



ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC FINDINGS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ATTENDING A TERTIARY CARE HOSPITAL IN EASTERN INDIA: A CROSS SECTIONAL STUDY

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ABSTRACT

BACKGROUND: COPD is characterized by chronic airflow limitation and a range of pathological changes in the lungs. In addition, COPD presents significant extrapulmonary effects and is associated with important comorbidities that may contribute to the disease severity. COPD affects pulmonary blood vessels, right ventricle, as well as left ventricle leading to the development of pulmonary hypertension, cor-pulmonale, right ventricular dysfunction, and left ventricular dysfunction. This study was undertaken to evaluate cardiac function with ECG and echocardiography in COPD patients which may further help to assess the prognosis and identifying the individuals likely to suffer increase morbidity and mortality.

METHODS: An observational, cross sectional study was conducted among 100 patients attending the Department of General Medicine of Burdwan Medical College and Hospital, diagnosed as having COPD wherein detailed history taking and clinical examination was done along with routine investigations such as complete blood count, renal functions, randomized blood sugar and further for a Chest X-ray, electrocardiography, and two-dimensional (2D)-echocardiography. Statistical analysis was done by SPSS version 19.0.

RESULTS: Majority of the COPD patients were male and belonged to GOLD stage 2. The most electrocardiographic finding was P-Pulmonale and Echocardiographic finding was PAH (Pulmonary Arterial Hypertension) with maximum patients having mild PAH. Most common clinical finding was pedal edema. Severity of the disease was found to have linear relation with severity of cardiac complications.

CONCLUSION: There is significant involvement of the cardiovascular system in COPD patients. The electrocardiographic and echocardiographic findings had linear relation with the severity of the disease. It is mandatory to investigate all the COPD patients with ECG and 2D ECHO as it aids in early detection and treatment of cor pulmonale.

KEYWORDS : COPD, Echocardiography, ECG, Pulmonary Arterial Hypertension

BACKGROUND:

Chronic obstructive pulmonary disease (COPD) is a global health issue with smoking being the most important risk factor. By 2020, it will be the third most leading cause of mortality and fifth leading cause of morbidity in the world.[1,2] There is a crude estimate of about 30 million people in India suffering from COPD, and the death rate is among the highest in the world, data suggests that about 556,000, i.e. (>20%) of total 2,748,000 die in India annually.[3,4]

COPD is characterized by chronic airflow limitation and a range of pathological changes in the lungs. In addition, COPD presents significant extrapulmonary effects and is associated with important comorbidities that may contribute to the disease severity. Chronic airflow limitation is associated with an abnormal inflammatory response of the lungs to noxious particles or gases, particularly cigarette smoke.[5]

COPD affects pulmonary blood vessels, right ventricle, as well as left ventricle leading to the development of pulmonary hypertension (PH), cor-pulmonale (COR-P), right ventricular dysfunction, and left ventricular dysfunction. Ischemic heart disease is one of the main causes of mortality in COPD.[6] Co-existence of both diseases is very common and has diagnostic, therapeutic, and prognostic implications.[7,8] Chronic bronchitis alone increases the risk of coronary deaths by 50%. Reduced ratio of forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC) is also an independent risk factor for coronary events, increasing the risk by 30%. With every 10% decrease in FEV1, all-cause mortality increases by 14% and an increase in cardiovascular mortality by 28%.[9] In more advanced COPD, cardiovascular diseases account for 20-25% of all deaths.[10]

COR-P is defined as an alteration in the structure and function of the right ventricle caused by a primary disorder of the respiratory system. PH is the common link between lung dysfunction and the heart in COR-P. COR-P can develop due to various cardiopulmonary diseases. COR-P usually has a slow and chronic progression, but acute onset and life-threatening complications can occur.[11]

Echocardiography provides a rapid, noninvasive portable, and almost accurate method to evaluate the right ventricle function, right ventricular filling pressure, tricuspid regurgitation, left ventricular function, and valvular functions. It has been studied that echocardiography measured pulmonary arterial pressure closely correlates with pressure measured by right heart catheterization.[12]

This study was undertaken to evaluate cardiac function with ECG and echocardiography in COPD patients which may further help to assess the prognosis and identifying the individuals likely to suffer increase morbidity and mortality.

