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Research Article

Evaluation of the frequency of Helicobacter pylori infection and atrophic gastritis in patients diagnosed with celiac disease

Çölyak hastalığı tanılı hastalarda Helicobacter pylori enfeksiyonu ve atrofik gastrit sıklığının değerlendirilmesi

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Abstract

Aim: Celiac disease (CD) is a chronic inflammatory enteropathy triggered by an autoimmune response to gluten. This study aimed to determine gastric pathologies accompanying CD, with a focus on the frequency of Helicobacter pylori (H. pylori) infection and atrophic gastritis.

Material and Methods: Between January 2010 and March 2018, 47 patients diagnosed with CD at the Gastroenterology Clinic of Kayseri Training and Research Hospital, who underwent gastric biopsy during endoscopy, were enrolled as the study group. The control group consisted of 47 age- and gender-matched patients who underwent endoscopy for dyspeptic complaints. The groups were compared regarding the presence of atrophic gastritis, H. pylori, lymphocytic gastritis, and intestinal metaplasia. Data were analyzed using IBM SPSS V23.

Results: A total of 94 patients (47 CD, 47 dyspepsia) were included. Both groups comprised 20 male and 27 female patients. Atrophy frequency was 27.7% in the CD group and 17.0% in the dyspepsia group ($p = 0.322$). H. pylori positivity was 61.7% in the CD group and 74.5% in the dyspepsia group ($p = 0.269$). Lymphocytic gastritis was present in 12.8% of the CD group but was not detected in the control group ($p = 0.011$). No statistical difference was found in metaplasia frequency ($p = 0.307$). Serum vitamin B12 levels were below 200 pg/mL in 80% of CD patients.

Conclusion: Gastric biopsy during endoscopy is recommended for celiac patients, particularly those with persistent anemia, dyspepsia, or B12 deficiency despite a gluten-free diet. While the frequencies of H. pylori infection and atrophic gastritis were similar to those in the control group, lymphocytic gastritis was significantly more common in CD patients. This finding underscores the importance of evaluating gastric mucosal changes to manage refractory symptoms and nutritional deficiencies effectively.

Keywords: celiac disease, helicobacter pylori, atrophic gastritis, lymphocytic gastritis, Vitamin B12

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Öz

Amaç: Çölyak hastalığı (ÇH), glutene karşı gelişen otoimmün yanıtın tetiklediği kronik inflamatuar bir enteropatidir. Bu çalışmada, ÇH'ye eşlik eden gastrik patolojilerin belirlenmesi, özellikle Helicobacter pylori (H. pylori) enfeksiyonu ve atrofik gastrit sıklığının saptanması amaçlanmıştır.

Gereç ve Yöntemler: Ocak 2010 ile Mart 2018 tarihleri arasında Kayseri Eğitim ve Araştırma Hastanesi Gastroenteroloji Kliniği'nde ÇH tanısı alan ve endoskopi sırasında gastrik biyopsi yapılan 47 hasta çalışma grubuna dahil edildi. Kontrol grubu, dispeptik şikayetler nedeniyle endoskopi yapılan benzer yaş ve cinsiyetteki 47 hastadan oluşturuldu. Gruplar; atrofik gastrit, H. pylori, lenfositik gastrit ve intestinal metaplazi varlığı açısından karşılaştırıldı. Veriler IBM SPSS V23 kullanılarak analiz edildi.

Bulgular: Toplam 94 hasta (47 ÇH, 47 dispepsi) çalışmaya dahil edildi. Her iki grupta da 20 erkek ve 27 kadın hasta mevcuttu. Atrofi sıklığı ÇH grubunda %27,7, dispepsi grubunda ise %17,0 olarak saptandı (p = 0,322$). H. pylori pozitifliği ÇH grubunda %61,7 iken kontrol grubunda %74,5 idi (p = 0,269$). Lenfositik gastrit ÇH grubunda %12,8 oranında görülürken, kontrol grubunda saptanmadı (p = 0,011$). Metaplazi sıklığında istatistiksel fark bulunmadı (p = 0,307$). ÇH hastalarının %80'inde serum vitamin B12 düzeyleri 200 pg/mL'nin altında saptandı.

