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Prevalence of Celiac Disease among Cases of Irritable Bowel Syndrome in Baghdad, Iraq

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Abstract

Celiac disease is a common illness need not to be mistaken as IBS or GI motility disorders and careful evaluation of IBS patients especially those with diarrhea predominant type may need to be considered.

This study disclose that about more than 12% of patients who had been already diagnosed as IBS is discovered to have positive serology of gluten sensitivity and the diagnosis of Celiac disease had been confirmed by histopathology study.

Though and careful evaluation of presumed cases of IBS especially those with poor response to conventional therapy or those who with atypical presentations is essentialin order to reach to an alternative diagnoses.

Keywords: *Celiac disease, Gluten sensitivity, Irritable bowel syndrome, Anti tissue transglutaminase, Gluten free diet.*

Introduction

Celiac disease is a common cause of malabsorption of one or more nutrients. Recent observations have established that it is a common illness with protean manifestations, a worldwide distribution is approximately 1%.[1]

Its incidence has been raised over the past five decades. Celiac disease has several other names, as nontropical sprue, celiac sprue, and gluten-sensitive enteropathy,the etiology of celiac disease is not completely understood, but immunologic; environmental; and genetic factors imply the major role in pathogenesis.

Celiac disease is considered an "iceberg" disease. A few number of patients have classic symptoms and manifestations linked to micronutrient malabsorption along with a varied natural history; the onset of symptoms can occur at all points of life, though the disease has two peaks of ages: the first is early in life, at approximately 2 years of age (after gluten containing diets has been introduced), or later in the second to fourth decades of life. It may first manifest after an attack of prolong diarrhea following gastroenteritis or even after abdominal surgery.[2]

A larger number of patients have "atypical celiac disease," with presentations that are not obviously linked to small intestine malabsorption (e.g., anemia, infertility, osteopenia, and neurologic and psychological manifestations). Even larger figure of patients have "silent celiac disease"; they are essentially asymptomatic despite abnormal small-intestinal histopathology and positive gluten sensitivity serology.

Other symptoms of patients with celiac disease may range from significant malabsorption of multiple nutrients, with diarrhea;weight loss; steatorrhea;and the consequences of nutrient depletion (i.e., metabolic bone disease and anemia), to the total absence of gastrointestinal symptoms despite evidence of the depletion of a singlenutrient (e.g., iron or folate deficiency;edema;osteomalacia from protein loss).[3]

Both IBS and gluten sensitivity are common in the general population and both can coexist with each other independently without necessarily sharing a common pathophysiological basis.[4]

Not all patient with IBS or IBS predominant diarrhea is candidate for screening for gluten sensitivity but testing should be considered in the following situations :

1. Patients with GI symptoms including recurrent or chronic diarrhea;weight loss;malabsorption and abdominalbloating or distension and severe lactose intolerance.
2. Patients with noalternative explanations for extraintestinal manifestations of combined nutritional deficiencies and/or anemia, persistent transaminitis, delayed puberty, short stature, females with recurrent abortions, hypofertility, recurrent aphthous ulcers, dental enamel hypoplasia, idiopathic peripheral neuropathy or cerebellar ataxia, or recurrent atypical migraine.
3. Patients with type 1 diabetes mellitus if they present with clinical manifestations of presumed celiac disease.
4. Asymptomatic first-degree relatives of patients with an established celiac disease.

These recommendations are consistent with the American College of Gastroenterology guidelines.[5]

The Rome III criteria can establish the diagnosis of IBS without further extensive testing and seeking for alternative diagnoses may be considered in cases of nocturnal diarrhea, symptoms unrelated to food or defecation. Alarm features that raise the concern of other diagnosis in presumed IBS cases are weight loss, anemia, bloody stool, positive family history of inflammatory bowel diseases, colonic cancer or celiac disease.

It is very important to remember that patients with celiac disease is at high risk of several malignancies like esophageal and intestinal adenocarcinoma, B- cell MALT lymphoma, hence increased mortality, so strict gluten free diet is essential.[2]

