DOI: 10.4274/gulhane.galenos.2026.42223
Gulhane Med J 2026;68(2):109-117

Hematological indices in children with *Helicobacter pylori* infection: a retrospective analysis

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Cite this article as: Ergen YM, Teke S. Hematological indices in children with *Helicobacter pylori* infection: a retrospective analysis. *Gulhane Med J.* 2026;68(2):109-117.

Date submitted:
22.10.2025
Date accepted:
20.01.2026
Publication Date:
16.06.2026

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Keywords: *Helicobacter pylori*, children, hematological indices, PLR, MPVLR

ABSTRACT

Aims: *Helicobacter pylori (H. pylori)* infection is a frequent chronic condition in childhood, and determining whether it provokes a systemic inflammatory imprint is clinically relevant. This study aimed to evaluate whether pediatric *H. pylori* infection was associated with alterations in complete blood count (CBC)-derived inflammatory indices, particularly the platelet-to-lymphocyte ratio (PLR) and the mean platelet volume-to-lymphocyte ratio (MPVLR).

Methods: This retrospective cross-sectional study included children aged 6-18 years who underwent upper gastrointestinal endoscopy for dyspeptic symptoms and had histopathological confirmation of *H. pylori* infection. Pre-procedural CBC and serum albumin levels were recorded, and CBC-derived inflammatory indices (such as the PLR and the MPVLR) were calculated. The primary endpoint was the association between *H. pylori* positivity and these inflammatory indices.

Results: A total of 453 children were included, of whom 171 were *H. pylori* positive and 282 were *H. pylori* negative [median age 13.4 years (interquartile range 10.8-15.7); predominantly female (65.6%)]. Children with *H. pylori* infection had significantly higher PLR (127.45 vs. 113.50; p<0.001) and MPVLR (4.45 vs. 4.02; p<0.001) values compared with controls. Neutrophil, lymphocyte, and monocyte counts were lower in the positive group (p<0.01 for all), while no meaningful differences were observed in other composite indices.

Conclusions: Pediatric *H. pylori* infection is associated with a measurable, low-grade systemic inflammatory response, as reflected by elevated PLR and MPVLR values.

Introduction

Helicobacter pylori (H. pylori) is a common bacterial pathogen in childhood; in the absence of treatment, it may persist in the host for many years. In children, the infection is frequently silent or accompanied only by vague, non-specific complaints; however, the resulting persistent gastric inflammation can facilitate the development of peptic ulcer disease and may elevate the long-term risk of malignancy later in life (1). In addition to gastric involvement, the organism has been linked to several extra-intestinal consequences, including impaired growth, iron deficiency anemia, and immune-mediated thrombocytopenia, which highlights the need for timely detection and management in childhood (2). Consequently, it is important to evaluate not only whether the bacterium is present but also how it influences the host's overall biology. In children, the immunological reaction elicited by *H. pylori* generally manifests as a mild, predominantly cell-mediated inflammatory response.

In pediatric patients, the immune response to *H. pylori* typically reflects a low-grade, cell-mediated inflammatory pattern. Sustained antigenic stimulation promotes persistent mucosal inflammation while simultaneously altering the balance of circulating neutrophils, lymphocytes, and platelets (3,4). These systemic changes indicate that the infection is not confined to the gastric mucosa but may also be indirectly monitored through peripheral hematological parameters.

In this context, hematological indices derived from the complete blood count (CBC) have gained increasing attention as non-invasive biomarkers for the evaluation of chronic inflammatory processes in children. Various CBC-derived ratios, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR), have been explored as indirect markers of systemic immune activation in a range of pediatric disorders (5). However, existing pediatric studies on *H. pylori* have reported heterogeneous diagnostic performance, and data correlating these indices with histopathological severity or bacterial density remain limited (6,7). This uncertainty highlights the need to better define the clinical utility of CBC-based composite markers in the non-invasive assessment of *H. pylori*-associated gastric inflammation in the pediatric population.

In light of these gaps, the present study was designed to characterize the hematological alterations associated with *H. pylori* infection in children with dyspeptic complaints and to determine whether CBC-based composite indices can support the identification of infection and approximate the histopathological severity. Through this investigation, we aimed to clarify the potential clinical value of these easily obtainable, inexpensive, and non-invasive parameters in routine pediatric practice.

Methods

Study design and participants

This study employed a descriptive retrospective cross-sectional design and used clinical data from pediatric patients who underwent endoscopic evaluation for dyspeptic complaints at a tertiary pediatric gastroenterology referral center between August 2023 and August 2025. Eligible participants were children aged 6-18 years who underwent upper gastrointestinal (GI) endoscopy under general anesthesia and whose gastric biopsy specimens were assessed for *H. pylori* status by histopathological examination. All information was extracted retrospectively from the institutional electronic medical records and analyzed after full de-identification.

