

Celiac Disease in Patients with Irritable Bowel Syndrome

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Abstract: Background and purpose: The symptoms of celiac disease are often confused with the symptoms of IBS, which makes diagnosing celiac disease that much more difficult. Between 5 and 15% of those diagnosed with celiac disease were originally diagnosed with IBS, suggesting that celiac disease testing in this population is very important. This study was done to detect celiac disease in IBS population as this will help to give proper treatment and have a better outcome. **Study design:** Cross sectional study. **Place:** Internal medicine department, Kasr Al Ainy Hospital, Internal Medicine department, Beni suef university hospital. **Subjects & Method:** 160 patients diagnosed with irritable bowel syndrome by using Rome IV criteria. Their age ranged from 18 to 45 years old. **Assessment:** The assessment was carried out by obtaining full personal history and diagnosing irritable bowel syndrome according to Rome IV criteria. Full clinical general and abdominal examination was done. Laboratory investigations were done in the form CBC, stool analysis, liver function tests and anti-tissue transglutaminase screen test for celiac disease. Anti-tissue transglutaminase test is a sensitive and specific test (98% and 96%) respectively. Patients with positive tests were submitted to duodenal biopsy to confirm the possibility of celiac disease. The gained measures were analyzed by using SPSS program were used to compare between groups. **Results:** This study included 160 patients with IBS diagnosed by Rome IV criteria, 22 of them were males and 138 females, the patients with age ranging from 18 to 45 years. Anti-Tissue-Transglutaminase screening and standard biopsy were taken detect prevalence of celiac disease among IBS patients was 2.5%.

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Key words: celiac disease /irritable bowel syndrome / Rome IV criteria

1. Introduction and rationale

Celiac disease is an inflammatory small bowel disease caused by intolerance to ingestion of gluten found in cereal grain. Classical symptoms of the disease in adults are abdominal cramps, abdominal distention and chronic diarrhea or constipation or both [1]. Irritable bowel syndrome (IBS) is a chronic condition that affects the large intestine. Symptoms of IBS include cramping, abdominal pain, bloating, gas, diarrhea and constipation. Symptoms can vary for each individual and can sometimes be controlled with managing diet, lifestyle and stress [2]. The symptoms of celiac disease are often confused with the symptoms of IBS, which makes diagnosing celiac disease that much more difficult. Between 5 and 15% of those diagnosed with celiac disease were originally diagnosed with IBS, suggesting that celiac disease testing in this population is very important [3]. The prevalence of celiac disease in people who also have IBS is 4 times greater than in the general population [2]. Because of the overlap between these two conditions, celiac disease is often missed or misdiagnosed as irritable bowel syndrome. But getting the right diagnosis is important. People need to know whether they have celiac disease or not as it is the best way to ensure that they get the correct diagnosis to

make changes to their diet and receive the proper treatment.

2. Patients and Methods

This study was done on 160 patients diagnosed with irritable bowel syndrome by using Rome IV criteria. Their age ranged from 18 to 45 years old. The assessment was carried out by obtaining full personal history and diagnosing irritable bowel syndrome according to Rome IV criteria. The Rome IV criteria require that patients have had recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with 2 or more of the following: Related to defecation (may be increased or unchanged by defecation), associated with a change in stool frequency and associated with a change in stool form or appearance. It only requires abdominal pain in defining this condition; "discomfort" is no longer a requirement owing to its non specificity, and the recurrent abdominal pain and differs in basing bowel habits on stool forms solely during days with abnormal bowel movements rather than on the total number of bowel movements [4].

Full clinical general and abdominal examination was done. Laboratory investigations were done in the form CBC, stool analysis, liver function tests and anti-

tissue transglutaminase screen test for celiac disease. Anti-tissue transglutaminase test is a sensitive and specific test (98% and 96%) respectively. Patients with positive tests were submitted to duodenal biopsy to confirm the possibility of celiac disease. The gained measures were analyzed by using SPSS program were used to compare between groups.

3. Results:

This study included 160 patients with IBS, 22 of them were males (13.8%) and 138 females (86.2%), the patients with age ranging from 18 to 45 years with mean age 31.04 ± 8.03 . The distribution of IBS patients according to the age group was illustrated in table (1).

As regards to IBS there were three types Constipation-predominant, Diarrhea-predominant and alternating constipation-diarrhea, the distribution of the IBS patients as regards to age showed that 46 patients with alternating constipation-diarrhea with mean age 31.78 ± 7.48 , 34 patients with Diarrhea-predominant with mean age 28.12 ± 6.632 and 80 patients with constipation-predominant with mean age 31.85 ± 8.74 .

Table (1): Frequency distribution of age group among IBS patients:

Age group	Number	Percent (%)
18-25	48	30
26-35	70	43.8
36-45	42	26.2
Total	160	100

The distribution of IBS patients according to the gender showed that 22 males who represented 13.75% of all IBS patients, 8 of them had Constipation-predominant IBS (5%), 10 with Diarrhea-predominant IBS (6.25%) and 4 with alternating constipation-diarrhea IBS (2.5%) while females who represented 138 of IBS patients found that 72 of them had Constipation-predominant IBS (45%), 24 with Diarrhea-predominant IBS (15%) and 42 with alternating constipation-diarrhea (26.25) with no significant difference between them as shown in table (2).

