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Research

Is Atopy Less Common in *Helicobacter pylori*-Positive Patients? A Retrospective Study

Helicobacter pylori-Pozitif Hastalarda Atopi Daha mı Az Görülüyor? Retrospektif Bir Çalışma

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ABSTRACT

Objective: *Helicobacter pylori* (*H. pylori*) has been implicated in modulating systemic immune responses and may potentially influence the onset of atopic disorders. Nevertheless, its specific relationship with systemic atopic markers remains unclear. We investigated the link between *H. pylori* infection and systemic indicators of atopy by analyzing serum immunoglobulin E (IgE) levels alongside peripheral inflammatory parameters.

Methods: In this retrospective analysis, data from 312 adult patients (246 females, 66 males) assessed for *H. pylori* infection between January 2023 and January 2025 were reviewed. Infection status was determined using stool antigen assays and/or histological examination of endoscopic biopsy specimens. Laboratory results included serum total IgE, eosinophil counts, complete blood count, C-reactive protein (CRP), and systemic inflammation markers, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio, systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and aggregate index of systemic inflammation. Comparative statistical evaluations were performed between *H. pylori*-positive and -negative groups.

Results: Serum IgE concentrations were not significantly different between *H. pylori*-positive and -negative individuals (median: 42.5 IU/mL vs. 37.5 IU/mL; p=0.891). Similarly, eosinophil counts and the majority of inflammatory indices exhibited no substantial variation. Notably, neutrophil counts were slightly elevated in the *H. pylori*-positive cohort (median: 4.00 vs. 3.60 x10^3/μL; p=0.043). Other markers, such as NLR, PLR, SII, SIRI, and CRP, did not differ significantly.

Conclusion: *H. pylori* infection in adults was not associated with significant alterations in systemic atopic markers, including serum IgE and eosinophil counts, or with prominent changes in inflammatory indices. A mild rise in neutrophil levels may suggest a subtle systemic immune response rather than a marked inflammatory state.

Keywords: Atopy, eosinophil, *Helicobacter pylori*, IgE, monocyte-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation, systemic inflammation response index

ÖZ

Amaç: *Helicobacter pylori'nin (H. pylori)*, sistemik bağışıklık yanıtını ve atopik hastalıkların gelişimini etkileyebileceği öne sürülmüştür. Ancak, *H. pylori* enfeksiyonun sistemik atopi belirteçleri üzerindeki etkisi belirsizliğini korumaktadır. Bu çalışmada, *H. pylori* enfeksiyonu ile sistemik atopi aktivitesi arasındaki ilişki, serum immünoglobulin E (IgE) düzeyleri ve periferik enflamatuvar indeksler ölçülerek değerlendirilmiştir.

Gereç ve Yöntem: Bu geriye dönük çalışmada, Ocak 2023 ile Ocak 2025 tarihleri arasında *H. pylori* enfeksiyonu açısından dışkı antijen testi ve/veya endoskopik biyopsi ile değerlendirilmiş toplam 312 yetişkin bireyin (246 kadın, 66 erkek) kayıtları incelendi. Katılımcılara ait serum toplam IgE düzeyleri, eozinofil sayımları, tam kan sayımı bulguları, C-reaktif protein (CRP) düzeyleri ve sistemik enflamasyon göstergeleri nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR), monosit/lenfosit oranı, sistemik immün-enflamasyon indeksi (SII), sistemik enflamatuvar yanıt indeksi (SIRI) ve toplam sistemik enflamasyon indeksi, analiz kapsamına alındı. *H. pylori*-pozitif ve -negatif bireyler arasındaki farklar uygun istatistiksel yöntemlerle karşılaştırıldı.

