Diagnostic Accuracy of Anti-Tissue Transglutaminase Antibodies (IgA) in Patients with Suspicion of Celiac Disease by Keeping Histopathology as Gold Standard

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ABSTRACT

Background: Celiac disease occurs in children with chronic diarrhea, weight loss, gastrointestinal symptoms, development of gastrointestinal cancer, vomiting, constipation, dental enamel defects, osteoporosis, dermatitis herpetiformis, short stature, persistent iron deficiency anaemia and delayed puberty and in asymptomatic individuals with type 1 diabetes, and first degree relatives of individuals with celiac disease.

Aim: To determine the diagnostic accuracy of anti-tissue transglutaminase antibodies (IgA) in patients with suspicion of celiac disease by keeping histopathology as gold standard

Design: It was a cross-sectional study.

Study settings: The study was conducted at indoor and outdoor patients at Pakistan Atomic Energy Commission General Hospital Islamabad for a period of 03-09-2017 to 02-03-2018.

Methods: Total 146 of both the genders were enrolled in this study. TTG (IgA) antibodies were done by ELISA method. Report was finalized by pathologist. Biopsy was performed at PAEC General Hospital Islamabad by gastroenterologist. Biopsy specimen was send to AFIP. The report was verified by histopathologist of same hospital. Statistical analysis was preformed to compute sensitivity, specificity, positive and negative predictive values by making 2x2 table taking small bowel biopsy as gold standard.

Results: In this study the mean age was 4.952 ±3.08 years and there were 70(47.95%) male and 76 (52.05%) female patients. Anti-tissue transglutaminase IgA antibodies were present in 84(57.5%) while 88 (60.3%) patients had positive findings on histopathology. There were 81(55.5%) patients who were diagnosed positive on both (histopathological findings and Anti-tissue transglutaminase IgA antibodies) and 55 (37.7%) patients were diagnosed negative on both (histopathological findings and Anti-tissue transglutaminase IgA antibodies).

Conclusion: Sensitivity and specificity of anti-tissue transglutaminase IgA antibodies was 92.05% and 94.83% respectively. The overall diagnostic accuracy was 93.15%. So, this test is recommended and should be used for diagnosis of celiac disease in children.

Keywords: Celiac disease, histopathology, TTG antibodies.

INTRODUCTION

Celiac disease (CD) is an immune mediated chronic inflammatory disorder of small bowel induced by ingestion of gluten containing grains in genetically susceptible persons. CD is a common cause of diarrhea, failure to thrive, abdominal distension, anemia, weight loss and short stature. During last decades, its occurrence has rose more quickly as previously only as smaller portion of CD patients were identified while a major portion remained concealed. Now as diagnostic facilities have improved, the criteria have been revised with sophisticated serological investigations including TTG IgA antibodies followed by gold standard proximal intestinal biopsy. In history of CD, identification of tissue transglutaminase was a major milestone. The only treatment of CD at present is gluten free diet strictly that ameliorates its symptoms and improves quality of life besides preventing occurrence of lymphoma, ulcerative jejunoileitis and refractory celiac disease.

For specific determination of IgA TTG antibodies, transglutaminase of human tissue is highly accurate as antigen. In comparison with antiendomysial antibodies assay, anti-tissue transglutaminase antibodies are cheaper and very simple, more sensitive for mass screening. The sensitivity and specificity of IgA TTG Enzyme-Linked Immunosorbant Assay (ELISA) is 90% and 95% respectively. There are some conflicting results on TTG diagnostic strength. The overall sensitivity and specificity of anti TTG range from 38%-92.5% and 74%-97.5% respectively.

The reason why IgA is used in the diagnosis of CD is that, celiac disease prevalence is on the rise and there is a need of a diagnostic method in order to timely screen and manage these patients.

The purpose of this study was to detect CD patients in our population with simple screening test because the prevalence of the disease is very high as previously thought. Locally only few studies are available and no study has been done in recent years and previous studies done showed variability in sensitivity and specificity of IgA antibodies. If results of this study proved good accuracy then this test would be recommended for diagnosis of celiac disease.
PATIENTS AND METHODS

This cross sectional study was conducted at indoor and outdoor patients at Pakistan Atomic Energy Commission General Hospital Islamabad for six months w.e.f 03-09-2017 to 02-03-2018 by selecting patients through consecutive non probability sampling. Sample size of 140 patients was calculated at 90% sensitivity and 95% specificity with expected prevalence of 16.6% at 95% confidence interval. Patients of both the genders with age between 6 months to 15 years were included in the study. Informed consent was taken from parents. In history, symptoms were failure to thrive, diarrhea, irritability, anorexia, abdominal distension, pallor, short stature, weight loss, foul smelling stool and abdominal pain. On examination, height, weight, muscle wasting, abdominal distension, edema and finger clubbing was observed. Then TTG (IgA) antibodies was done by ELISA method. TTG antibodies tests were free of cost of these patients from hospital lab. All the suspected cases were included in the study and then small bowel biopsy was performed. All above steps was clearly discussed with parents. Biopsy was performed at PAEC General Hospital Islamabad by gastroenterologist. Biopsy specimen was sent to AFIP. The report was verified by histopathologist of same hospital. Data was analyzed by using SPSS version-10. Relevant descriptive statistics was used as: frequency and percentage was computed to present categorical variables including presenting symptoms and signs, family history, Anti-tissue transglutaminase antibodies results and small bowel biopsy findings; quantitative variable like age, weight and height was presented by mean+SD. Statistical analysis was performed to compute sensitivity, specificity, positive and negative predictive values by making 2x2 table taking small bowel biopsy as gold standard.

