Original Article

The Role of High Sensitivity C-reactive Protein and Lipoprotein (a) in Chronic Obstructive Pulmonary Disease Cases as Severity and Early Atherogenic Markers

Thivyah Prabha AG[1], Synthia A[2], Rasheed Khan M[3], Gokul Kumar[4]

Abstract

Background : Chronic Obstructive Pulmonary Disease (COPD) is considered as a risk factor for atherosclerosis and a leading cause of mortality due to cardiovascular disease. The progression of atherogenic events in chronic obstructive disease patients is not due to the smoking and other cardio vascular risk factors. Lipoprotein (a) measures the hypercoagulable status.

Aims and Objectives : To evaluate the levels of High Sensitivity C-reactive Protein (hs-CRP) and Lipoprotein (a) in chronic Obstructive Pulmonary Disease patients and to find the role of them in the atherogenesis of COPD patients.

Materials and Methods : This Case control study was conducted in the Chennai Medical College hospital and research centre during January, 2014 - December, 2014. Eighty cases of COPD diagnosed by spirometry were included in the study and classified by GOLD staging. After informed consent, blood samples were collected and analysed for hsCRP and Lipoprotein (a) levels.

Results : There was a statistically significant elevation of hsCRP among cases and a positive correlation was observed among the severity of disease, obese individuals and smokers. In COPD patients Lipoprotein [a] levels were increased.

Conclusion : In COPD patients , hsCRP may be used as a marker for the disease severity and prognosis. Lipoprotein [a] may be used as an auxiliary marker for the prediction of risk of atherosclerosis among COPD patients for early intervention.

Key words : Lipoprotein (a), Chronic Obstructive Pulmonary Disease, High Sensitive C-reactive Protein, Atherogenetic Markers.

Chronic Obstructive Pulmonary Disease (COPD) is a Chronic Respiratory Disease characterized by progressive airflow limitation which is poorly reversible and often associated with systemic manifestations. Although COPD is a complex, heterogenous condition, it can be prevented as well as treated if identified earlier. Accounting for more than 3 million deaths worldwide in 2019, it is one of the leading causes of mortality as well as morbidity especially in low- and middle-income countries in patients under 70 years of age[1,2]. COPD patients have a significant systemic inflammation which can be identified by the elevated levels of a potential biomarker called high sensitivity C-reactive Protein (hs-CRP). With the recent advances in the methods used for measuring the elevated biomarkers in COPD patients we will be able to identify even low levels of hs-CRP. Systemic inflammation occurring in COPD patients leads to a hypercoagulable state with increased risk of atherogenesis even after the exclusion of smoking and other cardiovascular risk factors from the affected patients. This hypercoagulable state and atherogenesis in COPD patients can be identified using the marker Lipoprotein(a).

Editor's Comment :

- High-sensitivity C-reactive protein (hs-CRP) reflects systemic inflammation in Chronic Obstructive Pulmonary Disease (COPD) and correlates with disease severity, frequent exacerbations and declining lung function.
- Elevated Lipoprotein(a) [Lp(a)] acts as an independent early atherogenic marker, contributing to increased cardiovascular risk in COPD patients.
- Together, hs-CRP and Lp(a) serve as valuable biomarkers to identify high-risk COPD individuals who may benefit from early cardiovascular risk assessment and targeted preventive strategies.

Aims and Objectives

- To estimate the levels of bio markers [hs-CRP and Lipoprotein(a)] in COPD patients.
- To assess the correlation of hs-CRP with the severity of the disease and Lipoprotein(a) with the risk of atherosclerotic disease in COPD patients.
- To find out the association between the biomarkers and Socio-demographic variables

such as Age, Sex, BMI and smoking habits in COPD patients.

