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# Helicobacter pylori infection in pediatric patients with celiac disease: A single-center experience

# Çölyak hastalığı olan çocuk hastalarda Helicobacter pylori enfeksiyonu: Tek merkez deneyimi

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**Abstract**

**Aim:** There are numerous studies investigating the relationship between celiac disease (CD) and *Helicobacter pylori (H. pylori)*. In this study, we aimed to compare the prevalence of coexisting *H. pylori* infection and CD in pediatric patients diagnosed with celiac disease at our clinic versus an age-matched control group.

**Materials and Methods:** A total of 198 patients with celiac disease and 131 sex and age -matched controls undergoing upper gastrointestinal endoscopy due to dyspeptic complaints were included in this study. The prevalence of *H. pylori* was compared between the groups**.**

**Results:** Of the 198 patients with CD included in the study, 66 (33.3%) were male and 132 (66.7%) were female, while in the control group, 36 (27.5%) were male, and 95 (72.5%) were female. 89 (44%) of the patients with CD and 70 (53.4%) of the controls were *H. pylori*-positive. There was no statistically significant difference in the distribution of Marsh scores between the *H. pylori*-negative and -positive groups.

**Conclusion:** The association between celiac disease and *H. pylori* remains controversial. Thus, multicenter studies are warranted to evaluate the role of *H. pylori* in the pathogenesis of celiac disease.

**Keywords:** Celiac Disease, H. Pylori, Prevalence.

**Öz**

**Amaç:** Çölyak hastalığı ve *Helicobacter pylori* (*H. pylori*) arasındaki ilişkiyi araştıran birçok çalışma vardır. Biz çalışmamızda; kliniğimizde çölyak hastalığı tanısı almış hastalarda, Helicobacter pylori birlikteliğini ve yaş uyumlu kontrol grubu ile karşılaştırmayı amaçladık

**Gereç ve Yöntem:** Çalışmaya 198 çölyak hastası, yaş ve cinsiyet uyumlu, dispeptik şikayetleri nedeni ile üst gastrointestinal sistem endoskopisi yapılmış 131 kontrol hastası dahil edildi. İki grubun *H. pylori* prevalansları saptanarak aralarında farklılık olup olmadığı araştırıldı.

**Bulgular:** Çalışmaya alınan 198 çölyak hastasının 66 (%33,3)'sı erkek, 132 (%66,7)'si kız hasta ve kontrol grubunun 36 (%27.5)' erkek, 95 (%72.5) kız hasta idi. Çölyak hastalığı olan 198 hastanın 89'unda (%44), kontrol grubundaki 131 hastanın 70'inde(%53.4) *H. pylori* pozitif saptandı. *H. pylori* pozitif ve negatif gruplar arasında Marsh skoru dağılımı açısından istatistiksel anlamlı fark saptanmadı.

**Sonuç:** Çölyak hastalığı ile *H. pylori* arasındaki ilişki tartışmalı olmakla birlikte çölyak hastalığı patogenezinde *H. pylori*'nin rolünü değerlendirmek için çok merkezli çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** Çölyak Hastalığı, H. Pylori, Prevalans.

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## Introduction

Celiac disease (CD) develops in genetically predisposed individuals as a result of permanent sensitivity to dietary gluten, the protein fraction of cereals. CD is an autoimmune, systemic disease that is not limited to the gastrointestinal tract. While CD primarily affects the small intestine, it can manifest with a wide range of both intestinal and extra-intestinal signs and symptoms.[1] Atypical symptoms of CD have become more prevalent in the past few decades. Currently, CD is often initially detected in individuals presenting with a wide range of clinical disorders such as anemia, autoimmune conditions such as autoimmune thyroiditis, as well as certain neurological disorders. Globally, the estimated prevalence of celiac disease in the general population is 1%.[2]

*Helicobacter pylori* (*H. pylori*) is one of the most common bacterial pathogens involved in gastrointestinal (GI) infections. *H. pylori* is a leading cause of many GI diseases such as duodenal ulcer, stomach ulcer, chronic gastritis and malignancies.[3] In addition to autoimmune gastritis, it has also been associated with extra-gastrointestinal autoimmune diseases like immune thrombocytopenic purpura, multiple sclerosis, and psoriasis.[4] Both innate immune inflammatory responses and systemic humoral immune responses have been demonstrated in both CD and *H. pylori* infection.[5] For this reason, the association between CD and *H. pylori* has been examined in many recent studies. While some studies suggest a protective effect of *H. pylori* against celiac disease, many others argue that it has no effect or may predispose individuals to celiac disease.

