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Original Article *Özgün Araştırma*

CHRONIC GASTRITIS IN PEDIATRIC PATIENTS; HELICOBACTER PYLORI OR CELIAC DISEASE?

Çocuk Hastalarda Kronik Gastrit; Helikobakter pilori mi Çölyak mı?

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ABSTRACT

Objective: We aimed to determine the frequency of *Celiac disease* (CD) and *Helicobacter pylori* (Hp) infection, and the effect of Hp and chronic gastritis on patients with false positive CD serology in our center.

Material and Methods: We included 194 patients who had both stomach and small intestine biopsies and were diagnosed with chronic gastritis, between January 2021 and December 2022 in the study. Patients were divided into two groups: Hp-positive and Hp-negative.

Additionally, we evaluated the frequency and association of Hp in cases who were serologically suspected with CD but whose biopsies were not compatible with celiac disease histopathologically.

Results: Helicobacter pylori infection was detected in 76 of 194 gastric biopsies examined (39.1%). Hp positivity was detected in only 15 of 27 patients (55.5%) diagnosed with CD and CD serology was positive in 39 of 194 patients (20.1%), but histopathological changes compatible with CD were detected in only 27 (13.9%).

Conclusion: Although the relationship between chronic gastritis and Hp is clear, the relationship between Hp and CD remains unclear. We believe that studies with larger patient groups investigating Hp virulence and its effect on CD pathophysiology are needed to reveal this relationship.

Keywords: *Celiac disease, Helicobacter pylori, serology, gastritis*

ÖZ

Amaç: Merkezimizde kronik gastrit tanısı alan hastalarda Çölyak hastalığı (ÇH) ve Helikoobakter pilori (Hp) enfeksiyonu sıklığının, Hp ve kronik gastritin ÇH serolojisinde yanlış pozitiflik üzerine etkisinin belirlenmesi amaçlandı.

Gereç ve Yöntemler: Ocak 2021 ile Aralık 2022 tarihleri arasında mide ve ince bağırsak biyopsisi yapılan ve kronik gastrit tanısı alan 194 hasta çalışmaya dahil edildi. Hastalar Hp pozitif ve Hp negatif olarak 2 gruba ayrıldı. Ayrıca serolojik olarak ÇH şüphesi olan ancak biyopsisi histopatolojik olarak ÇH ile uyumlu olmayan olgularda Hp sıklığı ve aralarındaki ilişki değerlendirildi.

Bulgular: İncelenen 194 mide biyopsisinin 76'sında (%39.1) Hp tespit edildi. 27 olgunun 15'inde (%55,5) Hp saptandı ve aynı zamanda ÇH tanısı kondu. 194 hastanın 39'unda (%20,1) ÇH serolojisi pozitif bulunurken, yalnızca 27'sinde (%13,9) ÇH ile uyumlu histopatolojik değişiklikler saptandı.

Sonuç: Kronik gastrit ile Hp arasındaki ilişki açık olmasına rağmen, Hp ile ÇH arasındaki ilişki belirsizliğini korumaktadır. Bu ilişkinin anlaşılması için daha geniş hasta gruplarında Hp virülansının ve ÇH patofizyolojisi üzerine etkisinin araştırıldığı çalışmalara ihtiyaç olduğu kanaatindeyiz.

Anahtar Kelimeler: *Çölyak hastalığı, Helikobakter pilori, seroloji, gastrit*

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INTRODUCTION

Celiac disease (CD) is an autoimmune intestinal disorder, which is suspected to have a genetic basis and is triggered by gluten in susceptible individuals. The global prevalence of CD is estimated to be around 0.7% (ranging from 0.5% to 0.9%), with variations based on ethnicity and geography (1).

Helicobacter pylori (Hp) infection is a common gastrointestinal infection, which causes various diseases, ranging from chronic gastritis to gastric cancer. According to reports from the National Health and Nutrition Examination Survey (NHANES), the prevalence of Hp infection in the 6-19 age group was reported to be 24.8% in 1996 (2).