Bulgular: Serum IgE düzeylerinde *H. pylori*-pozitif ve negatif bireyler arasında anlamlı bir farklılık saptanmadı (medyan: 42,5 IU/mL vs. 37,5 IU/mL; p=0,891). Eozinofil düzeyleri ve çoğu enflamasyon parametresi açısından da gruplar arasında belirgin bir fark görülmedi. Bununla birlikte, nötrofil sayılarında *H. pylori*-pozitif bireylerde hafif bir artış gözlendi (medyan: 4,00 vs. 3,60 x10^3/μL; p=0,043). NLR, PLR, SII, SIRI ve CRP gibi diğer enflamatuvar göstergeler istatistiksel fark göstermedi.

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ÖZ

Sonuç: *H. pylori* enfeksiyonu, erişkin bireylerde sistemik IgE aracılı atopik aktivite ya da belirgin enflamatuvar değişikliklerle ilişkili bulunmamıştır. Nötrofil sayısındaki mütevazı artış, sınırlı bir sistemik enflamatuvar etkiyi yansıtabilir.

Anahtar Kelimeler: Atopi, eozinofil, *Helicobacter pylori*, IgE, monosit/lenfosit oranı, nötrofil/lenfosit oranı, sistemik immün-enflamasyon indeksi, sistemik enflamasyon, sistemik enflamasyonun birleşik indeksi, sistemik enflamatuvar yanıt indeksi

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a Gram-negative, microaerophilic microorganism colonizing the gastric mucosa and represents one of the most widespread chronic infections worldwide (1). Its association with peptic ulcer, chronic gastritis, and cancer is well established and has been thoroughly investigated (1,2). In recent years, increasing attention has been directed toward the bacterium's role in modulating immune responses, with particular interest in its potential involvement in autoimmune and atopic disorders (3-5).

In many industrialized nations, a decline in *H. pylori* prevalence has paralleled an increase in atopic diseases (4,6). This trend aligns with the hygiene hypothesis and the "old friends" theory, both of which propose that limited microbial exposure during early development may impair immunological tolerance and promote allergic sensitization (4,6,7).

Large-scale epidemiological data demonstrated a negative relationship between *H. pylori* colonization and atopy (5,8,9). This protective effect appears to be more pronounced when colonization occurs in early childhood (8,9). Immunologically, this may be explained by enhanced regulatory T-cell (Treg) activity, downregulation of Th2-mediated pathways, and modulation of dendritic cell signaling-all contributing to a more balanced immune state (10,11).

Animal model experiments have provided further insight into these mechanisms. For instance, certain *H. pylori* virulence factors, such as VacA and neutrophil-activating protein, have been shown to reduce immunoglobulin E (IgE) production, inhibit eosinophilic infiltration, and ameliorate allergic airway inflammation in mice (3,11,12). These findings suggest that *H. pylori* may influence systemic immunity beyond the gastric environment, potentially via immunologic communication along the gut-lung and gut-skin axes (5).

However, despite these promising findings, the relation of *H. pylori* and atopy is not entirely consistent across studies. Divergent results may reflect differences in bacterial strain virulence (e.g., presence of CagA or VacA), genetics, environmental factors, and most importantly, the age at initial colonization (9,10,13). While certain studies have explored biomarkers such as total IgE and eosinophil count, few have simultaneously evaluated these markers in the context of confirmed *H. pylori* infection.

The present study aimed to evaluate if *H. pylori* infection affects systemic atopic activity by evaluating total serum IgE levels and peripheral inflammatory indices. Comparisons were made between *H. pylori* infected patients and non-infected ones, and to assess whether the bacterium might be associated with immunological patterns indicative of protection against atopy. We hypothesized that *H. pylori* infection may be associated with reduced systemic indicators of atopic reactivity—namely, lower serum IgE levels and decreased eosinophil counts—when compared to uninfected individuals.

METHODS

Ethical Statement

The study was approved by the Koşuyolu High Specialization Training and Research Hospital Clinical Research Ethics Committee (approval no: 2025-KAEK-43, date: 28.01.2025). The authors complied with the Declaration of Helsinki and relevant national guidelines. Due to the retrospective nature of the study, previously collected data were used, and obtaining informed consent from participants was not required.

