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PULMONARY HYPERTENSION IN MILD-MODERATE COPD: AN EARLY LINK

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ABSTRACT: AIMS: To study right ventricular function and pulmonary artery pressure in patients with mild-moderate COPD by 2D echo Doppler. **METHODS:** This observational cross sectional study was carried out in JNMC, Wardha. 100 subjects with COPD in our hospital were interviewed. Detailed history and physical examination done and all patients were subjected to pulmonary function test (PFT) and categorised as per GOLD Criteria. The patients so selected were subjected to 2D ECHO Doppler examination. Hence, right ventricular (RV) systolic function was calculated with the help of Tricuspid Regurgitation (TR) jet, Pulmonary Regurgitation (PR) jet and Tricuspid Annular Plane Systolic Excursion (TAPSE). **RESULTS:** The mean age of present study population was 53.45±15.73 years. In the present study, males account for 74%, with a male: female ratio of 2.84:1 which was comparable to other study groups. 61 patients in the study group were smokers of which 53 patients had moderate COPD. This proves importance of smoking as a risk factor. Out of 100 patients 20% had mild COPD and 80% had moderate COPD. Study of PASP by TR jet with the use of 2D ECHO showed mild PASP in 68 patients out of 100 while moderate PASP in remaining 32 patients, while there were no patients with severe PASP. Study of TAPSE by 2D ECHO showed that 80 patients had abnormal TAPSE value while 20 patients had normal value. **CONCLUSION:** The study explains the incidence of pulmonary hypertension in mild-moderate COPD patients. Thus if subjected to ECHO, RV systolic function and pulmonary hypertension can be detected in early course of disease and hence early intervention may predict decreased morbidity and favourable outcome in patients of COPD.

KEYWORDS: COPD, Pulmonary hypertension, TR jet, TAPSE, PR jet.

INTRODUCTION: Chronic obstructive pulmonary disease (COPD) has been defined as a disease state characterized by airflow limitation that is not fully reversible.¹ The GOLD guidelines define COPD as "A preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in the individual patient. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases."²

COPD is the fourth leading cause of death and affects >16 million persons in the United States. COPD is also a disease of increasing public health importance around the world. GOLD estimates suggest that COPD will rise from the sixth to the third most common cause of death worldwide by 2020.¹

In India, COPD is 2nd most common lung disorder after pulmonary tuberculosis.³ The disease is frequently encountered in the middle aged patients and is rare below age of 35. It affects male more than female. It is equally prevalent in rural and urban areas.³

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The presence of pulmonary hypertension (PH) and cor pulmonale increases mortality and predicts hospital readmissions for exacerbations in patients with chronic obstructive pulmonary disease.^{4,5,6,7} Furthermore, the need to identify PH in patients with COPD has taken on new significance due to two developments.

First, the introduction of effective therapies for pulmonary arterial hypertension has renewed interest in treating other forms of PH, such as that associated with COPD,^{8,9} Secondly, the introduction of lung volume reduction surgery (LVRS) for advanced emphysema increases the need for a practical test to diagnose.

PH, which is contraindication to LVRS.¹⁰ It is a known fact that PH is always present in severe COPD, however it would be interesting to know the status of pulmonary artery pressure and right ventricular function in mild to moderate COPD, so that if so found, early intervention may be initiated which should predict a favorable outcome in patients of COPD. With the above facts in consideration this study was conducted.

AIM: To study pulmonary artery pressure and right ventricular in patients with mild – moderate COPD by 2D ECHO Doppler.

MATERIAL AND METHODS: This study was carried out in Acharya Vinova Bhave Hospital (AVBRH) (1200 bedded), a tertiary care hospital attached to JN medical college, Wardha in central India.

Type of Study: Observational Cross Sectional Study.

Duration of Study: September 2012 to September 2014

Subject Selection: 100 subjects with history consistent with COPD, from OPD/IPD in our hospital were interviewed. Detailed history and physical examination done and all selected patients will be subjected to Pulmonary function test (PFT). Based on PFT analysis, subjects were categorized as per GOLD Criteria.^{1,2}

Pulmonary function testing was done using RMS Helios 401 spirometer. Patient is requested to sit comfortably. The procedure is explained to patient and also demonstrated. Three satisfactory efforts were recorded and best effort was considered and documented. Bronchodilatation was done using 200 µg of inhaled salbutamol using a metered dose inhaler and test was repeated after 15 min. Final print out of report is obtained.

