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RESEARCH ARTICLE

Incidence of peptic ulcer in bronchial asthma and chronic obstructive pulmonary disease and its relation to *Helicobacter pylori* infection

Nesriene El-Margoushy[1], Ahmed M. A. Mansour[2], Nihad El-Nashar[3], Manal El-Nashar[4], Tamer Askar[5,6]

[1]Department of Internal Medicine, Faculty of Medicine, Taif University, Saudi Arabia, [2]Department of Medical Laboratory, Faculty of Applied Medical Science, Tarabah, Taif University, Saudi Arabia, [3]Department of Clinical Pathology, Faculty of Medicine, Taif University, Saudi Arabia, [4]Department of Pediatrics, Faculty of Medicine, Taif University, Saudi Arabia, [5]Department of Medical Clinic, Faculty of Applied Medical Science, Tarabah, Taif University, Saudi Arabia, [6]Department of Cardiovascular, Faculty of Medicine, Al-Azhar University, Egypt

Correspondence to: Ahmed Mansour, E-mail: mariam.amin09@yahoo.com

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ABSTRACT

Background: Asthma and chronic obstructive pulmonary disease (COPD) are characterized by a progressive airflow limitation. COPD is considered the fourth leading cause of death worldwide. *Helicobacter pylori* is a Gram-negative bacteria are closely associated with peptic ulcer development. **Aims and Objectives:** This study aimed to compare the incidence of peptic ulcer disease between asthmatic and COPD group of patients and evaluation of its relation to *H. pylori* infection. **Materials and Methods:** This study includes 50 patients with COPD from both sexes (M: 35/F: 15), 50 patients with bronchial asthma from both sexes (M: 30/F: 20) from King Abdul-Aziz Hospital, Taif area, and 25 healthy control volunteers (M: 17/F: 8) matched in age and sex. Total immunoglobulin E (IgE), pH, pO_2, pCO_2, forced vital capacity (FVC), forced expiratory volume in first second (FEV1)/FVC, and forced expiratory flow (FEF) 25-75 were measured and matched between various groups. **Results:** Total serum IgE T-IgE showed a non-significant increase in COPD patients compared to control (68.33 ± 16.74) while it increased significantly in asthmatic patients (243.65 ± 120.54) compared to control. Regarding pH, pO_2, and pCO_2 relation between control and asthmatic patients, the results are non-significant while it was significant ($P < 0.05$) for pH between control and COPD patients and was highly significant ($P < 0.001$) for pO_2 and pCO_2 in the two groups. For FVC, FEV1/FVC, and FEF 25-75 between control and asthma patients, results considered highly significant ($P < 0.001$) while it showed a significant difference ($P < 0.05$) for FEV1 in both groups. For FVC, FEV1/FVC, and FEF 25-75 between control and COPD patients, the results are considered highly significant ($P < 0.001$), and a very highly significant difference ($P < 0.05$) for control and COPD. **Conclusion:** Close interaction between the incidence of peptic ulcer disease with asthma and COPD group of patients in relation to *H. pylori* infection was confirmed.

KEY WORDS: Peptic Ulcer; Chronic Obstructive Pulmonary Disease; Bronchial Asthma; *Helicobacter pylori* Infection

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease characterized by a progressive airflow limitation due to chronic inflammation of the airways and lung parenchyma. The role of infections has also been mentioned in the pathogenesis and progression of the disease, where exacerbations in