Design

This research was conducted as a retrospective, observational study at a single medical center. Patient data were obtained from individuals evaluated in the internal medicine and gastroenterology outpatient clinics of the University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital between January 2023 and January 2025. The primary objective was to determine the prevalence of atopy and to analyze immunological parameters among patients diagnosed with *H. pylori* infection.

The inclusion criteria encompassed patients aged 18 years and older with *H. pylori* infection, diagnosed by either stool antigen testing or histopathological examination of gastric biopsies obtained during endoscopy. In routine clinical practice, the diagnostic modality was selected according to the clinical indication. Stool antigen testing was generally used

as a non-invasive first-line test, whereas endoscopic biopsy was performed in patients undergoing upper gastrointestinal endoscopy for clinical reasons. Therefore, not all patients underwent both diagnostic procedures. Patients were considered *H. pylori*-positive if either stool antigen testing or histopathological examination demonstrated infection.

Exclusion criteria included any history of immunodeficiency, cancer, autoimmune disorders, or current use of corticosteroids or other immunosuppressive agents. The control group consisted of *H. pylori*-negative individuals matched by age and sex, all of whom had undergone the same diagnostic procedures during the same period.

Clinical and Laboratory Data

All clinical and laboratory information was retrospectively obtained from patients' hospital records.

The variables mentioned below were recorded:

- Demographic characteristics, including age and sex,
- *H. pylori* infection status (positive or negative), determined via stool antigen testing and/or endoscopic biopsy,
- Patient-reported atopic history was extracted from electronic medical records and clinical documentation (diagnoses such as allergic rhinitis, asthma, or dermatitis were identified based on physician notes and/or ICD codes when available),
- Total serum IgE concentrations,
- Absolute eosinophil counts along with their respective percentages,
- Complete blood count (CBC),
- Levels of C-reactive protein (CRP).

Based on the CBC data, the following systemic inflammatory indices were calculated:

- Neutrophil-to-lymphocyte ratio (NLR): Neutrophil count/lymphocyte count ratio,
- Platelet-to-lymphocyte ratio (PLR): Platelet count/lymphocyte count ratio,
- Monocyte-to-lymphocyte ratio (MLR): Monocyte count/lymphocyte count ratio,
- Systemic inflammation response index (SIRI): Calculated as (neutrophil count×monocyte count)/lymphocyte count,
- Systemic immune-inflammation index (SII): Calculated as (neutrophil count×platelet count)/lymphocyte count,
- Aggregate index of systemic inflammation (AISI): Defined as (neutrophil count×monocyte count×platelet count)/lymphocyte count.

All test results were obtained from the most recent available laboratory data within a three-months period before or after the *H. pylori* diagnostic assessment.

Statistical Analysis

IBM SPSS Statistics software (version 25.0) was used for the statistical analyses. The distribution patterns of continuous variables were evaluated with the Shapiro-Wilk test. Normally distributed data were given as mean±standard deviation, whereas non-normally distributed variables were given as medians and interquartile ranges (IQR).

To compare individuals with and without *H. pylori*, an Independent Samples t-test was used. In cases where the data did not meet normality assumptions, the Mann-Whitney U test was used. Categorical data were presented as counts and percentages, and differences between groups were assessed using the chi-square test or Fisher's exact test, depending on the expected cell frequencies.

To evaluate the relationships between total serum IgE levels and inflammatory indices, Pearson's or Spearman's correlation coefficients were used. In all tests, a p-value below 0.05 (two-tailed) was considered statistically significant.

RESULTS

A total of 312 patients were evaluated in the study: 246 women (78.8%) and 66 men (21.2%). The average age was not significantly different between patients with and without *H. pylori* infection (52.01±12.68 vs. 52.60±14.77 years, respectively; p=0.725) (Table 1).

