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Original Research Article

Prevalence of pulmonary arterial hypertension in severe chronic obstructive pulmonary disease patients attending tertiary care centre Ernakulam

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is an irreversible bronchial inflammation of lung airways and parenchyma. Various factors play an important role in occurrence and severity of pulmonary arterial hypertension (PAH), a common in severe COPD. The objective of the study is to know the proportion of PAH in patients with severe COPD and to find the association between various factors.
Methods: 180 cases of severe COPD patients admitted in Government Medical College Ernakulum from January 2019-December 2019, were enrolled into this cross-sectional descriptive study. Subject's history, clinical examination, anthropometric measurements, vitals, Arterial Blood Gas (ABG) analysis were done.
Results: Among 180 subjects, 148 (82.22%) had mild PAH, 22 (12.22%) subjects had moderate PAH and 10 (5.56%) had severe PAH. Use of accessory muscle was the most elicited sign in the study with 174 (96.67%). 170 (94.44%) had cough and 169 (93.89%) had breathlessness which were the most reported symptoms. Demographic variables and clinical features had no significant mean pulmonary artery pressure (mPAP) association. Grade 3 PAH groups were elder than others, which was statistically significant ($p<0.047$). FEV1, Oxygen Saturation and ejection fraction were lowest in grade 3 PAH subjects. Respiratory rate, hemoglobin, PCV, tricuspid velocity, PaCO2 were highest in grade 3 PAH subjects being statistically significant ($p<0.0001$).
Conclusions: In our study, majority of severe COPD patients had mild PAH. There was an independent correlation between respiratory rate, hemoglobin, PCV, tricuspid regurgitant velocity and PaCO2 with severity of PAH.

Keywords: COPD, mPAP, PAH, Tricuspid valve regurgitant velocity

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is primarily characterised by the presence of airflow limitation resulting from airways inflammation and remodelling often associated with parenchymal destruction and the development of emphysema.[1] Approximately 50% of patients with very severe COPD who undergo lung volume reduction surgery (LVRS) or lung transplantation have moderate to severe PAH1, a common complication of COPD.[2] PAH defined by right-heart catheterization (RHC) showing precapillary pulmonary hypertension with a mean pulmonary artery pressure (mPAP) of >25 mmHg and a normal pulmonary artery wedge pressure (PCWP) of <15 mmHg.[3] PAH is usually mild to moderate and, nowadays, most of these patients in industrialised countries are undergoing long-term oxygen therapy which stabilises, attenuates, or sometimes reverses the progression of pulmonary hypertension.[2]

Potential causes proposed to explain the development of PAH in COPD include gas exchange abnormalities, destruction of the pulmonary vascular bed, alterations in

respiratory mechanics, changes in intrinsic pulmonary vessel tone, and increased blood viscosity.[4] Thrombosis and platelet dysfunction can be important in the development of PAH. Elevated plasma concentrations of D-dimers and fibrinopeptides A and B, in certain patients with PAH, are the proof of an abnormal intravascular coagulation process. Persistent dyspnea on exertion is the most frequent symptom; and it is present in almost patients even in the presence of mild hemodynamic abnormalities. Pulmonary function tests (PFT) will help to assess underlying lung abnormalities. Results of arterial blood gases usually show mild hypoxemia and hypocapnia. Transthoracic echocardiography (TTE) is a non-invasive screening test for patients with suspected Pulmonary Hypertension (PH). TTE estimates pulmonary artery systolic pressure (sPAP) and may provide additional information about the cause and consequences of PH.[5] An ejection fraction (EF) <50% is considered left ventricular dysfunction. Patients with COPD are at risk for left ventricular dysfunction; however, the results from the studies shows a disagreement regarding the association of LV dysfunction in COPD patients.[6,7] Furthermore, Forced Expiratory Volume in the first second (FEV1) evaluation is crucial in estimating the severity of airflow limitation and until recently guided the clinical management of the disease. In addition, there is a direct correlation between FEV1 levels with the prognosis of these patients.[8] In patients with COPD, malnutrition is often present and correlate with the severity of airway obstruction.[9] Malnutrition can be diagnosed based on the presence of a Body Mass Index (BMI) of less than 18.5 kg/m2 or based on weight loss (more than 10% irrespective of time or more than 5% over the last 3 months) combined with a reduced BMI (less than 20 kg/m2 or less than 22 kg/m2 if 70 years old or older).[10]