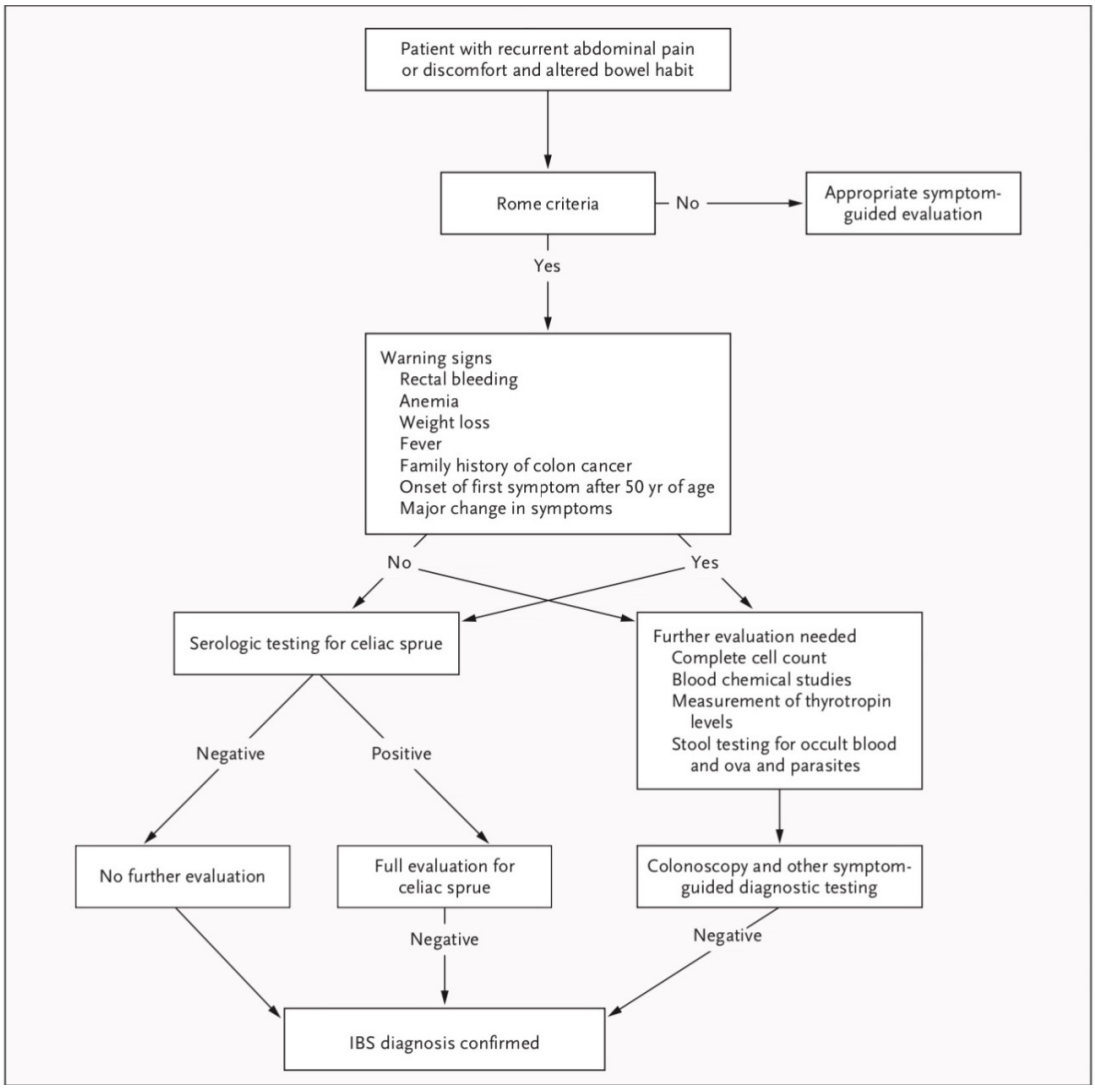

Figure 1 Testing for celiac disease in cases with diagnosed IBS depending on Rome criteria, especially in cases of diarrhea predominant IBD or there is possible alternative diagnosis other than IBS[6]

Diagnosis

Serum Antibody Assays:

1. IgA endomysial antibody (IgA EMA)
2. Immunoglobulins tissue transglutaminase antibody (IgA tTGA and IgG tTGA).
3. Immunoglobulins deamidated gliadin peptide (IgA DGP and IgG DGP)

All patients with Celiac disease express the HLA-DQ2 or HLA-DQ8 allele, although only a minority of people expressing DQ2/DQ8 have celiac disease. Absence of DQ2/DQ8 excludes the diagnosis of celiac disease.