COPD patients are commonly caused by respiratory tract infections.[1] COPD is considered the fourth leading cause of death worldwide. It is predicted to become the third leading cause of death worldwide by the year 2020. According to the global initiative for chronic obstructive lung disease (GOLD), COPD is defined as a preventable and treatable disease that leads to the narrowing of the airways and is not fully reversible.[2] Its main symptoms were including shortness of breath, cough, and sputum production.[3] It is defined by the history of respiratory symptoms such as shortness of breath, wheeze, cough, and chest tightness that vary over time and intensity, together with variable expiratory airflow limitation. Exacerbations of asthma often have identifiable triggers such as cold air, allergens, or exercise.[4] Immunoglobulin E (IgE) is crucial to the pathophysiological cascade that triggers allergic reactions and continues bronchial airway inflammation.[5] *Helicobacter pylori* are Gram-negative bacteria with a slow growing nature. They are characterized by the production of large quantities of urease. *H. pylori* are linked to the development of peptic ulcer disease, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue lymphoma. It has been classified by the WHO as a Class I carcinogen.[6] The bacteria undergoes colonization in the gastric mucosa causing a long-term immune response with local and systemic inflammation. Previous studies have provided extensive evidence on the role of *H. pylori* in chronic gastritis and peptic ulcer.[7] Recent studies have shown that there is a relationship between *H. pylori* infection and extra-gastric diseases as COPD, bronchiectasis, asthma, lung cancer, and lung tuberculosis.[8,9] The possible mechanism for the relationship between *H. pylori* and lung diseases might be the systemic effect of certain gastrointestinal peptides as gastrin, somatostatin, and cytokine release or due to direct injury and chronic inflammation of airways due to aspiration and inhalation. Due to the release of various inflammatory cytokines in chronic lung diseases, *H. pylori* eradication causes returning of these cytokines to their normal levels, most probably activation of inflammatory mediators by *H. pylori* is the pathogenic mechanism of extra-gastric manifestations of *H. pylori* infection.[10] Exposure to *H. pylori* can be determined by detection of immunoglobulin A, immunoglobulin G (IgG), or immunoglobulin M-class serum antibodies to the organism. Screening patients for the presence of antibody to *H. pylori* is a convenient, non-invasive means for assessing whether a patient has been exposed to *H. pylori* and whether gastrointestinal symptoms may be related to *H. pylori* infection.[11]

MATERIALS AND METHODS

This study enrolled 50 patients with COPD from both sexes (M: 35/F: 15), 50 patients with bronchial asthma from both sexes (M: 30/F: 20) from King Abdul-Aziz Hospital, Taif, Saudi Arabia, and 25 healthy control volunteers (M: 17/F: 8) matched in age and sex. Bronchial asthma, COPD was diagnosed on the basis of patient history, physical examination, and spirometric data.[12] All patients with upper respiratory tract infection during or within 4 weeks of the study were used for this study. Patients with other respiratory diseases are excluded.

Patients Selection

The local ethics committee approved the study, and written informed consent was obtained from each participant. Following a predefined protocol, between August and October 2015, 98 consecutive patients with COPD, diagnosed according to the Global Initiative for COPD guidelines, were recruited from the outpatient clinics. Briefly, COPD was diagnosed as the presence of a post-bronchodilator forced expiratory volume in first second (FEV1) <80% of the predicted value in combination with an FEV1/forced vital capacity (FVC) <70% in any patient who has symptoms of cough, sputum production, or dyspnea and/or a history of exposure to risk factors for the disease.[1] Exclusion criteria were applied as: (1) An exacerbation of COPD in the preceding month, as it does not represent baseline levels, (2) prior eradication therapy for *H. pylori*, (3) administration of any acid-suppressive drugs or antibiotics in the preceding 3 months, and (4) any history about upper gastrointestinal tract operations. Therefore, a total of 48 patients were excluded, and 50 patients were used for this study. The same method was used for asthmatic patients selection.

Surveys, Measurements, and Serological Parameters

History and physical examination with special attention to the symptoms of the chronic obstructive respiratory disease and asthma were considered. Blood sampling was carried out as following 10 ml of venous blood were drawn, and serum was separated from both groups for measurements of total IgE using RMA, serum *H. pylori* IgG using a commercially available kit ELISA imported by Biodiagnostics Labs, Dokki, Giza, Egypt. Moreover, arterial blood gases for both groups of patients. Pulmonary function tests were investigated in both groups. Comparison of the incidence of peptic ulcer between both groups of patients and evaluation of its relation to *H. pylori* infection was outlined.

Statistical Analysis

Data of the three groups were compared and analyzed using SPSS program version 16. Results were expressed as mean ± standard deviation. The mean values of the groups were compared using Student's unpaired *t*-test. Statistical significance was set at $P < 0.05$.

RESULTS

As shown in Table 1, there are no significant differences in age and smoking % of the control and COPD group of patients as well as the age and smoking % of the control and the asthmatic group of patients. The total IgE % in control and

asthmatic patients show a very highly significant difference ($P < 0.0001$) while the same measurement is not significant in control and COPD group of patients. Regarding, serum *H. pylori* IgG there is a highly significant difference between the control and the COPD group of patients ($P < 0.0001$), while the same measurement is highly significant between control and asthmatic patients ($P < 0.001$).

