

Lipoprotein Profile in Patients with Chronic Obstructive Pulmonary Disease in a Tertiary Care Hospital in South India

NIRANJAN M.R., DADAPEER K., RASHMI B.K.

ABSTRACT

Context: Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death world over. COPD has been defined as a disease state characterized by airflow limitation. Spirometric tests like Forced Expiratory Volume in first second (FEV_1) < 80% and FEV_1/FVC (ratio of Forced Expiratory Volume in first second to the Fixed Vital Capacity) 0.7 is the diagnostic criteria for COPD. In COPD smoking is the major risk factor and smoking affects the lipid profile of COPD patients.

Aims: To investigate the levels of total cholesterol (TCH), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL) and correlating FEV_1 and FEV_1/FVC ratio with lipid profile.

Settings and Design: A prospective cross-sectional case control study.

Methods and Materials: Fifty cases were selected on the basis of simple random sampling method.

The FEV_1 , FEV_1/FVC ratio and various lipoprotein levels like total cholesterol (TCH), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL) were studied and a group of 20 non-smoker healthy subjects were selected as controls. FEV_1 , FEV_1/FVC ratio were correlated with lipid profile.

Statistical Analysis: Comparison of various parameters were performed by "t" test, correlation between two variables were performed by Pearson's correlation co-efficient "r"

Results: Majority of the patients had moderate (50%) and severe (42%) airflow limitation. Mean LDL concentration among cases was 114.89 ± 19.61 (mg/dl) as against control group who had mean LDL concentration of 96.22 ± 19.96 (mg/dl), which was statistically significant (p-value < 0.05). However no significant difference in LDL, HDL and in triglycerides levels were observed.

Conclusion: Smoking significantly affects the lipid profile in COPD patients.

Key Words: COPD; Lipoprotein; FEV_1 , FEV_1/FVC ratio; Cholesterol; LDL; HDL; Triglycerides; VLDL

KEY MESSAGE

- Smoking increases LDL levels, hence all COPD patients who are smokers needs to check their lipoprotein levels.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases [1]. The clinical importance of hyperlipoproteinemia derives chiefly from the role of lipoproteins in atherogenesis.

In COPD, smoking is the major risk factor and smoking affects the lipid profile of COPD patients. The plasma β -lipoprotein, cholesterol and triglycerides concentration are higher and HDL cholesterol is lower in smoker than in non-smokers [2]. There are only few data in India where the lipoprotein in COPD were studied. Gupta et al. 2002 carried out a comparison of the lipid profile in bronchial asthma and COPD and concluded that LDL was significantly higher and VLDL was significantly lower in patients of bronchial asthma and COPD as compared to controls [3].

Hence an attempt was made to investigate the levels of total cholesterol (TCH), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL) in COPD patients. Moreover, correlation of FEV_1 (Forced Expiratory

Volume in first second) and FEV_1/FVC (forced expiratory volume in first second to the fixed vital capacity) ratio with lipid profile was carried out.

METHODS AND MATERIALS

In this study, 50 cases were selected on the basis of simple random sampling method from the Medical Wards, K.R. Hospital, Mysore from June 2005 to March 2006.

As per GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines [1] of COPD, any patient who has symptoms of chronic cough, sputum production, or dyspnoea, and / or a history of exposure to risk factors for the disease were considered and included in the study, and was further confirmed by spirometry. The values FEV_1 less than 80% of the expected value and ratio of FEV_1/FVC less than 0.7 (70%), after post bronchodilator inhalation, were included in this study. Patients with bronchial asthma, pulmonary tuberculosis, bronchiectasis, known congenital or acquired heart diseases, diabetes mellitus and hypertension, were excluded, and 20 non-smoker healthy subjects were selected as a control group.

All the 50 patients were subjected to a detailed history and thorough clinical examination including anthropometry. Chest X-ray Postero-Anterior view, spirometry was done on computerized spirometer (kit micro, COSMED, Srl, Rome Italy). Spirometry was performed when the patients were clinically stable with prior proper instructions as per ATS (American Thoracic Society) guidelines [4].