Endoscopic small bowel mucosal biopsy is the gold standard. Endoscopic biopsy is mandatory in suspected cases even if mucosalooks normal. As the histological changes can be patchy, multiple biopsies – usually, more than four biopsies from the second part of the duodenum in addition to one from the duodenal bulb – should be obtained.[7]

Histopathological feature mainly seen are villous atrophy or completely absent with a reduced villous-to-crypt ratio and crypts looks hyperplastic. There is increase in cellularity of the lamina propria with a mainly plasma cells and lymphocytes. The number of intraepithelial lymphocytes per unit length of absorptive epithelium is usually increased.[8]

Modified Marsh Classification of histologic findings in celiac disease (Oberhuber)

Marsh Type	IEL / 100 enterocytes – jejunum	IEL / 100 enterocytes - duodenum	Crypt hyperplasia	Villi
0	<40	<30	Normal	Normal
1	>40	>30	Normal	Normal
2	>40	>30	Increased	Normal
3a	>40	>30	Increased	Mild atrophy
3b	>40	>30	Increased	Marked atrophy
3c	>40	>30	Increased	Complete atrophy

- IEL/100 enterocytes, intraepithelial lymphocytes per 100 enterocytes
- Type 0: Normal; celiac disease highly unlikely.
- Type 1: Seen in patients on gluten free diet (suggesting minimal amounts of gluten or gliadin are being ingested); patients with dermatitis herpetiformis; family members of celiac disease patients, not specific, may be seen in infections.
- Type 2: Very rare, seen occasionally in dermatitis herpetiformis.
- Type 3: Spectrum of changes seen in symptomatic celiac disease.

Patients and Method

A cross sectional study conducted at Alyarmouk teaching hospital internal medicine outpatient clinic from the period of march 2018 to march 2019 involving 140 patients who had been labeled as IBS or presented with recurrent symptoms highly suggestive of IBS.

Inclusion criteria are patients had been previously diagnosed by general practitioner, physician, or gastroenterologist as having irritable bowel syndrome based on symptoms such as recurrent abdominal discomfort, colicky abdominal pain, altered bowel habits, and bloatingat time of presentation.

Exclusion criteria are patients with recent infectious diarrhea, history of inflammatory bowel disease, peptic ulcer disease, gastrointestinal malignancies, previous gastrointestinal surgeries, alcoholism and patients with advanced chronic illnesses (chronic renal failure, long term diabetes mellitus, and congestive heart failure).

The patients had been re-evaluated regarding the diagnosis either due non convincing response to IBS therapy, insufficient initial work up, or new symptoms had been developed.

Screening for gluten sensitivity had been done by using anti tissue transglutaminase (tTGA)assay then the patient with positive results undergone upper endoscopy and histopathological analysis of multiple biopsy specimens from second part of duodenum to confirm the diagnosis.

All the patients who had been diagnosed as Celiac disease undergone complete evaluation for anemia and micronutrient deficiency with CBC, serum ferritin, B12, and vitamin D level.

The patient who had been confirmed to have celiac disease established on gluten free diet and set for follow up.

Statistical Analysis: Analysis of data was carried out by available statistical package (version 25). Statistical significance was considered at (P value ≤ 0.05).

Findings: This study which in cover 140 IBS cases, in which each case had been assessed for possible gluten sensitivity and the results were 17 patients of 140 (12.1%) have positive serology for gluten sensitivity,all the cases with positive serology undergone upper endoscopy which confirm the diagnosis of celiac disease.

Fourteen of 17 patient (82.4%) who were positive were females and 3 (17.6%) were males in which it carry no statistical significance. P =0.585.

Most of these cases were diarrhea predominant IBS 10 of 17 (58.8%) where as 7 (42.2%) were constipation predominant type. Table 1

Table 1: Classification of patients according to age;gender and type variant of IBS in relation with positivity of tTGA

		Anti Tissue Transglutaminase						P value
		Total		Positive		Negative		
		No	%	No	%	No	%	
Age (Years)	<20y	9	6.4	1	5.9	8	6.5	0.405
	20---29	22	15.7	5	29.4	17	13.8	
	30---39	35	25.0	5	29.4	30	24.4	
	40---49	41	29.3	5	29.4	36	29.3	
	50---59	28	20.0	1	5.9	27	22.0	
	=>60y	5	3.6	-	-	5	4.1	
	Mean±SD (Range)	39.2±12.2 (15-79)		33.0±8.9 (19-50)		40.0±12.4 (15-79)		
Gender	Male	32	22.9	3	17.6	29	23.6	0.585
	Female	108	77.1	14	82.4	94	76.4	
Variant of Irritable Bowel	IBS-C	98	70.0	7	41.2	91	74.0	0.006*
	IBS-D	42	30.0	10	58.8	32	26.0	
*Significant difference between proportions using Pearson Chi-square test at 0.05 level.								

