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Relationship between chronic obstructive pulmonary disease and *Helicobacter pylori* infection

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Abstract

Introduction
There are insignificant observations and few research studies that indicate the action of *Helicobacter pylori* in the induction of extra-gastrointestinal tract diseases, which include autoimmune, skin, and vascular diseases, and also some pulmonary diseases. Moreover, it has been documented that the incidence of chronic bronchitis may be elevated in patients who experienced *H. pylori* infection.

Aim
To assess infection with *H. pylori* in patients with chronic obstructive pulmonary disease (COPD) and in control persons and also to determine the association between serology level of *H. pylori* and spirometry parameters in patients experiencing COPD.

Results
A total of 100 individuals experiencing COPD and 100 age-matched and sex-matched controls were included. The mean age in patients with COPD was 63.3 ± 8.4, whereas in controls was 60.8 ± 8.8. All participants of the current study underwent ELISA and immunoglobulin G (IgG) serology examination for *H. pylori*. The percentage of anti-*H. pylori* IgG seropositivity in patients with COPD was 78%, whereas in controls was 55% ($P < 0.001$). Moreover, patients experiencing COPD had a statistically highly significant elevated mean serum concentration of anti-*H. pylori* IgG antibodies. The mean level of anti-*H. pylori* IgG in patients with COPD was 120.5 ± 22.5 U/ml, whereas in the control group was 62.3 ± 11.6 U/ml ($P<0.001$). There was a highly significant reduction in forced expiratory volume in 1 s (FEV1) in *H. pylori*-positive patients with COPD than in *H. pylori*-negative patients with COPD. Mean FEV1 in patients with *H. pylori*-positive COPD was 49.56 ± 12.16, whereas in patients with *H. pylori*-negative COPD was 88.09 ± 2.24 ($P < 0.001$). There was also a statistically highly significant negative correlation between FEV1 value and serum concentration of anti-*H. pylori* IgG antibodies ($P < 0.001$).

Conclusion
The parameters indicate that there is a correlation between *H. pylori* infection and COPD.

Keywords: Chronic obstructive pulmonary disease, *Helicobacter pylori*, infection

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease of high burden all over the world. COPD affects ~300–600 million participants and leads to death of about one million patients per year. The pathogenesis of COPD has not been completely understood, investigated, or worked upon. Moreover, chronic inflammation is the main component. In addition to the inflammatory process of the lung, some patients with COPD show persistent systemic inflammation, and systemic inflammation is accompanied by increased symptoms and also poor outcomes of the patient condition, including both hospitalization and mortality. One of the major bacterial players in the gastrointestinal tract (GIT) is *Helicobacter pylori*. Many previous studies have stated that chronic infection with *H. pylori* is accompanied by endothelial dysfunction and persistent systemic inflammation; both of them found in patients experiencing COPD [1].

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Persistent systematic inflammation affects from 15 to 20% of the patients experiencing COPD and is accompanied by an elevated incidence of both exacerbation and mortality. The cause of this chronic inflammation and pathology in COPD is a major dilemma [2]. There is an observation that the GIT is the main driver and modulator of inflammation and that the GIT pulmonary axis may be perturbed in patients experiencing COPD [3].

Several research studies have been published to clarify the role of *H. pylori* infection in different diseases present in extra-GIT system. These systems include the immunological, cardiovascular, hepatobiliary, dermatological, neurological, hematological, endocrinological, ophthalmological, and gynecological systems [4]. The presence of an association between respiratory disease and *H. pylori* infection has been recently documented. Tuberculosis, lung cancer, and bronchiectasis are associated with elevated levels of *H. pylori* seroprevalence. Some previous studies, including few studies with few study samples, have found an association between COPD and *H. pylori* infection. The presence of a positive serology for *H. pylori* was identified to be raised in patients with COPD than in individuals who do not have COPD. A major relation between *H. pylori* serum positivity and forced expiratory volume in 1 s (FEV1) was recently identified [1].