RESULTS

In this study the mean age was 4.952 ±3.08 years with minimum and maximum age 0.5 years and 14 years respectively. According to gender distribution there were 70(47.95%) male and 76 (52.05%) female patients as given in table 1. Forty-three (29.5%) patients were reported as failure to thrive and anemia (Hb <7 mg/ dl) was seen in 85 (58.2%) of the patients. Diarrhea was present in 86(58.9%) patients the height was < 5th centile while height > 5th centile was seen in 43(29.5%) of the patients. Anemia (Hb<7 mg/dl) was seen in 43(29.5%) patients while > 5th centile weight was seen in 103(70.5%) of the patients. Anti-tissue transglutaminase IgA antibodies were present in 84(57.5%) while 88(60.3%) patients had positive findings on histopathology as mentioned in Table 2.

There were 81(55.5%) patients who were diagnosed positive on both (histopathological findings and Anti-tissue transglutaminase IgA antibodies) and 55 (37.7%) patients were diagnosed negative on both (histopathological findings and Anti-tissue transglutaminase IgA antibodies). A total of 3(2.1%) patients were diagnosed as positive on Anti-tissue transglutaminase IgA antibodies but were negative on histopathological examination and there were 7(4.8%) patients who were diagnosed as negative on Anti-tissue transglutaminase IgA antibodies but were positive on histopathological examination. The sensitivity and specificity of anti-tissue transglutaminase IgA antibodies were 92.05% and 94.83% respectively. Positive, negative predictive values were 96.43% and 88.71% with 93.15% diagnostic accuracy given in table 3.

DISCUSSION

Caused by a permanent sensitivity to gluten, celiac disease is an immune-mediated enteropathy in genetically susceptible masses.11 Its occurrence is high in females with F/M ratio 2:1. In the present study we also found that there were 70(47.95%) male and 76 (52.05%) female patients, showing the higher female ratio as compare to female. So the findings of our study are similar to other studies.12-13 We also found that Forty-three (29.5%) patients were reported as failure to thrive and anemia (Hb < 7 mg/ dl) was seen in 85 (58.2%) of the patients. Diarrhea was present in 86 (58.9%) of the patients while short stature was seen in 49
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(27.4%) of the patients. Moreover, in 40(27.4%) patients the height was < 5th centile while height > 5th centile was seen in 106 (72.6%) of the patients. According to weight distribution, <5th centile weight was seen in 43 (29.5%) while >5th centile weight was seen in 103 (70.5%) of the patients and these findings are similar to other studies.5,16

For specific determination of IgA TTG antibodies, human tissue transglutaminase is more accurate as antigen.5 Anti-tissue transglutaminase antibodies are cheaper and simpler, more sensitive for mass screening than antiretypesial antibodies assay. The sensitivity and specificity of IgA TTG Enzyme-Linked Immunosorbsent Assay (ELISA) is 90% and 95% respectively.6 There are some conflicting results on TTG diagnostic strength. The overall sensitivity and specificity of anti TTG range from 38%-92.5% and 74%-97.5% respectively.17-18

Similar findings were reported by Korponay-Szabó et al.19 who concluded that IgG anti-TTG ELISA had a sensitivity of 98.7% and a specificity of 98.6%, and the correlation with IgG EMA titres was high (rs=0.91). One coeliac patient, initially negative in all autoantibody tests, displayed both IgG anti-TTG antibodies and IgG EMA during later gluten exposure. IgG anti-TTG antibodies and EMA titres showed significant decreases (p<0.001) in treated patients. The short-term outcome of potential celiac disease in young children was described in a cohort study that prospectively followed children from birth if they had a first-degree relative with celiac disease; by a mean age of 29 ± 12 months, 96 of the children had developed serologic evidence of celiac disease and underwent intestinal biopsy.17 Moreover, Barker et al.20 also reported positive biopsy results.

A very strong limitation to the present study was that the study was limited to one hospital so its availability of facilities and expertise may have effect on results. In future this study is recommended as a multicenter study for more valid results.

CONCLUSION

Sensitivity and specificity of anti-tissue transglutaminase IgA antibodies 92.05% and 94.83% respectively. The overall diagnostic accuracy was 93.15%. So, this test is recommended and should be used for diagnosis of celiac disease in children.

REFERENCES