In our study, we aimed to determine the prevalence of celiac disease and *H. pylori* gastritis in biopsy materials obtained from pediatric patients diagnosed with CD at our center to identify whether there is a relationship between the two conditions.

## Materials and Methods

In this study, 198 pediatric (from 6 months to 18 years of age) patients with CD who were followed at our pediatric gastroenterology outpatient clinic between January 2018 and January 2022 were retrospectively evaluated. Additionally, a control group consisting of 131 age- and sex-matched children was included in the study. The control subjects were children who presented to the pediatric gastroenterology outpatient clinic due to dyspeptic complaints and underwent upper gastrointestinal endoscopy with gastroduodenal biopsy in whom celiac disease was ruled out histopathologically. The diagnosis of CD was established by a pathologist according to the Marsh classification in patients with symptoms suggestive of the disease, positive serologic celiac serology, and endoscopic examination with biopsy. Since villous lesions can be patchy in CD, multiple biopsies were obtained from the duodenal bulb and distal duodenum. The diagnosis of *H.pylori* was made based on upper gastrointestinal endoscopic examination, with two mucosal biopsies each taken from the gastric corpus and antrum, and demonstration of the bacterium with Giemsa staining of the biopsy materials. The control subjects were selected among patients with no exposure to proton-pump inhibitors or antibiotics in the last month and did not have chronic inflammatory bowel disease.

### Statistical analysis

Statistical analysis was performed using SPSS 26.0 (IBM Corp., Armonk, NY). Chi-square test was used to compare two different groups. P values less than0.05 were considered significant. The mean and standard deviation values of the variables were analyzed using Mann-Whitney U test.

### Ethics Committee Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was obtained from the Institutional Review Board of Adıyaman University Faculty of Medicine.

## Results

Among 198 patients with CD, 66 (33.3%) were boys and 132 (66.7%) were girls. The mean age was 120.98 ± 48.86 months for this group. In the control group, there were 36 (27.5%) boys and 95 (72.5%) girls with a mean age of 168.03 ± 42.70 months. When both

groups were compared, there was no difference in terms of sex (p = 0.261) and age distribution (p = 0.538). 89/198 (44%) of the patients with CD and 70/131 (53.4%) of controls were *H. pylori*-positive. No significant difference was observed between the groups with respect to *H. pylori* positivity (p = 0.132). Demographic characteristics of the study sample are presented in Table 1 (Table-1).

When the distribution of the Marsh scores was examined among *H. pylori*- positive CD patients, Marsh stage 3B was the most common (67.4%), followed by Marsh stage 3A (19.1%), and Marsh stage 3C (13.5%). In the *H. pylori*-negative patient group, Marsh 3B was also the most common stage (64.8%), followed by Marsh 3A (26.9%), and Marsh 3C (8.3%). There was no statistically significant difference in the distribution of Marsh scores between *H. pylori*-negative and -positive groups (p = 0.284) (Table-2).

**Table 1**. Demographic characteristics of patients with celiac disease (CD) and controls.

| | CD patients (n=198) | Controls (n=131) | *p*-value |
|---|---|---|---|
| **Age (months)** | 120.98 ± 48.86 | 168.03 ± 42.70 | 0.538 |
| **Sex (M/F), n (%)** | 66 (33.3%)/132 (66.7%) | 36 (27.5%)/95 (72.5%) | 0.261 |
| **Body weight (kg)** | 31.06 ± 13.99 | 46.97 ± 13.52 | 0.334 |
| **Height (cm)** | 133.7 ± 22.05 | 155 ±17.23 | 0.101 |
| **BMI (kg/m$^2$)** | 16.36 ± 3.06 | 18.90 ±2.85 | 0.503 |
| **BMI SDS** | -0.89 ± 1.34 | -0.67 ± 0.95 | 0.019 |
| ***H. pylori*-positive, n (%)** | 89 (44%) | 70 (53.4%) | 0.132 |

