Journal of Clinical and Translational Pathology **2026** | Epub
DOI: 10.14218/JCTP.2026.00021

Original Article

Eosinophilic Esophagitis with Concurrent Gastric *Helicobacter pylori* Infection: An Underappreciated Clinicopathologic Association

Jing Zhou, Katrina J. Jiang and Wei Xin*

Department of Pathology, University of South Alabama University Hospital, Mobile, AL, USA

Received: April 16, 2026 | **Revised:** June 06, 2026 | **Accepted:** July 09, 2026 | **Published online:** August 31, 2026

Abstract

Background and objectives: Eosinophilic esophagitis (EoE) is characterized by esophageal dysfunction and ≥15 eosinophils/high-power field on biopsy. The specific clinicopathologic characteristics and therapeutic outcomes of patients with concurrent gastric *Helicobacter pylori* infection and EoE remain poorly defined. This observational cohort study reexamines this relationship and evaluates the clinicopathologic features and outcomes of patients with concurrent diseases.

Methods: We retrospectively reviewed esophageal and gastric biopsies obtained between January 1, 2022, and December 30, 2025. Patients with a first-time diagnosis of EoE and concurrent treatment-naive gastric *H. pylori* infection were identified and confirmed by morphology and immunohistochemistry. Patients with a history of prior *H. pylori* eradication therapy or eosinophilic gastrointestinal disease were excluded. Clinical, pathologic, and follow-up data were analyzed.

Results: Among 5,443 patients undergoing concurrent esophageal and gastric biopsy evaluation, 197 (3.6%, 95% confidence interval [CI], 3.1–4.1%) met the diagnostic criteria for EoE, and 286 (5.3%, 95% CI, 4.7–5.9%) had gastric *H. pylori* infection. Twenty-eight patients with concurrent EoE and gastric *H. pylori* infection were initially identified, corresponding to an *H. pylori* prevalence of 14.2% (28/197) among patients with EoE. A significant association was identified between EoE and *H. pylori* infection (odds ratio, 3.20; 95% CI, 2.11–4.87; Fisher's exact test, $P < 0.001$). After exclusion of 1 patient with eosinophilic gastrointestinal disease and 3 patients with prior *H. pylori* treatment, 24 patients met the study inclusion criteria for the subsequent clinicopathologic analysis. Among these 24 patients (M:F = 7:1; mean age, 29.5 years; range, 8–82 years), 8 (33%) were children. The most common presentations (n = 18, 75%) were abdominal pain in children and dysphagia in adults. Atopy was present in 7 (29%) patients. Histologically, 5 (21%) cases exhibited classic features, while 19 (79%) showed nonclassic features with lower eosinophil density and a more uniform distribution of eosinophils within the epithelium. Among 10 patients with follow-up, 3/10 (30%) achieved resolution of both *H. pylori* infection and EoE after *H. pylori* eradication therapy with or without steroids; 5/10 (50%) had persistent *H. pylori* infection and persistent or recurrent EoE; 2(20%) achieved *H. pylori*-negative status but had persistent EoE; and fungal infection developed in 2 of 4 patients (50%) treated with steroids.

Conclusions: *H. pylori* infection may be associated with a nonclassic pattern of EoE. Recognition of this pattern may have implications for diagnosis and management.

Keywords: Eosinophilic esophagitis; *Helicobacter pylori*; Concurrent disease; Clinicopathologic correlation; Esophageal eosinophilia; Fungal infection; Targeted therapy.

***Correspondence to:** Wei Xin, Department of Pathology, University of South Alabama University Hospital, Room 113, Moore Building, Mobile, AL 36617, USA. ORCID: https://orcid.org/0000-0003-0987-0443. Tel: +1-251-4717795, E-mail: wxin@health.southalabama.edu

How to cite this article: Zhou J, Jiang KJ, Xin W. Eosinophilic Esophagitis with Concurrent Gastric *Helicobacter pylori* Infection: An Underappreciated Clinicopathologic Association. *J Clin Transl Pathol*. Published online: Aug 31, 2026. DOI: https://doi.org/10.14218/JCTP.2026.00021.

Introduction

Eosinophilic esophagitis (EoE) is a clinicopathologic diagnosis requiring the integration of three criteria: symptoms of esophageal dysfunction, at least 15 eosinophils per high-power field (eos/HPF) on esophageal biopsy, and exclusion of non-EoE disorders that cause or potentially contribute to esophageal eosinophilia.[1] In adolescents and adults, dysphagia and food impaction are the most

common presenting symptoms, although heartburn and chest pain may also be present; notably, patients frequently adopt food avoidance and modification behaviors to minimize dysphagia, which can lead to significant diagnostic delays.[1] Endoscopic evaluation is central to diagnosis, with typical findings including edema, fixed esophageal rings, white exudates, linear furrows, and strictures, systematically characterized using the EoE Endoscopic Reference Score; however, these findings are not pathognomonic and do not constitute formal diagnostic criteria.[1] Because EoE is a patchy disease histologically, at least 6 biopsies from at least 2 esophageal levels are recommended, as fewer biopsies risk missing the diagnosis; with 6 or more biopsies, diagnostic sensitivity approaches 100%.[1] The sole required histologic criterion remains the peak eosinophil count. However, additional features assessed by the EoE Histologic Scoring System, including basal zone hyperplasia, eosinophilic microabscesses, spongiosis, and eosinophil degranulation, are increasingly recognized as clinically relevant, as persistent basal zone hyperplasia and lamina propria fibrosis have been associated with ongoing symptoms even when eosinophil counts decline.[1] Although the etiology of EoE remains to be fully elucidated, genetic, immune, and environmental factors have been associated with its pathogenesis. If left untreated, chronic inflammation can lead to esophageal remodeling, strictures, and perforation.[2]

