ORIGINAL ARTICLE

Prevalence of Anti Tissue Transglutaminase Antibodies IGA and IGG Level in Patients with IBD

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ABSTRACT

Background: Celiac disease and IBD are inflammatory disorders of the gastrointestinal tract having some common genetic, immunological and environmental factors involved in their pathogenesis. Current guidelines do not suggest anti TTG antibodies screening in patients with IBD and these subjects are not considered to be at high hazard for Celiac disease.
Aim: To study the prevalence of anti-tissue transglutaminase (TTG) antibodies in inflammatory bowel disease other than celiac disease.
Methodology: This is a cross sectional study with non probability random method that assessed the prevalence of anti TTG antibodies in diseases other than celiac disease i.e. inflammatory bowel disease. The study was conducted on 145 patients, both male and females, from the age group of 02 years to 50 years with the suspicion of celiac disease (CeD). Anti-tissue transglutaminase antibody titers were done in all patients by ELISA. Endoscopies were carried out and numerous biopsies from distal part of duodenum, rectum, sigmoid and the last portion of colon were taken for proof of CeD and IBD in all the cases reviewed.
Results: 145 cases that had been assessed, 63(43.44%) cases satisfied the diagnostic criteria of CD, 77 (53.1%) patients had UC, remaining 5(3.46%) had non-specific enteritis and duodenitis, were recommended a recur biopsy. Out of the positive cases of CD and UC, 3(4.8%) and 4(5.1%) out of 63(100%) and 77(100%) cases had CeD respectively. Out of the positive 63(100%) CD cases, 48(76.1%) cases had < 10 anti TTG IgG antibodies and 15(23.8%) had >10 anti TTG IgG antibodies and 54(85.7%) had <10 anti TTG IgA level and 09(14.3%) cases had >10 anti TTG IgA level.
Conclusion: There is no any significant prevalence pattern of Anti tissue transglutaminase IgG antibodies as compared to IgA in CeD as it can be present in individuals with other conditions, including CD and UC. Anti-endomysial antibody test is more accurate in the diagnostic work-up of celiac disease, mainly in patients with known IBS. Endoscopic results and Histopathology results play a more accurate role in making diagnosis of CeD and IBD along with clinical presentation.
Keywords: Celiac Disease (CeD), Inflammatory bowel disease (IBD), Crohns Disease (CD), Ulcerative Colitis

INTRODUCTION

Celiac disease (CeD) is an autoimmune disorder evoked by gluten ingestion which is normally present in wheat, rye and barley which causes the damage to mucosa of the small intestine in genetically predisposed individuals and is characterized by a variable combination of intestinal and extraintestinal manifestations[1]. IBD comprises two major chronic inflammatory conditions of the gastrointestinal tract, Crohn's disease which can involve the whole gastrointestinal tract but is most common in the terminal ileum and colon and ulcerative colitis, which affects the colon. We are familiar with the well known concept that CeD can be associated with a number of autoimmune diseases, like rheumatoid arthritis, connective tissue disease, primary biliary cirrhosis, eosinophilic esophagitis and inflammatory bowel disease[2,3,4]. These autoimmune diseases demonstrate an extensive overlap in genetic basis. The possible explanation for this spread of autoimmunity may be the widespread distribution of anti tissue transglutaminase antibodies in various tissues in addition to the small bowel[5] and a common genetic susceptibility. Indeed, HLADQ2/DQ8 and HLA-B8DR3/DR4

region (associated with several autoimmune disorders) are in close linkage disequilibrium[6,7]. According to it, the association between Celiac disease and autoimmune diseases like rheumatoid arthritis, in particular Sjögren's syndrome (SjS), primary biliary cirrohsis, eosinophilic esophagitis, connective tissue disorders, systemic lupus erythematosus (SLE), (systemic sclerosis (SCL) polymyositis (PM), dermatomyositis (DM) and IBD has been demonstrated in several studies[8,14].

The prevalence of Celiac disease in patients with IBD is not clear. Several cases have been reported in literature which describes the coexistence of both diseases[15,16]. However, some authors believe that the prevalence of Celiac disease is similar between IBD patients and the general population[17]. We sought prevalence of anti tissue transglutaminase antibodies in patients with IBS with or without existence of celiac disease.

