

**PREVALENCE OF CARDIOVASCULAR COMORBIDITIES IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN SUBURBAN AREAS OF SOUTH-WEST INDIA**PRIYANKA ASWAL<sup>1</sup>, UPASANA BHUMBLA<sup>2\*</sup><sup>1</sup>Department of Pathology, Government Medical College, Haldwani, Uttarakhand, India. <sup>2</sup>Department of Microbiology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India. Email: [ucupasana124@gmail.com](mailto:ucupasana124@gmail.com)

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**ABSTRACT**

**Objective:** Chronic obstructive pulmonary disease (COPD) is the vital cause of morbidity and mortality in Western world, though it has become an increasing cause of mortality in India also in the past decade. Another concern is that COPD patients use medications that stimulate the cardiovascular system, including anticholinergic agents and sympathomimetic medications to study the prevalence of cardiovascular comorbidities in patients with COPD.

**Methods:** It was a prospective observational study, which was conducted on inpatient subjects diagnosed to have COPD based on GOLD guidelines 2020, for a period of 1 year in tertiary care hospital.

**Results:** The most of the patients were in 60–80 year age group (70%) and majority was males (87%). All the males (n=87) were smokers (62 ex-smokers and 25 present smokers) while all females (n=13) were non-smokers. The mean BMI for patients with CVD was 25.85±4.19 kg/m<sup>2</sup> while for patients without CVD, mean BMI was 27.46±3.98 kg/m<sup>2</sup>. About 63.2% of the males (n=87) had some cardiovascular comorbidity as compared to 38.5% of females (n=13). The prevalence of cardiovascular comorbidities in subjects with COPD was 60% in the present study. This was significantly higher in patients with COPD as compared to the reported prevalence value in the general population of comparable age group. The prevalence of associated cardiovascular abnormality in COPD patients with increased PCV (Packed cell volume), leukocytosis, and neutrophilia are 56.3%, 65%, and 60%, respectively. The most common cardiovascular comorbidity in subjects with COPD was ischemic heart disease (21%), followed by heart failure (20%), stroke (5%), arrhythmias (3%), and LVH (3%).

**Keywords:** Arrhythmias, Chronic obstructive pulmonary disease, Comorbidities

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**INTRODUCTION**

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity, mortality, and disability in the United States and around the world [1]. During 2000, COPD was responsible for 8 million physician office and hospital outpatient visits, 1.5 million emergency department visits, 726,000 hospitalizations, and 119,000 deaths [2]. It has been predicted that the problem of COPD will continue to escalate over the next 20–30 years. The World Health Organization (WHO) predicts by 2030, COPD will become the third leading cause of death (currently fourth) and the fifth leading cause of disability (currently 12<sup>th</sup>) worldwide [3,4].

Medications used in COPD patients stimulate the cardiovascular system, like anticholinergic agents and sympathomimetic medications which may contribute to increased heart rate and BP, which might instigate an ischemic episode of heart disease (e.g., angina or MI) or cerebrovascular disease (transient ischemic attack or stroke). Cardiovascular stimulation may also lead to arrhythmias, including potentially lethal arrhythmias such as ventricular tachycardia or ventricular fibrillation [5].

This study thus perpetuates the prevalence of cardiovascular diseases in COPD patients and to assess if the risk of cardiovascular disease increases with increasing severity of COPD. Through this study, we want to convey that when physicians are confronted by a patient experiencing a COPD exacerbation, they must resist the “knee-jerk” reaction of instituting anti-COPD interventions without adequately considering other possibilities for the patients worsening “respiratory” status especially cardiovascular causes which are so frequently the cause of the exacerbation rather than respiratory illness.

**METHODS**

It is a prospective and observational study, which was conducted on inpatient subjects diagnosed to have COPD based on GOLD guidelines 2021, for a period of 1 year in tertiary care hospital of South-west Rajasthan [6,7].

**Inclusion criteria**

All consecutive patients admitted to the ward with following inclusion criteria were enrolled into the study:

- Diagnosed to have COPD based on GOLD guidelines (Ratio of forced expiratory volume in 1 sec (FEV<sub>1</sub>) to forced vital capacity (FVC) of less than 70% after bronchodilator challenge)
- Ability to understand the study and perform the study procedures.

**Exclusion criteria**

Patients with chronic respiratory diseases other than COPD including sleep apnea-hyperpnea syndrome were excluded from the study.

**Ethics Committee**

Ethical clearance from the Institutional Ethics committee was obtained.

