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Original Article

Anaesthesia Section

Celiac Disease Prevalence in the Patients with Irritable Bowel Syndrome in the Ilam Province; A Cross Sectional Study from Western Iran

ALIREZA MAHMOODI[1], ALI JAFARIHAYDARLO[2], MASOOD YASEMI[3], KARIM HEMATI[4], HADI PEYMAN[5]

ABSTRACT

Introduction: Many studies have shown that the prevalence of celiac disease (CD) is increasing in the patients with irritable bowel syndrome (IBS), but the present evidences are controversy and all of the researches don't suggest evaluation of the patients with IBS for the CD.

Methods: In the cross-sectional study, 1000 patients that affected by IBS with the predominant feature of diarrhea who referred to the gastroenterology clinic were evaluated during 2009-2012 years. Blood samples were taken from the patients for ELISA of IgA tissue transglutaminase (TTG) Ab. Then biopsy was taken from the second part of duodenum of all of patients by endoscopy and the sample was referred to pathologist for histopathology evaluation in order to confirm diagnosis.

Results: About half of the patients with IBS were women (50.3%) and the mean age ± Standard deviation of the men and women was 29.59±11.41 and 28.42±11.73, respectively. The mean titer of TTG IgA Ab in the women and men affected by IBS was 5.25±17.77 and 7.22±25.4, respectively. 76 cases (7.6%) that affected by IBS had high serum level of Ab titer (TTG IgA.Ab≥10) that including 41 women and 35 men. In the patients with high serum level of Ab titer, 57 cases (75%) were affected by celiac disease (based on histopathology report). Therefore, the prevalence of CD was 5.7% among patients with IBS.

Conclusion: In the current study the incidence of CD was evaluated 5.7 cases per each 100 people with IBS. It's suggested that all of the patients with diarrhea predominant IBS and high serum level of TTG IgA Ab must be examined for evaluation of CD.

Keywords: Celiac disease (CD), Diarrhea, Irritable bowel syndrome (IBS), Ilam

INTRODUCTION

Celiac disease (CD) is an inflammatory and immune complex disease in the small bowel. Mucous damage of the small intestine is the feature of CD that the event occurs due to the immunologic damage by Gluten in the persons who are genetically susceptible. In such persons, consumption of gluten (exist in the wheat and barley) leads to the immunologic response and irritation of the bowel mucous (esp. duodenum). So it can make malabsorbtion and secondary complications in the patients and susceptible person. TTG IgA. Ab enzymes play the role of auto-antigen in CD [1].

Prevalence of the disease in the society is about (0.5%-1%)[1]. In some of epidemiologic studies that have been confirm based on biopsy, the prevalence of CD has been reported 1.3 to 1.5 in public populations [2]. In a broad study that was done in the US, the prevalence of CD was reported 1.33 in public population [3]. Similar results were reported in the Europe [3-5]. Some of the new studies have shown that the prevalence of CD is more than the past [3-6].

Many studies have shown the prevalence of CD is increasing among the patient with), Down syndrome [3,7], type 1 of diabetes [8,9], IgA deficiency [10], Turner syndrome [11], Williams syndrome[12] and auto immune thyroiditis[13]. CD can be appeared with the similar signs of the IBS such as diarrhea and constipation or other changes in the defecation 14,15].

It's possible that many of persons with the signs or symptoms such as diarrhea, vomiting, anorexia, anaemia and other gastrointestinal disorder or these signs remain as subclinical forever [16]. So, for overlapping of the signs (complications) of both disease and given that the early diagnosis of the CD can be useful in prevention from many of the disease complications.

Some researchers have been conducted in this field in the different countries and in one of the studies, prevalence of the CD among the patients affected by IBS was seven times more than of the normal people [17].

The current study was done according to the full of gluten nutritional regimes among the inhabitants of Ilam province (western Iran) and due to the complications and heavy economic load resulted from the delayed diagnosis of CD that can be preventive in early stage.

METHODS

In the cross-sectional study that has been done during the years of 2009-2012, 1000 patients were studied that had the Rome 2 criteria with appearance of diarrhea (IBS-D) that referred to the gastrointestinal clinic in Ilam city (in the west of Iran).

The patients with warning signs (weight loss, family history of Inflammatory bowel disease (IBD) and colon cancer, fever, anaemia, increase ESR, positive CRP, positive occult blood or parasite in stool exam, pregnant women, malignancy, heart failure (HF), Chronic obstructive pulmonary disease (COPD), liver disease, chronic renal failure (CRF), severe psychiatry disorder, Metabolic or endocrine disease, long-term and continuous consumption of the drug) were excluded from the study.

