

## EVALUATION OF C-RP AND LIPID PROFILE IN COPD AS A MARKER OF SYSTEMIC INFLAMMATION AND ATHEROGENIC LIPID PATTERN.

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**Article Info:** Received 15 June 2021; Accepted 03 August 2021

**DOI:** <https://doi.org/10.32553/ijmbs.v5i8.2035>

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**Conflict of interest:** No conflict of interest.

### Abstract

Chronic obstructive pulmonary disease (COPD), a progressive disease of the lungs characterized by persistent airflow limitation, is one of the main causes of morbidity and mortality worldwide. Epidemiological studies reported that COPD patients have various extrapulmonary comorbidities such as coronary heart disease (CHD), metabolic syndrome, and depression. Extrapulmonary comorbidities increase the risk of hospitalisation and mortality in COPD patients. An increasing number of COPD patients die from systemic comorbidities rather than respiratory failure. Purpose of present study was to measure serum C-reactive protein (C-RP) and lipid profile in COPD patient to establish its correlation as early predictor of risk factors CHD. **Aim:** To investigate the levels of serum C-RP, cholesterol (TCH), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL) in COPD patients and correlating FEV1 and FEV1/FVC ratio with lipid profile. **Settings and Design:** A prospective cross-sectional case control study. Method: 40 COPD patients 33 males (82.5%) and 7 females (17.5%) with mean age of 53.43±9.64 years, FEV1: 52±15 % pred., BMI: 29.4 ±4.5kg/m<sup>2</sup> with stable COPD enrolled in the study. We compared lipid profile in 40 patients with COPD and control group - 40 COPD patients. **Results:** Mean Cholesterol concentration was (257.30±56.39) (mg/dl), TG (Triglyceride) 253.18±58.98. LDL (191.17±86.17) (mg/dl), VLDL (51.31±11.79), HDL (30.98±5.21) (mg/dl) as against control group who had concentration of 188.58±39.59 (mg/dl), 112.56±55.44, 98.74±28.30, 31.59±11.56, 42.65±6.55 respectively. Which was statistically significant (p-value < 0.001).L/H Ratio (6.59±1.52) in cases compared to control Mean 3.98±1.84.C-RP mean concentration in cases 3.26±2.0, compared to control 0.48±0.38. **Conclusion:** The study established that there is decreased serum HDL LEVEL and increased cholesterol, TG, LDL, VLDL,L/H, C-RP, BMI in patients with COPD suggest C-Reactive Protein (hs-CRP) is considered as a marker of systemic inflammation. Increased LDL, cholesterol levels and decreased HDL cholesterol levels are indicative of an atherogenic lipid pattern.

**Keywords:** COPD, C-RP, Lipid Profile, Dyslipidemia, Systemic Inflammation

### Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive disease of the lungs characterized by structural changes such as emphysema, airflow limitation, dynamic hyperinflation, air trapping, and peribronchial fibrotic remodeling of the lungs with significant systemic inflammatory components, induced by chronic exposures to smoking and/or occupational or environmental sources [1,2]. It is the 5th leading cause of mortality and morbidity globally, and the World Health Organization (WHO) predicts that by 2030, it will step up to the 4th position with an increase of 160%, in contrast to a predicted decrease in mortality rates due to tuberculosis, malaria, and diarrheal infection [3]. CHD, also known as atherosclerotic heart disease and coronary artery disease, is common among patients with COPD. A strong association between CHD and COPD has been widely evaluated. COPD is an independent risk factor for CHD and, conversely, CHD is associated with the diagnosis and severity of COPD [4].

Metabolic syndrome is another common comorbidity of COPD. The prevalence of metabolic syndrome has been reported to be 20% to 50% in people with COPD [5,6].

The circulating CRP levels are associated with an increased mortality in COPD. CRP is found to be inversely associated with the FEV1 %, which is predicted in stable COPD. C-Reactive Protein (C-RP) is considered as a marker of systemic inflammation and this is also assessed for the primary stratification of the general population for the risk of CVD [7,8].

