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CLINICAL PROFILE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH SPECIAL REFERENCE TO CARDIAC RISK FACTORS AND AMBULATORY BLOOD PRESSURE MONITORING VALUES: A CROSS-SECTIONAL STUDY

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is described by airway obstruction, inflammation, and progressive lung function decline and is associated with multiple comorbidities, including cardiovascular disease (CVD), which is the leading cause of morbidity and mortality in COPD patients. This cross-sectional study is aimed to investigate the clinical profile of patients with COPD and their cardiac risk factors as well as ambulatory blood pressure monitoring (ABPM) values. **Methods:** The study was conducted on a sample of 75 COPD patients who were recruited from a tertiary care hospital. The patient's demographic characteristics, smoking history, COPD severity, and comorbidities were recorded. The cardiac risk factors were assessed by measuring, blood pressure, Blood glucose levels, LFT, USG of liver for NASH and lipid profile. **Results:** the study reveals that COPD patients have high rate of cardiac risk factors (36%) and abnormal ABPM values in form of non-dipping of blood pressure at night (24%) indicating the need for comprehensive evaluation and monitoring during their management. **Conclusion:** Due to coexistence of several risk factors, COPD patients have elevated risk of cardiovascular diseases. (CVD) ABPM is useful tool to detect early abnormalities of blood pressure. Judicious assessment of comorbidities and their control may lower the risk of CVD and improve the outcome in patients of COPD.

Key words: are COPD, ABPM, CVD, Cardiovascular risk factors

Introduction

COPD[(1,2)] A sedentary lifestyle, ageing, a history of smoking,(or other smoke exposures) diabetes, hypertension, dyslipidaemia and NASH as known the cardiovascular risk factors and many co-morbidities like cardiovascular diseases (CVD),stroke, peripheral vascular diseases are extremely common in COPD patients.[(3,4)] Hypertension, Ischemic heart disease,

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heart failure and cardiac arrhythmias are the most common CVDs in people with COPD. CVD associated with COPD is greatest in late-to-middle age [5]. Risk of Myocardial infarction is approximately double in COPD.[4,5,6] Patients with acute exacerbations are at greatest risk of bad CVD outcomes.[5] Calverely PM *et al.* reported that COPD patients with hypertension, diabetes or CVD had increased risk of hospitalizations and mortality.[7] The mortalty is worse in them than those without COPD[8] Arterial stiffness is a surrogate marker of CVD, stroke and peripheral arterial disease.[7,8] Bronchodilators LAMA and LABA which are mainstay of treatment in COPD and their use can worsen the situation. Increase in sympathetic activity due to these drugs predisposes them to tachyarrhythmias like atrial fibrillation, ventricular arrhythmias.[7,8]

It is extensively documented that the pathophysiological connections between COPD and atherosclerosis is due to sharing of common factors like chronic low grade systemic inflammation, oxidative stress, and enhanced platelet activation. The risk is pronounced in mid to late middle age.[9,10,11,12] Particularly elderly and smoker patients presenting with vague symptoms as dyspnea and fatigue, the differential diagnosis of cardiac disease may be difficult. The prevalence of hypertension is 50% and 75% in those over the age of 70 years in them. Cardiovascular dysfunction, pulmonary vasoconstriction, and arterial stiffness all improve with the administration of long-acting bronchodilators. An elevated level of inflammatory markers including fibrinogen and IL-6, which are connected to thrombosis and cardiovascular events, are also increased with lower respiratory tract infection, a typical cause of exacerbation in COPD patients [4,11,12]

Cardiovascular comorbidities are linked to several detrimental outcomes in COPD patients, including worse quality of life, more hospitalisations, and a higher risk of all-cause and CVD death.[10] Therefore to study the burden of cardiovascular risk factors in patients of COPD the present study was undertaken in the population of central India, along with the ambulatory blood pressure monitoring which is a diagnostic tool for detecting nocturnal non-dippers and hypertension in patients of COPD, which has harmful impact on cardiovascular diseases.