The prevalence of EoE has been steadily increasing since it was first described in the 1990s.[3] A recent multi-database analysis estimates a 5-fold increase in the prevalence of EoE since 2009. When standardized to the U.S. population, the prevalence rate is estimated at 142.5 cases per 100,000 people (approximately 1 in 700), or an estimated total of 472,380 cases.[4] While the drivers of this increase remain incompletely understood, improved socioeconomic conditions and hygiene, which reduce early microbial exposure and promote atopic sensitization, are often cited.[5]

Within this context, the role of the gastric microbiome, specifically *Helicobacter pylori*, in EoE remains a subject of significant debate. Given the parallel rising prevalence of EoE and decreasing prevalence of *H. pylori* infection over the past two decades,[6] some epidemiological studies have proposed an inverse association between *H. pylori* and atopy, allergy, and asthma, suggesting that *H. pylori* colonization may protect against atopy-associated conditions such as EoE via systemic immune modulation.[5,7] However, clinical data are conflicting, including a systematic review that concluded that *H. pylori* merely functions as a biomarker for poor household hygiene and failed to demonstrate any protective effect against atopic and allergic conditions.[8] Regarding EoE specifically, large multicenter studies have also found no protective effect.[9]

A critical gap in the literature further compounds this controversy: there are very limited data concerning the clinicopathologic features of EoE in the setting of gastric *H. pylori* infection. As a result, the specific clinicopathologic characteristics and therapeutic outcomes of patients with concurrent gastric *H. pylori* infection and EoE remain poorly defined. This study aimed to address this gap by retrospectively analyzing a cohort of patients with concurrent *H. pylori* infection and EoE at a single center.

Materials and methods

Study design and ethical approval

This single-center retrospective cohort study included esophageal and gastric biopsy specimens obtained between January 1, 2022, and December 30, 2025, at the University of South Alabama University Hospital, Mobile, Alabama. The study was conducted in accordance with the Declaration of Helsinki and was approved by the University of South Alabama Institutional Review Board (IRB Protocol No. 26-074). The requirement for informed consent was waived by the IRB because of the retrospective nature of the study and the use of existing, de-identified clinical pathology data. The study was reported in accordance with STROBE.

Case identification and selection

Cases were identified by searching for patients with esophageal eosinophilia on esophageal biopsy and/or *H. pylori* infection on gastric biopsy. Patients with a history of prior *H. pylori* eradication therapy (HPE) were excluded. Cases of eosinophilic gastrointestinal disease were also excluded. This was defined as the presence of gastrointestinal symptoms associated with pathologic eosinophilic infiltration of >20 eos/HPF in the gastrointestinal tract.

Histopathologic evaluation

All available hematoxylin and eosin- and immunohistochemistry-stained slides from eligible cases were independently re-reviewed by WX and JZ, who were blinded to the patients' clinical outcomes and follow-up data. Any discrepancies were resolved by joint review and consensus. The current diagnostic criteria for EoE, defined by esophageal dysfunction and the presence of ≥15 eos/HPF in esophageal biopsy specimens, were used for the study. At least 6 esophageal biopsies were obtained from at least two different esophageal levels (typically proximal/mid and distal esophagus). Peak eosinophil count was assessed in the area of greatest eosinophil density. *H. pylori* infection was confirmed when organisms were identified on hematoxylin and eosin sections and detected by immunohistochemistry staining.

Clinical data collection and outcome assessment

Demographic, clinical, and histopathologic data were extracted from the electronic medical record. Clinical parameters reviewed included age, sex, presenting symptoms, concurrent atopic diseases, laboratory findings, endoscopic findings, and the extent of gastrointestinal involvement. Treatment regimens and clinical outcomes were also reviewed. Information regarding the use of medications that could interfere with *H. pylori* detection, including proton pump inhibitors (PPIs) and antibiotics, was carefully documented. Outcomes were assessed based on histologic response at follow-up biopsy, defined as resolution of esophageal eosinophilia (≤5 eos/HPF in adults and 0 eos/HPF in children) and clearance of *H. pylori* infection.

Statistical analysis

Descriptive statistics were used to characterize the cohort. Categorical variables were summarized as frequencies and percentages. The prevalence of EoE, gastric *H. pylori* infection, and concurrent disease was calculated with corresponding 95% confidence intervals (CIs). The association between EoE and gastric *H. pylori* infection was evaluated using a two-tailed Fisher's exact test. Odds ratios (ORs) with 95% CIs were calcu-

