Original Article

Celiac Disease in Different Age Groups

Association of Anti-Tissue Transglutaminase Antibodies with Intestinal Damage in Celiac Disease

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ABSTRACT

Objective: To study the prevalence of celiac disease in different age groups ranging from 07 months-22 years in Multan and its periphery and the role of anti-tissue transglutaminase antibodies in the diagnosis of celiac disease.
Study Design: Descriptive / cross sectional study
Place and Duration of Study: This study was conducted at the Nishtar Medical College and Hospital Laboratory Multan from January 2016 to June 2016.
Materials and Methods: This study was conducted on 178 patients received at Nishtar medical unit III, both male and females, from the age group 07 months to 22 years with the suspicion of celiac disease(CD). All duodenal biopsy cases, in whom anti-tissue transglutaminase antibody test was conducted prior to duodenal biopsy, referred to Nishtar medical college and hospital laboratory Multan from the January 2016 to June 2016 were reviewed.All data was entered and analyzed by using statistical software SPSS version 23.1. Mean ± SD calculated for numerical data and categorical data was presented as frequency and percentages. Chi square test was applied to see effect modification and p value ≤ 0.05 considered as significant.
Results: Out of 178 cases that had been reviewed, 96 (53.93%)cases fulfilled the diagnostic criteria of CD, 76(42.70%) patients had non specific enteritis and duodenitis and 6 (3.37%)patients were suggested a repeat biopsy as celiac disease could not be ruled out. Out of these 96 cases, 35 (36.46%) had infiltrative hyperplastic stage marsh type 2 on histopathology, 34(35.42%) had 3a type and 27 (28.12%) had 3b type according to Marsh criteria. Out of these 96 patients, 49 (51%) had positive anti-tissue transglutaminase IgA antibodies. 24(48.98%) patients who had high titers ranging from >60->800 fell under 3b Marsh Type, 16(32.65%) patients had titers ranging from >25-300 had Marsh Type 3a, 09(18.37%) patients had titers ranging from >10-40 had Type 2 on histopathology.
Conclusion: Celiac disease may present at any age but predominantly in young age groups. Celiac disease is not a rare disease in Multan and its periphery. Duodenal biopsies play a significant role in diagnosis of CD as compared to serological tests. Anti TTG IgA is more sensitive and shows high titer only in severe cases of CD with Type 2 and above Marsh classification. However, Anti tissue transglutaminase IgG antibodies as compared to transglutaminase IgA didn't show any significant prevalence pattern.
Key Words: Celiac disease (CD), Anti-tissue transglutaminase (anti TTG), Gastroenterology, Marsh Classification.

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INTRODUCTION

Oslo's define celiac disease in 2013 as chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed individuals[1]. Celiac disease CD is known as condition of raised immune response of predisposed people to wheat products like barley, rye and oats[2]. Patients of celiac disease have to use glutin free diet throughout his life and should avoid from products that leads to difficult recovery or delayed recovery to normal morphology [3]. Families of such patients should also aware of glutin free diet and effects of celiac disease..

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Among histological disorder of intestinal mucosa in response to glutin free diet are divided into three phases known as glutin sensitive spectrum. This glutin sensitive spectrum has been designed by Marsh III and these phases described as raised amount of lymphocytes infiltrate in region of lamina propria was labeled as Marsh I to hypertrophy of villus with hyperplasia Marsh IIIc[4]. IgA anti-gliadin antibodies is a famous screening test for diagnosis of celiac disease and it can be measured via ELISA and EMA (anti-endomysium antibodies). These two markers estimated by measuring indirect immune fluorescence and measured a sensitivity and specificity range from 31% to 100% and 57% to 100% and from 85% to 100% and 95% to 100% for AGA and EMA, respectively.[5-7] But results of many studies are not in favour of AGA and EMA and claimed poor efficacy and reliability in clinical side. So, some new and advance scoring and diagnostic tests required[8-10].

In 2005 Dieterichet al.[11] reported that tissue transglutaminase enzyme is also a componentof human

body and it can be located through ELISA. He also reported sensitivity 90% and specificity 90 to 92 %[12, 13]. There is no study in favour of correlation evidence of this test (anti-tTG) and degree of damage but all above of this screening marker is a daily advised as a diagnostic investigation, since a lack correlation with slight histological damage may affect correct diagnosis. So, the aim of this study was to evaluate the prevalence of anti-tTG in different degrees of intestinal damage of celiac patients and whether there is a correlation between values of anti-tTG and increased degree of histological damage[12].

