

A Prospective Unicentric Study of the Prevalence of Celiac Disease in Patients with Irritable Bowel Syndrome (IBS).

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ABSTRACT

Background: Aim: To investigate the prevalence of celiac disease among those that fulfill the Rome III criteria for IBS. **Methods:** We conducted a prospective study to investigate prevalence of celiac disease in patients fulfilling Rome III criteria for IBS. Patient's with gastrointestinal alarm symptoms or signs like weight loss, blood in stool or vomitus, severe abdominal pain, pregnancy and HIV were excluded from study. Anti-tissue transglutaminase serology sent to recognize possible celiac disease cases. Endoscopic duodenal biopsy done to confirm diagnosis of celiac disease and histopathological staging done according to modified Marsh grading. Descriptive analysis of celiac disease in Irritable Bowel Syndrome presented in terms of percentage and its 95% confidence interval. Chi-square test was performed to assess prevalence of celiac disease in different types of IBS. **Results:** Out of 200 patients fulfilling Rome III criteria, IgA anti-tissue transglutaminase antibody was positive in 4 patients and duodenal biopsies confirmed the diagnosis in all of them. Thus, in this patient population with presumed IBS, 2% actually had Crohn's disease (CD). **Conclusion:** The prevalence of celiac disease in patients with presumed IBS is high therefore serological testing should be carried out in patients with symptoms of IBS particularly mixed type IBS (IBS-M) or Direct predominant IBS (IBS-D). Though larger multicenter studies required to confirm this association.

Keywords: Celiac Disease, Irritable Bowel Syndrome.

INTRODUCTION

Celiac disease is increasingly recognized autoimmune enteropathy caused by a permanent gluten intolerance. Gluten is the main storage protein of wheat, in genetically predisposed individuals, immune response to prolamins leads to injury to enterocytes. Celiac disease shares several symptoms which constitute some of the Rome criteria used for the diagnosis of irritable bowel syndrome (IBS), and as such many patients with underlying Celiac disease may be mistakenly diagnosed as having IBS. IBS can sometimes be difficult to distinguish clinically from adult-onset celiac disease.^[1,2] A broad spectrum of symptoms and signs may be associated with untreated CD. In fact, many patients - especially those presenting in adulthood - have minimal or atypical symptoms.^[3] The recent development of highly sensitive and specific serologic assays for CD has led to the increased realization that the disease is more common than it was believed.^[4,5]

This justifies the concern that some IBS-labeled patients may in fact have CD. Studies suggest that the prevalence of celiac disease is increased in individuals with IBS; however, evidence is conflicting, and current guidelines do not always recommend screening for celiac disease in these individuals. The aim of this study is to estimate the prevalence of CD in patients masquerading as IBS.

MATERIALS AND METHODS

Study Design

This is a prospective single centre study carried out at Lokmanya Tilak Municipal General Hospital between August 2011 and June 2013. An informed consent was taken from all patients. The institutional Ethics Committee clearance was taken.

Patients

The Rome III criteria for IBS were applied to 216 consecutive patients upon their first visit to our outpatient gastroenterology clinic in the period between August 2011 and June 2013.

Inclusion criteria

- Patients with irritable bowel syndrome diagnosed by Rome III criteria.
- Age > 18 years

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Exclusion criteria

- History of gastrointestinal alarm symptoms or signs like significant weight loss, blood in stool or vomitus, acute severe abdominal pain, fever, large volume diarrhoea , steatorrhea.
- Evidence of organic disease on USG or routine investigations.
- HIV positive
- Diabetes and dermatitis herpetiformis
- Unwillingness to be submitted to esophagogastroduodenoscopy.
- Pregnancy

Patients were approached in gastroenterology outpatient department of Sion hospital. Patients fulfilling the inclusion criteria were enrolled in the study after proper explanation about the study and were requested to participate. After an informed consent, patients were interviewed according to a specially prepared proforma. Total 204 individuals were eligible to participate in the study, and 4 of them did not give consent and thus were excluded from the study. So, total 200 patient’s detailed demographic profile and clinical history were taken regarding illness and complete examination was done. Patients based on the sub-type of IBS were classified as diarrhoea-predominant irritable bowel syndrome (D-IBS), constipation-predominant irritable bowel syndrome (C-IBS) and alternating symptoms (mixed type).