IBS-C irritable bowel syndrome – constipation, IBS-D irritable bowel syndrome - diarrhea

All the 17 cases with positive serology were undergone upper endoscopy and biopsy specimen had been obtained from second part of duodenum and sent for histopathological analysis.

The results of histopathological finding were positive for features of Celiac disease and were ranging from (2-3b) modified Marsh Classification of histologic finding in celiac disease (Oberhuber); 8 Patients type 2, 7 Patients type3a, and 2 patients type 3b. Figure 2

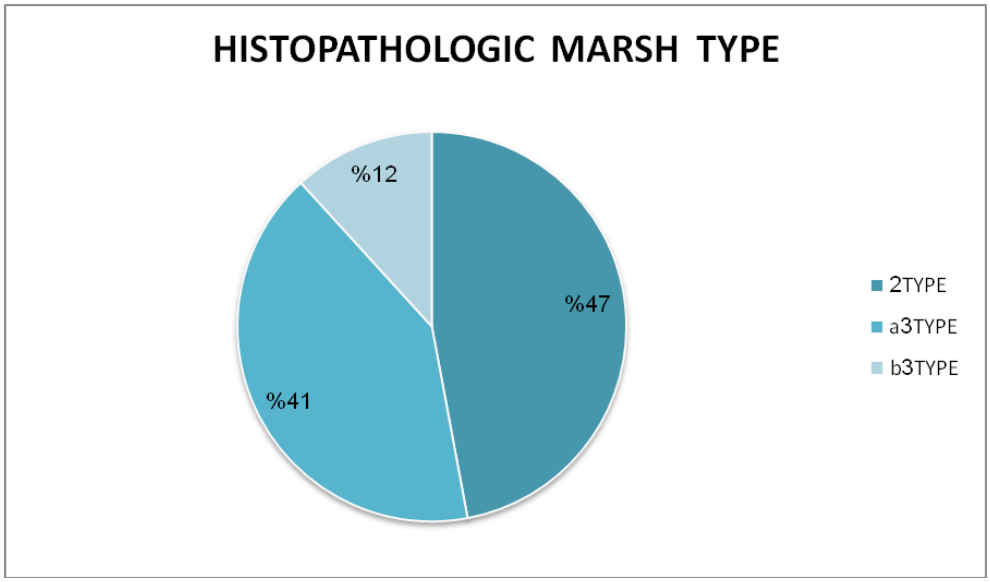

Figure 2: Histopathological finding in patient with positive anti tissue transglutaminase.

Among the total 17 patients, 10 has anemia (7 cases hypochromic microcytic anemia and the rest 3 has normochromic normocytic anemia and no cases of megaloblastic anemia seen despite that there were 3 cases discovered to have B 12 deficiency in which they were had normal hemoglobin and MCV level)Figure 3. All the 7 cases of hypochromic microcytic anemia is confirmed to be iron deficiency anemia as well as 2 cases of normochromic anemia and 3 non anemic patients were had below normal ferritin level; so the total number was 12 of 17 hashad iron deficiency state. Lastly all patients found to have vitamin D level below the reference range. Table 2.

All the cases who had been confirmed to be Celiac disease had been advised for gluten free diet and follow up.

