Original Article

The Diagnostic Value of Serum IgG-Antigliadin, IgA Anti-endomysial and IgA Anti-tissue Transglutaminase Antibodies for Pediatric Celiac Disease

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ABSTRACT

Background and Objective: **Celiac disease is an autoimmune disorder, characterized by inflammation, villous atrophy, and crypt hyperplasia of the small bowel mucosa. In this study we considered and compared sensitivity and specificity of serological tests in patients with celiac disease.**

Materials and Methods: **In this cross-sectional study we prospectively recruited children with suspected celiac disease. An intestinal biopsy specimen was obtained from all patients. Celiac disease diagnosed on the basis of histologic findings of Marsh classification. A serum sample was taken at the time of biopsy for serologic tests. Findings were analyzed using SPSS program, t-test, and chi-square tests.**

Results: **Out of a total of 134 children in this study, seventy (52.21%) patients were boy and sixty four (47.8%) patients were girl. Celiac disease was diagnosed in 14 (10.4%) of the patients. In serologic tests, 11 patients (78.6%) were positive for antigliadin-Ab, 4 (28.6%) for anti tissue-transglutaminase Ab, and 9 (64.3%) for antiendomysial antibody. Sensitivity of antigliadin-Ab was 78.6% and its specificity was 95.9%. Sensitivity of anti tissue-transglutaminase Ab was 28% and its specificity was 95%. Sensitivity of antiendomysial Ab was 64% and its specificity was 96%.**

Conclusion: **Positive serologic tests are supportive of the diagnosis in those with characteristic histopathologic changes on small intestinal biopsy. The best tests for this purpose are the IgA antiendomysial antibody or IgA anti tissue-transglutaminase, both of which are highly sensitive and specific.**

Key words: Celiac Disease, Gliadin, Transglutaminases, Antibodies

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Introduction

Celiac disease or gluten-sensitive enteropathy is an autoimmune disorder characterized by inflammation, villous atrophy, and crypt hyperplasia of the small bowel mucosa. The mucosal lesion develops in genetically susceptible individuals after ingestion of dietary gluten and recovers when gluten-containing cereals, wheat, rye, and barley are withdrawn from the diet (1). The disease should be detected as early as possible, because untreated celiac disease is associated with many severe complications such as intestinal lymphoma or cancer and osteoporesis (1-2). In untreated celiac disease, the characteristic abnormalities in the small bowel mucosa are villous atrophy, crypt hyperplasia, and an increased density of inflammatory cells in the epithelium and lamina propria. This type of lesion is nowadays uncommon in other conditions (3). The mucosal lesion recovers with a gluten-free diet and deteriorates further if the patient resumes a gluten-containing diet (1). The occurrence of circulating antibodies against gliadin or intestinal matrix further supports a diagnosis of celiac disease.

Various antibody assays have been developed to select patients for diagnostic small-bowel biopsy. Anti-reticulin and anti-gliadin antibodies (AGA) were the first tests to be employed in screening, the latter still being widely in use. In the context of celiac screening in asymptomatic patients and in various risk groups, however, the benefits of the more recent IgA class anti-endomysial antibody test (EMA-Ab) and the latest anti tissue-transglutaminase test (TTG-Ab) would now seem obvious (4).

In this study, we evaluated and compared sensitivity and specificity of these tests in patients with diagnosed celiac disease (CD).

Materials and Methods

In this cross-sectional study, from January 2006 to January 2008 we prospectively recruited children with suspected celiac disease who were referred to the division of Pediatric Gastroenterology at a pediatric hospital in Tehran (134 children). Presenting symptoms generally included failure to thrive (FTT), chronic diarrhea, abdominal distention, and steatorrhea. Patients were included if the intestinal biopsy was positive and if serologic tests were positive. Patients were excluded if pathology report of intestinal biopsy was negative or serologic tests were all negative or had been on a gluten- free diet. An intestinal biopsy specimen was obtained from all patients. At least 2 distal duodenal biopsy specimens, adequate in size and orientation, were examined by two experienced pathologists, blind to the serologic tests results. Celiac disease was diagnosed on the basis of histological findings of Marsh classification. A serum sample equal to 5-7 ml was taken at the time of biopsy and stored at -70 °C until testing for AGA, EMA-IgA and TTG-IgA. All antibodies were measured by immunometric enzyme immunoassay method using kits for in vitro diagnostic use (Orgentec diagnostica). Each run was checked against stated quality control requirements. Sensitivity or the lower detection limits for anti TTG-IgA and anti EMA-IgA were determined at 1.0 u/ml and for anti gliadin IgG were determined at 0.5 u/ml. Findings of pathologic examinations, serologic tests, gender, age, and family history, and clinical presentation were analyzed using SPSS program (version 11.5), and t test and chi-square tests.

Results

In this study, out of a total of 134 children, seventy patients were boy (52.2%) and sixty four patients were girl (47.8%). Celiac disease was diagnosed in 14 (10.4%) of the patients. Seventy nine of the patients were aged below six (58%). They included 42 girls (53.1%; five with positive celiac and thirty seven with negative celiac) and 37 boys (46.9%; four with positive celiac and thirty three with negative celiac). Fifty five (42%) patients belonged to the 6-12-years-old age group. They included 22 girls (three celiac-positive and 19 celiac-negative). Out of 134 examined children, 114 (85.1%) suffered from chronic diarrhea, 57 (42.5%) from steatorrhea, 114 (89.6%) from FTT, the entire 14 celiac-sufferer children, all (100%) had chronic diarrhea, 9 (64.3%) from steatorrhea, and 13 (92.9%) from FTT. Out of 134 cases, 12 (9%) had a family record of the disease and among celiac sufferers (14 children), one (7.1%) had a positive family record. Regarding stool exam tests carried out on 134 diagnosed patients, 49 (36.6%) had fatty drop and the average pH for the stool was 0.44 and SD = 5.59. In addition, 10 cases (71.4%) out of 14 patients

that suffered celiac had fatty drop on stool exams with average stool pH equal to 0.44 and SD = 5.22.