Investigations

Patients advised to get their complete blood count, liver profile, serum protein and albumin, renal function tests,ESR, thyroid profile, stool routine microscopy.

IgA anti-tTG test advised using the ELISA method. The sensitivity and specificity of this test in laboratory was previously estimated at 98% and 95%, respectively.

All patients advised ultrasonography at radiology department Sion hospital.

Upper G.I. endoscopy with duodenal biopsy (using standard biopsy forceps six specimens from second and third part of duodenum) done in those who were IgA anti tTG positive. Upper G.I. endoscopy and biopsy done free of cost and the samples evaluated by the Pathology Department, Sion hospital.Staging of biopsy specimen done according to modified Marsh classification.

ROME III criteria for irritable bowel syndrome:

- Onset of symptoms at least 6 months before diagnosis
- Recurrent abdominal pain or discomfort (uncomfortable sensation not described as pain) for >3 days per month during past 3 months
- Associated with 2 or more of the following:
 - Improvement with defecation
 - Associated with a change in frequency of stool
 - Associated with a change in form of stool

Table 1: The modified Marsh classification of celiac disease.

Type	Intraepithelial lymphocytes per 100 enterocytes	Crypts	Villi
0	< 40	Normal	Normal
1	>40	Normal	Normal
2	>40	Increased	Normal
3a	>40	Increased	Mild atrophy
3b	>40	Increased	Marked atrophy
3c	>40	Increased	Absent

Statistical analysis

Continuous data were described using mean, median, standard deviation, and range wherever appropriate. Categorical variables were described using proportions. The 95% confidence interval (CI) was used to calculate the interval estimate of the prevalence of CD. Differences in prevalence rates according to different types of IBS were tested using χ^2 test; a P-value of less than 0.05 was considered statistically significant.

RESULTS

Study included total of 200 patients (114 males, 86 females) with a mean age of 32years ,range 18 to 52years. Their distribution according to gender and type of IBS is shown in [Table 2].

Four patients, two IBS-D and two IBS-M tested positive for IgA anti tTG.Out of them 2 were male. Duodenal biopsy confirmed the diagnosis in all four patients. Modified Marsh criteria was used for grading histopathological changes. Among celiac disease patients two had Marsh grade 2 and two had Marsh grade 3A.Thus in these patient population with presumed IBS 2% actually had celiac disease. The prevalence of celiac disease in patients with IBS-D was (2 out of 28) 7.1% and in IBS-M was (2 out of 70) 2.8%. The age of patients with CD (2 females and 2 males) ranged from 25 to 32 years with a mean of 28.7years.Out of these 50% were IBS-D and 50% were IBS-M. No patient with IBS-C was positive for IgA anti tTG.

The demographic and clinical features of CD patients are summarised in [Table 5]. Duration of IBS symptoms before diagnosis of celiac disease range from 6 to 50 months with a mean of 24 months. Iron deficiency anaemia was present in 2 patients.No patients with celiac disease has BMI < 18.5, average BMI was 21.Gluten free diet leads to clinical improvement in IBS like symptoms in all patients after a period of 2 to 6 weeks.

Table 2: Distribution according to gender and type of IBS

	IBS-D	IBS-C	IBS-M
Male(114)	16	60	38
Female(86)	12	42	32
Total(200)	28	102	70

Table 3. Prevalence of celiac disease in different types of IBS

	Number of patients	No of Celiac disease	Percentage of celiac disease (95% CI)
IBS C	102	0	0
IBS D	28	02	7.1%(-2.41,16.61)
IBS M	70	02	2.8% (-1.06,6.66)
Total	200	04	2% (1.28,6.72)

Difference in prevalence of celiac disease between constipation type and non-constipation type is significant with P value 0.043(<0.05). Difference between IBS-D and IBS-M type is non significant with p value 0.36(>0.05). Difference between IBS-C and IBS-D is significant with p value 0.008(<0.05).