As part of the standard pre-endoscopy anesthesia protocol at our center, a CBC and a routine biochemistry panel (including albumin) were obtained after an overnight fast of approximately eight hours. For inclusion in the present analysis, these laboratory assessments had to have been performed no more than one week before endoscopy.

The *H. pylori*-positive group consisted of patients in whom the bacterium was identified by Giemsa or hematoxylin-eosin (H&E) staining of biopsy specimens. The control group was selected from children who presented with the same dyspeptic complaints and underwent endoscopy for clinical indications, but were histologically negative for *H. pylori* and showed no endoscopic abnormalities other than mild non-specific hyperemia. Individuals were not considered eligible if they had chronic systemic illnesses; had abnormalities in the esophagus or duodenum on endoscopy or histology; were taking medications such as antibiotics, corticosteroids, or immunosuppressants; an acute infection within the preceding four weeks; had signs of active systemic inflammation; or had missing laboratory or pathology data.

Endoscopic evaluation

All procedures were carried out while the children were under general anesthesia, which was administered and monitored by a pediatric anesthesia team. Upper GI endoscopy was performed by an experienced pediatric gastroenterologist using the Fujinon ELUXEO VP-7000/BL-7000 videoendoscopy system (Fujifilm Corporation, Tokyo, Japan); the endoscope diameter was selected according to the child's age and body size, and the procedure was performed in a child-friendly environment. The procedures were conducted in accordance with the recommendations of the 2023 ESPGHAN/NASPGHAN *H. pylori* guideline (8). Mucosal findings observed during the procedure (e.g., hyperemia, edema, nodularity, erosion, and ulceration) were recorded using a standardized protocol. From each patient, six gastric biopsies were systematically collected: three from the antral region and three from the corpus, to allow adequate histopathological evaluation. Additional biopsies were collected from macroscopically abnormal areas when present. All biopsy samples were labeled appropriately and fixed in 10% neutral-buffered formalin before being transferred to the pathology laboratory.

Histopathological evaluation

Gastric biopsy samples obtained from both the antrum and corpus were evaluated using the criteria defined in the Updated Sydney System (9). Diagnosis of *H. pylori* infection was based on these standardized histopathological findings. Rapid urease testing or culture/PCR is not routinely included in the initial diagnostic workflow for pediatric endoscopy at our center. To reduce the risk of misclassification, cases with equivocal histological findings were excluded. The degree of mucosal inflammation, inflammatory activity, glandular atrophy, intestinal metaplasia, and H. pylori burden were recorded using a four-tier grading system ranging from 0 (absent) to 3 (severe). The presence of *H. pylori* was evaluated using H&E and/or Giemsa

staining, and immunohistochemical confirmation was performed when deemed necessary. All evaluations were conducted by experienced pathologists at the institution.

Laboratory parameters and calculated hematological indices

All laboratory data were obtained retrospectively from the hospital information system. CBC and biochemistry results obtained as part of the standard pre-endoscopy anesthesia protocol constituted the laboratory dataset for this study. Only patients with laboratory tests performed during the same admission as the endoscopy were included in the analysis.

CBC parameters were measured using an automated hematology analyzer (Mindray BC-6000, Shenzhen Mindray Bio-Medical Electronics Co., Ltd., China) following routine quality-control procedures. The recorded parameters included white blood cell count, neutrophil count, lymphocyte count, monocyte count, erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), red cell distribution width (RDW), platelet count, mean platelet volume (MPV), platelet distribution width, and plateletcrit. Serum albumin levels were measured in the hospital biochemistry laboratory using the COBAS C8000 analyzer system (Roche Diagnostics, Mannheim, Germany), and all values were assessed according to internationally accepted laboratory standards.

In addition to raw CBC values, a set of CBC-derived inflammatory indices reflecting neutrophil-, lymphocyte-, and platelet-based systemic immune activity was calculated. Based on these measurements, CBC-derived hematological and composite inflammatory indices were calculated, including NLR, PLR, LMR, dNLR, systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), aggregate index of systemic inflammation (AISI), MPV-to-lymphocyte ratio (MPVLR), mean platelet volume-to-platelet ratio (MPR), RDW-to-platelet ratio (RPR), prognostic nutritional index (PNI), neutrophil-to-albumin ratio (NAR), and platelet-to-albumin ratio (PAR), with the corresponding formulas summarized in Table 1. All calculated ratios and raw laboratory values were included in the statistical analysis.

