Original Article

Prevalence and impact of diabetes, hypertension, and cardiovascular diseases in chronic obstructive pulmonary diseases: A hospital-based cross-section study

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is associated with important chronic comorbid diseases, including diabetes, hypertension and cardiovascular diseases. As very limited data is available in India, the aim of the present study was to determine the relationship between COPD and the common, chronic comorbid conditions of diabetes mellitus (DM), hypertension (HTN), and cardiovascular diseases (CVD) and also to determine how these affect the clinical course of COPD. **Methods:** All the COPD cohorts diagnosed as per Global Initiative for Chronic Obstructive Lung Disease-2013 (GOLD-2013) criteria were screened for DM, HTN, and CVD as per stipulated national and WHO guidelines.**Results:** The prevalence of DM, HTN, and CVD in the 2432 COPD subjects was 25.94%, 37.25%, and 13.93%, respectively. In multivariate analyses, very severe COPD was associated with a higher risk of DM (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.2–2), HTN (OR 1.6, 95% CI 1.4–1.9), and CVD (OR 2.5, 95% CI 1.9–3.0). **Conclusion:** A significant relationship was found between COPD and the presence of comorbid DM, HTN, and CVD. It was also found that subjects with advanced COPD were more likely to have at least two of these conditions and hugely affect the outcome of the disease. These findings suggest that the presence of COPD could provide a rationale to look for other comorbid disease and, conversely, that the presence of DM, HTN, or CVD might be the basis for the assessment of patients for airflow limitation and COPD as the tobacco smoking and advancing age were common risk factors.

Key words: COPD, diabetes, hypertension, cardiovascular diseases, comorbidities

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined by GOLD (Global Initiative for Chronic Obstructive Lung Disease) as a common, preventable, and treatable airflow limitation condition that is usually progressive and is associated with enhanced inflammation in the airways and lungs.[1] COPD is a major cause of morbidity and mortality around the world and projected to become the third leading cause of death worldwide by 2030.[2,3] Although defined by abnormal spirometry, it is well recognized that COPD is more than a respiratory ailment and its impact expands beyond the lungs with significant extrapulmonary consequences. Comorbidities, defined as the co-occurrence of other medical conditions along with COPD, considerably contribute to the severity of disease. Although not essentially associated with the disease, the existence of COPD may actually escalate the risk of other diseases. Comorbidities can occur in patients with

any degree of airflow limitation and are not restricted to patients with advanced COPD.[4] Furthermore, comorbidities are associated with increased morbidity and mortality and are a major determinant of health status, health expenditure, and prognosis in patients with COPD.[5]

Crude estimates suggest that there are 30 million COPD patients in India and contribute significantly to the growing percentage of COPD mortality, which is estimated to be among the highest in the world; that is more than 64.7 estimated age standardized death rate per 1,00,000 in both sexes. This would translate to about 556,000 cases in India (>20%) out of a world total of 2,748,000 annually. Such enormous volumes of disease have the potential to have devastating impact on the health systems and state economies.[6,7] In India, there is also escalating epidemic of chronic noncommunicable diseases (NCDs) like diabetes mellitus (DM), hypertension (HTN), and cardiovascular diseases (CVD).[8] If mortality due to comorbid conditions like DM, HTN, and CVD associated with COPD are taken together, then the convergence of these noncommunicable chronic diseases pose a great impact on the severity and outcome of the disease.

The presence of these common comorbidities is substantially affecting the outcome of COPD at various levels of healthcare services. As very limited data is available, the exact prevalence of these comorbidities in COPD patients in India is not known. The aim of the present study was to determine the relationship between COPD and the common, chronic comorbid conditions of DM, HTN, and CVD and also to determine how these affect the clinical course of COPD.

MATERIALS AND METHODS

Source of Data

Inpatient and outpatient Departments of Pulmonary Medicine, Internal Medicine, Endocrinology and Cardiology Departments at a tertiary care hospital at Belgaum district of Karnataka in India.

Population

All subjects aged more than 40 years and diagnosed as cases of COPD as per GOLD criteria.[1]

Study Design

A cross-section study.

Study Period

Primary data was collected between January 1, 2013 and December 31, 2014.

Inclusion Criteria

(1) Both male and female patients diagnosed with COPD.
(2) Age >40 years.

Exclusion Criteria

Patients were excluded from the study if they have any of the conditions like:

1. Any chronic lung disease other than COPD
2. HIV infection
3. Connective tissue disorders
4. Chronic renal failure
5. Chronic liver disease
6. Malignancies on long-term steroid or cytotoxic drug therapy
7. Chronic alcoholics.

