

Proportion of Gastroesophageal Reflux Symptoms in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Objective: To determine the proportion of gastroesophageal reflux symptoms in patients with chronic obstructive pulmonary disease and its association with the severity and worsening of the symptoms of chronic obstructive pulmonary disease (COPD).

Methods: A prospective, questionnaire based, case control, analytical study was conducted in the Department of Pulmonology, Jinnah Postgraduate Medical Centre, Karachi during June 2002 to January 2005. Gastroesophageal reflux symptoms were compared between 100 chronic obstructive pulmonary disease patients who fulfilled the inclusion criteria and 150 control subjects. Both groups were interviewed according to modified version of Mayo clinic GER questionnaire. Chronic obstructive pulmonary disease patients were divided into two groups according to pulmonary function tests (PFTs) results into FEV1 <50% and FEV1 >50%.

Results: Chronic obstructive pulmonary disease patients had more frequent gastroesophageal symptoms than controls (25% vs. 9.33% respectively; $p=0.001$), heartburn/acid regurgitation (70% vs. 43.33% and 56% vs. 30.66% respectively; p -value=0.001), dysphagia (15% vs. 4%; p -value=0.002) and chronic cough (89% vs. 29.33%; p -value=0.001). Twenty six COPD patients reported respiratory symptoms associated with reflux, whereas control subjects denied such association. Of the 11 patients with frequent gastroesophageal symptoms, 10 patients increased their inhaler use ($p=0.001$). Frequent gastroesophageal symptoms had shown a significant association with decreased FEV1 (25% vs. 0% p -value 0.001). In contrast Pulmonary function test results were similar among chronic obstructive pulmonary disease patients with and without gastroesophageal symptoms (48.13±20.81 vs. 50.94±23.33). Anti-reflux medication proton pump inhibitor and H2-blockers were utilized more by COPD patients as compared to control subjects.

Conclusion: A higher proportion of frequent gastroesophageal symptoms were noted by COPD patients than control subjects and higher proportion of gastroesophageal symptoms was present in severe COPD patients (JPMA 55:276;2005).

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality, and represents a substantial economic and social burden through out the world. It is the fifth leading cause of death worldwide.^{1,2} In U.K about 30,000 deaths per year are caused by COPD, and this accounts for about 6% of all male deaths and 4% of all female deaths. About 25% of all medical admissions occur as a result of respiratory disorders and more than 50% of these are chronic obstructive pulmonary disease.³

COPD is a chronic, slowly progressive disorder characterized by airflow obstruction (reduced FEV₁ and FEV₁/FVC ratio) which does not change markedly over several months. Most of the lung function remains fixed, though bronchodilator or other therapy can achieve some reversibility.⁴

Gastro esophageal reflux disease (GERD) has in recent times become an important public health issue owing to considerable health care resources utilized in its management and its deleterious effects on quality of life.⁵

GERD is a common condition affecting as much as 20%-36% of the population, particularly the elderly.⁶⁻¹⁰ GERD is defined as the movement of gastric contents into the esophagus.⁸ Reflux of gastric or intestinal contents result into damage to esophageal mucosa, causing deterioration of esophageal motility and symptoms of gastroesophageal reflux of which heartburn and/or acid regurgitation is characteristic.⁷ The normal anti-reflux mechanism consists of the lower esophageal sphincter (LES) and the anatomic configuration of gastroesophageal junction. Reflux occurs only when gradient of pressure between stomach and lower esophageal sphincter is lost. The decrease in LES tone may be due to muscle weakness or inappropriate sphincter relaxation mediated by inhibitory nerves. Secondary causes of LES incompetence include smoking, B2-agonist drugs, aminophylline, calcium channel blockers and nitrates. Abnormal activity of diaphragmatic crural muscle, which surrounds the esophageal hiatus in the diaphragm also, predisposes to gastroesophageal reflux.¹¹

The association between gastroesophageal symptoms and respiratory symptoms is well recognized in the setting of asthma.^{12,13} In U.S.A adult population it has been estimated that gastroesophageal symptoms occur at frequency of 7% daily, 14-19% weekly and 40% monthly.^{12,14,15}

In contrast to asthma, the prevalence and clinical consequences of GERD in COPD are not well characterized.^{12,15} Unlike asthma patients esophageal acid perfusion does not increase bronchoconstriction in COPD patients. Thus the relationship between gastroesophageal reflux and COPD symptoms is unclear.¹²

We conducted a study to assess the proportion of gastroesophageal reflux symptoms in patients with COPD as compared to control subjects without COPD attending the Department of Pulmonology, Jinnah Postgraduate Medical Centre, Karachi which is a tertiary care hospital and provides medical facilities to the patients from all over the country.

