

ORIGINAL ARTICLE

“Frequency of GERD in subjects with COPD: an experience from PNS SHIFA”

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ABSTRACT

Background—Gastro esophageal (GE) reflux is a known potential trigger of asthma, and aggressive anti reflux therapy may improve asthma symptoms and pulmonary function in selected patients. The same has not been adequately studied in patients with chronic obstructive pulmonary disease (COPD).

Objectives-

1-To measure the frequency of gastro esophageal reflux disease (GERD) in subjects with chronic obstructive pulmonary disease (COPD) presenting at the department of Pulmonology, PNS SHIFA.

2-To compare the frequency of occurrence of COPD exacerbations in subjects with and without GERD.

Design- Cross-sectional study.

Place and duration of study- This study was carried out between June-2006 to June-2007 at department of Pulmonology, PNS SHIFA, Karachi.

Subjects and methods- A total of 63 subjects with a diagnosis of COPD, confirmed through pulmonary function tests, were selected from a target population of patients attending PNS SHIFA out patient Pulmonology

department. These subjects were evaluated through GERD questionnaire for presence of GERD as per the criteria of Shimoyama et al; they were then followed up on two weekly basis for occurrence of COPD exacerbations.

Main outcome measures-Presence of GERD, COPD exacerbations

Results- The frequency of occurrence of GERD in subjects with COPD was 39.7%. COPD exacerbations, as defined by steroid use, antibiotics prescriptions and hospital admissions was higher among COPD subjects with GERD in comparison with subjects who did not have GERD.

Conclusion- The presence of GER symptoms appears to be associated with increased exacerbations of COPD.

KEYWORDS: **GERD:** Gastro esophageal reflux disease, **COPD:** Chronic obstructive pulmonary disease.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) has an extensive, adverse effect on both patients and the healthcare system. COPD causes physical impairment, debility, reduced quality of life, and death. It is the fourth-ranked cause of death in the United States, killing more than 100,000 individuals each year.¹ With respect to the healthcare system, COPD causes high resource utilization, which includes frequent clinician office visits, frequent hospitalizations due to acute exacerbations, and chronic therapy (eg, long-term oxygen therapy, medication).² The recent improvements in COPD management has not been able to reduce the associated long term morbidity and mortality. This has lead to the search for other possible etiological associations and pharmacological targets for COPD.³ Few studies have evaluated the association between gastro esophageal disease and COPD. The reason suggested by these studies is, vagal nerve-induced bronchospasm from gastric acid irritation of the esophagus and micro aspiration of gastric contents which can both lead to the observed association between GERD and pulmonary disease.⁴ Animal models have demonstrated that exposure of the esophagus to acid is associated with increase respiratory resistance, that could be ablated with bilateral vagotomy.⁵ Neural mechanisms underlying this pathway appear to involve the release of substance P which leads to plasma extravasations in the airways and the release of other tachynins from peripheral nerve terminals.⁶ Severe hyperinflation, vigorous cough and bronchospasm may increase intra abdominal pressure and change the relationship between diaphragm and lower esophageal sphincter, possibly

decreasing diaphragmatic contribution to sphincter tone and thereby promoting reflux of gastric contents.^(7,8)

Risk factors for acute exacerbations include airway irritation from active smoking, environmental factors, and/or upper respiratory tract infection.^{2, 9, 10, 11.} Most of the adverse clinical outcomes occur during the acute episode of COPD i.e. an exacerbation. The roles of smoking, socio-economic status, respiratory tract infections and predisposing environmental influences have been identified as definitive etiologies to the occurrence of an exacerbation of COPD in health care set up.¹⁰ Multiple studies have highlighted the need for the identification of other etiologies in the causation of COPD like exposure to environmental dust, organic antigens, and associated diseases like gastro esophageal reflux disease.^{12,10.} Some studies have also identified possible factors like racial and geographic influences which may play a role in COPD exacerbations.¹

Apart from the questionable relationship between GERD and COPD, there is not enough regional or international data describing this association. Keeping in view the above observations, a study was planned: 1) to measure the frequency of gastro esophageal reflux disease (GERD) in subjects with chronic obstructive pulmonary disease (COPD) presenting at the department of pulmonology, PNS SHIFA, and 2) to compare the frequency of occurrence of COPD exacerbations in subjects with and without GERD.

