

Clinical Profile of Patients with Chronic Obstructive Pulmonary Disease with Special Reference to Echocardiographic Finding

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Abstract: *Background:* Chronic obstructive pulmonary disease (COPD) is one of the major respiratory diseases causing high morbidity and mortality worldwide. The widespread use of tobacco and other tobacco products have increased its incidence. There are various patterns seen in the radiography and echocardiographic picture in the patients suffering from COPD. This study aims to know the various radiological and echocardiographic characteristics in these patients and compare the effectiveness of electrocardiogram and echocardiography in detecting the various cardiovascular changes in patients with COPD. *Method:* This study was conducted in ESIC PGIMS and Model hospital Basaidarapur in Medicine department. A total of 60 patients were selected who fulfilled our inclusion criteria. *Results:* In our study out of total 60 cases 46 were males and 14 were females. 38 patients were suffering from chronic bronchitis and 22 patients were suffering from emphysema. The majority of patients were farmers, labourers and housewives. In the present study, arrhythmias were found in 3 patients out of total 60. In the present study, P wave abnormalities in the form of P pulmonale was present in 13 (21.7 %) patients out of the total 60 and more common in case of chronic bronchitis (31.6%) than with emphysema (4.5%). Low voltage QRS complexes were seen in 21 cases (35%) of cases and were present in 9 cases of chronic bronchitis (23.7 %) and 12 cases of emphysema (54.5%). Clockwise rotation of heart was found in 11 cases (11.3%) and was higher in cases of emphysema (22.7% vs.15.8%). Echocardiographic abnormalities were found in as many as 56 patients (93.3%) and it was higher among patients with emphysema than with chronic bronchitis (94.5% vs.92.9%). Left ventricular diastolic dysfunction was found in 6 cases (10%) and was more common in chronic bronchitis than with emphysema (10.5% vs.9.1%). In the present study out of the total 60 patients 5 (8.33%) were found to have pericardial effusion. In the present study, 5 cases were found to be having co-existent dilated cardiomyopathy, which was statistically insignificant ($p=0.643$) and 11 patients had diminished LV ejection fraction (<50%) suggesting a systolic LV dysfunction, of which 5 had dilated cardiomyopathy. *Conclusion:* Echocardiographic as well as ECG findings were found in most of the patients suffering from chronic bronchitis and emphysema.

Keywords: COPD, Chronic Bronchitis, Emphysema, ECG changes, Echocardiographic findings

1.Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death in the world, and it affects million of patients worldwide. The risk factors for development of COPD include both active and passive cigarette smoking, occupational exposures, modern life style and increasing air-pollution. The diagnosis of COPD is normally made on the basis of history, clinical examination, radiology and lung function tests. COPD is often associated with several hemodynamic consequences. Pulmonary hypertension is the main complication of COPD. This can lead to right ventricular hypertrophy and eventually right sided congestive heart failure. The monitoring of electro-cardiographic (ECG) changes and echocardiography has enabled the physician to understand the underlying pathology and to detect abnormalities in respiration and cardiac functions due to respiratory diseases at the earliest. COPD includes chronic bronchitis, emphysema and small airway disease (a condition in which small bronchioles are narrowed).

The GOLD expert panel classified COPD into 4 stages, ranging from 1 to 4.

Stage 1 Mild COPD: FEV1/FVC<0.7 and FEV1 >80 %

Stage 2: Moderate COPD: FEV1/FVC <0.7 Characterised by FEV1>50% but <70%

Stage 3: Severe COPD: FEV1/FVC<0.7 and FEV1>30%BUT<50%.

Stage 4: Very Severe: FEV1/FVC<0.7 and FEV1<30%.

2.Materials and Methods

The present study consists of 60 cases of chronic obstructive pulmonary disease who were selected from the wards of the department of medicine, ESIC Hospital, New Delhi, fulfilling diagnostic criteria of COPD. These patients were evaluated in detail as per proforma and laboratory workup including complete blood count, chest x-ray, ECG, Echocardiography and pulmonary function test were carried out.

