DOI: https://doi.org/10.53350/pjmhs22168323

ORIGINAL ARTICLE

Diagnostic Accuracy of Serum Anti-Tissue Transglutaminase Antibody in Diagnosis of Pediatric Celiac Disease

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ABSTRACT

Background: Celiac disease (CD) is an immune mediated enteropathy that is caused by intolerance to gluten storage protein of wheat bartey and rice. Early diagnosis of celiac disease is highly imperative to institute early intervention in order to prevent profound macronutrient deficiencies as well as long term complications. Diagnostic investigation for celiac disease, the matter of controversy, with endoscopic duodenal biopsy remaining the gold standard but invasive, costly, painful, needing expertise and carrying risks of endoscopy, while serologic tests although noninvasive, cheap, easily available but with disputed specificity and sensitivity.

Objective: To find the accuracy and importance of anti-tissue transglutaminase IgA antibody in celiac disease diagnosis and determination in pediatric patients.

Place and Duration of Study: Department of Pediatrics, GMMMC Hospital Sukkur from 1st June 2019 to 30th November 2019.

Methodology: One hundred and fifty children were suspected celiac diseases were enrolled. Demographic data including age, gender was noted. Duodenal biopsy and upper GI endoscopy of all patients with positive anti-tTG was performed. At least 6 biopsy specimens were taken from first and second part of duodenum and duodenal bulb.

Results: Mean age of the children was 8.72±1.92 years. Sensitivity, specificity, PPV and NPV of tTG-IgA in evaluating celiac disease was 86.9%, 84.8%, 88%, 83.6% and 86% respectively.

Conclusion: Tissue transglutamianse (TTG) is an excellent screening test for celiac disease in high risk Paediatric population having diagnostic accuracy of 86%. Therefore, it can be safely recommended that patients having even fewer clinical features should be screened by TTG to detect celiac disease patients with minimal signs and symptoms.

Keywords: Celiac disease, IgA anti-tissue transglutaminase, Gastrointestinal endoscopy

INTRODUCTION

Celiac Disease (CD) is an immune mediated enteropathy that is caused by intolerance to gluten storage protein of wheat barley and rice, in genetically susceptible individuals.[1] Its prevalence is approximately 0.5-1% in general population.[2] Statistical data of 2010 showed that, approximately 2 million children below five years of age were suffering from CD. Early diagnosis of CD is highly imperative to institute early intervention in order to prevent profound macronutrient deficiencies as well as long term complications.[3]

Diagnosis of CD typically rests on appropriate clinical picture and ultimately serologic, endoscopic and histological findings as well as response to gluten free diet.[4] Clinical signs and symptoms of CD are variable, ranging from asymptomatic to a diverse spectrum of symptoms including diarrhea, fatigue, failure to thrive, anemia, clubbing, bloating, abdominal pain and distention.[5]

In symptomatic patients serologic tests are performed by measuring circulating disease associated antibodies. These antibodies are antigliadin IgA and igG, anti endomysial igA (EMA) and anti-tissue transglutaminase' (anti-tTG) igA.[6] Transglutaminase is determined to be the major enzyme that can prove helpful in diagnosis of the celiac disease as it is the major auto-antigen. ELISA based tTG-IgA is a powerful method that can be employed for diagnosis of CD.[7]

Duodenal biopsy is considered as primary diagnosis of celiac disease and severity of which can be ranged from Marsh I-III and only Marsh III is considered as indication of CD.[8] tTG-IgA is highly specific and sensitive serological test that helps in evaluating celiac disease without any invasive procedure.[9] Hashmi et al[9] also reported high sensitivity and specificity of this test. The varied specificity of anti-tissue transglutaminase IgA antibody but still it can prove to be useful tool for celiac disease screening.[10]

Diagnostic investigation for CD, the matter of controversy, with endoscopic duodenal biopsy remaining the gold standard but invasive, costly, painful, needing expertise and carrying risks of endoscopy, while serologic tests, although non-invasive, cheap, easily available but with disputed sensitivity and specificity. Current study is proposed with the rationale to evaluate the role of anti tTG in celiac disease diagnosis that can prove helpful in the diagnosis without the involvement of invasive procedure.

MATERIALS AND METHODS

This cross-sectional analytical study was performed at Department of Pediatrics, GMMMC Hospital Sukkur from 1st June 2019 to 30th November 2019 and 150 patients were enrolled. Age children aged 5-12years, suspected celiac disease and both genders were included. Children already diagnosed cases of CD, gluten free diet and total IgA deficiency (<0.07 g/lit) were excluded. Study was started after seeking permission for data collection from the Head of Department of pediatrics, Civil Hospital Sukkur and Ethical Committee of Hospital. Duodenal biopsy and upper GI endoscopy of all patients with positive anti tTG was performed. At least 6 biopsy specimens were taken from first and second part of duodenum and duodenal bulb. The biopsy specimen was examined by same expert histopathologist, blinded to the serological results of patients. The results of histopathology was graded according to Modified Marsh Classification and Marsh lll was regarded as indicative of CD taking histopathological findings as gold stranded. The collected data was analyzed through SPSS-20. Diagnostic accuracy was calculated in terms of sensitivity, specificity, positive predictive value and negative predictive value.

RESULTS

There were 57 (38%) patients belonged to age 5-8 years and 93 (62%) patients belonged to age 9-12 years. Fifty seven (38%) were males and 93(62%) were females (Table 1).

Table 1: Demographic information of the patients (n=150)

Variable	No.	%
Age (years)		
5- 8	57	38.0
9 -12	93	62.0
Gender		
Male	57	38.0
Female	93	62.0

The average age of the patients was 8.72±1.92 years and mean duration of disease was7.60±2.18 months (Table 2).