Baseline data was recorded which included age, sex, biomass fuel exposure, symptoms related to the respiratory system, DM, HTN, and CVD with duration of illness, level of dyspnea (Medical Research Council range [0–4]), smoking status (current or nonsmoker or ex-smoker), pack years, current treatment, previous medications, occupation, and number of exacerbations, that is, emergency hospital admissions or unscheduled hospital visits in the last 1 year. Also dyspnea score (D), level of airflow obstruction (O), current smoking status (S), and exacerbations (E) (DOSE) score were noted. Mortality has been found to be associated with patients with a DOSE index score >4.[9]

COPD Diagnosis

All the participants were subjected to spirometry and patients with post bronchodilator FEV1/FVC <70% predicted were considered as cases of COPD. Then they were categorized as mild, moderate, severe, and very severe COPD patients as per the GOLD guidelines.[1]

DM, HTN, CVD Screening

All the subjects enrolled in the study are screened for DM, HTN, and CVD as per stipulated national guidelines with cutoff thresholds in line with those recommended by WHO.[8]

In brief, fasting blood sugar (FBS) >126 indicates DM and FBS<110 mg/dL is normal. Patients whose diabetes status was uncertain underwent random blood sugar (RBS) testing, and if was more than 126 mg/dL, the subjects were further assessed with FBS and postprandial blood sugar (PPBS). If FBS was more than 126 mg/dL or PPBS more than 200 mg/dL the subjects were confirmed as having DM at the baseline.

Subjects were classified as having HTN if they reported physician diagnosis of HTN, were receiving treatment for HTN, or had evidence of same upon examination (diastolic blood pressure 90 mmHg or a systolic blood pressure 140 mmHg, based on three measurements).

Subjects reporting a diagnosis of a prior myocardial infarction, stroke, heart failure, angina, or transient ischemic attacks were classified as having cardiovascular disease at the baseline examination after panel discussion.

Panel Discussion

All participants were evaluated by a consensus panel that decided after plenary discussion whether a diagnosis of DM, HTN, or CVD was present, possible, or absent. The panel was consisted of pulmonologist, general physician, and a cardiologist. Diagnosis of COPD was confirmed as per the guidelines of the GOLD program, which provides standard diagnostic criteria, severity staging as well as recommendations for prevention and management of COPD. The panel confirmed diagnosis of DM, HTN, and CVD if the subjects met the WHO criteria for these disorders. Characteristics of the participants in the screening were tabulated against the COPD status defined as no comorbidity "COPD +0," COPD with any one of three comorbidities "COPD +1," COPD with any two of three conditions "COPD +2," and finally COPD with all three conditions as "COPD+3."

RESULTS

The final cohorts consisted of 2432 COPD patients with 1648 (67.76%) males and 784 females (32.24%). About 1351 (55.55%) were smokers whereas 653 (26.85%) had history of biomass fuel exposure (Table 1). Analyses showed that increasing age, a higher BMI, lower education status, longer duration of COPD, higher pack years of smoking, high DOSE score and male sex were associated with a higher risk of DM, HTN, and CVD (Table 2). In multivariate analyses, very severe COPD was associated with a higher risk of DM (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.2–2), HTN (OR 1.6, 95% CI 1.4–1.9), and CVD (OR 2.5, 95% CI 1.9–3.0). Similar findings were seen for other stages of COPD (Table 3).

In the present study cohort, 912 (37.5%) subjects had no comorbid disease, 852 (35.03%) had one comorbid disease, 461 (18.5%) had two comorbid diseases, and 207 (8.5%) had three comorbid diseases (Table 1). Multinomial logistic regression showed that compared to subjects with normal lung function, those with very severe COPD were more likely to have one (OR 1.8, 95% CI 1.4–2.3), two (OR

Table 1: Patients included in this study.

	N	%
COPD subjects in the study	**2432**	
Males	1648	67.76
Females	784	32.24
Tobacco smokers	1351	55.55
Subjects with biomass exposure	653	26.85
Patients with "0" comorbidity—"COPD + 0"	912	37.5
Patients with "1" comorbidity—"COPD + 1"	852	35.03
Patients with "2" comorbidities—"COPD + 2"	461	18.95
Patients with "3" comorbidities—"COPD + 3"	207	8.5
Subjects with DM	631	25.94
Subjects with HTN	906	37.25
Subjects with CVD	339	13.93

Table 2: Baseline demographic characteristics of all subjects.

DATA	COPD+0	COPD+1	COPD+2	COPD+3
Number	912	852	461	207
Age	54 ± 8.2	59 ± 9.13	63 ± 7.3	67 ± 10.28
BMI	18.34 ± 2.48	19.23 ± 3.63	22 ± 4.21	22 ± 4.68
Smoking (pack years)	6.34 ± 3.9	7.21 ± 2.3	8.16 ± 3.2	8.20 ± 2.28
Duration of COPD (years)	6.83 ± 2.8	8.21 ± 2.3	9.42 ± 3.9	10.41 ± 8.93
Mean FEV1% predicted	68.38 ± 13.8	63.2 ± 12.1	57.14 ± 8.9	51 ± 13.26
Dose score	2.18 ± 2.3	2.96 ± 1.06	4.96 ± 1.04	5.56 ± 1.96

Table 3: Multivariate regression analysis predicting DM, HTN, and CVD.