[1]MD, Associate Professor, Department of Biochemistry, St Peter's Medical College, Hospital and Research Institute, Hosur, Tamilnadu 635130 and Corresponding Author
[2]MD, Assistant Professor, Department of Biochemistry, KAP Viswanatham Government Medical College, Tiruchirappalli, Tamil Nadu 620001
[3]MD, Associate Professor, Department of Biochemistry, Srinivasan Medical College and Hospital, Tiruchirappalli, Tamil Nadu 621112
[4]MD, Asssociate Professor, Department of Community Medicine, St Peter's Medical College, Hospital and Research Institute, Hosur, Tamilnadu 635130

Received on : 28/10/2024
Accepted on : 20/03/2025

How to cite this article : The Role of High Sensitivity C-Reactive Protein and Lipoprotein (a) in Chronic Obstructive Pulmonary Disease Cases as Severity and Early Atherogenic Markers. Thivyah Prabha AG, Synthia A, Khan MR, Kumar G. *J Indian Med Assoc* 2026; **124(3):** 34-6.

Materials and Methods

This was a case-control study conducted by the Department of Biochemistry, Chennai Medical College Hospital and Research Centre for a duration of one year from January, 2014 to December, 2014. The study included 80 COPD patients and out of those 80 patients, 50 were Cases and remaining 30 are Controls. We used GOLD criteria to diagnose the COPD patients by Spirometry. Those patients having other co-morbidities like acute infections, bronchial asthma, inflammatory diseases, connective tissue disorders, disorders of thyroid, malignancy, renal failure (acute and chronic), stroke and diabetic ketoacidosis were not included in the study. After obtaining the necessary approval from the Institutional Ethical Committee, all the study participants were explained the purpose of the study, procedures involved and assured regarding the confidentiality of their results. Written informed consent was obtained from all the patients included in the study. About 5ml of venous blood was collected from each patient and centrifuged at 3500 rpm for a duration of 10 minutes at -20ºC, serum samples were stored and used for analysis. Immuno-turbidimetry was used for analysing the serum samples for both high sensitivity C-reactive protein and Lipoprotein(a). Serum total cholesterol estimation was carried out using Enzymatic cholesterolesterase method, Colorimetric Enzymatic method GPO was used for serum triglycerides and Phosphotungtistic acid method was used for estimation of serum High density Lipoprotein. Statistical analysis of data was done by calculating mean, Standard Deviation, p-value by applying student 't' test, ANOVA and Bonferroni.

Observation and Results

The mean age of the patients was around 60 years and in the Control group it was around 45 years and this difference was found to be statistically significant ($p<0.05$). Males and females were equally distributed between the Case and Control groups. Among the Cases, patients were equally distributed in all four stages of the Spirometry. About 54% of the cases have of BMI within the normal range and the remaining 44% were either Overweight or Obese. We used ANOVA test to identify the difference in the mean BMI levels of four groups according to the Spirometry staging. Among the cases, 80% of them had COPD for more than 10 years and 16% have COPD for more than 20 years. The duration of addiction was more than ten years among the smokers in Cases group. The mean pack years was used as a measure for estimation of the magnitude of smoking. The mean smoking pack years was significantly increased in stage 4 and vice versa and was correlating with the disease severity. The mean hsCRP levels in Cases was 12.66 mg/L and in Controls was 3.5 mg/L and it was statistically significant. ANOVA test was used to study the statistical significance in the mean hsCRP between the four groups. There was a statistically significant ($p<0.005$) difference in mean hsCRP levels in different stages of COPD as per the Bonferroni test. The mean hsCRP levels change with the severity of the disease. The mean Lipoprotein (a) levels were 211mg/dl in Cases group and 143 mg/dl in Control group. There was statistical significance among the Lipoprotein (a) value of cases and controls. There was no statistical significance in the Lipoprotein (a) value of different stages, as the data was analysed by ANOVA test. Lipid parameters were high in Cases as compared to the Controls and the difference in the mean levels of Lipid parameters were significant except Low Density Lipoprotein (LDL) and Total cholesterol levels. The increase in hs CRP levels in serum were correlating with the BMI levels and the increase was in the same direction. The correlation between High Density Lipoprotein (HDL) and Body Mass Index (BMI) was in opposite direction and negative correlation was seen. Statistically no significance was observed between the disease duration, hs-CRP, Lp(a) and lipid profile. The Odd ratio was statistically significant and the risk of COPD increased by 14% as the age increases by one unit and the correction of other variables have been done in the model. For each unit increase of hs-CRP in the serum, the COPD risk will increase by 25% after adjusting the other variables. For each unit increase of Lp (a) in the serum, the COPD risk will increase by 7% after adjusting the other variables. Odds ratio was not statistically significant for the females in the Cases group as compared to the Control group even though the females were having high risk. In 62.5% of variability was explained by the Nagelkerke's pseudo-R square in the possibility of occurrence of COPD. Statistically significant correlation in positive direction was present between the serum Lipoprotein (a) levels and Total cholesterol levels in serum (Tables 1-3).

