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Original Article

The prevalence of coeliac disease in patients fulfilling Rome III criteria for irritable bowel syndrome

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ABSTRACT

Background and study aim: The clinical presentation of coeliac disease can vary from a classical malabsorption syndrome to more subtle atypical gastrointestinal manifestations similar to irritable bowel syndrome (IBS). The aim of this study was to investigate the prevalence of coeliac disease in Egyptian patients with clinically diagnosed diarrhoea-predominant IBS (according to Rome III criteria).
Patients and methods: This study was conducted on 100 patients with clinically diagnosed diarrhoea-predominant IBS (fulfilling Rome III criteria). They were subjected to complete clinical evaluation, routine laboratory investigations, abdominal ultrasonography and serum anti-tissue transglutaminase antibody (anti-tTG) test as a predictor marker for coeliac disease. All patients who tested positive for serum anti-tTG underwent upper gastrointestinal endoscopy with four to eight biopsy samples collected from the second part of the duodenum.
Results: All of the studied 100 patients presented with abdominal pain or discomfort, flatulence and diarrhoea. Eight patients (8%) exhibited high levels of serum anti-tTG, and their duodenal biopsy samples satisfied the histopathological criteria of coeliac disease. The studied patients were divided into two groups: Group I comprising 92 patients with IBS and negative anti-tTG results and Group II comprising eight patients with IBS and positive anti-tTG results. A non-significant difference was noted between the two groups in age, gender and duration of abdominal pain ($p > 0.05$). The haemoglobin level was found to be significantly reduced in anti-tTG-positive patients ($p < 0.01$), as was the Na level in anti-tTG-negative patients ($p < 0.05$). A highly statistically significant inverse correlation was noted between anti-tTG and both serum total protein and serum albumin.
Conclusion: Some symptoms overlap between coeliac disease and IBS. A lack of awareness may lead to a diagnostic delay in these patients.

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterised by abdominal pain and altered bowel habits in the absence of a specific organic pathology. It is the most commonly diagnosed gastrointestinal condition, accounting for approximately 30% of all referrals to gastroenterologists [1].

Its prevalence varies in the human population and in the majority of the related literature; it is more common in females than in males [2]. IBS commonly affects the younger population, with the majority of new cases appearing before the age of 45 [1].

The Rome III criteria system was developed to classify functional gastrointestinal disorders based on clinical symptoms. Each disorder has its own set of criteria. The Rome III criteria for IBS are as follows: symptoms of recurrent abdominal pain or discomfort and a marked change in bowel habit for at least 6 months, with symptoms experienced on at least 3 days of at least 3 months. Two or more of the following criteria must be satisfied [3]:

- Pain is relieved by bowel movement.
- Onset of pain is related to a change in the frequency of stool.
- Onset of pain is related to a change in the appearance of stool.

Coeliac disease (CD), also known as gluten-sensitive enteropathy or coeliac sprue, is defined as a permanent intolerance to

Abbreviations: Anti-tTG, anti-tissue transglutaminase antibody; IBS, irritable bowel syndrome.

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ingested gluten (the storage protein components of wheat, barley and rye). Previous studies in Egypt have reported a prevalence of CD among Egyptian children ranging from 0.53% to 6.4% [4,5]. The prevalence of CD among adult Egyptian patients with chronic non-bloody diarrhoea was reported to be 14.2% [6].

The clinical presentation of CD can vary from a classical malabsorption syndrome to more subtle atypical gastrointestinal manifestations (similar to IBS) or extra-intestinal presentations (for example, infertility, osteoporosis and iron-deficiency anaemia). It can be clinically silent, often detected by serologic screening of subjects at risk, presenting villous atrophy in the intestine. An individual may have a latent predisposition to CD, which is defined by positive serological results in the absence of villous atrophy in the small intestine [7].

The most sensitive antibody tests for diagnosing CD are of the immunoglobulin A (IgA) class. The available tests include those for anti-gliadin antibodies; connective tissue antibodies (anti-reticulin and anti-endomysial antibodies); and antibodies directed against tissue transglutaminase, the enzyme responsible for the deamidation of gliadin in the lamina propria [8].

The aim of this study was to investigate the prevalence of CD in Egyptian patients with clinically diagnosed IBS (according to Rome III criteria) (with predominant diarrhoea).

Patients and methods

This prospective randomized study was conducted on 100 consecutive patients with clinically diagnosed IBS (fulfilling Rome III criteria [3] with predominant diarrhoea), who presented to the Internal Medicine and Tropical Medicine Departments, and outpatient clinics at Ain the Shams University Hospital, from March 2014 to July 2015.

