

Helicobacter pylori seroprevalence in patients with lung cancer

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Abstract

AIM: To assess *Helicobacter pylori* (*H pylori*) seroprevalence in a cohort of Greek patients with lung cancer.

METHODS: Seventy-two lung cancer patients (55 males and 17 females, aged 58.2±11.7 years) and 68, age and gender-matched, control subjects were enrolled. All subjects underwent an enzyme-linked immunosorbent assay IgG serologic test for *H pylori* diagnosis.

RESULTS: A correlation between age and *H pylori* IgG level was detected for both lung cancer patients ($r = 0.42$, $P = 0.004$) and controls ($r = 0.44$, $P = 0.004$). Seropositivity for *H pylori* did not differ significantly between patients with lung cancer and controls (61.1% vs 55.9%, $P > 0.05$). Concerning the mean serum concentration of IgG antibodies against *H pylori*, no significant difference between the two groups was detected (32.6±19.1 vs 27.4±18.3 U/mL, $P > 0.05$).

CONCLUSION: No significant association between *H pylori* infection and lung cancer was found.

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INTRODUCTION

Helicobacter pylori (*H pylori*) infection of the gastric mucosa affects approximately 50% of the world's population^[1]. It seems to be the main cause of chronic antral gastritis^[2] and is strongly associated with peptic ulcer disease^[3], gastric cancer^[4], and gastric MALT-lymphoma^[5]. In the past few years, a variety of extradigestive disorders, including cardiovascular, skin, rheumatic and liver diseases, have also been associated with *H pylori* infection^[6,7]. As regards respiratory diseases, an increased *H pylori* seroprevalence has been found in active bronchiectasis^[8], chronic bronchitis^[9,10] and active pulmonary tuberculosis^[11]. The activation of inflammatory mediators by *H pylori* seems to be the common pathogenetic mechanism underlying the observed associations^[12].

It is well known that the prevalence of lung cancer in peptic ulcer patients is increased 2 to 3 fold compared with findings in ulcer-free controls^[13-18]. The major factor underlying this association seems to be the impact of cigarette smoking on both diseases. However, a recent pilot study, in a small number of patients, showed that *H pylori* infection, *per se*, might be implicated in lung cancerogenesis^[19]. It suggested that the prolonged release of gastrin and cyclooxygenase (COX)-2 in *H pylori* infected patients might account for the stimulation of lung cancer growth and tumor neoangiogenesis^[19]. However, insufficient information is available on the prevalence of *H pylori* infection in lung cancer patients.

Therefore, in order to further investigate the relationship between *H pylori* infection and lung cancer, we assessed *H pylori* seroprevalence in a cohort of Greek patients with lung cancer and control subjects.

MATERIALS AND METHODS

Study subjects

The present study was conducted at the 9th Department of Pulmonary Medicine, "Sotiria" Chest Diseases Hospital (Athens, Greece). The local ethics committee approved the study and written informed consent was obtained from each participant. Following a predefined protocol, between March 1, 2002 and April 30, 2001, 104 consecutive patients with, histologically verified, primary lung cancer were recruited from our department. Exclusion criteria were: (1) prior *Helicobacter* eradication therapy, (2) consumption of acid suppressive drugs or antibiotics in the preceding 6 mo and (3) a history of vagotomy or operations of the upper gastrointestinal tract. A total of 32 patients were excluded. Therefore, 72 patients were eligible for analysis.

Controls were selected randomly from subjects who attended courses designed for public health education during the period of the study. Exclusion criteria for controls were: (1) a known history of lung cancer and (2) a known history of gastrointestinal tract pathology. Finally, we selected 68 controls out of 99 healthy subjects and we matched them with the patients for sex, age (within 2 years) and socioeconomic status.

Methods

All subjects enrolled (lung cancer patients and controls) underwent an enzyme-linked immunosorbent assay (ELISA) IgG serologic test for *H pylori* diagnosis (HEL-P test, Park Co, Athens, Greece), in accordance with the manufacturer's guidelines. A positive, borderline or negative result was assigned when the concentration of IgG antibodies against *H pylori* was greater than 25, between 20 and 25 and less than 20 U/mL respectively. The specificity and sensitivity of the serology test, validated in our local population, were 95% and 85% respectively.

Statistical analysis

Results are expressed as mean±SD. Significance of difference between groups was assessed by unpaired Student's *t*-test for continuous variables and χ^2 -test for proportions. Correlation coefficients between variables were determined using conventional

Pearson's correlation analysis. Statistical analysis was performed using SPSS program (SPSS Inc, IL, USA) and *P*-values were two-tailed analyzed. *P* less than 0.05 was considered statistically significant.

