Celiac Disease in Patients with Irritable Bowel Syndrome

Masoodi M[1], Sadeghi S[2], Moosavi A[3]

[1] Assistant Professor, Department of Internal Medicine, Tropical and infectious Disease Research Center, Hormozgan University of Medical Sciences

[2] Research Fellow, Department of Internal Medicine, Hormozgan University of Medical Sciences

[3] Assistant Professor, Department of Pathology, Hormozgan University of Medical Sciences

ABSTRACT

Background

Celiac disease occurs primarily in whites of northern European ancestry. Previous beliefs about epidemiology of celiac disease in Iran has changed after recent studies on the disease.

The aim of this study is to find the frequency of celiac disease among patients with irritable bowel syndrome.

Materials and Methods

During one-year period (2006-07), patients with irritable bowel syndrome with Rome II criteria referred to the University Clinic in Bandar Abbas, Hormozgan, South of Iran, were studied to identify those who had also celiac disease. Serologic tests were used to screen patients for celiac disease. If the serologic test became positive, a duodenal biopsy was taken to confirm the diagnosis.

Results

150 patients fulfilling Rome II criteria for irritable bowel syndrome were evaluated. 19 (12.7%) patients were found to have tissue transglutaminase (tTG) antibody; out of these 19 patients, 15 (10% of total cases) had abnormal intestinal pathology according to the modified Marsh classification,5 had type I, 6 type II, 3 type IIIA and 1 had type IIIB lesions.

Conclusions

Celiac disease is a relatively common finding among patients with irritable bowel syndrome.

Keywords: Celiac disease, Irritable bowel syndrome, Iran

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INTRODUCTION

Irritable bowel syndrome (IBS)-a complex, multifaceted condition, broadly characterized by abdominal pain/discomfort associated with altered bowel habits-is among the most prevalent gastrointestinal motility disorders and is one the commonest conditions seen by gastroenterologists in their daily practice.(1), In clinical practice, a positive diagnosis of IBS is usually made by symptom criteria as the main finding along with limited paraclinical evaluation to exclude organic gastrointestinal diseases.(2)

It is generally accepted that IBS is a multifactorial condition, and patients having this disease are actually a heterogeneous group with different underlying mechanisms which are so far unknown.(3)

Corresponding author:
Department of Internal Medicine, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar abbas, Iran.
Tel: +98 912 317 8080
Fax: +98 761 334 8722
E-mail: Masoodi47@yahoo.com

Other gastrointestinal disorders may present with IBS; one such disorder is celiac disease.(3), Celiac disease is relatively common, affecting one in 120-300 persons in both Europe (4-6) and North America.(7), Celiac disease is also found in parts of Northwest India. It may be underdiagnosed in South America, North Africa, and Asia.(8), The diagnosis of celiac disease is increasingly being made in adult. About 20% of patients occur in those who are older than 60 years.(9), Many adults present with episodic or nocturnal diarrhea, flatulence, and weight loss.(10), Abdominal discomfort and bloating are common and often lead to a mistaken diagnosis of IBS.(10), The availability of highly-sensitive and specific serologic markers greatly facilitates the diagnosis of celiac disease.(8), Clinical studies showed that presentation with non-specific symptoms or no symptoms is as common in the Middle East as in Europe and that clinical manifestations of celiac disease vary markedly with age of the patient, and the duration and the extent of the disease.(11)

There are few reports on the prevalence of celiac disease in Iran. A previous report from Iran indicated an estimated prevalence of up to 1/166 for celiac disease.(12), In another case-control study from Iran, Shahbazkhani, *et al.,* reported that among 105 patients with IBS, 12 (11.4%) had celiac disease too.(3), We conducted this study to investigate the prevalence of celiac disease among known patients with IBS in Hormozgan province, southern Iran.

MATERIALS AND METHODS

From January 2006 to January 2007, all patients who attended the Gastroenterology Clinic of Hormozgan Medical University and who diagnosed as IBS by internists, were invited to enroll into this study. The objectives of the study were explained for the participants and it was made clear that it might be necessary that they underwent upper endoscopy for taking duodenal biopsy. All patients gave informed written consents. The study was approved by the ethics committee of Hormozgan University of Medical Sciences.