Inclusion Criteria

- 1)History suggestive of chronic bronchitis and emphysema.
- 2)History suggestive of emphysema or emphysema with cor pulmonale involved.

- 3) Evidence of pulmonary hypertension due to chronic obstructive lung disease.
4) Evidence of right ventricular hypertrophy.

- 1) Evidence of pulmonary hypertension
2) Criteria for radiographic diagnosis of emphysema
3) Evidence of right ventricular enlargement if any

Radiological criteria for selection of cases (Simon G, Principal of Chest X-ray and diagnosis, 4th Ed; London, Butterworth 1978)

Exclusion Criteria

Patients suspected of having congenital heart disease, rheumatic heart disease, or coronary artery disease and active respiratory disease other than chronic obstructive lung disease were excluded from the present study.

The standard postero-anterior view of chest skiagram was taken. The radiological diagnosis of chronic obstructive lung disease (chronic bronchitis and emphysema) and bronchial asthma was suggestive on the most of the following observations.

3.Result

38 patients were suffering from chronic bronchitis and 22 patients were suffering from emphysema.

Chronic Bronchitis	38	63.30%
Emphysema	22	36.70%
Total	60	100%

In our study out of total 60 cases, 46 were males and 14 were females.

Sex	Total		Chronic Bronchitis		Emphysema		P Value
	Frequency	%	Frequency	%	Frequency	%	
F	14	23.33%	12	31.60%	2	9.10%	0.061
M	46	76.67%	26	68.40%	20	90.90%	
Total	60	100%	38	100%	22	100%	

In the present study, out of the 60 cases, only 5 cases were 40 years or less (8.3%), while the rest were above 40 years of age (91.7%). Maximum prevalence was in the 6th decade.

AGE GROUPS	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
<=40	5	8.30%	0	0.00%	5	22.70%	0.002
41-50	6	10%	4	10.50%	2	9.10%	0.858
51-60	27	45%	19	50%	8	36.40%	0.306
61-70	22	36.70%	15	39.5%	7	31.80%	0.553
TOTAL	60	100%	38	100%	22	100.00%	

The majority of patients were farmers, labourers and housewives. In the present study, arrhythmias were found in 3 patients out of total 60.

In the present study, P wave abnormalities in the form of p pulmonale was present in 13 (21.7 %) patients out of the total 60. It was more common in case of chronic bronchitis (31.6%) than with emphysema (4.5%).

P Pulmonale	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
No	47	78.33%	26	68.40%	21	95.50%	0.021
Yes	13	21.67%	12	31.60%	1	4.50%	
Total	60	100.00%	38	100.00%	22	100.00%	

In the present study low voltage QRS complexes were seen in 21 cases (35%) of cases and was more common in emphysema (54.5%) than chronic bronchitis (23.7 %).

Low Voltage	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
No	39	65.00%	29	76.30%	10	45.50%	0.016
Yes	21	35.00%	9	23.70%	12	54.50%	
Total	60	100.00%	38	100.00%	22	100.00%	

In the present study, clockwise rotation of heart was found in 11 cases (11.3%) and was higher in cases of emphysema (22.7% vs.15.8%).

Clock wise Rotation	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
No	49	81.67%	32	84.20%	17	77.30%	0.503
Yes	11	18.33%	6	15.80%	5	22.70%	
Total	60	100.00%	38	100.00%	22	100.00%	

Lead I Sign

In the present study, lead I sign was seen in 4 cases (6.6%), of which 2 cases were having chronic bronchitis (5.3%) and 2 had pulmonary emphysema (9.1%).

S1 S2 S3 Pattern:

In the present study, S1S2S3 pattern was found in 3 cases (5%) of which 2 cases had chronic bronchitis (5.3%) and 1 had pulmonary emphysema (4.5%).