Ethical Approval

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki (1975), as revised in 2013. Because this research was conducted as a retrospective chart review with no direct patient contact or intervention, the approving ethics committee waived the requirement for written informed consent. The study protocol was reviewed and approved by the University of Health Sciences Türkiye, Gülhane Scientific Research Ethics Committee (approval no: 2025-417, date: 30.09.2025).

Statistical Analysis

All statistical computations were carried out with IBM SPSS Statistics software (version 26.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro-Wilk test. Non-normally distributed data were presented as median (minimum-maximum), whereas categorical variables were presented as frequencies and percentages.

Comparisons between the *H. pylori* positive and negative groups were performed using the Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Multiple comparisons were controlled using the Benjamini-Hochberg false discovery rate (FDR) procedure. Effect sizes, together with 95% confidence intervals, were calculated to complement p-values.

Table 1. Calculation formulas of hematological and composite inflammatory indices

Abbreviation	Full name	Formula
NLR	Neutrophil-to-lymphocyte ratio	NEU/LYM
PLR	Platelet-to-lymphocyte ratio	PLT/LYM
LMR	Lymphocyte-to-monocyte ratio	LYM/MON
dNLR	Derived neutrophil-to-lymphocyte ratio	NEU/(WBC-NEU)
SII	Systemic immune-inflammation index	(PLT×NEU)/LYM
SIRI	Systemic inflammation response index	(NEU×MON)/LYM
AISI	Aggregate index of systemic inflammation	(NEU×MON×PLT)/LYM
MPR	Mean platelet volume-to-platelet ratio	MPV/PLT
MPVLR	Mean platelet volume-to-lymphocyte ratio	MPV/LYM
RPR	Red cell distribution width-to-platelet ratio	RDW/PLT
PNI	Prognostic nutritional index	(10×Alb [g/dL])+(0.005×LYM [/µL])
NAR	Neutrophil-to-albumin ratio	NEU/Alb
PAR	Platelet-to-albumin ratio	PLT/Alb

NEU: Neutrophil, LYM: Lymphocyte, MON: Monocyte, PLT: Platelet, RDW: Red cell distribution width, MPV: Mean platelet volume, Alb: Serum albumin

The discriminatory ability of each index was evaluated using receiver operating characteristic (ROC) curve analysis; in addition, area under the curve (AUC), optimal cut-off values, sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios (LR^+ and LR^-) were reported with 95% confidence intervals. Variables that remained significant in univariate analyses were subsequently included in a multivariable logistic regression model, adjusted for age, sex, hemoglobin, and albumin, to identify independent predictors of *H. pylori* positivity. A two-tailed p-value <0.05 was considered statistically significant.

In a subgroup of patients for whom a post-eradication hemogram was available in the hospital electronic records, a short-term within-patient comparison was conducted to evaluate the responsiveness of PLR and MPVLR following eradication. Because the distribution of paired differences deviated from normality (Shapiro-Wilk test), the Wilcoxon signed-rank test was applied to both indices, and effect sizes were summarized using Cliff's delta.

Results

Demographic and histopathological characteristics

A total of 453 children were included in the study, of whom 171 were *H. pylori* positive and 282 were *H. pylori* negative. The median age was 14.0 years (IQR 11.0-16.0) in the *H. pylori* positive group and 13.0 years (IQR 10.0-15.0) in the control group (difference: +1 year; 95% CI: -0.3 to +2.1; p=0.152). Sex distribution was comparable between the two groups (36.2% vs. 34.0% boys; p=0.545).

Among *H. pylori* positive patients, histopathological grading according to the Updated Sydney System demonstrated mild (17.5%), moderate (53.8%), and severe (28.7%) inflammation; mild (29.8%), moderate (50.3%), and severe (19.9%) activity; and mild (25.7%), moderate (47.4%), and severe (26.9%) bacterial density.

Hematological and biochemical parameters

There were no significant differences in hemoglobin, platelet count, MCV, mean corpuscular hemoglobin (MCH), MCH concentration, MPV, eosinophil count, or serum albumin levels between the groups (all p_FDR >0.05). In contrast, neutrophil, lymphocyte, monocyte, and RDW values were significantly higher in the *H. pylori* negative group (all p_FDR <0.05). The distribution of these differences is illustrated in Figure 1 using box-plot visualizations, and the detailed hematological and biochemical measurements are presented in Table 2.

