



Medicine

STUDY OF CLINICAL PROFILE AND ELECTROCARDIOGRAPHIC CHANGES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT **AIMS:** To analyse the ECG changes in COPD patients and to correlate them with the severity of the disease.
MATERIAL AND METHODS: COPD patients were clinically examined and underwent chest radiograph, ECG, 2D Echo and spirometry
RESULTS: 82% were males and 18% were females. The mean duration of symptoms was 9.88 ± 6.123 years. The mean FEV1 was 42.14 ± 11.63 percentage of predicted. The most common at presentation was tachypnoea (88%) followed by loud P₂ (46%). 36% of patients had features suggestive of right heart failure. 24% of the patients had cyanosis and 10% of the patients had clubbing. The most common ECG abnormality is right axis deviation of P wave (64%) followed by right axis deviation of QRS complex (60%).
CONCLUSIONS: ECG is better than clinical methods in detecting right ventricular dysfunction in COPD.

KEYWORDS : Chronic Obstructive Pulmonary Disease ECG

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important cause of morbidity, mortality and health-care costs worldwide. It is a global health issue, with cigarette smoking being an important risk factor, other factors such as occupational hazards, exposure to indoor and outdoor air pollution, and infections are also important.

The major morbidity of COPD is due to its impact on the cardiac performance caused by pulmonary arterial hypertension. Lung function tests in particular FEV₁, remains the reference marker for the diagnosis, assessment of severity and prognosis of COPD. ECG is a simple bedside investigation. Hence it would be of great importance, if a high degree of correlation between ECG changes and spirometric studies can be established, which indicate the severity of COPD. This study attempts to correlate the ECG changes with the severity of the disease as assessed by lung function tests.

AIMS OF THE STUDY

- To analyse the clinical signs and symptoms of COPD patients.
- To analyse the ECG changes in COPD patients and to correlate them with the severity of the disease.

METHODOLOGY

Patient admitted in Osmania General Hospital with the diagnosis of COPD whom met inclusion criteria were analysed clinically and underwent investigations like ECG, chest x ray and spirometry. Data was analysed using mean, standard deviation and Chi square test.

RESULTS

In the present study 50 patients with COPD who met the inclusion and exclusion criteria were randomly selected and the results of this study are as follows. In this study 82 % (41) were males and 18 % (9) were females.

The mean age of presentation in this study group is 66.86 ± 7.29 years and range is 52 to 87 years. In this study maximum number of COPD patients are clustered in the age group of 60 to 79 years that is in the seventh and eighth decade (78%). Duration of the Disease: The mean duration of symptoms was 9.88 ± 6.123 years, ranged between 2 and 25 years. Severity of the disease: The mean FEV₁ was 42.14 ± 11.63

percentage of predicted, ranged between 25 and 66 percent of predicted. Duration of tobacco use: The mean duration of tobacco use was 56.9 pack years with range from 24 to 110 pack years. Majority of the patients (64%) had history of tobacco exposure for more than 40 pack years. Correlation of tobacco exposure with disease severity: All patients in this study had history of more than 20 pack years of tobacco exposure. Majority of the patients with severe disease (i.e. 18/29 patients) and very severe disease (i.e. 4/7 patients) had history of more than 40 pack years of tobacco exposure. Symptoms at presentation: All patients in this study had history of cough with sputum production and breathlessness at presentation. 38% of the patients presented with swelling of the legs and 24% of the patients presented with symptoms suggestive of carbon dioxide narcosis like headache, drowsiness, lethargy. Physical signs at presentation: The most common at presentation was tachypnoea (88%) followed by loud P₂ (46%). 36% of patients had features suggestive of right heart failure (elevated JVP, pedal oedema, tender hepatomegaly). 24% of the patients had cyanosis and 10% of the patients had clubbing.