	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
S1S2S3	3	5.00%	2	5.30%	1	4.50%	1
Lead I Sign	4	6.67%	2	5.30%	2	9.10%	0.619

Mean QRS axis

In the present study right axis deviation was seen in 9 cases (23.7%). It is evident from that RAD was higher in emphysema than with chronic bronchitis (31.7% vs.23.7%).

QRS AXIS	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
Indeterminate Axis	2	3.33%	0	0.00%	2	9.10%	0.059
LAD	1	1.67%	0	0.00%	1	4.50%	0.185
Normal	41	68.33%	29	76.30%	12	54.50%	0.081
RAD	16	26.67%	9	23.70%	7	31.70%	0.492
Total	60	100.00%	38	100.00%	22	100.00%	

Right Ventricular Hypertrophy in COPD

In present study RVH (by ECG criteria) was found in 19 cases (31.6%). The incidence was higher in case of chronic bronchitis than with emphysema (34.2% vs.27.3%).

RVH	TOTAL		CHRONIC BRONCHITIS		EMPHYSEMA		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
No	35	58.30%	18	47.40%	17	77.30%	0.024
Yes	25	41.70%	20	52.60%	5	22.70%	
Total	60	100.00%	38	100.00%	22	100.00%	

Echocardiographic Features in COPD

Echocardiographic abnormalities were found in as many as 56 patients (93.3%) and it was higher among patients with emphysema than with chronic bronchitis (94.5% vs.92.9%). A normal echocardiogram was reported in only 4 patients.

Echocardiographic evidence of cor-pulmonale and RV size.

In the present study, echocardiographic features of cor-pulmonale as evident by a dilated right atrium and ventricles or both were found in 33 cases of chronic bronchitis (86.8%) and 14 patients of emphysema (63.6%) which comes to a total of 47 patients (76.7%) which was Statistically significant ($p=0.036$).

Tricuspid Regurgitation in COPD

In the present study, tricuspid regurgitation was found in 6 patients (15.8%) of chronic bronchitis and 9 patients of emphysema (40.9%) with RV dilatation and was statistically significant ($p=0.030$).

LV systolic dysfunction and LVEF in COPD

In the present study out of the total of 60 patients, 11 patients had a diminished LV ejection fraction (<50%) suggesting a systolic LV dysfunction, of which 5 had dilated cardiomyopathy. Apart from these only 1 patient had severely diminished LVEF (2.6%) indicating systolic Impairment of LV function is not a significant Occurrence in COPD ($p=0.443$).

Left Ventricular Hypertrophy in COPD

In the present study, left ventricular hypertrophy (LVH) was found by echocardiography in 4 patients out of the total 60 which was statistically insignificant ($p=0.619$).

In the present study out of the total 60 patients 5 (8.33%) were found to have pericardial effusion. In the present study, 5 cases out of the total of 60 cases were found to be having co-existent dilated cardiomyopathy, which was statistically insignificant ($p=0.643$). In the present study out of the total of 60 patients, 11 patients had diminished LV ejection fraction.

	TOTAL		CHRONIC BRONCHITIS (n=38)		EMPHYSEMA (n=22)		P VALUE
	FREQUENCY	%	FREQUENCY	%	FREQUENCY	%	
Corpulmonale	47	78.33%	33	86.80%	14	63.60%	0.036
LV Diastole dysfunction	6	10.00%	4	10.50%	2	9.10%	1
Pericardial Effusion	5	8.33%	2	5.30%	3	13.60%	0.346
LVH	4	6.67%	2	5.30%	2	9.10%	0.619
DCM	5	8.33%	4	10.50%	1	4.50%	0.643
Normal study	4	6.77%	3	7.90%	1	4.50%	1

4. Discussion

Gender Distribution

In the present study 38 cases of chronic bronchitis were studied out of which 26 patients were male (68.4%) and 12 were female (31.6 %). The disease was more common in males than in females. Present series Consists of 22 cases of emphysema out of which 20 were males (90.9%) and 2 were females (9.1%). This is in accordance to the study conducted by Jindal et al¹.