METHODOLOGY:

This institutional based cross sectional, observational study was included 100 consecutively selected COPD patients by convenience sampling admitted in General Medicine Ward of our Institution over a period of 18 months. After approval from the Ethical Committee, Informed consent from each adult patient was taken. All the patients selected were asked for the detailed history of respiratory as well as cardiovascular symptoms and were clinically examined for the signs of ventricular hypertrophy, cardiomegaly, PH and/or heart failure. Patients were investigated for routine investigations

such as complete blood count, renal functions, randomized blood sugar and further for a Chest X-ray, electrocardiography, and two-dimensional (2D)-echocardiography. All patients were subjected to resting two-dimension transthoracic Doppler echocardiography .

Echocardiography was done to assess the pericardium, valvular anatomy and function, left and right side chamber size and cardiac function. Tricuspid regurgitant flow was identified by colour flow Doppler technique and the maximum jet velocity was measured by continuous wave Doppler without the use of intravenous contrast. Right ventricular systolic pressure was estimated based on the modified Bernoulli equation and was considered to be equal to the sPAP in the absence of right ventricular outflow obstruction: sPAP (mmHg) = right ventricular systolic pressure = trans-tricuspid pressure gradient (TTPG) right atrial pressure (RAP), where trans-tricuspid gradient is $4v$ (v = peak velocity of tricuspid regurgitation, m/s). RAP was empirically estimated as 15 mmHg before 1997. Since 1997, RAP was estimated to be 5, 10, or 15 mmHg based on the variation in the size of inferior vena cava with inspiration as follows: complete collapse, RAP = 5 mmHg; partial collapse, RAP = 10 mmHg; and no collapse, RAP = 15 mmHg.[13] Pulmonary hypertension was defined in this study as sPAP \geq 30 mmHg. [14] This value was chosen according to the definition of PH. PH was classified into mild, moderate, Severe and severe category as sPAP 30-50, 50-70, $>$ 70 mmHg, respectively (using Chemla formula, mean pulmonary arterial pressure (MPAP) = 0.61 PASP + 2 mmHg and putting value of 25-35, 35-45, and $>$ 45 mmHg of MPAP for mild, moderate, and severe PH, respectively). [14] Right ventricle dimension was measured by M-Mode echo and right ventricular dilation or cor pulmonale was said to be present when it exceeded the normal range of 0.9–2.6 cm. Right ventricle contractility was also noted and right ventricular systolic dysfunction was said to be present when it was hypokinetic. Left ventricular function was also assessed by using the following parameters: EF (ejection fraction) is a measure of how much end-diastolic value is ejected from LV with each contraction (56%–78%). FS (fractional shortening) is a percentage change in LV dimension with each LV contraction (28%–44%). LV mass = left ventricular mass (88–224 g). E/A = diastolic filling of left ventricles usually classified initially on the basis of the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A). In normal subjects LV elastic recoil is vigorous because of normal myocardial relaxation, therefore more filling is completed during early diastolic, so left ventricular diastolic dysfunction (LVDD) is said to be present when E/A is $<$ 1.3 (age group 45–49 years), $<$ 1.2 (age group 50–59 years), $<$ 1.0 (age group 60–69 years), and $<$ 0.8 (age group \geq 70 years).[15]

Inclusion criteria of the study included subjects between the age of 35-80 years with informed and written consent and diagnosed as a case of COPD by Spirometry. Exclusion criteria included cases of pneumonia, tuberculosis bronchial asthma, interstitial lung disease, carcinoma lung, any congenital heart disease, Left ventricular failure, Dilated cardiomyopathy. Descriptive statistical analysis of data has been done. The age and sex distribution of all patients, their body mass index (BMI), severity of COPD, echocardiography findings, the frequency of COR-P and its relation to COPD has been represented graphically. Correlation between the cardiac parameters on echocardiography findings and pulmonary parameters on spirometry findings have been done to find out the relation. The mean and standard deviation (SD) of FEV1 and PH of all the patients has been calculated along with Pearson correlation value. Analysis was done with the help of SPSS version 19.0.

RESULTS:

Table 1: Sex Distribution of COPD patients aged above 35 years:

| Age Patients above 35 years of age | Male | | Female | |
|------------------------------------|---------------------|----|--------|----|
| | No | % | No | % |
| | 72 | 72 | 28 | 28 |
| Total | 100 Patients | | | |

Male cases were more in number than female. Male patients were 72% and female were 28 % of total sample size respectively.