**Table 2**. *H. pylori*-positivity according to Marsh classification scores in patients with celiac disease.

| | *H. pylori*-positive | *H. pylori*-negative |
|---|---|---|
| **Marsh 3A** | 17 (19.1%) | 29 (26.9%) |
| **Marsh 3B** | 60 (67.4%) | 70 (64.8%) |
| **Marsh 3C** | 12 (13.5%) | 9 (8.3%) |
| **Total** | 89 (100%) | 108 (100%) |

## Discussion

Celiac disease (CD) is an autoimmune enteropathy triggered by exposure to gluten proteins found in cereals and cereal products in genetically susceptible individuals.[6] *H. pylori* is one of the infectious agents that can induce autoimmune diseases by modulating the inflammatory and immune responses in the small intestine. There are studies evaluating the relationship between *H. pylori* and inflammatory markers.[7] Many studies have been conducted to investigate the link between *H. pylori* gastritis and celiac disease, which reported mixed results[8-10] While some studies suggest that *H. pylori* infection may further exacerbate CD as well as duodenal mucosal damage, others advocate a protective role of *H. pylori* against CD.

In this study, *H. pylori* positivity rate was 44% in patients with CD versus 53.4% in the control group. In a study, Luzza et al.[11] reported a *H. pylori* prevalence of 18.5% in 81 pediatric patients with CD and 17.3% in 81 pediatric controls. Rostami-Nejad et al. found an *H. pylori* prevalence of 82.0% in patients with CD versus 86.0% in the control group.[12] In Jocefczuk et al.'s study, pediatric patients with CD showed a *H. pylori* prevalence of 5.8% versus 6.4% in pediatric controls, with a nonsignificant difference between the groups.[13] In a study from Turkey involving adults with CD, *H. pylori* was identified in 52.6% of the patients, which is in line with our findings.[14]

In a study by Crabtree et al. examining the prevalence of *H. pylori* among patients with or without celiac disease, no significant difference was found.[15] *H. pylori* may potentially reduce the immunogenicity of ingested gluten by altering gastric pH or through its proteases[16], which supports the claim that *H. pylori* infection might protect against celiac disease. Villanacci et al. reported less severe villous atrophy in patients with CD and *H. pylori* infection.[8] In a study by Narang et al. involving 324 patients with CD, *H. pylori* was identified in 37 (11.4%) patients, and an inverse relationship was observed between CD and *H. pylori*, suggesting that *H. pylori*

infection may confer protection against the development of CD.[17] In a meta-analysis of 25 studies, Yue Min et al. found that the frequency of *H. pylori* infection was lower among CD patients compared to controls, suggesting that *H. pylori* infection may be a protective factor.[18] The mechanism underlying the potential protective nature of *H. pylori* infection for celiac disease has also been debated. T-regulatory lymphocytes activated by *H. pylori* have systemic effects, and they may also play a role in the pathogenesis of celiac disease, as the downregulation of the cellular responses mediated by T-regulatory lymphocytes in the intestinal wall is diminished in patients with CD.[16]

In our study, no difference was found between *H. pylori*-negative and -positive patients with celiac disease and pathological Marsh stage. A similar study in a Turkish sample also reported no significant difference between *H. pylori*-positive and -negative individuals in terms of Marsh scores.[19]

## Limitations of the study

A number of limitations should be noted for this study. Dietary habits and socioeconomic status of the patients were unknown. In addition, the sample size was relatively small, and the study had a retrospective design.

## Conclusion

Multicenter systematic prospective studies are required to establish the relationship between *H. pylori infection* and celiac disease.

## Ethics Committee Approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was obtained from the Institutional Review Board of Adıyaman University Faculty of Medicine.

## Informed Consent

All study data were collected with the permission of the Adıyaman Provincial Health Directorate.

## Authors Contributions

All authors contributed equally at each stage of the study

## Conflict of Interests

The authors have no conflicts of interest to declare.

## Financial Disclosure

No financial support was received for this study from a person or organization.

## Statements

The results of this study were not published or presented anywhere previously. Data related to the study is available on request.

## Peer-review

Externally peer-reviewed.

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