Methodology

A cross-sectional hospital-based study was performed in the department of medicine & chest medicine of a tertiary care hospital for two years. Total 75 patients were enrolled with the application of appropriate sample size technique and use of consecutive sampling method. After obtaining approval from the institutional ethical committee and consent from the participant, the study was initiated. The research was carried out in patients who were over 18 years old, had been clinically diagnosed with COPD, were admitted to the medicine ward, and met all criteria other qualifying requirements. Patients with conditions affecting neuro-autonomic function like neuropathies, psychiatric illness, with primary diagnosis of unstable angina, congestive heart failure and respiratory diseases other than COPD, such as asthma, restrictive disorder, obstructive sleep apnea-hypopnea syndrome, and lung cancer were excluded from the study. For the enrollment of the patients, the diagnosis was made with the help of clinical features (dyspnoea, sputum, and cough), pulmonary function test, chest radiographs and GOLD criteria Patient's assessment was done by thorough history taking, a clinical examination, and pertinent investigations. After the individual rested for 20 minutes in a sitting posture, blood pressure was measured using a sphygmomanometer three times at roughly 5-minute intervals. The office BP was computed as the mean of these three readings. Then, employing an ABPM equipment, all individuals completed 24-hour ambulatory blood pressure monitoring. All the data such as demographic details, relevant chief complaint, body mass index (BMI), and other laboratory blood test values were entered in Excel sheet and later data analysis was performed.

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Data Analysis

Appropriate Z-test statistics were used for calculating sample size. Descriptive data was collected presented in the form mean, standard deviation, range, frequency, and percentage. The data analysis was done by using SPSS version 23.0 Statistical software. The relationship between ambulatory blood pressure and cardio-vascular risk variables was examined using the Chi square test.

Results

As per age distribution of the study population, it was seen that majority 52 % of patients were in the age group of less than 50 years, followed by 46% in age group of 51 to 70 years and only 2% were more than 71 years. Mean age was 51.78 $\pm$ 6.67 years. The gender distribution showed that majority (84%) were males and 16% were females. Overall 54.7%of the patients were exposed to smoke from various sources. The exposure was for 15 to 30 years in 36%, followed by 12% for less than 15 years and 6.7% for more than 30 years (Table 1) (Figure-1)

Table 1: Distribution of subjects depending on exposure to smoke(n=75)

Smoke Exposure	**Male**	**Female**	**Total**	**Percentage**
Yes	32	9	41	54.7
No	31	3	34	45.3
Total	**63**	**12**	**75**	**100**

