Frequency of Serological Tests Positive Findings for Celiac Disease at the First Relative of Children with Celiac Disease

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Goal: The research was undertaken with the aim to determine the frequency of positive findings of serological tests for celiac disease of the first relatives of children with celiac disease. Materials and methods: The study included 175 first relatives of 68 children suffering from celiac disease. Of that number, 75 (40 mothers and 26 fathers), 4 sisters and five brothers agreed to be tested for the presence of antibodies to celiac disease. For each subject were done tests on presence of anti-gliadin IgA, IgG anti-gliadin antibodies and IgA antibodies on tissue transglutaminase in the Polyclinic for Laboratory Diagnostics - Institute for Microbiology-Department of Immunology, University Clinical Centre (UCC) Tuzla. Results: Of 175 first relatives of children with celiac disease 75 consented to serologic screening. Positive anti-gliadin IgG antibodies had 13.3%; anti-gliadin IgA antibodies had 2.6%, whereas antibodies on tissue transglutaminase were positive in 7.5% of respondents. With positive findings of anti-gliadin IgG were only two brothers. Fifteen subjects with positive findings of serological tests for celiac disease were confirmed by diagnosis of small bowel mucosal biopsy in 4%. Conclusion: In our study the incidence of positive serological tests for celiac disease among first relatives of children with celiac disease was 20%. All of our respondents with positive antibody findings had no symptoms that could indicate celiac disease. After establishing the diagnosis of celiac disease in children, it should be mentioned that testing must be done with the first relatives. This would, along with further diagnostic testing discover a significant number of asymptomatic patients and atypical forms of celiac disease. Key words: Celiac disease, high risk groups, screening.

1. INTRODUCTION
Celiac disease - gluten enteropathy is a chronic disease, predominantly of proximal intestine, which occurs due to inadequate immune reaction in contact with gluten in genetically predisposed individuals. Its essential features are: permanent intolerance of gluten, a different degree of damage (morphological and functional) lining the small intestine and a diverse array of clinical symptoms, of which not all the consequences of malabsorption. Removing gluten from food leads to the disappearance of histological and clinical signs of disease, and its re-introduction is causing recurrent intestinal histological changes, while the clinical symptoms may be absent. The disease occurs in children and adults, but the “classic” clinical disease is more common in the first years of life (1).
opsy of the small intestine, was analyzed the five major studies in England during the 1970’s and ranged from 5.5% to 22.5% (7, 8, 9). Serological screening for celiac disease performed on the first relatives, in various studies showed a high prevalence of 12% (10, 11), while biopsy confirmed celiac disease ranged from 5.5% to 10% (12, 13, 14). Large multi-center study conducted in America (since February 1996 until May 2001), using serological tests and a biopsy of the small intestine, showed the prevalence of celiac disease of 1:56 in patients with symptoms, 1:22 in the group of first relatives, 1:39 in second line relatives, while the prevalence of the risk-free, the control group was 1:133 (15).

At the time of establishing the diagnosis, anti-gliadin IgA antibodies (AGA IgA) and anti-gliadin IgG antibodies (AGA IgG) were present in most patients with celiac disease. The clinical studies demonstrated the specificity for IgA-class AGA of 97% and sensitivity of 71% and for AGA IgG class showed specificity of 91% and sensitivity of 87% (16).

In 1997 Dietrich et al. found gluten epitopes (tTG) as auto antigens for antibodies anti-endomisial and recommended them for clinical use, because they shows higher sensitivity of 90%, and the high specificity of 95%, with small variations in utilization of various tests (17). Diagnostic significance of determining the titer of antibodies to tTG was noted in a study by Hill and Holmes, where they recorded 100% predictive accuracy of serological tests in people with celiac disease. Results obtained in this study significantly altered attitude on biopsy of the small intestine mucosa as a “gold standard” for definitive diagnosis of celiac disease (18). This is confirmed by experience using serological tests by Colina et al. (2005), who founded the diagnostic algorithm for the diagnosis of celiac disease using serological tests (19).

People with untreated celiac disease are more prone to develop non-malignant and malignant complications. Recent studies suggest that people with celiac disease have twice the mortality than other healthy populations, especially in the first three years of diagnosis (20).

The study was undertaken with the aim of the first relatives of children with celiac disease determines the frequency of positive findings of serological tests for celiac disease.

### 2. MATERIALS AND METHODS

The study includes 175 first degree relatives of 68 children suffering from celiac disease. Of that number, with the prior written and oral explanation of the diagnosis of celiac disease, 112 relatives of 344 first degree relatives who agreed to be tested 1 Anti-gliadin antibodies IgA, 2 Anti-gliadin antibodies IgG, 3 Antibodies and tissue transglutaminase IgA.

The frequency of positive results of serological tests for diagnosis of celiac disease in first relatives who agreed to be tested 1 Anti-gliadin antibodies IgA, 2 Anti-gliadin antibodies IgG, 3 Antibodies and tissue transglutaminase IgA.

