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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

# Duodenal Ig E and Adult Celiac Disease

## Duodenal Ig E ve Erişkin Çölyak Hastalığı

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## ABSTRACT

**Aim**: The coexistence of Celiac disease (CD) and food allergies is not fully explained. That is why, in the present study, we aimed to determine IgE, related to food allergies, in duodenum with adult CD.

**Material and Method**: Duodenum biopsy samples of 16 celiac patients, aged between 22 and 55, and 14 non-celiac patients, aged between 24 and 59, were evaluated by IgE immunohistochemical examination.

**Results**: Strong and diffuse IgE staining cells were not detected in any case. Sparse IgE-positive cells were detected in 5 (31%) of the celiac patients, while it was detected in 4 (24%) patients in the control group. No statistically significant difference was found between the two groups. The obtained data were evaluated statistically.

**Conclusion**: According to the results of our study, no increase in IgE was detected in the duodenum samples of newly diagnosed celiac patients compared to the duodenum samples of the control group. However, to reach definitive results for the relationship between CD and food allergy, need for a wide series of studies that include gluten-free diet patients and child patients.

**Keywords**: IgE, celiac disease, allergy

## ÖZ

**Amaç**: Çölyak hastalığı (ÇH) ile gıda alerjilerinin birlikteliği tam olarak açıklanamamıştır. Bu nedenle bu çalışmada erişkin çölyak hastalarında duodenumda gıda alerjisi ile ilişkili olan IgE'nin belirlenmesini amaçladık.

**Gereç ve Yöntem**: Yaşları 22 ile 55 arasında değişen 16 çölyak hastası ve 24 ile 59 arasında çölyak hastası olmayan 14 hastanın duodenum biyopsi örnekleri IgE immünhistokimyasal incelemesi ile değerlendirildi. Elde edilen veriler istatiksel olarak değerlendirildi.

**Bulgular**: Hiçbir vakada yaygın IgE boyanan hücreler tespit edilmedi. Çölyak hastalarının 5 tanesinde (%31) seyrek IgE pozitif hücre saptanırken, kontrol grubunda 4 (%24) hastada pozitiflik saptandı. İki grup arasında istatistiksel olarak anlamlı bir fark bulunamadı.

**Sonuç**: Çalışmamızın sonuçlarına göre yeni tanı alan çölyak hastalarının duodenum örneklerinde kontrol grubunun duodenum örnekleri ile karşılaştırıldığında IgE pozitif hücrelerde artış saptanmadı. Ancak ÇH ile besin alerjisi arasındaki ilişkiye yönelik kesin sonuçlara ulaşmak için glutensiz diyet uygulayan hastalar ile çocuk hastaları da kapsayan geniş serili çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler**: IgE, çölyak hastalığı, alerji

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## INTRODUCTION

The small intestine is a major organ involved in the digestion of food and absorption of nutrients and minerals. The duodenum, which is the first part of the small intestine and connects to the stomach, is a primary site in the digestion and absorption of food (1).

Celiac disease (CD) is an immune-mediated gluten-dependent enteropathy that affects the small bowel (2).

Gluten is a protein found in wheat and other grains and causes disease with its alcohol-soluble prolamin portion (3). It is known that in gluten enteropathy, mucosal damage occurs due to overstimulation of cellular and humoral immunity, and gamma interferon (γ-INF) produced by gluten-specific T cells is activated. It has been found that humoral immunity is also stimulated in untreated celiac patients. The increase in the number of IgA-secreting plasma cells in the intestinal mucosa of these patients is remarkable (4-5).

The type I hypersensitivity responses of classic allergic reactions are mediated by allergen cross-linking of immunoglobulin E (IgE) bound to FcεRI receptors on the surface of tissue mast cells and blood basophils. GI tissues are an important reservoir for allergen-specific IgE-positive plasma cells in allergic participants and could contribute significantly to allergen-specific serum IgE in the tissues and perhaps systemically (6).

