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ORIGINAL ARTICLE

Helicobacter pylori in celiac disease and in duodenal intraepithelial lymphocytosis: Active protagonist or innocent bystander?

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Summary
Background and objective: *Helicobacter pylori* (*H. pylori*) infection influences duodenal inflammation. Consequently, in celiac disease and in duodenal intraepithelial lymphocytosis, the bacterium could affect the clinical-histological manifestations. The aim of this work was to evaluate the prevalence and the potential role of *H. pylori* infection in celiac disease and duodenal intraepithelial lymphocytosis.
Methods: *H. pylori* status was reviewed in 154 patients with celiac disease or duodenal intraepithelial lymphocytosis and in a control population. This retrospective study was performed at Molinette hospital, university of Torino, Italy.
Results: *H. pylori* prevalence was 36% in celiac disease patients, 19% in case of duodenal intraepithelial lymphocytosis and 41% in controls ($P < 0.05$ vs. duodenal intraepithelial lymphocytosis). *H. pylori* prevalence was not significantly different between celiac disease patients with or without iron deficiency anemia (22% vs. 39%) and it was higher in patients with milder duodenal lesions: 50% in Marsh-Oberhuber classification type 1—2 vs. 33% in type 3. Celiac disease patients had a mean intraepithelial lymphocytes count greater than that of duodenal intraepithelial lymphocytosis patients (52 vs. 44 intraepithelial lymphocytes per 100 epithelial cells). Both in celiac disease and in duodenal intraepithelial lymphocytosis patients, *H. pylori* infection was associated with an increase in intraepithelial lymphocytes count, but this difference was not significant.

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Conclusion: *H. pylori* prevalence was similar in celiac disease patients and in controls and higher in patients with milder duodenal lesions. There was no association between *H. pylori* infection and duodenal intraepithelial lymphocytosis.

Introduction

There are several studies on *Helicobacter pylori* prevalence in celiac disease (CD) patients, but they are extremely heterogeneous. A work by Villanacci et al. suggested that *H. pylori* infection is more frequent in CD patients with low grade than in those with high grade duodenal lesions [1]. In the duodenum, the increase of intraepithelial lymphocytes (IELs), defined duodenal intraepithelial lymphocytosis (DIL), can be an early manifestation of CD as well as the epiphenomenon of *H. pylori* infection itself [2,3].

Lymphocytic gastritis (LG), defined as the presence of more than 25 IELs per 100 epithelial cells [4], has been associated with many other diseases, among which *H. pylori* infection, CD and duodenal nodular lymphoid hyperplasia [5].

The aim of this retrospective case-control study was to evaluate the prevalence of *H. pylori* infection in patients with CD or DIL.

Material and methods

The database of the pathology department of Molinette hospital, Torino, Italy, was retrospectively analysed, identifying the patients who underwent esophago-gastro-duodenoscopy (EGDS) with gastroduodenal biopsies (at least six samples taken from the second part of the duodenum) between January 1st 2003 and March 31st 2012. The cohort included 4227 patients, among which 1107 had a duodenal biopsy with a diagnosis of damage type 1, 2, or 3 according to Marsh-Oberhuber classification [6,7]. Eight hundred subjects were excluded because gastric biopsies were not taken, and *H. pylori* status could not be determined. Also excluded from the study were 153 patients with absence of correct serology or of DQ2 and DQ8 genotyping. The study design is schematically reported in Fig. 1. The study population included 154 patients. A diagnosis of CD (anti-endomysial Ig A antibodies and/or anti-tissue transglutaminase positive) or DIL (both antibodies negative with normal level of total IgA, DQ2 and DQ8 negative) was made in 73 and in 81 patients, respectively. An additional review of medical records of patients without CD, but with increased IELs, was performed to ascertain that no further diagnosis compatible with increased IELs was present.

As controls, 404 subjects suffering from constipation, with negativity for both anti-endomysial IgA antibodies and anti-tissue transglutaminase antibodies and with normal level of total IgA, who underwent 13C-urea breath test (UBT) for study purposes were included. The controls were subjects evaluated for constipation in the same hospital. Subjects undergoing EGDS were not chosen as control because these patients have symptoms, such as dyspepsia and epigastric pain, usually related to a high prevalence of *H. pylori* infection.

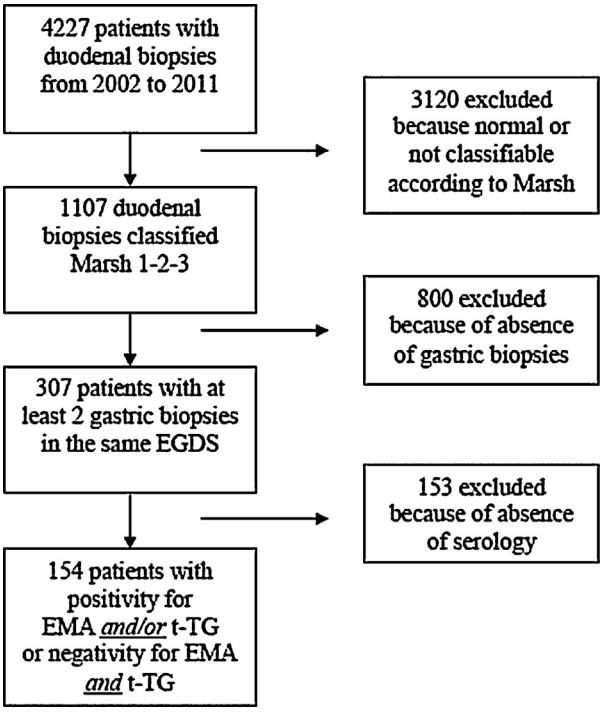

Figure 1 Flow diagram of patients included in the final analysis. EGDS: esophago-gastro-duodenoscopy; EMA: anti-endomysial antibodies; t-TG: anti-tissue transglutaminase.

The histological features of gastritis were evaluated according to the Sydney System classification [8], with the limitation that not in all cases 5 gastric biopsies (as Sydney System's protocol suggest) were available. *H. pylori* infection was diagnosed on hematoxylin & eosin (H&E) stained sections. Duodenal alterations were classified according to Marsh [6] (modified by Oberhuber et al. [7]) and to Corazza-Villanacci [9] classifications. A villus/crypt ratio of 3:1 (with normal IELs count) was considered normal, while a reduction of this ratio was defined ''atrophy''. As generally accepted, the normal value for IELs in superficial epithelium was considered 25 IELs per 100 epithelial cells [10]. In all cases, an immunohistochemical evaluation with CD3 monoclonal antibody was performed to confirm the H&E count of T lymphocytes [11].

Statistical analysis was conducted with SPSS 16.0 software. In order to evaluate the different influences of independent variables on the prevalence of *H. pylori*