DIAGNOSTIC ACCURACY OF SERUM IGA ANTI-TISSUE TRANSGLUTAMINASE ANTIBODY IN THE DIAGNOSIS OF CELIAC DISEASE

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ABSTRACT

Objective: To determine the diagnostic accuracy of serum IgA anti-tissue transglutaminase antibody in the diagnosis of celiac disease taking histopathology as gold standard.
Study Design: Cross-sectional survey.
Place and Duration of Study: This study was conducted at the department of Pediatrics, Military Hospital Rawalpindi from April 2015 to July 2016.
Patients and Methods: Ninety-five consecutive children presenting with suspicion of celiac disease were included in this study after taking written informed consent. A predesigned proforma was used to record patient's demographic details. Anti-tTG level of ≥25 U/ml was taken as diagnostic of celiac disease while results of histopathology on endoscopic biopsy were taken as gold standard.
Results: The mean age of the patients was 6.48 ± 3.20 years and majority (n=53, 55.8%) of the children were aged between 5 to 10 years. The serum anti-tTG level ranged from 8.0 U/ml to 759.0 U/ml with a mean of 298.75 ± 225.51 U/ml. Taking a cut-off value of ≥25 U/ml for anti-tTG, 81 (85.3%) children were suspected of celiac disease. Histopathology of endoscopic biopsy confirmed celiac disease in 68 (71.6%) children with 62 true positive, 19 false positive, 6 false negative and 8 true negative cases. It yielded 91.18% sensitivity, 29.63% specificity and 73.68% accuracy for anti-tTG (≥25 U/ml) in the diagnosis of celiac disease with positive and negative predictive values of 76.54% and 57.14% respectively.
Conclusion: IgA anti-tissue transglutaminase antibody (≥25 U/ml) was found to be highly sensitive test for the detection of celiac disease in children.

Keywords: Anti tissue transglutaminase IgA, Celiac disease, Sensitivity and specificity.

INTRODUCTION

Endoscopic small bowel biopsy currently the 'gold standard' for the diagnosis of celiac disease (CD) however, the severity of injury ranges from Marsh I to Marsh IV and only Marsh stages III and IV have largely been considered to be indicative of celiac disease[1,2]. But, endoscopy and duodenal biopsy is cumbersome, painful and costly[2]. The dawn of serological tests, therefore, offered the ever welcomed opportunity of diagnosing celiac disease without the need for endoscopy. The detection of auto-antibodies is frequently used as a first-line test to recognize individuals who might need a duodenal biopsy[1,2]. Historically, screening for celiac disease has been performed with a diagnostic test for malabsorption (D-xylose) or serological tests for anti-endomysial antibodies (anti-EMA) and anti-gliadin antibodies (AGA). These serological tests have become vital in the identification and diagnosis of celiac disease[2]. After Dieterich et al. revealed that tTG was the main (or the sole) auto antigen recognized by anti-endomysial antibody (EMAs) in CD patients, the use of an ELISA based on tTG was suggested and widely established for the diagnostic assessment of such patients[3]. Anti-tTG testing is highly sensitive and remains the single serological test of choice for diagnosis and screening of celiac disease. It is notable that tTG antibody levels fluctuate depending on the degree of intestinal damage. Recent guidelines recommend that if anti-tTG IgA is elevated more than 10 times then HLA-DQ2 and DQ8 are performed and if any one of

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them is positive it is confirmatory of celiac disease. But this is debated now. Thus, a negative test is likely in a patient with marginal pathology (i.e., Marsh I lesion) and does not essentially rule out milder forms of celiac disease. Repeat testing may offer important clinical insight and help decide the appropriate timing for a biopsy or observing dietary compliance[2]. The reported specificity of anti-tTG greatly varies in the existing literature from as low as 9.5%[4] to as high as 100%[5]. With a low specificity of 9.5% anti-tTG may not be a good diagnostic tool and should only be used for screening while with a high specificity of 100% it can confirm the celiac disease without the need for endoscopic biopsy.

The purpose of the current study was to evaluate the role of anti-tTG antibody in the diagnosis of celiac disease with a hope that the results of the present study may provide a screening or diagnostic tool limiting the need for endoscopic biopsy in children suspected of celiac disease.