Histopathology confirmed the prevalence of celiac disease was 56% (84/150). Sensitivity, specificity, PPV, NPV and accuracy of tTG-IgA in evaluating CD was 86.9%, 84.8%, 88%, 83.6% and 86% respectively (Table3).

Table 2: Descriptive statistics of the patients

Variable	Mean±SD	95% Confidence Interval for mean	
		Lower bound	Upper bound
Age (years)	8.72±1.92	8.41	9.03
Weight (kg)	23.11±4.76	22.23	23.88
Height (cm)	122.86±9.96	121.25	124.47
Duration of symptoms (months)	7.60±2.18	7.25	7.95

Table 3: Diagnostic accuracy of tTG-IgA antibody in celiac disease diagnosis

Serum IGA anti-tissue transglutaminase antibody	Celiac disease on histopathology		Total
	Yes	No	
Yes	73	10	83
No	11	56	67
Total	84	66	150

Sensitivity = 86.9% Specificity = 84.8%
PPV = 88.0% NPV = 83.6%
Accuracy = 86%

DISCUSSION

Celiac disease is an auto-immune disorder in which body gets sensitive to gluten consumption which is mainly present in wheat, barley and rye. Its prevalence is different in different regions of the world.[11] Statistics of 2010 reveals that almost 2 million children below 5 years were more vulnerable to celiac disease.[12]

Serological testing; antigliadin IgG antibody has diagnostic accuracy reaching 100%for the diagnosis of CD in children <2.[13] TTG and anti-endomysial IgA (EMA) antibody testing have been shown to be highly sensitive and specific for celiac disease.[14] TTG and/or EMA have a high accuracy (sensitivity 90-98% and specificity 95-99%).[15,16] Diagnosis of celiac disease is a matter of discrepancy. The very high specificity and sensitivity of anti-tissue transglutaminase (TTG), recommending it as sufficient evidence of starting gluten-free diet.[17] Others suggest strongly positive TTG (>10 folds cut off) as diagnostic, and values less than 10 times need further confirmation by duodenal biopsy and histopatholgy.[18] Some studies have suggested that using double anti-body testing with TTG and EMA.[19,20] Yet others have suggested using TTG anti-body and anti-gliadin antibodiestogether.[21]

Celiac disease is an auto-immune disorder in which immune cells attack villi of small intestine and lead to various diseases.[11] The number of subclinical cases of CD is very high due to subtle manifestations closely mimicking other common conditions, such as primary malnutrition and inflammatory bowel syndrome. Frequency of CD in study population of present study, which includes high-risk population, was 63.33%. This result closelycorrelates with the results of Aziz et al. who studied similar high risk population in Karachi.[22]

The average age of the patients was 8.72±1.92 years and mean duration of disease was 7.60±2.18 months. In Hashmi et al[23] study the total number of patients was 60 with age ranging from 2 to 13 years (mean = 5.85±3.36 years)

In the present study there were 38% male and 62% female (ratio 1:1.6) which is in close concordance with previous studies which also show a female preponderance.[24] Hashmi et al[23] also reported the male to female was 1:1.23

This study showed that frequency of CD was 56%. This is a well- recognized trend towards non-GI presentation observed worldwide, and results partly correlate with previous studies such as conducted by Ehsani-Ardakani et a.[24] Sensitivity, specificity, PPV, NPV and accuracy of tTG-IgA in evaluating CD was 86.9%, 84.8%, 88%, 83.6% and 86% respectively. These results appear representative as they closely correlate with the results of Samasca et al., showing a high sensitivity, specificity and positive predictivevalue[14], but a relatively low negative predictive value. On the other hand, Alessio et al[18] and Bürgin-Wolff et al[25] demonstrated better sensitivity, specificity, positive and negative predictive values. Hashmi et al[23] reported that the sensitivity of TTG was calculated to be 86.84%. Specificity of TTG was 81.82%. Positive predictive value was 89.19% and negative predictive value was 78.26%.

It is evident from the above discussion that TTG provides an excellent screening tool for CD with high specificity and sensitivity. Strongly positive TTG value, i.e. TTG >50 IU/ml, provides a positive predictive value of100%; suggesting sufficient diagnostic accuracy to obviate the need for endoscopic duodenal biopsy and histopathologic examination of duodenal mucosa.

Therefore, a strongly positive TTG is diagnostic of CD. Histopathology is the time tested invasive procedure for celiac disease diagnosis. Moreover, it requires necessary expertise and costly equipment, which is not freely available in many centers of the country. Endoscopy and duodenal mucosal histopathology should be reserved for cases with TTG positivity <50 IU/ml, and TTG negative cases with strong clinical suspicion of CD.

The only satisfactory treatment for celiac disease is lifelong strict adherence to a gluten-free diet. Prospective research is aimed at developing alternative therapies which may permit an unrestricted diet including proteolytic enzymes that degrade gluten, desensitizing vaccines, anti inflammatory drugs, polymeric binders, inhibitors of transglutaminase 2, and HLA-DQ2 blockers. However, these have not been proven effective enough to replace gluten-free diet.[26]

It is evident from the discussion that diagnosis is the most key step in the management of CD. This is because of protean clinical features of CD, which are at times very diverse and subtle. Scenario is made more complex by large number of sub-clinical cases having no clinical features. Early diagnosis is of utmost importance in determining the course of disease and possible complications, being a potentially curable condition, makes early diagnosis even more important.

CONCLUSION

Tissue transglutamianse is an excellent screening test for CD in high risk paediatric population having 86.9% sensitivity and 84.8% specificity. Therefore, it can be safely recommended that patients having even fewer clinical features should be screened by TTG to detect CD patients with minimal signs and symptoms.

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