Table 1: Frequency of occurrence of ECG changes

| ECG abnormality | Number of cases | Percentage (%) |
|------------------------------------------------------------|-----------------|----------------|
| RAD of QRS complex | 30 | 60 |
| P pulmonale | 21 | 42 |
| RAD of P wave | 32 | 64 |
| R wave amplitude in V ₁ or V ₆ <5 mm | 14 | 28 |
| R/S ratio in V ₁ or V ₆ <1 | 12 | 24 |
| RBBB | 21 | 42 |
| R wave amplitude in V ₁ >7mm | 4 | 8 |
| R/S ratio in V ₁ >1 | 16 | 32 |
| Others | 5 | 10 |

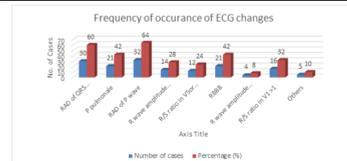


Table 2: Correlation of ECG findings with severity of the disease

| ECG Findings | Moderate N=14 | | Severe N=29 | | Very severe N=7 | | X ² | p | Significance |
|-----------------------------------------------------------|---------------|------|-------------|------|-----------------|------|----------------|-------|--------------|
| | No | % | No | % | No | % | | | |
| RAD of P wave axis | 8 | 57 | 22 | 75 | 2 | 28 | 6.79 | 0.045 | S |
| R wave amplitude in V ₁ or V ₆ <5mm | 0 | 0 | 12 | 41.3 | 2 | 28 | 11.58 | 0.003 | HS |
| R/S ratio in V ₁ or V ₆ <1 | 0 | 0 | 10 | 34.5 | 2 | 28 | 9.369 | 0.009 | HS |
| RBBB | 6 | 42.8 | 14 | 48.2 | 1 | 14 | 2.998 | 0.223 | NS |
| R wave amplitude in V ₁ >7mm | 1 | 7 | 3 | 10.3 | 0 | 0 | 1.382 | 0.501 | NS |
| R/S ratio in V ₁ >1 | 5 | 35.7 | 8 | 27.5 | 3 | 42.8 | 0.715 | 0.699 | NS |

S= significant, HS= highly significant, NS= Not significant.

Table 3: Correlation of ECG findings with duration of disease

| ECG findings | 1-9 yrs. N=26 | | 10-19yrs N=19 | | >20yrs N= 5 | | X ² | p | S |
|-----------------------------------------------------------|---------------|------|---------------|------|-------------|----|----------------|-------|----|
| | No. | % | No. | % | No. | % | | | |
| RAD of P wave axis | 16 | 61.5 | 13 | 68.4 | 3 | 60 | 0.266 | 0.875 | NS |
| R wave amplitude in V ₅ or V ₆ <5mm | 5 | 19.2 | 5 | 26.3 | 4 | 80 | 6.934 | 0.031 | S |
| R/S ratio in V ₅ or V ₆ <1 | 3 | 11.5 | 6 | 31.5 | 3 | 60 | 0.082 | 0.047 | S |
| RBBB | 11 | 42.3 | 8 | 42.1 | 2 | 40 | 0.009 | 0.995 | NS |
| R amplitude in V ₁ >7mm | 1 | 3.8 | 1 | 5.2 | 2 | 40 | 4.834 | 0.089 | NS |
| R/S ratio in V ₁ >1 | 8 | 30.7 | 6 | 31.5 | 2 | 40 | 0.161 | 0.922 | NS |
| RAD of QRS | 4 | 15.3 | 10 | 38.4 | 3 | 60 | 8.762 | 0.015 | S |

In the present study R wave amplitude in V₅ or V₆ <5mm and R/S ratio in V₅ or V₆ <1 were found to significantly correlate with the duration of the disease. But other ECG parameters like right axis deviation of P wave, right bundle branch block, R wave amplitude in V₁ >7 mm, R/S ratio in V₁ >1 were not found to correlate with duration of the disease.

DISCUSSION

1. Sex distribution

The higher incidence of COPD in males can be attributed to higher incidence of smoking amongst men. In this study none of the women were smokers, but all of them had history of cooking with dried wood fuel and other biomass exposure.

Table 4: Comparison of sex distribution

| Author and Year | Percentage of Males |
|--------------------------------------|---------------------|
| V. K. Singh et al 1989 ³⁸ | 94.6 |
| Chappell A. G. 1966 ²⁰ | 81.5 |
| Present study | 82 |

2. Age Distribution

The highest number of COPD patients (39/50) in this study was in the age group of 60 to 79 years with mean age 66.87(±7.21) years.

Table 5: Comparison of age distribution

| Authors and Year | Mean Age |
|-----------------------------------------------|--------------|
| 1. Keller & Shepard et al, 1986 ³⁹ | 59±7 yrs |
| 2. Putnik and Povazan, 1998 ⁴⁰ | 59.25 yrs |
| 3. Present study | 66.87(±7.21) |

3. Duration of Symptoms

In this study most of the patients (26/50) gave history of symptoms of 1 to 9 years duration, with a mean duration of dyspnoea 7.013 ± 5.0439 and cough of 9.092±6.303years.