MATERIALS AND METHODS

This cross-sectional study was conducted at the department of Pulmonology, PNS SHIFA hospital, Karachi from June- 2006 to Dec-2007. The target population constituted of subjects who presented at PNS SHIFA out patient department of Pulmonology for follow up of their COPD status. Subjects with a previous diagnosis of COPD (n=107) were assessed further for inclusion into the study. The individuals with known esophageal disease such as cancer, achalasia, stricture or active peptic ulcer disease and age < 40 years were excluded from further study. Finally selected subjects (n=84) provided informed consent, and were explained the detailed procedural aspects of the study. These individuals were later evaluated with detailed history, clinical examination and pulmonary function tests through spirometry, and were then followed up for a further period of six months for development of COPD exacerbation.

Operational definitions-

- a. **COPD-**A diagnosis of COPD was accepted as:
 - i. If age > 40 years
 - ii. Smoker with smoking \geq 20 cigarettes/day, and
 - iii. FEV1/FVC ratio \leq 70% on pulmonary function tests
- b. **GERD-**These subjects were questioned through a GERD questionnaire for the presence of GERD, as per criteria of Shimoyamo et al.¹³

These subjects were followed up for duration of six months for development of COPD exacerbation.

- c. **COPD exacerbations-** COPD exacerbation was defined as per the criteria of “Global Initiative for Chronic Obstructive Lung Disease (GOLD)”.¹⁴ An acute COPD exacerbation was defined as worsening dyspnoea, increasing volume of sputum, or purulent sputum in conjunction with physician-initiated use of corticosteroids or antibiotics and hospital admission.

During the course of study nine subjects were lost to follow up, and were excluded from the secondary objective analysis. Thus sixty-three subjects finally participated in the study.

Statistical analysis-All data was entered into SPSS- version 15. Descriptive statistics in terms of mean and standard deviations were calculated for age. Chi square statistics were used to measure the significance of association of presence of GERD in subjects with COPD exacerbations indices, including steroid use, antibiotic requirements and hospital admissions. The differences for age between subjects with and without GERD in total data set were evaluated through t-statistics. A p-value of < 0.05 was considered as significant.

RESULTS

The mean age among our subjects was 56 ± 4.50 years. Sixty (60) patients were male and only three (03) patients were females. The frequency of occurrence of GERD in subjects with COPD was 39.7 %. The presence of COPD exacerbations was higher among COPD subjects with GERD in comparison to subjects with only COPD (Steroid use: $p=0.025$, Antibiotic prescriptions: $p=0.000$ and hospital admissions= 0.000) [figure 1-3]. The difference for age among subjects with and without GERD in our selected population was non-significant ruling out age as probable reason to overall differences. [Figure-4]