Sonuç: Çölyak hastalarında, özellikle glutensiz diyete rağmen persistan anemi, dispepsi veya B12 eksikliği olanlarda endoskopi sırasında gastrik biyopsi yapılması önerilir. H. pylori enfeksiyonu ve atrofik gastrit sıklığı kontrol grubuyla benzer olsa da lenfositik gastrit ÇH hastalarında anlamlı derecede daha yaygındır. Bu bulgu, dirençli semptomların ve beslenme yetersizliklerinin etkin yönetimi için gastrik mukoza değişikliklerinin değerlendirilmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: çölyak hastalığı, helicobacter pylori, atrofik gastrit, lenfositik gastrit, vitamin B12.

Introduction

Celiac disease (CD) is an immune-mediated enteropathy that occurs in genetically predisposed individuals upon ingestion of gluten-containing grains. It is characterized by villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes in the small intestinal mucosa. The pathogenesis involves an abnormal immune response to gliadin, a component of gluten, triggering autoimmune processes, particularly in individuals with HLA-DQ2 and HLA-DQ8 genotypes [1,2].

The classic form of the disease presents with malabsorption symptoms (weight loss, diarrhea, steatorrhea, bloating), while atypical or silent forms, increasingly recognized, may manifest with iron deficiency anemia, osteopenia, infertility, neurological symptoms, and elevated liver enzymes [3-5]. This highlights CD as a systemic disease affecting multiple organs.

Pathological changes may also occur in the gastric mucosa in celiac disease. Lesions such as lymphocytic gastritis (LG) and atrophic gastritis (AG) have been frequently reported. LG, characterized by increased intraepithelial lymphocytes in the gastric mucosa, is observed in approximately 10% of celiac patients [6,7]. These findings may explain dyspeptic complaints that persist despite a gluten-free diet.

Helicobacter pylori (H. pylori) infection is a global health issue and a key etiological factor for atrophic gastritis. H. pylori contributes to chronic gastritis, peptic ulcer disease, and gastric adenocarcinoma. Some studies suggest that H. pylori may coexist with celiac disease and potentially trigger autoimmune mechanisms [8-10].

However, the relationship between H. pylori and celiac disease remains unclear. While some studies propose that the bacterium may facilitate CD development, others suggest a protective effect [11,12]. These contradictory findings indicate that the role of H. pylori in CD pathogenesis is not fully understood.

This study aimed to examine the frequency of H. pylori, lymphocytic gastritis, and atrophic gastritis in gastric biopsies of celiac patients, compare the results with a dyspepsia control group, and evaluate the clinical significance of gastric mucosal changes.

Material and Methods

This retrospective cross-sectional study included 47 patients diagnosed with CD at the Gastroenterology Clinic of Kayseri Training and Research Hospital between January 2010 and March 2018, who underwent gastric biopsy during the same endoscopic session. The control group consisted of 47 age- and gender-matched patients who presented with dyspeptic complaints and underwent gastric biopsy.

The diagnosis of celiac disease was based on clinical findings, serological positivity for anti-endomysium and/or anti-tissue transglutaminase antibodies, and histopathological evidence of villous atrophy according to the Marsh classification (Marsh 2 and above).

All patients underwent a standard biopsy protocol with at

least two biopsies from the antrum and two from the corpus. Biopsies were evaluated by a single experienced pathologist using an Olympus BX53 light microscope. H. pylori was detected by Giemsa stain, and intestinal metaplasia was identified by PAS-Alcian Blue staining. Histological assessments followed the Sydney classification.

Lymphocytic gastritis was diagnosed when more than 25 intraepithelial lymphocytes per 100 epithelial cells were present. Atrophy was graded as mild, moderate, or severe, but for analysis, a binary (present/absent) classification was used.

This study was conducted in the Department of Internal Medicine at the University of Health Sciences Kayseri Training and Research Hospital. Approval for the study was obtained from the Medical Specialization Education Board of our hospital (Decision No: 13, dated March 20, 2018). The study was carried out in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data were analyzed with IBM SPSS v23.0. Continuous variables were assessed for normality using the Kolmogorov-Smirnov test. The Student's t-test was used for comparisons between two independent groups, and the Chi-square test was applied for categorical data. A p-value < 0.05 was considered statistically significant.

Results

The study included 94 patients (47 CD, 47 dyspepsia). The CD group consisted of 27 females and 20 males, with a similar gender distribution in the control group ($p > 0.05$). The mean age was 37.3 ± 14.0 years in the CD group and 37.4 ± 15.3 years in the control group.