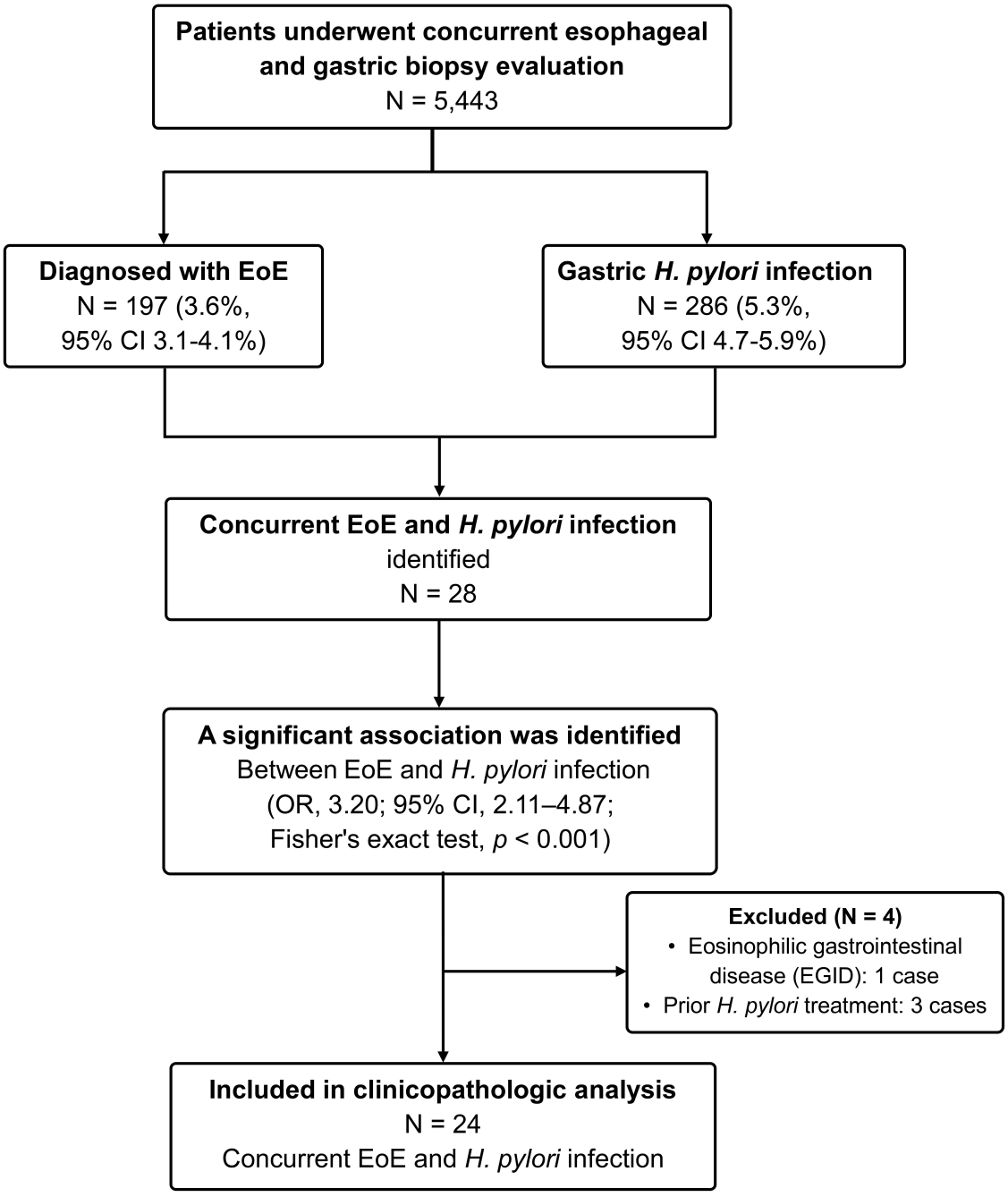

Fig. 1. Study flow chart. CI, confidence interval; EGID, eosinophilic gastrointestinal disease; EoE, eosinophilic esophagitis; *H. pylori*, *Helicobacter pylori*; OR, odds ratio.

lated to estimate the strength of association. A two-sided *P*-value < 0.05 was considered statistically significant.

Results

Patients were identified through the electronic medical record system (Fig. 1). Among 5,443 patients undergoing concurrent esophageal and gastric biopsy evaluation, 197 (3.6%, 95% CI, 3.1–4.1%) met the diagnostic criteria for EoE, and 286 (5.3%, 95% CI, 4.7–5.9%) had gastric *H. pylori* infection. Twenty-eight patients with concurrent EoE and gastric *H. pylori* infection were initially identified, corresponding to an *H. pylori* prevalence of 14.2% (28/197) among patients with EoE. A significant association was identified between EoE and *H. pylori* infection (odds ratio, 3.20; 95% CI, 2.11–4.87; Fisher's exact test, $P < 0.001$) (Table 1). After exclusion of 1 patient with eosinophilic

gastrointestinal disease and 3 patients with prior *H. pylori* treatment, 24 patients met the study inclusion criteria for the subsequent clinicopathologic analysis.

Table 1. Prevalence estimates and association between EoE and gastric *Helicobacter pylori* infection

Variable	Estimate	95% CI
EoE prevalence	197/5443 = 3.6%	3.1–4.1%
H. pylori prevalence	286/5443 = 5.3%	4.7–5.9%
H. pylori among EoE patients	28/197 = 14.2%	10–19.8%
Concurrent EoE and *H. pylori*	28/5443 = 0.51%	0.34–0.74%
Association between EoE and *H. pylori*	OR = 3.20	2.11–4.87

EoE, eosinophilic esophagitis; CI, confidence interval; OR, odds ratio. OR was calculated based on 24 cases included.

The clinical characteristics of patients with concurrent EoE and *H. pylori* infection are summarized in Table 2. The cohort consisted of 24 patients with a marked male predominance (male-to-female ratio, 7:1) and a mean age of 29.5 years (range, 8-82 years). Eight patients (33%) were pediatric (<18 years). The most common presenting symptoms were abdominal pain in children and dysphagia in adults, accounting for 75% (n = 18) of cases overall. Obesity and atopic diseases were documented in 6 (25%) and 7 (29%) patients, respectively.

