Celiac disease and \textit{Hp} infection association in Iran

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ABSTRACT

Background: we assessed the prevalence, the related symptoms, and the endoscopic and histologic gastric features of celiac disease (CD) in patients with \textit{Helicobacter pylori} (Hp).

Methods: 450 dyspeptic patients were studied. Biopsies of gastric antrum and duodenum, CD serology, and total IgA were obtained. Histological findings were scored with the Marsh-Rostami criteria.

Results: 411 (91.3\%) patients were \textit{Hp} positive. Duodenal histology was normal in 385 (85.6\%) patients, 124 (27.5\%) had duodenitis and 28 (6.2\%) showed duodenal abnormalities (Marsh I-IIc). Twenty three/28 (82.1\%) patients with malabsorption pattern were also \textit{Hp} positive. Serological analysis: 12 of 31 (38.7\%) positive patients had abnormal histology (Marsh I,-IIIc). Nine out 450 patients were IgA deficient; none of them was serologically positive for CD.

Conclusion: although a high prevalence of \textit{Hp} infection was found in this study, the relationship between \textit{Hp} infection and CD was similar to that reported in other geographic areas.

Key words: Celiac disease. \textit{H. pylori}.

INTRODUCTION

Celiac disease (CD) is frequently associated with abnormalities in gastric function and histology (1-8). \textit{Helicobacter pylori} (\textit{Hp}) is the causative agent in more than 90\% of cases of chronic gastritis, peptic ulcer disease, primary gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer (9). A high prevalence of this infection would be also expected in patients with celiac disease (1-8). Atrophic gastritis with an increased prevalence of parietal cell antibodies seems to be common in some studies (1), but others have found little evidence to support this in CD (10).

Although the pathogenesis of CD is relatively well understood, the possibility that a chronic gastric infection capable of inducing duodenal ulcers could influence the inflammatory and immune responses in the small intestine and, therefore, the development and evolution of CD, should be considered (11,12).

\textit{Hp} is now recognized as a major etiological factor in most patients with non-autoimmune chronic gastritis (2). In developing countries, \textit{Hp} infects the majority of the population; for instance, the Iranian population displays a rate of infection of more than 90\% (13).

Even though epidemiological studies have failed to reveal a connection between gastritis and CD (11,12), some studies showed that patients with \textit{Hp} gastritis are more likely to have increased numbers of intraepithelial lymphocytes in the duodenal mucosa, and that this can be reversed by the eradication of \textit{H. pylori} (14,15). Other works have focused on \textit{Hp}-related lymphocytic gastritis in CD (16-19) and on the link between anemia and \textit{Hp} infection in celiac patients (20,21).

Purposes of the present study were to assess the prevalence of celiac disease, its related symptoms, and endoscopic features, and to compare the histopathological and clinical features in patients with associated \textit{Hp} infection.
PATIENTS AND METHODS

In the period January 2007-December 2008, four hundred and fifty patients (211 men, 239 women, mean age 36 years, range 15-83 years) who underwent upper endoscopy for dyspeptic symptoms were recruited in the out-patient clinic of Taleghani hospital. After obtaining a written informed consent from all subjects upper endoscopy with gastric and duodenal biopsies was carried out. Two biopsy specimens were obtained from the gastric antral mucosa and two to four samples from different portions of the duodenum. Biopsies were fixed overnight in buffered formalin, embedded in paraffin, cut to 3-µm thickness, and stained with hematoxylin-eosin for routine histological evaluation. Giemsa staining was also used for gastric specimens, to identify \( H. pylori \). The slides were blindly evaluated by two expert gastrointestinal pathologists.

In accordance with the Updated Sydney System (22), the degree of gastric mucosal inflammation, polymorphonuclear cell infiltration, glandular atrophy, and intestinal metaplasia was classified into four grades as follows: 0 = none, 1 = mild, 2 = moderate and 3 = severe. \( H. pylori \) infection was considered positive if present at least in one of the biopsies examined.

The diagnosis of CD was based on the characteristic histological finding of increased intra-epithelial lymphocytes, villous atrophy, and crypt hyperplasia, classified according to the standard classification proposed by Marsh (23,24) and subsequently modified by Rostami et al. (25) (Table I).

Before endoscopy, a blood sample was drawn for serum anti-tissue transglutaminase (tTGA) and stored at -70 °C until tested. Patients who had normal biopsies, but tested positive for tTGA in their serum, were asked to undergo retest and an intestinal biopsy 12 months later. IgA-tTGA levels were measured by a commercially available ELISA method (AESKULISA tTGA, Germany). Serum values of tTGA higher than 15 U/mL were considered positive. Total serum IgA values were measured by an immunoturbidimetric assay ( Pars Azmoon, Iran), and serum levels below 70 U/mL were considered indicative of IgA deficiency. Immunoglobulin G (IgG) tTGA values were further obtained in individuals with IgA deficiency by an ELISA method (AESKULISA tTGG, Germany).