The study was aimed to conclude the prevalence of anti tissue transglutamniase antibodies IgA and IgG in the serum of patients with the identification of IBD.
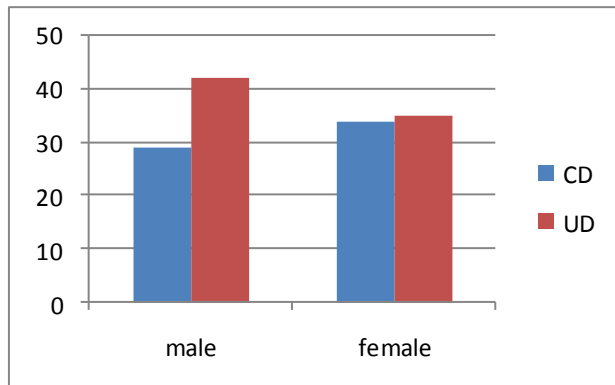
METHODOLOGY

This is cross sectional sydy.Total of 145 suspected cases of inflammatory bowel disease, received at CMH, Nishtar and BAMDC Multan, of those persons in which anti tissue transglutaminase antibody test was carried out, from Jan 2017 to Oct 2018. All data was collected.Anti tissue transglutaminase antibody test was performed by ELISA method using kits supplied by National Institute of Health according to manufacturer's instructions .The cut-off value of 10, provided by the manufacturer, was used. Patients with positive anti TTG antibodies were further tested for antiendomysial antibodies, and those found positive underwent duodenal biopsy to confirm a possible diagnosis of CD. Patients who had endoscopic and pathologic evidence of IBD were identified, and their pathology was reviewed. All the data including biochemical parameters was entered and analyzed by using SPSS. Prevalence of anti TTG antibodies in inflammatory bowel disease other than celiac disease was determined. We compared patients with positive anti TTG antibodies in IBD that coexists with CeD, positive anti TTG antibodies in IBD with no evidence of CeD on histopathology and positive anti TTG antibodies without CeD and IBD.

RESULTS

Out of the total 145 cases that had been assessed, 63(43.44%) cases carried out the diagnostic criteria of CD, 77 (53.1%) patients had UC, remaining 5(3.46%) had non-specific enteritis and duodenitis and were recommended a recur biopsy.

Out of the total 145(100%) cases of CD, we had 76(52.4%) male patients and 69 (47.6%) female patients. In 63(43.44%) positive CD patients; we had 29(46%) male patients and 34(54%) female patients. While out of the 77(53.1%) UC cases, we had 42(54.5%) male patients and 35(45.5%) female patients. It was observed from our results that CD was more prevalent among females than males and UC was more prevalent among males than females (Fig. 1).
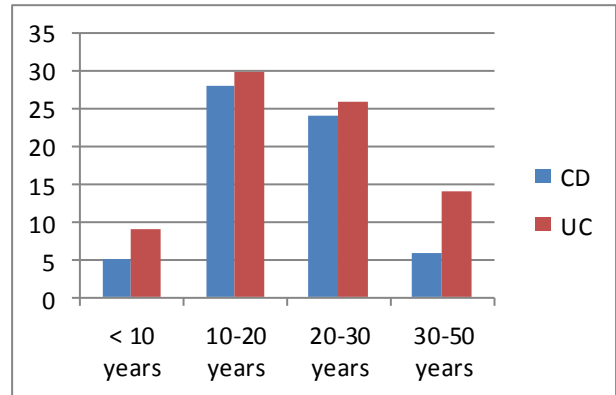
Fig.1: Gender distribution among CD and UD cases

Our study included patients from the age group of 2 years to 50 years; among the positive 63(43.44%) CD cases, 5(8%) persons had less than 10 years age, 28(44.4%) of them had the age ranged between 10 to 20

years, and 24(38.1%) persons were between 20 to 30 years of age and 06(9.5%) were between 31 to 50 years of age. While in the positive 77 (53.1%) UC cases, 7(9%) persons had less than 10 years of age, 30 (39.1%)were between 10 -20 years of age, 26(33.8%) had the age ranged between 20 -30 years and remaining 14(18.1%) had the age between 31- 50 years. (Fig. 2)

Fig.2: Age Distribution among CD and UD cases

Out of the positive cases of CD and UC, 3(4.8%) and 4(5.1%) out of 63(100%) and 77(100%) cases had CeD respectively (Table 1).

Table 1: Prevalence of CeD in IBD.

| | | celiac disease | | Total |
		Positive	negative	
IBD	CD Cases	3	60	63
	UD Cases	4	73	77

Out of the positive 63(100%) CD cases, 48(76.1%) cases had < 10 anti TTG IgG antibodies and 15(23.8%) had >10 anti TTG IgG antibodies and 54(85.7%) had <10 anti TTG IgA level and 09(14.3%) cases had >10 anti TTG IgA level. While out of the positive 77(100%) cases of UC, 43(55.8%) cases had anti TTG IgG level less than 10 and 34(44.2%) cases had anti TTG IgG more than 10 and 69(89.6%) cases were having titers of anti TTG IgA level <10 and 8(10.4%) had anti TTG IgA values >10 (Table 2,3)

The remaining 5(3.46%) cases had non-specific enteritis and duodenitis and were suggested a repeat biopsy.