In the same time, Table 2 demonstrates that pH, pO_2, and pCO_2 are without significant between control and asthmatic patients, while it was significant ($P < 0.05$) for pH between control and COPD patients, and for pO_2 and pCO_2 in the two groups, it showed a highly significant difference ($P < 0.001$). Table 3 shows that FVC, FEV1/FVC, and forced expiratory flow (FEF) 25-75 for control and asthmatic patients are highly significant ($P < 0.001$) while for FEV_1 in both groups show a slight significant ($P < 0.05$) difference. When we compared FVC, FEV_1/FVC, and FEF 25-75 between control and COPD patients, the results were highly significant ($P < 0.001$) while for FEV_1 in both groups, it showed the highly significant difference ($P < 0.05$) as seen in Table 3. Finally, comparison between asthmatic and COPD patients based on the changes on total IgE % and pylori IgG were investigated and outlined (Table 4). Serum *H. pylori* IgG, incidences of peptic ulcer

Table 1: Demographic and laboratory data of asthmatic and COPD patients comparing to controls

Parameters	Controls (*n*=25)	Asthmatic patients (*n*=50)	COPD patients (*n*=50)
Ages (years)			
Mean±SD	54.38±6.18	52.40±3.10	56.20±7.60
P value		NS	NS
M/F	17/8	30/20	35/15
Smoking %	69	65	73
P value		NS	NS
Total IgE %			
Mean±SD	60.42±06.75	243.65±120.54	68.33±16.74
P value		<0.0001	NS
Serum *H. pylori* IgG (u/ml)			
Mean±SD	59.20±39.00	40.37±5.00	109.13±68.81
P value		<0.001	<0.0001

Values are means±SD for different categories. *P*<0.001-Highly significant. *P*<0.0001-Very highly significant. NS: Non-significant, SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, IgG: Immunoglobulin G, *H. pylori*: *Helicobacter pylori*, IgE: Immunoglobulin E

Table 2: Comparison of ABG of asthmatic and COPD patients with ABG of the control group

Parameters	Controls (*n*=15)	Asthmatic patients (*n*=25)	COPD patients (*n*=50)
pH			
Mean±SD	7.41±0.04	7.43±0.05	7.33±0.03
P value		NS	<0.05
pCO_2			
Mean±SD	34.10±6.10	32.20±5.31	55.18±9.1
P value		NS	<0.001
pO_2			
Mean±SD	91.8±9.20	86.10±7.80	60.88±10.8
P value		NS	<0.001

Values are means±SD for different categories. *P*<0.05-Significant. *P*<0.001-Highly significant. NS: Non-significant, SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, ABG: Arterial blood gases

Table 3: Comparison of PFTs of asthmatic and COPD patients with PFTs of the control group

Parameters	Controls (*n*=25)	Asthmatic patients (*n*=50)	COPD patients (*n*=50)
FVC			
Mean±SD	92±9.25	71.27±19.3	57.00±11.82
P value		<0.001	<0.001
FEV1			
Mean±SD	93±7.32	67.10±15.26	42.30±14.39
P value		<0.05	<0.0001
FEV1/FVC			
Mean±SD	85±5.28	69.80±5.74	62.05±9.00
P value		<0.001	<0.001
FEF 25-75			
Mean±SD	80±5.4	66.32±5.78	62.20±6.15
P value		<0.001	<0.001

Values are means±SD for different categories. *P*<0.001-Highly significant, *P*<0.0001-Very highly significant. PFTs: Pulmonary function tests, SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, FVC: Forced vital capacity, FEV1: Forced expiratory volume in first second, FEF: Forced expiratory flow

Table 4: Comparison between asthmatic patients and COPD patients

Parameters	Asthmatic patients (*n*=50)	COPD patients (*n*=50)
% Total IgE		
Mean±SD	243.65±120.54	68.33±16.74
P value		<0.0001
Serum *H. pylori* IgG (u/ml)		
Mean±SD	40.37±5.00	109.13±68.81
P value		<0.0001
Incidences of peptic ulcer		
n (%)	7 (14)	39 (78)
P value		<0.0001
Complicated peptic ulcer		
n (%)	1 (14)	15 (38)
P value		<0.0001

P<0.0001-Very highly significant. SD: Standard deviation, COPD: Chronic obstructive pulmonary disease, IgG: Immunoglobulin G, *H. pylori*: *Helicobacter pylori*, IgE: Immunoglobulin E

number (%), and complicated peptic ulcer number (%) were the highly significant difference ($P < 0.0001$) and were correlated.