The objective of this study is to find the proportion of PAH in severe COPD patients and to find out the association between PAH and variables like haematological parameters, anthropometric measurements, vital signs, Forced Expiratory Volume (FEV1), EF and ABG.

METHODS

Patients admitted in Government Medical College Ernakulum from January 2019-December 2019, were enrolled into this cross-sectional descriptive study.

A total 180 COPD patients after applying the formula 4pq/d2. As per study of Samareh et al, the prevalence of severe PH (p value) is 13.7%.11 Q value= 86.3; d value (precision) =5. All consecutive Severe COPD patients admitted in medical wards and ICU of Govt. Medical College, Ernakulum till the sample size is attained.

Inclusion and exclusion criteria

Inclusion criteria for the study were all COPD exacerbation patients (as per GOLD criteria) whose airway obstruction, based on spirometric results, had an FEV1/FVC ratio less than 0.7; also, they were given two puffs of salbutamol inhaler and, after 15 min, if there was a not a 12% or 200 cm3 increase in FEV1, and the possibility of all other obstructive pulmonary diseases, such as bronchectasis, were ruled out. And FEV1<50%.

Data collection

Study began after obtaining permission from research committee and institutional review board. As per the inclusion criteria COPD patients are selected. Thorough history and clinical examination done. After obtaining informed consent various tests are done. Initially anthropometric measurements are taken with weighing machine, measuring tape. Vitals are monitored with pulse oximeter, sphygmomanometer. ABG also done by taking blood in heparinised syringe and analysed using ABG analyser. EF and tricuspid regurgitant flow velocity is calculated using echocardiogram. Tricuspid more than 3.4m/s is considered significant. Doppler Echo can approximate pulmonary artery systolic pressure (PASP) using

tricuspid valve velocity (4v2 = TV pressure gradient), estimated CVP (=RA pressure), Bernoulli equation, PASP = RVSP (in the absence of RVOTO or pulmonic stenosis)

RVSP = 4v2 + CVP

Mean PAP can be approximated because mPAP = 0.61•sPAP + 2. Based on the echo PAH is classified into mild (20-40 mmHg), moderate (41-55 mmHg) and severe PAH (>55 mmHg). Then each variable is compared univariably for its association with PAH.

Data management and statistical analysis

Data was analysed using Statistical package for social sciences (SPSS) statistical software. Descriptive statistics was used to find out mean, standard deviation, minimum, maximum and range for the quantitative variables. The association between the demographic variables and grades of pulmonary artery pressure were analysed by chi square test. Chi square test was used to find out association between clinical features and grades of PAH. One way ANOVA was used to find out the difference between grades of pulmonary artery pressure for age and other quantitative variables such as BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse, saturation, respiratory rate (RR), total count, FEV1, platelet, tricuspid regurgitant velocity, partial pressure of carbon dioxide (PaCO2) etc.

RESULTS

Basic characteristics

A total of 180 patients were recruited in the study, in which 167 (92.78%) were male and 13 (7.22%) were female. The mean age of the patients was 63.49. Table 1 shows the

descriptive statistics for demographic and outcome variables related to the patients.

Among 180 subjects, 148 (82.22%) had mild PAH, 22 (12.22%) subjects had moderate PAH and 10 (5.56%) had severe PAH. Use of accessory muscle was the most elicited sign in the study with 174 (96.67%). 170 (94.44%) had cough and 169 (93.89%) had breathlessness which were the most reported symptoms (Table 2).