MATERIALS AND METHODS

We conducted a cross sectional study of 178 duodenal biopsy cases at Nishtar medical unit III, and reviewed at Nishtar medical college and hospital laboratory, Multan, from January 2016 to June 2016, those individuals in whom anti tissue transglutaminase antibody test was performed.

Anti-tissue transglutaminase antibody test was performed by ELISA method and samples were collected before performing duodenal biopsies. Anti-tissue transglutaminase antibody results were expressed in terms of titers by calculating observed values with cut off values. Cut of value was 10. All cases with results less than 10 were considered negative. And those with results more than 10 were considered positive. Upper gastrointestinal endoscopies were performed and multiple duodenal biopsies from distal part of duodenum were taken for confirmation of CD in all the cases reviewed. Histopathology results were expressed according to Marsh Classification criteria of CD.[8] All data was entered and analyzed by using statistical software SPSS version 23.1. Mean ± SD calculated for numerical data like age and categorical data was presented as frequency and percentages like ender and grade of Marsh classification. Chi square test was applied to see effect modification and p value ≤ 0.05 considered as significant.

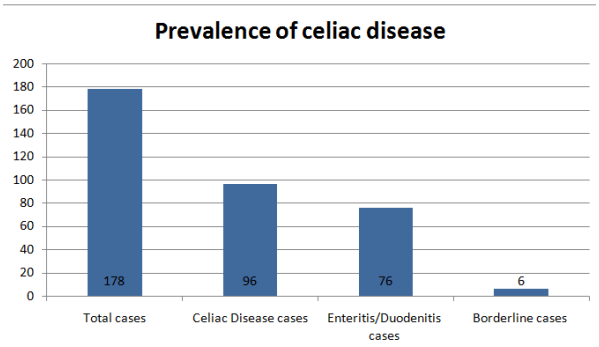
RESULTS

In our study, among the 178 cases, 96 (53.93%) were found to have celiac disease, 76 (42.70%) had nonspecific enteritis and duodenitis, while there were 6 patients who had mild focal increase in lymphocytes in sub epithelial region of their mucosa and increase anti tissue transglutaminase IgG level on ELISA who were suggested a repeat biopsy as CD could not be ruled out in those patients (graph-1).

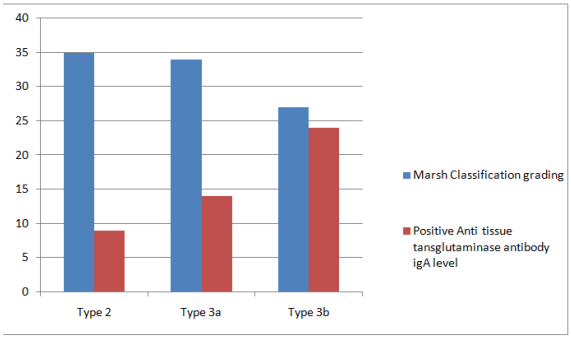
Among the 96 cases who were found to have celiac disease, 57 (59.4%) were male patients and 39(40.6%) were female patients. Among different age groups ranging from 07 months to 22 years, children up to the age of 15 years were seemed to be more affected with CD. The mean age was found to be 5.5 ± 2.8 years.

Out of these 96 CD cases, 35 (36.46%) had infiltrative hyperplastic stage Marsh Type 2 on histopathology, 34 (35.42%) had Marsh 3a Type and 27 (28.12%) had 3b Type according to Marsh criteria. Out of these 96 patients, 49 (51%) had positive anti tissue transglutaminase IgA antibodies, 24 (48.98%)patients who had high titers ranging from >60->800 fell under 3b Marsh Type, 16(32.65%) patients had titers ranging from >25-300 had Marsh Type 3a, 09(18.37%) patients had titers ranging from >10-40 had Type 2 on histopathology (graph-2).