4. Severity of the disease

Table 6: Comparison of severity of the disease

| FEV1 | Higham et al ⁴² , 1988 n(%) | Present n(%) |
|--------|-------------------------------------------|-----------------|
| 50-79% | 12(16.4%) | 14(28) |
| 30-49% | 19(26%) | 29(58) |
| < 30% | 42(57.6%) | 7(14) |

Table 7: Comparison of mean FEV₁ (SD)% of predicted

| Study (Year) | Mean FEV ₁ (SD) (% of predicted) |
|------------------------------------|---------------------------------------------|
| Keller et al, (1986) ³⁹ | 33(14) |
| M.A. Higham et al ⁴² | 39.4(19.7) |
| Present study | 42.145(11.63) |

5. Duration of tobacco use and correlation to severity of disease

In this study, majority of the patients (18/50) had a history of tobacco use, more than 40 pack years, with a mean of 56.9(±23.9) pack years. And according to BTS guidelines most patients with COPD have at least 20 pack years of smoking history⁴⁹. Our finding correlates well with this study.

6. Symptoms at presentation

All patients had breathlessness and cough with expectoration at presentation.

7. Physical signs at presentation

Most of the patients in the present study had tachypnoea(44/50) at presentation. Most of them had signs of hyperinflation, and also diminished breath sounds with prolonged expiratory phase. Clinical signs of pulmonary hypertension were present in 46% (23/50) of the patients.

8. ECG findings

1. Right axis deviation of QRS

Right axis deviation of QRS was present in 60% (30/50) of the patients in the present study. According to Murphy & Hutcheson²⁷, right axis deviation is one of the most reliable criteria of RVH, and is more common in patients with RVH secondary to COPD than in those with RVH secondary to congenital heart disease and has a specificity of 95%. Millard²⁵ concluded that in chronic pulmonary disease, the position of mean QRS axis provided a good indication of right ventricular hypertrophy as any other electrocardiographic sign. Our findings are in agreement with the above studies.

Table 8: Comparison of Right Axis Deviation of QRS

| Author and Year | Incidence (%) |
|--------------------------------------------|---------------|
| Milnor, 1957 ⁴⁴ | 18.75 |
| Padmavathi and Pathak, 1959 ⁴⁵ | 74 |
| Silver and Calatayud, 1971 ⁴⁶ | 19 |
| Padmavathi and Raizada, 1972 ⁴⁷ | 43.2 |
| Murphy and Hutcheson, 1974 ²² | 28 |
| Present study | 60 |

1. R/S ratio in V1 > 1

Table 9: Comparison of R/S in V1 > 1

| Author and Year | Incidence (%) |
|----------------------------------------|---------------|
| Murphy & Hutcheson, 1974 ²² | 7.5 |
| Silver & Calatayud, 1971 ⁴⁶ | 7 |
| Present study | 32 |

3. R wave amplitude in V1 > 7mm

Table 10: Comparison of R wave amplitude in V1 > 7 mm

| Author and Year | Incidence (%) |
|--------------------------------------------|---------------|
| Silver and Calatayud, 1971 ⁴⁶ | 21 |
| Padmavathi and Raizada, 1972 ⁴⁷ | 2.6 |
| Murphy & Hutcheson, 1974 ²² | 9.4 |
| Present study | 8 |

4. R/S ratio in V5 or V6 < 1

Table 11: Comparison of R/S ratio in V5 or V6 < 1

| Author and Year | Incidence (%) |
|------------------------------------------|---------------|
| Silver and Calatayud, 1971 ⁴⁶ | 21 |
| Padmavathi & Raizada, 1972 ⁴⁷ | 77.9 |
| Murphy and Hutcheson, 1974 ²² | 23 |
| Present study | 24 |

5. Incomplete RBBB

Table 12: Comparison of Incomplete RBBB

| Author and Year | Incidence (%) |
|--------------------------------------------|---------------|
| Padmavathi and Raizada, 1972 ⁴⁷ | 12.9 |
| Murphy and Hutcheson, 1974 ²² | 2 |
| Present study | 38 |

6. P-pulmonale

Table 13: Comparison of P pulmonale

| Author and Year | Incidence (%) |
|------------------------------------------|---------------|
| A. G. Chappell, 1966 ²⁰ | 10 |
| Silver and Calatayud, 1970 ⁴⁶ | 46.2 |
| Padmavathi & Raizada, 1972 ⁴⁷ | 95 |
| Murphy & Hutcheson, 1974 ²² | 26.4 |
| Present study | 42 |