Table 2: IBD anti tissue transglutaminase level IgA Crosstabulation

| | | Anti tissue transglutaminase level IgA | | Total |
		less than 10	more than 10	
IBD	CD	54	9	63
	UC	69	8	77
Total		123	17	140

Table 3: IBD anti tissue transglutaminase level IgG Crosstabulation

| | | Anti tissue transglutaminase level IgG | | Total |
		less than 10	more than 10	
IBD	CD	48	15	63
	UC	43	34	77
Total		91	49	140

DISCUSSION

We are familiar with the association of several autoimmune diseases with celiac disease[18]. However, there is no conclusive evidence that proves a close relationship between CeD and other autoimmune diseases neither by gluten exposure or due to injury of the intestinal barrier function and a common genetic background.

Our study strongly supports the hypothesis that anti tissue transglutaminase antibodies , more specifically IgG has been found in patients with several other conditions , including inflammatory bowel disease other than celiac disease. We would like to hypothesise that anti IgG antibodies as compared to anti tissue transglutaminase IgA antibodies didn't show any major prevalence pattern. Anti-tissue transglutaminases IgG antibodies were more detectable as compared to anti tissue transglutaminase IgA antibodies in the serum of patients diagnosed with inflammatory bowel disease, and that they are related to disease activity. All patients with positive anti tissue transglutaminase activity should undergo anti-endomysial antibody test. In our study, Tissue transglutsminase antibody IgA was found in patients with IBD in whom Celiac disease coexist while higher titers of anti TTG IgG were seen in UC and CD patients without existence of CeD. Endoscopic results and Histopathology results play a more accurate role in making diagnosis of CeD and IBD along with clinical presentation. Tissue transglutaminase antibodies are of little significance in making a diagnosis of CeD as they coexist in variety of other diseases. Serological anti tissue transglutaminase IgG and IGA screening testing for CeD is not recommended in IBD patients, unless there is a relevant clinical suspicion of CeD.

Our findings concluded that moderate number of patients with IBD had high titers of anti TTG antibodies. Although different studies have revealed conflicting results in this regard but M G Farrace et al[19]. Similarly, several studies have demonstrated a link between CD and rheumatic diseases including RA, PM, DM, SLE, SCL, SjS and MCTD[20]. Le Fevre et al had a similar conclusion in his study; he concluded that anti TTG Ab level was elevated in almost one-quarter of our total Eosinophilic esophagitis cohort cases[21]. Likewise there are studies which have analyzed improvement of clinical symptoms by introduction of gluten free diet in inflammatory bowel disease[22]. There are studies which have suggested that the presence of complicated CeD should be considered in IBD patients who do not respond to immunosuppressive or biological treatments[23]. Current international guidelines for CeD screening[24] do not consider patients with IBD to be at more risk, despite growing evidence on a possible association between CeD and other autoimmune disorders. In this study, we found prevalence of CeD in complicated cases of IBD who weren't showing response to treatment, and the frequency was same as compared with the general population. Our data suggest that adult patients presenting with deteriorating IBD features may be at risk for CeD, and therefore they should be considered for serological screening of CeD by anti EMA. Because of the several benefits of gluten free diet, the identification of CeD is expected to improve outcomes in IBD patients.

CONCLUSION

There is no any significant prevalence pattern of Anti tissue transglutaminase IgG antibodies in contrast to IgA in CeD as it can be present in individuals with other conditions, including CD and UC. Anti-endomysial antibody test is more precise mainly in patients with known IBD. Endoscopic results and Histopathology results play a more accurate role in making diagnosis of CeD and IBD along with clinical presentation. Tissue transglutaminase antibodies are of little significance in making a diagnosis of CeD as they coexist in variety of other diseases. However, the occurrence of anti TTG antibodies is not a common feature in IBD and current international guidelines for CeD screening, do not consider patients with IBD to be at risk.

RECOMMENDATIONS

We suggest serological screening in IBD patients in whom symptoms deteriorate even after initiation of treatment in order to identify CeD, in these patients gluten avoidance should be combined with specific immunosuppressive treatment to improve symptoms. Anti-endomysial antibody test should be done for the diagnostic work-up of celiac disease. Complicated CeD should be considered in IBd patients who do not respond to immunosuppressive or biological treatments.

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