**SUMMARY**

**Objectives:** A high *Helicobacter pylori* (*H. pylori*) seroprevalence has been found in many extragastrointestinal disorders. Moreover, it has been reported that the tuberculosis (TB) risk may be increased in patients with a history of peptic ulcer disease. The aim of this study was to assess the *H. pylori* seroprevalence in patients with newly diagnosed pulmonary TB, before the initiation of antituberculosis treatment.

**Methods:** We evaluated all patients with newly diagnosed pulmonary TB presenting to our hospital during a 2-year period. We evaluated 80 patients with pulmonary TB and 70, age and sex–matched, control subjects. All enrolled subjects (tuberculosis patients and controls) underwent an enzyme-linked immunosorbent assay (ELISA) IgG serologic test for *H. pylori* diagnosis.

**Results:** A correlation between age and *H. pylori* IgG level was detected for both TB patients (r=0.42, p=0.004) and controls (r=0.44, p=0.004). The *H. pylori* seropositivity in the TB group was significantly higher than that of controls (87.5% vs 61.4%, p=0.02). The mean serum concentration of IgG antibodies against *H. pylori* was also significantly higher in TB patients than in control subjects (39.0– 25.2 U/ml vs 26.1–21.2 U/ml, p=0.001).

**Conclusions:** *H. pylori* infection may be associated with pulmonary TB. Further studies should be undertaken to confirm our results and to clarify the potential underlying pathogenetic mechanisms.

**Key words:** *Helicobacter Pylori*, Prevalence, Tuberculosis

**INTRODUCTION**

*Helicobacter pylori* (*H. pylori*) infection of the gastric mucosa affects approximately 50% of the world’s population. It seems to be the main cause of chronic antral gastritis and is strongly associated with peptic ulcer disease, gastric cancer, and gastric MALT – lymphoma. A high *H. pylori* seroprevalence has also been found in many extra gastrointestinal disorders, including coronary heart disease, rosacea and growth failure in childhood.

In 1992, Mitchell et al found that a history of pulmonary TB might be associated with an increased prevalence of *H. pylori* infection. More recently, Woeltje et al assessed the prevalence of tuberculin skin test (TST) positivity in a cohort of 346 newly hospitalized patients. A history of peptic ulcer disease was one of the identified risk factors for a positive TST test. However, insufficient information is available on the prevalence of *H. pylori* infection in TB patients. A previous study showed no difference in *H. pylori* seroprevalence between patients on antituberculosis chemotherapy and control subjects. However, antituberculosis regimens, including Rifampicin and Streptomycin may eradicate *H. pylori* infection and subsequently decrease serum concentrations of *H. pylori* IgG antibodies. As far as we know, there are no studies focused on the seroprevalence of *H. pylori* in TB patients, before the initiation of antituberculosis treatment.

In order to investigate the relation between *H. pylori*...
infection and TB, we assessed the \textit{H. pylori} seroprevalence in patients with newly diagnosed pulmonary TB, before the commencement of antituberculosis treatment.

\textbf{MATERIALS AND METHODS}

The present study was conducted at the 9th Department of Pulmonary Medicine, at “Sotiria” Chest Diseases Hospital (Athens, Greece). Following a predefined protocol, between January 1, 1998 and January 31, 2001, we studied all consecutive patients with newly diagnosed pulmonary TB. Only patients with a proven bacteriologically and/or histological diagnosis were included in the study. The local ethics committee approved the study and written informed consent was obtained from each participant.

The diagnosis of TB was based on one or more of the following criteria: 1) positive sputum culture for \textit{Mycobacterium tuberculosis}, 2) positive sputum smear for acid fast bacilli and 3) presence of necrotic caseous granulomas in lung biopsy. Patients who had only criteria 2) and/or 3) had to show clinical and radiological improvement with antituberculosis chemotherapy. Exclusion criteria were: 1) compromised immunity (e.g. patients receiving corticosteroids or diagnosed as having acquired immunodeficiency syndromes), 2) critical illness, 3) prior \textit{H. pylori} eradication therapy, 4) consumption of acid suppressive drugs or antibiotics in the preceding 6 months and 5) a history of vagotomy or operations on the upper gastrointestinal tract.

Our control group included healthy subjects, well matched for age, sex and socio-economic status, who attended courses designed for public health education. None of the control subjects had a known history of TB or upper gastrointestinal tract pathology. All subjects (patients and controls) were questioned on the number of patients living in the same household. Moreover, social status was graded from 1 to 3 (low, mean or high) on the basis of family income.

All subjects enrolled (tuberculosis patients and controls) underwent an enzyme-linked immunosorbent assay (ELISA) IgG serologic test for \textit{H. pylori} diagnosis (HEL-P test, Park Co, Athens, Greece), in accordance with the manufacturer’s guidelines. A positive, borderline and negative result was assigned when the concentration of IgG antibodies against \textit{H. pylori} was greater than 20, between 12.5 and 20 and less than 12.5 U/ml respectively. The specificity and sensitivity of the serologic test validated in our local population were 95% and 85% respectively.\cite{13}

Results are expressed as mean ± one standard deviation (±SD). Significance of difference between groups was assessed by unpaired Student’s t-test for continuous variables and \chi^2-test for proportions. Correlation coefficients between variables were determined using conventional Pearson’s correlation analysis. The statistical analysis was performed using the SPSS program (SPSS Inc, IL, USA). P values of less than 0.05 were considered statistically significant.