7. Right axis deviation of P wave.

In the present study 32/50 patients were found to be having right axis deviation of P wave (64%). In the study by R.L. Agarwal and Dinesh kumar⁴¹ 64.3 % patients had normal P wave axis and 35.7% patients LAD or RAD or indeterminate axis while majority patients that is 97.8% patient in whom COPD was absent had normal P wave axis

8. Complete Right bundle branch block (RBBB)

In the present study, only two patients had evidence of complete RBBB (4%). Similarly in the study by Padmavathi and Raizada²⁴ 4 patients out of 544 patients had RBBB and Chappell¹⁹ study had 2 cases out of 122 patients. Milnor (1957)¹² is of the opinion that presence of RBBB is more commonly due to coronary disease than RVH is also found in persons without heart disease.

6. Arrhythmias

In this study only two patients had transient atrial fibrillation. In a study by Chappell¹⁹ of 112 patients, one patient had atrial flutter and another had paroxysmal atrial fibrillation. Arrhythmias (usually transient and usually supraventricular) are common especially during acute exacerbations of the disease and disappear once hypoxia is corrected.

7. Others

One patient in our study had inverted T wave in V1 and V2. T wave is upright in V1 and V2 but of decreased amplitude, gets inverted in chronic cor pulmonale. One patient found to have qS in V1-4 and three patients had S1S2S3 syndrome in limb leads. S1S2S3 syndrome indicates extreme axis deviation that is northwest region⁴⁷

11. Correlation of ECG findings with severity of the disease

In the present study no patients were found in the category of mild degree of COPD according GOLD criteria. Statistical analysis showed significant correlation between ECG findings like right axis deviation of P wave, R wave amplitude in V5 or V6 < 5mm and R/S ratio in V5 or V6 < 1 and severity of the disease. But ECG findings like RBBB, R wave amplitude in V1 > 7mm and R/S ratio in V1 > 1 did not correlate with the severity of the disease.

Most of the patients in our study belonged to the category of severe degree (58%) of COPD according to GOLD criteria, followed by moderate degree (28%) of COPD. Caird and Wilcken (1962), observed that 'P' pulmonale and evidence of RVH are much more frequent when FEV1 falls below 45% of normal than above it. The likely explanation given by them is that a ventilatory capacity of < 45% of predicted is inadequate to maintain normal blood gases in the face of inequalities of ventilation and V/Q ratios and it has been repeatedly shown that pulmonary hypertension is correlated with degree of arterial oxygen desaturation and hypercapnea.

A. G. Chappell²⁰ studied 112 patients, dividing them into 2 groups, one with FEV1 < 1200 ml and other with > 1200 ml and found that, right ventricular hypertrophy, 'P' pulmonale and vertical 'P' axis occurred more frequently in patients with widespread emphysema than in the other group.

M. K. Tandon²¹ also found increasing incidence of P-pulmonale, right axis deviation of QRS and dominant S in V5 or V6 < 1 with increasing severity of the disease as defined by FEV1/FVC ratio.

V.K. Singh and his coworkers³² also found increasing incidence of 'P' pulmonale, R/S ratio in V5 or V6 < 1, QRS axis > 90° and R wave amplitude in V6 < 5 mm, as the FEV1 / FVC ratio was decreasing, which was statistically significant and explained that this trend was due to increased alveolar air trapping and blood gas derangement.

12. Correlation of ECG findings with duration of disease.

R wave amplitude in V5 or V6 < 5mm, R/S ratio in V5 or V6 < 1 and right axis deviation of QRS complex which are ECG signs of RVH, are found with increasing incidence as duration of disease increases.

CONCLUSIONS

The following conclusions can be drawn from this study

- COPD is more common in males and in the 6th and 7th decade.
- Most of the patients have fairly advanced disease at presentation.

ECG is better than clinical methods in detecting right ventricular dysfunction in COPD.

REFERENCES

- Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380 (9859): 2095-128.
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006; 3 (11): e442.
- Shapiro SD, Gordon L, Snider, Rennard SI, Chronic Bronchitis and Emphysema. In Mason RJ, Broaddus VC, Murray JF, Nadel JA, editors. *Murray and Nadel's Text Book of Respiratory Medicine*, 4th ed., vol 1, Philadelphia, Elsevier Saunders, Health Sciences Right Department. 2005: 1115-62.