There are many studies in the literature showing that the frequency of allergic diseases increases in CD (7-9). Recently; many studies show that there is increased Ig-E-related food allergy in CD, especially in children (10-12).

The coexistence of Celiac disease (CD) and food allergies is not fully explained. That is why, in the present study, we aimed to determine IgE related to food allergies in duodenum with adult CD.

## METHOD

The study was carried out with the permission of the KTO Karatay University Non-interventional Clinical Researches Ethics Committee (Date: 25/12/2020, Decision No: 2021.006). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

30 patients whose pathological samples were evaluated in our department between 2019 and 2020 years, were included. The histopathological appearance of 16 of them was compatible with CD.

The CD diagnosis was established according to standard criteria, histological analysis of small intestinal biopsy. Intestinal biopsies were evaluated for villous architecture, heights of the crypts, and intraepithelial lymphocytes and scored according to the Marsh classification modified by Oberhuber. All CD patients were confirmed with serological test results by the hospital information system. Control samples with normal intestinal histology were obtained from non-CD 14 individuals undergoing biopsies for screening procedures for abdominal symptoms and excluded for CD diagnosis. All patients' age and blood eosinophil counts were obtained from the hospital information system.

The paraffin blocks of patients' duodenal biopsy samples and hematoxylin-eosin-stained preparations were obtained from the hospital's pathology archive. In preparing tissue sections, poly-L-lysine (PPL) was used to coat glass slides for IgE immunocytochemical staining. The primary antibody was anti-human IgE (rabbit, Abcam, polyclonal, prediluted, Ab75673).

Immune-stained and hematoxylin-eosin-stained glasses were evaluated under a light microscope. All cases were classified two according to whether they contained IgE-positive cells and

H&E images of all biopsies were reviewed (**Figure 1-4**).

