

## Demographic Features and High Prevalence of Celiac Disease in Patients with Irritable Bowel Syndrome in Khoram Abad, Lorestan

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### ABSTRACT

#### Background:

Many patients with irritable bowel syndrome (IBS) may have undiagnosed celiac disease (CD). Diagnosis of CD is important because early diagnosis can prevent serious complications. The purpose of this study was to investigate the demographic features and prevalence of CD in patients with IBS in Khoram Abad, Lorestan.

#### Materials and Methods:

This descriptive cross-sectional study was conducted on 369 patients with IBS who were diagnosed based on Rome III criteria and attended to gastrointestinal clinic of Shohada-y-Ashayer Hospital in KhorramAbad from June 2015 until March 2016. 31 patients did not accept to participate so were excluded from the study. Serological tests were performed and seropositive cases were underwent upper gastrointestinal endoscopy and duodenal biopsy. Data were analyzed using descriptive statistics, t test and Chi-square test through SPSS software version 22.

#### Results:

The mean age of the patients with CD was 31±12 years and most of them (72.7%) were women. Most of CDs were diarrheal dominant IBS (77.3%). Among 338 patients who completed the study, 25 patients (7.4%) were seropositive, and CD was confirmed in 22 of them (6.5%) according to the Marsh classification. Marsh I was reported in seven cases, Marsh II in four, and Marsh III in 11 cases.

#### Conclusion:

Considering the high prevalence of CD (6.5%) in patients with IBS, the overlap of the symptoms, as well as the importance of timely diagnosis of CD, it is suggested to screen CD in patients with IBS.

**Keywords:** Irritable bowel syndrome, Celiac disease, Prevalence

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#### INTRODUCTION

Celiac disease (CD) is an intestinal malabsorption syndrome occurring in genetically predisposed individuals who are exposed to gluten-containing diet (1-3). CD symptoms are varied depending on the patient's age, disease duration, and the extent of the disease. In children, symptoms manifest as malnutrition and growth retardation. Adults may have no symptoms or gastrointestinal symptoms (such as diarrhea, abdominal pain, bloating, steatorrhea etc.) or non-gastrointestinal

symptoms (such as weight loss, anemia, etc.) (4,5).

Diagnosis of CD is on the basis of clinical symptoms, and positive serology with duodenal pathological findings (6). Non-invasive serological tests including anti-endomysial antibody (anti-EMA, IgA) and anti-tissue transglutaminase antibody (anti-TTG, IgA) with a sensitivity of over 98% and specificity of nearly 100% are used for CD diagnosis (7). Various symptoms of the disease often lead to delays in diagnosis, which may result in serious complications (8,9).

The prevalence of CD is variable in different regions of the world (10). Previous studies have reported its prevalence as about 1% in general population in European countries as well as Iran (11,12). Studies have shown that most of the patients with CD present with symptoms suggesting irritable bowel syndrome (IBS) such as recurrent abdominal discomfort, bloating, and diarrhea, and no alarming signs (13). Therefore, the differentiation between IBS and CD (adult onset) is difficult (14-16) and these patients may be misdiagnosed as having IBS (17,18).

IBS is one of the most common diseases diagnosed by gastroenterologists (19,20). It is a chronic functional gastrointestinal disorder (21), which is characterized by abdominal pain/discomfort and changes in bowel habits and stool consistency, without organic disorder (20,22,23). There is no biochemical test, pathological, or radiological tests for diagnosis of IBS and the diagnosis is only based on the Rome III criteria, and ruling out other diseases with similar symptoms (24,25). Symptoms of CD and IBS are similar (26,27). In fact, many patients diagnosed as having IBS, are more likely to have an undiagnosed CD. The importance of diagnosis of CD is that its early detection can prevent serious complications (19,20). In general, there are contradictory studies on the prevalence of CD in the patients with IBS (28,29). In the study by Cash and colleagues, the prevalence of CD in the US was 7.3% (30). Shahbazkhani and co-workers have reported that the prevalence of CD in patients with IBS was 11.4% (31). On the other hand in the study by Emami and others in Isfahan, no relationship was observed between CD and IBS. In their study, none of the 275 patients with IBS (based on anti-TTG and IgA) had CD (9). Therefore, this study aimed to determine the demographic features and prevalence of CD in patients with IBS in Khoram Abad, Lorestan.

## MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in the gastrointestinal clinic of Shohada-y-Ashayer Hospital in Khorram Abad (west of Iran) from July 2015 to March 2016. IBS was diagnosed according to the Rome III criteria.

The Rome III criteria are defined as follows: abdominal pain or discomfort for at least 3 days per month in the past three months, along with two or more of the following characteristics: 1- pain relief with defecation 2- change in the frequency of defecation 3- change in stool consistency, and the onset of symptoms at least 6 months prior to the diagnosis (32).

After a complete physical examination performed by a gastroenterologist, necessary laboratory tests were done for the patients such as complete blood count (CBC), ferritin, calcium, ESR (erythrocyte sedimentation rate), stool examination (to rule out parasitic diseases especially *Giardia*), occult blood, TSH (thyroid-stimulating hormone), and liver and renal function tests. If the results were normal, the individuals would be enrolled in the study.

Individuals with the following criteria were excluded from the study: significant systemic disease, abdominal surgery (except for caesarean section, appendectomy, hysterectomy), inflammatory bowel disease (ulcerative colitis and Crohn's disease), pregnant and lactating women, family history of colon cancer and inflammatory bowel disease, alarming signs (anemia, blood or leukocyte in stool exam, unintentional weight loss), the onset of symptoms after 50 years of age, nocturnal diarrhea, abdominal mass, and recent use of antibiotics, metformin, or anti-depressants.

### Serology

Anti-tissue transglutaminase antibody (anti-TTG, IgA) has a sensitivity of more than 98% and specificity of about 100% for the diagnosis of CD (7). Therefore, this antibody was used for initial screening. Anti-TTG was measured by ELISA method using generic assay kit with a normal upper limit of 20 u/mL. Serum IgA was determined by nephelometry and binding assay kit with a normal IgA range of 70-400 mg/dL. In the case of low serum IgA titer, anti-TTG antibody (IgG) was used by ELISA method with a normal range of less than 20 u/mL.

Prevalence of Celiac Disease in Patients with IBS

Table 1: Demographic data of all subjects

	No (%)
Age (mean±SD)	31 ± 9
Male/female	173 (51.2) / 165 (48.8)
IBS-diarrhea	232 (68.6)
IBS-constipation & diarrhea	79 (23.4)
IBS-constipation	27 (8)

IBS: Irritable bowel syndrome

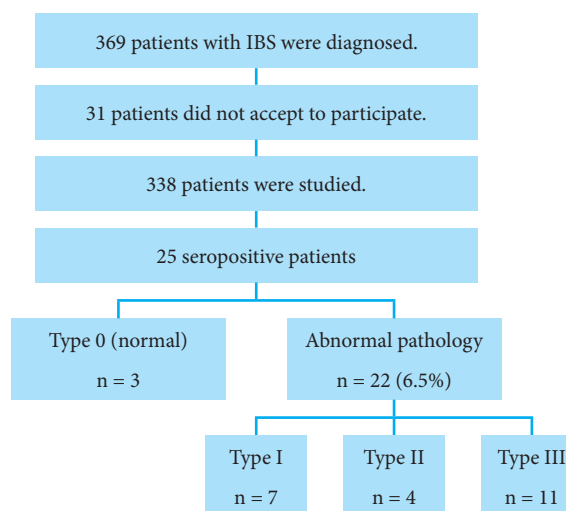


Fig.1: The study design

Table 2: Symptoms in patients with irritable bowel syndrome

	N	Diarrhea	Constipation	Abdominal pain	Bloating	GERD	Early satiety	Dyspepsia	Nausea
IBS-D	232	232	51	207	97	151	78	91	59
IBS-C	27	4	27	19	22	16	19	5	12
IBS-CD	79	79	79	76	56	36	26	14	6
Total	338	315	157	302	175	203	123	110	77

Endoscopy

In the seropositive cases (anti-TTG [IgA] or anti-TTG [IgG] in IgA deficient cases), a gastroenterologist performed upper endoscopy and six biopsy specimens were taken from the second part of the duodenum (D2) and Bulb.