Lymphocytic gastritis was significantly more frequent in the celiac group than in the control group ($p = 0.011$). No significant differences were observed between the groups regarding atrophy, H. pylori infection, or intestinal metaplasia (Table 1).

Table 1. Positivity rates by groups.

Parameter	Celiac (n = 47)	Dyspepsia (n = 47)	p
Atrophy	27.7%	17.0%	0.322
H. pylori	61.7%	74.5%	0.269
Lymphocytic gastritis	12.8%	0	0.011
Metaplasia	6.4%	2.1%	0.307

Table 2 demonstrates that serum Vitamin B12 deficiency (<200 pg/ml) was observed in the majority of celiac patients (80%). The deficiency was slightly more common among females (85%) compared to males (77%). These findings suggest that Vitamin B12 deficiency is highly prevalent in celiac disease, likely due to both malabsorption and associated atrophic or autoimmune gastritis.

The decrease in vitamin B12 levels may be associated with the presence of atrophy or autoimmune gastritis in the gastric mucosa. In particular, B12 deficiency was observed in all cases with severe atrophy.

Table 2. Serum vitamin B12 levels in celiac patients.

Group	Low Serum B12 (<200 pg/ml)
All patients (n=47)	80%
Male (n=20)	77%
Female (n=27)	85%

Additional analyses showed no significant correlation between H. pylori infection and the presence of atrophic gastritis or lymphocytic gastritis (Table 3). However, Vitamin B12 levels were significantly lower with increasing atrophy severity (Table 4).

Table 3. Relationship between H. pylori and gastric pathologies.

Parameter	H. pylori Positive	H. pylori Negative	p
Atrophic gastritis	31.0%	25.0%	0.48
Lymphocytic gastritis	15.0%	10.0%	0.61
Intestinal metaplasia	8.0%	4.0%	0.39

Table 4. Vitamin B12 levels according to atrophy severity.

Atrophy Severity	Mean Vitamin B12 (pg/ml)	p
Mild	190 ± 35	0.04
Moderate	160 ± 28	0.02
Severe	125 ± 21	<0.01

Discussion

This study evaluated histopathological changes in the gastric mucosa of celiac patients and compared the frequencies of H. pylori infection, atrophic gastritis (AG), lymphocytic gastritis (LG), and intestinal metaplasia (IM) with a dyspepsia control group. LG was significantly more frequent in the CD group. Although no statistical difference was observed in AG and H. pylori rates, the numerically higher AG frequency in celiac patients is noteworthy. Additionally, low serum vitamin B12 levels support the clinical impact of gastric mucosal pathologies [1,4,5].

Lymphocytic gastritis is a rare histological finding characterized by increased intraepithelial lymphocytes in the gastric mucosa. In this study, LG was present in 12.8% of celiac patients but absent in controls ($p = 0.011$). Literature reports LG frequencies of 7–13% in CD patients, consistent with our findings [6,7]. Although its pathogenesis is not fully understood, the immune response to gluten may induce similar lymphocytic infiltration in the gastric mucosa [13]. The migration of activated T lymphocytes from the small intestine to the gastric mucosa via systemic circulation is a proposed mechanism. Some studies

indicate that LG may regress with a gluten-free diet, suggesting it may be a manifestation of CD. However, LG can also cause persistent dyspepsia, nausea, or epigastric pain despite dietary compliance [14]. Therefore, gastric biopsy in CD patients provides valuable diagnostic and symptomatic insights.

In our study, AG frequency was 27.7% in celiac patients and 17% in the dyspepsia group. Although not statistically significant, the higher rate in CD patients is clinically relevant. AG, characterized by loss of gastric glands and mucosal thinning, often results from H. pylori infection or autoimmune processes (8,9). Its frequent occurrence in CD suggests a shared autoimmune predisposition [15]. Some studies have reported parietal cell antibody positivity in celiac disease, potentially linked to autoimmune gastritis [13,18]. This may explain vitamin B12 deficiency resulting not only from malabsorption but also from autoimmune destruction of gastric mucosa [18,19].

The clinical significance of AG is substantial, as progressive mucosal atrophy reduces gastric acid secretion and intrinsic factor production, impairing vitamin B12 absorption and leading to megaloblastic anemia [9,10]. The finding that 80% of our CD patients had low serum B12 levels supports this pathophysiological mechanism [18].