The relationship between CD and Hp remains unclear. While some studies suggest a positive correlation between CD and Hp infection, others indicate no significant association (3,4). Interestingly, there are studies proposing a protective role of Hp infection on CD as well (5).

In this study, we aimed to investigate the frequency of CD and Hp in patients diagnosed with chronic gastritis by endoscopy in our center, to examine the impact of Hp on false seropositivity in CD, and to explore the interaction between CD and Hp.

MATERIALS AND METHODS

This is a retrospective observational study that was conducted on 194 pediatric patients who underwent upper gastrointestinal endoscopy and who had both stomach and small intestine biopsies diagnosed with chronic gastritis between January 2021 and December 2022. Plasma total immunoglobulin A (IgA) and anti-tissue transglutaminase IgA (IgA tTG) were used as screening tests for CD. In cases with low IgA levels, anti-tissue transglutaminase IgG (IgG tTG) was employed to control CD seropositivity. Marsh classification was used for histopathological CD diagnosis (6). The diagnosis of Hp was made by histological examination of the stomach biopsy samples. The frequency of Hp gastritis and CD, and the relationship between Hp gastritis and CD were assessed. Statistical analyses were conducted using the Statistica Version 13.3 program. The chi-square test and Fisher exact test were used to compare proportions. The level of significance was set as $p<0.05$ with a 95% confidence interval.

This study was approved by the Ankara Training and Research Hospital Clinical Research Ethics Committee under decision number E.22/1013.

RESULTS

Among 194 patients, 76 (39.2%) were diagnosed with Hp gastritis, and 27 (13.9%) were diagnosed with CD. In the Hp-positive group, 24 out of 76 cases (31.5%) showed positive celiac serology; however, only 15 cases (19.7%) had small intestine biopsies compatible with CD.

In the Hp-negative group, 15 of 118 patients (12.7%) showed positive celiac serology however only 12 cases (10.1%) had small intestine biopsies consistent with CD. The prevalence of CD was higher in the Hp-positive group than Hp-negative group but there was no statistically significant relationship between them (p=0.06).

The false positivity rate in the Hp-positive and Hp-negative groups was found 37.5% and 11.1% respectively (p=0.215) (Table 1).

Among the 27 cases with both CD-compatible biopsies and gastritis, 15 cases (55.5%) were Hp-positive.

Table 1: The relationship between Helicobacter pylori and Celiac seropositivity.

Hp + N (%)			**Hp –** N (%)		
76 (39.2)			118 (60.8)		
Seropositive	Seronegative		Seropositive	Seronegative	
24 (31.5)	52 (68.5)		15 (12.7)	103 (87.3)	
CD +	CD -		CD +	CD -	
15 (19.7)	9 (11.8)		12 (10.1)	3 (2.5)	

DISCUSSION

Celiac Disease is an autoimmune intestinal disorder triggered by gluten in genetically susceptible individuals. However it is believed to extend beyond the small intestine, it affects the other segments of the gastrointestinal tract (7). The reason behind this based on assumption that the immune-mediated lymphocytic response to gluten, which plays a role in the pathophysiology of CD, occurs not only in the small intestine of CD patients but also in the gastric epithelium (8).

In a retrospective study evaluating 240 CD children, Levine et al. identified non-Helicobacter pylori-related gastritis in 9.6% of cases (9). Furthermore, in the pathogenesis of the disease, the activation of the structural and acquired immune system in the intestine by gluten leads to enteric inflammation and destruction. So, in sensitive individuals, the increased uptake of luminal enzyme-resistant gluten peptides, elevated production of IL-15 and IFNy, deamidation and transamidation of gluten, proliferation of TCD4+ cells, and activation of macrophages contribute to both intestinal and extraintestinal inflammatory process (10). Oderda et al. revealed mucosal damage in children with CD to be 29.4% in those with good dietary compliance and 43.5% in the group with poor compliance (11).