Symptoms like abdominal distension, pedal edema, abdominal pain, reduced urinary output, Hemoptysis, JVP and FEV1 were found to be statistically significant with association of grades of PAH (Table 3).

The association between different grades of PAH and variables are shown in Table 4. SPO2, RR, Hb, PCV, FEVI, Tricuspid regurgitant velocity, PaCo2 showed statistically significant difference.

There was no statistically significant difference between different grades of pulmonary artery pressure and age group (p>0.69), gender (p>0.257) and socio-economic status (p>0.222).

Table 1: Descriptive statistics for demographic and outcome variables.

Variance	Range	Minimum	Maximum	Mean	SD
Age	57	35	92	63.49	9.92
SBP	102	86	188	133.77	16.81
DBP	58	42	100	79.71	8.71
Pulse	72	54	126	81.21	12.55
BMI	11.30	17.60	28.90	22.79	2.53
SPO_2	7	87	94	91.66	1.54
RR	23	19	42	25.11	4.50
Hb	5.40	13	18.40	15.52	1.29
PCV	53.40	4.60	56	45.77	4.97
Platelet	2	1.50	3.5	2.43	0.52
TC	7322	6130	13452	9177.38	1626.93
FEV_1	23	26	49	39.33	6.87
Tricuspid regurgitant velocity	2.80	1.60	4.40	2.50	0.62
EF	66	4	70	56.55	8.06
$PaCO_2$	39	36	75	47.86	6.94
PAP	45.75	17.25	63	30.10	10.46

Table 2: Frequency distribution of variables.

Variables		Frequency	Percentage
Age group	<40	2	1.11
	41-50	10	5.56
	51-60	53	29.44
	61-70	73	40.56
	71-80	33	18.33
	81-90	7	3.89
	>90	2	1.11
Gender	Male	167	92.78
	Female	13	7.22
Socioeconomic	Upper	10	5.56
	Upper middle	28	15.56
	Lower middle	72	40.00
	Upper lower	55	30.56
	Lower	15	8.33
Breathlessness	Absent	11	6.11
	Present	169	93.89
Abdominal Distension	Absent	146	81.11
	Present	34	18.89
Pedal edema	Absent	151	83.89
	Present	29	16.11
Abdominal Pain	Absent	166	92.22
	Present	14	7.78

Continued.

Variables		Frequency	Percentage
Reduced urinary output	Absent	167	92.78
	Present	13	7.22
Chest pain	Absent	169	93.89
	Present	11	6.11
Hemoptysis	Absent	173	96.11
	Present	7	3.89
Cough	Absent	10	5.56
	Present	170	94.44
Fever	Absent	162	90.00
	Present	18	10.00
Jaundice	Absent	170	10(94.44
	Present	10	5.56
Clubbing	Absent	165	91.67
	Present	15	8.33
Accessory muscles	Absent	6	3.33
	Present	174	96.67
Jugular venous pressure (JVP)	Absent	156	86.67
	Present	24	13.33
Pulmonary artery pressure (PAP)	Mild	148	82.22
	Moderate	22	12.22
	Severe	10	5.56

Table 3: Association of grades of PAH and symptoms.