Discussion

Chronic Obstructive Pulmonary Disease is the leading cause of morbidity and mortality among the major public health problems. To understand and control the disease progression, biomarkers implicating severity and atherogenesis are needed. The biomarker of low grade systemic inflammation is hs-CRP[3]. The levels of hs-CRP

Table 1 — *Distribution of the cases according to Spirometry staging and smoking as continuous variable (in pack-years) (n=50)*

Spirometry staging	N	Mean smoking pack-years	STD Deviation	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
Stage I	13	11.81	9.2478	6.219	17.396
Stage II	14	12.11	12.6691	4.792	19.422
Stage III	13	15.42	15.1215	6.285	24.561
Stage IV	10	29.95	11.2779	21.882	38.018
Total	50	16.46	13.8372	12.528	20.392

Table 2 — *Correlation matrix between BMI, serum markers and Lipid parameters among cases (n=50)*

	BMI	hs-CRPmg/L	Lp(a)mg/L	Total Cholesterol mg/dl	Triglycerides mg/dl	HDL-Cmg/dl	LDL-Cmg/dl	VLDL-Cmg/dl
BMI	1	0.640**	-0.40	-0.191	-0.224	-0.311*	-0.068	-0.224

Table 3 — *Correlation matrix between disease duration, serum markers and Lipid parameters among cases (n=50)*

	Disease duration	hs-CRPmg/L	Lp(a)mg/L	Total Cholesterol mg/dl	Triglycerides mg/dl	HDL-Cmg/dl	LDL-Cmg/dl	VLDL-Cmg/dl
Disease duration	1	0.099	0.098	0.073	0.013	0.0111	0.047	0.013

among the cases were (12.66 ± 3.92) and its significantly higher than the control group (3.5 ± 1.57) and the p=0.001. Similar observations were found in a study by Lisatileman, Lena Ginder, *et al*[4] and Sanjamarevic, *et al*[5]. The correlation between the levels of hs CRP and disease severity and stages of the disease (as gold criteria) was shown by Tahia H Saleem, *et al*[3] and SA Alavi, *et al*[6] In our study the levels of hs CRP were significantly elevated among the smokers and it was even correlating with the packyears and the same was observed in a study by SA Alavi, *et al*[6] Yannick MTA, *et al*[7] and Rehuaarwal, *et al*[8]. Studies by SA Alavi, *et al*[6], Breyer MK, *et al*[9] and PO Bridevaux, *et al*[10] have shown there is significant correlation between the increase of hs-CRP levels and BMI levels and the same was observed in our study also. But no correlation was observed between the hs-CRP levels and disease duration, in a study done by Daianatolz, *et al*[11] among 100 patients for a period of >1 year. Significant negative correlation was observed between HDL and hs-CRP in this present study. In developed countries Cardiovascular diseases are the potent killers among the COPD patients. The cardiovascular risk is high in COPD cases as there is basic underlying chronic inflammation of lung with systemic features also. Moreover Cardiovascular diseases are causing more deaths among the COPD patients[12]. Lipoprotein (a) is the important and sensitive risk factor for Coronary Artery Diseases in COPD patients[10]. The mortality and morbidity is increased due to the changes in the Lipoprotein metabolism and hence the increased Cardiovascular risk[13]. Thus the Lipid parameter abnormalities are highly important. The 20 year follow-up study of ARIC cohort among the African Americans and Caucasians have found that Lp (a) are associated with similar degree of cardiovascular risk[14]. The role of Lipoprotein (a) as an independent risk factor for Coronary Heart Disease has been shown in the meta-analysis by the Emerging Risk factors collaboration evaluation with 126,634 subjects of 36 prospective studies. In contrast to previous studies that suggested Lp(a) was only relevant as a risk factor when levels were extremely elevated, the meta-analysis demonstrated that risk and that Lp(a) levels are continuously associated with CHD risk[15].