Endoscopic findings frequently included linear furrows, esophageal rings, stricture, and edema, with at least one of these features observed in approximately 80% (n = 19) of cases. Histologically, all cases demonstrated eosinophil degranulation and dilated intercellular spaces within the esophageal squamous epithelium. Additional features included basal cell hyperplasia, elongation of lamina propria papillae, and lamina propria fibrosis. Five cases (21%) showed dense eosinophilic infiltration with superficial layering and eosinophilic microabscess formation, consistent with classic EoE. In contrast, the remaining 19 cases (79%) demonstrated lower eosinophil density with a relatively even distribution throughout the squamous epithelium, representing a distinct, nonclassic histologic pattern observed in the setting of *H. pylori* infection (Fig. 2).

All pediatric patients in this cohort were educated on an elimination diet. PPI therapy was used as first-line treatment in all patients. Overall treatment regimens included HPE alone (n = 7, 29%), PPI therapy alone (n = 9, 37.5%), HPE combined with corticosteroids (n = 6, 25%), and PPI combined with corticosteroids (n = 2, 8%). HPE therapy in this cohort primarily consisted of standard bismuth-based quadruple regimens (PPI, bismuth, tetracycline, and metronidazole) or clarithromycin-based triple therapy (PPI, amoxicillin, and clarithromycin), administered for 14 days. Follow-up data were available for 10 patients: 3 (30%) achieved histologic resolution of both *H. pylori* infection and EoE following HPE with or without corticosteroids. Five (50%) patients had persistent *H. pylori* infection with persistent or relapsing EoE; notably, 2 of these belonged to the nonclassic group and did not receive HPE. Two (20%) patients became *H. pylori*-negative but had persistent EoE; both were treated with PPI alone and had a single follow-up. Fungal infection developed in 2 of 4 patients (50%) treated with combined HPE and corticosteroids (Fig. 3). One additional patient underwent a single follow-up with gastric biopsy only (without a concurrent esophageal biopsy) and was therefore excluded from the follow-up outcome analysis, which required assessment of both *H. pylori* infection and EoE status.

Table 2. Patient characteristics

Features	n (%)
Age (mean, median, range) (*y*)	29.5, 23, 8–82
Children (age <18 y)	8 (33%)
Male	21 (87.5%)
Obesity	6 (25%)
Atopic disorders	7 (29%)
Esophagogastroduodenoscopy indication	
Dysphagia	13 (54%)
Abdominal pain/dyspepsia	5 (21%)
Heartburn	2 (8%)
Others	4 (17%)
Endoscopic abnormality	19 (79%)
Peak eosinophil count (/HPF)	
15–40	16 (67%)
45–80	6 (25%)
85–105	1 (4%)
110–200	1 (4%)
PPI as first-line treatment	24 (100%)
HPE regimen	13 (54%)
Steroid use	8 (33%)
Candida infection	2 (20%)*
Resolution rate (*H. pylori*-, EoE-)	3 (30%)*

*Based on available follow-up data for 10 patients. *H. pylori*-, EoE-, resolution of both *H. pylori* infection and EoE. HPF, high-power field; PPI, proton pump inhibitor; HPE, *Helicobacter pylori* eradication therapy; EoE, eosinophilic esophagitis.

Discussion

EoE is considered an immune-mediated disease characterized by symptoms of esophageal dysfunction and eosinophilic infiltration of the esophageal mucosa (≥15 eos/HPF), with exclusion of other causes of eosinophilia. Like many immunologic entities, the exact etiology of EoE remains unknown, and it is believed to be secondary to a combination of environmental triggers (food, medication, infection, etc.), genetic predisposition, and host immune response. Whether *H. pylori* infection represents one such trigger has not been well characterized. This retrospective cohort

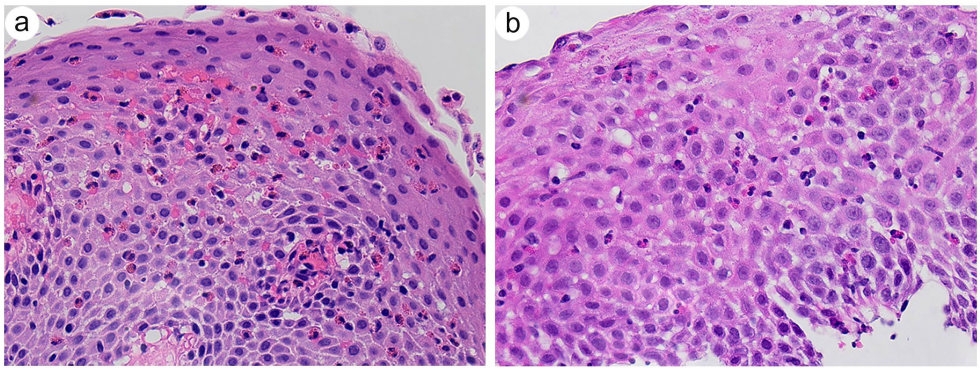

Fig. 2. Histologic changes in eosinophilic esophagitis (EoE) with concurrent gastric *Helicobacter pylori* infection. (a) Classic EoE. (b) *H. pylori*-associated EoE. Hematoxylin and eosin stain, 400×. In addition to eosinophilia, other histologic abnormalities include basal cell hyperplasia, dilated intercellular spaces, and lamina propria fibrosis.

study describes the clinicopathologic characteristics and treatment outcomes of patients with EoE and concurrent gastric *H. pylori* infection. Our findings suggest that *H. pylori* infection may be associated with a subset of EoE that, histologically, tends to differ slightly from classic EoE and is characterized by lower eosinophil density and a relatively even distribution of eosinophils within the squamous epithelium. This *H. pylori*-associated EoE might also respond to targeted eradication therapy.