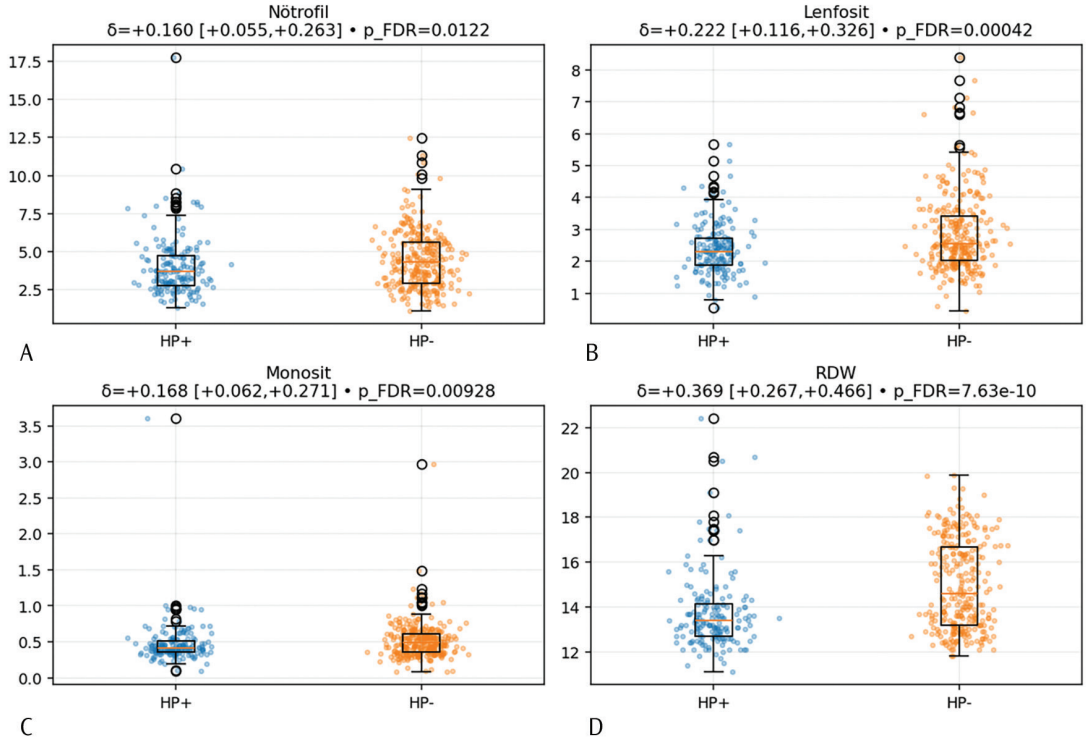

Figure 1. Hematological and biochemical parameters with significant differences

Boxplots showing hematological and biochemical parameters with significant intergroup differences between HP positive and HP negative groups: (A) Neutrophil, (B) Lymphocyte, (C) Monocyte, and (D) RDW. Boxes indicate interquartile ranges and median values, while individual jittered dots represent the distribution of observations. All p-values were adjusted for multiple comparisons using the Benjamini-Hochberg FDR method, and effect sizes are reported as Cliff's δ with 95% confidence intervals

FDR: False discovery rate, RDW: Red cell distribution width, HP: *Helicobacter pylori*

Table 2. Comparison of hematological and biochemical parameters between HP positive and HP negative groups

Parameter	HP positive (n=171)	HP negative (n=282)	Cliff's δ (95% CI)	p_FDR
Hb (g/dL)	13.40 (12.55-14.10)	13.40 (12.70-14.30)	+0.057 (-0.053 to +0.168)	0.427
Platelet (×10³/μL)	294.00 (255.00-338.00)	298.00 (259.00-350.00)	+0.042 (-0.069 to +0.152)	0.557
MCV (fL)	84.40 (80.40-87.95)	85.00 (81.50-88.20)	+0.055 (-0.054 to +0.160)	0.427
MCH (pg)	27.70 (26.00-29.00)	27.90 (26.50-29.10)	+0.066 (-0.046 to +0.175)	0.409
MCHC (g/dL)	32.60 (31.85-33.30)	32.80 (32.10-33.30)	+0.086 (-0.028 to +0.197)	0.232
MPV (fL)	10.20 (9.60-10.95)	10.20 (9.60-10.90)	-0.008 (-0.123 to +0.103)	0.891
Neutrophil (×10³/μL)	3.68 (2.77-4.76)	4.31 (2.93-5.62)	**+0.160 (+0.055 to +0.263)**	**0.012**
Lymphocyte (×10³/μL)	2.31 (1.88-2.73)	2.54 (2.04-3.42)	**+0.222 (+0.116 to +0.326)**	**0.0004**
Monocyte (×10³/μL)	0.41 (0.36-0.52)	0.49 (0.36-0.61)	**+0.168 (+0.062 to +0.271)**	**0.009**
Eosinophil (×10³/μL)	0.12 (0.07-0.21)	0.12 (0.06-0.21)	-0.013 (-0.126 to +0.098)	0.863
RDW (%)	13.40 (12.70-14.20)	14.60 (13.20-16.70)	**+0.369 (+0.268 to +0.466)**	**<0.0001**
Albumin (g/dL)	4.70 (4.50-4.80)	4.70 (4.50-4.90)	+0.030 (-0.079 to +0.136)	0.701