H. pylori positivity was 61.7% in the CD group and 74.5% in controls ($p = 0.269$). Although not significantly different, the high infection rate is notable. The prevalence of H. pylori in Turkish adults is approximately 70% [10], aligning with our findings. The effect of H. pylori on celiac disease is controversial. While some studies suggest it may suppress CD development by modulating mucosal immunity [11], others propose that it exacerbates chronic inflammation and triggers autoimmunity [12]. The lack of difference between groups in our study suggests no direct causal relationship. However, H. pylori infection may influence symptom severity in CD. Chronic gastritis can reduce gastric acid production, further impairing iron absorption and worsening anemia [2]. Therefore, H. pylori eradication in CD patients, particularly those with refractory anemia, is a reasonable consideration [16].

The high prevalence of vitamin B12 deficiency (80%) in celiac patients underscores the multifactorial pathogenesis of anemia in this population. Villous atrophy impairs iron absorption proximally and folate/B12 absorption distally [1,3]. However, the observed rate cannot be attributed solely to intestinal malabsorption. The coexistence of B12 deficiency with atrophic or autoimmune gastritis indicates that parietal cell damage also contributes [18]. Similar findings have been reported, especially in CD patients with parietal cell antibodies [9,18]. Therefore, regular monitoring of iron, B12, and folate levels is recommended in CD management [17,19]. Additional analyses showed no significant association between H. pylori positivity and gastric histopathology. However, the progressive decline in vitamin B12 levels with increasing atrophy severity supports an autoimmune component (Tables 3,4). Our findings align with prior literature. Villanacci et al. [6] reported LG in 11% of 111 celiac patients, while Miceli et al. [7] detected LG in 9%. These rates support our 12.8% finding. Atrophic gastritis rates in the literature range from 15–30% [14,15], our finding of 27.7% suggests that autoimmune gastritis frequently accompanies CD. H. pylori infection rates vary geographically. In Europe, rates in CD patients are around 30–40%, while in endemic regions like Turkey, they exceed 60% [16]. Our findings reflect this geographical variation [10,16].

This study reinforces the diagnostic value of gastric biopsy in celiac disease. Biopsies from the antrum and corpus during endoscopy are crucial for detecting accompanying gastritis, atrophy, or metaplasia [4,5]. In CD patients with persistent anemia, B12 deficiency, or dyspepsia despite a gluten-free diet, gastric pathology should be investigated [3,18]. As H. pylori eradication may reduce the risk of atrophic gastritis, treatment should be considered in positive patients [8-10]. Regular follow-up of patients with LG on a gluten-free diet is important for monitoring symptom and histological improvement [19].

Limitations of the study

The main limitations of this study are its retrospective design and limited sample size. Prospective, multicenter studies could clarify the role of H. pylori in CD pathogenesis [11,12,16]. Systematic evaluation of autoimmune gastritis markers (anti-parietal cell antibody, anti-intrinsic factor) would better elucidate the relationship between gastric and small intestinal immune responses (15,18). Future studies should investigate gastric mucosal changes in CD at the molecular level. Examining cytokine profiles, T lymphocyte subsets, and microbiota differences will enhance our understanding of the complex interplay between gluten sensitivity and gastric immune response [14,15,17].

In conclusion, this study demonstrates that lymphocytic gastritis is significantly more common in the gastric mucosa of celiac patients, while the frequencies of H. pylori infection and atrophic gastritis are similar to those in the general population. The high prevalence of vitamin B12 deficiency underscores the multifactorial nature of nutritional deficits in CD. We recommend gastric biopsy for celiac patients with persistent anemia, dyspepsia, or B12 deficiency despite a gluten-free diet. This approach facilitates early detection of accompanying pathologies such as lymphocytic or atrophic gastritis and guides appropriate management strategies.

Declaration of conflicting interests

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Ethics approval

The study was approved by the Medical Specialization Education Board of the University of Health Sciences Kayseri Training and Research Hospital (Decision No: 13, dated March 20, 2018).

Authors' contribution

G.A.: Study Design, Data Collection, Data Analysis and Interpretation, Manuscript Drafting and Revision, Final Approval. E.Ç.: Study Design, Manuscript Drafting and Revision, Final Approval. All authors have read and approved the final manuscript.

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