The most recent meta-analysis reported a prevalence of *H. pylori* infection among patients with EoE ranging from 1.6% to 37.4%, with an overall prevalence of 5.03%.[10] The 14.2% observed in our cohort falls within this range. While some studies have proposed an inverse association, suggesting that *H. pylori* may exert a protective effect on EoE,[5] others have attributed this relationship to coincidental divergence in disease trends or confounding factors such as socioeconomic status and hygiene, rather than a true biologic effect.[6,9] The significant association observed in our cohort supports a close relationship between these conditions. However, rather than demonstrating a protective effect, our findings, particularly the predominance of nonclassic histologic features in 79% of cases, raise the possibility of a pathogen-associated mechanism of esophageal eosinophilia that is distinct from classic immune-mediated EoE.[11] To our knowledge, the predominance of this nonclassic histologic pattern in patients with concurrent gastric *H. pylori* infection has not been previously described.

Similarly, *H. pylori* has previously been reported in association with symptomatic eosinophilic gastritis and hypereosinophilia, both of which have been reported to resolve completely with eradication therapy alone.[12,13] These observations provide a plausible mechanism by which chronic *H. pylori* infection may potentiate eosinophilic inflammation in susceptible individuals.[14] Interestingly, *H. pylori* eradication has also been associated with improvement or resolution of chronic urticaria, a separate non-IgE-mediated allergic condition, with anti-*H. pylori* IgG levels being significantly elevated in affected patients compared with controls.[15] While the mechanisms may differ, these observations suggest that *H. pylori* can modulate immune pathways across non-IgE-mediated allergic conditions. EoE is widely considered an atopic disease based on evidence from animal models, genetic studies, the frequency of comorbid allergic disorders, and the clinical efficacy of elimination diets.[8] However, evidence suggests that EoE is not primarily IgE-mediated but rather represents a Th2-mediated immune response in which interleukin (IL)-4, IL-5, and IL-13 induce expression of eotaxin-3, a potent chemokine responsible for eosinophil migration and activation.[16] Activated eosinophils subsequently release additional factors such as transforming growth factor-beta, which contributes to chronic injury and fibrostenotic remodeling of the epithelium.[17,18]

Treatment outcomes in our cohort further support this proposed mechanism. Among patients achieving *H. pylori* eradication, several demonstrated concurrent resolution of EoE, whereas persistent *H. pylori* infection was associated with relapsing or refractory EoE. A clinically notable finding was the development of fungal infection in 2 of 4 patients treated with corticosteroids. Although esophageal candidiasis is a recognized complication of topical steroid therapy in EoE,[19,20] the relatively high frequency observed in this small cohort raises the possibility that concurrent mucosal inflammation, epithelial barrier dysfunction, or immune alterations associated with *H. pylori* infection may contribute to susceptibility in some patients.[21] We propose, in these cases, targeted HPE as the primary treatment approach and reserve steroids for persistent eosinophilia after confirmed *H. pylori* eradication. Of note, the entire cohort was treated first-line with PPI alone or as a component of other regimens, which is in line with current international consensus guidelines for EoE management; the potential confounding effect of PPI therapy on esophageal eosinophilia cannot be excluded.[22,23] Moreover, Okimoto *et al.*[24] reported that more than 60% of patients who discontinued PPI therapy experienced recurrence of symptoms and/or esophageal eosinophilia. It is plausible that persistent gastric *H. pylori* infection may contribute to EoE persistence or recurrence in a subset of these patients.

Although our findings raise the possibility of a pathogen-associated pattern of EoE in the setting of gastric *H. pylori* infection, this proposed mechanism remains speculative. *H. pylori* infection is known to promote chronic mucosal inflammation through activation of innate and adaptive immune pathways, including Th1-, Th17-, and epithelial-derived cytokine responses.[25] These immune effects may alter epithelial barrier function, antigen presentation,

Patient	Treatment	Follow-up 1	Follow-up 2	Follow-up 3	Follow-up 4
Non-classic EoE ★ Candida					
1	PPI	—	—	—	—
2	PPI	—	—	—	—
3	PPI	—	—	—	—
4	PPI	—	—	—	—
5	PPI	—	—	—	—
6	PPI	*H. pylori* − EoE +	—	—	—
7	PPI	*H. pylori* + EoE +	—	—	—
8	PPI	*H. pylori* + EoE +	*H. pylori* + EoE +	—	—
9	HPE	—	—	—	—
10	HPE	—	—	—	—
11	HPE	—	—	—	—
12	HPE	—	—	—	—
13	HPE	—	—	—	—
14	HPE	*H. pylori* − EoE −	—	—	—
15	HPE	*H. pylori* − EoE −	—	—	—
16	HPE + steroid	*H. pylori* + † EoE not evaluated	—	—	—
17	HPE + steroid	*H. pylori* − EoE +	*H. pylori* + EoE + ★	*H. pylori* + EoE +	*H. pylori* + EoE +
18	HPE + steroid	*H. pylori* + EoE − ★	*H. pylori* + EoE +	*H. pylori* + EoE +	*H. pylori* + EoE − ★
19	PPI + steroid	—	—	—	—
Classic EoE					
1	PPI	*H. pylori* − EoE +	—	—	—
2	HPE + steroid	—	—	—	—
3	HPE + steroid	*H. pylori* + EoE +	—	—	—
4	HPE + steroid	*H. pylori* − EoE −	*H. pylori* − EoE −	—	—
5	PPI + steroid	—	—	—	—

