ORIGINAL ARTICLE

Celiac disease: Serologic prevalence in patients with irritable bowel syndrome

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Background: The prevalence of irritable bowel syndrome (IBS) in the community is 10%–20% and have symptom based diagnostic criteria. Many symptoms of celiac disease (CD) with 1% prevalence in some communities can mimic IBS. Sensitive and specific serologic tests of CD can detect asymptomatic cases. The purpose of this study was to compare the level of anti-tissue-transglutaminase (tTG) IgA in IBS patients and controls group. **Materials and Methods:** This case–control study was performed at a University hospital in which 107 patients with IBS who met the Rome II criteria for their diagnosis were compared with 126 healthy age and sex-matched controls. Both groups were investigated for CD by analysis of their serum tTG IgA antibody with human recombinant antigen. Titers were positive containing over 10u/ml and borderline if they were between 4 and 10 u/ml. **Result:** 86 percent of IBS patients were female. The mean antibody level was 0.837 u/ml in IBS group and 0.933 u/ml in control group without any significant difference. **Discussion and Conclusion:** Results of this study may intensify disagreement on the situation of CD in IBS patients.

Keywords: Celiac disease, irritable bowel syndrome, tissue-transglutaminas antibodies

INTRODUCTION

Irritable bowel syndrome (IBS) is one of the most common cases referred to a general practitioner and consultation with gastroenterologists.[1,2] Based on the Rome II criteria, 10%–20% of people in different communities have IBS, which is two times more common in women.[1,3] Celiac disease (CD) has many symptoms which imitate IBS and sometimes it is difficult to differentiate them based on clinical symptoms.[2,4]

It has been thought that CD or gluten-sensitive enteropathy is rare, but recent studies estimate 1% of some community with nine times more common in adult than children. [5,6]

Clinical presentation of celiac includes gastrointestinal manifestations like abdominal pain, bloating, and diarrhea; their intensity depends on the extent of mucosal damage and nongastrointestinal symptoms, such as fatigue, arthralgia, skin eruption, or as an asymptomatic or silent one. [4,6]

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In patients with CD presenting in adulthood, minimal or atypical symptoms are often encountered.[7,8] The low levels of awareness and clinical suspicion among physicians led to a delayed unrecognized case, which was eight times more common than the recognized one.[8,9] Despite the fact that IBS is a chronic disorder without improvement and have limited management modality, gluten-free diet improves the quality of life and prevents long-term complication of celiac.[10-12] With the advent of sensitive and specific serologic tests, the diagnosis of asymptomatic cases has been simplified.[13] In many studies, percentage of the patients with IBS which had CD is increasing.[4,14] These studies compared levels of anti-tissue-transglutaminase (tTG) IgA in patients with IBS and control.

MATERIALS AND METHODS

This case-control study was performed on the 107 patients with IBS and 126 healthy age and sex-matched control individuals. Based on the formulas comparing of proportion level and 90% power of test and consider P1 = 0.114 and P2 = 0.009, [5,14] the minimum sample size of 105 for each group was determined. Gastroenterology clinic of Imam Khomeini Hospital of Tehran were used. Sampling of IBS patients based on Rome II criteria and relatives who not fulfill clinical criteria of Rome II for IBS as control group were performed. Control group included relatives of admitted and outpatient accompanying of University hospital.

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Patients with diabetes and dermatitis herpetiform were excluded. From each sample subjects, 4 ml of blood were taken and serums were isolated and maintained at temperature of –70°C and kept the samples in a series of 80, expose to the low levels of antibody of human recombinant IgA anti-tTG and used orgentec Germany ELISA kit. The amount of IgA anti-tTG was determined with concentrations of 0, 5, 10, 25, 75, and 200u/ml, by standard calibrators in kit. Reading the test results was performed by drawing standard curve with point to point method which show IgA anti-tTG concentration in one column and optical absorption of standards in the other. In this calculation after drawing standard optical absorption curve and tests on a curve, IgA anti-tTG concentration is calculated. Based on the information in the kit's brochure, antibody titer more than 10u/ml was considered as positive, less than 4 u/ml as negative, and 4–10 u/ml as a borderline response. Data collected by check list, mean and standard deviation of quantitative data, and frequency of qualitative data were calculated. Average levels of antibodies in the two groups based on Leven's test for equality of variance and independent *t*-test were compared. To compare antibody levels in the two groups based on other background variables after categorizing, the level of antibodies and for diagnosis of CD a layering chi-square test were used.

Statistical analysis was performed by using SPSS software version 11.5 (SPSS Inc, Chicago, IL) and *P* value less than 0.05 considered statistically significant

RESULTS

107 patients with IBS (45.9%) and 126 healthy individuals (54.1%) were evaluated. Female in both groups were 210 (90.1%) and male 23 (9.9%). Percentage of female in IBS group was 86% and in control group 93.7% ($P = 0.5$) [Table 1]. Antibody level in the healthy group was less than 4 u/ ml (mean 0. 933 ± 0.548 u/ml) and in IBS group with the exception of one case with 4.2 u/ml others had less than 4 u/ ml with mean level of 0.837 ± 0.637 u/ml ($P = 0.215$).