In the combined analysis according to *H. pylori* status assessed by stool antigen and endoscopic biopsy, patients with stool antigen positivity were significantly younger than those who were negative (median age: 51.0 vs. 55.5 years; p=0.048), and hemoglobin levels were slightly lower in the stool antigen-positive group (p=0.037), while no other hematologic or biochemical parameters differed significantly. In contrast, based on endoscopic evaluation, biopsy-proven *H. pylori*-positive patients were significantly older than biopsy-negative individuals (median age: 58.0 vs. 52.0 years; p=0.037), and lymphocyte counts were higher in the biopsy-positive group (p=0.035), whereas the remaining parameters showed no significant differences (Table 2).

Serum total IgE levels were slightly higher in *H. pylori*-positive individuals, with a median of 42.5 IU/mL (IQR: 19-92.25), compared to a median of 37.5 IU/mL (IQR: 15-108) in the negative group; however, this difference was not statistically significant (p=0.891) (Figure 1). Similarly,

Table 1. General characteristics of the study population (n=312)

Variable	Value
Gender	
Female	246 (78.8%)
Male	66 (21.2%)
Atopy	
Negative	311 (99.7%)
Positive	1 (0.3%)
***H. pylori* in stool**	
Negative	128 (41.0%)
Positive	184 (59.0%)
Endoscopic *H. pylori*	
Negative	273 (87.5%)
Positive	39 (12.5%)
Age (years)	52.18±13.30
IgE (IU/mL)	93.49±187.97
Eosinophil count (x10^3/µL)	0.18±0.14
Lymphocyte count (x10^3/µL)	2.29±0.69
Monocyte count (x10^3/µL)	0.43±0.23
Neutrophil count (x10^3/µL)	4.17±1.63
Platelet (x10^3/µL)	269.41±72.23
CRP (mg/L)	3.49±7.40
Hemoglobin (g/dL)	13.26±1.53

H. pylori: *Helicobacter pylori*, IgE: Immunoglobulin E, CRP: C-reactive protein

no significant difference was noted in eosinophil counts between the two groups (p=0.348) (Table 3, Figure 2).

Regarding systemic inflammatory profiles, neutrophil counts were significantly elevated in the *H. pylori*-positive group [median: 4.00 (IQR: 3.27-5.00)] in comparison to the uninfected group [median: 3.60 (IQR: 3.00-4.50); p=0.043]. On the other hand, inflammatory markers—including NLR, PLR, MLR, SII, SIRI, and AISI—and CRP levels did not show statistically significant differences between the groups (all p-values >0.05). Levels of hemoglobin, lymphocytes, monocytes, and platelets were also similar between the two groups (Table 3). The modest increase in neutrophil counts among *H. pylori*-positive patients may reflect a low-grade systemic inflammatory response. Although not accompanied by elevations in CRP or other markers, this finding aligns with prior studies suggesting that *H. pylori* infection may sustain chronic, subclinical inflammation.

A full comparison encompassing both stool antigen and endoscopic findings for *H. pylori* is presented in Table 4.

In conclusion, while the majority of immunological and hematological parameters appeared comparable between the groups, a slight elevation in neutrophil counts was observed among *H. pylori*-positive individuals, potentially indicating a low-grade systemic inflammatory effect. Differences in age and lymphocyte levels were also noted in subgroup analyses stratified by diagnostic method (stool antigen versus biopsy); however, these variations did not reflect significant systemic immune alterations.