Fig. 3. Treatment regimens and outcomes of eosinophilic esophagitis (EoE) with concurrent gastric *Helicobacter pylori* infection. Different colors indicate treatment regimens and follow-up outcomes. Blue boxes indicate histologic resolution of both *Helicobacter pylori* infection and EoE (*H. pylori*$_-$/EoE$_-$); light blue boxes indicate eradication of *H. pylori* with persistent EoE (*H. pylori*$_-$/EoE$_+$); red boxes indicate persistent *H. pylori* infection with persistent EoE (*H. pylori*$_+$/EoE$_+$); light orange boxes indicate resolution of EoE but persistent *H. pylori* infection (*H. pylori*$_+$/EoE$_-$). ★indicates biopsy-proven *Candida* infection. † Gastric biopsy only; concurrent esophageal biopsy unavailable. This patient was excluded from follow-up outcome analyses (n = 10). HPE, *H. pylori* eradication therapy; PPI, proton pump inhibitor.

DOI: 10.14218/JCTP.2026.00021 | 2026

and downstream inflammatory signaling.[26] Such immune modulation could theoretically influence esophageal inflammation by affecting type 2 immune pathways, eosinophil recruitment, or epithelial barrier integrity.[11,26] However, *H. pylori* is also known to exert complex and sometimes opposing effects on host immunity.[14] Due to the small cohort size and observational nature of this study, our findings should not be interpreted as proof of causality but rather as hypothesis-generating evidence that gastric *H. pylori* infection might contribute to eosinophilic esophageal inflammation in a subset of patients. Future prospective studies incorporating cytokine profiling, tissue-based immune markers, microbiome analysis, and standardized post-eradication follow-up are needed to clarify whether this association reflects a true pathogen-driven mechanism.

The relationship among EoE, gastroesophageal reflux disease (GERD), and PPI-responsive esophageal eosinophilia remains complex and incompletely understood.[16] Contemporary guidelines recognize substantial overlap among these entities, and PPI responsiveness is no longer considered sufficient to exclude a diagnosis of EoE.[1] Because objective reflux testing was not routinely performed and PPI therapy was administered as first-line treatment in all patients, the independent contribution of GERD and acid suppression cannot be fully determined. Consequently, PPI-responsive esophageal eosinophilia and reflux-associated eosinophilia cannot be completely excluded in some cases. However, all patients had symptoms of esophageal dysfunction, endoscopic findings typical of EoE (furrows, rings, or strictures), and peak eosinophil counts ≥15 eos/HPF, and the majority demonstrated additional histologic features characteristic of EoE, including eosinophil degranulation, basal zone hyperplasia, and lamina propria fibrosis. Therefore, while PPI therapy and GERD may have contributed to esophageal eosinophilia in a subset of patients,[27] they are unlikely to fully account for the clinicopathologic patterns observed in this cohort.

Limitations

We acknowledge several limitations of this study. First, this is a single-center study with a limited number of cases, and a relatively high rate of loss to follow-up was observed, suggesting that this condition may be underrecognized or not consistently managed in routine clinical practice. Unfortunately, as this was a retrospective study, the specific reasons for loss to follow-up could not be reliably determined from the medical records. Possible explanations include transfer of care, failure to return for scheduled follow-up, symptom resolution, or care received outside our health care system. Furthermore, the relatively small cohort, wide age range, and limited follow-up constrain the interpretation of treatment response and long-term clinical outcomes. Therefore, analysis for potential confounding using multivariable regression was not performed. Second, some may argue that the nonclassic cases represent reflux-associated eosinophilia. In our opinion, these entities are not mutually exclusive, and it may not be feasible to fully distinguish them in routine clinical practice. Supporting this, the LOTUS trial included 1.8% (9 of 512) of GERD patients with EoE-type pathology at baseline.[28] O'Connor has further suggested that the increasing prevalence of EoE may be partially driven by elevated gastric acid secretion associated with the rising prevalence of GERD.[29] Third, we strictly adhered to the ≥15 eos/HPF threshold for EoE diagnosis, which may have excluded cases with EoE morphologic features but lower eosinophil counts. In practice, repeat biopsy may be warranted in such cases given the patchy distribution of eosinophilic infiltration in EoE.[30,31] Finally, as this study focuses on patients with concurrent diseases, direct comparison with EoE patients without *H. pylori* infection was not contributory and thus was not performed.

Conclusions

Our findings identify gastric *H. pylori* infection as a potential contributor in a subset of patients with EoE and describe a distinctive clinicopathologic pattern characterized by relatively lower eosinophil counts and a more uniform distribution of eosinophilic inflammation. Although confirmation in larger prospective studies is warranted, this study expands the current understanding of EoE and highlights a potentially underrecognized, clinically relevant subtype associated with *H. pylori* infection.

Acknowledgments

Prior Presentation: This study was presented in abstract form at the United States and Canadian Academy of Pathology (USCAP) Annual Meeting, San Antonio, Texas, March 2026, and published in the Laboratory Investigation abstract supplement.

Funding

This research did not receive any funding from public, commercial, or not-for-profit sectors.