Age Distribution

In the present study, out of the 60 cases, only 5 cases were 40 years or less (8.3%), while the rest were above 40 years of age (91.7%). Maximum prevalence was in the 6th decade.

This was in accordance to the reports by Viejo et al (2006)¹ and Vishwanathan et al². Viejo et al (2006)³, in his study had reported the mean age of COPD to be 67 years (+/-10.7 years).

Electrocardiographic Anomalies in COPD

Rate and Rhythm

In the present study, arrhythmias were found in 3 patients out of total 60. There was 1 case of atrial fibrillation (1.6%) who had predominant chronic bronchitis (2.6%) and 2 cases of occasional VPCS (3.3%) of which one had a predominant chronic bronchitis pattern (2.6 %) and the other emphysema (4.5%).

Friedberg⁴ (1958) attributed the development of arrhythmias to pH fluctuations. Respiratory acidosis and pH changes due to CO₂ retention may play a significant role in the production of arrhythmias.

P Wave

In the present study, P wave abnormalities in the form of p-pulmonale was present in 13 patients out of the total 60 (21.7 %). It was more common in case of chronic bronchitis (31.6%) than with emphysema (4.5%).

This was consistent with the study of Kemper et al (1970)⁵ who found p-pulmonale in 10 out of the total 47 cases he studied (21%). While Murphy et al (1974)⁶ found p-pulmonale in 35% of patients with COPD. Zuckerman et al (1948)⁷ observed that increased amplitude of P wave may be due to verticalisation of the heart.

QRS Complex

In the present study (Table 11 (f)), low voltage QRS complexes were seen in 21 cases (35%) of cases. Low voltage complexes were present in cases of chronic bronchitis (23.7 %) and 12 cases of emphysema (54.5%).

This was in accordance with the observations of Kemper et al (1970)⁵. Kemper et al (1970) observed low voltage complex in 51% cases (24 cases) of COPD.

Vishwanathan et al² and Fowler et al⁸ also reported higher incidence of low voltage QRS Complexes in emphysema.

Lead I Sign

In the present study, lead I sign was seen in 4 cases (6.6%), of which 2 cases were having chronic bronchitis (5.3%) and 2 had pulmonary emphysema (9.1%).

Fowler et al (1965)⁸ reported 15 patients with severe pulmonary emphysema with cor-pulmonale. They found that 5 patients (33%) showed the lead I sign. In 13 control patients with pulmonary thrombo-embolism or idiopathic pulmonary hypertension, only one patient showed the "lead I sign". This patient had normal lung function tests.

S1 S2 S3 Pattern:

In the present study, S1S2S3 pattern was found in 3 cases (5%) of which 2 cases had chronic bronchitis (5.3%) and 1 had pulmonary emphysema (4.5%).

This observation was similar to the observations by Kemper et al (1970)⁵ and Perlman et al (1971)⁹.

Mean QRS axis

In the present study right axis deviation was seen in 9 cases (23.7%) and RAD was higher in emphysema than with chronic bronchitis (31.7% vs.23.7%).

This was supported by the findings of Vishwanathan et al (1965)² who in his study, observed ORS axis of +90degree or more in 30.4% cases.

Rotation of the heart

In the present study, clockwise rotation of heart was found in 11 cases (11.3%) and was higher in cases of emphysema (22.7% vs.15.8%). This was supported by Vishwanathan et al (1960)² and Millard (1967)¹⁰ who also observed clockwise rotation to be higher in case of emphysema than with chronic bronchitis.

Right Ventricular Hypertrophy in COPD

In present study RVH (by ECG criteria) was found in 19 cases (31.6%). The incidence was higher in case of chronic bronchitis than with emphysema (34.2% vs.27.3%).