**RESULTS**

The most of the patients were in 60–80 years age group (70%) and majority was males (87%). The mean age of patients with CVD was 68.40±8.65 years while for patients without CVD, it was 67.25±9.14 years. The difference was not statistically significant (p=0.526). All the males (n=87) were smokers (62 ex-smokers and 25 present smokers) while all females (n=13) were non-smokers. The mean BMI for patients with CVD was 25.85±4.19 kg/m<sup>2</sup> while for patients without CVD, mean BMI was 27.46±3.98 kg/m<sup>2</sup>. This result

was of borderline statistical significance ( $p=0.057$ ) and indicated a trend of the lower BMI in COPD patients with CVD as compared to those without CVD.

The mean FEV1 in patients with CVD was  $40.09 \pm 14.42\%$  of predicted normal while in those without CVD was  $46.09 \pm 17.61\%$ . This result was of borderline statistical significance ( $p=0.065$ ) and showed a declining trend in FEV1 values in patients with CVD.

The prevalence of cardiovascular comorbidities among COPD patients in this study was 60%. It is depicted in Table 1.

About 63.2% of the males ( $n=87$ ) had some cardiovascular comorbidity as compared to 38.5% of females ( $n=13$ ). This difference was of no statistical significance ( $p=0.163$ ) but indicated a trend of higher prevalence of cardiovascular comorbidities in males as compared to females. About 74.5% of subjects with systemic hypertension ( $n=51$  and  $p=0.005$ ) and 81.5% of subjects with dyslipidemia ( $n=27$  and  $p=0.015$ ) had some cardiovascular comorbidity as compared to 44.9% and 52.1% of subjects without systemic hypertension and dyslipidemia, respectively. This difference was of high statistical significance and indicated that COPD patients with systemic hypertension and dyslipidemia had higher risk of cardiovascular disease as compared to those without. About 72.2% of subjects with diabetes mellitus ( $n=36$  and  $p=0.097$ ) and 48% of obese subjects ( $n=30$  and  $p=0.239$ ) had some form of cardiovascular comorbidity as compared to 53.1% and 64% of subjects without diabetes mellitus and obesity, respectively, as shown in Table 2.

**Table 1: Prevalence of cardiovascular comorbidities in chronic obstructive pulmonary disease patients**

Type of CVD	Frequency	Percentage
Ischemic heart disease	21	21
Congestive heart failure	20	20
Stroke	5	5
Arrhythmias	3	3
Left ventricular hypertrophy	3	3
Alular heart disease	2	2
Peripheral vascular occlusive disease	2	2
Hypertrophic obstructive cardiomyopathy	2	2
Pulmonary embolism	1	1
Aortic aneurysm	1	1
Total	60	60

CVD: Cardiovascular disease

**Table 2: Risk factors associated with cardiovascular comorbidities in chronic obstructive pulmonary disease patients**

Risk factor	Percentage of patients with CAD	p
Sex		
Male (87)	63.2	0.163
Female (13)	38.5	
Hypertension		
Yes (51)	74.5	0.005
No (49)	44.9	
Diabetes (36)		
Yes (36)	72.2	0.097
No (64)	53.1	
Dyslipidemia (27)		
Yes (27)	81.5	0.015
No (73)	52.1	
Obesity (BMI>30)		
Yes (25)	48.0	0.239
No (75)	64.0	
Smoking status		
Non-smoker (13)	38.5	0.071
Ex-smoker (62)	58.1	
Current smoker (25)	76.0	

At admission, in all the patients, full hemogram along with erythrocyte sedimentation rate (ESR) was done. The prevalence of associated cardiovascular abnormality in COPD patients with increased packed cell volume (PCV), leukocytosis, and neutrophilia are 56.3%, 65%, and 60%, respectively. The difference is not statistically significant. Although prevalence of associated cardiovascular abnormality in COPD patients with raised ESR is also not statistically significant, yet, it shows a trend of higher prevalence of cardiovascular abnormality in such patients. Furthermore, sputum and blood culture examination was performed to identify the etiological causes. Table 3 depicts as follows. In five of these patients who also had Type II diabetes mellitus, sputum smear-positive pulmonary TB was diagnosed at the time of admission.

The prevalence of cardiovascular comorbidity among patients with Stage 1 and Stage 2 COPD was 44.4%, Stage 3 COPD was 61.5%, and Stage 4 COPD was 66.7%. This difference was of no statistical significance ( $p=0.298$ ); however, trend toward increasing cardiovascular comorbidities with increasing severity of COPD was depicted and it is shown in Table 4.