METHODS:

1. 2D ECHO examination was done using Philips HD 11 XE machine, with 2-4 MHZ multifrequency linear probe.
2. Examination was carried out with the patient in supine and left lateral decubitus position. Various views including subcostal view obtained (4chamber, 2chamber, PLAX, subcostal).
3. TR jet and PR jet visualized. Pressure gradient of these jets measured by Doppler. PASP and PADP thus calculated. (Pulmonary artery systolic pressure) (Pulmonary artery diastolic pressure).
4. Gradient of TR jet is measured by placing continuous Doppler cursor, parallel to TR jet. The

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value in mm of Hg thus obtained is RVSP (Right Ventricular Systolic Pressure). To this is added RA pressure, so as to measure PASP.¹¹

$$\text{PASP} = \text{RVSP} + \text{RAP.}$$

RA pressure calculation is done as IVC size and collapsibility, as below.

1. IVC diameter < 2.1cm that collapses > 50% with a sniff suggest normal RA pressure of 3 mm of Hg. (0-5 mm of Hg).
2. IVC diameter > 2.1cm that collapses < 50% with a sniff suggest high RA pressure of 15mm of Hg(10-20 mm of Hg).
3. IVC diameter and collapse do not fit this paradigm; an intermediate value of 8 mm of Hg (5-10 mm of Hg) may be used.^{12,13,14}

The method for RV function assessment, selected for present study is tricuspid valve annular motion during systole. Tricuspid annular velocity is surrogate for global RV systolic function.^{1,15,16,17,18}

Apical⁴ chamber view is visualized and M-mode/TDI cursor is placed parallel/aligned to the lateral tricuspid annulus and image thus obtained shows movement of tricuspid annulus. The excursion of annulus is measured in distance in mm.

Inclusion criteria: All patients of

1. Mild (FEV1/FVC <0.7 and FEV1 80% predicted).
2. Moderate (FEV1/FVC <0.7 and 50% FEV1<80% predicted) COPD, who give consent to study.

Exclusion criteria:

1. Patients with acute exacerbation of COPD.
2. K/c/o systemic hypertension.
3. Cardiac diseases – IHD, Valvular disease, Cardiomyopathy.
4. Any respiratory condition like asthma apart from COPD.
5. Poor echocardiography / acoustic window.
6. Any other systemic disease that secondarily leads to respiratory involvement. E.g. Cirrhosis, sepsis.

Observation will be discussed. Statistical analysis will be done using Pierson's correlation coefficient.

Results and observations are discussed ahead.

H/O Smoking	No. of patients	Percentage (%)
Smoker	61	61.0
Non-Smoker	39	39.0
Total	100	100

Table1: Distribution of patients according to H/O smoking

Out of 100 patients included in the study, 61 were smokers while 39 were non-smokers.

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PFT	No. of patients	Percentage (%)
Mild	20	20.00
Moderate	80	80.00
Total	100	100

Table 2: Distribution of patients according to pulmonary function test (PFT)

Out of 100 patients who underwent PFT for the study, 20 had mild COPD while 80 had moderate COPD

PASP	PFT(COPD)	
	Mild	Moderate
Normal(≤ 25 mmHg)	0	0
Mild(26-50 mmHg)	20	48
Moderate(51-80 mmHg)	0	32
Severe(> 80 mmHg)	0	0
Total	20	80
28-Value	11.76	
p-value	0.001, S, $p < 0.05$	

Table 3: Correlation of PFT with PASP

The above table describes the correlation of COPD staging by PFT with pulmonary artery systolic pressure by TR jet. The chi square value being 11.76 and p value being 0.001 which was significant for $p < 0.05$.^{17,19,20,21,22,23}

PR-JET	PFT(COPD)	
	Mild	Moderate
Normal(≤ 10 mmHg)	0	0
Abnormal (> 10 mmHg)	6	55
No PR-JET	14	25
Total	20	80
2 χ -value	10.09	
p-value	0.001, S, $p < 0.05$	

Table 4: Correlation of PFT with PADP17

Correlation of PFT with pulmonary artery diastolic pressure by PR jet was done which was statistically significant for $p < 0.05$.