Dyslipidemia, a major risk factor for CHD and metabolic syndrome, is characterized by a cluster of lipid abnormalities such as an elevated level of triglyceride (TG), a reduced level of high-density lipoprotein cholesterol (HDL) and an increased level of low-density lipoprotein cholesterol (LDL). A number of studies have evaluated the relationship between COPD and blood lipid profiles with inconsistent results.

The objective of the present study was to investigate the association between COPD serum C-RP levels & the serum levels of HDL, LDL, total cholesterol (TC), and TG.

### Methods

This study was the duration based case control study for a period of one year conducted on 40 patients with clinically confirmed chronic obstructive pulmonary disease visiting departments of Medicine, Chest and TB at Vydehi Institute of Medical Sciences & Research Centre, Bengaluru and 40 age/sex matched healthy

male/female as a controls visiting the hospital for routine health check-up and also hospital staff members included, with approval of Institutional Ethical Committee. Informed consent was taken both from cases and control. Demographic histories such as age, sex and smoking so on were recorded. Cases had FEV1/FVC <70% and FEV1<80% predicted in their spirometry and asthma was ruled out in them by assessing their clinical history and response to bronchodilators (less than 12% increase in FEV1 after inhaling salbutamol 400>g). After detailed clinical history blood was collected from both cases and controls. Patients suffering from alcoholic, autoimmune, liver, kidney, malignant disorders, bronchial asthma, bronchiectasis, cardiovascular diseases, diabetes mellitus, pleural effusion, pulmonary tuberculosis, osteoarthritis, Patients on medications like steroids and antioxidants are excluded. 5 ml of blood from each of the mentioned subjects was collected from median cubital vein by venipuncture avoiding hemolysis into an evacuated vacuum

tube. The samples were aliquoted and kept at - 20° C until analysis was done. C-RP was measured by Nephelometrically using (IMMAGE 800) (Serum <0.75mg/dL).lipid profile analysed by DXC 860I Beckman analyser. Body mass index is calculated weight in kg divided by square of height in meters. They were further classified as per Indian Council for Medical Research classification.

Underweight <18, normal 18-23, overweight 23-25, obese >25. The data were expressed as mean±SD. Student t test (two tailed, independent) has been used to find the significant mean difference of study parameters between control and COPD patients. Results were analysed statistically by One-way ANOVA (Analysis Of Variance) using standard statistical software package of social science (SPSS) version 20. The difference was considered significant if p <0.05. Pearson's correlation has been used to find the strength of relationship between the proportion of study features and the associated parameters.

### Results

The mean age in controls was 48.03±11.30 and in cases it is 53.43±9.64, the difference in age is not statistically significant (p<0.127). There were 70% of males and 30% of females in controls and in cases 82.5% of them are males, 17.5% of them are females with p=0.189. In our study the C-RP values are significantly higher in COPD patients (3.26±2.0 mg/dL) compared to controls (0.48±0.38mg/dl).

TBMI also found high in COPD patients (29.5 ± 3.6 kg/m<sup>2</sup>) than controls (19.95±3.17kg/m<sup>2</sup>)

**Table 1: comparison of gender in cases and control**

Gender	Controls		Cases	
	No	%	No	%
Male	28	70.0	33	82.5
Female	12	30.0	7	17.5
Total	40	100.0	40	100.0

Samples are gender matched with p=0.189

70% of males and 30% of females in controls. In cases 82.5% of them are males, 17.5% of them are females. Thus Samples are gender matched with p=0.189

**Table 2: comparison of BMI in cases and control**

	Controls	Cases
Male	19.95±3.17	24.5 ± 3.6
Female	20.56 ±3.4	29.5 ±4.5

**Table 3: Comparison of pulmonary function test between case and control groups.**

Pulmonary function test			
Variable	control	cases	p value
FEV1 (l)	52.4 ± 4.36	40.2 ± 5.2	0.001*
FVC (l)	64.8 ± 10.1	50.2 ± 9.9	0.001*
FEV1/FVC (%)	90.8 ± 9.4	76.3 ± 11.1	0.001*