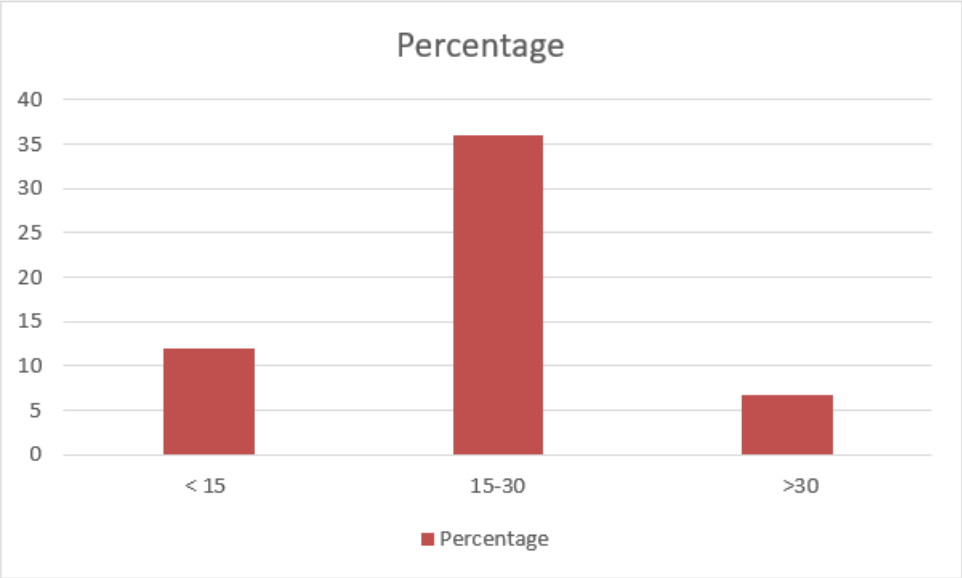

Figure 1: Distribution depending on exposure to smoke in years

Among those exposed to smoke majority were themselves smoker and of them 24% were bidi smokers, 18% were cigarette smokers, 33% were exposed to indoor smoke like chulha, 16% were exposed to passive smoke and 10% were exposed to smoke at their occupation.

The clinical history revealed that 93.3% patients had breathlessness, 73.3% had cough with expectoration, 53.3% had chest pain, 8% had wheeze, and 14% had fever as presenting symptom.

On chest x ray evaluation majority cases had hyperinflated lungs (45.3%), 16% had flattened diaphragm, 13.3% had increase in volume of retrosternal air space and 10.7% had rapid

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tapering of vascular markings. Fasting plasma glucose level in majority (53.3%) was <100 mg% 17.3% had FBS in range of 100-125, 16% had 126-200 and 13.3% patients had FBS >200mg%.42% cases had HbA1c <5.7%, 8% had HbA1C between 5.7-6.4%, and 20% had HBA1c between 6.5 to 8%, 16% had value of 8 to 10% and 13.3% had jt as >10%. Majority cases 86.7% had triglyceride level <150mg/dl, 17.3% had >150mg/dl level.

LFT showed that 65% patients had SGOT and SGPT ratio between 1-2; followed by 18% having a ratio of less than 1; 15% cases have ratio >2. On USG 22% had fatty liver and 78% had normal liver.

As per the exercise status of patients 56% cases did exercise sometimes, 28% never did it and only 16% did daily regular exercise. Number of exacerbations in past one year among the study population showed that majority (84 %) had less than 2, and 16 % had more than 2 episodes.

Table 2 shows distribution as per **GOLD's Criteria,** majority patients (55%) had moderate COPD, followed by 22% had mild COPD, 19% had severe COPD and 4% had very severe COPD.

Table 2: Distribution depending on GOLD's Criteria based on FEV1 %

Severity of COPD As per FEV1	**Frequency**	**Percentage**
Mild (FEV11 >80%)	17	22
Moderate (50-80 %)	41	55
Severe (50-30 %)	14	19
Very Severe (< 30 %)	3	4
Total	**75**	**100**

On ambulatory blood pressure monitoring (ABPM) for 24 hours, it was found out that mean systolic blood pressure was more in day time as compared to night whereas mean diastolic blood pressure was more at night. Mean blood pressure of 24 hours was 133.4 mmHg systolic and 75.6 mmHg diastolic.

Table 3: Distribution as per average Blood pressure at day and night time

Blood Pressure in mmHg Mean		Mean	SD	t value	P value
Day	Systolic	128.1	6.1	8.7	<0.001
Night	Systolic	121.3	3.4		
Day	Diastolic	72.3	4.5	2.8	0.005
Night	Diastolic	74.9	6.5		

The overall frequency CV risk factors among the subjects with COPD was 36%. The most common risk factors of our study population was smoking in 42 .6%, hypertension in 37.3%, Diabetes mellitus 32 %, followed by obesity in 28%, sedentary lifestyle 25.3%, and dyslipidemia seen in 18%. Multiple risk factors (>2) were noted in 13% (Table 4).

Table 4: Distribution of CV risk factors among COPD cases

Cardiac risk factors	**Frequency**	**Percentage**
1. Smoking	32	42.6
2. Hypertension	28	37.3
3. Diabetes Mellitus	24	32

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4. Obesity	21	28
5. Sedentary lifestyle	19	25.3
6. Dyslipidemia	14	18.6
7. Multiple risk factors >2	10	13

Discussion

As implied in their age and an array of typical cardiovascular risk factors, COPD patients have a substantial risk of cardiovascular diseases.