Written consent was taken from both cases and controls, ethical committee clearance were also obtained.

After 12 hour of overnight fast, 5 ml blood samples were drawn in the morning before breakfast from the subjects and controls. Total cholesterol, HDL and triglycerides were directly analysed by using ERBA Mannheim diagnostic equipment (Model-EM 360, V21.0, MADE IN INDIA). LDL cholesterol was calculated by using Friedewalds equation (LDL cholesterol = (Total cholesterol) – (HDL cholesterol) – (Triglycerides/5)). VLDL cholesterol was calculated by using the equation, VLDL cholesterol = Triglyceride/5.

STATISTICAL ANALYSIS

Comparison of various parameters among male and female subjects with COPD were performed by “t” test, correlation between two variables were performed by Pearson’s correlation co-efficient “r”, analysis was done by using SPSS+ 10.0 computer package for statistics.

RESULTS

Fifty cases of COPD were studied and out of 50 cases studied 44 were males and 6 were females. Mean age of the male patients among cases was 63.32±10.73 years and that of the female in the study was 63±10.18 years.

Majority of the patients in the cases studied were males constituting 88%. The male-female ratio was 7.33:1. Among controls males were 16 and females were 4 in number. The mean age of the males among controls was 57.87±10.20 and that of females was 57.50±8.20

In the present study the duration of illness ranged from 2-20 years with majority belonging to the 6-10 years range.

In our study smoking was the major risk factor. All the 44 male patients were smokers, while history of exposure to smoke of burnt fuels was present in all the female cases [Table/Fig-1].

There was a dose response relationship between the number of pack-years of smoking and decline in lung function. In our study, duration of smoking ranged from 20 pack-years to 60 pack-years (1 pack= 10 cigarettes, calculated by number of packs of cigarette smoked per day multiplied by number of years smoked, which constitutes one pack year). Majority were in 30-50 pack-years of duration of exposure.

Majority of the patients had BMI of < 25.

On viewing chest x-ray, 56% of patients had chronic bronchitis with emphysema. Twenty two percent had chronic bronchitis, 22% had normal chest x-rays. Chest x-rays of all the subjects in the control group were normal.

In spirometry, the expected value is the value given by the computerized spirometer for each patient considering the patient’s age, sex, race, height and weight. The actual value is what the percentage or volume of air the patient breathes out.

The present study [Table/Fig-2] showed the actual mean of FVC was 2.22±0.50 litres, though the expected mean of FVC was 2.92±0.43

litres. The actual mean of FEV₁ was 1.12±0.34 litres, and the expected mean of FEV₁ would be 2.30±0.35 litres. Among the FEV₁% and FEV₁/FVC ratio the actual mean were 49.76±14.25% and 53.01 ±14.22% respectively.

All the control group had normal spirometric parameters.

Out of 50 cases studied, 60% of patients were present in FEV₁/FVC ratio of 51-70%, 34% of patients were present in 31-50% group. 6% of patients were present in 21-30% group.

It was observed that mean LDL concentration among cases was 114.89±19.61(mg/dl) as against control group who had mean LDL concentration of 96.22±19.96(mg/dl), which was statistically significant (p-value < 0.05). All other lipid parameters such as Total cholesterol, triglycerides, HDL cholesterol, and VLDL cholesterol were within normal range when compared to controls [Table/Fig-3].

In this study patients with moderate airflow obstruction had mean total cholesterol, HDL, LDL, and triglyceride concentration 180.36±13.80 (mg/dl), 39.88±12.57 (mg/dl), 114.44±20.96 (mg/dl), 135.60±46.18 (mg/dl) respectively [Table/Fig-4].