RESULTS

The demographic data of both patients and controls are shown in Table 1. There was no statistical difference in age or gender between the two groups. The majority of lung cancer patients were current cigarette smokers (60 patients, 83.3%) or ex-smokers (10 patients, 13.9%) and only 2 patients (2.8%) had never smoked. On the other hand, 40 out of 68 control subjects (58.8%) were never-smokers, 20 (29.4%) were current and 8 (11.8%) were previous smokers.

A correlation between age and *H pylori* IgG level was detected for both lung cancer patients ($r = 0.42$, $P = 0.004$) and controls ($r = 0.44$, $P = 0.004$). Among the lung cancer patients, 44 (61.1%) were anti-*H pylori* IgG positive, 2 (2.8%) had borderline values and 26 (36.1%) were seronegatives. Of the control subjects 38 (55.9%) were anti-*H pylori* IgG positive, 2 (2.9%) were borderline and 28 (41.2%) were seronegatives.

H pylori seropositivity did not differ significantly between patients with lung cancer and controls ($P > 0.05$) (Table 1). Concerning the mean serum concentration of IgG antibodies against *H pylori* no significant difference between the two groups was detected ($P > 0.05$).

Table 1 Demographic data and *H pylori* serologic parameters

Parameter	Control (n = 68)	Lung cancer (n = 72)	<i>P</i>
Age (yr)	54.8±12.1	58.2±11.7	0.79
Male gender (%)	73.5	76.3	0.88
<i>H pylori</i> IgG level (U/mL)	27.4±18.3	32.6±19.1	0.18
<i>H pylori</i> IgG seropositivity (%)	55.9	61.1	0.23

DISCUSSION

Data in literature on the relationship between *H pylori* infection and lung cancer are poor. Recently, Gocyk *et al.* carried out a pilot study in a sample of 50 Polish patients with lung cancer and showed an increased *H pylori* seroprevalence (89%). Moreover, they proposed that the seropositive patients might be considered for *H pylori* eradication in order to reduce the hypergastrinemia and COX-2 expression^[19], provoked by this bacterium. As both overexpression of COX-2 in lung tissue^[20-22] and increased serum levels of gastrin^[23] have been reported in lung cancer patients, a pathogenetic link between *H pylori* infection and lung cancer seems to exist.

Our study is the first one focusing on seroprevalence of *H pylori*, in a relatively large population of Greek patients with lung cancer. According to our results, *H pylori* seroprevalence in lung cancer patients did not differ significantly from that of the control subjects. The age-related pattern of infection, which in our study was detected for both lung cancer patients and controls, was common in developed countries and explained by the cohort effect^[24]. The socioeconomic status, which was related with both *H pylori* infection and risk of lung cancer, was similar between the two groups. Tobacco use could be another confounding factor. Cigarette smoking was the most important etiologic factor of lung cancer and seemed to fully account for the, observed in previous studies, association between peptic ulcer and lung cancer^[13-18]. However, data on the relationship between *H pylori* infection and smoking habits are controversial. The prevalence of *H pylori* infection in smokers has been variously reported as low^[25], normal^[26], and high^[27]. In the present study, we did not match patients with

control subjects in smoking habits. As the relation between smoking and *H pylori* infection has not been clarified yet, the possible impact of cigarette smoking on both lung cancer and *H pylori* infection should be regarded as a potential study limitation.

The present study did not focus on the potential pathogenetic mechanisms underlying a possible association between *H pylori* infection and chronic bronchitis. This association might reflect either susceptibility induced by common factors or a kind of causal relationship between these diseases. As far as we know, there are no common factors implicated in the susceptibility to both lung cancer and *H pylori* infection. However, we can not rule out this possibility, as the predisposing conditions to *H pylori* infection have not been clarified yet. With regard to the aetio-pathogenetic role of *H pylori* infection in lung cancer development, it has been suggested that the prolonged release of gastrin and cyclooxygenase (COX)-2 in *H pylori* infected patients might stimulate lung cancer growth and lead to tumor neoangiogenesis^[19]. The spilling or inhalation of *H pylori* or its exotoxins into the respiratory tract might also lead to their accumulation in lung tissue. However, as far as we know, neither identification of *H pylori* species in human bronchial tissue, nor isolation of *H pylori* from bronchoalveolar lavage (BAL) fluid has been achieved yet^[24]. Studies estimating the relative risk of developing lung cancer for *H pylori* infected patients and the effect of *H pylori* eradication on the natural history of chronic bronchitis are also needed to further investigate these hypotheses.

In conclusion, the present study suggests that *H pylori* seroprevalence in lung cancer patients did not differ significantly from that of control subjects. Our results should be confirmed in a larger number of patients. Further studies are needed to clarify the pathogenetic mechanisms, if those exist, underlying a possible association between these two diseases.

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