

## The prevalence of celiac disease in healthy school children in Van City, east of Turkey: a screening study using a rapid test

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### Abstract

**Objective:** Celiac disease is seen by increasing rates in the whole world. It may have a silent course besides having classical symptoms. It may result in serious complications if the diagnosis is delayed such as anemia, fatigue, vitamin K deficiency, excessive bruising and bleeding. The aim of this study is to detect celiac patients who have not been diagnosed yet in healthy school children.

**Materials and Methods:** Present study performed was in 1003 school children who are between 5-18 years old in Van city, east of Turkey. Celiac disease was investigated via rapid celiac testing (Biocard<sup>TM</sup> stick test).

**Results:** Percentages of the cases, 51.2% were female and 48.8% male. Test was positive in two (0.2%) patients. Ten (1%) patients had immunoglobulin A deficiency. In addition to these patients, one patient had been diagnosed as celiac disease beforehand.

**Conclusion:** The prevalence of celiac disease in Van city, east of Turkey in our study, shows a lower prevalence than in study which performed in our country previously

**Keywords:** Celiac disease, children, prevalence, rapid test

### Introduction

As European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) defined, celiac disease (CD) is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations, CD-specific antibodies, HLA-DQ2 or HLA-DQ8 haplotypes, and enteropathy (1). CD is a permanent sensitivity to gluten, resulting in a disorder of inflammatory enteropathy with various degrees of severity, and a wide range of gastrointestinal and extraintestinal problems (2).

Different clinical classification of CD has been made: the typical, atypical, silent, potential, and latent. Today, the number of applicants with typical gastrointestinal symptoms is decreasing compared to atypical ones. The term "silent CD" is used for patients with positive serology, HLA-DQ2/DQ8 and histopathology, but without any suggestive clinic for CD. Latent CD has been defined for patients with HLA-DQ2/DQ8 positivity, without enteropathy, but had enteropathy for a particular time of the life either before or after. These patients may have or not positive CD antibody serology or symptoms and signs.

The potential CD explains patients without histopathology despite the presence of positive CD antibody serology and HLA-DQ2/DQ8. These patients may or may not have symptoms and may or may not develop CD in the future. Today, patients with a diagnosis of CD are actually the tip of the iceberg above the water (2,3).

In our study, recognition of the patients remaining silent as well as determining CD prevalence in school-age children in Van city which is located at the eastern Turkey have been aimed by CD screening in school-age children considered to be healthy.

### Material and Methods

**Study group:** The study was planned to be conducted on a total of 1000 patients among the school-age children in Van city aged between 5 and 18. Van City Directorate of National Education was applied to carry out the study in schools. Quick celiac tests were conducted at the designated schools by two doctors and two allied health personnel. Patients with positive test results were invited to pediatric gastroenterology clinic in our hospital and for conventional serum anti-tTG IgA antibody study and it was palled to confirm the diagnosis by duodenal biopsy.

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## Description of Biocard testing

For CD screening study used a rapid and easy immunoglobulin A-class whole blood point-of-care test (Biocard™, Ani Biotech, Finland) which measure to immunoglobulin (Ig) A tissue transglutaminase (TTG) antibodies (anti-tTG) and total IgA according to instructions for use. One drop capillary blood, obtained by performing a finger prick with a sterile lancet, is mixed with the reagent solution in a capillary tube. Three drops of this mixture were applied to the test stick having two separate fields, test and control ones. Anti-tTG IgA antibodies bind to antigen in the test strip to form a visible line and provide results within 10 minutes. Two lines in both field indicate positive result for CD, one line in only control field negative result. If there is no line, IgA deficiency should be suspected.

## Ethical approval and funding

Ethical permission was taken from Yuzuncu Yil University, Faculty of Medicine, Clinical Research Ethics Committee (Approval number: 05.12.2013/01). This work was supported by Research Fund of the Yuzuncu Yil University (Project Number: 2014-TF-B161).

## Results

1003 patients including 51.2% female and 48.8% male were included in the study. The age and gender distribution of the children who participated in the study are presented in Table 1. According to test results, positivity for CD was detected in two children (0.2%). IgA deficiency was detected in ten (1%) patients. One patient was previously diagnosed with CD. The patients whose tests were verified positive did not apply to the hospital despite being invited for the test verification and if necessary for duodenal biopsy. If the patient pre-diagnosed with CD is included, test positivity was detected at the rate of 0.3%.