Patients of advanced age ($\geqslant$65 years), with one or more alarming symptoms (weight loss, family history of inflammatory bowel disease or cancer, fever, abnormal physical findings, arthritis, dermatitis, severe anaemia, leucocytosis, high erythrocyte sedimentation rate (ESR) or presence of occult blood in stool), with abnormal upper or lower gastrointestinal endoscopic findings, with concomitant metabolic or endocrine diseases and those with other co-morbidities were excluded.

All included patients were subjected to the following investigations after signing a written consent form: (1) A complete clinical evaluation was implemented. (2) Routine laboratory investigations including complete blood count (CBC; using an Automated Cell Counter), ESR (by the Westergren manual method), random blood sugar, liver profile, renal function tests and stool analysis were carried out. (3) Abdominal ultrasonography was performed. (4) The presence of serum anti-tissue transglutaminase antibody (anti-tTG) was tested as a predictor marker for CD. Whole blood specimens were collected and allowed to clot, and the serum was separated by centrifugation. The specimens were stored at −20 °C. All patient samples were diluted to 1:100 with a sample buffer before assaying. Then 10 μl of the sample was combined with 990 μl of the sample buffer in a polystyrene tube. Specific IgA and IgG antibodies against tTG were detected using a commercial ELISA kit with recombinant human tTG as the antigen (Eu-tTG umana IgA; Eurospital, Trieste, Italy). Human recombinant tissue transglutaminase antigen was bound to the microwells. Antibodies against this antigen, if present in the diluted serum or plasma, bound to the respective antigens. Upon washing the microwells, unspecific serum and plasma components were removed. Horseradish peroxidase (HRP)-conjugated anti-human IgG and IgA could detect patient antibodies forming a conjugate/antibody/antigen complex. The unbound conjugate was removed by washing the microwells. An enzyme substrate in the presence of the bound conjugate underwent hydrolysis to form a blue colour. The addition of an acid stopped the reaction, forming a yellow end product. The intensity of this yellow colour was measured photometrically at 450–630 nm. The amount of colour was directly proportional to the concentration of IgG and IgA antibodies present in the original sample. The anti-tTG findings were considered normal at a level of $\leqslant$15 U/ml and positive at >15 U/ml [9]. (5) All patients testing positive for serum anti-tTG antibody underwent upper gastrointestinal endoscopy with the Pentax video endoscope EG 3440; four to eight biopsy samples were collected from the second part of the duodenum. Lesions were classified histopathologically based on the modified Marsh classification [10,11] as follows:

- Grade 0: normal or chronic inflammation with no increase in lymphocytes
- Grade I: increased intra-epithelial lymphocytic infiltration
- Grade II: crypt hyperplasia
- Grade IIIa: partial villous atrophy
- Grade IIIb: subtotal villous atrophy
- Grade IIIc: total villous atrophy

Informed consent was obtained from all of the included patients, and the study protocol was approved by the ethics guidelines committee.

Statistical analysis

This was performed using the mean, standard error, Student's *t*-test and chi-square by SPSS V18. Fisher's exact test and Yates' corrected chi-square were computed for 2 × 2 tables. Pearson's correlation coefficients were used to assess the relation between two studied parameters with quantitative data.

The confidence interval was set to 95%, and the margin of error accepted was set to 5%. Thus, the significance of the *p*-value was decided as follows:

$p > 0.05$: non-significant
$p < 0.05$: significant
$p < 0.01$: highly significant

Results

This study included 100 Egyptian patients diagnosed with IBS fulfilling Rome III criteria with predominant diarrhoea. Their ages ranged between 16 and 54 years (mean age: 35.1 ± 10.9 years). All of the studied patients presented with abdominal pain or discomfort, flatulence and diarrhoea.

Among the studied 100 patients, eight patients (8%) (six female and two male) exhibited high serum levels of anti-tTG with a high risk of CD. To confirm the diagnosis, all patients with positive serological results underwent upper gastrointestinal endoscopy with four to eight biopsy samples collected from the second part of the duodenum. These biopsy samples were found to satisfy the histopathological criteria of CD.

According to previous data, the studied patients were divided into two groups:

Group I: This included 92 patients with IBS and negative anti-tTG results, 42 female (45.65%) and 50 male (54.35%), with a mean age of 35.37 ± 11.1 years.

Group II: This comprised eight patients with IBS and positive anti-tTG results, six female (75%) and two male (25%), with a mean age of 45.75 ± 8.5 years. Their mean serum level of anti-tTG was 23.000 ± 4.243 U/ml. Based on the modified Marsh grading system, these patients were histopathologically classified as follows: two patients (25%) Grade II, three patients (37.5%) Grade IIIa and three patients (37.5%) Grade IIIb.