About 91.3% of subjects with elevated levels of brain natriuretic peptide (BNP) ( $n=23$ ) had some form of cardiovascular comorbidity as compared to 50.6% with normal levels of BNP. This difference was of high statistical significance ( $p=0.001$ ) indicating that COPD patients with elevated levels of BNP have higher prevalence of cardiovascular disease as compared to those with normal BNP levels. A trend of higher prevalence of cardiovascular disease in those with elevated Troponin I levels is seen. About 66.7% of subjects with elevated levels of CK-MB ( $n=27$ ) had some form of cardiovascular comorbidity as compared to 57.5% with normal CK-MB levels.

## DISCUSSION

The present study showed a 60% prevalence of cardiovascular comorbidities in patients with chronic obstructive pulmonary disease which is substantially higher than that found in the general population of similar age group. The prevalence of cardiovascular disease in general population in India was estimated to be 3–4% in rural areas and 8–10% in urban areas according to the population-based cross-sectional surveys.

**Table 3: Hematological parameters associated with cardiovascular comorbidities in chronic obstructive pulmonary disease patients**

Hematological parameters	Percentage of patients with CAD (%)	p
Increased PCV (PCV>54% in men, >49% in women)		
Yes (48)	56.3	0.2328
No (52)	42.3	
Leukocytosis ( $>11 \times 10^3/\text{mm}^3$ ), ( $>11 \times 10^9/\text{l}$ )		
Yes (60)	65.0	0.4265
No (40)	55.0	
Neutrophilia (>70%)		
Yes (65)	60	0.5391
No (35)	51.4	
Elevated ESR (>20 mm at the end of the first hour)		
Yes (52)	63.4	0.1166
No (48)	45.8	

PCV: Packed cell volume, ESR: Erythrocyte sedimentation rate

**Table 4: Relation between severity of chronic obstructive pulmonary disease and prevalence of cardiovascular disease**

COPD stage	Percentage of patients with CVD	p
Stage 1 and 2 (18)	44.4	0.298
Stage 3 (52)	61.5	
Stage 4 (30)	66.7	

CVD: Cardiovascular disease, COPD: Chronic obstructive pulmonary disease

The prevalence of cardiovascular comorbidities among COPD patients in this study was 60%. The overall prevalence of cardiovascular disease in COPD patients in various studies ranged from 28% to 70% [7,8]. In the evaluation of COPD longitudinally to identify predictive surrogate end-points (ECLIPSE) study, "heart trouble" was reported in 26% of 2164 COPD patients, compared with 11% of 337 smoking controls, and MI was reported in 9% versus 3% [9].

In two large population-based studies (atherosclerosis risk in communities [ARIC] and the cardiovascular health study [CHS]) comprising 20296 patients over the age of 44 years, the prevalence of cardiovascular disease in COPD patients was between 20 and 22% compared with 9% of subjects without COPD [9,10]. Aggressive search for CVS comorbidities in the present study could have contributed to detection of high proportion of patients with comorbidities.

The most of the patients in this study were in 6<sup>th</sup> and 7<sup>th</sup> decade of life (70%) and majority was males (87%). The mean age of patients with CVD was 68.40±8.65 years whereas that for patients without CVD was 67.25±9.14 years (p=0.526). Although an increasing trend of cardiovascular morbidity was seen in patients with increasing age, the difference was not statistically significant. In a similar study by Curkendall *et al.*, the majority of patients were 65 years or older (74%) and most were males (54%) [11]. One of the major factors accounting for higher incidence of COPD and cardiovascular comorbidities in males could be the higher prevalence of smoking among males as compared to females especially in developing countries like India.

In congruence with existing literature, the mean FEV1 values in patients with CVD were lower (40.09±14.42%) as compared to those without CVD (46.09±17.61%) in our study. This indicated an increasing trend of cardiovascular disease with falling FEV1 values and an inverse relationship between the two. This result was of borderline statistical significance (p=0.065). Two studies have reported that the relative risk for CVD increased with increasing severity of airflow limitation [12,13].