Pathology

Biopsy samples were studied by an experienced pathologist for diagnosis of CD, according to the newly revised Marsh classification (33).

Among the patients attended to the clinic, 338 patients with the Rome III criteria were selected for this study. This study was approved by the Ethics Committee of Lorestan University of Medical Sciences (lums.rec. 1394, 28). Patients with IBS were included in the study and a written informed consent was obtained from all the patients.

To analyze the data, descriptive statistics (mean, standard deviation, and frequency) and inferential statistics of Chi-square and t tests were used. The

level of significance was considered as less than 0.05. Data were analyzed using SPSS software version 22.

RESULT

In this descriptive cross-sectional study, 369 patients with IBS according to the Rome III criteria participated in the study. 31 patients did not accept to participate and were excluded. Finally 338 patients completed the study (figure 1).

Of the 338 studied patients, 173 patients (51.2%) were male and 165 patients (48.8%) were female with the mean age of 31 ± 9 years (with a minimum age of 12 and maximum age of 58 years). 232 patients (68.6%) had diarrhea-dominant IBS. Demographic data of the subjects are shown in table 1. Diarrhea and abdominal pain were the most prevalent symptoms among the patients with IBS, respectively (table 2). 24 subjects (7.1%, 16 female and 8 male) had positive anti-TTG antibody (IgA) (20 u/mL ≤). Of the seven patients (2%) with low serum IgA titer (≤ 70mg/dL) one had positive anti-TTG antibody (IgG) (≥ 20 u/mL).

**Table 3: Symptoms in patients with celiac disease**

	N	diarrhea	constipation	Abdominal pain	bloating	GERD	Early satiety	dyspepsia	nausea	anemia	steatorrhea	Weight loss	
<b>Patients with celiac disease</b>	IBS-diarrhea	17	17	4	15	9	5	9	7	2	6	5	3
	IBS-constipation	2	0	2	1	1	0	1	0	1	1	0	0
	IBS-constipation & diarrhea	3	3	3	2	1	0	0	2	1	1	2	0
<b>Total</b>		22	20	9	18	11	5	10	9	4	8	7	3

**Table 4: Variables between patients with CD and patients without CD**

		Celiac		P value
		No	Yes	
		No (%)	No (%)	
<b>Sex</b>	Male	167(52.8)	6(27.3)	0.02*
	Female	149(47.2)	16(72.7)	
<b>Age (years)</b>	≤25	94(29.7)	10(45.5)	0.048*
	25-40	157(49.7)	5(22.7)	
	≥40	65(20.6)	7(31.8)	
<b>Symptoms</b>	Diarrheal dominant	215(68)	17(77.3)	0.536
	Constipation dominant	25(7.9)	2(9.1)	
	Intermittent Diarrhea- Constipation	76(24.1)	3(13.6)	

\* Statistically significant

therefore, 25 seropositive patients underwent upper endoscopy and 22 patients (6.5%) had abnormal pathology according to the Marsh classification. Marsh I was reported in seven cases (31.8%), Marsh II in four (18.2%), and Marsh III in 11 cases(50%). Among the patients with CD, 16 patients (72.7%) were female and 6 patients (27.3%) were male with the mean age of 31 ± 12 years. Among the patients with CD, 17 patients (77.3%) had diarrhea-dominant IBS, 2 patients (9.1%) had constipation-dominant IBS, and 3 patients (13.6%) had intermittent diarrhea and constipation. The most prevalent symptom was diarrhea. Other symptoms are shown in table 3. Variables of age, sex, and clinical symptoms were compared between the two groups of patients with and without CD. No significant relationship was observed between the clinical symptoms of IBS in the patients with CD and others ( $p = 0.536$ ), while sex and age were significantly different between the two groups ( $p = 0.02$  and  $0.048$ ) (table 4). Most of the patients with CD (72.7%) were women and

45.5% of them were younger than 25 years. All the patients with the diagnosis of CD were provided with necessary education about the disease and underwent gluten-free diet. All the patients referred for follow-up and re-visit after two months. At follow-up visit, the patients presented no clinical symptoms and also, in serological tests a significant decrease of antibody titer was observed.