Table 2. Comparison of clinical and laboratory parameters according to *H. pylori* status (stool vs. endoscopic) (n=312)

Parameter	Stool *H. pylori* negative	Stool *H. pylori* positive	p-value	Endoscopic *H. pylori* negative	Endoscopic *H. pylori* positive	p-value
Age (years)	55.50 (46.00-63.75)	51.00 (42.25-60.00)	0.048*	52.00 (42.00-61.50)	58.00 (58.00-62.00)	0.037*
IgE (IU/mL)	37.50 (14.20-98.25)	43.00 (20.70-93.00)	0.521	41.00 (18.45-96.00)	42.00 (12.00-76.00)	0.591
Eosinophil count (x10^3/µL)	0.2 (0.1-0.2)	0.2 (0.1-0.2)	0.562	0.2 (0.1-0.2)	0.2 (0.1-0.2)	0.613
Lymphocyte count (x10^3/µL)	2.2 (1.8-2.7)	2.2 (1.8-2.7)	0.730	2.2 (1.8-2.61)	2.5 (1.9-3.0)	0.035*
Monocyte count (x10^3/µL)	0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.464	0.4 (0.3-0.5)	0.4 (0.3-0.6)	0.174
Neutrophil count (x10^3/µL)	3.7 (3.02-4.6)	4.05 (3.2-4.9)	0.107	3.9 (3.1-4.8)	3.9 (3.3-5.1)	0.524
Platelet (x10^3/µL)	265.00 (223.00-302.00)	257.50 (214.25-312.00)	0.873	260 (217-308.5)	265 (223-289)	0.770
CRP (mg/L)	1.85 (0.82-3.16)	1.62 (0.87-3.64)	0.941	1.64 (0.84-3.42)	2.08 (0.95-3.69)	0.375
Hemoglobin (g/dL)	13.40 (12.52-14.40)	13.10 (12.10-14.00)	0.037*	13.2 (12.3-14.2)	13.6 (12.5-14.4)	0.198

*Statistically significant
H. pylori: *Helicobacter pylori*, IgE: Immunoglobulin E, CRP: C-reactive protein

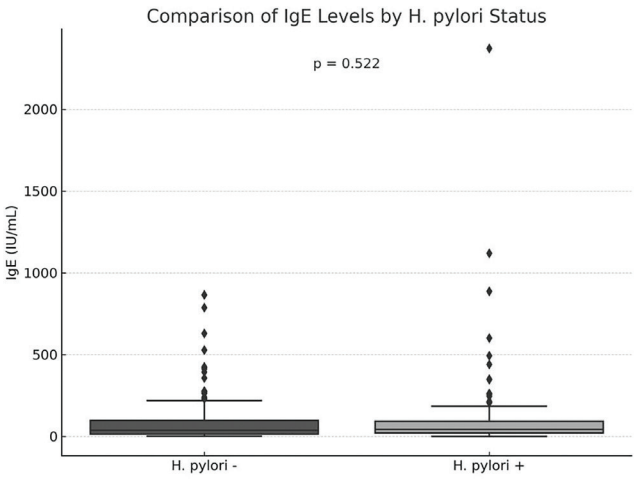

Figure 1. IgE levels by *H. pylori* status
IgE: Immunoglobulin E, *H. pylori*: *Helicobacter pylori*

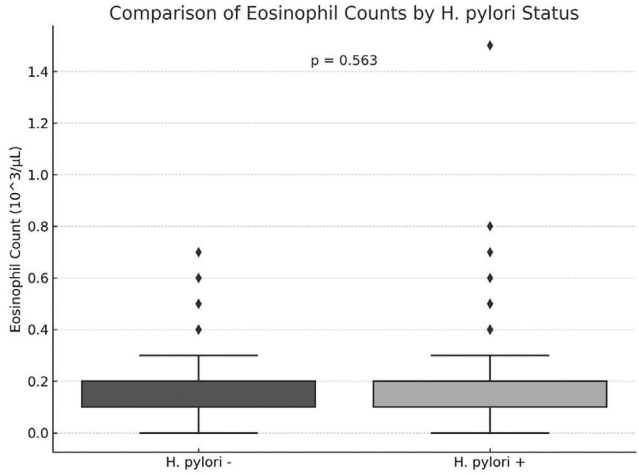

Figure 2. Eosinophil counts by *H. pylori* status
H. pylori: *Helicobacter pylori*

