Diagnostic Value of Serologic Tests in Celiac Screening

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ABSTRACT

Objectives: Celiac disease is one of the malabsorption syndromes leads to growth and development retardation in children. There is no test lonely can definitely diagnose celiac; however, the collection of clinical findings, serologic tests, intestinal biopsy, and response to treatment may diagnose it. Although diagnostic value is variable in different studies, they are used a non-invasive and appropriate screening methods today. This study aimed to evaluate diagnostic value of celiac serologic tests in children less than 15-year-old.

Methods: During two years, this study conducted on children referred to Al-Zahra hospital (Isfahan, Iran). All the children who had duodenal biopsy tests were evaluated in terms of serologic tests and clinical symptoms due to suspected celiac. The results were analyzed through descriptive statistics, chi-square and Fisher's exact tests using SPSS software.

Results: 15.8 percent of children were under 2 years, 37.3 percent between age range of 2 to 12 years and 10.5 percent were above 12 years. 8.1 percent of children with negative anti-endomysial antibody (EMA) suffered from celiac; while 20.0 percent of children with positive EMA suffered from celiac. 15.4 percent of children with negative anti-gliadin antibody (AGA) had celiac; while 11.6 percent of those with positive AGA suffered from it. 11.1 percent of those with negative tissue transglutaminase antibody (tTG) and 37.5 percent with positive tTG suffered from celiac.

Conclusions: According to our study results, there is no correlation between gastrointestinal symptoms such as vomiting diarrhea, anorexia, bulimia, and failure to thrive (FFT) with celiac. TTG was the best screening test method to diagnose celiac disease and other tests such as AGA and EMA do not have high diagnostic value.

Keywords: Celiac, Malabsorption, Anti-gliadin antibody, Anti-endomysial antibody, Tissue transglutaminase antibody

Original Article

INTRODUCTION

Celiac disease is one of the malabsorption syndromes in children which is featured as small intestinal mucosal damage due to immune intolerance toward gluten in cereal.[1] In this disease, gluten in food damages the proximal small intestine mucosa;

malabsorption due to this disease is associated with watery, acidic or steatorrhea diarrhea. However, lack of diarrhea and even presence of normal feces would not reject malabsorption disorder.[2] Disease signs and symptoms will not emerged until gluten containing foods start for patient. It is seen more among Northern Europe People and their generation migrated to other parts of the world. However, it is not seen only among Caucasians; it is also among Spaniards, Indian, Sudanese, Chinese, Caribbean African and Middle Eastern.[3] The average incidence and prevalence of celiac in Europe is one in a thousand live births (1 in 250 in Sweden and 1 in 40,000 in Denmark). In Great Britain, it was reported 1 in 300 though screening test and its confirmation by intestinal biopsy.[4]

Screening 200 blood tests in the United States reported the prevalence of endomysial antibody 1 in 250 people.[5,6]

In Iran, wheat consumption is higher than the global average and this can be effective on prevalence of this disease in Iran.[7] In a study, the prevalence of celiac in blood donors in Tehran was 1 in 166 people.[8] The prevalence of at least 1% and calculation of silent celiac cases of 2% were estimated.

For celiac diagnosis, malabsorption screening tests are not much useful; because their values in children with celiac are normal. However, anemia and hyperproteinemia may exist.[9,10]

Serologic markers in order for diagnosis of celiac include anti-gliadin antibody (AGA), anti-endomysial antibody (EMA) and tissue transglutaminase antibody (tTG). Anti-gliadin antibodies are as IgG and IgA in the blood. In children, the sensitivity of IgG and IgA anti-gliadin antibody reported 100% and 89% respectively. It is estimated that 2-3 percent of patients with celiac have IgA-deficiency.[11]

Anti-gliadin antibodies are in other diseases such as cow's milk intolerance, Crohn's disease, nephropathy IgA, eosinophilic enteritis, tropical Sprue and dermatitis herpetiformis. EMAs are as IgA antibodies. Its sensitivity is 100% and specificity also is 98%. Using anti-gliadin antibody and anti-endomysial antibody together can increase the estimation of positive and negative cases to 100% in celiac screening.[12]