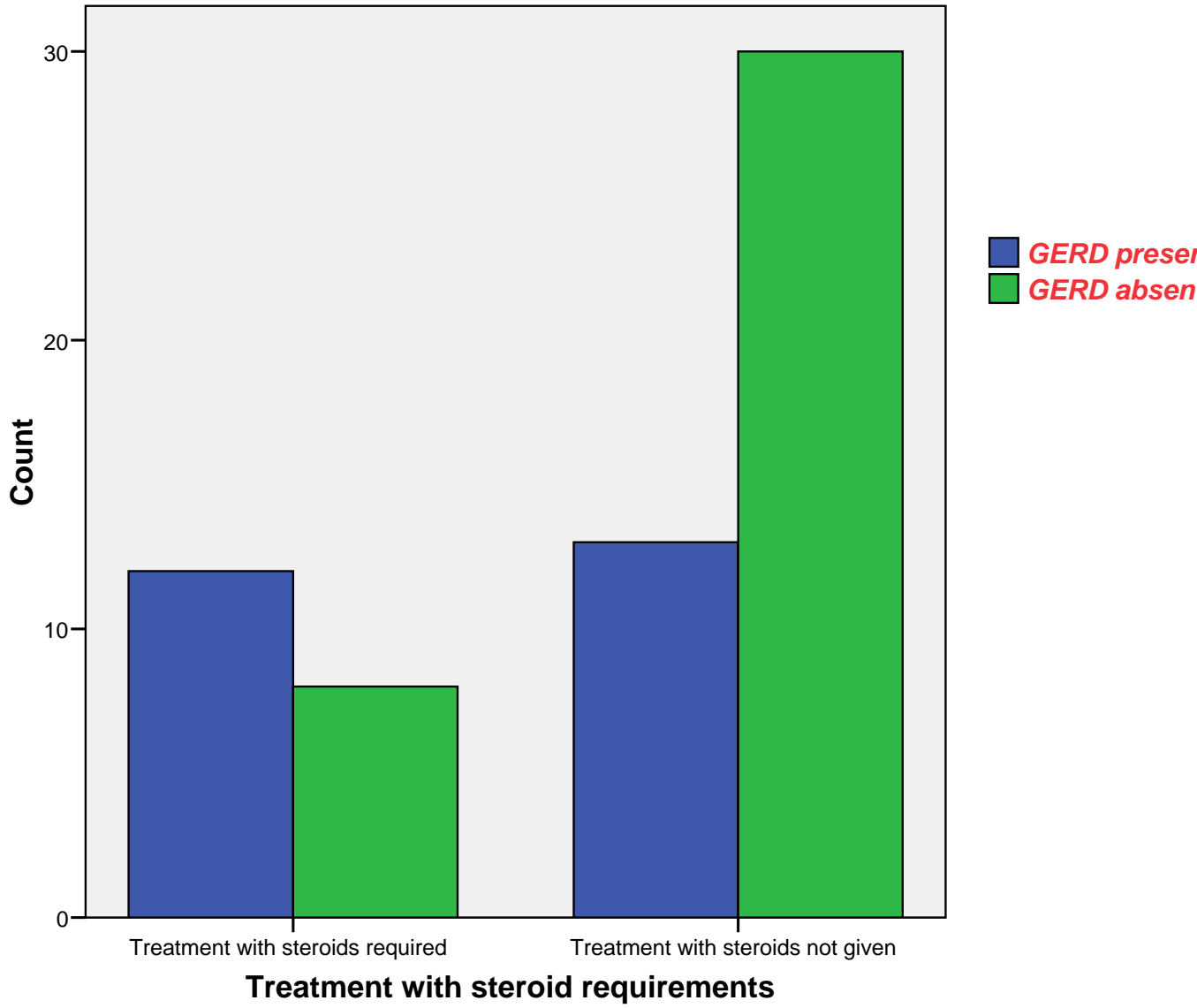


Figure-1: Differences between subjects with and without GERD in terms of steroids requirements as treatment (p=0.025)