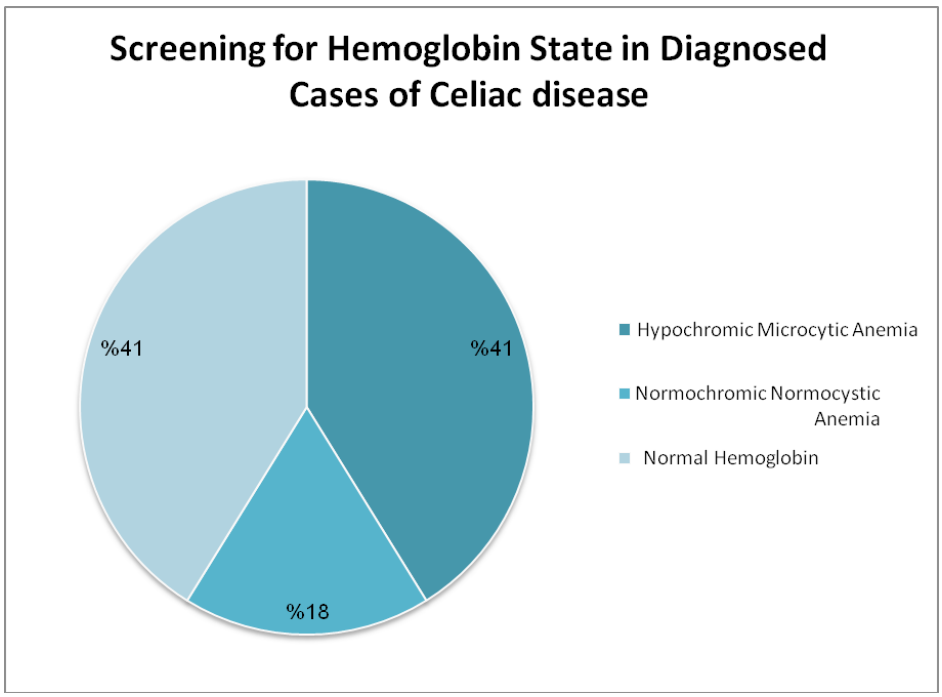

Figure 3: Hemoglobin state in cases of Celiac disease

Table 2: Micronutrient State in cases with Celiac disease

Screening for micronutrient deficiency in Diagnosed cases of Celiac Disease					
Vitamin D3		Vitamin B12		Iron State	
Normal	Deficient	Normal	Deficient	Normal	Deficient
0 (0%)	17 (100%)	14 (82%)	3 (17.6%)	5 (29.4%)	12 (70.5%)

Discussion

Celiac disease is one of the most readily missed illnesses in practice due to the complexity of gastrointestinal symptoms associated with this disease, such as flatulence,diarrhea or rarely constipation, abdominal cramps and fullness which may overlap with other various gastrointestinal illnesses, such as inflammatory bowel diseases, chronic infections and helminth infestation, other food allergies, lactose intolerance, motility disorders and irritable bowel syndrome.

The lack of history or features of micronutrients deficiency, mineral bone diseases and other cutaneous and neurological manifestations of celiac disease does not exclude the presence of this syndrome. So thorough evaluation for gluten sensitivity is essential in presumed cases of IBS which not respond to conventional dietary and medical approaches and carry the same importance of excluding inflammatory bowel disease or other pathologies that may simulate IBS.

Although it has to be pointed that some IBS cases with no evidence of gluten sensitivity may surprisingly get significant benefit in improvement of their symptoms after exclusion of gluten containing food from their diet.

According to this study there is significant number of those patients who had been diagnosed and managed as IBS are actually haveCeliac disease, especially those with diarrhea predominant subtype.

The usual work up of patients who present with symptoms suggestive of IBS does not involve regularly screening for gluten sensitivity or any form of food allergies unless the patient has features of malabsorption ofmicronutrients, diarrhea, steatorrhea, weight loss or coexistence of dermatitis herpetiformis.

Still early diagnosis of Celiac disease and establishment of gluten free diet is essential to prevent long term serious complications other than vitamin and minerals malabsorption such us ulcerative jejuno-ileitis, small intestinal lymphoma and small bowel adenocarcinoma.[9]

As compared with the study*The prevalence of celiac disease in patients with irritable bowel syndrome and its subtypes* byDanuta Domżał-Magrowskawho had been published in Przegląd Gastroenterologiczny 2016 in which concomitant positive result of genetic testing and any elevated serum antibodies specific to celiac disease was found in 12.5% of IBS patients.[10]

So this study carry a highly comparable results, Screening for anemia and micronutrient deficiency in the cases who had been confirmed to have Celiac disease reveals that anemia is present in 10 of 17 cases (58.8%) that was mainly of iron deficiency which is the most common type of nutritional anemia in Celiac disease, there is also significant number of cases with iron deficiency state to be added to cases of IDA to be a total of 12 of 17 (70.1%).

Mainly because of small size of sample there is no case with megaloblastic anemia detected but still there are 3 cases with low serum B12 level. It is also important to be referred that there is no data available about folate statues in our study because lack of availability of reliable test for red blood cell folate in our facility at time of the study and the level of serum folate does not reflect the actual folate level state.

Vitamin D deficiency is present in all cases who had been diagnosed as Celiac disease but it may reflect the high prevalence of vitamin D deficiency among Iraqi patients in general as well as the effect of Celiac disease on lipid soluble vitamins absorption.

Finally it is important to follow up all the patients who had been diagnosed as celiac disease regarding improvement in their GI symptoms following exclusion of gluten from their diet, if not, the coexistence of IBS or other GI pathologies still possible and careful clinical re-evaluation is warranted.

Conclusions

There is significant number of celiac disease patient had been diagnosed and managed as IBS cases (mainly diarrhea predominant type) and there may be coexistence of both illnesses in the same patient.

Ethical Clearance: No

Source of Findings: Self

Conflict of Interest: Nil

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