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Association of *Helicobacter pylori* infection with chronic obstructive pulmonary disease

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a disease that is systematically characterized by an abnormal inflammatory response affecting the airways, interstitium and vascular bed through reactions to gas and particles, especially cigarette smoking. Recent studies have shown an association between *Helicobacter pylori* infection and various inflammatory diseases. *H. pylori* is a gram-negative, microbial bacterium that can be resistant to acidic stomach conditions and can interfere with gastric urease production. In this study, we examined the relationship between *H. pylori* infection in patients with COPD and the prevalence of *H. pylori* infection.
Objectives: Determining the association between *H. pylori* infection and COPD.
Patients and Methods: This case-control study is based on the Persian cohort study of patients who were referred to the digestive disease research center after being identified in the pulmonary clinic for *H. pylori* fecal antigen. Information on demographic variables and other related variables were obtained. Finally, the collected information was entered into SPSS software version 24 and the results were displayed descriptively using distribution and frequency tables and graphs and analytical statistics were analyzed using *t* test and logistic regression.
Results: Out of 250 patients, 134 (53.6%) tested positive for *H. pylori* and 116 (46.4%) tested negative. Out of a total of 250 non-infected people; 106 patients (42.4%) were positive and 144 patients (57.6%) were negative. The two groups were statistically significantly different based on the chi-square test ($P = 0.012$).
Conclusion: Our study showed a direct and significant relationship between *H. pylori* and COPD, which can be due to the effect of bacteria on lung growth in early life and also the development of systemic inflammation throughout life.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic disease characterized by airflow restriction and systemic inflammation and it is associated with pulmonary and extra-pulmonary complications and effects about 300-600 million people and kills three million people annually (1,2).

Objectives

The clinical impact of *Helicobacter pylori* infection on the prevalence of COPD and lung function may vary depending on the regional prevalence of *H. pylori*. So far, few studies have been performed on the relationship between *H. pylori* infection and COPD and the effect of *H. pylori* infection on lung function and the results have been contradictory. Due to the high prevalence of *H. pylori* infection in Ardabil, this study was performed to determine the relationship between *H. pylori* infection and COPD.

Key point

Based on the analysis of this case-control study results we showed a direct and significant relationship between *Helicobacter pylori* infection and chronic obstructive pulmonary disease in studied cases.

Patients and Methods

Study design

This study was a case-control study that was conducted from September 2020 to September 2021 in Ardabil hospital. The case group was 250 people with COPD and the control group was 250 healthy people who referred to Ardabil gastroenterology and liver research center. The case and control groups were matched for gender and age. In the present study, the presence of COPD was diagnosed by spirometry. After being identified in the lung clinic, patients were referred to the gastroenterology research center for *H. pylori* fecal antigen. Information

on demographic variables and other related variables was obtained from patients and patients with other lung diseases (such as asthma) were excluded from the study. Informed consent was obtained from all patients to participate in the study. Informed consent was obtained from all patients to participate in the study.

Data analysis

After collecting the required information, the data were analyzed in SPSS 21 with descriptive statistics methods in the form of tables and graphs and descriptive and analytical statistical methods using chi-square, *t* test and logistic regression method. The significant level was set as $P<0.05$.

Results

In the present study total of 500 subjects were included in the study who were randomly divided into two groups of 250 cases and controls. The mean age of the case group was 57.99 years and the control group was 56.84 years. In terms of gender, in both groups, 190 (0.76%) were male and 60 (24.0%) female. There was no significant difference between the two groups in terms of age and gender however smoking was significantly higher in the case group than the control group (Table 1).

Out of 250 patients, 134 (53.6%) tested positive for *H. pylori* and 116 (46.4%) tested negative for the case group. Out of 250 patients in the control group, 106 (42.4%) were positive and 144 (57.6%) negative and the two groups were statistically significant (0.012) (Table 2).

There was a significant relationship between smoking, hookah use and the number of pack-years cigarettes with COPD severity among patients in the case group. Therefore, the severity of the disease was higher in smokers, hookah users and people with pack-years (Table 3).

There was a significant relationship between patients' jobs and the severity of COPD ($P=0.025$).

According to the logistic regression test, the result of *H. pylori* test was significantly associated with COPD and the odds ratio (OR) was 0.637 (95% CI: 0.448-0.907). Hookah use, drugs and occupation were not significantly associated with COPD. Cigarette smoking was significantly associated with COPD (Table 4).