Table 2: GOLD staging of COPD:

| GOLD guideline | No of patients | Percentage |
|------------------------|----------------|------------|
| Stage I (Mild) | 00 | 00 |
| Stage II (Moderate) | 37 | 37 |
| Stage III (Severe) | 33 | 33 |
| Stage IV (Very Severe) | 30 | 30 |
| Total | 100 | 100 |

The patients diagnosed with COPD disease as per GOLD guideline, and we found maximum number of patients had stage II (Moderate) i.e 37 %, 33% patients belonged stage III (Severe), 30.0 % patients had stage IV (Very severe) and not a single patients had found in stage I (Mild).

Table 3: Electrocardiographic finding of COPD patients

| ECG Findings | Moderate COPD (n=37) | Severe COPD (n=33) | Very severe COPD (n=30) | Total (n=100) | percentage |
|--------------|----------------------|--------------------|-------------------------|---------------|------------|
| | No | No | No | No | |
| p Pulmonale | 4 | 13 | 23 | 40 | 40 |
| R/S in V1>1 | 2 | 9 | 12 | 23 | 23 |
| R/S in V6<1 | 2 | 6 | 11 | 19 | 19 |
| RAD | 4 | 3 | 4 | 11 | 11 |
| RBBB | 0 | 3 | 4 | 07 | 07 |
| AF | 0 | 1 | 3 | 04 | 04 |
| VPC | 1 | 2 | 3 | 06 | 06 |

The most common electrocardiographic finding is P-Pulmonale (40.0%) seen in most of the very severe group of COPD. The next common finding is R/S in V1 $>$ 1 found in 23.0 % and R/S in V6 $<$ 1 found in 19.0%. Right axis deviation alone was found in 11.0%. 7.0 % had RBBB, AF was found in 4.0 % and VPC was found in 6.0 % in severe and very severe groups of COPD in the present study. All the ECG changes except right axis deviation and RBBB had significant relation with the severity of the disease. The insignificance of RAD, RBBB, AF and VPC may be attributed to small sample size of the study.

Table 4: Echocardiographic findings present in COPD patients:

| Echocardiography findings | Moderate COPD (n=37) | Severe COPD (n=33) | Very severe COPD (n=30) | Total (n=100) | percentage |
|---------------------------|----------------------|--------------------|-------------------------|---------------|------------|
| | No | No | No | No | |
| PAH | 6 | 24 | 27 | 57 | 57 |
| RA dilatation | 5 | 17 | 27 | 49 | 49 |
| RV dilatation | 5 | 14 | 27 | 46 | 46 |
| TR | 5 | 19 | 20 | 44 | 44 |
| RVH | 5 | 9 | 20 | 34 | 34 |
| IVMA | 1 | 5 | 12 | 18 | 18 |
| LVH | 1 | 7 | 4 | 12 | 12 |
| EF | 0 | 1 | 12 | 13 | 13 |
| LV Dilatation | 0 | 1 | 8 | 09 | 09 |
| LVDD | 0 | 2 | 4 | 07 | 07 |

In the present study having 100 COPD patients, 71.0 % had 2D ECHO findings and 29.0 % had normal study. Of these 29

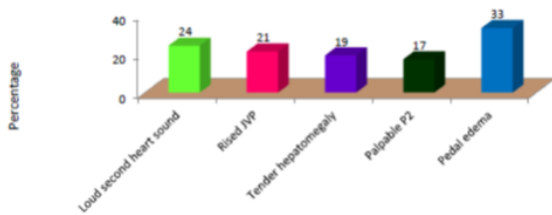
patients, with normal ECHO, 4 had electrocardiographic changes. 4 patients in the total study had absolutely normal ECG but had significant echocardiographic changes. The most common echocardiographic finding in the study was pulmonary artery hypertension observed in 57.0% followed by right atrial dilatation and right ventricular dilatation seen in 49.0% & 46.0 % of cases respectively. Right ventricular hypertrophy was found in 34.0 % and inter ventricular septal wall motion abnormality is found in 18.0 %. 12% had left ventricular hypertrophy. 7.0 % of the cases had left ventricular diastolic dysfunction. 44.0 % of the cases had tricuspid regurgitation. 13 % cases had EF and LV Dilatation also found in 9 %. The findings of pulmonary arterial hypertension, right ventricular dilatation, right atrial dilatation, right ventricular hypertrophy and interventricular wall motion abnormality are found to have increased incidence with duration and severity of illness and found mostly in severe(stage-3 GOLD) and very severe(stage-4 GOLD) classes of COPD. The p values for 2D ECHO were calculated using Fissure t test. All the findings except LVH and LVDD had highly significant correlation with the severity of the disease, the incidence being high in very severe disease.