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TAPSE	PFT(COPD)	
	Mild	Moderate
Normal(> 16 mmHg)	9	11
Abnormal (≤ 16 mmHg)	11	69
Total	20	80
28-Value	9.76	
p-value	0.002, S, p<0.05	

Table 5: Correlation of PFT with TAPSE

TAPSE was compared with COPD staging by PFT which was statistically significant for $p < 0.05$, chi square value being 9.76.^{17,18,24,25,26}

Parameters	Unstandardized Coefficients		Odd's ratio	T	n-value
	B	Std. Error			
PFT(COPD)	1.319	0.277			
PASP	0.217	0.083	0.253	2.617	0.010 S, p<0.05
PADP	-0.129	0.084	0.158	1.541	0.127 NS, p>0.05
TAPSE	0.208	0.098	0.208	2.117	0.037 S, p<0.05

Table 6: Multiple Regression Analysis

The above table of multiple regression analysis shows that when COPD staging by PFT was compared for its impact on PASP, PADP and TAPSE as independent variables, PASP and TAPSE were found to be statistically significant. ($p < 0.05$) Thereby indicating that in present study PASP and TAPSE were the most sensitive indicators of RV function and pulmonary hypertension.

LINE OF REGRESSION: $PFT = 1.319 + 0.217 * TR\text{-}JET - 0.129 * PR\text{-}JET + 0.208 * TAPSE$.

DISCUSSION: The Present study entitled "Study of Right Ventricular Function and Pulmonary Artery Pressure in Mild and Moderate COPD by 2D Echo and Doppler Evaluation" was carried out in the Department of Medicine, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha during the period September 2012 to September 2014.

Total 100 cases were included in this study from IPD as well as OPD of AVBRH JNMC Wardha. 100 patients undergoing study were subjected to spirometry and pulmonary function test. Mild and moderate COPD patients were selected and 2D ECHO was performed and PASP by TR jet, PADP by PR jet and TAPSE was calculated.

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AGE: The mean age of present study population was 53.45 ± 15.73 years which was Comparable to Michel Miguères et al.²⁷ and Prasanta R Mohapatra et al.²⁸ Studies.

SEX: In the present study, males account for 74%, with a male: female ratio of 2.84:1 which was comparable to other study groups mentioned below. Higher Prevalence in males may be attributed to smoking and exposure to various dusts and allergens at workplace.

In the study of Prasanta R Mohapatra et al.,²⁸ male were 93.33% while female were 6.77%.

In study of Michel Miguères et al.,²⁸ Male were 96% while female were 4%.

SMOKING STATUS: 61 patients in the study group were smokers of which 53 patients had moderate COPD. This proves importance of smoking as a risk factor. It was comparable to Prasanta R Mohapatra et al.,²⁷ study in which 88% were smoker while in study of Higham et al.,²⁹ 49% were smoker.

S.K.Jindal et al.,³⁰ and David Stav et al.,³¹ in 2006 and 2007 respectively studied prevalence of COPD in smokers and established positive correlation.

SEVERITY OF COPD: In our study out of 100 patients 20% had mild COPD and 80% had moderate COPD. Severe COPD patients were excluded from the studies as presence of pulmonary hypertension is a known fact in severe cases. In study of Higham et al.,²⁹ 25% were mild while 43% were moderate. In study of Gupta et al.,³² 58.8% were mild while 23.5% were moderate.

PASP: Study of PASP by TR jet with the use of 2D ECHO showed mild PASP in 68 patients out of 100 while moderate PASP in remaining 32 patients, while there were no patients with severe PASP. Mean value of PASP was 42.63 while standard deviation being 9.74. Correlation of PASP by TR jet with COPD staging was done in our study. It came out to be statistically significant, chi square value being 11.76 and p value being 0.001 which is significant for $p < 0.05$. While comparing PASP with COPD staging by PFT, it was found that 68 patients had mild PASP and 32 had moderate PASP. Among 68 mild PASP patients, 20 had mild COPD while 48 had moderate COPD. Remaining 32 patients had moderate COPD and all had moderate PASP. Further comparison by age, revealed that moderate COPD patients with mild PASP were relatively younger at mean age of 52.25 yrs whereas moderate COPD patients with moderate PASP were of mean age of 59.75yrs.

N K Gupta et al.,³² in their study of echocardiographic evaluation of COPD in 40 patients, tricuspid regurgitation (TR) was observed in 27/40 cases (67.5%). Pulmonary hypertension (PH) was observed in 17/27 (63%) cases in which prevalence of mild, moderate, and severe PH were 10/17 (58.82%), 4/17 (23.53%), and 3/17 (17.65%), respectively. The frequencies of PH gradually increases with increase in the severity of COPD.

PutnikM et al.,³³ studied sixty patients of COPD by performing ECG and 2D ECHO. They found that all patient had increased RV dimension and TR jet in a range of pulmonary hypertension.