The patients with severe airflow obstruction had mean total cholesterol, HDL, LDL, and triglyceride concentration 176.61 ± 17.76 (mg/dl), 41.43 ± 8.23(mg/dl), 114.93±15.90(mg/dl), 137.08±41.15(mg/dl) respectively. As the severity of airflow

	Male	Female	Total	% age
History of smoking	44	0	44	88
Exposure to smoke of burnt fuels	0	6	6	12
Total	44	6	50	100

[Table/Fig-1]: Risk factors for COPD

Test	Range	Mean	SD
FVC (litres)	1.03–3.21	2.22	0.50
FEV ₁ (litres)	0.53–1.84	1.12	0.34
FEV ₁ %	25.70–77.0	49.76	14.25
FEV ₁ /FVC%	21.50–70.0	53.01	14.22

[Table/Fig 2]: Range and mean values of spirometric parameters among cases

Lipid Profile	Cases (mg/dl) (N=50)	Controls (mg/dl) (N=20)	p-value
Total cholesterol	178.36±17.55	171.25±20.49	0.149(NS)
HDL	39.70±12.47	44.57±8.57	0.115(NS)
Triglycerides	129.38±41.81	138.80±35.62	0.379(NS)
VLDL	33.24±22.03	32.01±16.73	0.822(NS)
LDL	114.89±19.61	96.22±19.96	0.001(S)
Total Cholesterol/HDL	3.59±1.38	3.12±1.21	0.191(NS)

[Table/Fig 3]: Showing serum mean concentration of lipid parameters S- Significant; NS- Not significant.

Lipid Profile	Mild (FEV ₁ >80%)	Moderate (FEV ₁ 50-80%)	Severe (FEV ₁ <50)	p-value
Total cholesterol	–	180.36±13.80	176.61±17.76	0.729(NS)
HDL	–	39.88±12.57	41.43±8.23	0.715(NS)
LDL	–	114.44±20.96	114.93±15.90	0.982(NS)
Triglycerides	–	135.60±46.18	137.08±41.15	0.362(NS)

[Table/Fig 4]: Showing correlation of lipid profile with severity of COPD S- Significant; NS- Not significant.

obstruction increased, no significant difference in lipid profile was observed.

Discussion: Cigarette smoking is clearly the single-most important identifiable etiological factor in COPD [5]. About 85% people with COPD develop the disease because of cigarette smoking [6].

COPD is a disease of late adulthood. As the age advances the lung function (FEV_1) declines and other risk factors add to the disease process [7]. In the present study the mean age was 63.16 ± 10.45 . COPD is a male dominant disease, the prevalence in males due to higher prevalence of smoking in this sex, and also males are more susceptible to smoking than females [7]. In our study males accounted for 88%, with a male-female ratio of 7.33:1. In the present study all males were smokers, while all 6 female patients were non-smokers but all of them were exposed to smoke of burnt fuels which is very common in rural population. In this part of the country, cooking is predominantly carried out by using wood and cow dung. In a study by Behera and Jindal (1996) respiratory symptoms in India were reported in 13 percent of 3608 non-smoking women involved in domestic cooking [8]. In the study by Mishra et al (1990), it was observed that the female population had exposure to kitchen smoke due to cooking with wood, cow dung and coal [9]. In a New Guinea household pollution, due to heating and cooking within a small space was responsible for COPD commonly in women than men [10]. A study from Jindal et al (2006) showed that the exposure to solid fuel combustion is also shown to be an additive risk factor along with environmental tobacco smoke exposure in causing COPD [11]. Hence domestic environmental factors may be of great importance in the aetiology of COPD.

Smoking is a very important risk factor for COPD, seen in 85% of patients who develop COPD. In the present study all males were smokers, when compared with the Thiruvengadam et al (1977) study group, who also had smoking history in all males [12].

Present study consisted of mean value of $FEV_1/FVC\%$ ratio 53.01 ± 14.22 . According to GOLD criteria majority of the patients in the present study belonged to moderate to severe airflow obstruction, which was comparable with that of Tandon (1973) [13] and Singh and Jain (1989) [14] which consisted of FEV_1/FVC ratio 56.70% and 48.45% respectively.