GOLD Category	DM	HTN	CVD
Very severe	1.6 (1.2–2)	1.6 (1.4–1.9)	2.5 (1.9–3)
Severe	1.5 (1.2–1.7)	1.4 (1.3–1.5)	2.4 (1.9–2)
Moderate	0.9 (0.7–1.2)	1.3 (1.2–1.4)	2.5 (1.5–2.6)
Mild	1.2 (1.1–1.4)	1.2 (1.1–1.3)	2.4 (2.1–2.5)
Normal	1	1	1

Table 4: Multivariate logistic regression predicting the presence of comorbidities

	Comorbidities		
Gold Category	1	2	3
Very severe	1.8 (1.4–2.3)	3.6 (2.6–3.4)	4 (3.6–4.9)
Severe	1.5 (1.3–1.6)	3.2 (2.4–4)	3.9 (2.9–4.9)
Moderate	1.4 (1.4–1.7)	3.2 (2.6–3.6)	3.8 (2.8–4.6)
Mild	1.4 (1.4–1.6)	3 (2.6–3.5)	3.6 (2.8–4.2)
Normal	1.0	1.0	1.0

3.6, 95% CI 2.6–3.4), or three (OR 4, 95% CI 3.0–4.1) comorbid diseases, with similar observations in other groups too (Table 4).

DISCUSSION

NCDs, including COPD, DM, HTN, and CVD are the major global health problem of the century.[10] They are the world leading cause of disease burden and mortality and are increasing in prevalence even in low- and middle-income countries like India. The costs incurred by the convergence of these uncontrolled diseases are substantial with momentous impact on each others' outcome.[11] The association is bidirectional as COPD is known to escalate the prevalence and severity of these NCDs and vice versa. COPD is the major respiratory NCD in our country along with DM and HTN. As far as our knowledge extends, this is the first kind of study in which association between COPD and these NCDs was assessed.

The understanding of COPD has changed considerably over the past two decades. The definition of the disease has moved from a simple airflow limitation (forced expiratory volume in 1 s, FEV_1)-centric view of the disease to the understanding that COPD as a complex and heterogeneous condition. It is important to highlight that, "complex" means that COPD has a number of intrapulmonary and extrapulmonary components whose dynamic interactions along time are not linear, whereas "heterogeneous"[12] indicates that not all of these components are present in all individuals at any given time point. The presence of multiple comorbidities adds to the complexity and heterogeneity of COPD. The universal aging of the world's population is reinforcing this trend, partly due to the fact that the prevalence is higher in age groups. Epidemiological studies and large clinical trials have helped us to understand the importance of comorbidities.[13–15] Greater understanding of the pathophysiology of COPD, focused on the concept of systemic inflammation, has also helped to explain the high frequency of major comorbidities (cardiovascular, DM, HTN) in addition to coexisting illnesses that one would naturally expect due to the patients' advanced age and due to the shared risk factors such as tobacco smoking, sedentary life style, etc.

The present study revealed that prevalence of DM in study cohorts was 25.94%, which is considerably higher than the national average of 8%.[16,17] COPD is known to be novel risk factor for development of DM via multiple pathophysiological modifications such as inflammation, oxidative stress, insulin resistance, weight gain and alterations in metabolism of adipokines.[18] In the present study, the risk of DM increased with the severity of COPD (odds ratio [OR] 1.6, 95% confidence interval [CI] 1.2–2 in very severe COPD). Instabilities in glucose metabolism are more frequent in COPD patients than in non-COPD individuals. Also, almost half of all COPD patients suffer from other medical problems frequently linked to diabetes, such as HTN and higher levels of cholesterol. The combination of these medical problems is sometimes referred to as "metabolic syndrome" and is considered a cause for various cardiovascular complications in COPD patients.[19] Similarly, many studies have found that DM causes an accelerated decline in lung functions as compared to nondiabetics.