Out of the 178 patients who had anti TTG antibody ELISA test, 46 patients had positive anti tissue transglutaminase IgA level and these 49 were diagnosed as CD on duodenal biopsy and by giving a trial of gluten free diet ,all these patients showed a reverse of their symptoms. 49(51%) out of 96 diagnosed cases of CD had positive anti-TTG IgA levels, while 57 patients showed a positive anti tissue transglutaminase IgG level, out of these 57 cases, 39(68.43%) patients had villous atrophy on histopathology and they responded to a gluten free diet, while 16(28.07%) patients had nonspecific enteritis/ duodenitis on histopathology and didn't show any improvement to gluten free diet and 02(3.5%) patients were suggested a repeat biopsy.



Graph No.1: Prevalence of Celiac disease



Graph No.2: Type of Marsh grading

DISCUSSION

In this study it is reported that celiac disease is an abnormality of small intestine which disturbs the absorption capacity of villi and hyperplasia of crypts develop, this condition ultimately leads to the malabsorption of and generation of IgA antibody and

IgG antibody in response of glutin food. Against of this problem availability of glutin free diet is a common issue in our environment[10].

This study showed that almost 53.93% cases are suffering from celiac disease, with males more prone to the disease. In addition, CD may present at any age but predominantly in young age groups with children aged up to 15 years, with the mean age of 5.5 ± 2.8 years, were seemed to be more affected with the disease as we reviewed data at Nishtar medical college and hospital laboratory which is mainly referred by Children Hospital Multan so it largely consists of young age groups. In many western studies, the disease mainly affects children but in recent studies the true prevalence of celiac disease increases over time.[10] However, in our study we conclude that celiac disease is not a rare disease in Multan and its periphery among children.

Duodenal biopsies play a significant role in the diagnosis of CD as compared to serological tests.[6,7,8] Histopathology is the gold standard in the confirmation of diagnosis along with a trial of gluten free diet.[11,12] Our data showed that Anti TTG IgA antibody level is more sensitive than anti tissue transglutaminase IgG antibody test,[13,14] as it shows a 100% correlation with the disease but only in severe cases of CD with >2 Type Marsh classification on histopathology. With the intake of gluten as the severity of villous atrophy increases, likewise the anti -TTG IgA level increases in the serum of the affected individual.

It is therefore suggested that screening strategies to detect the level of anti-tissue transglutaminase IgA& IgG antibody should be addressed before duodenal biopsy in suspected cases but mucosal biopsies should be performed in all cases with low anti TTG antibody titers for confirmation as many patients with CD has low titers. However, Anti tissue transglutaminase IgG antibodies against transglutaminase IgA didn't show any significant prevalence pattern.[13,14As] out the 57 patients with positive titers, 39 (68.43%) had villous atrophy on histopathology and showed response to gluten free diet while the remaining 18(31.57%) were not found to have CD. The level of the anti TTG IgG antibody are less specific to CD, however people who are IgA antibody deficient, their IgG levels could be a helpful tool for diagnosis.[15,16,17]

Small bowel biopsy is also a diagnostic test for celiac disease but Barkers et al [18] suggested that small bowel biopsy is not necessary investigation for diagnosis of raised titer tTG in celiac disease and its subtypes. Later on Vivas et al recommended that duodenal biopsy should be avoided in children who's tTG antibody is definitely positive[19]. Europian Society for Gastroenterology also updated their protocols for diagnosis of celiac disease after 20 years and decided to omit this diagnostic technique (mall bowel biopsy) from the diagnostic criteria in patients, whose EMA was confirmed. Zanini et al [20] also suggested that ULN 5 times more than normal shows duodenal atrophy and in these patients duodenal biopsy for diagnosis of celiac disease is a dangerous decision and also observe that tTG greater than 90 U/ml means 97.2% sensitivity for Marsh II.

The prevalence of celiac disease in Iran is similar to many western countries and results of these studies shows that screening test of tTG is helpful for the diagnosis of celiac disease even in patients of much raised titers of serum antibodies (five to ten fold raised than normal). Its confirmation must be done with EMA and other clinical and laboratory evidences.