This was in accordance with Seizer (1966)¹¹, Millard et al (1967)¹⁰ and Katsutoshi et al (2007)¹².

Echocardiographic Features in COPD

Echocardiographic abnormalities were found in as many as 56 patients (93.3%) and it was higher among patients with emphysema than with chronic bronchitis (94.5% vs.92.9%). A normal echocardiogram was reported in only 4 patients.

Echocardiographic evidence of cor-pulmonale and RV size

In the present study, echocardiographic features of cor-pulmonale as evident by a dilated right atrium and ventricles or both were found in 33 cases of chronic bronchitis (86.8%) and 14 patients of emphysema (63.6%) which comes to a total of 47 patients (76.7%) which was Statistically significant ($p=0.036$). This is in accordance with the results of Rasche et al (2007)¹³ who have reported the prevalence of echocardiographically defined cor-pulmonale in COPD to be 80%. While according to Fishman (1976)¹⁴ the actual prevalence of cor pulmonale in COPD patient's is more than 40% based on autopsy studies.

In the present study, right ventricular (RV) size was found to be dilated in 32 cases of chronic bronchitis (81.6%) and in 15 patients of emphysema (72.7%).

Tricuspid Regurgitation in COPD

In the present study, tricuspid regurgitation was found in 6 patients (15.8%) of chronic bronchitis and 9 patients of emphysema (40.9%) with RV dilatation and was statistically significant ($p=0.030$). Tricuspid regurgitation was found only in one case of chronic bronchitis without

any associated RV dilation indicating that presence of tricuspid regurgitation in COPD is a secondary effect because of the dilatation of RV as a result of cor-pulmonale. Overall tricuspid regurgitation was found in 15 patients (26.7%) which is in accordance with the findings of Tamarin et al (1991)¹⁵ who found that 30% of COPD patients had Tricuspid regurgitation echocardiographically.

Other Echocardiographic findings in COPD

1) LV diastolic dysfunction

In the present study left ventricular diastolic dysfunction was found in 6 cases (10%). LV diastolic dysfunction was higher in chronic bronchitis than with emphysema (10.5% vs.9.1%). However, the presence of LV diastolic dysfunction in COPD was not statistically significant ($p=1.0$)

This finding was supported by Baum et al (1976)¹⁶ and Suchon et al (2007)¹⁷.

2) LV systolic dysfunction and LVEF in COPD

In the present study out of the total of 60 patients, 11 patients had a diminished LV ejection fraction (<50%) suggesting a systolic LV dysfunction, of which 5 had dilated cardiomyopathy. Apart from these only 1 patient had severely diminished LVEF (2.6%) indicating systolic Impairment of LV function is not a significant occurrence in COPD ($p=0.443$).

This was supported by the findings of Niederman et al (1986)¹⁸ Buda et al (1979)¹⁹ and Steele (1975)²⁰, all of whom have reported that systolic function of LV and its LVEF are not significantly affected in case of COPD.

3) Dilated Cardiomyopathy in COPD

In the present study, 5 cases out of the total of 60 cases were found to be having co-existent dilated cardiomyopathy, which was statistically insignificant ($p=0.643$). A similar observation was found by Steven et al (1995)²¹. Even in this present study, all the patients having DCMP did have prior history of treatment with beta-agonists.

4) Left Ventricular Hypertrophy in COPD

In the present study, left ventricular hypertrophy (LVH) was found by echocardiography in 4 patients out of the total 60 which was statistically insignificant ($p=0.619$). This was in accordance with the findings of Fluck et al (1966)²² and Murphy et al (1974)²³.

5) Pericardial effusion in COPD

In the present study out of the total 60 patients 5 (8.33%) were found to have pericardial effusion which was statistically insignificant ($p>0.05$). Pericardial effusion was higher in emphysema than with chronic bronchitis (13.6% vs.5.3%) No reports were found in this regard.