Hsiao S H et al.,³⁴ R.Tramarin,³⁵ Kassim M. Sultan et al.,³⁶ also did similar studies showing severity of pulmonary hypertension in COPD.

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PADP: Study of PADP by PR jet with use of 2D ECHO showed that PR jet was abnormal in 61 patients while in remaining 39 patients PR jet was not found. Mean value being 13.25 while standard deviation being 2.45. Correlation of PADP by PR jet with COPD staging was done in our study. It came out to be statistically significant, chi square value being 10.09 and p value being 0.001 which was significant for $p < 0.05$.

Comparing PADP with COPD staging revealed that 61 patients had PR jet and 39 had no PR jet. Out of 61 patients, 55 were moderate COPD while 6 were mild COPD with abnormal PR jet.

Thus higher COPD severity correlates well with abnormal PADP (Mean PADP = 13.25 mm of Hg).

R. Tramarin³⁵ studied 100 COPD patients by 2D ECHO and showed that Doppler echocardiographic evaluation of pulmonary artery pressure with the help of TR jet velocity and PR velocity were found to be useful screening tools.

TAPSE: Study of TAPSE by 2D ECHO showed that 80 patients had abnormal TAPSE value while 20 patients had normal value. Mean being 14.87 and standard deviation of 1.68.

Correlation of TAPSE with COPD staging was done in our study. It came out to be statistically significant, chi square value being 9.76 and p value being 0.002 which was statistically significant for $p < 0.05$.

Moderate COPD patients had lower TAPSE values as compared to mild COPD patients. Hence, higher COPD severity correlates well with proportionately lower TAPSE.

N. F. Chaisson et al.,³⁷ A. Chelliah et al.,³⁸ Forfia PR et al.,³⁹ Charlotte Uggerhøj Andersen et al.,⁴⁰ conducted about efficacy of TAPSE in predicting RV function in COPD patients.

Tamborini G et al.,⁴¹ studied patients of COPD by 2 D ECHO to assess RV systolic function by TAPSE and other parameters and found useful correlation.

Saxena N et al.,⁴² showed tricuspid annular systolic velocity (TAPSE) is a useful measurement in determining right ventricular systolic function regardless of pulmonary artery pressures in a study of 52 patients.

MULTIVARIATE REGRESSION ANALYSIS: As a further probe, sensitivity of independent variables such as PASP, PADP and TAPSE were assessed for their impact on COPD patients by PFT analysis. The study shows good correlation and PASP and TAPSE were found to be most sensitive indicators.

SUMMARY: The Present study entitled 'Study of Right Ventricular Function and Pulmonary Artery Pressure in Mild and Moderate COPD by 2D Echo and Doppler Evaluation' was carried out in the Department of Medicine Jawaharlal Nehru Medical College, Sawangi, Wardha during the period September 2012 to September 2014.

Total of 100 patients including IPD and OPD were selected on the basis of PFT/spirometry for COPD staging and later for the 2D ECHO and Doppler evaluation for measuring parameters like PASP, PADP and TAPSE.

The aim was to study right ventricular function and pulmonary artery pressure in those selected as mild and moderate COPD patients. Objective was to find the presence of pulmonary hypertension in these mild and moderate patients at an early stage so that early diagnosis can

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help in early intervention and proper management of patient thus favoring good prognosis.

The study revealed striking correlation of COPD with pulmonary hypertension, all 100 patients studied were found to have mild/moderate pulmonary hypertension (PASP), whereas 80 patients were found to have altered TAPSE indicating abnormal RV systolic function.

Probing further, it was found that severity of COPD correlated with proportionately severe pulmonary hypertension (PASP).

Smoking, as is well documented, was found to be an important risk factor in this study. Majority of smokers had proportionately severe COPD. Lastly, ECHO Doppler parameters to assess pulmonary hypertension and RV function, such as PASP and TAPSE were found to be the most sensitive indicators and correlated well with COPD severity in our study.

CONCLUSION:

1. Severity of COPD correlated very well with proportionate changes in RV function and PASP (Pulmonary Hypertension).
2. The present study and its conclusions makes it imminent that ECHO Doppler evaluation of COPD patients should be used as a risk stratification tool for assessing RV function and pulmonary artery pressure and should constitute part of a periodic screening tool for all COPD patients.
3. This study helps to identify individuals at risk of increased morbidity and mortality, warranting close monitoring and aggressive treatment to prevent/delay complication (Pulmonary Hypertension).

Further studies of similar nature across various geographical locations would go a long way in substantiating the conclusions found in the present study.

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