**Table 4: Comparison of lipid parameters between case and control groups.**

	case	control	P value
Cholesterol mg/dl	257.30±56.39	188.58±39.59	<0.001**
Triglycerides mg/dl	253.18±58.98	112.56±55.44	<0.001**
HDL mg/dl	30.98±5.21	42.65±6.55	<0.001**
LDL mg/dl	191.17±86.17	98.74±28.30	<0.001**
VLDL mg/dl	51.31±11.79	31.59±11.56	<0.001**
L/H Ratio	6.59±1.52	3.98±1.84	<0.001**
C-reactive protein (mg/dl)	0.48±0.38	3.39±1.31	<0.001**

**Inference:** Total cholesterol, triglyceride, LDL, VLDL, L/H ratio elevated in cases compared to control. HDL levels decreased in cases than control. Elevated C-reactive protein (>0.75mg/dl) is significantly more in Cases compared to Controls with p<0.001\*\*: That is highly statistically significant.

**Table 5: Pearson correlation of C-RP and Lipid profile in cases.**

Lipid parameters	r value	Correlations	p value	Significance
C-RP /Cholesterol mg/dl	0.6445	Positive	0.001	<0.001**
C-RP /Triglycerides mg/dl	0.5426	Positive	0.001	<0.001**
C-RP /HDL mg/dl	-0.4965	Negative	0.003	<0.001**
C-RP /LDL mg/dl	0.3584	Positive	0.002	<0.001**
C-RP /VLDL mg/dl	0.2245	positive	0.05	<0.10
L/H RATIO	0.3416	positive	0.002	<0.001**
C-RP/ FEV1	-0.3965	Negative	0.003	<0.001**

Inferences: C-RP and total cholesterol triglyceride, LDL, L/H ratio showed positive correlation and C-RP and HDL Showed negative correlation with cases of COPD, which is statistically significant

#### Discussion:

Chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD) frequently occur together and their coexistence is associated with worse outcomes than either condition alone. Pathophysiological links between COPD and CVD include lung hyperinflation, systemic inflammation and COPD exacerbation. Therefore, the novel COPD definition perceives COPD as the pulmonary component of systematic endothelial disease whereby various inflammatory processes simultaneously affect multiple organs causing multi morbidity.

Low dose of short-term corticosteroids [9] as well as oxidative stress caused by cigarette smoking [10] have been proven to affect plasma lipid values in COPD patients

Lipid profile is usually acknowledged as a good predictor for cardiovascular disease. High blood cholesterol and high triglycerides are part of metabolic syndrome and can be caused by medical conditions or bad dietary habits Mitra, et al.[11] found significantly high serum levels of all lipoproteins TC, TG, LDL in COPD cases than controls. HDL levels were also significantly decreased in cases than controls. In our study total cholesterol and Triglyceride levels were significantly high well correlated with serum C-RP and Body Mass Index (BMI) and Increase in BMI may increase triglyceride levels in COPD patients. Our result consistent with their study

Attaran D, et al. evaluated the serum lipid profile in chemical warfare patients with COPD and found statistical difference in cholesterol and triglyceride levels between patients and controls but none of the lipid parameter showed any correlation with severity of airflow limitation assessed by FEV1.[12] Our result consistent with their study.

Beti Zafirova-Ivanovska and colleagues reported that hypercholesterolemia in COPD patients significantly increases with disease severity [13]. Overall, a definitive demonstration of dyslipidemia in COPD and its association with disease severity remains uncertain.