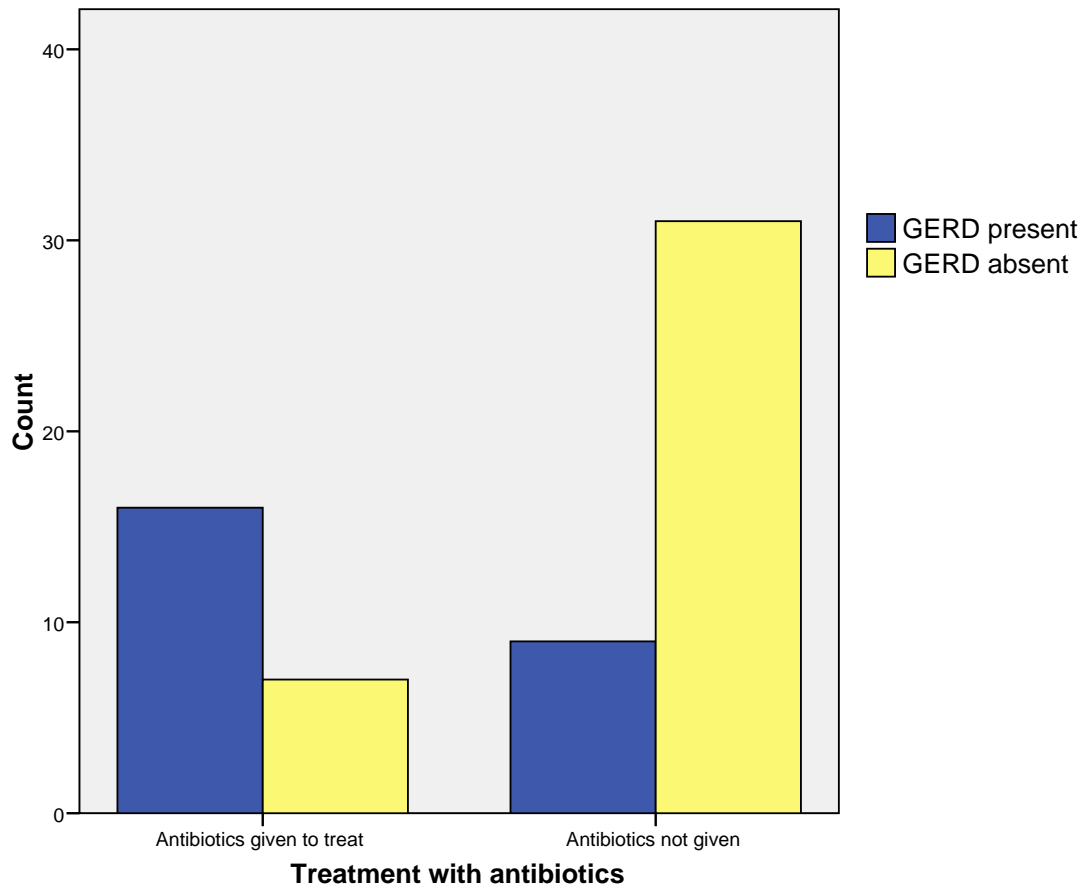


Figure-2: Differences between subjects with and without GERD in terms of antibiotics requirements as treatment (p=0.000)