Discussion

The study by Wang et al, on the relationship between COPD and *H. pylori* was meta-analyzed and showed a significant association between *H. pylori* and COPD (17). In the study of Sze et al using immunoassay method, *H. pylori* immunoglobulin (IgG) antibody titers were measured in serum samples of 4765 patients with mild to moderate COPD. Then, using multiple regression analysis, their relationship with individual FEV1 and the rate of FEV1 reduction and mortality over 11 years was determined. According to this study, *H. pylori* infection was associated with COPD (18). The study conducted by Tabaru et al on *H. pylori* infection in chronic obstructive pulmonary disease in Turkey, showed the presence of *H. pylori* infection in patients with COPD effects pulmonary function; however, the effects of *H. pylori* infection on the respiratory tract and COPD in their study was not clear (19). The study by Roussos et al, on the prevalence of *H. pylori* in patients with chronic obstructive pulmonary disease, showed an increased frequency of *H. pylori* infection in patients with COPD (20). Hashemi showed an association between *H. pylori* infection and the incidence of COPD, which was consistent with the present study (21). Moreover, Gencer et al showed serum level of *H. pylori* specific IgG was significantly higher in patients with COPD versus control group. Based on their study, a direct relationship between *H. pylori* IgG levels and the severity of COPD was detected, which was consistent with the results of the present study (16).

In our study, out of 250 patients, 134 (53.6%) tested

Table 1. Demographic variables and smoking in the study groups

Variable		Case group		Control group		*P* value
		Number	Percent	Number	Percent	
Gender	Man	190	76.0	190	76.0	1.000
	Female	60	24.0	60	24.0	
Smoking	Yes	76	30.4	204	8.6	<0.001
	No	174	69.6	46	18.4	
		Mean	Standard deviation	Mean	Standard deviation	
Age (year)		55.99	11.82	56.86	10.46	0.248

Table 2. *Helicobacter pylori* test results

Variable		Case group (affected)		Control group		*P* value
		Number	Percent	Number	Percent	
Helicobacter pylori	Negative	116	46.4	144	57.6	0.012
	Positive	134	53.6	106	42.4	
Total		250	100	250	100	

Table 3. Relationship between demographic variables and COPD severity in the case group

Variable (Qualitative)		Intensity of COPD				*P* value
		Slight	Middle	Intense	Very intense	
Gender	Man	24 (12.6)	58 (30.5)	81 (42.6)	27 (14.2)	0.519
	Female	5 (8.3)	24 (40.0)	24 (40.0)	7 (11.7)	
Location	City	22 (11.2)	61 (31.1)	84 (42.9)	29 (14.18)	0.572
	Village	7 (13.0)	21 (38.9)	21 (38.9)	5 (9.3)	
Smoking	Yes	9 (11.8)	34 (44.7)	26 (34.2)	7 (9.2)	0.049
	No	20 (11.5)	48 (27.6)	79 (45.4)	27 (15.5)	
Hookah use	Yes	20 (11.1)	51 (28.3)	79 (43.9)	30 (16.7)	0.029
	No	9 (12.9)	31 (44.3)	26 (37.1)	4 (5.7)	
Narcotic	Yes	27 (11.6)	81 (34.9)	94 (40.5)	30 (12.9)	0.145
	No	2 (11)	1 (6)	11 (61)	4 (22)	
Helicobacter pylori test	Negative	13 (11.2)	38 (32.8)	52 (44.8)	13 (11.2)	0.717
	Positive	16 (11.9)	44 (32.8)	53 (39.6)	21 (15.7)	
Variable (quantitative)		**Intensity of COPD**				***P* value**
		Slight	**Middle**	**Intense**	**Very intense**	
Age (year)		58.90(13.97)	56.11 (11.99)	58.69 (11.30)	59.62(10.93)	0.356
Number of packs per year		21.58(9.63)	22.19(6.55)	27.11(6.58)	30.25(7.29)	<0.001

Table 4. The effect of age, sex and *Helicobacter pylori* test result and COPD in subjects