Values are presented as median (interquartile range). Statistical comparisons were performed using the Mann-Whitney U test
This table summarizes peripheral blood hematological and biochemical findings in the HP-positive and HP-negative (control) groups. Although hemoglobin, erythrocyte indices (MCV, MCH, MCHC), platelet count, MPV, eosinophil count, and albumin levels were comparable between the two groups, neutrophil, lymphocyte, monocyte, and RDW values were significantly higher in the HP-negative group
Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, MPV: Mean platelet volume, RDW: Red cell distribution width, HP: *Helicobacter pylori*, FDR: False discovery rate

Hematological indices

When hematological indices derived from CBC parameters were compared, PLR and MPVLR were significantly higher in the *H. pylori* positive group, whereas RPR, NAR and PNI were significantly higher in the *H. pylori* negative group (all p_FDR <0.05). Detailed comparative results are presented in Table 3, and representative distributions of the significant indices are illustrated in Figure 2. Although PLR and MPVLR values showed statistically significant differences between groups, the effect sizes were small, and therefore, their biological relevance should be interpreted with caution.

Among *H. pylori* positive patients, post-eradication hemogram data were available in the electronic hospital records for 36 patients, enabling a paired short-term evaluation. In this subgroup, neither PLR nor MPVLR showed a significant change following treatment. PLR decreased from a mean of 139.86 to 128.00 (mean difference -11.86; Wilcoxon W=305; p=0.870; Cliff's δ=-0.086), whereas MPVLR decreased from a mean of 4.754 to 4.477 (mean difference -0.277; Wilcoxon W=315; p=1.000; Cliff's δ=0.029). These findings indicate that only a small fraction of the *H. pylori* positive cohort had system-level post-eradication CBC follow-up data available; in this subset, no early measurable shift in PLR/MPVLR was observed.

Correlation between hematological parameters and histopathological findings

Spearman's correlation analysis demonstrated only weak and non-significant associations between the evaluated indices (NLR, PLR, LMR, SII, SIRI, AISI, MPVLR, MPR, RPR, NAR, PAR, and PNI) and *H. pylori* density, histological activity, or inflammation scores (all p>0.05). Similarly, conventional laboratory parameters such as RDW, MPV, and albumin showed no significant relationships with histopathological severity. The correlation coefficients (ρ) ranged from -0.10 to +0.23, indicating minimal effect sizes that were neither clinically nor statistically significant. These findings suggest that peripheral hematological and biochemical markers do not reliably reflect the histological severity or inflammatory activity of *H. pylori* associated gastritis in children; see Supplementary Figure S1.

ROC analysis

Exploratory ROC analysis showed that PLR and MPVLR had the highest, yet still modest, discriminative performance in identifying *H. pylori* infection, with AUC values around 0.60. Other indices, including NAR, RPR, and PNI, demonstrated poor diagnostic ability (AUC ≤0.43). Accordingly, the complete ROC curves are presented in the Supplementary Material (Supplementary Figure S2).

Discussion

In this study, we observed that both primary hematological parameters and CBC-derived inflammatory indices significantly differed between *H. pylori* positive and *H. pylori* negative children. The *H. pylori* positive group exhibited significantly higher PLR and MPVLR values, whereas neutrophil, lymphocyte, and monocyte counts were lower than those in controls. In contrast, RDW values were significantly higher in the *H. pylori* negative group, while hemoglobin and MCV levels remained comparable between the two groups.

Table 3. Comparison of hematological indices between HP positive and HP negative groups