5. Summary and Conclusion

- [1] In the present series, the incidence of COPD was highest in the 51-60 years age group (45%), while it was least below 41 years (1.67%)
- [2] In the present series, 46 patients (76.66%) were males (23.34%) were females. The percentage of males was higher in case of emphysema than with chronic bronchitis (90.9% vs.68.4%).
- [3] In the present series, majority of patients were either labourers or farmers (both 23.5%), while the least was private sector or businessmen (both 11.7%). The p value is significant in labourers.
- [4] In the present series, 40 patients presented within the first five years (75%), while it was least above 15 and 20 years (6.7% and 5% respectively).
- [5] The main ECG changes were sinus tachycardia (25%), presence of P-pulmonale (21.7%), low voltage QRS complexes in limb leads (35.0%), right axis deviation of QRS complex (26.6%), clockwise rotation of the heart (18.3%), right ventricular hypertrophy (41.7%), the S1S2S3 sign (5.0%) and the lead I sign (6.7%).
- [6] In the present series, echocardiographic abnormalities were found in as many as 56 patients (93.3%) and it was higher among patients with emphysema than with chronic bronchitis (94.5% vs.92.9%).
- [7] In the present series, echocardiographic evidence of cor-pulmonale was found in 47 patients (78.3%) and dilated right ventricle were found in 47 patients (78.3%) of COPD and cor-pulmonale was higher in patients with chronic bronchitis (86.8. %) than with emphysema (63.6%).
- [8] In the present series there was a definite co-relation between the duration of illness and the incidence and severity of cor-pulmonale.
- [9] In the present series, tricuspid regurgitation was found in (11.6%) of chronic bronchitis and 9 patients of emphysema (26.67%). Only 1 patient had tricuspid regurgitation without associated dilated right ventricle indicating that presence of tricuspid regurgitation in COPD as a secondary effect because of the dilatation of RV as a result of cor-pulmonale.
- [10] In the present series, 11 patients had diminished LV ejection fraction (<50%) suggesting a systolic LV dysfunction, of which 5 had dilated cardiomyopathy. Apart from these only 2 patients had a diminished LVEF (3.5%) indicating systolic impairment of LV function is not a significant occurrence in COPD.
- [11] In the present series, 5 cases were found to be having CO-existent dilated cardiomyopathy, all of whom had prior history of treatment with beta-agonists. However this finding was not statistically significant.
- [12] In the present series the other main echocardiographic findings were LV diastolic dysfunction (10.0%), pericardial effusion (8.3%) and left ventricular hypertrophy (6.66%). None of these findings were however statistically significant.

6. Conclusion

Chronic obstructive pulmonary disease occurs primarily in the 6th and 7th decade with a definite male preponderance.

Incidence of COPD was highest among labourers and farmers and among the rural population.

It is exacerbated by dust exposure and exercise and is more common during the winter seasons. Breathlessness and cough with expectoration were the important clinical symptoms.

X-ray chest do not give much help in the diagnosis. The patients showed ECG abnormalities like the classical p-pulmonale, low voltage QRS complexes, clockwise rotation of the heart, signs of right ventricular hypertrophy, the lead I sign and the S1 S2 S3 `sign.

Echocardiographic abnormalities were found in 56 patients (93.3%), with features of cor-pulmonale in as many as 47 patients (78.3%), clearly indicating the superiority of Echocardiography over ECG in patients with COPD. This becomes very important because development of cor-pulmonale is regarded as a poor prognostic indicator in the course of COPD and hence its detection at the earliest is important. Hence Echocardiography as a screening test may be advisable in all patients with COPD to detect cor-pulmonale and other abnormalities at the earliest even before they become clinically manifest.

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Conflicts of Interest

There are no conflicts of interest.