The most common cardiovascular disease in the present study was found to be ischemic heart disease (21%), followed by congestive heart failure (20%), stroke (5%), arrhythmias (3%), left ventricular hypertrophy (LVH) (3%), alular heart disease (2%), peripheral vascular occlusive disease (2%), hypertrophic obstructive cardiomyopathy (2%), pulmonary embolism (1%), and aortic aneurysm (1%). The prevalence of ischemic heart disease ranged between 4.7 and 60% among patients with COPD in various studies while the prevalence of heart failure ranged from 7.1 and 31.3% [10,12,13]. The prevalence of heart failure in ECLIPSE study in a cohort of COPD patients was 7% [14]. The prevalence of arrhythmias in various studies ranged from 0.3–29% and for stroke was 6.9–9.9% [13–15]. The most common form of arrhythmia was atrial fibrillation which is more common with increasing severity of airflow limitation [16]. In a large survey of primary care records of 12,04,100 members of the general population aged ≥35 years, the prevalence of stroke was 9.9% in those with COPD compared with 3.2% in rest of the population [17]. In the follow-up study, COPD was associated with 2.8 fold increase in the incidence of acute stroke. Two studies investigated the risk of peripheral vascular disease and reported adjusted RR estimates of 1.11 (range 1.05–1.19) and 5.50 (range 4.90–6.18) in patients with COPD as compared to those without COPD [18].

Of all the patients with systemic hypertension (n=51), 74.5% of patients had some cardiovascular comorbidity as compared to 44.9% among those who did not have systemic hypertension. This difference was highly statistically significant (p=0.005) and indicated that COPD patients with systemic hypertension had significantly higher risk of cardiovascular disease as compared to those without systemic hypertension. The prevalence of systemic hypertension in the present study was 51%. Systemic hypertension is reported in 40–60% of COPD patients [5,16]. In the ARIC and CHS population-based cohorts, the prevalence of hypertension was 34% in normal subjects but 40% in GOLD Stage I

COPD patients, 44% in GOLD Stage II and 51% in GOLD Stage III and IV COPD patients, with an odds ratio of having hypertension of 1.4 in GOLD Stage II and 1.6 in GOLD Stage III and IV patients compared with normal subjects [18]. Thus, the prevalence of systemic hypertension in COPD patients in the present study was higher than the prevalence of systemic hypertension in general population which is estimated to be 20–40% among urban and 12–17% among rural adults [19]. Hypertension is an independent risk factor for cardiac events.

In the present study, the overall prevalence of diabetes mellitus in COPD patients was 36%. The reported prevalence of diabetes mellitus among patients with COPD ranges from 2% to 16% in various studies [19,20]. This is higher than the study on normal subjects conducted by Indian Council of Medical Research (ICMR) which estimated the prevalence of diabetes in general population as 3.8% in rural areas, compared with 11.8% in urban areas [20,21]. In the present study, 72.2% diabetic subjects (n=36) had some form of cardiovascular co morbidity as compared to 53.1% of subjects without diabetes. Although this difference was of borderline statistical significance (p=0.097), it indicated a trend toward higher prevalence of cardiovascular comorbidities among COPD patients with diabetes than those without this disease [21].

Studies	Unspecified CVD	HTN	DM	DLP
Van <i>et al.</i> [18]	13	23	5	-
Mapel [19]	65	45	12	-
Walsh [20]	50	52	16	51
Eclipse [12]	26	-	10	-
Present study	60	51	36	27

The prevalence of dyslipidemia in the present study was 27%. Among all patients with dyslipidemia (n=27), 81.5% of patients had some form of cardiovascular comorbidity as compared to 52.1% among those without dyslipidemia. This difference was statistically significant (p=0.015) substantiating an increased prevalence of cardiovascular comorbidities among patients with dyslipidemia than among those without dyslipidemia. The reported prevalence of dyslipidemia in COPD patients in various studies is 9–51% [7,21].

## CONCLUSION

The prevalence of cardiovascular comorbidities in subjects with COPD was 60% in the present study. This was significantly higher in patients with COPD as compared to the reported prevalence value in the general population of comparable age group. The most common cardiovascular comorbidity in subjects with COPD was ischemic heart disease (21%), followed by heart failure (20%), stroke (5%), arrhythmias (3%), and LVH (3%).

The prevalence of cardiovascular comorbidities was numerically higher in subjects with severe stages of COPD although this relationship was not statistically significant (p=0.298). BMI was inversely related to stage of COPD as well as to prevalence of cardiovascular disease. Using multiple linear regression analysis, systemic hypertension, dyslipidemia, and elevated serum BNP levels were found to be the most significant factors associated with the presence of cardiovascular comorbidities in subjects with COPD in the present study.

## CONFLICT OF INTEREST

There is no conflict of interest

## FUNDING

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