- American Lung Association Epidemiology and Statistics Unit. Trends in COPD (Chronic bronchitis and Emphysema): Morbidity and Mortality. 2013 <http://www.lung.org/assets/documents/research/copd-trend-report.pdf> (accessed 12 August 2016).
- Rabe KF, Beghe B, Luppi F, Fabbri LM. Update in chronic obstructive pulmonary disease 2006. *Am J Respir Crit Care Med* 2007; 175: 1222-32.
- Shahab L, Jarvis MJ, Britton J, West R. Prevalence, diagnosis, and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006; 61: 1043-47.
- Jindal SK, Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, et al. A multicentric study on epidemiology of chronic obstructive pulmonary disease and its relationship with tobacco smoking and environmental tobacco smoke exposure. *Indian J Chest Dis All Sci*; 2006; 48: 23-29.
- Reilly J, Jr., Silverman EK, Shapiro SD. Chronic obstructive pulmonary disease. In Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL et al. editors. *Harrison's principles of internal medicine*. 19th ed., vol 2, New York, McGraw Hill, Health Professions Division, 2008; 1635-42
- Macnee W. Chronic bronchitis and emphysema. In. Seaton A, Seaton D, Leitch AG editors. *Crofton and Doughlas's respiratory diseases*, 5th ed., vol 1, Blackwell Science Ltd, London. 2000: 616-95.
- Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5 year survival than airway obstruction in patients with COPD. *Chest* 2002; 121: 143-40.
- Fletcher CM. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). *BMJ* 1960; 2: 1662.
- Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007; 370 (9589): 765-73
- Barbera JA, Peinado VJ, Santos S. Pulmonary hypertension in chronic obstructive pulmonary disease. *Eur Respir J* 2003; 21: 892-905.
- Jackson H, Hubbard R. Detecting chronic obstructive pulmonary disease using peak flow rate : cross sectional survey. *BMJ* 2003; 327 (7416): 653-4.
- Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J* 2005; 26(2): 319-38.
- Pellegrino R, Viegi G, Brusasco V et al. Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26(5): 948-68.
- Kessler R, Fallner M, Weitzenblum E, Chaouat A, Aykut A, Ducloux A et al. "Natural History" of Pulmonary Hypertension in a series of 131 patients with chronic obstructive lung disease. *Am J Respir Crit Med* 2001; 164: 219-24.
- Fabbri LM, Luppi F, Beghe B, Rabe KF. Update in chronic obstructive pulmonary disease 2005. *Am J Respir Crit Care Med* 2005; 173 (10): 1056-65
- Schamroth L. Emphysema: chronic obstructive airway disease. In. Schamroth C editor, *An introduction to electrocardiography*. 7th ed. Berlin, Blackwell Science Ltd. 1990; 233-38.
- Chappell AG. The electrocardiogram in chronic bronchitis and emphysema. *Brit Heart J* 1966; 28: 517-22.
- Tandon MK. Correlation of electrocardiographic features with airway obstruction in chronic bronchitis. *Chest* 1973; 63: 146-48.
- Murphy ML, Hutcheson F. The electrocardiographic diagnosis of right ventricular hypertrophy in chronic obstructive pulmonary disease. *Chest* 1974; 65: 622-27
- Kok-Jensen A. simple electrocardiographic features of importance for prognosis in severe chronic bronchial obstruction. *Scand J Respir Dis* 1975; 56(5): 273-84.
- Smith JM, Burema J, May JF, Postma DS, Smither HJ, Steinhuis EJ. Prognosis in severe chronic obstructive pulmonary disease with regard to the electrocardiogram. *J Electrocardiol* 1983 Jan; 16(1): 77-86.
- Mittal SR, Jain SC, Sharma SK, Sethi AK. The role of oesophageal electrocardiography in the diagnosis of right ventricular hypertrophy in chronic obstructive pulmonary disease. *Int J Cardiol* 1986 May; 11(2): 165-73.
- Oswald - Mammosser M, Oswald T, Nyankiye E, Dickle MC, Grange D, Weitzenblum E. Non-invasive diagnosis of pulmonary hypertension in chronic obstructive pulmonary disease. Comparison of ECG, radiological measurements, echocardiography and myocardial scintigraphy. *Eur J Respir Dis* 1987 Nov; 71(5): 419-29.