The difference between mean antibody level of younger and older than 40 years of both groups and between men and women in both groups was not significant [Table 1]. In IBS group, 78.5% had gastrointestinal symptoms and bloating was the most common symptom [Table 2]. The difference between mean antibody level in a patient with and without clinical symptoms was not significant [Table 2].

DISCUSSION

Screening test of CD was not positive in any of the groups, thus it seems that the majority of peoples with IBS do not accompany CD. This result was also seen in the study of Ozdi Kl on 60 IBS Turkish patients, which evaluates with anti-endomycium IgG and anti-gliadin IgA antibodies, and Emami *et al*. on166 IBS patients with anti-t-TG IgA in Isfahan, both based on Rome II criteria that did not find any cases of CD.[15,16] While IBS is a disorder considered high risk for CD,[10] the statistical analyses show that serologic test for CD in patients with IBS has an acceptable cost when the prevalence of CD is above 1% and is the dominant strategy when the prevalence exceeds 8%.[17]

Shahbazkhani *et al*. has reported 11.4% positive anti-endomyosial antibodies (AEM) in patients with IBS and in 1 of every 166 healthy Iranian individuals.[14,18] Saber Firoozi also showed less than 0.5% prevalence of positive anti-tTG IgA antibodies in the general population of Shiraz by screening of 1440 healthy individuals.[19] Mein *et al*. study also revealed that 3% of patients with IBS had positive anti-tTG IgA antibodies and concluded that serologic test of CD with this prevalence is cost-effective and almost all cases of CD in IBS can be identified with this method.[20] Screening for CD with IgA AEM with respect to the sensitivity of 98%–75%

Table 1: Distribution of age and sex and average antibody levels of patients with IBS and matched control group

Variables	Groups		*P* value
	IBS (*n* = 107) %	Control (*n* = 126) %	
Age	32.68 ± 10.22	32.15 ± 10.10	0.7272
Female (*n*)	86.0	93.7	0.5
Antibody levels	1.020 ± 0.8222	0.825 ± 0.495	0.944
Male	0.808 ± 0.5642	0.940 ± 0.5689	0.95
Female	0.802 ± 0.5010	0. 913 ± 0.5615	0.117
Age under 40	0.946 ± 0.8608	0.981 ± 0.5671	0.850
Age over 40			

Results are expressed as mean ± SD, *n* = number (%)

Table 2: Frequency of symptoms and mean ± SD of antibody levels in IBS patients with and without symptoms

Symptoms	Frequency in IBS %	Symptomatic	Asymptomatic	*P* value
Bloating	93.5	0.839 ± 0.6218	0.814 ± 0.3485	0.918
Constipation	92.5	0.837 ± 0.6170	0.837 ± 0.4926	1
Abdominal fullness	78.5	0.817 ± 0.5731	0.913 ± 0.7257	0.918
Heartburn	57.9	0.755 ± 0.4295	0.951 ± 0.7798	0.918
Diarrhea	57.9	0.853 ± 0.7052	0.816 ± 0.4431	0.78
abdominal discomfort or pain	57.9	0.826 ± 0.6222	0.853 ± 0.5911	0.818
Passing mucus	29.9	0.803 ± 0.6141	0.852 ± 0.6070	0.705

and specificity of 100%–96% approved.[14] But in a recent study, the sensitivity of this test was lower than the anti-tTG IgA antibody which has a sensitivity of 94% and specificity of 97%.[6,21] On the other hand, with the regard of specific IgA deficiency of 2.5% in CD, absence of these antibodies would not reject CD.[5, 21] Despite the advent of newer tests, IgA anti-tTG ELISA is the standard test of choice in most communities.[22] The diagnostic kit of tTG with guinea pig antigen has high false positive, but in this study kit of recombinant human tTG antigen with higher specificity was used. [23-25] This subject elevates the quality of this study and it seems necessary to review the results of previous studies. Iran is one of the highest wheat- consumption parts of the worlds with a per capita consumption of up to 150 kg/year.[26,27] Continues ingestion of high concentration of wheat protein induces some degree of immune tolerance, so milder manifestation of CD and lower occurrence of CD are estimated.[14,28] Indeed, only some CD patients present the classical symptoms, while many of them are oligo-symptomatic and they usually display very mild complaints or with silent forms of CD (the so-called celiac iceberg). For example in India, Middle East, North Africa, and Latin America, the majority of CD patients presented atypical complaints, such as short stature, failure to thrive, and refractory anemia, which are the result of delayed diagnosis.[29] But recent studies showed more than 10% prevalence of celiac with IBS.[18] The results of this study about CD intensify a significant study difference of IBS and CD in Iran.

CONCLUSION

It was concluded that serum tTg IgA antibody level with human recombinant antigen was not different between IBS and control groups. Although studies were performed on very few patient samples and therefore definite conclusions could not be drawn but with more samples and especially the use of recombinant human tTG antigen kit, better assessment of the situation of CD and relation with IBS in Iran is estimated.

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