Parameter	HP positive (n=171)	HP negative (n=282)	Cliff's δ (95% CI)	p_FDR
NLR	1.56 (1.12-2.23)	1.49 (1.11-2.13)	+0.017 (-0.093 to +0.125)	0.547
dNLR	0.86 (0.82-0.89)	0.87 (0.83-0.90)	+0.010 (-0.102 to +0.121)	0.491
LMR	5.41 (4.30-6.80)	5.58 (4.35-6.86)	+0.018 (-0.094 to +0.130)	0.485
SII	461.19 (334.60-692.72)	449.59 (322.94-629.40)	-0.008 (-0.119 to +0.103)	0.547
SIRI	0.65 (0.44-0.97)	0.71 (0.48-1.10)	+0.044 (-0.067 to +0.156)	0.485
AISI	186.94 (133.37-318.31)	218.10 (131.00-352.67)	+0.040 (-0.072 to +0.154)	0.491
MPR	0.03 (0.03-0.04)	0.03 (0.03-0.04)	+0.022 (-0.094 to +0.136)	0.603
PAR	63.83 (53.55-73.92)	63.71 (54.06-75.62)	+0.012 (-0.098 to +0.123)	0.870
PLR	127.45 (102.24-165.81)	113.50 (88.92-145.09)	**-0.205 (-0.308 to -0.098)**	**0.0004**
MPVLR	4.45 (3.57-5.70)	4.02 (3.02-5.05)	**-0.210 (-0.316 to -0.106)**	**0.0004**
RPR	0.05 (0.04-0.06)	0.05 (0.04-0.05)	**+0.152 (+0.044 to +0.259)**	**0.007**
NAR	0.76 (0.60-1.05)	0.91 (0.63-1.18)	**+0.150 (+0.045 to +0.256)**	**0.007**
PNI	58.60 (55.62-61.75)	60.25 (57.11-64.21)	**+0.229 (+0.122 to +0.330)**	**<0.001**

Values are presented as median (interquartile range). Statistical comparisons were performed using the Mann-Whitney U test. p-values were adjusted for multiple comparisons using the Benjamini-Hochberg FDR method, and effect sizes were reported as Cliff's δ with 95% confidence intervals. Bold p-values indicate statistically significant differences after FDR correction (p_FDR <0.05)

Among CBC-derived indices, PLR and MPVLR were significantly higher in the HP-positive group, while RPR, NAR, and PNI were significantly higher in the HP-negative group (all remained significant after FDR correction). No significant intergroup differences were observed for NLR, dNLR, LMR, SII, SIRI, AISI, MPR, or PAR

NLR: Neutrophil-to-lymphocyte ratio, dNLR: Derived neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, AISI: Aggregate index of systemic inflammation, MPVLR: Mean platelet volume-to-lymphocyte ratio, MPR: Mean platelet volume-to-platelet ratio, RPR: Red cell distribution width-to-platelet ratio, NAR: Neutrophil-to-albumin ratio, PAR: Platelet-to-albumin ratio, PNI: Prognostic nutritional index, HP: *Helicobacter pylori*, FDR: False discovery rate, CI: Confidence interval

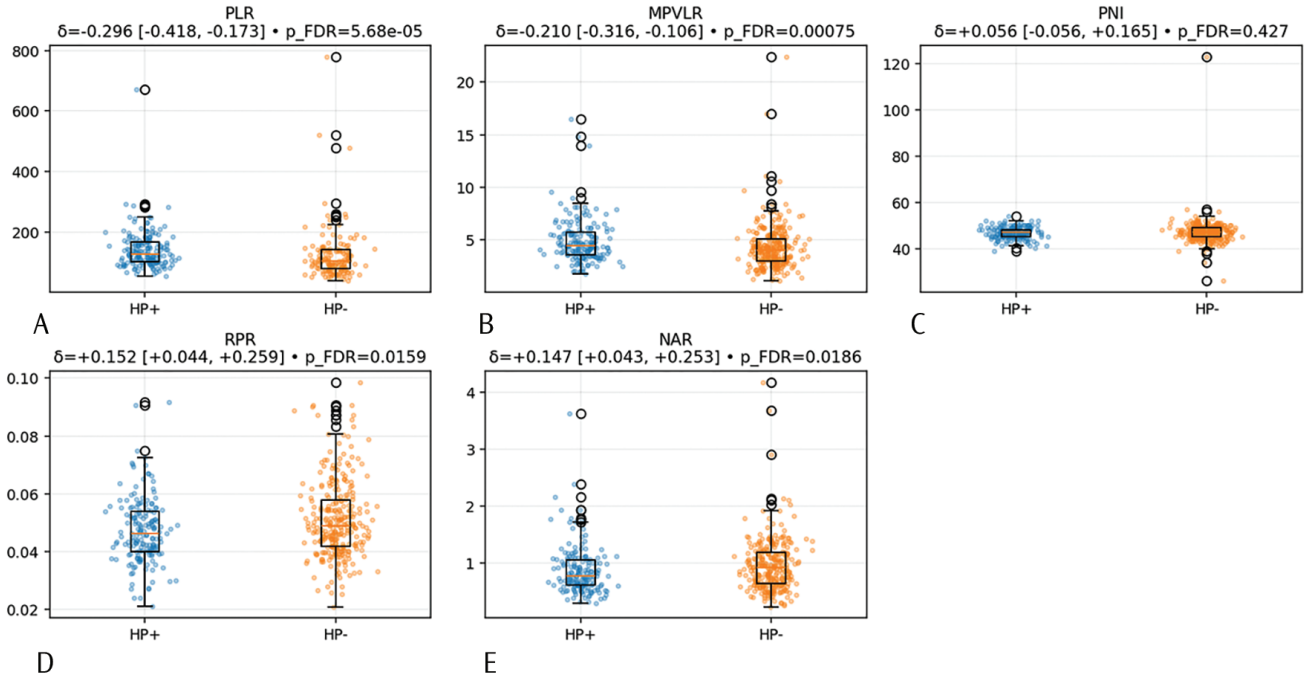

Figure 2. Significant hematological indices between HP positive and HP negative groups