Specificity and sensitivity of tTG are equal to anti-endomysial antibody test which is easier to be standardized and requires no animal or human tissue. IgA/tTG measurement has 98/95% sensitivity and 94/92% sensitivity respectively. In patients with celiac who have IgA deficiency, IgG/tTg will be positive through ELISA. Positive diagnostic value of this test confirmed for patients with biopsy 70-83 percent. This screen test may diagnose the children at the risk of symptomatic celiac and leads to early treatment.[13]

Celiac is a lifelong disease and if it is not diagnosed timely, it will cause failure to thrive (FTT) in children and delayed puberty in higher ages.[14] In patients with celiac, esophageal, gastric, pharynx and intestinal malignancy would increase.[15] Early diagnosis and onset of gluten-free diet can reduce these outcomes.[16] This study aimed to review the diagnostic value of serologic tests in celiac through comparing its results with intestinal biopsy. The results could be effective in correct screening and early diagnosis of celiac.

METHODS

In this cross-sectional retrospective study, all the less than 15 years children suspected to celiac underwent intestinal biopsy in Al-Zahra Hospital, Isfahan, Iran.

Children with intestinal biopsy, suspected to celiac with serologic tests who had intestinal biopsy sample in Pathology Center of Al-Zahra Hospital enrolled in the study.

Children without intestinal biopsy and those underwent intestinal biopsy due to another reason except the celiac as well as children with Giardia were excluded from the study.

Sampling was done through convenient sampling method. Sample size calculated 57 subjects based on sample size formula. The files of the

children were assessed after obtaining required permissions and the required data such as amount of AGA and EMA and also the result of duodenal biopsy and a short history recorded in a checklist.

In this study, 0-1 stages of Marsh score considered non-celiac, stages 2, 3a and 3b as high celiac suspected and 3c considered as proved celiac.

The findings were analyzed through descriptive statistics, t-test, chi-square test, Fisher's exact test and ANOVA using Software SPSS.

RESULTS

In this study, the files of 57 under 15 years children suspected to celiac underwent duodenal biopsy evaluated. Nine children (15.8%) were under 2 years, 42 children (37.3%) were between age range 2 to 12 years and 6 children (10.5%) were above 12 years. There were 23 males (40.4%) in the study.

64.9 percent of the study subjects diagnosed negative EMA and 35.1 percent also had positive EMA. 8.1 percent of children with negative EMA suffered from celiac and 24.3 percent of children were suspected celiac and also, 67.6 percent did not suffer from celiac. While 20.0 percent of children with positive EMA suffered from celiac and 40.0 percent of them were suspected to celiac and 40.0 percent also did not suffer from it.

Chi-square test showed that there was not a significant correlation between positive EMA and presence or high probability celiac in children (P = 0.118); however, this test showed that there was a significant correlation between positive EMA and biopsy results (P = 0.02).

Sensitivity and specificity of EMA test for celiac was calculated 50 and 75.75 percent; respectively. On the other hand, positive and negative predictive value for this test calculated 60.0% and 67.56% respectively.

In terms of AGA, 23.2 and 76.8 percent of children reported negative and positive AGA. 15.4 percent of children with negative AGA suffered from celiac and 38.5 percent of children were suspected to celiac and 46.2 percent did not suffer from celiac. 11.6 percent of children with positive AGA suffered from celiac and 27.9 percent of children were suspected to celiac and 60.5 percent also did not suffer from celiac.

Chi-square test showed that there was no significant correlation between positive AGA and celiac (P = 0.658) and positive biopsy and positive AGA (P = 0.18).

Sensitivity and specificity of AGA test for celiac based on intestinal biopsy was calculated 70.83 and 18.75 percent; respectively. On the other hand, positive and negative predictive value for this test calculated 39.53% and 46.15% respectively.

According to the results, 81.8 percent of children had negative tTG and 18.2 percent also had positive tTG. 11.1 percent of those with negative tTG suffered from celiac and 16.7 percent had suspected celiac and 72.2 percent also did not suffer from it. While 37.5 percent of children with positive tTG suffered from celiac, 62.5 percent had suspected celiac and none of the children were healthy.

Chi-square test showed that there was a significant correlation between positive tTG and celiac disease in children (P = 0.001). In addition, Fisher's exact test showed that there was a significant correlation between positive tTG and biopsy result (P = 0.0001).

Sensitivity and specificity of tTG test for celiac was calculated 44.44 and 100 percent; respectively. On the other hand, positive and negative predictive value for this test calculated 100% and 60% in our study; respectively.

