

Prevalence of celiac disease among dyspeptic patients: A community-based case-control study

Dispepsili hastalarda çölyak hastalık serolojisi: Toplum temelli vaka-kontrol çalışması

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Background/aims: To determine the relation between undiagnosed celiac disease and dyspepsia in the community. **Methods:** Patients presenting to the gastroenterology outpatient clinic of Mersin University Hospital, aged between 18 and 70 years and with no malignancy, malabsorption, chronic diarrhea, inflammatory bowel disease, diabetes mellitus, heart failure or renal failure, were asked to complete a questionnaire for functional bowel disease (based on Rome II criteria for irritable bowel syndrome and dyspepsia). The patients diagnosed with dyspepsia based on Rome II criteria formed the dyspepsia group and those with gastrointestinal complaints other than dyspepsia and irritable bowel syndrome formed the control group. Serum tissue transglutaminase antibody (anti-tTG) was determined in all patients. The patients with anti-tTG levels of >20U/ml underwent endoscopic duodenal biopsy. **Results:** The study included a total of 137 patients, of whom 69 (50.4%) were assigned into the dyspepsia group and 68 (49.6%) into the control group. Of 137 patients, 24 (17.5%) had an anti-tTG level of ≥20U/ml: 14 in the dyspepsia group (20.3%) and 10 in the control group (14.7%), with no significant difference between the groups (p=0.39). Of the 24 patients positive for anti-tTG, 15 (64.5%) underwent endoscopy, and of these 15 patients, 8 (53.3%) had endoscopic duodenal biopsy. Biopsy revealed that of the 4 patients in the dyspepsia group, 3 (75%) had Marsh type 0 histology (IEL<40, normal crypt) and 1 (25%) had Marsh type 3a histology. Of the 4 patients in the control group, 3 (75%) had Marsh type 0 histology and 1 (25%) had Marsh type 3a histology. Histopathological examinations showed celiac disease in 2 out of the 8 patients (25%) positive for anti-tTG who underwent biopsy. Intention to treat analyses revealed that 1 of 69 patients in the dyspepsia group (1.44%) and 1 of 68 patients in the control group (1.47%) had celiac disease. **Conclusions:** Celiac disease in this patient population had a high prevalence. Further studies with larger sample sizes are needed to confirm the relation between dyspepsia and celiac disease.

Key words: Celiac disease, tissue transglutaminase antibody, dyspepsia

INTRODUCTION

Celiac disease is an immune-mediated enteropathy involving intolerance to gluten, exacerbated by wheat, barley and rye and occurring in geneti-

Amaç: Toplumda tanı konulmamış çölyak hastalığının dispepsi ile ilişkisini saptamak. **Yöntem:** Hastanemiz gastroenteroloji polikliniğine başvuran malignitesi, malabsorpsiyonu, kronik diyarezi, inflamatuvar barsak hastalığı, diyabetes mellitusu, kalb yetmezliği ve böbrek yetmezliği olmayan 18-70 yaş arası hastalara fonksiyonel barsak hastalığı ile ilgili anket (Roma II İrritabl Barsak Sendromu ve dispepsi sorgulaması) yapıldı. Roma II ölçütleri ile dispepsi tanısı alan hastalar dispepsi grubunu, dispepsi ile İrritabl Barsak Sendromu dışı diğer gastrointestinal yakınmaları olan hastalar kontrol grubunu oluşturdu. Çalışmaya alınan her hastanın serum doku transglutaminaz antikor (antiTTg) düzeyi ölçüldü. Serum antiTTg düzeyi pozitif (>20U/ml) saptanan hastalar endoskopik duodenal biyopsi için yönlendirildi. **Bulgular:** Toplam 137 hasta çalışmaya alındı. Çalışmaya alınan hastalardan 69'u (%50.4) dispepsi grubu, 68'i (%49.6) kontrol grubu olarak ayrıldı. Serum antiTTg düzeyi 137 hastanın 24'ünde (%17.5) >20 U/ml üzerinde saptandı. Dispepsi grubunda 69 hastanın 14'ünde (%20.3), kontrol grubunda 68 hastanın 10'unda (%14.7) serum antiTTg düzeyleri >20 U/ml olarak saptandı. Dispepsi grubunda antiTTg yüksekliği fazla olmasına karşın istatistiksel olarak anlamlı değildi (p= 0.39). AntiTTg pozitifliği saptanan 24 hastanın 15'ine (%62.5) endoskopi, 15 hastanın 8'ine endoskopik duodenal biyopsi (%53.3) yapıldı. Biyopsi raporu sonucu dispepsi grubunda 4 hastanın 3'ünde (% 75) Marsh tip 0 (IEL <40, kript normal), 1'inde (%25) Marsh tip 3a, kontrol grubunda yine 4 hastanın 3'ünde (%75) Marsh tip 0, 1'inde (%25) Marsh tip 3a olarak raporlandı (p=1). AntiTTg (+) olan ve duodenal biyopsi yapılan 8 hastanın 2'sinde (%25) histopatolojik olarak çölyak hastalığı saptandı. [ITT'e göre çölyak sıklığı dispepsi grubunda 1/69 (%1.44) ve kontrol grubunda 1/68 (%1.47)]. **Sonuçlar:** Bu çalışma grubundaki hastalarda çölyak hastalığı sıklığı %1.4 gibi yüksek oranda olmakla birlikte dispepsi ile çölyak hastalığı arasındaki belirgin bir ilişki saptanmadı.