- Caruso G, Trovato GM, Corsaro A, Sciuto V. Correlative evaluation of electrocardiographic changes and spirometric parameters in pulmonary cardiopathy secondary to chronic obstructive bronchopneumopathy. *Recenti Prog Med*; 1989 Sep; 80(9): 468-70.
- Bhan AK, Mittal SR, Lalgadiya M. Importance of recording lead V1 in the seventh right intercostals space in diagnosing cor pulmonale. *Int J Cardiol* 1994 Jan; 43(1): 99-100.
- Inclazi RA, Fuso L, De Rosa M, Di Napoli A, Basso S, Pagliari et al. Electrocardiographic signs of chronic cor pulmonale. A negative prognostic finding in chronic obstructive pulmonary disease. *Circulation*; 1999; 99: 1600-05.
- Inclazi RA, Pistelli R, Fuso L, Cocchi A, Bonetti MG, Giordano A. Cardiac arrhythmias and left ventricular function in respiratory failure from chronic obstructive pulmonary disease. *Chest* 1990; 97: 1092-97.
- Balajepally R, Spodick DH. Electrocardiographic screening for emphysema: the frontal plane P axis. *Clin Cardiol* 1999 Mar; 22(3): 226-28.
- Nayak SK, Dash AK, Padhi PK, Barik BK, Das P. Electrocardiographic and echocardiographic profile of COPD patients. *JAPI* 2008 Apr; 56: 289.
- Vij A, Bhardwaj, Kapila S, Vij C, Sachdeva GS, Gill BS et al. Study of electrocardiographic and echocardiographic profile of COPD patients. *JAPI* 2008 Apr; 56: 290.
- Stewart AG, Waterhouse JC, Howard P. The QTc interval, autonomic neuropathy and mortality in hypoxaemic COPD. *Respir Med*; 1995; 89: 79-84.
- Zulli R, Donati P, Nocosia F, De Vecchi M, Tantucci C, Romanelli G et al. Increased QTc dispersion: a negative prognostic finding in chronic obstructive pulmonary disease. *Intern Emerg Med*; 2006; 1(4): 279-86.
- Asad N, Vanessa MP, Johnson, Spodick DH. Acute right atrial strain: regression in normal as well as abnormal P-wave amplitude with treatment of Obstructive Pulmonary Disease. *Chest* 2003; 124: 560-64.
- McCord J, Borzak S. Multifocal atrial tachycardia. *Chest* 1998; 113: 203-09.
- Singh VK and Jain SK. Effects of Airflow limitation on the electrocardiogram in COPD. *Indian Journal of chest diseases and Allied sciences*, 1989; 31(1): 1-8.
- Kellar CA, Shepard JW Jr., Chun DS, Vasquez P, Dolan GF. Pulmonary Hypertension in Chronic Obstructive Pulmonary disease. Multivariate analysis. *Chest* 1986; 90(2): 185-192.
- Putnik M, Povazan D, Vindisjesic M. Electrocardiography and echocardiography in the diagnosis of chronic cor pulmonale (Article in Serbo Croatian (Roman)). *Med Pregl*, 1998; 51(11): 528-31.
- Global Initiative for Chronic Obstructive Lung Disease - Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary disease. <http://www.goldcopd.com>.
- Higham MA, Dawson D, Joshi J, Paulos PN, Morell NW. Utility of echocardiography in assessment of pulmonary hypertension secondary to COPD. *Eur. Respir. J.* 2001; 17: 350-355.
- Millard FJC. The electrocardiogram in chronic lung disease. *British Heart Journal* 1967; 29: 43-50.

44. Milnor WR. Electrocardiogram and Vectorcardiogram in right ventricular hypertrophy and right bundle branch block. *Circulation* 1957; XVI. : 348-367.
45. Padmavathi S, Pathak SN. Chronic cor-pulmonale in Delhi. A study of 127 cases. *Circulation* 1959; 20: 343-352.
46. Silver HM, Calatayud JB. Evaluation of QRS criteria in patients with COPD. *Chest* 1971 ; 59(2) : 153-159.
47. Padmavathi S and Raizada V. Electrocardiogram in chronic cor pulmonale. *British Heart Journal* 1972; 34 : 658-667
48. Agarwal RL, Kumar D, Gurpreet, Agarwal DK, Chabra GS. Diagnostic values of electrocardiogram in chronic obstructive pulmonary disease (COPD). *Lung India* 2008; 25: 78-81.
49. Chang. Chronic obstructive pulmonary disease and Cor pulmonale, *Text book of Clinical Electrocardiography*; 28(9): 380-388.