Patients and Methods

We enrolled 100 consecutive chronic obstructive pulmonary disease patients who attended the OPD or were admitted in the Department of Pulmonology, Jinnah Postgraduate Medical Centre, Karachi. The inclusion criteria for COPD patients was: (1) H/O 20 pack-year smoking, (2) Abnormal findings on Spirometry demonstrating non-reversible airway obstruction based on British Thoracic Society criteria (FEV1 <80% or FEV1/FVC ratio < 70% of predicted and 200ml or <15% improvement in FEV1 after inhaling salbutamol). The exclusion criteria were the following (1) patients with respiratory disorders other than COPD, (2) Normal Spirometry, (3) Active peptic ulcer disease and (4) patients with known esophageal disorders such as cancer, stricture, Achalasia.

COPD patients were divided into two groups according to pulmonary function tests (PFTs) results into FEV1 <50% and FEV1 >50%. A total of 150 subjects were taken as control group which included the persons accompanying the COPD patients who attended the Out-patient department of Pulmonology Department or the attendants of Indoor COPD patients, who denied having respiratory symptoms such as dyspnoea and chronic sputum production or had previous diagnosis of asthma or chronic obstructive pulmonary disease. Before entering the study, informed consent was obtained from each subject.

Both chronic obstructive pulmonary disease patients and control subjects completed a modified version of a previously validated Mayo clinic GER questionnaire developed by Locke and associates.¹⁶ First 50 questions out of 80 questions of GER questionnaire were asked to examine the four symptoms of gastroesophageal reflux disease including

heartburn, acid regurgitation, dysphagia and chronic cough. First question for each symptom served as branch point. If answer was "no", subjects were asked to proceed to the next symptom. The next two questions for each symptom addressed the frequency and severity of the symptom in last year. Modified version included eight questions to assess the effects of gastroesophageal (GER) symptoms on shortness of breath, cough, and wheezing and increased inhaler use. The remainder questions assessed patient's demographic data, smoking history, tea/coffee/alcohol use and over-the counter antacids or prescription of antireflux medication. This questionnaire was simple, understandable and well accepted by the COPD patients and control subjects. The questionnaire was pretested¹², and it was completed in < 25 minutes. Statistical analysis consisted of t-test for comparing means and for association between variables x²-square test was employed.

Results

One hundred COPD patients and 150 control subjects were included in the study. All the subjects in both groups were male. Patients in COPD on average were older than controls (mean age 56.8±7.8 years vs 49.5±5.18 years respectively p=0.001). The smoking pack-year exposure was greater in chronic obstructive pulmonary disease patients (29.9±9.9 pack-year vs. 6.83±6.91 pack-year; p=0.001). The pack-year data was obtained by number of cigarettes smoked per day multiplied by years of smoking divided by 20. Body Mass Index (BMI) of COPD patients and control group was (19.9±3.3 vs. 20.58±4.86 respectively; p=0.26). Tea consumption was also greater in COPD group as compared to control subjects (8.4±7.8 cups/day vs. 2.78±1.38 cups/day; p= 0.003). Only one COPD patient had used alcohol. There was no difference in the amount of smoking and tea consumption between COPD patients with frequent gastroesophageal reflux symptoms and COPD patients without gastroesophageal reflux symptoms (Table 1).

Table 1. Demographics of control subjects and COPD patients.

Variables	COPD Patients (n=100)	Control Subjects (n=150)	p-value
Age (years)	56.8 ± 7.8	49.5 ± 5.18	0.001
Weight (Kg)	54.5 ± 8.4	60.48 ± 14.13	0.001
Height (m)	1.6 ± 0.1	1.71 ± 0.7	0.001
Body Mass Index(Kg/m ²)	19.9 ± 3.3	20.58 ± 4.86	0.26
Smoking (Pack year)	29.9 ± 9.9, n=100	6.83 ± 6.91, n=36	0.001
Tea (Cup/day)	8.4 ± 7.8	2.78 ± 1.38	0.003

Data are presented as mean ± SD.

Negative sign showed a decrease from COPD patients to Control subjects.

CI=Confidence Interval.

Among COPD patients 76 had experienced gastroesophageal reflux symptoms while in control group 69 had gastroesophageal reflux symptoms (p-value 0.001). Out of 76 patients 25 had frequent gastroesophageal reflux symptoms (once or more than once a week), while in control group 14 subjects experienced frequent symptoms (25% vs. 9.33%; p=0.001).

The proportion of heartburn/acid regurgitation among patients with COPD and control subjects was (70% vs. 43.33% and 56% vs. 30.66% respectively; p-value 0.001), dysphagia (15% vs. 4%; p-value=0.002) and chronic cough (89% vs. 29.33%; p-value=0.001). These results suggest that gastroesophageal reflux symptoms were more common in COPD patients as compared to control group.

Measures of spirometry showed that acid regurgitation (30% vs. 26%; p-value=0.05), dysphagia (15% vs. 0%; p-value=0.001) and chronic cough (45% vs. 44%; p-value=0.05) were more significant gastroesophageal reflux symptoms in COPD patients with FEV1 <50% as compared to FEV1 >50%. However, heartburn was similar among COPD patients with FEV1 <50% and FEV1 >50% (35% each; p-value=0.12). Thus the results suggest that patients with more severe COPD may also experience more frequent gastroesophageal reflux symptoms (Table 2).