Table (2): Frequency distribution of patients according to gender and IBS types:

IBS	Gender				Total	p-value
	Male		Female			
	No	%	No	%		
C/D-IBS	4	18.8	42	30.34	46	0.109 (NS)
D-IBS	10	45.45	24	17.39	34	
C-IBS	836.36		72	52.17	80	
Total	22	100	138	100	160	

By applying of Rome (IV) criteria, IBS can be diagnosed that patients had recurrent abdominal pain on average at least 1 day per week during the previous 3 months that is associated with changing in defecation, a change in stool frequency and associated with a change in stool form or appearance. Also, requires abdominal pain in defining this condition, we classified symptoms of IBS according to their types as shown in table (3).

Table (3): Flatulence, Colic and pain relieved defecation among different types of IBS patients:

Symptoms	C/D-IBS		D-IBS		C-IBS		Total	P-value
	No	%	No	%	No	%		
Flatulence								0.5
Yes	28	60.86	26	76.47	58	72.5	112	
No	18	39.13	8	23.53	22	27.5	48	
Total	46	100.0	34	100.0	80	100.0	160	
Colic								0.735
Yes	36	78.2	24	70.6	64	80	124	
No	10	21.8	10	29.4	16	20	36	
Total	46	100.0	34	100.0	80	100.0	160	
Pain								0.053
Yes	42	91.3	20	58.8	62	77.5	124	
No	4	8.9	14	41.2	18	22.5	36	
Total	46	100.0	34	100.0	80	100.0	160	

By analysis of the CBC results of the 160 IBS patients, found that 110 patients had normal hemoglobin (HB above 13mg/dl for male and above 12mg/dl for female), 48 with anemia (HB 8-12mg/dl) and only two patients with severe anemia (HB below 8mg/dl) and also biochemical profile of the patients showed that all IBS patients had normal kidney

function test including serum creatinin, serum Na and blood urea but 16 of them had hypokalemia (10 D-IBS and 6 C-IBS) as well as liver function test including bilirubin, ALT, AST and prothrombin concentration were normal in all IBS patients but 14 of them showed hypokalemia (10 D-IBS, 2 C-IBS and 2 C/D-IBS) as illustrated in table (4).

Table (4): CBC, serum potassium and Albumin level among different types of IBS patients:

	C/D-IBS		D-IBS		C-IBS		Total	P-value
	No	%	No	%	No	%		
Hemoglobin								
Normal	34	73.9	22	64.7	54	67.5	110	0.4
Anemia	12	26.1	10	29.41	26	32.5	48	
Severe	0	0	2	5.88	0	0	2	
Total	46	100.0	34	100.0	80	100.0	160	
Serum potassium								
Normal	46	100	24	70.6	74	92.5	144	0.007*
Hypokalemia	0	0	10	29.4	6	7.5	16	
Total	46	100.0	34	100.0	80	100.0	160	
Albumin								
Normal	44	95.6	24	70.58	78	97.5	146	0.003*
Hypoalbuminemia	2	4.34	10	29.4	2	2.5	14	
Total	46	100.0	34	100.0	80	100.0	160	

The table showed that there was significant difference between IBS types and hypokalemia with p-value 0.007 and with hypoalbuminemia with p-value 0.003 which mean that IBS is a risk factor for hypokalemia and hypoalbuminemia.

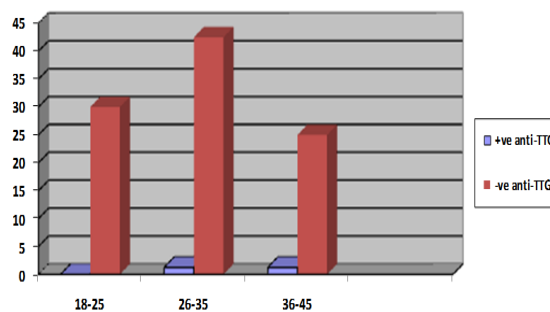
By using Anti-Tissue-Transglutaminase screening using ELISA method and also standard biopsy were taken from the second and third portion of duodenum to detect prevalence of celiac disease among IBS patients the following results found.

Table (5): The prevalence of celiac disease in different types of IBS:

	C/D-IB (n=46)	D-IBS (n=34)	C-IBS (n=80)	Total	P-value
No of positive of anti-tTG	2	2	0	4	0.57 (NS)
No of villous atrophy	2	10	0	12	
No of celiac disease	2	2	0	4	
Prevalence of celiac disease	1.25%	1.25%	0	2.5%	

As regards to the frequency distribution of different age group among patients with celiac disease found that about 50% of celiac disease patients (1.25% of total IBS) were between age 26-35 and 50% were between age group 36-45 years old as illustrated in graph (1):

As regards of laboratory measurements among the celiac and non-celiac patients, there was no significant regarding the serum potassium while the was high significant difference between them regarding albumin level which mean that IBS is a risk factor for hypoalbuminemia as showed in table (7).