<table>
<thead>
<tr>
<th>Table 1. Frequency of positive results of serological tests for diagnosis of celiac disease in first relatives who agreed to be tested</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Father (n = 26)</td>
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<tr>
<td>Mother (n = 40)</td>
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<tr>
<td>Brother (n = 5)</td>
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<td>Sister (n = 4)</td>
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</table>

The research results are presented in absolute and relative numbers.

### 3. RESULTS

Positive AGA IgA antibodies had two mothers, whereas IgG AGA was positive in seven mothers, one father and two brothers. Detection of IgA antibodies to tTG was positive in three mothers. On biopsy of the small intestine mucosa of fifteen subjects with positive serological tests agreed three relatives and for them on the basis of a positive pathohistological findings confirmed the diagnosis of celiac disease.

The total serum IgA tests were done only in four subjects with non-determined innate selective IgA deficiency. For other subjects total serum IgA was not made.

### 4. DISCUSSION

In our first study of 175 relatives of children with celiac disease 75 agreed to serologic screening. A positive IgG AGA had 13.3%, AGA IgA 2.6%, whereas antibodies to tTG were positive in three mothers, or 7.5% of respondents. With positive findings AGA IgG were only two brothers. Fifteen subjects with positive findings of some of the serological tests for celiac disease diagnosis are biopsy of the small intestine mucosa was confirmed in 4%.

According to latest figures from 2008 obtained by the research in the USA by Rubio-Tapia et al. among the first degree relatives of children with celiac disease was reported 11% prevalence of celiac disease. Of the total number of 344 first degree relatives who agreed to testing, positive anti-tTG antibodies had 14% of respondents, while the diagnosis of celiac disease by the biopsy of the small intestine mucosa was set in 11% of respondents (21). The importance of screening...
for celiac disease among relatives of children with celiac disease, are confirmed by the results of studies made in Slovenia by Dolinske et al. (2004) where was noted that from a total of 106 first degree relatives had positive 5.7% of all antibodies to celiac disease, one parent was positive only for IgA EMA antibodies, while 8.5% had positive AGA IgA antibodies (22). These results partially agree with the results obtained in our study, especially if we take into account the relationship between the percentage of our respondents with positive findings of some of the antibodies and the number of relatives who agreed to confirm the diagnosis by small intestine mucosal biopsy. In a study by Sunad et al. 2007 from 183 relatives (154 first and 29 second degree), it was noted that a total of 32 had positive findings, at one of the serological tests, while in 13.1% of respondents by the small intestine mucosal biopsy was diagnosed celiac disease (23).

In our study there was a first degree relative at the age of 8 years who had a negative finding of celiac disease antibodies in the first test. After three years after was made the first test of this boy, because maintained in addition to anemia and iron preparations was repeated serologic screening and seroversion was recorded with the presence of a high titer of antibodies to tissue transglutaminase. This confirms that once tested first degree relatives with negative serological tests due to seroversion and development opportunities for celiac disease in the future must be subjected to serological screening for celiac disease every 2-3 years (24, 25). There were two subjects with positive findings to some of the antibodies for celiac disease who have not agreed to biopsy of the small intestine, but they agreed to undergo gluten free diet. In these subjects there was a significant improvement of health status. So one mother after years of treatment of secondary sterility became pregnant. Mother in which the biopsy of the small bowel confirmed the diagnosis of celiac disease, which did not adhere to strict gluten free diet, she had epilepsy resistant to antiepileptic drugs followed by most of the various forms of mental disturbance.

In our study there was a significant response of parents of children with celiac disease on serological screening, especially if we take into account that a large number of children in the period covered by our research were older than age for treatment at the clinic for child diseases. In support of an important response of parents to be tested for antibodies to celiac disease is the fact that during the hospitalization and gastroenterology specialist monitoring on several occasions conducted educational discussions about the importance of this disease and the frequency of its occurrence among first degree relatives.

4.1. Limitations of the research

In our study only in four parents besides tests on antibodies specific for celiac disease were made the test of total serum IgA antibodies. Because of the possibility of innate selective IgA immunodeficiency that is associated with celiac disease (26) there is some probability that the certain number of relatives had false-negative finding of antibodies for celiac disease.

5. CONCLUSION

The frequency of positive serological tests for celiac disease among first relatives of children with celiac disease was 20%. All of our respondents with positive antibody findings had no symptoms that could indicate celiac disease. Given the fact that today the serologic tests for celiac disease are commercially available, relatively cheap, that their use is simple and that they have high specificity and sensitivity in diagnosing celiac disease, after establishing the diagnosis of celiac disease in children, it should be mentioned that testing must be done with first degree relatives. In this way, with further diagnostic testing a significant number of patients with asymptomatic forms of celiac disease would be detected, and thus prevented the appearance of possible complications of untreated disease.

REFERENCES