Aim

The present study aimed to determine *H. pylori* infection in patients with COPD in comparison with control individual and also to evaluate the association between *H. pylori* serology state and spirometry values in patients with COPD.

Patients and methods

This study was carried out on 100 patients with COPD, who were diagnosed and classified according to the GOLD criteria. Moreover, 100 apparently healthy nonsmoking volunteer participants who were match with the patients with COPD for age, socioeconomic status, and sex, were taken as a control group. The patients were recruited from Al Sahel Teaching Hospital. The study was approved by the local ethics committee of general organization of Teaching Hospital and Institutes (GOTHI). Written fully informed consent was obtained from every participant.

Inclusion criteria for patients with COPD included the following:

(1) Symptoms of chronic bronchitis.
(2) Evidence of airway narrowing according to the GOLD study.
(3) No improvement in FEV1 of more than 10% after inhalation of 200 mg salbutamol.

Exclusion criteria for patients with COPD were as follows:

(1) Exacerbation of COPD in the past 30 days, as in those cases, measurement of ventilatory parameter values does not represent baseline reading.
(2) Prior *H. pylori* eradication treatment.
(3) Taking of any acid-suppressive treatment or antibiotics in the past 6 months.
(4) Any history of operations like vagotomy operation or upper GIT operation.

Exclusion criteria for the controls were as follows:

(1) A known history of COPD.
(2) A known history of GIT pathology, including *H. pylori* infection.
(3) Consumption of acid-suppressive treatment or antibiotics in the preceding 6 months.

All participants were subjected to the following:

(1) Full clinical history, including personal, familial, smoking, alcohol intake, drug therapy, environmental risk factors and past history, and also history of the patient's conditions including symptoms and signs of COPD.
(2) Thorough clinical examination, including general as well as local examination.
(3) Pulmonary function tests.

The following were recorded:

(1) Forced vital capacity (FVC).
(2) FEV1.
(3) FEV1/FVC.

In all patients, postbronchodilation spirometry values (FEV1, FVC, and FEV1/FVC) were detected. The best results of three maneuvers were expressed as a percentage of the predicted value, and classification of COPD severity was performed according to GOLD guidelines.

(a) ELISA immunoglobulin G (IgG) serologic test for *H. pylori*.

Statistical analysis

Review of data and coding was occurred; the results was entered and analyzed through SPSS program, software ((IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). results were expressed as mean ± one standard deviation (± SD). *P*-values of less than 0.05 was considered statistically significant. Significance of difference between groups was assessed by unpaired Student's *t*-test for continuous variables and X2 test for proportions.

Results

This work was carried out on 100 patients with COPD. They were diagnosed and classified according to the GOLD criteria. Moreover, 100 apparently healthy nonsmoker volunteer participants, match with the patients with COPD for age, socioeconomic status, and sex, were taken as a control group. The patients were recruited from Al Sahel Teaching Hospital.

The mean age of the patients with COPD was 63.3 ± 8.4, whereas the mean age of the control was 60.8 ± 8.8. Both groups are well matched according to sex and age distribution ($P = 0.149$) (Table 1).

The distribution of patients with COPD according to COPD severity was as follows: 24% had mild disease (Gold 1), 37% had moderate disease (Gold 2), 24% had severe COPD (Gold 3), and 6% had very severe disease (Gold 4) (Fig. 1).

Anti-*H. pylori* IgG serum positivity was elevated in COPD than in controls. The percentage of anti-*H. pylori* IgG seropositivity in patients with COPD was 78%, whereas in controls was 55% (P<0.001).

Moreover, patients with COPD had a statistically significant increase in mean serum concentration of anti-*H. pylori* IgG antibodies. The mean level of anti-*H. pylori* IgG in patients with COPD was 120.5 ± 22.5 U/ml, whereas in the control group was 62.3 ± 11.6 U/ml (P<0.001) (Table 2).

There is a highly statistically significant difference between *H. pylori*-infected patients with COPD and uninfected patients regarding FEV1 values. The mean FEV1 in *H. pylori*-positive COPD was 49.56 ± 12.16, whereas in *H. pylori*-negative COPD was 88.09 ± 2.24 (Table 3). Moreover, there is a highly statistically significance negative correlation between FEV1 values and anti-*H. pylori* IgG level (Fig. 2).