Patients were then interviewed by a medical resident using a standard questionnaire which addressed the Rome II criteria.(2), Complete physical examination was done for each patient. Serum samples were taken from all patients. The lab tests performed for each patient included a complete blood count, serum chemistry, thyroid function tests, and stool for occult blood, ova and parasites. If clinically indicated, other paraclinical work-ups were requested. This included upper endoscopy, sigmoidoscopy, colonoscopy, small bowel barium study and abdominal ultrasonography. The diagnosis of IBS was made according to Rome II criteria. Exclusion criteria included any abnormalities or organic diseases found in paraclinical tests, and not consenting to enter the study.

IgA and IgG antibodies against neo-epitopes of tissue transglutaminase (tTG) in human serum were measured in all patients. The method used was a solid phase enzyme immunoassay for the combined quantitative and qualitative detection of IgA and IgG antibody employing human recombinant tTG (Aeskulisa CeliCheck, Wendelsheim, Germany). The determination of IgG antibodies to tTG is the only available specific serologic test for those 2%-5% of patients who have IgA deficiency. The diagnostic sensitivity and specificity of tTG antibodies for celiac disease is 98%-100%, and 95%-100%, respectively.(13)

Patients who found positive for antibodies against tTG were invited for upper endoscopy and biopsy was taken from the second portion of their duodenum. All biopsies were reviewed by one pathologist experienced in celiac disease and graded according to the modified Marsh criteria. Patients found to have positive serologic tests, if confirmed by histologic findings, were considered to have celiac disease too.

Collected data were coded and analyzed by

SPSS ver 10 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used.

RESULTS

During the study period, 150 (78 female and 72 male) patients with IBS were included. The mean ± SD age of patients was 36.7±11.3 years. Among theses 150 patients, 35 (23.3%) had predominant constipation, 50 (33.3%) predominant diarrhea, and 65 (43.3%) intermittent diarrhea and constipation. Nineteen (12.7%; 7 female, 12 male) of 150 patients were found positive for combined IgA and IgG antibodies against tTG. Ten of patients with positive tests had diarrhea-predominant IBS and nine had intermittent constipation and diarrhea. From these 19 patients, 15 (10% of total case) had also abnormal intestinal pathology, according to the modified Marsh classification. Biopsy of the small intestine revealed that four patients had type 0, five had type I, six type II, three type IIIA, and one had type IIIB lesions (Table 1). There were no other significant pathologic changes (e.g., parasites and eosinophilia in pathology samples). All of these patients had neither history of milk intolerance nor good clinical response to lactose-free diet. We had recommended use of gluten-free diets to these patients. However, most of them did not tolerate the dietary regimen for a long time due to non-adherence and no good substitution for bread. Only five patients tolerated gluten-free diets for almost six months with good clinical response. Antibody titer against tTG decreased in three patients but we had no follow-up pathology sample after the treatment.

Table 1. Clinical and pathologic findings in patient with positive combined IgA and IgG antibodies against tissue-transglutaminase

	No of patients
No of patients (M/F)	19 (7/12)
Mean±SD age (yr)	35.4 ± 12.2
Range	17-58
Diarrhea predominant	10
Intermittent constipation and diarrhea	9
Biopsy of the small intestine (Modified Marsh classification)	
Type 0	4
Type I	5
Type II	6
Type IIIA	3
Type IIIB	1

DISCUSSION

The management of patients with IBS is frequently unsatisfactory. If we can find a definitive treatment for even a small group of these patients, it would be an important progress. Considering the possible confusion of Rome II criteria with symptoms common in celiac disease, it is rational to consider celiac disease as a possible diagnosis among patients with IBS.[2, 3], The availability of a sensitive and specific serologic test for the diagnosis of celiac disease during the last two decades, and a better knowledge of this disease, has permitted the identification of those with atypical presentations of celiac disease. It is now well-established that a considerable number of patients with celiac disease do not have demonstrable clinical or functional characteristics of the disease.[14-18], These patients are described as latent or potential celiac disease. The concept of latent and potential celiac disease has recently been introduced into the pathogenesis of IBS.[19]

