Original Article

Correlation Between Transglutaminase Antibody (TGA) Ratio and Histological Findings of Villous Atrophy in Celiac Disease By Marsh Grading

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Objective: To assess the correlation between TGA ratio and degree of duodenal damage by using histologic Marsh grading in patients with CD.

Methods: This present study was conducted in the Department of Histopathology, Shaikh Zayed hospital, Lahore. After taking informed consent (from the patients and guardians in case of minors), endoscopic biopsy from the distal duodenum was taken routinely. Data was computerized with window SPSS version 22. P value ≤ 0.05 was considered significant.

Results: In our study, the mean age of the patients was 32.23±16.37 years and male to female ratio was 1.08:1. The mean TGA ratio of the patients was 16.51±7.37. A strongly positive correlation was found between the Marsh grading of CD and TGA ratio of the patients i.e. r=0.872. Statistically, a highly significant difference was found between Marsh grading and TGA ratio.i.e. p-value=0.006

Conclusion: The results of our study concluded that the titer of TGA ratio is strongly correlated with duodenal histologic Marsh grading in patients of CD.

Keywords: Marsh grading, TGA ratio, CD, correlation, small Intestine

Introduction

Celiac Celiac disease has now emerged as the most common genetically based food intolerance. Celiac disease was initially considered to be a disease of western society. However, it has now been detected in many other parts of the world including Africa, Middle East and Asia with the highest prevalence in Saharawi population living in Algeria.[1] Regarding Pakistan, no specific figure has been documented for its prevalence.[2] In 1940's, the association between the dietary wheat component (gluten) and CD was described by the Dutch paediatrician Dicke.[3] The features characteristic of Celiac disease are villous atrophy of the duodenal mucosa, intraepithelial lymphocytosis and crypt hyperplasia.[4] The result is decrease in the mucosal surface area of absorption. It ultimately leads to malabsorption, diarrhea and growth failure.[5]

There are multiple complications of untreated Celiac disease. Some of these include growth failure in children, anaemia, osteoporosis, infertility and development of lymphoma in the small intestine.[6]

Diagnosis

The diagnosis of Celiac disease should comprise of: history, clinical symptoms, serology & histo-pathology of the proximal duodenum[7]. However, a definite diagnosis relies on the histological findings. The grading of these changes is done by a classification system proposed by Marsh[8].

The best serological test used to screen patients of Celiac disease is considered to be anti-TGA assay. Anti-TTG assay has a high sensitivity and positive predictive value as compared to anti-endomysium antibodies. However, the gold standard for diagnosis is biopsy of the proximal duodenum, although it has many limitations due to patchy distribution of mucosal changes.[9]

The researchers are currently trying to discover non-invasive and economical methods for the diagnosis of CD, especially in children. It has encouraged them to find if any correlation exists between TGA levels and mucosal damage and whether it has a PPV sufficient to be used for the diagnosis of CD. Recent evidence has suggested that the duodenal changes correlate with the TTG titers. Accordingly, duodenal biopsy can be ignored in strongly positive TTG levels provided additional symptoms and history are suggestive of CD.[10]

It has been claimed that high level of TGA has a positive predictive value of almost 100% for diagnosing Celiac disease and in such cases a duodenal biopsy can be avoided. Hence, a gluten free diet can be prescribed based on confirmed greatly positive TGA result.[11] The TGA level five times the upper limit of normal is 100% specific for villous atrophy. By using a

this cut-off value, biopsy can be avoided in 1/3 of patients.[12]

It was a cross sectional analytical study, conducted in the Department of Pathology, Shaikh Zayed hospital, Lahore.Study was completed in one year after approval of research synopsis.The estimated sample size was 100. It was calculated by using 95% confidence interval, 8% precision level with expected sensitivity and specificity of anti-tissue transglutaminase antibody, 91% with expected frequency of positive cases 50%.

A designed proforma was used to collect the consent and data of patients.Patients of both genders with malabsorption, diarrhea and/or risk factors suggestive of CD were included.

Patients with other autoimmune disease, viral or parasitic infection, drugs, gastro-intestinal malignancy were excluded.

Study Protocol: The study was carried out in one year. Patients were selected from the Department of Gastroenterology and Paediatric Medicine, ShaikhZayed Hospital Lahore, who had been advised anti-tissue transglutaminase antibody level or had already got serology report and were suspected of having biopsy positive CD.Informed consent regarding the inclusion of the endoscopic biopsy in this study was obtained from the patients & the parents/guardians (in case of minor patient) before entering into the study. Endoscopic biopsy was taken routinely (which was free of cost for admitted patients).

Data analysis plan:

\Data was computerized with window SPSS version 22. The strength of association of both parameters was seen by Pearson's correlation curve. P value ≤ 0.05 was considered significant.

Results& Discussion:

In this present study, a total of 100 random patients from either gender were enrolled with age range from 17 months to 80 years.

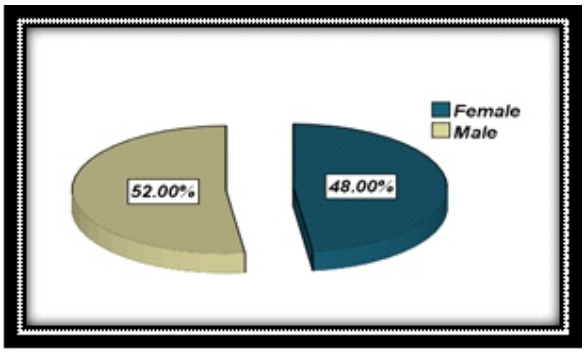

Fig-1: Male to female ratio.