Conflict of interest

WX is a member of the Editorial Board of the *Journal of Clinical and Translational Pathology*. Other authors have no conflict of interest related to this publication.

Author contributions

Writing – review & editing (JZ, KJJ, WX), writing – original draft (JZ, KJJ, WX), methodology (JZ, WX), formal analysis (JZ, WX), data curation (JZ), conceptualization (JZ, WX), resources (WX), investigation (WX), and supervision (WX). All authors have approved the final version and publication of the manuscript.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024). Ethical approval was obtained from the Institutional Review Board of the University of South Alabama (IRB Protocol No. 26-074). The requirement for informed consent was waived by the IRB because of the retrospective nature of the study and the use of existing, de-identified clinical pathology data.

Data sharing statement

The datasets generated and analyzed during the current study are

not publicly available because they contain protected health information and are subject to institutional review board and privacy restrictions. De-identified data may be made available from the corresponding author upon reasonable request and with appropriate institutional approval.

References

[1] Dellon ES, Muir AB, Katzka DA, Shah SC, Sauer BG, Aceves SS, *et al*. ACG Clinical Guideline: Diagnosis and Management of Eosinophilic Esophagitis. Am J Gastroenterol 2025;120(1):31–59. DOI: 10.14309/ajg.0000000000003194, PMID: 39745304.

[2] Muir A, Falk GW. Eosinophilic Esophagitis: A Review. JAMA 2021;326(13):1310–1318. DOI: 10.1001/jama.2021.14920, PMID: 34609446.

[3] Attwood SE, Smyrk TC, Demeester TR, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. Dig Dis Sci 1993;38(1):109–116. DOI: 10.1007/BF01296781, PMID: 8420741.

[4] Thel HL, Anderson C, Xue AZ, Jensen ET, Dellon ES. Prevalence and Costs of Eosinophilic Esophagitis in the United States. Clin Gastroenterol Hepatol 2025;23(2):272–280.e8. DOI: 10.1016/j.cgh.2024.09.031, PMID: 39486752.

[5] Dellon ES, Peery AF, Shaheen NJ, Morgan DR, Hurrell JM, Lash RH, *et al*. Inverse association of esophageal eosinophilia with Helicobacter pylori based on analysis of a US pathology database. Gastroenterology 2011;141(5):1586–1592. DOI: 10.1053/j.gastro.2011.06.081, PMID: 21762663.

[6] Shah SC, Tepler A, Peek RM Jr, Colombel JF, Hirano I, Narula N. Association Between Helicobacter pylori Exposure and Decreased Odds of Eosinophilic Esophagitis-A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 2019;17(11):2185–2198.e3. DOI: 10.1016/j.cgh.2019.01.013, PMID: 30659992.

[7] Spinelli I, Porcari S, Esposito C, Fusco W, Ponziani FR, Caruso C, *et al*. Meta-Analysis: Inverse Association Between Helicobacter pylori Infection and Eosinophilic Oesophagitis. Aliment Pharmacol Ther 2025;61(7):1096–1109. DOI: 10.1111/apt.70042, PMID: 39991954.

[8] Miftahussurur M, Nusi IA, Graham DY, Yamaoka Y. Helicobacter, Hygiene, Atopy, and Asthma. Front Microbiol 2017;8:1034. DOI: 10.3389/fmicb.2017.01034, PMID: 28642748.

[9] Molina-Infante J, Gutierrez-Junquera C, Savarino E, Penagini R, Modolell I, Bartolo O, *et al*. Helicobacter pylori infection does not protect against eosinophilic esophagitis: results from a large multicenter case-control study. Am J Gastroenterol 2018;113(7):972–979. DOI: 10.1038/s41395-018-0035-6, PMID: 29545632.

[10] Gutiérrez-Ramírez L, Garcia-Dionisio SL, Feo-Ortega S, González-Cervera J, Tejera-Muñoz A, Lucendo AJ, *et al*. The Association Between *Helicobacter* pylori Infection and Eosinophilic Esophagitis: Systematic Review and Meta-Analysis. Helicobacter 2025;30(2):e70038. DOI: 10.1111/hel.70038, PMID: 40249184.

[11] Racca F, Pellegatta G, Cataldo G, Vespa E, Carlani E, Pelaia C, *et al*. Type 2 Inflammation in Eosinophilic Esophagitis: From Pathophysiology to Therapeutic Targets. Front Physiol 2022;12:815842. DOI: 10.3389/fphys.2021.815842, PMID: 35095572.

[12] Papadopoulos AA, Tzathas C, Polymeros D, Ladas SD. Symptomatic eosinophilic gastritis cured with Helicobacter pylori eradication. Gut 2005;54(12):1822. DOI: 10.1136/gut.2005.075077, PMID: 16284301.

[13] Alshurafa A, Sied M, Elkhdier M, Abdalhadi AM, Yassin MA. Helicobacter pylori infection manifesting as Hypereosinophilic syndrome and immune thrombocytopenia complicated by portal vein thrombosis and ischemic colitis. IDCases 2022;27:e01451. DOI: 10.1016/j.idcr.2022.e01451, PMID: 35242558.

[14] Doulberis M, Kountouras J, Rogler G. Reconsidering the "protective" hypothesis of Helicobacter pylori infection in eosinophilic esophagitis. Ann N Y Acad Sci 2020;1481(1):59–71. DOI: 10.1111/nyas.14449, PMID: 32770542.