## DISCUSSION

The prevalence of CD is estimated as 1% in general population in European studies (18). In a study conducted on the general population in Khuzestan, the prevalence of positive anti-TTG (IgA) antibody was reported to be about 1% (34) and the same results were obtained in a study in Gonbad-e Kavos (35). Also, in a study in Kerman and Sari, the prevalence of positive anti-TTG (IgA) was reported to be 1 in 104 in the general population (36). While, the prevalence of IBS in the general population is approximately 15-25% (22). Many patients with IBS may be diagnosed as having

CD (19,20) and considering the similarity between the symptoms of IBS and CD, patients with CD are likely to be misdiagnosed as having IBS. So, the prevalence of CD is expected to be higher in the population suffering from IBS than in the general population.

In the present study out of the 338 patients, 25 had positive serological tests and therefore CD was confirmed in 22 (6.5%) of them according to the pathological findings. In Ahvaz, Shayesteh and colleagues in a study on 465 patients with IBS, showed that of the 47 cases with positive serology (anti-TTG or anti-gliadin or both in some cases), CD was diagnosed in 13 cases with the prevalence of 2.8% (37). In the present study, the prevalence of CD is higher, that can be due to using serum IgA in addition to anti-TTG for IgA deficiency. These methods are more sensitive in the diagnosis of the disease. So, no patient with CD was missed due to IgA deficiency.

Shahbazkhani reported that the prevalence of CD in patients with IBS in Tehran was 11.4% (31), which is higher than our findings and could have been influenced by factors such as sampling site (a referral center in Tehran), as well as different diagnostic criteria used to diagnose IBS (Rome II). In the study of Emami and colleagues in Isfahan, none of the 275 patients with IBS had positive titer of anti-TTG (IgA), while among 60 cases of duodenal biopsy, 7 CD cases were diagnosed as Marsh 1 to 3a (9) suggesting the lack of sensitivity of serological tests. Also, the prevalence of CD in our study was higher than the results obtained by Ahmadi and co-workers in Kerman (2.79%) (37), and Akhondi Meybodi and colleagues in Yazd (3.2%) (38). The reason for the differences in these results can be attributed to: differences in sample size, different diagnostic criteria for CD and IBS, different sensitivities of diagnostic tests, different prevalence in the general population of studies as well as the effects of genetic and environmental factors. In the study of Jafari and others in Ilam in 2013, the prevalence of CD in patients with IBS was 5.7% (39), which is close to the results of our study. In comparison with the studies performed in other countries, the prevalence of CD in this study was higher than the study done by Sanchez Vargas and colleagues in Mexico (2.5%) (40). Considering the different prevalence of CD and IBS in different regions and populations, different prevalence of IBS in patients is not unexpected. Also the prevalence of

CD in patients with IBS in the present study is higher than the study of Sharma and co-workers in India that reported a prevalence of 0.8% (41). The prevalence of CD in patients with IBS in the present study was lower than a study in Bangladesh by Chowdhury (9%) (42), affected by the age, sex, and other factors related to the studied population.

In our study, most of the cases with CD had diarrhea-dominant IBS, which was consistent with the results of many studies (9,18), while other studies do not confirm our findings. For example in Shayesteh and colleagues study, CD was more likely to be diagnosed in patients with particular clinical manifestations (diarrhea, constipation, or a combination of both) but not statistically significant (43). Most of the patients with CD were female (72.7%), which is consistent with most studies (43-45). The mean age of the patients with CD was 31±12 years, similar to what reported by Shayesteh and co-workers (33 years) (43). While in the study of Shayesteh et al, most of the cases (69%) were reported as Marsh 1 and 2, showing the diagnosis of CD before worsening of the disease (43), which may be influenced by genetic, ethnical, and environmental factors such as the time of first exposure to gluten and the amount of wheat in individuals' diet (3,46).

## CONCLUSION

Considering the high prevalence of CD (6.5%) in the patients with IBS and the overlap of the two diseases as well as the importance of timely diagnosis of CD, high-sensitivity serological tests are suggested to be performed for the screening of CD in patients with IBS.

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## CONFLICT OF INTEREST

The authors declare no conflict of interests related to this work.

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