Boxplots of hematological indices with significant intergroup differences between HP positive and HP negative groups: (A) PLR, (B) MPVLR, (C) PNI, (D) RPR, and (E) NAR. Boxes indicate interquartile ranges and medians; individual jittered dots show the distribution of observations. All p-values were adjusted for multiple comparisons using the Benjamini-Hochberg FDR method, and effect sizes are reported as Cliff's δ with 95% confidence intervals

PLR: Platelet-to-lymphocyte ratio, MPVLR: Mean platelet volume-to-lymphocyte ratio, RPR: Red cell distribution width-to-platelet ratio, NAR: Neutrophil-to-albumin, PNI: Prognostic nutritional index, HP: *Helicobacter pylori*, FDR: False discovery rate

During *H. pylori* infection, pro-inflammatory cytokines such as interleukin-1β (IL-1β), IL-6, tumor necrosis factor- α (TNF-α), and IL-8 are upregulated within the gastric mucosa, initiating a local immune response that subsequently influences hematopoietic pathways. Among these, IL-6-mediated upregulation of hepatic thrombopoietin enhances megakaryocyte activation and platelet production, whereas TNF-α and IL-8 promote lymphocyte recruitment to the site of inflammation, leading to a relative decline in peripheral lymphocyte counts (10). The combined effect of increased platelet activity and reduced lymphocyte levels translates into higher PLR and MPVLR values. Conversely, the absence of a pronounced neutrophil-dominant response and the predominantly low-grade, mucosa-restricted inflammatory pattern of *H. pylori* gastritis explain why neutrophil-weighted markers such as NLR did not differ significantly between groups. This pathophysiological mechanism may partially explain the lack of correlation between histopathological severity and hematological indices observed in our cohort, given that CBC-based markers reflect systemic inflammatory activity, whereas histopathology reflects strictly local inflammatory activity.

Previous studies assessing the relationship between *H. pylori* infection and hematological indices have yielded heterogeneous findings. Some reports have demonstrated elevated NLR, whereas others with larger sample sizes have found no meaningful differences in NLR or MPV. This heterogeneity is also evident across the limited pediatric literature, where some cohorts report mild elevations in CBC-derived indices while others demonstrate no significant systemic signal. The absence of a difference in NLR in our study aligns with the latter group and suggests that pediatric *H. pylori* infection may be characterized by a limited systemic inflammatory imprint without a dominant neutrophilic response. In contrast, the significant elevation in PLR parallels findings from studies emphasizing platelet-driven immune activation (11-13). Notably, the concomitant increase in MPVLR observed in our cohort appears to be the first reported evidence of this finding in the pediatric population, underscoring its potential relevance as a surrogate marker of platelet functional activation in this age group.

A key contribution of our study is the first demonstration that MPVLR is significantly elevated in pediatric *H. pylori* infection. In the adult literature, MPVLR has been proposed as a marker of pro-inflammatory activation in cardiovascular and autoimmune disorders; however, its clinical relevance in childhood disease has not previously been explored (14). The elevation of MPVLR in *H. pylori* positive children reflects the combined effect of enhanced platelet activation and reduced peripheral lymphocyte counts. This finding further supports the view that inflammation in childhood *H. pylori* infection is not neutrophil-dominant but rather is organized along a platelet-lymphocyte axis, which in turn reinforces the observed increase in PLR and suggests that MPVLR may serve as a marker of this pathway. Rather than indicating definitive systemic inflammation, our findings might reflect subtle hematological alterations associated with *H. pylori* infection and should be interpreted as hypothesis-generating.

Although an expanded RDW has been reported in conditions associated with gastric inflammation, it is noteworthy that RDW was higher in the *H. pylori* negative group in our cohort (15). This finding suggests that RDW is influenced more strongly by non-infectious factors, such as micronutrient status, dietary variation, or subtle alterations in erythropoiesis, than by serving as a reliable marker of the inflammatory response specific to *H. pylori*.