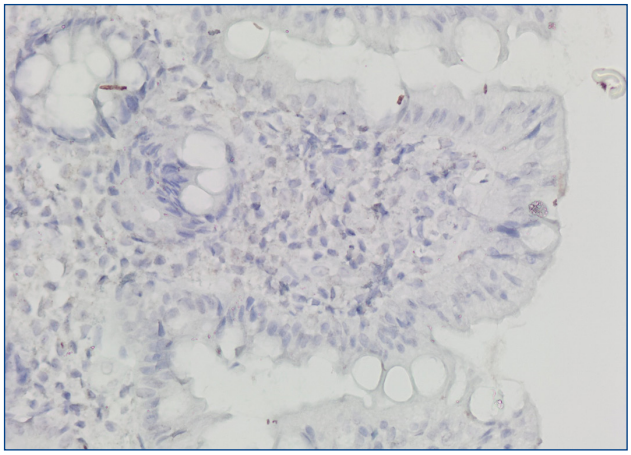

**Figure 1:** No Ig-E positive cell in the celiac patient's duodenum (400X)

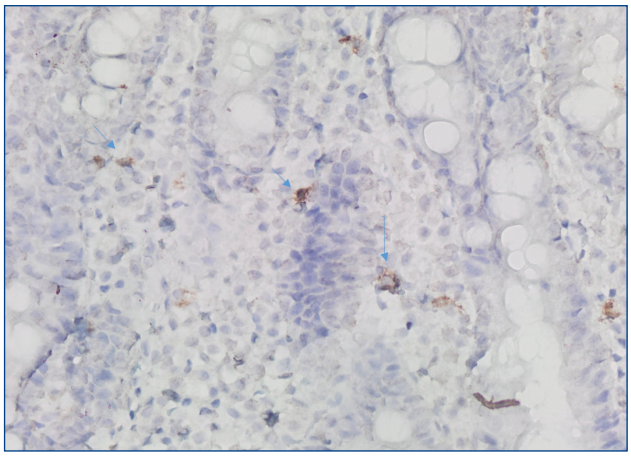

**Figure 2:** IgE-positive mast cells in celiac patient's duodenum (400X) (blue arrows)

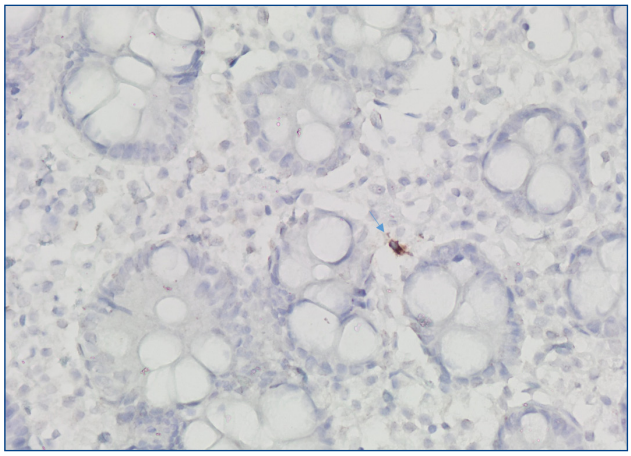

**Figure 3:** IgE positive mast cell in control patient's duodenum (400x) (blue arrow)

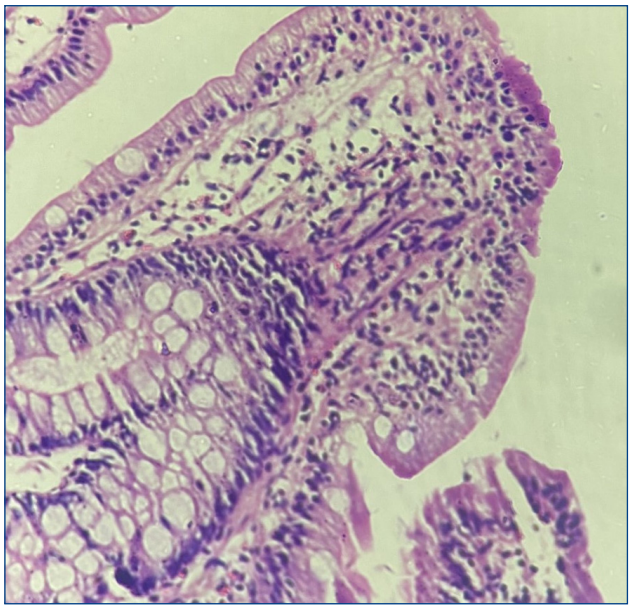

**Figure 4:** H&E image of one of the celiac patient's duodenum with broad and short villus (400x)

While the differences between both groups were determined by the Mann-Whitney U test for numerical variables, the chi-square test was used to investigate the categorical variables. A p-value of <0.01 was considered statistically significant.

## RESULTS

Our study included a total of 30 patients, 16 with CD diagnosis and 14 non-celiac patients diagnosed with non-specific chronic duodenitis. The study participants were classified as the study group consisting of 16 CD patients and the control group composed of 14 non-celiac patients diagnosed with chronic duodenitis. CD and non-CD patients consist of groups with similar age distributions.

As a result of the examination of all cases under the light microscope, strong and remarkable IgE staining was not detected in any case. Sparsely dispersed IgE-containing mast cells were detected in some cases in both groups. Sparse IgE antibody was detected in 5/16 (31%) of the celiac patients, while it was detected in 4/14 (24%) patients in the control group (Table). In these 9 positive cases containing IgE-positive mast cells, IgE was very weakly and sparsely stained. No stained cells were found in the other 21 cases. No statistically significant difference was found between the two groups. (p>0,05) (**Table**).