We also demonstrated that the risk of HTN and CVD is significantly high in COPD subjects compared to general population. We noted that the risk of HTN and CVD also increased significantly with severity of COPD. In an analysis of worldwide data for the global burden of HTN, 20.6% of Indian men and 20.9% of Indian women were suffering from HTN in 2005. The rates for HTN in percentage are projected to go up to 22.9 and 23.6 for Indian men and women, respectively by 2025.[20] However, in present analysis prevalence of HTN in COPD patients is much more higher than this projected data. HTN exerts a substantial public health burden on COPD subjects and severely affects quality of life of these subjects. Also exerts greater risk of CVD. It is interesting to note that of a total of 9.4 million deaths in India in 1990, CVD caused 2.3 million deaths (25%). A total of 1.2 million deaths were due to coronary heart disease and 0.5 million due to stroke. It has been projected that by 2020, there would be a 111% increase in CVD deaths in India. This increase is much more than 77% for China, 106% for other Asian countries, and 15% for economically developed countries.[21] Such an alarming escalation of epidemics of HTN and CVD will be further augmented by the presence of COPD itself.

Our observations that increasing age, a higher BMI, lower education status, longer duration of COPD, higher pack years of smoking, high DOSE score, and male sex were associated with a higher risk of DM, HTN, and CVD in present cohorts is in agreement with the study by Mannino *et al.*[22] We also established that increase in number of comorbidities in COPD leads to increase in the severity of the disease, high symptom score, exacerbations, frequent emergency visits, limited physical activity, and poor quality of life as per DOSE score data. In the current study number of tobacco smokers was notably high. Tobacco exposure is common risk factor for both COPD and the comorbidities discussed here. There are about 120 million smokers in India, which is corresponding to 12% of the world's smokers. Approximately 900,000 people die every year in India due to smoking as of 2009. According to 2002 WHO estimate, 30% of adult males in India smoke. Among adult females, the figure is much lower at between 3 and 5%. Tobacco is usually consumed in the form of bidis in rural areas, which are smaller than cigarettes and contain only about a quarter as much raw tobacco, wrapped in the leaf of another plant.[23]

Smoking is projected to delay the millennium development goals of WHO. The present study as well as many studies discussed above emphasizes the urgent need for smoking cessation programs at all levels of healthcare services. It is essential to note that interventions to decrease the prevalence of smoking among patients with COPD (or in the general population) may have an important impact on the incidence of COPD and comorbidities. The interventions including counseling and pharmacological treatment for cessation of smoking in COPD patients are still far from being implemented in routine clinical practice, particularly in countries like India where high proportions of COPD patients continue to smoke and come from remote rural dwellings.

High proportion of subjects in the current study was older than 60 years and we observed advancing age was significant risk for multimorbidity in COPD subjects. Mean age of "COPD+3" subjects was 67±10.28, which was remarkably more than other groups in the study. It is worth mentioning here that the world is experiencing the dramatic change in the demographics of the population with the strata of older individuals growing faster than the younger individuals due to decreasing population growth rate and increased life expectancies. United Nations Population Division reported that the global share of older people (aged ≥60 years) increased from 8% in 1950 and 9% in 1990 to 12% in 2013, and will continue to grow to an estimated 21% by 2050. By 2045–2050, life expectancy is projected to reach 83 years in the more developed regions of the world and 75 years in the less developed regions of the world. There is another important noteworthy epidemiological transition, which is the movement from communicable diseases toward NCD, through the world.[23,24]

COPD is one of the important NCD in the world and accelerated prevalence of other NCD like DM, HTN, and CVD will have profound negative impact on disease outcome. Hence it is imperative to screen all COPD patients for DM, HTN, and CVD. The increased understanding of COPD as a systemic disease has significantly changed the understanding of pathophysiology of comorbidities. In addition to conventional pharmacological therapy focused on treating chronic airflow limitation, management of COPD now requires a more holistic approach, including the diagnosis and appropriate treatment for comorbid conditions like DM, HTN, and CVD.

Strengths of the study are-

1. Large sample size.

2. It focuses on a specific group of subjects (COPD) at high risk of DM, HTN, and CVD: those who are symptomatic and elderly.

3. The screening was based not only on the symptomatology but also on a detailed individual assessment by a multidisciplinary panel (pulmonologist, a general physician, and a cardiologist) that took into account clinical history,

risk factors, physical examination, blood tests, and all other relevant investigations to arrive at the diagnosis of comorbidities.

Limitations: The study is limited by the fact that it is a single centric cross-section study and hence the outcomes of the trial cannot be generalized. COPD exhibits many other comorbidity like skeletal muscle dysfunction, depression, etc., that were not involved in the study might as well contribute to the outcome. A further study with involvement of different geographic populations with wide range of comorbidities is worth exploring.

CONCLUSION

In conclusion, a significant relationship was found between COPD and the presence of comorbid DM, HTN, and CVD. It was also found that subjects with advanced COPD were more likely to have at least two of these conditions and hugely affect the outcome of the disease. These findings suggest that the presence of COPD could provide a rationale to look for other comorbid disease and, conversely, that the presence of DM, HTN, or CVD might be the basis for the assessment of patients for airflow limitation and COPD as the tobacco smoking and advancing age were common risk factors.

Conflicts of Interest

None declared.

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