The absence of correlation between *H. pylori* density and hematological indices, according to the Sydney classification, further supports the notion that *H. pylori* infection in children is characterized by a predominantly local rather than systemic inflammatory response. A similar observation has been reported in adults, where hematological markers were able to reflect the presence of infection but not the histological severity of mucosal injury (16). This parallel reinforces the concept that these indices lack sufficient sensitivity to gauge the extent of mucosal damage in both pediatric and adult populations.

ROC analysis demonstrated that although PLR and especially MPVLR achieved statistical significance in discriminating *H. pylori* positivity, their diagnostic performance remained modest. AUC values hovering around 0.60 indicate that these markers are unlikely to serve as stand-alone diagnostic tools and should, at best be interpreted as adjunctive indicators. The post-hoc power analysis, which confirmed adequate statistical power for medium effect sizes (power ≈ 0.87), further supports the interpretation that the limited AUC values stem not from sample size constraints but from the intrinsically limited diagnostic capacity of these biomarkers.

A short-term paired analysis in the subgroup with available post-eradication CBCs likewise showed no significant reduction in PLR or MPVLR, indicating that these indices do not meaningfully improve in the early post-treatment period. This supports the interpretation that their utility is limited to cross-sectional detection rather than follow-up monitoring.

Among the main strengths of this study are its large sample size (n=453), the histopathological confirmation of *H. pylori* infection, and the exclusion of potential confounders such as active infection, immunosuppressive therapy, and systemic disease. Furthermore, the simultaneous assessment of multiple hematological and composite indices allowed for a comprehensive characterization of the systemic immune profile associated with *H. pylori* infection in children.

Study Limitations

However, several limitations should be considered. The retrospective, cross-sectional design precludes the establishment of causality. Moreover, the absence of additional

biomarkers, such as ferritin, iron indices, CRP, or cytokine panels, limited the biological interpretability of the hematological alterations. In our center, these biomarkers are not routinely collected prior to endoscopy, which limits their availability for analysis. Although this may reduce the granularity of systemic inflammatory profiling, the lack of intergroup imbalance in baseline measures such as body mass index, hemoglobin, and albumin suggests that any residual confounding is likely minimal. Additionally, *H. pylori* infection was diagnosed solely on the basis of histopathological findings. Although standardized antral and corpus sampling enhances diagnostic accuracy, the absence of a second confirmatory invasive test, such as a rapid urease test or culture, as recommended by the current ESPGHAN and NASPGHAN guidelines, may have resulted in diagnostic misclassification in cases with low bacterial density, which could have biased the associations observed in this study toward the null. Finally, the control group consisted of children undergoing endoscopy for dyspeptic symptoms rather than completely healthy subjects; non-specific markers, such as RDW, may have been influenced by factors unrelated *to H. pylori*.

Conclusion

From a clinical perspective, CBC-derived indices such as PLR and MPVLR may reflect subtle hematological alterations associated with *H. pylori* infection; however, given their low discriminative performance, they cannot serve as diagnostic tools and should be interpreted with caution. These indices may provide supportive information during preliminary assessment, but cannot replace histopathological confirmation via endoscopy or biopsy. Prospective studies incorporating post-eradication follow-up could better elucidate the temporal dynamics of these hematological markers, while the integration of data on iron metabolism, nutritional indices, and cytokine profiles would help delineate the true systemic boundaries of *H. pylori*-associated inflammation in children.

Our findings indicate that pediatric *H. pylori* infection may be associated with subtle hematological alterations, particularly in platelet- and lymphocyte-related indices. These changes likely reflect a mild and predominantly mucosa-restricted inflammatory response rather than definitive systemic inflammation. Although PLR and MPVLR demonstrated statistically significant differences between groups, their limited discriminative accuracy precludes any diagnostic application. Therefore, these markers should be considered exploratory and hypothesis-generating rather than clinically actionable parameters. Prospective studies incorporating systemic inflammatory biomarkers and post-eradication follow-up are required to clarify whether such hematological alterations have meaningful clinical implications for this population.

Ethics

Ethics Committee Approval: The study protocol was reviewed and approved by the University of Health Sciences Türkiye, Gülhane Scientific Research Ethics Committee (approval no: 2025-417, date: 30.09.2025).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Concept: Y.M.E., Design: Y.M.E., S.T., Data Collection or Processing: Y.M.E., S.T., Analysis or Interpretation: Y.M.E., S.T., Literature Search: Y.M.E., Writing: Y.M.E., S.T.

Conflict of Interest: The authors declared no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

Supplementary Figures: https://d2v96fxpocvxx.cloudfront.net/688d2d00-d207-464d-89b6-73f393f4f50c/content-images/696c2741-2bb7-4a3a-87c1-6ea82a52a3ce.pdf

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