[15] Watanabe J, Shimamoto J, Kotani K. The Effects of Antibiotics for *Helicobacter pylori* Eradication or Dapsone on Chronic Spontaneous Urticaria: A Systematic Review and Meta-Analysis. Antibiotics (Basel) 2021;10(2):156. DOI: 10.3390/antibiotics10020156, PMID: 33557074.

[16] Molina-Infante J, Bredenoord AJ, Cheng E, Dellon ES, Furuta GT, Gupta SK, *et al*. Proton pump inhibitor-responsive oesophageal eosinophilia: an entity challenging current diagnostic criteria for eosinophilic oesophagitis. Gut 2016;65(3):524–531. DOI: 10.1136/gutjnl-2015-310991, PMID: 26685124.

[17] Zhu C, Weng Q, Gao S, Li F, Li Z, Wu Y, *et al*. TGF-β signaling promotes eosinophil activation in inflammatory responses. Cell Death Dis 2024;15(8):637. DOI: 10.1038/s41419-024-07029-2, PMID: 39214980.

[18] Arias-González L, Rodríguez-Alcolado L, Laserna-Mendieta EJ, Navarro P, Lucendo AJ, Grueso-Navarro E. Fibrous Remodeling in Eosinophilic Esophagitis: Clinical Facts and Pathophysiological Uncertainties. Int J Mol Sci 2024;25(2):927. DOI: 10.3390/ijms25020927, PMID: 38256003.

[19] Dellon ES, Woosley JT, Arrington A, McGee SJ, Covington J, Moist SE, *et al*. Efficacy of Budesonide vs Fluticasone for Initial Treatment of Eosinophilic Esophagitis in a Randomized Controlled Trial. Gastroenterology 2019;157(1):65–73.e5. DOI: 10.1053/j.gastro.2019.03.014, PMID: 30872104.

[20] Cameron BA, Xue AZ, Kiran A, LaFata S, Ocampo AA, McCallen J, *et al*. Esophageal Candidiasis Is Strongly Associated With Treatment Response to Topical Steroids in Eosinophilic Esophagitis and Could Be a Marker of Adherence. Gastro Hep Adv 2024;3(5):612–614. DOI: 10.1016/j.gastha.2024.03.003, PMID: 39165420.

[21] Naumann M, Ferino L, Sharafutdinov I, Backert S. Gastric Epithelial Barrier Disruption, Inflammation and Oncogenic Signal Transduction by Helicobacter pylori. Curr Top Microbiol Immunol 2023;444:207–238. DOI: 10.1007/978-3-031-47331-9_8, PMID: 38231220.

[22] Franciosi JP, Mougey EB, Dellon ES, Gutierrez-Junquera C, Fernandez-Fernandez S, Venkatesh RD, *et al*. Proton Pump Inhibitor Therapy for Eosinophilic Esophagitis: History, Mechanisms, Efficacy, and Future Directions. J Asthma Allergy 2022;15:281–302. DOI: 10.2147/JAA.S274524, PMID: 35250281.

[23] Chakraborty S, Sharma A, Marella S, Rizza CF, O'Brien PA, Ganesan V, *et al*. Unique epithelial proliferative transcriptomic signature in proton pump inhibitor-responsive pediatric eosinophilic esophagitis. JCI Insight 2025;10(19):e178595. DOI: 10.1172/jci.insight.178595, PMID: 41059573.

[24] Okimoto E, Ishimura N, Ishihara S. Clinical Characteristics and Treatment Outcomes of Patients with Eosinophilic Esophagitis and Eosinophilic Gastroenteritis. Digestion 2021;102(1):33–40. DOI: 10.1159/000511588, PMID: 33202408.

[25] Algood HMS. T Cell Cytokines Impact Epithelial Cell Responses during Helicobacter pylori Infection. J Immunol 2020;204(6):1421–1428. DOI: 10.4049/jimmunol.1901307, PMID: 32152211.

[26] Kabir S. The role of interleukin-17 in the *Helicobacter* pylori induced infection and immunity. Helicobacter 2011;16(1):1–8. DOI: 10.1111/

j.1523-5378.2010.00812.x, PMID: 21241406.

[27] Katzka DA. The complex relationship between eosinophilic esophagitis and gastroesophageal reflux disease. Dig Dis 2014;32(1-2):93–97. DOI: 10.1159/000357080, PMID: 24603388.

[28] Fiocca R, Mastracci L, Engström C, Attwood S, Ell C, Galmiche JP, *et al*. Long-term outcome of microscopic esophagitis in chronic GERD patients treated with esomeprazole or laparoscopic antireflux surgery in the LOTUS trial. Am J Gastroenterol 2010;105(5):1015–1023. DOI: 10.1038/ajg.2009.631, PMID: 19904246.

[29] O'Connor HJ. Forty years of *Helicobacter* pylori infection and changes in findings at esophagogastroduodenoscopy. Helicobacter 2023;28(6):e13026. DOI: 10.1111/hel.13026, PMID: 37818739.

[30] Collins MH, Arva NC, Bernieh A, Lopez-Nunez O, Pletneva M, Yang GY. Histopathology of Eosinophilic Esophagitis. Immunol Allergy Clin North Am 2024;44(2):205–221. DOI: 10.1016/j.iac.2023.12.008, PMID: 38575219.

[31] Collins MH. Histopathologic features of eosinophilic esophagitis and eosinophilic gastrointestinal diseases. Gastroenterol Clin North Am 2014;43(2):257–268. DOI: 10.1016/j.gtc.2014.02.007, PMID: 24813514.