Variable	B	SE	*P* value	Odds ratio	95% CI	
					Upper	Lower
H. pylori	-0.451	0.80	0.012	0.637	0.907	0.448
Smoking	-0.472	0.499	<0.001	0.031	0.083	0.012
Hookah use	-1.255	0.670	0.061	0.285	1.061	0.077
Narcotic	-1.388	0.594	0.589	0.250	0.800	0.078
Job	-1.848	1.595	0.158	0.247	1.593	0.007

positive for *H. pylori* and 116 (46.4%) tested negative. Out of a total of 250 non-infected people; 106 patients (42.4%) were positive and 144 patients (57.6%) negative. There was a statistically significant difference between the two groups ($P=0.012$). Our study was consistent with other similar studies. In this case, the decrease in lung function may be due to the effect of bacteria on lung growth early in the life and the development of systemic inflammation throughout life. Furthermore the study by Lee et al showed an association between *H. pylori* positivity and the severity of COPD. In addition, *H. pylori* infection did not affect the rate of decline in lung function in this population (22). Therefore, our study is not in line with the above study and more studies are needed. According to the study by Kojima et al, the incidence of COPD in smokers was significantly higher than in non-smokers. They also showed a direct relationship between smoking and COPD (23).

In our study, smoking was significantly higher in the case group than the control group ($P<0.001$). The result of the present study was consistent with the above study and based on this finding, it can be concluded that inflammation of the pulmonary ducts caused by exposure to cigarette smoke can cause COPD. To find the predictors of mortality individuals with COPD, Esteban et al found that, the amount of smoking can be related to the severity of COPD as well as the resulting mortality (24). According to the study by Tzanakis et al, the overall prevalence of COPD in the population over 35 years of age with a history of smoking more than 100 cigarettes in a lifetime was 8.4% and the severity of smoking and age were significantly associated with the prevalence of COPD in men and women (25). In our study, there was a significant relationship between smoking and hookah use and the number of pack-years cigarettes with the severity of COPD. The severity of the disease was significantly higher in smokers, people with hookah use and people with higher pack-years. Therefore, our study was consistent with the study by Esteban et al. It is possible that with increasing exposure to external factors (such as smoke), the amount of inflammation in the lung ducts also increases and the disease intensifies. Rodríguez et al conducted study on the effect of occupational exposure on the intensity of COPD. This cross sectional study was conducted on 185 male patients with COPD. Patients underwent primary spirometry and a questionnaire was collected from patients including respiratory symptoms, hospitalization due to COPD, smoking, current employment status and work history. Exposure to biological dust, inorganic dust, gases and vapors was examined. According to the results of this study, occupational exposure is independently

related to the severity of airflow restriction, respiratory symptoms and inactivity in patients with COPD (26). During our study, a significant relationship was found between patients' jobs and the severity of COPD ($P=0.025$). Our study was also in line with the study by Rodríguez et al (26). We interpreted that vapors, dust and gases in the workplace can act as allergens to stimulate the inflammatory process in the lung tissue and thus restrict the flow of lung air. According to the study by Tzanakis et al, the prevalence of COPD by gender was 11.6% for men and 4.8% for women. The severity of smoking and age were also significantly associated with the prevalence of COPD in men and women (25). In our study, age and gender were not significantly associated with COPD since our study was not in line with that of Tzanakis et al, which could be due to cultural, economic, occupational and lifestyle differences.

Conclusion

The results of the present study showed a direct and significant relationship between *H. pylori* and COPD, which could be due to the effect of bacteria on lung growth in early life and also the development of systemic inflammation throughout life. Considering the ethnic and cultural diversity in the country and the impact of lifestyle on the course of COPD, it is suggested that a similar study be conducted on a national scale and the association and impact of other infectious or gastrointestinal diseases with COPD be investigated. It is also suggested that using the results of this study, the possibility of *H. pylori* in COPD patients be considered and if necessary, diagnostic and therapeutic measures be conducted.

Limitations of the study

This is a preliminary study with a limited number of patients. We suggest further investigation on this feature of COPD patients.

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Authors' contribution

SH, SMK, FP, MB and MA were the principal investigators of the study. SH, SMK and MS were included in preparing the concept and design. FP and MB revisited the manuscript and critically evaluated the intellectual contents. FP and MA were helped in data collection and analysis. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interests

The authors declare no conflict of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Ardabil University of Medical Sciences approved this study (IR.ARUMS.REC.1399.183). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D thesis of Masoud Aslani at this university (Thesis#899). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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