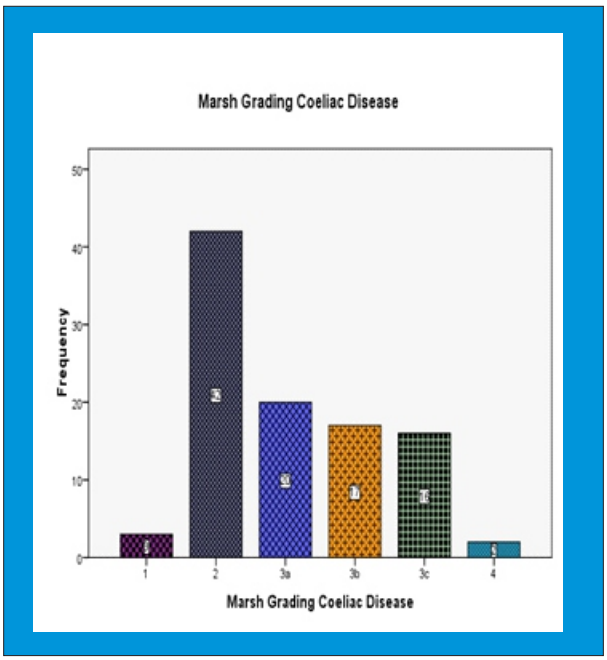

Fig-2: Frequency of various Marsh grades.

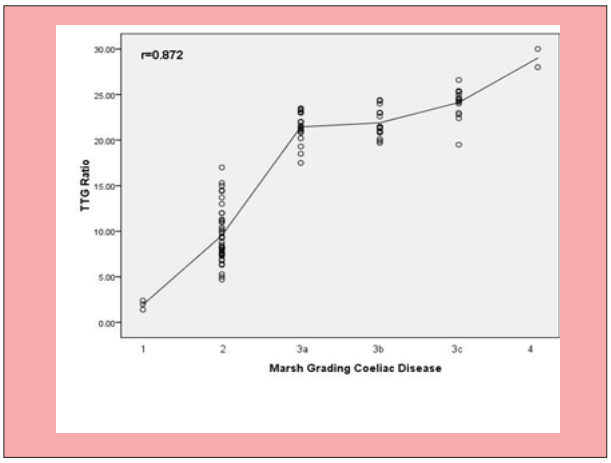

Fig-3: TTG ratio in various Marsh Grades.

In our study, 52% of the patients were males and 48% of the patients were females. The male to female ratio of the patients was 1.08:1. **(Fig-1)**

Frequency of various Marsh Grades is shown in **(Fig-2).** A positive correlation was found between the Marsh grading of Celiac disease and TGA ratio of the patients. i.e r=0.872 **(Fig-3).**

Statistically, a highly significant difference was found between Marsh grading and TGA ratio of the patients i.e. p-value<0.05.

In our study, the mean age of the patients was 32.23±16.37 years and the male to female ratio of the patients was 1.08:1. A weakly negative correlation was found in our study between the TGA ratio and age of the patients (r= -0.030). On the other hand, a highly

positive correlation was observed between the TGA ratio and Marsh grading of Celiac disease i.e. r=0.872. Some of the studies which support the findings of our study are as follows.

Rahmati et al showed in their study that the mean TGA titers were considerably higher in patients with Marsh grade 3 (p=0.003). They found that a correlation exists between TGA titers and degrees of duodenal damage in patients of Celiac disease.[13]

In another study, Vivas et al concluded that the levels of TGA correlate with the Marsh grades (r = 0.661, p< 0.0001). Furthermore, in children, the diagnosis of Celiac disease might be considered when the TGA titer is very high.[14] In another study, it was suggested by Diamanti et al that in symptomatic patients, a strong correlation is present between TGA levels and degree of mucosal injury, and further demonstrated that TGA value ≥20 U/mL can predict mucosal atrophy.[15] Alessio et al carried out a study and investigated an almost complete correspondence (99.8%) between TGA ratio >20 with atrophic lesions (Marsh 3) and 100% positive predictive value for Celiac disease.[16] A study carried out by Zulfiqar et al at the Histopathology laboratory, Karachi concluded that a strong correlation exists between the serological TGA levels and histological findings as graded by Modified Marsh classification.[17] Another study by Parizade et al conducted in the paediatric age group found that in high risk population, high level of antibody can predict villous atrophy with high sensitivity.[18]

However, few studies which showed contradicted findings to this study are as follows:

A study by Evans et al demonstrated that the serology cannot entirely replace histology. Therefore, definite diagnosis should be based on positive antibodies in the presence of villous atrophy[19]. Sweis Rami et al have also reported in their study that a small but significant number of cases of Celiac disease will be missed if only serology is considered.[2] A study conducted by Arevalo et al showed that the frequency of positive serology is low in patients who have had biopsy compatible with Celiac disease[21]. It was shown in another study conducted by Emami et al that the sensitivity of TGA is lower in patients with lesser degree of villous atrophy. Therefore, cases with low Marsh grades can be missed if serology is used as a sole source of diagnosis.[22]

Conclusion

The results of our study concluded that the levels of TGA ratio are strongly correlated with duodenal histologic Marsh grading in patients of Celiac disease.

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