PATIENTS AND METHODS

This was a cross sectional survey conducted at the department of Pediatrics, Combined Military Hospital Rawalpindi over 16 months period from April 2015 to July 2016. Ninety five (95) children aged between 2 months to 14 years presenting with persistent diarrhea, abdominal pain, vomiting, abdominal distension, constipation, failure to thrive (FTT), idiopathic short stature, unexplained anaemia or iron deficient anaemia unresponsive to treatment and lassitude/weakness were included in the study after taking written informed consent from parents or legal guardian of the patient. Serum anti-tTG levels were determined and a cut-off value of ≥25 U/ml was taken as diagnostic of celiac disease. These patients underwent endoscopic biopsy of the duodenal mucosa. At least four biopsy specimens were taken from first and second part of the duodenum and one sample was taken from duodenal bulb. The results of histopathology were taken as gold standard and the diagnostic accuracy of anti-tTG was judged accordingly. Children with inflammatory bowel disease, abdominal tuberculosis, cystic fibrosis, and other established causes of FTT and short stature were excluded from the study. A predesigned proforma was used to record patient's demographic details, anti-tTG and histological diagnosis. All the patients were assessed by a single consultant pediatrician and all the histological reports were

Table I: Demographic features of study participants.

Characteristic	Study Participant (n=95)
Age (years)	6.48 ± 3.20
Age Groups	
<5 years	34 (35.8%)
5-10 years	53 (55.8%)
10-14 years	8 (8.4%)
Gender	
Male	47 (49.5%)
Female	48 (50.5%)
Anti-tTG (U/ml)	298.75 ± 225.51

Table II: To determine diagnostic accuracy of anti-tTG.

Anti-tTG Diagnosis	Histopathological Diagnosis		Total
	Celiac Disease	No	
Celiac Disease	62	19	81
No	6	8	14
Total	68	27	95

acquired from the same laboratory to eliminate bias. Confounding variables were controlled by exclusion. SPSS version 16 was used to analyze the data.

RESULTS

The age of the patients ranged from 7 month to 14 years with a mean of 6.48 ± 3.20 years. Majority (n=53, 55.8%) of the children were aged between 5 to 10 years followed by 34 (35.8%) children aged under 5 years and 8 (8.4%) children aged between 10 to 14 years. There were 47 (49.5%) male and 48 (50.5%) female children. The serum anti-tTG level ranged from 8.0 U/ml to 759.0 U/ml with a mean of 298.75 ± 225.51 U/ml as shown in table-I.

Taking a cut-off value of ≥25 U/ml for anti-tTG, 81 (85.3%) children were suspected of having celiac disease. Histopathology of duodenal biopsy confirmed celiac disease in 68 (71.6%) children with 62 true positive, 19 false positive, 6 false negative and 8 true negative cases. It yielded 91.18% sensitivity, 29.63% specificity and 73.68% accuracy for anti-tTG (≥25 U/ml) in the diagnosis of celiac disease with positive and negative predictive values of 76.54% and 57.14% respectively (table-II).

DISCUSSION

The immune response in celiac disease involves the production of antibodies against the intestinal enzyme tissue transglutaminase. These auto antibodies are either immunoglobulin G (IgG) or immunoglobulin A (IgA). The level of anti tTG IgA in the blood is more reliable for the detection of disease because it is formed in the small intestine, where gluten is responsible for inflammation in gluten-sensitive people[6]. In the present study, the prevalence of celiac disease was 71.58%. Hashmi et al[7] reported similar disease prevalence of 63.33% in children presenting at Benazir Bhutto Hospital, Rawalpindi. Javaeed et al[8] however reported much lower prevalence of 11.57% among adults presenting at Khyber Medical University, Peshawar. Eremic et al[5] and Emami et al[9] reported similar prevalence of 8% and 6% in Serbian and Irani such children. IgA anti-tissue transglutaminase antibody (≥25 U/ml) was found to be 91.18% sensitive, 29.63% specific and 73.68% accurate in the diagnosis of celiac disease taking histopathology as gold standard with positive and negative predictive values of 76.54% and 57.14% respectively. The results of the present study are similar to those of Bayram et al[4] who reported similar higher sensitivity (93.3%) but low specificity (9.5%) of anti-tTG in Turkish children. Better sensitivity and specificity has been reported in other local studies where Hashmi et al[7] reported 86.84% sensitivity and 81.82% specificity and Javaeed et al[8] reported 85.70% sensitivity and 99.1% specificity of anti-tTG in Pakistani children with celiac disease. Dutta et al[10] also reported better sensitivity and specificity of 77.8% and 89.1% respectively in Indian population. Eremic et al[5] reported much higher specificity of 100% with relatively lower sensitivity of 75% in Serbian population.

The low specificity observed in the presents study can be partly due to the difference of laboratory test systems. Another explanation for this difference from previous studies can be the hypothesis that proteins other than tissue transglutaminase (tTG) may act as antigens in some patients for anti-tTG antibodies[11]. Based on the results of the present study, high sensitivity and low specificity of anti-tTG make it a better screening tool where positive children should undergo endoscopic biopsy for the confirmation of diagnosis.

CONCLUSION

IgA anti-tissue transglutaminase antibody (≥25 U/ml) was found to be 91.18% sensitive, 29.63% specific and 73.68% accurate in the diagnosis of celiac disease taking histopathology as gold standard with positive and negative predictive values of 76.54% and 57.14% respectively.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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