Table 3. Laboratory parameters by *H. pylori* status (n=312)

	***H. pylori* negative**	***H. pylori* positive**	**p-value**
Age (years)	52.60±14.77	52.01±12.68	0.725
IgE (IU/mL)	37.5 (15-108)	42.5 (19-92.25)	0.891
Eosinophil count (x10³/µL)	0.17 (0.10-0.20)	0.20 (0.10-0.20)	0.348
Lymphocyte count (x10³/µL)	2.24 (1.80-2.60)	2.20 (1.80-2.80)	0.337
Monocyte count (x10³/µL)	0.40 (0.30-0.50)	0.40 (0.30-0.50)	0.835
Neutrophil count (x10³/µL)	3.60 (3-4.50)	4 (3.27-5)	0.043
Platelet (x10³/µL)	265.5 (226.5-304.5)	261 (215-308.25)	0.805
CRP (mg/L)	1.79 (0.80-3.23)	1.69 (0.90-3.61)	0.672
Hemoglobin (g/dL)	13.48±1.37	13.17±1.59	0.112
NLR	1.79 (1.28-2.22)	1.78 (1.33-2.40)	0.456
PLR	117.08 (97.79-153.12)	116.95 (93.34-148.45)	0.550
MLR	0.18 (0.16-0.22)	0.17 (0.14-0.22)	0.417
SII	459.54 (327.13-571.73)	459 (329.45-632.56)	0.438
SIRI	0.66 (0.50-0.95)	0.71 (0.48-1.09)	0.402
AISI	177.60 (121.28-249.28)	179.75 (127.05-280.42)	0.429

H. pylori: *Helicobacter pylori*, IgE: Immunoglobulin E, CRP: C-reactive protein, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, AISI: Aggregate index of systemic inflammation

DISCUSSION

In the present study, no statistically significant difference was found in total IgE between individuals having *H. pylori* infection or not having *H. pylori* infection. This suggests that colonization with *H. pylori* may not have a direct effect on IgE-mediated systemic allergic responses.

To evaluate the potential association between *H. pylori* and allergic predisposition, both humoral and cellular aspects of the immune response were taken into account. Total serum IgE, a well-established marker of atopic sensitization, reflects the activity of Th2-driven B cells and is typically elevated in allergic conditions such as asthma, allergic rhinitis, and atopic dermatitis.

In addition to serum IgE measurements, this study included several inflammation-based indices derived from standard hematologic tests: namely NLR, PLR, MLR, SII, SIRI, and AISI. These markers have garnered increasing attention as indicators of low-grade systemic inflammation. While not specific to allergic responses, they offer valuable insight

Table 4. Overall comparison of clinical and laboratory parameters according to combined *H. pylori* status (stool antigen and endoscopic diagnosis)

	H. pylori		
	Negative	**Positive**	**p-value**
Age (years)	52.60±14.77	52.01±12.68	0.725
IgE (IU/mL)	37.5 (15-108)	42.5 (19-92.25)	0.891
Eosinophil count (x10^3/µL)	0.17 (0.10-0.20)	0.20 (0.10-0.20)	0.348
Lymphocyte count (x10^3/µL)	2.24 (1.80-2.60)	2.20 (1.80-2.80)	0.337
Monocyte count (x10^3/µL)	0.40 (0.30-0.50)	0.40 (0.30-0.50)	0.835
Neutrophil count (x10^3/µL)	3.60 (3-4.50)	4 (3.27-5)	0.043*
Platelet (x10^3/µL)	265.5 (226.5-304.5)	261 (215-308.25)	0.805
CRP (mg/L)	1.79 (0.80-3.23)	1.69 (0.90-3.61)	0.672
Hemoglobin (g/dL)	13.48±1.37	13.17±1.59	0.112
NLR	1.79 (1.28-2.22)	1.78 (1.33-2.40)	0.456
PLR	117.08 (97.79-153.12)	116.95 (93.34-148.45)	0.550
MLR	0.18 (0.16-0.22)	0.17 (0.14-0.22)	0.417
SII	459.54 (327.13-571.73)	459 (329.45-632.56)	0.438
SIRI	0.66 (0.50-0.95)	0.71 (0.48-1.09)	0.402
AISI	177.60 (121.28-249.28)	179.75 (127.05-280.42)	0.429

