

# Immunopathology of Pediatric Celiac Disease Associated with *Helicobacter pylori* Infection

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**Abstract** Celiac disease percentage is continuously increasing in recent years. *Helicobacter pylori* infection is found in more than 50% of the population. Recent studies have attempted to discover a link between celiac disease and *H. pylori* infection. We analyzed the main immunopathological aspects of celiac disease associated with *H. pylori* infection. If celiac disease is associated with *H. pylori* infection, clinical evidence can occur: gastric lymphocytosis, duodenal lymphocytosis.

**Keywords:** celiac disease, *helicobacter pylori*, immunology, pathology

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## 1. Introduction

Previous studies showed a so-called Th1 immune response with an increased production of IFN- $\gamma$ , TNF- $\alpha$  and other pro-inflammatory cytokines that occur in the stomach, when the subject is infected with *Helicobacter pylori*, as well as in the small intestine, when the subject with celiac disease (CD) eats normal bread [1]. Today, this possible immunological association between *H. pylori* infection and CD is linked to the hygiene hypothesis. Hygiene hypothesis revealed that low exposure to bacterial antigens can trigger autoimmunity. *H. pylori* and CD are inversely related [2]. A low prevalence of Crohn's disease and CD was seen in *H. pylori*-positive patients [3].

Although the stomach was a hostile environment, *Helicobacter pylori* infection has been extensively studied since 1984 [4]. It is also well known that bacterial species prevail in the intestinal microbiota of patients with celiac disease (CD) [5] but little evidences were related linked to existing of *H. pylori* in the gut of patients with CD. Recent studies highlighted *H. pylori* infection and CD as main aspects of pediatric gastroenterology in recent years [6].

The aim of this study was to find current state of immunopathological knowledge about association of *H. pylori* infection and CD. A potential link between *H. pylori* and CD was analysed. We searched in PubMed database with the following keywords: *H. pylori*, CD, immunopathology. Only relevant papers were included in our present study.

## 2. Gastric Lymphocytosis

Early studies showed that lymphocytic gastritis was associated with CD, but *H. pylori* infection was not showed in children with lymphocytic gastritis [7] and the relationship between lymphocytic gastritis and CD required further elucidation [8]. Lymphocytic gastritis occurred most often in CD, but rarely with other entities [9]. More recent studies have shown that CD might be associated with *H. pylori* gastritis, but clinical presentation of CD was not affected [10]. A pathogenic relationship between CD and lymphocytic gastritis was highlighted. *H. pylori* might be another cause of lymphocytic gastritis in children [11]. So the main causes of lymphocytic gastritis were *H. pylori* infection and CD [12]. When the histopathological result showed lymphocytosis alone, lymphocytic gastritis was associated with CD and not with *H. Pylori* infection. But when the histopathological result showed significant infiltration of neutrophils, the diagnosis would be "chronic active gastritis", often associated with *H. pylori* infection [13].

## 3. Duodenal Lymphocytosis

The first studies showed that in some patients, increased duodenal intraepithelial lymphocytes could be due to an autoimmune response to *H. pylori* [14]. The presence / absence of *H. pylori* were independent of

normalization of duodenal mucosa to CD patients [15]. The most common duodenitis etiology were: CD (32%), Crohn's disease (13%), ulcerative colitis (3%) and *H. pylori* infection (6%) [16]. There were no statistically significant differences of duodenal intraepithelial lymphocytes according to *H. pylori* status among children with CD: 73.1 ( $\pm$  26.1) positive vs. 72.6 ( $\pm$  26.5) negative [17]. *H. pylori* prevalence was similar in patients with CD and controls, and higher in patients with minor duodenal injuries [18]. *H. pylori* infection seems to be less frequent in patients with CD and villous atrophy suggesting that histological damage appears to be similar in patients with *H. pylori* infection [19]. Therefore, *H. pylori* infection is one of the main causes of duodenal lymphocytosis and together with HLA are strong predictors for CD development [20].

## 4. Conclusions

There are many “for” and “against” conclusions on immunopathological association between CD and *H. pylori* infection. But if celiac disease is associated with *H. pylori* infection, clinical evidence can occur: gastric lymphocytosis, duodenal lymphocytosis.

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