**Table 1.** Distribution of study group (n=1003) according their ages and genders.

Age Year	Gender		Rapid test positivity	IgA deficiency
	Girl	Boy		
5	31	38	-	-
6	76	76	-	1
7	123	126	1	1
8	85	100	-	3
9	46	40	1	1
14	34	18	-	-
15	17	29	-	1
16	44	26	1	2
17	43	30	-	1
18	15	6	-	-
<b>Total</b>	<b>514</b>	<b>489</b>	<b>3</b>	<b>10</b>

## Discussion

The incidence and diagnosing of CD have increased with the development and widely use of serologic tests with high sensitivity and specificity. With serological screening tests, prevalence was determined as 1:105 in the United States, 1:100 in the UK, 1:77 in Sweden, 1:133 in Russia, 1:251 in Australia, 1:157 in Israel, 1:166 in Iran and 1:310 in India (4). In our country, in the study with the broad participation conducted in healthy school children, CD prevalence proved with biopsy was determined 1:212. On including the patients with high serological antibody titer positivity that cannot be biopsied and the previously diagnosed with CD, prevalence of CD has reached a value of 1:58 that indicates that it is fairly common in our country (5). CD is seen in all the world in varying rates but increasing incidences. In an earlier study conducted in our country, a small number of participation was from the province of Van city. In our study, we aimed to determine the prevalence in Van city. Test positivity for CD have been found at the rate of 0.2% in 1003 children. On including the previously diagnosed child, this value would be 0.3%. These values are considered as lower than expected. Both patients with test positivity did not come to the hospital in spite of being invited for performing verification and duodenal biopsy.

In our study, unlike previous studies in our country, rapid celiac test has been used instead the conventional method. Rapid celiac tests have been widely used in the world because of ease of application outside the hospital and getting quick results. However, there are studies indicating relatively low sensitivity. Serum anti-TTG IgA antibody studied by conventional method have a sensitivity of 96.4%, specificity of 97.7 (6). Biocard testing detects anti-TTG in capillary whole blood rapidly.

Mooney et al., in their study (7), investigated Biocard test and deaminated gliadin peptide antibodies (DGP) in 55 patients with positivity for endomysial antibody (EMA) and determined sensitivity 72.2% in Biocard test, and 94.4% in DGP test. Singh et al., in their study (8), conducted conventional anti-TTG and Biocard test with duodenal biopsy in 319 children suspected with CD, and determined sensitivity/specificity 93.8%/96.4% for conventional anti-TTG, and 83.6%/90% for Biocard test. Mooney et al., in another study (9) assessed Biocard rapid test, serum anti-TTG, EMA, and upper GI endoscopy with duodenal biopsies at the same visit in 523 patients had no prior diagnosis of CD, and 53 patients had known CD coming for reassessment. Sensitivity, specificity, positive predictive value, and negative predictive value of Biocard test were 70.1%, 96.6%, 85.4%, and 91.8%, respectively, sensitivity and specificity of TTG were 91.0% and 83.5%, respectively, and EMA were

83.8% and 97.5%, respectively. In comparison, they indicated that anti-TTG and EMA both performed significantly better than the rapid test, and proposed that the performance of rapid test was disappointing compared with standard serology and cannot at present be recommended within the context of an endoscopy unit. Korponay-Szabó et al. (10) scanned 2690 patients in primary care with rapid test. They found that rapid testing had a 78.1% sensitivity and 100% specificity for a final diagnosis of CD by biopsy, while sensitivity was 65.1% and specificity was 100% compared with combined results of IgA and IgG laboratory tests. According to these studies, it can be considered that rapid test has low sensitivity but high specificity.

Pichler et al., in their study (11), have applied Biocard test in 196 first and second degree relatives of CD patients and have found positivity in 3 patients. These 3 patients were later confirmed by serology and histology. Doğan et al., in their study (12), analyzed anti-TGG in 195 first-degree relatives of CD patients with conventional method, and detected a high level of positivity at the rate of 9.5%. Popp et al. (13) have detected positivity at the rate of 8% with Biocard test in first-degree relatives of CD patients. Oliveira et al. (14) detected Biocard test positivity at the rate of 4.5% in 268 first-degree relatives of children with CD, and diagnosed CD with histology at the rate of 2.6%.

Korkut et al. (15) have detected positivity in 2 of 100 patients with Biocard test in their study where they investigated prevalence of CD in adult patients fulfilling the Rome III criteria for irritable bowel syndrome. Kansu et al. (16) have investigated CD with Biocard test in 1047 children with abdominal pain-associated functional gastrointestinal system disorders, have found positivity in 13 patients and confirmed the diagnosis of CD in 10 of them.

Alarm et al. (17) have made a screening with a rapid test in Libyan Children, and have found positivity in 50 out of 2920 (1.7%). 20/50 have been confirmed by the ELISA determination. Biopsy-confirmed CD diagnosis was confirmed in 19 out of these 20. In addition, they found that serum ELISA anti-TTG IgA antibody was positive in 4 out of 800 rapid test negative children. CD prevalence was 0.79-1.13%. Karakoyun et al. (18) have found positivity in 4 out of 502 students of the department of nutrition and dietetics and medical school for CD screening with Biocard testing and confirmed the diagnosis with biopsy. IgA deficiency had not been detected on any of them. In our study, IgA deficiency was a ratio of 1%.

### Conclusion

As a result, in our study, CD prevalence was found to be 0.3% in school-age children considered to be healthy (if the patient previously diagnosed with CD is

included and if they were also proven by biopsy). This value is lower than expected. Biocard test's having a high specificity as seen in previous studies and low sensitivity is considered to contribute to this value being lower. The number of the test methods used for the diagnosis of CD is increasing. There is a need for the studies investigating the correlation of these methods with each other.

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