Helicobacter pylori seroprevalence in patients with chronic bronchitis

Mehmet Kanbay*, Gurden Gur, Sule Akcay, Ugur Yilmaz

Faculty of Medicine, Department of Internal Medicine, Baskent University, Ankara, Turkey

Received 2 February 2005

Summary
Aim: A high rate of seropositivity for antibodies against Helicobacter pylori has been found in many extragastrointestinal diseases. In addition, it has been reported that the risk of chronic bronchitis may be increased in subjects infected with H. pylori. This study was designed to determine the H. pylori seroprevalence in patients with and without chronic bronchitis.

Materials and methods: This study enrolled 68 patients with chronic bronchitis (40 men and 28 women, aged 50.5 ± 16.2 years (mean ± standard deviation) and 95 control subjects (60 men and 35 women, aged 51.8 ± 15.9 years) matched for age and sex. An enzyme-linked immunosorbent assay immunoglobulin (Ig) G test for H. pylori diagnosis was performed on all enrolled subjects (those with chronic bronchitis and controls).

Results: Forty-five of 68 patients with chronic bronchitis (66.1%) and 48 of 95 subjects in the control group (57.7%) tested positive for H. pylori (P = 0.008). Rates of H. pylori infection are higher in patients with chronic bronchitis than in the control group.

Conclusion: The main conclusion of this study is that H. pylori infection is associated with an increased prevalence chronic bronchitis. Further studies should be planned to understand the potential pathogenetic mechanisms that might underlie this association.

© 2005 Elsevier Ltd. All rights reserved.

Introduction
Worldwide, Helicobacter pylori infection is the most common chronic bacterial infection of humans. Seroepidemiologic studies have revealed that approximately half of all adults in developed countries and approximately 90% of adults in developing countries are positive for serum antibodies against H. pylori. H. pylori is strongly associated with type B antral gastritis, peptic ulcer, gastric MALT lymphoma, and gastric adenocarcinoma.

H. pylori infection often triggers a marked local inflammatory response and a chronic systemic immune response. One hypothesis is that the
persistent inflammatory response related to *H. pylori* infection could induce vascular disorders through an immune-mediated release of substances associated with vasospasm or platelet aggregation. Mediators that have been considered to participate in the pathogenesis of extradigestive diseases include interleukin-1 (IL-1), tumor-necrosis factor alpha (TNF-alpha), interferon gamma (IFN gamma), leukotriene C4 (LT C4) and platelet-activating factor (PAF).5,6

A high rate of seropositivity for antibodies against *H. pylori* has also been found in many extradigestive disorders, including coronary heart disease, rosacea, growth failure in childhood, active bronchiectasis, and asthma.7-9 It is also well known that the prevalence of chronic obstructive pulmonary disease in patients with peptic ulcer is 2–3 times greater than in ulcer-free controls.10 An epidemiological study in Danish adults also suggested that chronic bronchitis might be more prevalent in women who were seropositive for Ig G antibody against *H. pylori* than in uninfected subjects.12 However, there are insufficient data about the prevalence of *H. pylori* infection in patients with chronic bronchitis.

This study was designed to determine the relation between *H. pylori* infection and chronic bronchitis. We assessed the rate of seropositivity for antibodies against *H. pylori* in a cohort of subjects with chronic bronchitis and bronchitis-free control subjects.

**Materials and methods**

This was a cross-sectional study of patients visiting the Department of Internal Medicine outpatient clinic of a university hospital in Turkey between March 2004 and October 2004 was approved by the local ethics committee. Sixty-eight consecutive patients with chronic bronchitis, diagnosed according to the American Thoracic Society Guidelines, were recruited from the outpatient clinic. Briefly, chronic bronchitis was diagnosed as “the presence of chronic productive cough for 3 months in each of successive years, in a patient in whom other causes of chronic cough have been excluded. Exclusion criteria were (1) an exacerbation of chronic bronchitis in the preceding month (the exacerbation was defined as “increased dyspnea associated with change in the quality or quantity of sputum, which led the patient to seek medical attention”); (2) prior therapy to eradicate *H. pylori* infection; (3) use of acid-suppressive drugs or antibiotics in the preceding 6 months; and (4) a history of vagotomy or operations on the upper gastrointestinal tract.

Control patients were selected randomly from our outpatient clinic during the period of study. Exclusion criteria for controls were (1) a known history of chronic bronchitis; (2) prior therapy to eradicate *H. pylori*; (3) use of acid-suppressive drugs; and (4) a known history of gastrointestinal pathology. We selected 95 controls and we matched them with the patients for age, sex, and socio-economic status.