Various studies also show similar age & sex distribution of COPD patients as seen by us. [11,12,13.21] Male preponderance was noted by many studies [13,20,21] Occupational smoke exposure is responsible for 20 % cases of COPD in this study. Considering the smoke exposure, the majority of the cases were active addicted smokers (78%), and 61% were exposed to indoor smoke like chullas, and 19.5% were related to occupational exposure to the smoke, values are consistent with other studies. The other studies reported that 86.5% and 64.45% and 49.9%were active smokers respectively. [13,12,18]. In this study 22% patients of COPD were mild cases,55%were moderate,19% were severe and 5% were in very severe category as per GOLD criteria. In one study, an increased risk of high blood pressure has been observed to be associated with airflow restriction reflected by the FEV1 [20].The presenting clinical symptoms were noted as breathlessness (93.3%) followed by cough with expectoration 73.3%, 53.3% had chest pain, 8% had wheeze, and 14% had fever all comparable with other studies.[15]

Less number of our patients were hypertensive (37.3%) in comparison with other studies which show 63.2%, 52.1%,53% prevalence respectively. [16,17,18,] It is said that there is link between COPD and hypertension; "pulmonary hypertension, or high blood pressure in the blood vessels that link the heart and lungs, can be fatal." The larger circulatory system may also be impacted by the airflow restriction caused by COPD, raising blood pressure in a number of other body systems.[17] Mean blood pressure of 24 hours was 133.4 systolic and 75.6 diastolic. Other studies similarly noted mean SBP as 119.7, 145 and 129.1 whereas DBP were 73.3,82 and71.9 and respectively.[11,20,21] The two most important markers are circadian variation, the overnight non-dipping and the morning surge, constitute a stronger marker of the target organ involvement and cardiovascular (CV) morbidity, and mortality. An increased likelihood of cardiovascular fatalities and left ventricular hypertrophy is associated with a lack of a night time drop. [18] To enhance the prognosis for hypertensive patients, night time blood pressure (BP) control should be a new focus of therapy objective in addition to ambulatory or home daytime BP and 24-ho mean BP.[11,18]) In present study dipping of blood pressure was seen in majority of cases (76%) and in (24%) no dipping was seen, as contrast to other studies. A study noted non-dipping of BP in 94.44% patients of COPD while reverse dipping was noted in 5.56%. [21]

Difference between systolic daytime BP and night was significant with p value of <0.001. The diastolic BP difference between day and night records was statistically significant. Similar findings were noted in another study. [20]

ABPM monitoring plays vital role in detecting blood pressure abnormalities in 24 hours.[6]

COPD is an independent risk factor for CVD morbidity in addition to clustering of various risk factors. In this study overall frequency of CVD was 36% .The studies done by others also have similar findings. Cui *et al.*[19] had 51.7%, Joseph F[15] had 28% and Caram *et al.* (18) had 48% prevalence of CVD.

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Cardiovascular diseases present in our patients were hypertension in 37.3% followed by heart failure (17.3%) cor-pulmonale in (9.3%) Supraventricular arrhythmia total (8.2%), atrial fibrillation (3%) ventricular arrhythmia (1.5%) myocardial infraction (4%), stroke (2.7%); which were comparable with the other studies.[15,19,20])

It is established by a meta-regression of RCT data that BMI is related to the extent of lung function deterioration in COPD. Low BMI is linked to a quicker fall in FEV1 compared to normal BMI, whereas high BMI is linked to a slower decline.[11] and our study showed 28% were obese and 18% were overweight and low BMI was noted in 10% while 44% had normal BMI. Mean waist circumference was 94.32 cm, and majority subjects had waist circumference in normal range in this study. BMI distribution in study population was comparable with others studies 27.58 + 4.89 [13] Another study showed that mean BMI was 25 kg/m2. [18] A study by Sulhattin,Arslan *et al.* showed that mean BMI was 27.2 kg/m2.[11]