Table 4: Distribution of cases with celiac disease

IgA anti t TG positive patients	Age (year)	Sex (M/F)	Type of IBS (D/C/M)	Marsh grade in duodenal biopsy
1	28	F	M	II
2	30	F	D	IIIA
3	25	M	M	IIIA
4	32	M	D	II

Table 5: Demographic and clinical profile of patients with celiac disease

Gender	
Male	2(50%)
Female	2(50%)
Age	
18-35yrs	4(100%)
36-60yrs	0
BMI(Mean)	21
Duration of symptoms in months (Mean)	24
Iron deficiency anaemia	2(50%)

DISCUSSION

The prevalence of celiac disease in a recent population based study from India was 1.04%.^[5] Studies from North America and Europe have shown that upto 0.5 to 1% of adult population may have celiac disease.^[6,7] In contrast to its high prevalence in Western countries, CD is considered rare in non-Western populations. However, recent studies from the Middle East, Africa and India showed prevalence as high as 7.6% in selected groups of patients.^[8-10] In meta analysis of seven studies the pulled prevalence of biopsy proven celiac disease was 4.1% in IBS patients.^[11] Case control study of 300 subjects fulfilling Rome II criteria for IBS, Sander's and colleagues found that patients were 7 times more likely to have celiac disease than matched controls.^[2] Prevalence of celiac disease in patients with

presumed IBS was 2% in present study. This implies that even after strict application of Rome III criteria IBS patients may have undetected celiac disease. Previously regarded as a mainly childhood problem it is now recognized that celiac disease affects mostly adults with about 25% patients have been diagnosed over 60years of age. In present study mean age of IBS patients who diagnosed as celiac disease was 28.5yrs. In study by Makharia et al mean age of patients with celiac disease was 28.7years.^[3] Up to 50% of the patients with celiac disease may present with atypical or non gastro intestinal manifestations of celiac disease.^[3] Celiac disease can present with spectrum of insidious symptoms that can mimic IBS. Patients often have few or no gastrointestinal symptoms and can even be obese.^[12,13] In fact in present study none of the patients had typical features of celiac disease and, the majority of them had BMI in normal range.

No patients with IBS-C had positive celiac serology. So, routine screening for celiac disease in this subgroup of patients may not be cost effective. But this finding requires further validation in large study. All four patients, who diagnosed with celiac disease by serology as well as biopsy, were belong to either IBS-M or IBS-D. IBS-D has somewhat different pathogenesis than it's constipation associated counterpart. Patients with IBS-D have several underlying organic abnormalities such as small intestinal bacterial overgrowth, lactose intolerance and celiac disease.^[14,15] Similar to finding in our study, Jadallah et al reported celiac disease in 6.8% of IBS-D as compared to 1.68% of IBS-C patients.^[16]

Contrary to popular belief that total villous atrophy routinely seen in patients with celiac disease, no patients in our study had either subtotal or total villous atrophy. This finding correlate with lack of obvious malabsorption features in celiac disease patients in present study. Only two patients found to have iron deficiency anaemia, this suggests low grade inflammation rather than florid total villous atrophy leads to IBS like manifestations in patients with celiac disease. Celiac disease causes neuromyopathy of the gut muscle, which may result in symptoms similar to irritable bowel syndrome.^[17] There are some limitations in the present study. Ig A levels were not tested in present study which may lead to false negative results. IgA deficiency has been found in 2.5% of patients with celiac disease & 0.2% to 0.5% of general population.

CONCLUSION

The prevalence of celiac disease in patients with presumed IBS is high therefore serological testing should be carried out in patients with symptoms of IBS particularly IBS-M or IBS-D. Though larger multicenter studies required to confirm this result.

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