References

- [1] Jindal S K, Indian Journal of Medical Research, Dec (2006)
- [2] Vishwanathan R and Leela Shourie. Ind. J. c. doct1960; 11: 4
- [3] Viejo-Bañuelos J L, Pueyo-Bastida A, Fuevo-Rodriguez A. Respir Med DEC 2006; 100 (12): pp 2137-43
- [4] Friedberg C. K. Disease of the Heart 2nd Ed.1958. Saunders Philadelphia p.386.
- [5] Kemper D. Chovtechauan Fowler, Noble O. Am. H. J., 1970; 80: 445-452
- [6] Murphy L. Marvin and Fred Hutcheson. Chest, July 1974; Vol.65: 622-627
- [7] Zuckerman R, Coveracosia E, Fishleder BL. Am. H. J.1948; 35: 421-437
- [8] Fowler N O, Deniels C, Scott R C. Am. J. Cardiol, 1965; 16: 500-505
- [9] Perlman LV, Higgins MW, Chiang BN, Ostrander JD and Keller JB. Am. Rev. of Resp. Disease, 1971; 104: 443-447.
- [10] Millard FJ. Brit. H. J.29; 43-50, 1967.
- [11] Seizer A. Limitations of the electrocardiographic diagnosis of ventricular hypertrophy, J. Amer Med. Assoc., 1966; 195: 1051
- [12] Katsutoshi M, N Kunhiro, N Akio. Studies of Electrocardiographic Diagnosis of Right Ventricular

- Hypertrophy and of the Incidence of Arrhythmias and Left Ventricular Abnormalities in Patients with Chronic Obstructive Pulmonary Disease with Moderate to Severe Pulmonary Hypertension. *Shimane journal of medical science*, 2007; Vol.4, No 2 (19801200): 109-120.
- [13] Rasche K, Orth M, Kutscha A, Duchna H W. Pulmonary diseases and heart function, *Internist (Berl)*, March 2006; 48 (3): pp 276-82
- [14] Fishman A, Chronic cor pulmonale, *Amer Rev Respir Dis* 1976; 114: 775-794
- [15] Tramarin R, Torbicki A, Marchandise B, Laaban J P, Mörpurgo M. Doppler echocardiographic evaluation of pulmonary artery pressure in chronic obstructive pulmonary disease, A European multicentric study. *Eur Heart J*, 1991; 12: pp 103-111
- [16] Baum G L, Schwartz A, Llamas R, Castillo C. Left ventricular function in chronic obstructive lung disease, *N Engl J Med* 1971; 285: 361–365
- [17] Suchoń E, Tracz W, Podolec P, Pieculewicz M, Plazak W, Prokop A, Nalepa P. *Pol Arch Med Wewn*, march 2007; 117 (3): pp 26-30
- [18] Niederman MS, Matthay R A. Cardiovascular function in secondary pulmonary hypertension, *Heart and Lung*, 1986; 15: 341-351
- [19] Buda AJ, Pinsky MR, Ingels, NB (Jr.), et al. Effect of intrathoracic pressure on left ventricular performance, *N Engl J. Of Medicine*, 1979: 301; pp 453-459.
- [20] Steele P, Ellis J H, Van Dyke D, et. al. Left ventricular ejection fraction in severe chronic obstructive airways disease, *Am., J. Med.*, 1975; 5
- [21] Steven Kadiev, Jeremy A. Falk, Gerard J. Criner, Steven M. Scharf, Omar A. Minai, and Philip Diaz *Proc Am Thorac Soc.* 2008 May 1; 5 (4): 543–548.
- [22] Cardiac Disease in Chronic Obstructive Pulmonary Disease doi: 10.1513/pats.200708-142ET PMID: 18453369
- [23] Fluck D C, Chandrasekar RG, Gardner F V. Left ventricular hypertrophy in chronic bronchitis, *Br. Heart J.* 1966; 921-927
- [24] Murphy L. Marvin and Fred Hutcheson. *Chest*, July 1974; Vol.65: 622-627