Table 5: Distribution of pulmonary artery hypertension in various stages of COPD

| GOLD COPD staging | Mild PAH (<30 mmHg) | Moderate PAH (30 – 50 mm Hg) | Severe PAH (>50 mm Hg) |
|-------------------|---------------------|------------------------------|------------------------|
| Stage II | 13 | 0 | 0 |
| Stage III | 24 | 12 | 2 |
| Stage IV | 12 | 10 | 16 |
| Total | 49(49.0 %) | 22 (22.0 %) | 18 (18.0 %) |

In the present study 56.0 % of cases had pulmonary artery hypertension (PAH) of which 49.0 % had mild PAH, 22.0 % had moderate PAH and 18.0 % had severe PAH.

Figure 1: Clinical profile of cor-pulmonale



Pedal edema was the most common sign of cor pulmonale observed in 33.0 % of patients. 24.0 % had loud second heart sound, 21.0 % had raised JVP, 19% had tender hepatomegaly and 17.0 % had palpable P2.

DISCUSSION:

In our study males and females more than 35 years of age with history suggestive of chronic obstructive pulmonary disease. We have found male cases was higher than female. Male patients was 72% and female was 28 % respectively. This in accordance with the study by Hideki Katsura et al.[16] where male : female ratio in COPD is approximately 3:1. In our study, maximum number of patients 37% diagnosed with COPD as per GOLD guideline had stage II disease(Moderate), 33% patients belonged stage III (Severe), 30.0 % patients had stage IV (Very severe) and not a single patients was found in stage I (Mild). We observed in the present study that, pedal edema was the most common sign of cor pulmonale observed in 33.0 % of COPD patients. 24.0 %had loud second heart sound, 21.0 % had raised JVP, 19% had tender hepatomegaly and 17.0 % had palpable P2.The most common

electrocardiographic finding is p Pulmonale (40.0%) seen in most of the very severe group of COPD. p values were calculated using fissure t test with 2x3 contingency table. All the ECG changes except right axis deviation and RBBB had significant relation with the severity of the disease. The insignificance for RAD RBBB, AF and VPC may be attributed to small sample size of the study. In the present study total 100 COPD patients, 71.0 % had 2D ECHO findings and 29.0 % had normal study. Of these 29 patients, with normal ECHO, 4 had electrocardiographic changes. 4 patients in the total study had absolutely normal ECG but had significant echocardiographic changes. The most common echocardiographic finding in the study was pulmonary artery hypertension observed in 57.0% of cases followed by right atrial dilatation and right ventricular dilatation seen in 49.0% & 46.0 % of cases respectively. Right ventricular hypertrophy was found in 34.0 % and inter ventricular septal wall motion abnormality is found in 18.0 %. 12% had left ventricular hypertrophy. 7.0 % of the cases had left ventricular diastolic dysfunction. 44.0 % of the cases had tricuspid regurgitation. The findings of pulmonary arterial hypertension, right ventricular dilatation, right atrial dilatation, right ventricular hypertrophy and interventricular wall motion abnormality are found to have increased incidence with duration and severity of illness and found mostly in severe(stage-3 GOLD) and very severe(stage-4 GOLD) classes of COPD. The p values for 2D ECHO were calculated using Fissure t test. All the findings except LVH and LVDD had highly significant correlation with the severity of the disease, the incidence being high in very severe disease. In the present study 56.0 % had pulmonary artery hypertension (PAH) of which 49.0 % had mild PAH, 22.0 % had moderate PAH and 18.0 % had severe PAH. There is no exact data of PH prevalence in COPD; pulmonary artery pressures were seen elevated in about20–90% of patients when measured by right heart catheterization, with evidence of changing severity in pulmonary hemodynamics with the severity in airflow obstruction.