*Statistically significant
H. pylori: *Helicobacter pylori*, IgE: Immunoglobulin E, CRP: C-reactive protein, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, AISI: Aggregate index of systemic inflammation

into the overall inflammatory status in immune-mediated conditions, including both allergic and autoimmune disorders.

By simultaneously evaluating IgE levels and inflammation-related indices, the study sought to determine whether *H. pylori* exerts its effects on allergic responses via conventional IgE-mediated mechanisms, through alternative immune regulation, or potentially by engaging both pathways. This integrated strategy enabled a broader analysis of immune activity, encompassing both adaptive and innate components potentially influenced by *H. pylori* colonization.

Numerous prior studies, both epidemiological and experimental, have described an inverse correlation between *H. pylori* presence and allergic manifestations. Findings from large-scale population studies and meta-analyses indicate that being exposed to *H. pylori* in early years of life may be associated with reduced risk of atopic disorders such as asthma and allergic rhinitis (5,8,9). These protective effects have been attributed to the bacterium's capacity to enhance Treg cell responses, inhibit Th2-dominant immunity, and influence dendritic cell behavior (3,10,11). Experimental models further support this hypothesis: *H. pylori*-derived components such as VacA and neutrophil-activating protein have been shown to suppress IgE synthesis, reduce eosinophil-driven inflammation, and limit histamine release (3,11). In murine studies, *H. pylori* colonization has been linked to reduced allergic airway inflammation and fewer dermatitis-like skin lesions (12).

In contrast to earlier reports, our results indicate that *H. pylori* colonization in adults does not result in a detectable decrease in systemic IgE concentrations. This inconsistency may be attributed to factors such as host genetic variability, environmental influences, or strain-specific differences in *H. pylori* virulence. Although no IgE-lowering effect was observed, the possibility of broader immunoregulatory roles for *H. pylori*, independent of IgE-mediated mechanisms, cannot be excluded.

As a prevalent cause of chronic infections globally, *H. pylori* has a prolonged and complex interaction with the human immune system (14). The absence of significant differences in atopic parameters between infected and uninfected individuals in this study does not necessarily contradict prevailing theories that reduced microbial exposure—including the decline of *H. pylori*—may add to the rising incidence of atopy, particularly in developed countries (4). According to the hygiene hypothesis and the related "old friends" theory, insufficient microbial contact during early life may impair immune regulation by limiting Treg cell maturation and favoring a Th2-skewed immune profile (1,4).

Although the anti-inflammatory effects of *H. pylori* have traditionally been examined in the context of gastrointestinal disorders, more recent evidence points to its potential impact on distant mucosal immune responses via the gut-lung and gut-skin axes (5).

Inflammatory indices such as NLR, PLR, and SII are increasingly regarded as sensitive markers for detecting low-grade systemic inflammation. Their utility in identifying underlying immunologic activity in both allergic and autoimmune diseases is becoming more widely recognized (15,16). Nonetheless, in the present study, no statistically significant differences in these indices were observed between *H. pylori*-positive and -negative individuals.

Discrepancies in findings across the literature may be partially attributable to variations in *H. pylori* virulence determinants, particularly the presence of CagA and VacA (17). Certain studies have failed to confirm a protective effect, potentially due to differences in bacterial strain, the age at infection onset, host genetic background, or environmental exposures (9,10). Notably, *H. pylori* colonization occurring earlier in life appears to exert a more pronounced immunomodulatory influence compared to infections acquired later (8,9).