In serologic tests, 16 patients (11.9%) was positive for anti-gliadin antibody, 10 patients (7.5%) for TTG-Ab, and 14 patients (10.4%) for EMA-Ab. In addition, 11 (78.6%) cases out of 14 patients that suffered from celiac were positive for anti-gliadin antibody, 4 (28.6%) patients were positive for TTG-Ab, and 9 (64.3%) were positive for EMA-Ab. Meanwhile, 20 cases (14.9%) out of 134 patients were positive following small intestinal biopsy. Sensitivity of AGA test was 78.6% and its specificity was 95.9%. Sensitivity of TTG-Ab test was 28% and its specificity was 95%. Sensitivity of EMA-Ab was 64% and its specificity was 96%.

Discussion

The results of the past studies have shown that the EMA-IgA and the human recombinant TTG-IgA are the most sensitive and specific serologic tests for identifying individuals who need to undergo an intestinal biopsy examination to diagnose CD (5-11). For the EMA-IgA test, the majority of studies report a sensitivity in excess of 95% and all but 1 study found the specificity to be in excess of 95% (5-11) (Table 1). In our study, the sensitivity and the specificity stand respectively at 64 and 96 percent. The specificity is close to one, but the inconsistency between the sensitivities might be related to the difference in the volume of samples or the sensitivity of kits or the difference in the stage of disease.

Table 1: Sensitivities and specificities for the EMA-IgA test

Author	Date	Age group	Sensitivity(%)	Specificity(%)
Bonamico et al[5]	2001	Children	95	98
Delecea et al[6]	1996	Children	88	90
West et al[7]	2002	Adults	94	100
Tesei et al[8]	2003	Adults	86	100
Carroccio et al[9]	1996	Children	97	100
Bugin-walkff et al[10]	1991	Children	90	98
Dileo et al[11]	1999	Children	100	97

An initial review of the data for TTG-IgA might suggest it is less sensitive and specific than the EMA-IgA (5, 12-15), but direct comparison between the human recombinant TTG-IgA and the EMA-IgA failed to show any significant differences (12, 16-18) (Tables 2-3). In our study, the sensitivity and the specificity stand respectively at 28 and 95 percent. The specificity is close to one, but the inconsistency between the sensitivities might be related to the difference in the volume of samples or the sensitivity of kits or the difference in the stage of disease. For these different sensitivities, it is suggested that the study be conducted with one more sample and a specific criterion for diagnosis of the disease and the consistency between Abs titers and the stage of the disease.

Table 2: Sensitivities and specificities for the TTG-IgA test

Author	Date	Age group	Sensitivity(%)	Specificity(%)
Bonamico et al[5]	2001	Children	90	100
Dickey et al[12]	2001	Adults	77	98
Vitoria et al[13]	1994	Mixed	61	91
Ascher et al[14]	1996	Mixed	91	98
Leon et al[15]	2001	Not Stated	99	99

Table 3: Studies comparing EMA-IgA and TTG-IgA

Author	Date	EMA-IgA		TTG-IgA	
		Sensitivity(%)	Specificity(%)	Sensitivity(%)	Specificity(%)
Bonamico et al[12]	2001	95	98	90	100
Baldas et al[16]	2000	93	100	100	98
Sulkanen et al[17]	1998	93	99	95	91
Sblaterro et al[18]	2000	93	100	98	99

The sensitivities and specificities for the AGA tests were not only highly variable but generally were lower than those for the EMA-IgA and TTG-IgA (9-10, 19-20). For the AGA-IgG, most studies reported a sensitivity of less than 90%, whereas the specificity was below this level for all of the samples (21). Specificity for the AGA-IgA was better than that for the AGA-IgG, with the majority of studies reporting levels of 90% or more, but the sensitivity was poor (9-10, 19-20) (Table 4). In our study, the sensitivity and the specificity stand respectively at 78.6 and 95.9 percent.

Table 4: Sensitivities and specificities for the AGA-IgG test

Author	Date	Age group	Sensitivity(%)	Specificity(%)
Wolters et al[19]	2002	Not stated	83	80
Carroccia et al[9]	1996	Children	89	72
Burgin-wolff et al[10]	1991	Children	89	65
Lerner et al[20]	1994	Children	88	92

Based on these findings, either the EMA-IgA or TTG-IgA test is best suitable to identify those individuals who require an intestinal biopsy examination to diagnose CD while avoiding an unnecessary biopsy examination in those who do not have the condition. Because of the variable and generally lower sensitivity and specificity associated with the AGA, these tests are less suitable for screening purpose there are no data to show that a combination of tests is better than a single test using either EMA-IgA or TTG-IgA (21-22).

There have been no other studies that specifically evaluated whether the performance of the serologic tests varied in different racial or ethnic groups. With regard to age group difference, the past data suggest the AGA-IgG may be more sensitive in children compared with adults. There was no clear difference between children and adults for the AGA-IgA test.

Conclusion

In clinical practice, serologic tests for CD are frequently used to identify both symptomatic and asymptomatic at-risk individuals who require an intestinal biopsy examination to confirm the diagnosis. A positive test is also supportive of the diagnosis in those with characteristic histopathology change on small intestinal biopsy examination. Based on our study, the best tests for this purpose are the EMA-IgA or TTG-IgA, both of which are highly sensitive and specific.

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