Smoking affects the lipid profile in the following ways. The plasma β -lipoprotein, cholesterol and triglycerides concentration are higher and HDL cholesterol is lower in smoker than in non-smokers. Free fatty acid concentration tends to be variable, but inhalation during smoking produces an immediate increase of free fatty acids of about 30% through stimulation of the adrenal medulla, by nicotine which increases the concentration of epinephrine in the plasma and the urinary excretion of catecholamine and their metabolites [15].

In addition, the plasma cortisol concentration may increase by as much as 40% within 5 minutes of the start of smoking, although the normal diurnal rhythmicity of cortisol is unaffected. Smokers excrete more 5-hydroxy indole acetic acid than do non-smokers [15].

The study by Gupta et al (2002) showed a significantly higher LDL and significantly lower VLDL levels when compared to controls [3]. The present study also showed significantly elevated LDL levels when compared with controls but VLDL was normal. This may be due to the fact that the present study group had 88% of smokers, which increases VLDL levels also.

The study by Don and Paul (2003) showed no significant differences in the LDL or HDL concentrations and even with severe airflow obstruction, had slightly lower serum concentrations of triglycerides [16]. Present study showed no significant difference in LDL, HDL and also in triglycerides levels. This may be due to the study population studied which was much larger ($N=6629$) in the former study as compared to the present ($N=50$) study. Moreover, the former study had 73.7% of severe form of COPD patients but present study had only 50%.

In an analysis of the 1988-1994 National Health and Nutritional Examination Survey of 18,162 randomly selected adults in the US, Cassano and co-authors explored that higher HDL was associated with better lung function, total cholesterol had little or no association with lung function and lower LDL was associated with better function [6].

Fekete and Mosler (1987) studied plasma lipoprotein fractions in 29 patients with chronic obstructive pulmonary disease (COPD) and compared with non-COPD subjects and found triglycerides were significantly lower in COPD females only, the other parameters being almost identical [17]. Marquis et al. (2005) studied 16 men and 18 women with COPD to evaluate the metabolic syndrome in COPD patients who participated in a pulmonary rehabilitation program and concluded that metabolic syndrome was frequent in patients with COPD and waist circumference, fasting lipid profile, blood pressure and fasting glucose should be obtained in all COPD patients, beginning pulmonary rehabilitation program and this would allow a better cardiovascular risk assessment [18].

Bahar et al. (2003) studied lipid profile in 20 patients with COPD and 20 healthy controls and concluded that COPD patients did not show an atherogenic lipid pattern and that the increased HDL levels might be related to the drugs used by these patients [19].

In conclusion smoking significantly affects the lipoprotein profile in COPD patients in the form of increases in LDL levels. Hence all COPD patients who are smokers needs to check their lipoprotein levels. However there was no correlation with severity of airflow obstruction and dyslipidemia, and there is a need for more detailed studies to understand these relationships.

REFERENCES

- [1] Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of COPD. NHLBI/WHO Workshop Report, Executive Summary; 2004; 1-21.
- [2] Burtis A Carl, Ashwood R Edward. Lipids, lipoproteins and apolipoproteins. In: Burtis A Carl, Ashwood R Edward editors, Tietz Textbook of Clinical Chemistry, 3rd edition. Philadelphia: WB Saunders Company 1993; 61-62.
- [3] Gupta R, Bhadoria DP, Mittal A, Bhadoria P, Gupta S. Lipid profile in obstructive airway disorders. *J Assoc Physicians India* 2002; 50:186-87.
- [4] American Thoracic Society. Lung function testing: Selection of reference values and interpretative strategies. *Am Rev Respir Dis* 1991; 144:1202-17
- [5] Doll R, Peto R. Mortality in relation to smoking: 10 years observation on British doctors. *Br Med J* 1976; 2:1525.
- [6] Susan Lang. Good cholesterol may be healthy for the lungs, too. *Am J Epidemiol* 2002; 155(9):842-48.
- [7] Postma S Dirkje and Kerstjens AM Huib. Epidemiology and natural history of chronic obstructive pulmonary disease. In: Gibson G John, Geddes M Duncan, Costabel Ulrich, Sterk J Peter, Corrin Bryan, editors. *Respiratory Medicine*. 3rd ed. Saunders 2003; 2:1109-20.
- [8] Behera D, Jindal SK. Respiratory symptoms in Indian women using domestic cooking fuels. *Chest* 1991; 100 : 385-88.
- [9] Mishra VN, Malhotra M, Saroj Gupta. Respiratory disorder in females of Delhi. *J Indian Med Assoc* 1990; 88:77-80.