Two studies by Kessler R. et.al and Oswald-Mamosser M. et.al have shown an abnormal increase in MPAP (Ppa) in COPD of 0.4–0.6 mmHg per year. These studies illustrate that PH in COPD progresses slowly and occur in mild as well as severe forms of disease.[17,18] Study by Higham MA et.al demonstrated the 5 years survival rate being 50% in patients with mild PH (20–30 mmHg),30% in those with moderate and severe PH (30–50 mmHg),and 0% in small group of patients suffering from severe PH (>50 mmHg). This study finding reveals 48% patients of varying severity of COPD have findings for PH that is almost similar to the previous studies. The frequencies of PH in moderate and severe COPD were 33.33% and 66.66%,respectively which is comparable to other study in which findings were 43% and 68%, respectively.[19] Previous studies showed the frequency of severe PH in COPD about 1–3% it has shown a high rise of 12% which could be explained as the study included only moderate and severe COPD cases. Approximately, about 25% patients of COPD develop COR-P.[29] One of the autopsies in a study by Gupta NK et.al showed 40% patients of COPD had COR-P.[20] The cause of LVDD in COPD patients could be due to chronic hypoxemia leading to the changes in myocardial relaxation, distension, and lung hyperinflation making the parietal pleura stiff and similarly the walls of cardiac fossa adding the load to the walls of ventricle and also due to ventricular interdependence. In our study, LVDD was present in 58% of patients as compared to 47.5% seen in the study done by Gupta NK et. al [21] Studies by Murphy ML et.al , Fluck DC et.al and Render ML et.al indicate that LV function remains normal in persons with COPD, whereas others suggest that LV dysfunction may be present. [22,23] Abnormal LV performance in persons with COPD may be due to a number of factors, such as hypoxemia and acidosis; concurrent coronary artery disease; ventricular interdependence (because the right

ventricle (RV) and LV share a common septum, RV dilatation may lead to bulging of the septum into the LV, which would in turn increase LV end-diastolic pressure, decrease venous return, and diminish LV stroke volume and cardiac output (CO) and large swings in intrathoracic pressure (pronounced negative pleural pressure would increase Ppa and diminish LV stroke volume due to ventricular interdependence, negative pleural pressures may also increase LV after load).[24] Left ventricular systolic dysfunction (LVSD) is present in 7.5% patients, in previous studies by Vizza CD et.al, Jardin F et.al, Louridas G et.al and Funk GC et.al, it was present in 4%–32% patients of COPD.[25-28] LVDD was seen in COPD patients with normal pulmonary arterial pressure and it increased with right ventricular after load in a study by NK Gupta et.al.[29] Poddar AK et al, concluded[30] LVDD is present in 47.5% of patients, out of which 16 patients had PH and 3 did not have PH, various mechanisms might explain the presence of left diastolic dysfunction in COPD patients. This may be due to chronic hypoxemia leading to abnormalities of myocardial relaxation, lung hyperinflation, and distension leading to increased stiffness of the parietal pleura and thus of the wall of cardiac fossa leading to added load on ventricle, and also due to ventricular interdependence. Left ventricular hypertrophy (LVH) was present in 22.5%. In a study by Poddar AK et al, LVH was found in 25%–60% patients dying of COPD mainly in patients who also had right ventricular hypertrophy.[30]

CONCLUSION:

There is significant involvement of the cardiovascular system in COPD patients. The electrocardiographic and echocardiographic findings had linear relation with the severity of the disease. It is mandatory to investigate all the COPD patients with ECG and 2D ECHO as it aids in early detection and treatment of cor pulmonale.

To conclude, the present study shows high prevalence of pulmonary hypertension, cor pulmonale, left ventricular dysfunction complicating COPD, more so with severe COPD. We suggest screening of all COPD patients for cardiac complications. This would contribute to the assessment of prognosis in these patients and assist in identifying individuals likely to suffer increased mortality and morbidity warranting close monitoring and intense treatment.

Limitations of this study :

This study had a short time frame. So, long term follow up was not possible. It was also a hospital based study with a relatively small number of study population. Investigations like computed tomography or angiography were not incorporated in this study.

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