RESULTS

Out of 450 patients 411 (91.3%) were \( H. pylori \) positive; associated symptoms/diseases were diabetes 26 (5.8%), anorexia 99 (22%), weight loss 143 (31.5%), nausea and vomiting 145 (32.2%), heartburn 261 (58%), bloating 320 (71.1%), flatulence 140 (31.1%), a concomitant stressful condition 117 (26%), and abdominal discomfort 351 (78%). Nine out of 450 recruited patients were IgA deficient and none of them were positive for IgG tTGA.

Duodenal histology was normal in 385 (85.6%) patients, 124 (27.5%) had duodenitis, and 28 (6.2%) showed mucosal abnormalities compatible with CD (Marsh I-IIIc) (Table II).

Twenty three out of 28 patients (82%) with positive histology for CD had gastric biopsies positive for \( H. pylori \) (Fig. 1). The prevalence of \( H. pylori \) in patients without CD (86.2%) was slightly but not significantly higher. \( H. pylori \) in-
Infection was more prevalent in patients younger than 40; as expected, most (91.4%) Hp-positive patients had moderate to severe chronic gastritis, whereas only 12 out of 39 (30.7%) Hp-negative patients had moderate or severe chronic gastritis.

Serological analysis showed that 12 out of 31 (38.7%) tTGA-positive patients had abnormal histology (four Marsh I, two Marsh II (Fig. 2) one Marsh IIIa, three Marsh IIIb (Fig. 3) and two Marsh IIIc (Fig. 4). In this group, one had mild chronic gastritis, three moderate chronic gastritis, two moderate active chronic gastritis, three severe chronic gastritis, and the last three had severe active chronic gastritis.

**DISCUSSION**

In this study we found that, in this geographic area of the Middle East, the prevalence of Hp infection in dyspeptic patients was higher than 90%. Patients with a malabsorption pattern had 42.8% positive serologies for CD, with sensitivity values ranging from 33.4% in Marsh IIIa patients to 100% in Marsh IIIc, which is in agreement with previously published results (26-28). According to literature results, in our series also only 33.4% of Marsh I patients showed positive serology. The Marsh degree in 5 patients who were Hp-negative included one Marsh I, one Marsh II, two Marsh IIIa and one Marsh IIIc. Moderate chronic gastritis was more prevalent in Hp-infected patients.

Out of 31 serology positive patients, 19 patients had normal histology. In contrast, in the 28 patients with a malabsorption pattern, 16 had negative serology. Therefore, only 12 patients had both abnormal histology and positive serology related to CD.

Hp has been positively identified as the main cause of active chronic gastritis and its major complications (peptic ulcer disease, gastric adenocarcinoma, and primary gastric MALT lymphoma), with numerous studies carried out to explore the possible etiological role of this bacterium in a variety of both gastrointestinal and extra-intestinal conditions (28,29). Investigations on the relationship between Hp infection and CD have yielded conflicting results (11,12), probably because of the different prevalence of Hp in the populations studied.

As shown in table II, in our series 23/28 patients with a malabsorption pattern (Marsh I-IIIc) were also Hp-positive. Histological findings in these patients included six mild chronic gastritis, eight moderate chronic gastritis, three moderate active chronic gastritis, two severe chronic gastritis, and four severe active chronic gastritis cases.
The four patients with Marsh I (two patients), Marsh II and IIIb who were positive for Hp and tTG-A had mild chronic gastritis, moderate active chronic gastritis, and severe active chronic gastritis, respectively. Two patients with Marsh II had moderate chronic and moderate active chronic gastritis. For Marsh IIIa, one patient had severe chronic gastritis. Three patients with Marsh IIIb had moderate chronic gastritis, severe chronic gastritis and severe active chronic gastritis. Two patients with Marsh IIIc had severe active chronic gastritis. These results showed that 9 out of 12 with serology positive for CD were infected with Hp. On the other hand 24/31 tTG positive were also positive for Hp.

It should be noted that, concerning Hp positivity, the percentage of Hp-positive celiac patients is lower than that of non-celiac patients and, as recently shown (29), the clinical features of CD patients are unrelated to the simultaneous presence of Hp gastritis, and there is no relation between gastritis and severity of mucosal damage in CD.

In conclusion, the prevalence of Hp infection in Iranian patients complaining of dyspeptic symptoms is high, and the relationships between Hp and CD are similar to those described in other geographic areas.

REFERENCES