Graph (1): Frequency distribution of different age group among the studied patients.

Table (7): Hemoglobin level, serum potassium and albumin level among positive and negative anti-TTG patients:

	Positive anti-TTG		Negative anti-TTG		Total	P-value
	No	%	No	%		
Hemoglobin						
Normal	2	50	64	41	66	NS
Anemia	2	50	88	56.41	90	
Severe	0	0	4	2.56	4	
Total	4	100.0	156	100.0	160	
Serum potassium						
Normal	2	50	142	91.08	144	0.056
Hypokalemia	2	50	14	8.9	16	
Total	4	100.0	156	100.0	160	
Albumin						
Normal	0	0	146	93.58	146	0.000*
Hypoalbuminemia	4	100	10	6.4	14	
Total	4	100.0	156	100.0	160	

Interestingly, only two (50%) of celiac disease patients had signs of intestinal malabsorption on further laboratory testing, with anemia and hypoalbuminemia being the most common abnormality. The other patient has normal laboratory findings. All patients diagnosed with celiac disease were started on a gluten-free diet, with subsequent improvement of their IBS-like symptoms.

4. Discussion

This study included 160 patients with IBS, 22 of them were males (13.8%) and 138 females (86.2%), the patients with age ranging from 18 to 45 years with mean age 31.04 ± 8.03 . As regards to IBS there were three types Constipation-predominant, Diarrhea-predominant and alternating constipation-diarrhea, the distribution of the IBS patients as regards to age showed that 46 patients with alternating constipation-diarrhea with mean age 31.78 ± 7.48 , 34 patients with Diarrhea-predominant with mean age 28.12 ± 6.632 and 80 patients with constipation-predominant with mean age 31.85 ± 8.74 . The distribution of IBS patients according to the gender showed that 22 males who represented 13.75% of all IBS patients, 8 of them had Constipation-predominant IBS (5%), 10 with Diarrhea-predominant IBS (6.25%) and 4 with alternating constipation-diarrhea IBS (2.5%) while females who represented 138 of IBS patients found that 72 of them had Constipation-predominant IBS (45%), 24 with Diarrhea-predominant IBS (15%) and 42 with alternating constipation-diarrhea (26.25) with no significant difference between them.

The most frequent reasons for CD screening in our study in IBS cases were 112/160 presenting with bloating, 34/160 with diarrhea, 80/160 with constipation and 124/160 with colicky abdominal

pain. By analysis of the CBC results of the 160 IBS patients, found that 110 patients had normal hemoglobin (HB above 13mg/dl for male and above 12mg/dl for female), 48 with anemia (HB 8-12mg/dl) and only two patients with severe anemia (HB below 8mg/dl) and also biochemical profile of the patients showed that all IBS patients had normal kidney function test including serum creatinine, serum Na and blood urea but 16 of them had hypokalemia (10 D-IBS and 6 C-IBS) as well as liver function test including bilirubin, ALT, AST and prothrombin concentration were normal in all IBS patients but 14 of them showed hypokalemia (10 D-IBS, 2 C-IBS and 2 C/D-IBS). The table showed that there was significant difference between IBS types and hypokalemia with p-value 0.007 and with hypoalbuminemia with p-value 0.003 which mean that IBS is a risk factor for hypokalemia and hypoalbuminemia.

In the current study the frequency distribution of different age group among patients with celiac disease found that about 50% of celiac disease patients (1.25% of total IBS) were between age 26-35 and 50% were between age group 36-45 years old As regards of laboratory measurements among the celiac and non-celiac patients, there was no significant regarding the serum potassium while the was high significant difference between them regarding albumin level which mean that IBS is a risk factor for hypoalbuminemia. Only two (50%) of celiac disease patients had signs of intestinal malabsorption on further laboratory testing, with anemia and hypoalbuminemia being the most common abnormality. The other patient has normal laboratory findings. All patients diagnosed with celiac disease were started on a gluten-free diet, with subsequent improvement of their IBS-like symptoms. In a study

done by **Catassi et al. [5]** in North America included 976 participant with a symptom associated with CD including IBS with serologically tested for CD. A diagnosis of CD was established in 22 patient and the prevalence of CD was in the sample was 2.25%.

In a case-control study performed by **Zobeiri et al., [6]** 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. 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% ($P = 0.5$). 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 ($P = 0.215$).

While in the study of **Shahbazkhani et al. [7]** has reported 11.4% positive anti-endomyosial antibodies (AEM) in patients with IBS and in 1 of every 166 healthy Iranian individuals. **Saberi-Firouzi [8]** 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. **Mein and Ladabaum [9]** 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. Screening for CD with IgA AEM with respect to the sensitivity of 98%–75% and specificity of 100%–96% approved. 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% **[10]**.

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