Six ml blood was taken from each patient for Serologic test. Serologic tests such as anti-TTG IgA Ab, the serum level of IgA for IgA deficiency and IgG anti-gliadin were performed for all patient in order to the screening of celiac patients. Anti-TTG IgA Ab was quantitavely measured for the entire patients and the rate of more than 10AU was considered positive.

Then gastroduodenoscopy was done for all of patient with IBS disease and 6 samples of duodenum (3 from proximal part and 3 from the second part) of the IBS patients were taken and the sample was referred to pathologist to confirm Diagnosis of CD. This study

Variables	Age group					≥50
	≥10	30-40	20-30	30-40	40-50	
patients number	43 (4.3%)	226 (22.6%)	283 (28.3%)	271 (27.1%)	143 (14.3%)	34 (3.4%)
Positive titer IgATTG.Ab (number)	2	27	22	21	2	2
Nagative titer (Number) IgATTG.Ab	41	199	261	250	141	32
Celiac(+)	2	23	16	13	2	1
Celiac(-)	41	203	267	258	141	33
Titer (AU) IgATTG.Ab	4.90	8.84	5.85	5.87	2.98	10.62

[Table/Fig-1]: Frequency distribution of participant based on age groups and celiac disease prevalence

Variables	Gender		p value
	Female	Male	
Celiac (+)	36	21	0.04
Celiac(-)	467	476	
Age (Mean ± SD)	29.59 ±11.41	28.42 ± 11.73	0.17
IgATTG.Ab titer (SD±Mean)	7.22 ± 25.40	5.25 ± 17.71	0.15

[Table/Fig-2]: Frequency distribution of participant based on gender and pathology of CD

Celiac (+)	Celiac (-)	IgATTG.Ab
Pos Ab titer	19	57
Neg Ab titer	924	0

[Table/Fig-3]: Sensitivity, specificity, PPV and NPV of IgATTG. Ab test

was certified by research committee of Ilam University of medical science. Data were analysed by SPSS software and the significant level (p-Value) was considered lower than 0.05 (p-Value≤0.05). The Kolmogorov-Smirnov Test was used for normality distribution of data.

RESULTS

From 1000 patient affected by IBS, 503 patients (50.3%) were women. The mean age ± standard deviation of patient was 29.02 ±11.58. The mean titer of TTG IgA Ab of the patients with IBS was 6.24±21.94 and titer average of anti-TTG IgA Ab in the patients with CD was obtained 53±66.

The highest and lowest frequency of the IBS patients were in the age groups of 20 to 30 y (28.3%) and groups of +50 y (3.4%), respectively[Table/Fig-1]. Most of the patients with positive Ab titer were in the age groups of 20-30 y (28.3%) and least of them were in the age group of above 50 (≥50) y old.

Based on Kolmogorov-Smirnov Test age and Ab titer hadn't normal distribution. The spearman test showed an inverse significant correlation between age and Ab titer (r=-0.071, P<0.02). There was no significant difference between gender with age and Ab titer.

Totally, from 1000 patients with IBS, 57 patients (5.7%) affected by CD. Among patients with CD 36 patients (63.1%) were women. The mean age of cases affected by CD (24.33±10.15y) was lower than non-affected cases (29.29±11.6 y) (P<0.001) and Most of the cases (40.3%) affected by the disease were in the age group of 10 to 20 y [Table/Fig-1]. The prevalence of CD among female was more than men (P<0.04)[Table/Fig-2].

The mean of Ab titer in the cases affected by CD were 52.91±66, respectively (P=0.000). Sensitivity and specificity of the Anti-TTG IgA Ab test were 100% and 97.9% respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 75% and 100%, respectively[Table/Fig-3].

DISCUSSION

Celiac disease (CD) that also is called celiac sprue and sensitive enteropathy to Gluten is an auto-immune disorder, until the past decade, celiac disease was considered as an uncommon disease; but the many studies show that the disease is prevalent and is common among all of the races. In the other studies, the prevalence of CD has been estimated 1-2% in the public population, that according to the epidemiologic estimations, this rate is lower than the real prevalence [3, 5].