Discussion

In the current study, we identified a significant association between anti-*H. pylori* IgG and COPD. Moreover, we identified an association between *H. pylori* bacterial infection and the degree of severity of COPD. Few previous research studies have shown elevated serum prevalence of *H. pylori* IgG levels in patients experiencing COPD. One previous research found that there is an association between anti-*H. pylori* IgG and COPD [5]. Moreover, one previous seroepidemiological study found an association between *H. pylori* and respiratory diseases [6].

Although there are many previous research studies relating a raised *H. pylori* serum prevalence to chronic bronchitis [7], these studies about the relation of *H. pylori* infection with COPD are considered small in number [8], and a relationship between *H. pylori* IgG levels and ventilatory functions has not been detect in patients with COPD so far. In the present study, *H. pylori* serum prevalence and concentration of *H. pylori* IgG in serum were statistically highly significantly higher in patients with COPD than in the healthy participants. Moreover, there was a highly significant reduction in FEV1 in

Table 1: Demographic results of patients with chronic obstructive pulmonary disease and controls and spirometry parameters of patients with chronic obstructive pulmonary disease

Parameters	COPD	Control	*P*
Age per year	63.3±8.4	60.8±8.8	0.149
Male sex (%)	83	80	0.912
FEV1	58.04±19.32	105.90±8.20	<0.001
FEV1/FVC	57.40±10.76	101.60±8.87	<0.001

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Table 2: Serology values in chronic obstructive pulmonary disease and control group

Parameters	COPD	Control	*P*
Anti-*Helicobacter pylori* IgG seropositivity (%)	78	55	<0.001
Anti-*Helicobacter pylori* IgG level U/ml	120.5±22.5	62.3±11.6	<0.001

COPD, chronic obstructive pulmonary disease; IgG, immunoglobulin G.

Table 3: Comparison of spirometry results of *Helicobacter pylori*-positive and *Helicobacter pylori*-negative patients with chronic obstructive pulmonary disease

Parameters	*Helicobacter pylori* positive	*Helicobacter pylori* negative	*P*
FEV1	49.56±12.16	88.09±2.24	<0.001

FEV1, forced expiratory volume in 1 s.

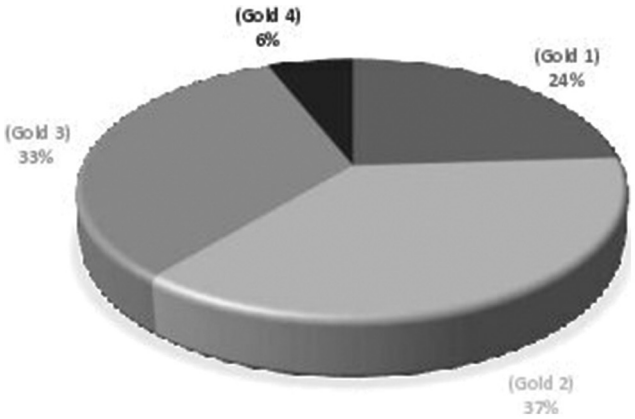

Figure 1: The percentage of patients with COPD according to the severity. COPD, chronic obstructive pulmonary disease.

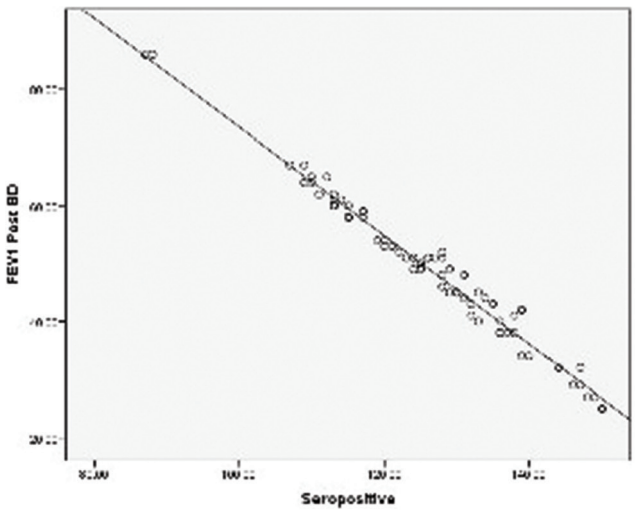

Figure 2: Correlation between FEV1 values and anti-*Helicobacter pylori* IgG level. FEV1, forced expiratory volume in 1 s; IgG, immunoglobulin G.