Study Limitations

First, this being a retrospective study, the analysis cannot establish causality between *H. pylori* infection and systemic markers of atopy. The findings are based solely on existing clinical and laboratory records, without prospective follow-up or in-depth clinical assessments of allergic diseases.

Another limitation relates to the diagnostic methods used to determine *H. pylori* infection. Because the study was retrospective and based on routine clinical records, the diagnostic modality was selected according to clinical indications rather than by a predefined research protocol. Non-invasive stool antigen testing was generally used as an initial diagnostic approach, whereas histopathological examination of gastric biopsies was performed in patients undergoing upper gastrointestinal endoscopy for clinical reasons. Consequently, not all patients underwent both diagnostic procedures. Although this reflects real-world clinical practice, the use of different diagnostic pathways may have introduced a degree of diagnostic heterogeneity between subgroups.

Third, atopy was evaluated indirectly using laboratory surrogates, primarily total serum IgE concentrations and eosinophil counts. While these biomarkers are informative, they do not capture the complete clinical spectrum of allergic conditions and may not accurately represent the severity or presence of atopy in every case.

The inflammatory indices assessed—such as NLR, PLR, and SII—are non-specific markers that may be affected by a wide range of confounding variables, including acute or chronic infections, comorbid conditions, and medication use. In our retrospective dataset, detailed information on potential confounders such as smoking status, body mass index, chronic diseases (e.g., diabetes, cardiovascular conditions), and use of antihistamines or immunomodulatory agents was not consistently available. As a result, these factors could not be fully accounted for in the analysis and may have introduced bias or masked subtle differences between the study groups.

Additionally, data on *H. pylori* virulence-related factors, including CagA and VacA status, timing of infection onset, and any history of eradication therapy, were unavailable. These variables likely play a crucial role in modulating immune responses and therefore represent key avenues for future research.

Moreover, due to the retrospective design, we lacked access to cytokine panel measurements [e.g., interleukin (IL)-4, IL-5, IL-10], which could have deepened our understanding of immune polarization (Th1/Th2 balance) in *H. pylori*-infected individuals.

No a priori sample size or power analysis was performed because of the retrospective design. While the sample size was adequate for preliminary group comparisons, it may not have been sufficient to detect smaller effect sizes.

Because the study was conducted in a single tertiary referral center, the results may not be broadly generalizable. Differences in population demographics, environmental exposures, and regional microbiological patterns could influence the associations observed and limit the extrapolation of these findings to wider settings.

CONCLUSION

These findings suggest that *H. pylori* colonization in adulthood does not appear to be associated with significant alterations in systemic atopic markers, including total IgE levels and eosinophil counts. In many industrialized nations, *H. pylori* prevalence has been progressively decreasing, largely as a result of widespread antibiotic use and enhanced hygiene standards. Although this study does not demonstrate a direct link between the bacterium's decline and the increasing incidence of allergic disorders, the findings are consistent with broader hypotheses suggesting that reduced microbial exposure—including the disappearance of *H. pylori*—may impair normal immune system development. These alterations in the microbial landscape underscore the importance of ongoing research

into how such ecological changes may influence immune regulation.

Prospective studies initiated in early life are warranted to clarify the potential protective role of early *H. pylori* colonization in atopy development.

ETHICS

Ethics Committee Approval: The study was approved by the Koşuyolu High Specialization Training and Research Hospital Clinical Research Ethics Committee (approval no: 2025-KAEK-43, date: 28.01.2025).

Informed Consent: Retrospective study.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: M.E., İ.K., Concept: M.E., İ.K., Design: M.E., İ.K., Data Collection or Processing: M.E., Analysis or Interpretation: E.G.Ö., Literature Search: M.E., İ.K., Writing: İ.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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