Anahtar kelimeler: Çölyak hastalığı, doku transglutaminaz antikor, dispepsi

cally susceptible people. The prevalence of the disease has been reported to increase 10-fold in a North American community in the past 50 years

(1). Recent screening studies have revealed that the frequency of celiac disease is 1% in various populations (2-6). It is known that celiac disease may have such atypical forms as functional dyspepsia and irritable bowel syndrome apart from conventional symptoms such as anemia, diarrhea and weight loss (7, 8). It has been reported that about 20-40% of the patients diagnosed with celiac disease have dyspepsia (9). Functional bowel diseases are quite frequent and cause symptoms related to the upper and lower gastrointestinal system that may not be explained completely. Due to atypical symptoms, celiac disease may be overlooked, especially in patients with dyspepsia and irritable bowel syndrome (10, 11). There have been several studies to determine the frequency of celiac disease among patients with irritable bowel syndrome and to show the need for serological screenings for celiac disease. Therefore, we aimed to determine the prevalence of celiac disease in patients with gastrointestinal complaints other than dyspepsia and irritable bowel syndrome.

MATERIALS AND METHODS

The study included a total of 137 patients aged between 18 and 70 years and presenting to the gastroenterology outpatient clinic of Mersin University Hospital between January 2004 and December 2004. Exclusion criteria were malignancy, malabsorption, chronic diarrhea, inflammatory bowel disease, diabetes mellitus, heart failure and renal failure. All patients completed a questionnaire for functional bowel disease (based on Rome II criteria for irritable bowel syndrome and dyspepsia).

The patients diagnosed with dyspepsia based on Rome II criteria were assigned into the dyspepsia group and those with gastrointestinal complaints other than dyspepsia and irritable bowel syndrome were assigned into the control group. Serum tissue transglutaminase antibody (anti-tTG) levels were determined in all patients. Anti-tTG levels were measured with commercial kits (INOVA Diagnostics, Inc., San Diego, CA). The patients found to be positive for anti-tTG antibodies underwent endoscopic duodenal biopsy. One biopsy specimen was obtained from the second half of the duodenum and three biopsy specimens from other parts of the duodenum. Histopathological features were evaluated according to Marsh classification (13).

Statistical Analyses

The confidence interval for the rates of positive and negative tTg titers was 95%. Student's t test was used to determine the distribution of the patients by age, chi-square test to determine the significance level of anti-tTG positivity between the two groups, and Pearson correlation test to determine the relation between anti-tTG titers and age. $P < 0.05$ was considered significant. Statistical analyses were made with SPSS for Windows (Version 10.0).

Intention to treat analyses were made to evaluate the rates of the patients diagnosed with celiac disease based on the histopathological features of the disease determined according to Marsh classification (14, 15).