H. pylori-positive COPD than in *H. pylori*-negative COPD. There is also a highly significant negative correlation between FEV1 value and serum level of anti-*H. pylori* IgG antibodies.

The etiology for raised *H. pylori* seroprevalence in patients with COPD is still unexplained. Whether more advanced age, hygiene status, or poor socioeconomic conditions are the etiologies of susceptibility to *H. pylori* infection in patients with COPD also remains to be determined. However, in the present study groups, socioeconomic and age status did not show difference between the groups.

Roussos *et al*. [8] found elevated serum *H. pylori* IgG positivity and serum *H. pylori*-specific IgG levels in patients with COPD, but they did not find an association with lung function values.

Eisa *et al*. [9] found a statistically significant association between anti-CagA and both disease severity and FEV1 values. This also goes in agreement with Gencer *et al*. [10], who reported a negative association between FEV1 and *H. pylori* serum IgG parameters in patients with COPD.

Although the action of *H. pylori* in the pathology of COPD is still under investigation, the induction and mediators of inflammation activation by the *H. pylori* infection and through the COPD disease may clarify the etiopathogenetic action of *H. pylori*. CagA + *H. pylori* strains activate the release of inflammatory mediators and cytokines like interleukin-1 (IL) 1, IL8, and tumor necrosis factor α [11]. Serum levels of cytokines return back to normal following eradication medications of *H. pylori* [12]. Alternatively, inflammatory reaction is the main pathological finding in COPD and is accompanied with activation of inflammatory cells like macrophages and neutrophils in bronchial mucosa and causes the release of mediators of inflammation [13].

Multiple research studies have found that mediators and cytokines are stimulated through *H. pylori* infection and in the disease of COPD and its exacerbation of COPD [11]. This finding strengthens that infection with *H. pylori* has a stimulatory and proinflammatory action in COPD. Serology and epidemiology research studies have found an association between *H. pylori* infection and diseases of extra-GIT [14]. Systemic inflammatory reaction activated by *H. pylori* is considered the cause of these associations. Kowalski *et al*. [15] have stated an association between *H. pylori* bacterial infection and the diseases of the coronary artery. Moreover, they studied the effect of inflammatory substances that are toxic like inflammatory mediators and cytokines. Many previous research studies have stated an association between *H. pylori* infection and pulmonary diseases like lung cancer, chronic bronchitis, and bronchiectasis and have emphasized that inflammatory responses that affect stomach mucosa may also affect bronchial mucosa [11]. This action is stimulated by the mediators of systemic inflammation. Alternatively, Bayraktaroğlu *et al*. [16] stated that despite the high production of cytotoxins that come after an inflammation response owing to *H. pylori*, levels of IL6, IL8, and tumor necrosis factor α in the serum are not raised. So, these cytokines might form and release locally in bronchial tract secretions. In addition, finding of *H. pylori* in the bronchial mucosa secretion can potentiate its association with pulmonary diseases. More research studies detecting *H. pylori* specifics DNA, histological alteration of the bronchial tree tissue, and the action of eradication treatment of *H. pylori* on COPD are required to show the effect of *H. pylori* infection throughout the course and disease of COPD [17].

Conclusion

The present study detected an association between *H. pylori* infection and COPD, and *H. pylori* IgG parameters are negatively associated with the stage of severity of COPD. More research studies are needed to determine the action of *H. pylori* infection on the pathology of COPD and investigate the action of *H. pylori* eradication treatment on COPD.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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