The chest radiograph is gold standard investigation to assess severity of the COPD and the majority of the cases had hyper-inflated lungs 45.3%, 16% had flattened diaphragm, 13.3% had raised volume of retrosternal air space and 10.7% had rapid tapering of vascular markings [21] Different laboratory tests were conducted and diabetes was found in 32% patients, The fasting blood glucose in majority (53.3%) was <100 mg%, and only 13.3% had FBS >200 mg%. HBA1C in majority cases (42%) was <5.7%. Our study showed that 86.7% subjects had serum triglyceride level < 150mg/dl,17.3% had levels >150mg/dl. As diabetes predisposes to ischemic cardiac events it needs attention in COPD patients. Prevalence of diabetes was 21% in one study[28]. Complications due to diabetes were seen in 21.18%[28] and 23% in another study.

Overall dyslipidaemia was present in 18% of our patients. A study by Fisk M showed high mean Triglyceride levels [20] and in stable COPD patients than healthy individuals as noted by Lingling Xuan,Feifei Han [27]

In present study majority cases (65%) had SGOT and SGPT ratio between 1-2; followed by 18% having a ratio of less than 1, and 15% cases had ratio >2. On USG 22% had fatty liver and 78% had normal liver. NASH is found to be prevalent (59%) in patients of COPD patients as per some studies [26] Non-alcoholic steatohepatitis (NASH) is common in COPD patients as they have a high risk of increased visceral fat that is inflammatory and lipophilic and can lead to the deposition of free-fatty acids in the liver. Additionally, the presence of nocturnal hypertension increases the likelihood of non-alcoholic fatty liver disease in COPD patients.[23]

The exercise status of our patients showed that only 16% did daily exercise and had active life. These findings also corroborate with a study by Joseph Finkelstein *et al.* in which, 58% did exercise sometimes and 42% never did exercise. [15] Sedentary behaviour is common risk factor for increased chances for CVD.[24] In present study the number of exacerbations in past one year among the study population was less than 2 in 82%, and 16 % had more than 2 episodes. Mean number of exacerbations in past were 1.69 + 0.9. In a study by Abolhassan H *et al.* ,66.5% had < 2 exacerbations and 33.35 had > 2 exacerbations. [12] .

GOLD criteria helps in assessing severity of COPD and the present study noted that majority cases had moderate COPD with FEV1/FVC ratio of less than 0.7 similar to study done by Radha TG *et al.*[25]

To conclude, the presence of CV risk factors among COPD cases in this study was 36%, compared with other studies which reported 28%, [16,] 48% ([17]) and 51.7% [20]. The intermittent hypoxia, chronic inflammatory state, sympathetic hyperactivity that COPD patients experience, has serious consequences for the cardiovascular system, including a higher chance of hypertension, type 2 diabetes, myocardial infarction, stroke, and fatal cardiovascular events [4].

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Concomitant diseases and CV risk factors in the patients with COPD would affect the quality of life, worsen life expectancy and increased hospitalizations. "The shared pathophysiological pathways, high prevalence of both diseases, adverse effects of medications, pulmonary exacerbations of COPD contribute to CVD, and can be potentially worsening for COPD and vice versa, are all possible reasons of strong association between CVD and COPD.

Limitations of study

As this study was carried out on the small number of patients from single study centre the results cannot be generalized to the large population, and lack follow-up also is a limiting factor.

Conclusion

This study provides insight into the menace of cardiovascular diseases in COPD patients and its association with the risk factors that can elevate the threat, such as smoking, hypertension, diabetes mellitus, dyslipidaemia, NASH and sedentary lifestyle. Non-dipping of the BP at night and rise of day time SBP are early markers of hypertension and are commonly seen in COPD patients. Hence use of ABPM which accurately correlates with target organ damage should be advocated. Occupational exposure is one of the important hidden factor for COPD, knowledge of which can control this occupational risk and would prevent future events. Hence to improve the wellbeing of the COPD patients, the physicians must be aware of the risk factors and complications related to heart while treating such patients. And controlling various comorbidities might be the key factor to decrease the mortality in such patients.

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