The prevalence rate of different symptoms in the study subjects are illustrated in Table 1.

According to the analysis, there was no significant correlation between celiac and symptoms of diarrhea (P = 0.353), chronic vomiting (P = 0.796), abdominal distention (P = 0.684), anorexia (P = 0.302), bulimia (P = 302) and FTT (P = 0.758) but there was only a significant correlation between celiac and irritability (P = 0.026).

Table 1. The prevalence rate of different symptoms in patients with suspected celiac according to biopsy results

Result	Biopsy result [n (%)]			Overall Prevalence
Symptom	Positive	Suspected	Negative	Positive
Diarrhea	5 (71.4)	9 (52.9)	14 (42.4)	28 (49.1)
Chronic vomiting	4 (57.1)	9 (52.9)	15 (45.5)	28 (49.1)
Abdominal distention	1 (14.3)	2 (11.8)	2 (6.1)	5 (8.8)
Anorexia	0 (0)	9 (52.9)	8 (24.2)	5 (29.8)
Bulimia	0 (0)	1 (5.9)	0 (0)	1 (1.8)
Muscle atrophy	0 (0)	0 (0)	0 (0)	0 (0)
FTT	3 (42.9)	8 (47.1)	12 (36.4)	23 (40.4)
Irritability	0 (0)	6 (35.3)	3 (9.1)	9 (15.8)

The study showed that there was no significant correlation between biopsy result and age in the study subjects (P = 0.18).

Furthermore, there was no significant difference between age of celiac and non-celiac children (P = 0.68). There was no significant correlation between celiac and sex in children (P = 0.693).

DISCUSSION

This study aimed to determine the diagnostic value of serologic tests in celiac screening in children suspected to this disease.

As results indicated, there was no significant correlation between positive EMA and celiac in the studied children. Therefore, positive results of EMA in children lonely cannot be a sufficient reason for existence of celiac in them. On the other hand, there was a significant correlation between positive result of biopsy and EMA. Therefore, patients with celiac probably would have positive EMA. The study results of Mahjoub et al. supported this finding.[15]

As indicated in the results, there was no significant correlation between positive AGA and celiac in the studied patients. Besides, positive results of biopsy and celiac had no significant correlation with positive results of AGA. Therefore, in addition that AGA is not an appropriate test to determine patients with celiac, the possibility of positive AGA also is very few.

The results of the present study was in accordance with results of Bhatnagar and Tandon.[16] They also found low diagnostic value of AGA for diagnosis of patients with celiac; however, diagnostic value of EMA was higher than AGA and EMA seemed more appropriate for celiac.

Furthermore, out results showed that there was a significant correlation between positive result of tTG and celiac; in other words, those with celiac much probably had also positive tTG. Therefore, tTG has high sensitivity and specificity to diagnose celiac in children of our society. This finding was in accordance with study result of Gupta.[17]

According to the results of our study, there was no significant correlation between existence of celiac and diarrhea in children. Furthermore, diarrhea cannot be an appropriate symptom for suspecting to celiac. Therefore, in children with chronic diarrhea, celiac assessment seems unnecessary.

Moreover, there was no significant correlation between existence of celiac and vomiting and abdominal distention. Besides, in celiac patients, signs such as vomiting and abdominal

distention are not common. Therefore, patients with vomiting and abdominal distention do not need celiac assessment.

In addition, the results showed that there was no significant correlation between existence of celiac and anorexia and bulimia and these patients are low correlated with these signs. Therefore, patients with anorexia and bulimia do not need celiac assessment.

In addition, the results showed that there was no significant correlation between celiac and FTT and the probability of FTT seem very low in such patients. However, in some studies which there was a significant correlation between FTT and celiac and FTT children should be evaluated in terms of celiac;[11,15-17] perhaps the results of the present study is due to low number of sample size and/or lack of full files and records in the hospital; but reviewing this issue in fact is so important.

The results of this study indicated that patients with celiac suffered from irritability; however, every children with irritability necessarily do not have celiac. Therefore, children with irritability do not need celiac assessment.

One of the other obtained results in this study was lack of a significant correlation between gender and age with celiac which was in correlation with other studies.[15-17] As we know, celiac is a chronic and a lifelong disease and therefore there would be no correlation between age and celiac.