An Immulite (chemiluminescent) analyzer (Diagnostic Products Corp, Los Angeles, CA, USA) was used to tested for serum antibodies against *H. pylori* infection. This kit has a sensitivity of 97% and a specificity of 98.8%, according to the manufacturer’s guidelines.

Results are presented as mean±SD (standard deviation). Statistical analysis was carried out using SPSS software (Statistical Package for the Social Sciences, version 11.0, SSPS Inc, Chicago, Ill., USA), and the *w*² and Student *t*-tests. A value for *P* less than 0.05 was considered statistically significant.

**Results**

Altogether 68 consecutive subjects with chronic bronchitis and 95 control subjects were recruited into this study. The demographic and clinical details of these subjects are shown in Table 1. There was no significant difference in age, sex, or social status between the study and control groups (*P* > 0.05). The majority of patients with bronchitis were current cigarette smokers (48 patients; 70.5%). Seropositivity for antibodies against *H. pylori* in the group of patients with chronic bronchitis was significantly higher than in the control group (*P* = 0.008) (Fig. 1). If we subdivide the chronic bronchitis and control group as smoker

<table>
<thead>
<tr>
<th>Table 1 Basic patient and control subject characteristics.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n = 68)</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male (%)</td>
</tr>
<tr>
<td>Smoking (%)</td>
</tr>
<tr>
<td>Hp seropositivity (%)</td>
</tr>
</tbody>
</table>
and nonsmoker, the seroprevalence of *H. pylori* was not statistically significant \((P > 0.05, \text{ Table 2})\).

**Discussion**

Rates of seropositivity for antibodies against *H. pylori* have been reported to be higher in populations of patients with many extradigestive disorders (including ischemic heart disease, stroke, and particularly chronic inflammatory diseases such as rosacea, urticaria, and Henoch-Schönlein purpura) than in the corresponding populations of persons without these disorders. \(^5\)–\(^9\) Interestingly, the clinical status of patients with the latter three conditions has been reported to improve after eradication of *H. pylori*. \(^10\)

The results of this study show that the population of patients with chronic bronchitis has a significantly higher rate of seropositivity for antibodies against *H. pylori* than the population of subjects without chronic bronchitis. Earlier data about the relationship between *H. pylori* infection and chronic bronchitis are limited. Three previous studies investigated the association between *H. pylori* seropositivity and chronic bronchitis. Gaselli et al. found an 81.6% seroprevalence of antibodies against *H. pylori* in 60 consecutive patients with chronic bronchitis and a 57.9% seroprevalence in 69 control subjects \((P = 0.008)\). \(^12\) In another study in Danish women, they found that the presence of antibodies against *H. pylori* was associated with chronic bronchitis. \(^11\) In a case-control study, Roussos et al. found a significant association between chronic bronchitis and *H. pylori*. \(^13\) While these studies suggest an association between chronic bronchitis and *H. pylori*, the potential pathogenetic mechanism remains unclear. In fact, patients with chronic bronchitis receive antibiotics frequently, and one might expect that the prevalence of antibodies against *H. pylori* would be lower than in a healthy population. Chronic bronchitis had been associated with gastroduodenal ulcer many years before *H. pylori* infection was identified as a cause of peptic ulcer. Three epidemiological studies found that the prevalence of chronic bronchitis in patients with peptic ulcer was 2–3 times higher than that in ulcer-free controls. \(^10,14\) Possible confounding factors for this association are age, sex, smoking, and socioeconomic status. \(^15\) It is possible that *H. pylori* infection
promotes atherosclerosis by generating a persistent low-grade inflammatory stimulus. *H. pylori* is a gram-negative bacterium and thus contains lipopolysaccharide, a substance that stimulates the production many cytokines, including interleukin-1, interleukin-6, and tumor necrosis factor-α. The eradication of *H. pylori* leads to normalization of serum cytokine levels. Recent studies showed that the same cytokines might be released during the course of chronic bronchitis and exacerbations of it. As a result, we emphasize that *H. pylori* infection might play a proinflammatory role and co-trigger chronic bronchitis.

In conclusion, this study showed that *H. pylori* seropositivity is high in patients with chronic bronchitis. Our results must be confirmed by other studies. The present study has not focused on the potential pathogenetic mechanisms underlying the association between *H. pylori* infection and chronic bronchitis. A prospective case control study should be planned to determine the effects on chronic bronchitis of eradication therapy for *H. pylori* and to understand the possible pathogenetic mechanisms. Investigation of *H. pylori* infection especially in chronic recurrent cases with bronchitis may also help to understand the relationship and pathogenesis.

References