\textbf{RESULTS}

A total of 80 TB patients and 70 control subjects were recruited into this study. 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.

Among the TB patients 70 (87.5%) were anti-\textit{H. pylori} IgG positive, 2 (2.5%) had borderline values and 8 (10%) were seronegative. Of the control subjects 43 (61.4%) had positive values, 2 (2.9%) were borderline and 25 (35.7%) were seronegative. A correlation between age and \textit{H. pylori} IgG level was detected for both TB patients (r=0.42, p=0.004) and controls (r=0.44, p=0.004).

Table 1 shows analytically the serologic parameters. The \textit{H. pylori} seropositivity in the TB group was significantly higher than that of controls (p=0.02). The mean serum concentration of IgG antibodies against \textit{H. pylori} was also significantly higher in TB patients than in con-

\begin{table}[h]
\centering
\caption{Demographic data and \textit{H. pylori} serologic parameters}
\begin{tabular}{llll}
\hline
\textbf{Parameters} & \textbf{Controls} & \textbf{TB patients} & \textbf{P-value} \\
 & (n=70) & (n=80) & \\
\hline
Age & 56.8±15.9 & 55.2±14.8 & 0.78 \\
Male gender (%) & 54.3 & 57.5 & 0.42 \\
\textit{H. pylori} IgG level (U/ml) & 26.1±21.2 & 39.0±25.2 & 0.02 \\
\textit{H. pylori} IgG seropositivity (%) & 61.4 & 87.5 & 0.007 \\
\hline
\end{tabular}
\end{table}
DISCUSSION

Data in the literature on the relationship between H. pylori infection and pulmonary TB are poor. A previous epidemiological study, in a Southern China population, suggested that a history of tuberculosis might be associated with increased prevalence of H. pylori infection. Poor socio-economic and sanitary conditions during childhood could explain these results, as it is well known that in developing countries acquisition of both H. pylori and Mycobacterium tuberculosis occurs early in life. Recently, Sanaka et al showed no difference in H. pylori seroprevalence between patients on antituberculosis chemotherapy and control subjects. However, in that study the decrease in serum concentration of H. pylori IgG antibodies due to the eradication of H. pylori by antituberculosis drugs could not be excluded. Rifampicin and Streptomycin, two drugs commonly used in antituberculosis regimens, are effective against H. pylori and decrease in H. pylori seroprevalence during antituberculosis therapy has been reported.

Our study is the first focused on the seroprevalence of H. pylori in TB patients, before the initiation of antituberculosis treatment. According to our results, the H. pylori seroprevalence in patients with pulmonary TB is significantly higher than that of the control subjects. The socio-economic status, which is related to both H. pylori seroprevalence and risk of pulmonary TB, is similar in the two groups. Unfortunately, we did not perform a tuberculin skin test in control subjects. Although we primarily focused on active pulmonary TB, this omission should be regarded as a potential limitation of our study. A possible common route of transmission could be another confounding factor. However, neither the H. pylori nor the Mycobacterium tuberculosis has been cultured from traditional environmental reservoirs such as water, insects, pets or farm animals. Moreover, the airborne transmission of Mycobacterium tuberculosis occurs even without physical contact, whereas H. pylori usually spreads via close physical contact. Thus, the observed association between H. pylori infection and pulmonary TB seems to be real and cannot be attributed to transmission-associated confounding factors.

The present study has not focused on the potential pathogenetic mechanisms underlying the association between H. pylori infection and development of pulmonary TB. This association might reflect susceptibility to both infections induced by common host genetic factors. It has been suggested that HLA-DQ serotype may contribute to enhanced mycobacterial survival and replication. Recent studies showed that this serotype is also associated with increased susceptibility to H. pylori infection. On the other hand, the role of chronic H. pylori infection as a predisposing factor for development of pulmonary TB is unknown. An increased risk of TB for persons who had undergone partial gastrectomy or vagotomy for peptic ulcer disease has previously been reported. With regard to the pathogenetic role of H. pylori infection in peptic ulcer disease, we could hypothesize that H. pylori infection per se may be related to the risk of pulmonary TB.

However, the common genetic predisposition to both bacteria and the consideration of H. pylori infection as a predisposing factor for development of pulmonary TB are only hypotheses. We cannot exclude the possibility that other factors, linked to the host or bacterial strains, may be responsible for the observed association between the two infections.

In conclusion, the present study suggests that patients with pulmonary TB have an increased seroprevalence of H. pylori infection. Our results must be confirmed in a larger number of patients. Further studies should be undertaken to clarify the pathogenetic mechanisms underlying the possible association between H. pylori infection and pulmonary TB.

REFERENCES