with measurable alterations in circulating acute-phase reactants (14-17).

Helicobacter pylori infection has been shown to induce both localized gastric mucosal inflammation and low-grade systemic inflammatory responses, reflecting its role as a common cause of chronic gastritis. Previous pediatric studies have demonstrated that this low-grade systemic inflammation may be detected through cell-based inflammatory indices, such as neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios, which appear to correlate with the presence and severity of *H. pylori* infection (18).

In contrast, the C-reactive protein/albumin ratio represents a composite marker of the acute-phase response and may require a more pronounced or diffuse systemic inflammatory burden to show consistent alterations. Although *H. pylori* infection is associated with localized gastric inflammation and low-grade systemic inflammatory responses, this level of inflammation may be insufficient to induce measurable changes in serum acute-phase reactants in pediatric patients. This pathophysiological difference may explain the lack of association observed in the present study between the C-reactive protein/albumin ratio and gastric chronic inflammation grade, gastric inflammatory activity grade, or *H. pylori* colonization density.

Study Limitations

The limitations of this study include its retrospective design, a relatively small sample size, and the absence of an *H. pylori*-negative control group, which limit the evaluation of the diagnostic performance and the cut-off value of the C-reactive protein/albumin ratio. In addition, serum CRP and albumin levels are non-specific parameters that may be influenced by various clinical conditions unrelated to gastric inflammation. Despite these limitations, the study provides a detailed histopathological evaluation based on the standardized Sydney classification and offers novel insight into the relationship between a widely used systemic inflammatory marker and localized gastric inflammation in pediatric *H. pylori* gastritis.

Conclusion

Although median CAR values tended to be higher in children with significant *H. pylori* colonization than in those with mild or moderate colonization, the difference did not reach statistical significance. The findings of this study indicate that the CAR does not reliably reflect the severity of chronic gastric inflammation, gastric inflammatory activity, or *H. pylori* colonization density in pediatric patients. These results suggest that systemic acute-phase reactants may have limited utility in assessing localized gastric inflammation associated with *H. pylori* infection in children. Further large-scale prospective studies are needed to validate these findings.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the University of Health Science Türkiye, Gulhane Scientific Research Ethics Committee (approval number: 2022-207, date: 26.05.2022).

Informed Consent: Written informed consent was waived due to the retrospective nature of the study; however, general consent for diagnostic procedures was obtained from all patients and/or their legal guardians.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.K., N.B., B.U., Concept: H.K., N.B., B.U., Design: H.K., N.B., B.U., Data Collection or Processing: H.K., M.A., C.F.O., E.G.B., N.B., Analysis or Interpretation: H.K., M.A., C.F.O., E.G.B., Literature Search: H.K., M.A., Writing: H.K., M.A., N.B.

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