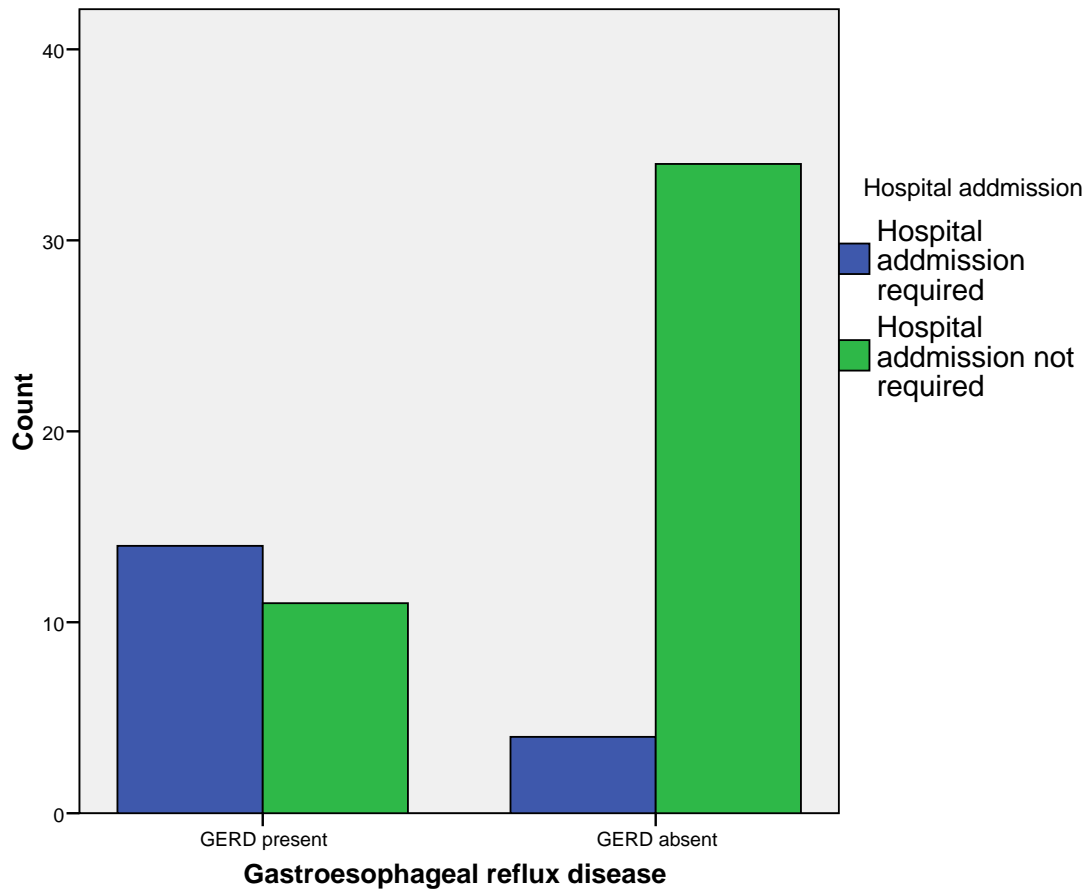


Figure-3: Differences between subjects with and without GERD in terms of hospital admissions ($p=0.000$)

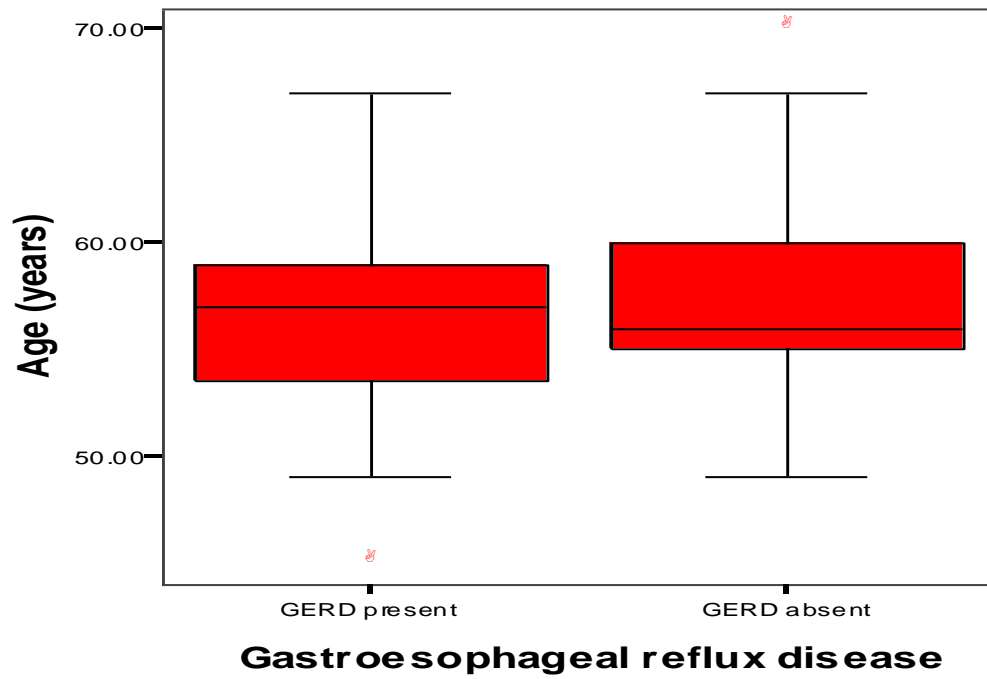


Figure-4: Differences for age between subjects with and without GERD (P=0.481)