Table 2. Comparison of GER symptoms in COPD patients and control subjects.

GER symptoms	Control group	COPD group	p-value
Heart burn	65 (43.33%)	70 (70%)	0.001
Acid regurgitation	46 (30.66%)	56 (56%)	0.001
Dysphagia	6 (4%)	15 (15%)	0.002
Chronic cough	44 (29.33%)	89 (89%)	0.001
Frequent symptoms	14 (9.33%)	25 (25%)	0.001
Infrequent symptoms	45 (30%)	51 (51%)	0.001

Data is presented as number (percentage).

Among 76 COPD patients with gastroesophageal reflux symptoms, 25 (32.89%) had frequent reflux symptoms and 51 (67.10%) patients had infrequent reflux symptoms (p-value 0.001). Among 25 patients with frequent gastroesophageal reflux symptoms 11 (44%) experienced increased symptoms of COPD (dyspnoea, wheezing, cough) while this was noticed in 15 (29.41 %) patients with infrequent symptoms. Of the 11 COPD patients with frequent gastroesophageal reflux symptoms, 10 patients increased their inhaler use (p-value=0.001). In control subjects no association between gastroesophageal reflux symptoms and respiratory symptoms was detected. Thus these results suggest a greater association between

gastroesophageal reflux symptoms and respiratory symptoms (Table 3).

Table 3. Association of GER symptoms with severity of COPD.

GER symptoms (n=76)	p-value	
Frequent	25 (32.89%)	0.001
Infrequent	51 (67.10%)	
COPD symptoms (n=76)	0.001	
No change	50 (65.78%)	0.001
Increased	26 (34.21%)	

GER symptoms	COPD patients		p-value
	FEV1 ≤50% (n=45)	FEV1 ≥50% (n=55)	
Heart burn	35	35	0.12
Acid regurgitation	30	26	0.05
Dysphagia	15	0	0.001
Chronic cough	45	44	0.05

Data is presented as number (percentage).

There was no significant difference for antacid anti-reflux medication use; however H2-blockers (31.5% vs. 11.59% p-value 0.001) and proton pump inhibitor (13.1% vs. 0% p-value 0.001) were more often used by COPD patients as compared to control group. Taken together these results indicate that anti-reflux medication use was greater in COPD patients as compared to control group. (figure)

Figure. Anti-reflux medication use in COPD Patients and Controls.

Discussion

The aim of our study was to determine the proportion of gastroesophageal reflux symptoms in COPD patients and its association with severity of airway obstruction. The most important finding of our study was that frequent gastroesophageal reflux symptoms (once or more than once per week) are more prevalent in patients with COPD as compared to control subjects. We utilized the modified version of GER symptoms questionnaire of Mayo

clinic that accurately reflects the presence of gastroesophageal reflux symptoms and its association with respiratory symptoms.¹² We also noted that there is direct relationship between severity of airway obstruction detected by FEV₁ and gastroesophageal reflux symptoms (25% vs. 0%, p-value 0.001). In addition patients with COPD consumed more tea as compared to control subjects.

Our study primarily involved the elderly male patients. All control subjects were asymptomatic without a complaint of respiratory disease, however it is difficult to rule out occult COPD in control subjects because none of them underwent the pulmonary function tests (PFT's) and many had a smoking history. In our study we demonstrated that frequent gastroesophageal reflux symptoms occur in 25% of patients with COPD having FEV₁ <50%. This is considerably less than patients with asthma 25% vs. 80%).^{14,16} The proportion of dysphagia was similar in our population and previous study (15% vs. 17% respectively).¹²

There are several mechanisms by which gastroesophageal reflux can induce symptoms in patients with asthma and chronic obstructive pulmonary disease. One mechanism suggests that reflux induces microaspiration whereas other suggest that acid induces vagally stimulated reflex bronchoconstrictin.¹⁷⁻¹⁹ Reflux associated dyspnoea may increase minute ventilation promoting air trapping and hyperinflation in patients with obstructive airway disease. Severe hyperinflation, vigorous cough and bronchospasm may increase intra-abdominal pressure and change the relationship between lower esophageal sphincter and diaphragm, decreasing diaphragmatic contribution to sphincter tone therefore promoting reflux of gastric contents.^{12,18}

In conclusion, our study shows that a higher proportion of gastroesophageal reflux symptoms is present in COPD patients compared to control subjects. A higher proportion of frequent gastroesophageal reflux symptoms is seen in patients with severe COPD detected by pulmonary function tests. Anti-reflux medication use is higher in chronic obstructive pulmonary disease patients compared to control subjects.

This study, which comprised highly selected patients of COPD, is unlikely to reflect true proportion of gastroesophageal reflux symptoms in COPD patients. Further studies are recommended which include the patients with COPD in non-smokers exclusively.

In clinical practice the relationship between gastroesophageal reflux and pulmonary diseases should be consid-

ered routinely, in order to initiate early and effective treatment and to end the vicious circle.

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