Variables		Mild	Moderate	Severe	Total	Chi-square	P value
Breathlessness	Absent	10	1	0	11	0.85	>0.654
	Present	138	21	10	169		
Abdominal distension	Absent	136	10	0	146	72.42	<0.0001
	Present	12	12	10	34		
Pedal edema	Absent	140	11	0	29	83.31	<0.0001
	Present	8	11	10	151		
Abdominal pain	Absent	146	16	4	166	58.2	<0.0001
	Present	2	6	6	14		
Reduced urinary output	Absent	146	16	5	13	48.12	<0.0001
	Present	2	6	5	167		
Chest pain	Absent	140	20	9	11	0.73	>0.694
	Present	8	2	1	169		
Hemoptysis	Absent	145	21	7	7	19.64	<0.0001
	Present	3	1	3	173		
Cough	Absent	8	2	0	10	1.12	>0.571
	Present	140	20	10	170		
Fever	Absent	134	18	10	8	2.8	>0.247
	Present	14	4	0	162		
Jaundice	Absent	144	19	7	10	16.42	<0.0003
	Present	4	3	3	170		
Clubbing	Absent	137	19	9	15	1	>0.607
	Present	11	3	1	165		
Accessory muscles	Absent	6	0	0	6	1.34	>0.512
	Present	142	22	10	174		
JVP	Absent	138	7	7	152	56.7	<0.0001
	Present	10	15	3	28		
$PaCO_2$	<45	66	3	1	70	11.44	<0.003
	>45	82	19	9	110		
FEV_1	32-50	144	14	3	161	18.29	<0.0001
	<30	4	8	7	19		

Table 4: Comparison of quantitative variables with different grades of pulmonary arterial pressure.

Variable	Grade I	Grade II	Grade III	P value
Age	62.66±9.92	66.77±9.88	68.60±8.14	<0.047
SBP	133.59±16.65	132.18±17.96	139.80±18.07	>0.477
DBP	79.93±8.76	77.64±10.02	81.00±3.68	>0.466
Pulse	80.53±11.92	83.09±14.11	87.10±17.65	>0.211
BMI	23.00±2.40	22.05±3.07	21.36±2.71	>0.475
SPO2	92.02±1.19	90.45±1.84	88.90±1.52	<0.0001
RR	23.57±2.78	31.27±4.31	34.40±2.76	<0.0001
Hb	14.90±0.92	16.97±0.91	17.95±0.30	<0.0001
PCV	44.44±4.28	50.73±2.80	54.46±1.69	<0.0001
Platelet	2.41±0.52	2.48±0.51	2.54±0.55	>0.666
TC	9101.79±1595.32	9758.91±2065.96	9016.80±678.84	>0.202
FEV1	40.90±6.02	33.36±6.48	29.20±3.43	<0.0001
Tricuspid regurgitant velocity	3.11±0.30	4.21±0.21	4.84±0.08	<0.0001
EF	57.61±7.94	52.14±8.03	50.60±4.06	<0.0005
PaCO2	46.26±5.70	54.50±7.78	56.90±7.14	<0.0001

DISCUSSION

In this cross-sectional descriptive study, the prevalence and predictors associated with patients with COPD were examined. The male preponderance evident in this study was similar to the one conducted by Mahishale et al which was also focussed in India (Karnataka), had 73.9% of male patients and study by Fekri et al in Iran, also had male predominance of 75%.[12,13]

Among 180 patients, 148 (82.22%) patients had mild PAH, 22 (12.22%) had moderate PAH and 10 (5.56%) had severe PAH. The study conducted by Fekri et al showed severe PH at 13.7%.[11] The prevalence of severe PH in COPD patients range from 5 to 13.5% and, in most cases, the prevalence has been 10%.[11] Indian study by Gupta et al also showed prevalence of severe PAH was 17.65% in COPD patients.[14] So in our study the prevalence of severe PAH is lower than the studies conducted earlier.

FEV1, oxygen saturation and ejection fraction was lowest in grade 3 pulmonary arterial hypertension subjects. Respiratory rate, hemoglobin, PCV, tricuspid velocity, PaCO2 were highest in grade 3 pulmonary arterial hypertension subjects which was statistically significant. In the study conducted by Fekri et al also showed the progressive development of PAH in COPD patients and their relationship with increased PCV, ejection fraction, and hypoxia.[11] Fekri et al in his study also showed association of BMI with PAH but our study did not show any association. This may be because of our small sample size of 180 compared to 1477 and also our study period was of 1 year duration.

CONCLUSION

In our study, majority of severe COPD patients had mild PAH. There was an independent correlation between respiratory rate, hemoglobin, PCV, tricuspid regurgitant velocity and PaCO2 with severity of PAH.

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