- [10] Pride NB, Stockley RA. Chronic obstructive pulmonary disease. In: Weatherall DJ, Ledingham JGG, Warrell DA Eds. Oxford Textbook of Medicine, Oxford Medical Publications 1996; 2766-78.
- [11] Jindal SK, Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, *et al.* Asthma Epidemiology Study Group. 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 Allied Sci* 2006; 48 :23-27.
- [12] Thiruvengadam KV, Raghavan TP, Bhardwaj KV. Survey of prevalence of chronic bronchitis in madras city. In: Viswanathan R, Jaggi OP, editors. Advances in chronic obstructive lung disease. Delhi; Asthma and Bronchitis Foundation of India 1977; 59-69.
- [13] Tandon MK. Correlation of electrocardiographic features with airway obstruction in chronic bronchitis. *Chest* 1973; 63(2):146-48.
- [14] Singh VK and Jain SK. Effects of airflow limitation on the electrocardiogram in chronic obstructive pulmonary disease (COPD). *Indian J Chest Dis & All Sci* 1989; 31(1):1-8.
- [15] Burtis A Carl, Ashwood R Edward. Lipids, lipoproteins and a polipo- proteins. In: Burtis A Carl, Ashwood R Edward editors, Tietz Textbook of Clinical Chemistry, 3rd Edition. Philadelphia: WB Saunders Company 1993; 61-62.
- [16] Sin D Don, Man Paul SF why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular disease? *Circulation* 2003; 107:1514-19.
- [17] Fekete T, Mosler R. Plasma lipoproteins in chronic obstructive pulmonary disease. *Horm Metab Res* 1987; 19(12):661-62.
- [18] Marquis K, Maltais F, Bezean AM, Jobin J, LeBlanc P, Poirer P *et al.* Evaluation of the metabolic syndrome in patients with chronic obstructive pulmonary disease who participated in a pulmonary rehabilitation program. *Journal of Cardiopulmonary Rehabilitation* 2005; 25(4):226-32.
- [19] Ulubab Bahar, Clmen Filiz, Eryyluaz, Buddaycy Resul, Calykodlu Mukadder. Lipid profile in patients with chronic obstructive pulmonary disease. *Turkish Respiratory Journal* 2003; 4(3):120-22.

AUTHOR(S):

1. Dr. Niranjan M.R.
2. Dadapeer K.
3. Rashmi B.K.

PARTICULARS OF CONTRIBUTORS:

1. MD (General Medicine), DNB., MNAMS
Assistant Professor, Department of Medicine,
Hassan Institute of Medical Sciences,
Hassan 573201, Karnataka, India.
2. MS (Ophthalmology), DNB., Hassan Institute of Medical
Sciences, Hassan, Karnataka, India.
3. MBBS, Medical Officer, District Tuberculosis Centre,
Hassan Institute of Medical Sciences, Hassan 573201

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Niranjan M.R.
Assistant Professor, Dept. of General Medicine,
Hassan Institute of Medical Sciences, Hassan 573201,
Karnataka, India.
Phone: 09448672501
E-mail: dnrniranjanmr@yahoo.co.in

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