DISCUSSION

Our study has demonstrated that the association between gastro esophageal reflux disease and chronic obstructive pulmonary disease is significant. This finding is in accordance with studies found in literature, Sonnenberg et al in a retrospective study noted an increase risk of COPD as well as other pulmonary disease in patients with reflux oesophagitis,¹⁵ similarly Mokhlessi et al through a questioner based study demonstrated a higher prevalence of GER symptoms in patients with COPD ⁷. Moreover, our study has also shown that COPD exacerbations are more frequent if there was an associated GERD. Review of available literature suggests that other studies have yielded similar findings, David et al diagnosed GERD in 29 (61%)out of 47 COPD patients using PH monitoring for 03 hrs after meals ¹⁷ ,DuculoneE et al also reported presence of GERD in 17 of 30 patients with severe COPD (57%) using sinti scanning and short term PH monitoring for 03 hrs after meals ¹⁸ similarly Mokhlessi et al ,using a modified version of a validated GERD questionnaire given to more than 100 patients observed a high prevalence of GERD in patients with COPD ⁷, finally Casanova et al demonstrated the presence of GERD in 26(62%) of 42 patients with COPD using 24 hrs esophageal PH monitoring ²⁰. There are however, few studies which have shown these exacerbations not to be related ,Orr et al using 24 hrs PH monitoring did not find GERD in 12 patients in COPD ,even though the majority of the patients had a positive history of reflux related symptoms ^{19,24}. The frequency of observed COPD exacerbations in subjects with a combined diagnosis of COPD and GERD was found to be quite higher in our study than

some other studies, Ivan et al have shown the frequency of COPD exacerbations in patients with GER symptoms to be only twice as high compared to non-GERD cases.¹⁶ The factors attributed to these differences seem multi factorial. Smoking has been identified as a common culprit in both the pathogenesis of COPD and GERD.^{21,22} We know that smoking in our part of the world is still a culture-on-the-rise, but developed and educated societies are trying to reduce the trends in smoking, not only in terms of quantity but also quality. The kind of smoking cultural differences, we are experiencing in our society include earlier age of onset of smoking and use of unfiltered brands on account of low cost. There can be a possibility that our “traditional diets” may have some components that can accelerate both the disease processes at the same time. Similarly, as highlighted by some studies, the variations between races and genotypes may be the possible reasons to the stronger association observed between GERD and COPD in our study.²³ However, the above explanations linking the stronger association between GERD and COPD require the elucidation of pathogenesis and etiological agents thru some randomized controlled trials in our population. Certain limitations in our study must be acknowledged: Firstly, the sample size mainly constituted of male population due to non-probability convenience sampling. This has probably resulted due to the reason that the male gender has been more associated with smoking habit in this part of the world as compared to the western population. Secondly, the data from the study reflects regional data only, so the interpretations from this particular study must not be applied to other population groups.

The study has many clinical implications. GERD is a medically modifiable disease; however it can become a source of increased morbidity, mortality and rising health care costs once it is associated with COPD. At present the recommended algorithms do not suggest the concomitant treatment of GERD in subjects with COPD. In the light of our finding, and in tandem with some international studies, this kind of therapy is likely to become a standard protocol in treatment of patients with underlying/associated GERD in patients with COPD. However, it is recommended that some randomized clinical trials be carried out in a feasible set up to further augment or disapprove our findings.

CONCLUSIONS

We conclude that COPD patients with GER symptoms are more likely to be hospitalized, receive antibiotics and are given steroids as compared to GERD (-ve) COPD patients.

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