**Table: Patients' IgE containing results of duodenum biopsies, ages, and blood eosinophil counts**

| Patient group | Ig E positive cell | Age | Blood eosinophil count |
|---|---|---|---|
| CD | No | 34 | 0.01x $10^3$ /µl |
| CD | No | 54 | 0.06 x $10^3$ /µl |
| CD | Yes | 45 | 0.05 x $10^3$ /µl |
| CD | No | 23 | 0.15 x $10^3$ /µl |
| CD | Yes | 31 | 0.15 x $10^3$ /µl |
| CD | No | 46 | 0.02 x $10^3$ /µl |
| CD | No | 22 | 0.08 x $10^3$ /µl |
| CD | No | 34 | 0.12 x $10^3$ /µl |
| CD | Yes | 26 | 0.24 x $10^3$ /µl |
| CD | No | 41 | 0.21 x $10^3$ /µl |
| CD | No | 25 | 0.12 x $10^3$ /µl |
| CD | Yes | 20 | 0.08 x $10^3$ /µl |
| CD | Yes | 27 | 0.22 x $10^3$ /µl |
| CD | No | 55 | 0.16 x $10^3$ /µl |
| CD | No | 23 | 0.16 x $10^3$ /µl |
| CD | No | 40 | 0.1 x $10^3$ /µl |
| Control | No | 48 | 0.14 x $10^3$ /µl |
| Control | No | 54 | 0.24 x $10^3$ /µl |
| Control | No | 37 | 0.25 x $10^3$ /µl |
| Control | No | 24 | 0.17 x $10^3$ /µl |
| Control | Yes | 37 | 0.07 x $10^3$ /µl |
| Control | No | 35 | 0.07 x $10^3$ /µl |
| Control | No | 38 | 0.08 x $10^3$ /µl |
| Control | No | 37 | 0.18 x $10^3$ /µl |
| Control | No | 38 | 0.07 x $10^3$ /µl |
| Control | Yes | 38 | 0.08 x $10^3$ /µl |
| Control | No | 59 | 0.04 x $10^3$ /µl |
| Control | Yes | 36 | 0.02 x $10^3$ /µl |
| Control | Yes | 51 | 0.13 x $10^3$ /µl |
| Control | No | 59 | 0.15 x $10^3$ /µl |

(CD: Celiac disease)

The normal range for blood eosinophil count is 0-0.5x 103 /µl and in the two groups, no patients have eosinophilia and no difference between the two groups' blood eosinophilic count (p>0,05).

## DISCUSSION

Nowadays, various studies have investigated the association between CD and IgE-related allergic diseases (7-9). In our study, the fact that no difference was determined between the two groups by examining the

IgE in the duodenum biopsies of initial CD and non-celiac patients' duodenum biopsies yielded results never studied before.

Given the findings related to IgE antibodies in the tissues, there are studies in the literature evaluating only food allergies in the duodenum (6,13-15) As a result of such studies, the detection of IgE in the duodenum tissue was found to be highly predictive and sensitive in detecting food allergies (15). Therefore, the IgE we detected in the duodenum of celiac patients would be significant in terms of food allergy.

In addition to not finding a significant difference between the CD and control groups in our results, we did not detect any significant and remarkable IgE staining in any of the CD and non-CD cases. In a small number of cases where staining was observed, expression was detected in very rare cells. According to our results, no relationship with other food allergies was detected, at least in the initial stage of adult CD.

In the literature, the relationship between CD and IgE-related allergies has been predicted in some studies, but in our study, no difference was found compared to the control group (11). Majsiak et al. say that; the elimination of wheat from the diet of patients with CD may lead to a loss of immune tolerance and to the development of sensitization, which may even manifest as anaphylaxis (11). In all the cases in our study, duodenal biopsy samples were taken from patients at the first diagnosis stage who were not yet on a gluten diet. In our study, no patients had started a gluten-free diet, this may be the reason why we couldn't find any difference.

We included blood eosinophil counts in our study to confirm the absence of another disease that could cause eosinophilia and IgE elevation in both groups.

The limitation of our study is that celiac patients who followed a gluten-free diet and child patients were not included in our study.

## CONCLUSION

According to the results of our study, no increase in IgE was detected in the duodenum samples of newly diagnosed celiac patients compared to the duodenum samples of the control group. However, to reach definitive results for the relationship between CD and food allergy, need for a wide series of studies that include gluten-free diet patients and child patients.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Ethical Committe of Faculty of KTO Karatay University (Date:25.12.2020, Decision No: 2021-006).

**Informed Consent:** Informed consent form did not obtained from the participants due to the nature of the study.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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