Also, among the persons affected by IBS, the prevalence of CD has been estimated 3 to 11% [4]. Sandoz et al., (2001) reported that the celiac disease prevalence is 4.7% in the people affected by IBS [17] . Also in the present study, the prevalence of CD was 5.7% in these patients. In a study that has been done by Akhondi et al (2010) in the yazd city, the prevalence of CD was reported 3.2% in the affected persons [18]. While, shahbazkhani et al (2002) have reported this rate 11.4% in the Tehran (22), comparison of the study results with the other researches shows that the frequency of our patients that affected by CD was in the average range of the other studies that have been done in the Iran and the world. But according to the various prevalence of celiac and IBS in the different regions, naturally prevalence of IBS will be various in the different regions. Based on many of the studies that have been done, celiac disease is more prevalent in the women and its reason is attributed to the auto-immune mechanism of this disease.

In some of the studies, CD prevalence in the women even has been reported more than 80%. In the present study, this rate was partly higher in the women than men. On the other hand some of the studies have reported the ration of women to the men affection is 1:2 to 1:1.3 [19,20].

Few studies exist about celiac prevalence in the Iran[21]. Previously, it was thought that it is very uncommon in the Iran. But researches that have been done in the recent years have changed this subjectivity. In a study in the Tehran city, the prevalence of CD has been reported 1 in every 166 people among the health blood donors. Of course, this study has been done through administration of the test of anti-gliadin anti-body and anti-endomysium anti body. The several studies show the increasing of CD in IBS but their results are contraversy [22-24].

In the present study, the age average of the persons affected by celiac (24. 33 ± 10.15) was lower than the persons affected by IBS (29 ±1.57). Also, in the similar studies the age average of the persons was in the range of 28 to 32 y and generally the disease is prevalent from the childhood to adolescence. But, about 20% of the patients have more than 60 y old during the diagnosis [25,26].

Serologic and biochemical tests of the small intestine are the most accurate tests of the diagnosis of celiac disease. According to most of the studies, for the diagnosis of this disease, at first, estimation is done with the serologic tests and when the serologic test was positive, sampling of the small intestine should be done for its confirmation. Anti- gliadin anti body has low sensitivity and high false positive results of this test is common. Thus the test hasn't any application for the screening and the primary diagnose of CD [27]. Based on the conducted researches, serologic tests (antiendomysium antibody and tissue Trans glutamines antibody have high sensitivity and specificity. Also, the existence of this antibody is related to the degree of atrophy of villis [27,28]. In a study that was done in the khoozestan, the prevalence of IgA anti-TTG was reported about 1% in the population [29]. In another study in the Kerman (southeast Iran) and Sari cities (North of Iran) [30], high prevalence of IgA anti- TTG in the population was obtained 1 in 104 and it is a high prevalence[. Also, in Iran, a study shows that the patients who are diagnosed based on the clinical evidences and those who are diagnosed by the screening have the ratio of 1 to 7 [21,25,26]. Also, in the study of Akbari et al the best diagnosed test

has been mentioned IgA anti- TTG antibody [27]. But, in a study that was done in the Esfahan city [29], positive case of IgA anti-TTG antibody has not been reported from 275 cases affected by IBS, while in the study that have been done in the Hormozgan, from 150 cases of IBS, 19 cases of IgA anti- TTG antibody have been reported [31]. In a research that has been conducted by Maki et al (2003) on 3654 students in the age range of 7-16 y, 27 cases of 56 cases of the positive IgA anti- TTG antibody that have been reported were affected by celiac[32].

In the present study, the sensitivity and specificity of the IgA anti-TTG test for the diagnosis of CD were respectively 100% and 97.9% and it confirm the effective role of this antibody in the diagnosis approach the celiac disease.

CONCLUSION

According to the 5.7% of celiac disease prevalence in the evaluated society in the study (persons affected by IBS with the predominant feature of diarrhea) and due to the overlapping of the signs of both disease and given that the early diagnosis importance of CD can prevent from many complications of the disease, thus we can say that CD should be considered as an important differential diagnosis in the persons affected by the chronic diarrhea and based on the study results it is suggested that all of the persons affected by IBS with the predominant feature of diarrhea should be evaluated for CD.

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PARTICULARS OF CONTRIBUTORS:

1. Student Research Committee, Ilam University of Medical Sciences, Ilam, Iran.
2. Assistant Professor of Gastroenterology, Dept of Internal Medicine, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
3. Student Research Committee, Ilam University of Medical Sciences, Ilam, Iran.
4. Assistant Professor of Anesthesia, Department of Anesthesiology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
5. Student Research Committee, Ilam University of Medical Sciences, Ilam, Iran.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Karim Hemati,
Assistant Professor of Anesthesia, Department of Anesthesiology, Faculty of Medicine,
Ilam University of Medical Sciences, Ilam, Iran.
Phone : +989124249129, E-mail : khematy@gmail.com

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