DISCUSSION

Current findings reported an increase in the levels of serum IgE and were considered to be mostly a reflection for the allergic inflammation of the airways. We found that the total IgE T-IgE showed a non-significant increase in COPD patients in comparison to control (68.33 ± 16.74) while its increase is very highly significant in asthmatic patients (243.65 ± 120.54) in comparison to control group. This suggests a role of atopy even in COPD. Similar results were obtained in other study of total serum IgE level in COPD patients and deduced that there was a high prevalence of elevated serum T-IgE in patients with COPD without obvious atopy.[13] Moreover, serum T-IgE levels were found to be associated with symptoms such as dyspnea and impairment of lung function.[14] It has been shown that the prevalence of elevated serum T-IgE in patients with COPD, implying that even among COPD patients without obvious atopy, hypersensitive inflammation of the lower airways may exist, probably representing the real proportion of the allergic phenotype in patients with COPD.[13] Regarding T-IgE levels in asthmatic patients, other study reported that it was highly and extremely variable.[14] While, another study explained that IgE plays a major role in allergic diseases he stated that IgE binds to allergens and triggers the release of substances from mast cells that can cause inflammation, when IgE binds to mast cells, a cascade of allergic reaction can begin starting immunological reactions that eventually lead to allergic and asthmatic symptoms.[15]

Serum *H. pylori* IgG revealed that asthmatic patients have a much lower decrease in *H. pylori* IgG compared to control group with a highly significant difference. Similar results were obtained as *H. pylori* infection in patients with selective IgE deficiency revealed the inverse relation between peptic and duodenal ulcer and concluded that IgE deficiency is associated with higher rates of *H. pylori*-associated gastritis and peptic duodenal ulcers.[16] There is a hypothesis that childhood acquisition of *H. pylori* is associated with reduced risks of asthma and allergy.[17] Consistent with the present findings, asthma, and allergic arhinitis were less frequent in The Third National Health and Nutrition Examination Survey, 1988-1994 participants seropositive for hepatitis A virus, *Toxoplasma gondii*, and herpes simplex virus 1 than in seronegative persons.[18]

When we talk about the incidence of peptic ulcer in asthma and COPD group of patients, our study revealed 39 COPD patients having peptic ulcer while only 7 asthmatic patients had peptic ulcer disease. These results were in accordance to those of as he studied the relationship between *H. pylori* seropositivity and COPD.[3] It is also associated with systemic inflammation and increased risk of cardiovascular mortality in patients with COPD.[3] A positive association between *H. pylori* infection, peptic ulcer, and COPD seropositivity were confirmed.[19] On the same time, patients with COPD have an increased seroprevalence of *H. pylori* infection, especially with virulent (CagA) strains.[20] Therefore, we can postulate that the activation of inflammatory mediators by *H. pylori* infection might be the pathogenetic mechanism of the disease. In parallel, high incidence of peptic ulcer in COPD patients by various reasons was confirmed.[21] They considered the first suggest that COPD is characterized by chronic local and systemic inflammation. Thus, patients are exposed to oxidative stress secondary to chronic hypoxia and produce reactive oxygen species that may damage gastric or small intestinal mucosa. Another reason that COPD patients often need steroids for controlling lung inflammation.[22] Steroid-induced peptic ulcer disease is controversial, but steroids reportedly increase the incidence of peptic ulcer. A meta-analysis done by study showed that the association between *H. pylori* and asthma; he found that asthmatic patients have a significantly lower prevalence of *H. pylori* infection than controls.[22] Concerning the pathogenic mechanisms behind the supposed protective effect, *H. pylori* is able to stimulate the Th1 immune response, promoting persistent infection but conferring protection against asthma.[23] On the contrary, another study disagrees with our results as there is no inverse relationship between *H. pylori* infection and adult asthma with peptic ulcer.[24] Current results must be confirmed in a larger number of patients. Further, studies are needed to clarify the pathogenic mechanisms underlying the possible association between these diseases and *H. pylori*. The current study stabilized the limitation and the interaction between the incidences between certain diseases and *H. pylori* infection.

CONCLUSION

Close interaction between the incidence of peptic ulcer with asthma and COPD group of patients in relation to *H. pylori* infection was confirmed.

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