RESULTS

This study included a total of 137 patients, with a mean age of 39 years (range: 18-70 years). Of the 137 patients, 103 (75.2%) were female and 34 (24.8%) were male. Sixty-nine patients (50.4%) (48F [69.6%], 21M [30.4%]) were assigned into the dyspepsia group and 68 patients (49.6%) (55F [80.1%], 13M [19.1%]) into the control group. There was no significant difference in age between the groups. Fourteen patients in the dyspepsia group (20.3%) and 10 patients in control group (14.7%) had a serum anti-tTG level of ≥ 20 U/ml, with no significant difference ($p=0.39$). There was no significant relation between age and anti-tTG positivity ($p > 0.05$). As age increased, anti-tTG levels slightly and insignificantly increased ($p=0.015$). Out of 24 patients found to be positive for anti-tTG, 15 (62.5%) had endoscopy and of those 15, 8 had endoscopic duodenal biopsy (53.3%). On endoscopy, the duodenum was normal in 7 dyspeptic patients and 1 dyspeptic patient had hyperemia. In the control group, the duodenum was normal in 2 patients, 3 patients had hyperemia and edema and 2 patients had scalloping. Of all patients who underwent endoscopy, 4 patients in the dyspepsia group and 4 patients in the control group had biopsy. According to Marsh classification, histological features were Marsh type 0 (IEL $<$ 40, normal crypt) in 3 dyspeptic patients (75%) and Marsh type 3a in 1 dyspeptic patient (25%). In the control group, histological features were Marsh type 0 in 3 patients (75%) and Marsh type 3a in 1 patient (25%). Intention to treat analyses revealed that the frequency of celiac disease was 1/69 (1.45%) in the dyspepsia group and 1/68 (1.47%) in the control group (Table 1).

Table 1. Demographic features, serological results, endoscopic findings and results of endoscopic biopsy

	Dyspepsia Group	Control Group
Number of patients (n)	69	68
Gender		
Female	48	55
Male	21	13
Anti tTg (+)	14	10
Features of the duodenum on endoscopy	8	7
Scalloping in the second half of the duodenum	1	1
Hyperemic	1	3
Normal	6	3
Number of patients who underwent endoscopic biopsy	4	4
Results of endoscopic biopsy		
Marsh type 0	3	3
Marsh type 3a	1	1

DISCUSSION

We attempted to determine the frequency of celiac disease in patients with dyspepsia and those with non-specific gastrointestinal complaints and the need for serological screening. The frequency of dyspepsia was quite high. Serological tests help to diagnose celiac disease, but the gold standard for a firm diagnosis of the disease is to obtain multiple biopsy specimens from the distal part of the duodenum (16). Duodenal appearance on endoscopy is very important in the diagnosis of celiac disease. It has been reported that villous atrophy on endoscopy is 82%-100% specific for celiac disease (17-19). It is difficult and expensive to perform endoscopy routinely to diagnose celiac disease. The sensitivity and specificity of the anti-tTG test were 91% and 96%, respectively, in patients diagnosed with celiac disease (20). However, the positive predictive value of the anti-tTG test is 30-35% in population screenings (21). It has been reported that the frequency of celiac disease in people with dyspeptic complaints is 0.5-8%, which is two to nine times higher than in the normal population (8, 22-25). In this study, we first performed serologi-

cal tests in patients with dyspeptic complaints and then carried out endoscopy when the serological tests were positive for celiac disease. Consistent with the results of the present study, Lima et al. (26) found that serological tests were positive for celiac disease in 17% of the patients, but they reported that biopsy confirmed the diagnosis of the disease in 1.4% of those patients. In this study, anti-tTG was positive in 20.3% of the patients with dyspepsia and endoscopic biopsy showed celiac disease in 1.45% of the patients. In the control group, anti-tTG was positive in 14.7% of the patients and endoscopy showed celiac disease in 1.47% of the patients. There was no significant difference in the frequency of celiac disease between the groups. It has been reported that the prevalence of asymptomatic celiac disease is 0.7-1% in the Turkish population (4-27-28). We found that the prevalence of celiac disease, the diagnosis of which was confirmed on endoscopy, increased two-fold compared to the normal population. However, further studies with larger sample sizes are needed to establish the relation between celiac disease and dyspepsia.

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