Generally, the present study showed that among the serologic tests, tTG is the only test with high diagnostic value for diagnosis of celiac and patients with high tTG probably suffer from celiac. Although, EMA is not useful in diagnosis and screening the celiac patients, it has a high prevalence in celiac patients.

Finally, AGA has a high diagnostic value in patients with celiac and not in non-celiac patients. Intestinal biopsy should only be implemented with positive tTG and in terms of negative tTG, other test should be used.

The following items are suggested according to the results:

1. Considering the importance of celiac and irreparable outcomes, such a study should be done with higher sample size

2. the results of the present study should be given to the physicians, particularly to pediatricians

3. Given to high prevalence of celiac disease and its complications, retraining classes should be hold for medial staff in addition with explaining the features, importance and early diagnosis of celiac.

4. According to similar studies, a test for celiac screening should be selected in order to avoid from high costs of other tests and implementation of invasive measures as well as avoiding from costs of endoscopy based on test results without high positive predictive value.

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REFERENCES

1. Behrman RE, Kliegman R, Jenson HB. Nelson textbook of pediatrics. 17th ed. Toronto: Saunders; 2004.
2. Maki M, Collin P. Coeliac disease. The Lancet 1997; 349(9067): 1755-9.
3. Wyllie R, Hyams JS. Pediatric gastrointestinal disease: pathophysiology, diagnosis, management. 2nd ed. Philadelphia: W.B. Saunders Co; 1997.
4. Talley NJ, Valdovinos M, Petterson TM, Carpenter HA, Melton LJ, III. Epidemiology of celiac sprue: a community-based study. Am J Gastroenterol 1994; 89(6): 843-6.
5. Goggins M, Kelleher D. Celiac disease and other nutrient related injuries to the gastrointestinal tract. Am J Gastroenterol 1994; 89(8 Suppl): S2-17.
6. Ferguson A. New perspectives of the pathogenesis of coeliac disease: evolution of a working clinical definition. J Intern Med 1996; 240(6): 315-8.
7. van Overbeek FM, Uil-Dieterman IG, Mol IW, Kohler-Brands L, Heymans HS, Mulder CJ. The daily gluten intake in relatives of patients with coeliac disease compared with that of the general Dutch population. Eur J Gastroenterol Hepatol 1997; 9(11): 1097-9.

8. Nasr K, Haghighi P, Abadi P, Lahimgarzadeh A, Hedayati H, Halstead JA, et al. Idiopathic enteropathy: an evaluation in rural Iran with an appraisal of nutrient loss. Am J Clin Nutr 1976; 29(2): 169-76.
9. Mansoor AA, Strak SK. Prevalence of celiac disease among patients with iron deficiency anemia: Personal experience and review of literature. pakistan journal of medical sciences 2012; 21(4): 413-6.
10. Zenkl V, Andrysek O. Malabsorption (celiac) syndrome with idiopathic hypoproteinemia. Cesk Pediatr 1963; 18: 947-52.
11. Hill ID. What are the sensitivity and specificity of serologic tests for celiac disease? Do sensitivity and specificity vary in different populations? Gastroenterology 2005; 128(4 Suppl 1): S25-S32.
12. Poddar U. Celiac disease: clinical features and diagnostic criteria. Indian J Pediatr 1999; 66(1 Suppl): S21-S25.
13. Alsaigh N, Odze R, Goldman H, Antonioli D, Ott MJ, Leichtner A. Gastric and esophageal intraepithelial lymphocytes in pediatric celiac disease. Am J Surg Pathol 1996; 20(7): 865-70.
14. Adams S. Growth Hormone Deficiency Found in Children with Celiac Disease. Clinical Endocrinology 2005; 62(3): 372-5(4).
15. Mahjoub F, Farahmand F, Siamand R. Small bowel biopsy and serologic test results in children with suspected celiac disease in anti Ndvmyzyal Children's Medical Center, the years 1380-1383. Tehran University Medical Journal 2006; 64(8): 96-102.
16. Bhatnagar S, Tandon N. Diagnosis of celiac disease. Indian J Pediatr 2006; 73(8): 703-9.
17. Gupta C. Tissue transglutaminase antibodies in the diagnosis of celiac disease in Indian children. Indian J Gastroenterol 2006; 25(6): 322.

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