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Bonaszkiewicz et al. found persistent gastritis in 25.4% of children with CD when diagnosed, highlighting its separate occurrence from villous atrophy (12). In our study, 13.9% of patients with diagnosed chronic gastritis had small intestine biopsies compatible with CD, and all patients' small intestine biopsies were consistent with Marsh 3.

The findings enhance the comprehension of the complex nature of CD, indicating that the disease's effects go beyond the small intestine to affect the gastric epithelium. The found correlation between chronic gastritis and CD in our study underscores the necessity for additional research to clarify the complex mechanisms that underlie the association between these conditions.

Therrien et al. determined that the prevalence of chronic gastritis in individuals with CD was 31.3%. Interestingly, the cases with gastritis had higher antibody titers regardless of the extent of villous atrophy. The article suggested that this could be due to having a longer duration of the disease or a potential role of gastric mucosa in gluten-mediated immune reactions (13).

In our study, among 39 patients with positive celiac-specific antibodies, 27 were histopathologically proven CD, and all of these patients had chronic gastritis. Furthermore, a total of six patients presenting with concurrent duodenitis and one patient presenting with bulbitis were identified as possible cases of CD and were further monitored. During follow-up, the antibody titers of four patients became negative which led us to consider the possibility of false antibody positivity in chronic gastritis.

The results of studies on the relationship between Hp and CD in the literature are conflicting. Studies by Nitelim, Ciacci et al., and Rostami et al. emphasized that Hp is less common in individuals with CD (14-16). However, there are also studies supporting the idea that Hp infection has no effect on the occurrence of CD or suggesting a positive association between Hp and CD (3,4).

These contradictory findings highlight the complexity of the interaction between Hp and CD, requiring additional research into the processes that may explain their connection. The presence of chronic gastritis in CD patients, as observed in our study, introduces an additional level of intricacy to this complex association, necessitating further extensive investigation to elucidate the intricate interconnections among these entities.

In our study, the prevalence of CD in those with Hp positive gastritis was found to be 19.7%, whereas it was 10.1% in the negative group but no statistically significant relationship was observed (p=0.06). We found the prevalence of false positive CD antibody rate to be 37.5% in Hp-positive cases while it was 11.1% in Hp-negative cases. However, there was no statistically significant correlation identified (p=0.215). This data has prompted us to contemplate the potential occurrence of cross-reactivity between antibodies generated as a result of Hp and antibodies specific to CD or Hp may serve as a mechanism to enhance the immune response against gluten. Nevertheless, the literature on this subject presents conflicting findings, necessitating additional research to arrive at a definitive conclusion. Similarly, there are studies suggesting that gastric pathologies can affect the duodenum, and with colonizing the gastric mucosal epithelium Hp infection leads to the development of duodenitis. Therefore, these studies recommend taking samples from both the stomach and the duodenum in patients with duodenal pathology (17). Our study supports this information.

There are some limitations in our study. Due to the retrospective nature of the investigation, we were unable to validate the false positive findings in a different laboratory and, focus on pediatric participants limited the ability to conduct post-treatment histopathology assessment after dietary and/or Hp elimination.

In conclusion, the prevalence of CD among patients attending hospitals with a variety of symptoms is increasing in the modern world. Due to deteriorating dietary habits and crowded living spaces, gastrointestinal complaints, especially gastritis, are encountered more frequently. Hence, while dealing with patients who are suspected of having CD, it is important to take into account the potential presence of both gastritis and Hp, and vice versa, for individuals who have dyspeptic complaints. On the other hand, we believe that bulb and duodenum materials should be sampled during upper gastrointestinal endoscopies. Furthermore, especially in patients with low levels of celiac-specific antibody titers, it is essential to consider the non-celiac causes. So, to get a conclusive determination, it is needed to investigate the virulence of Hp and the pathogenesis of CD in larger cohorts of patients, with a longer period of observation.

Conflict of Interest: The author have indicated no conflicts of interest regarding the content of this article.

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