CONCLUSION

Celiac disease may present at any age but predominantly in young age groups. Celiac disease is not a rare disease in Multan and its periphery. Duodenal biopsies play a significant role in diagnosis of CD as compared to serological tests. Anti TTG IgA is more sensitive and shows high titer only in severe cases of CD with Type 2 and above Marsh classification. However, Anti tissue transglutaminase IgG antibodies as compared to transglutaminase IgA didn't show any significant prevalence pattern.

Recommendation

- Therefore, celiac disease is prevalent in our surroundings but we recommend further studies with large data to find out the true prevalence of this disease.
- All those patients with malabsorption and gastrointestinal abnormalities should go for anti-tissue transglutaminase IgA level detection tests for the correct diagnosis before invasive procedures unless the patient is IgA deficient.
- Though duodenal biopsy and evidence of histological changes in intestinal mucosa along with a strict trial of gluten free diet are the basic diagnostic criteria's of CDand should be performed in all suspected cases to detect all the undiagnosed cases.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Jonas F L, Daniel A L, Julio C B, Federico B, Alessio F, Peter H R G, et al. The Oslo definitions for coeliac disease and related terms. Gut 2013;62:43–52.
2. Marsh MN. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue') Gastro-enterol 1992;102:330–54.

3. Green PH. The many faces of celiac disease: clinical presentation of celiac disease in the adult population. Gastroenterol 2005;128:S74–8.
4. Green PH, Cellier C. Celiac disease. N Engl J Med 2007;357:1731–43.
5. American Gastroenterological Association medical position statement: Celiac Sprue. Gastroenterol 2001;120:1522–5.
6. Abdulkarim AS, Murray JA. Review article: The diagnosis of coeliac disease. Aliment Pharmacol Ther 2003;17:987–95.
7. Rashtak S, Murray JA. Tailored testing for celiac disease. Ann Int Med 2007;147:339–41.
8. van der Windt DA, Jellema P, Mulder CJ, et al. Diagnostic testing for celiac disease among patients with abdominal symptoms: a systematic review. JAMA 2010;303:1738–46.
9. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol 1999;11(10):1185–1194
10. American Gastroenterological Association medical position statement: Celiac Sprue. Gastroenterol 2001;120:1522–5.
11. Hill ID, Dirks MH, Liptak GS, et al; North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2005;40(1):1–19.
12. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. Gastroenterol 2001;120(3): 636–651
13. Giersiepen K, Lelgemann M, Stuhldreher N, et al. Espghan Working Group on Celiac Disease Diagnosis. Accuracy of diagnostic antibody tests for coeliac disease in children: summary of an evidence report. J Pediatr Gastroenterol Nutr 2012;54(2):229–241
14. Husby S, Koletzko S, Korponay-Szabó IR, et al. Espghan Working Group on Celiac Disease Diagnosis; ESPGHAN Gastroenterology Committee; European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of celiac disease. J Pediatr Gastroenterol Nutr 2012;54(1):136–160
15. Mäki M, Hällström O, Vesikari T, Visakorpi JK. Evaluation of a serum IgA-class reticulin antibody test for the detection of childhood celiac disease. J Pediatr 1984; 105: 901–905.
16. Korponay-Szabo IR, Halttunen T, Szalai Z, Laurila K, Kiraly R, Kovacs JB et al. Evaluation of IgG antibodies against tissue transglutaminase as a diagnostic tool for coeliac disease. Gut 2003; 52: 1567–1571.
17. Collin P, Mäki M, Keyriläinen O, Hällström O, Reunala T, Pasternack A. Selective IgA deficiency and coeliac disease. Scand J Gastroenterol 1992; 27: 367–371.
18. Barker CC, Mitton C, Jevon G, Mock T. Can tissue transglutaminase antibody titers replace small-bowel biopsy to diagnose celiac disease in select pediatric populations? Pediatrics 2005;115:1341-6.
19. Vivas S, Ruiz de Morales JG, Riestra S, Arias L, Fuentes D, Alvarez N. et al. Duodenal biopsy may be avoided when high transglutaminase antibody titers are present. World J Gastroenterol 2009;15:4775–80.
20. Zanini B, Magni A, Caselani F, Lanzarotto F, Carabellese N, Villanacci V. et al. High tissue-transglutaminase antibody level predicts small intestinal villous atrophy in adult patients at high risk of celiac disease. Dig Liver Dis 2012;44: 280–5.