However, in our study lipid levels, C-RP were elevated in COPD compared to controls but were abnormally high. These observations reveals that etiological factors for COPD might contribute for cardiovascular complications in patients with COPD. Cigarette smoking is markedly the most important etiological factor for COPD which disarranges lipid parameters.[14,15]

#### In conclusion,

COPD is considered as a chronic systemic disease according to much concomitant comorbidity in patients. These comorbidities will have significantly impact on patient outcomes and hospitalization. Evidence for this approach has been provided by strong associations with increased rates especially with cardiovascular diseases, metabolic syndrome, anemia, musculoskeletal disease and pulmonary malignancies. A number of studies have shown a high connectivity between COPD and cardiovascular morbidity and mortality and pulmonary embolism.

Hypercholesterolemia probably is hugely responsible for those events which we proved in our study.

### Acknowledgements

Authors gratefully acknowledge the HOD and other teaching staff of Biochemistry department of Vydehi Institute of Medical Sciences and Research Centre, White Field, Bangalore, for their kind support throughout the study.

Funding: No funding sources

Ethical approval: The study was approved by the Institutional Ethics Committee

### References

- Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*. 2007;370:765–73.
- Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2013;187:347–65
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006;3:e442.
- Williams MC, Murchison JT, Edwards LD, Agusti A, Bakke P, Calverley PM, et al. Coronary artery calcification is increased in patients with COPD and associated with increased morbidity and mortality. *Thorax*. 2014;69:718–723. doi: 10.1136/thoraxjnl-2012-203151.
- Lam KB, Jordan RE, Jiang CQ, Thomas GN, Miller MR, Zhang WS, et al. Airflow obstruction and metabolic syndrome: the Guangzhou Biobank Cohort Study. *Eur Respir J*. 2010;35:317–323.
- Park SK, Larson JL. The relationship between physical activity and metabolic syndrome in people with chronic obstructive pulmonary disease. *J Cardiovasc Nurs*. 2014;29:499–507.
- Man SFP, Connett JE, Anthonisen NR, Wise RA, Tashkin DP, Sin DD. C reactive protein and mortality in mild to moderate chronic obstructive pulmonary disease. *Thorax [Internet]*. *BMJ Group*. 2006;61(10):849–53.
- Ridker PM. High-Sensitivity C-Reactive Protein: Potential Adjunct for Global Risk Assessment in the Primary Prevention of Cardiovascular Disease. *Circulation [Internet]* 2001 Apr 3 [cited 2012 Oct 17];103(13):1813–8.
- W.H. Ettinger, H.F. Klinefelter, P.O. Kwiterovitch Effect of short-term, low-dose corticosteroids on plasma lipoprotein lipids *Atherosclerosis*, 63 (1987), pp. 167-172
- U. Can, F.H. Yerlikaya, S. Yosunkaya Role of oxidative stress and serum lipid levels in stable chronic obstructive pulmonary disease *J Chin Med Assoc*, 78 (12) (2015 Dec), pp. 702-708
- Ritabrata Mitra, Subinay Datta, Mrinal Pal, Kaushik Ghosh, Debajoity Paul, et al. (2015) Lipid profile status in chronic obstructive pulmonary disease and association with interleukin 8. *British Journal of Medicine & Medical Research* 9: 1-7.
- Attaran D, Towhidi M, M Lari Sh, Ayatollahi H, Asadi A, et al. (2014) Lipid Profile Status in Mustard Lung Patients and Its Relation to Severity of Airflow Obstruction. *J Cardiothorac Med* 2: 113-117.
- Zafirova-Ivanovska B, Stojkovicj J, Dokikj D, Anastasova S, Debresliovska A, et al. (2016) The level of cholesterol in COPD patients with severe and very severe stage of the disease. *Open Access Maced J Med Sci* 4: 277-282.
- Doll R, Peto R (1976) Mortality in relation to smoking: 20 years' observation on British doctors. *Br Med J* 2: 1525-1536.
- Wendy Y Craig, Glenn E Palomaki, James E Haddow (1989) Cigarette smoking and serum lipid and lipoprotein concentrations: an analysis of published data. *BMJ* 298: 784-788.