Wheat is a major component of the Iranian diet for many centuries. It may be argued that the continuous and high level of exposure to wheat proteins has induced some degrees of immune tolerance, leading to milder symptoms that may be misdiagnosed as IBS or unexplained gastrointestinal disorders. Many items in the Rome-II criteria, such

as diarrhea, abdominal cramps, improvement by defecation, distention and many others, are also seen in patients with celiac disease.(11)

Sanders, *et al.*, measured the anti-gliaden (IgA, IgG) and endomysial antibody in 300 patients with suspected IBS and in 300 age- and sex-matched asymptomatic controls. Positive tests were followed by endoscopic duodenal biopsies. Sixty-six (22%) patients with suspected IBS had positive test, and 14 (4.7%) had histologic evidence of celiac disease compared with two (0.7%) of controls.(20), In another study from Iran by Shahbazkhani, *et al*, 12 (11.4%) of 105 patients with IBS proved to have celiac disease (3); a frequency close to our findings in Hormozgan, although we had no control group. Other investigators also believe in testing patients with IBS for celiac disease. In a systematic review by Cash, et al, it was concluded that given the relatively high pre-test probability for celiac disease, routine serologic testing may be justified in patients meeting the clinical criteria for IBS.(21)

A hallmark of histology is the presence of villous atrophy. However, villous atrophy can be patchy, and may also be present in a variety of other disorders that should be considered in appropriate clinical settings. In our study, only four of 19 patients positive for antibodies against tTG had Marsh III lesions. Increased intra-epithehal lymphocyte count per se is not absolutely specific for celiac disease and a series of infrequent diseases have to be ruled out. The differential diagnoses include giardiasis, cow's milk protein intolerance or other food protein intolerances. Furthermore, increased intra-epithehal lymphocyte count may be found in some patients free of any recognizable diseases. However, because serum IgA endomysial and tTG antibody tests have a high diagnostic accuracy, pathologic changes in our other patients can be due to celiac disease; nonetheless, but we did not have a good follow-up due to non-adherence of our patients for gluten-free diets. O'Leary, *et al*, studied IBS among celiac disease. In this study, 30 (20%; CI95%: 13.6-26.4) of 150 patients with celiac disease fulfilled the Rome criteria, whereas only 5% of controls had IBS.(22), Traditionally, it was believed that celiac disease is either non-existent or very rare in Iran. However, a recent study has shown that, on the contrary, celiac disease is rather common in this area, although the majority of cases are asymptomatic or have only atypical symptoms.(12)

The management of celiac disease is administration of a gluten-free diet for life. Consult with a skilled dietitian, education about the disease, life-long adherence to a gluten-free diet, identification and treatment of nutritional deficiencies, access to an advocacy group, continuous long-term follow-up by a multidisciplinary team are key elements in the management of individuals affected by celiac disease. In Shahbazkhani, et al, study from Iran, 11 of 12 suspected patients with celiac disease adhered to a gluten-free diet and after six months, all 11 patients had significant improvements in symptoms and three became totally asymptomatic. Six allowed repeated endoscopy after six months of gluten-free diet, of which five showed improvement in histological findings.(3), However, in our study, lesser patients adhered to a gluten-free diet-probably due to lower socioeconomic status, for lack of access to gluten-free diet, lack of a good follow-up by a multidisciplinary team, and the distance of patients from a medical center. Therefore, public awareness of this disease is imperative. Education of physicians, registered dietitians, and other health providers is needed.

CONCLUSION

Celiac disease seems to be unrecognized and under-investigated in patients with symptoms of IBS. It may constitute the etiology of over 5% of patients with IBS in Iran. We believe that it is now reasonable to add the serologic tests for celiac disease to the tests routinely performed in patients being evaluated for IBS.

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