Conclusion

hs-CRP is a biomarker for indicating the progression and severity of disease in COPD patients and for initiating the preventive and therapeutic strategies for the patients. Lipoprotein (a) is an auxillary marker to predict the risk of atherosclerosis in COPD patients.

Funding : None.

Conflict of Interest : None.

References

1 Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. [Updated 2016]. Available from: https://goldcoped.org/.
2 WHO Fact sheet: the top 10 causes of death dated 24 May 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/thetop-10-causes-of-death. Accessed May 14, 2019.
3 Saleem TH, Manal AM, Mandour — High Sensitivity C- Reactive Protein as a biomarker for Chronic Obstructive Pulmonary Disease. *AAMJ* 2011; **9:** 36-46.
4 LisaT, LenaGindner, Franz M — Differences in Local And Systemic Inflammatory Markers in patients with Obstructive Airway Disease. *Prim Care Respir J* 2011; **20(4):** 407-13.
5 Marevic S, Vrkic N, Sanja P, Ivana C — TNF Alpha, CXCL8 And Hs CRP In COPD Patients. *Croatica Chemical ACTA CCACAA* 2008; **81(1):** 211-7.
6 Alavi SA, Soati F, Amani H, Forghanparast K — Hs CRP in patients with Acute Exacerbation Of COPD. *Iranian Red Crescent Medical Journal* 2011; **13(10):** 713-18.
7 Yannick M, VanDurme T, Guy G, Bruslee, Bruno HC, Stricker — CRP Levels Haplotypes And The Risk Of Incident COPD. *Am J Respir Crit Care Med* 2009; 375-82.
8 Agarwal R, ShoaibZaheer M — The Relationship between C-Reactive Protein and prognostic factors in Chronic Obstructive Pulmonary Disease. *Multidisciplinary Respiratory Medicine* 2013; **(8):** 63.1-5.
9 Breyer MK, Spruit MA, Celis AP — Highly Elevated CRP Levels In Obese Patients With COPD. *Clin Nutr* 2009; **28:** 642-7.
10 Bridevaux PO, Wgerbase M, Cschindler — Sex specific effect of body Weight Gain On Systemic Inflammation in subjects with COPD: Results from the SAPALDIA Cohort Study 2. *European Respiratory Journal* 2009; **34:** 332-9.
11 Stolz D, Christ M, Crain, Joachim SBM, Michael T — Copeptin, CRP, Procalcitonin as Prognostic Biomarkers in Acute Exacerbation Of COPD. *Chest* 2007; **131:** 1058-67.
12 Maclay JD, MacNee W — Cardiovascular Disease in COPD. *CHEST* 2013; **143(3):** 798-807.
13 Begum K, Begum MK, Sarker ZH, Dewan MRK — Lipid Profile Status of Chronic Obstructive Pulmonary Disease in Hospitalized Patients. *Bangladesh J Med Biochem* 2010; **3(2):** 42-5.
14 Virani SS, Brautbar A, Davis BC, Nambi V, Hoogeveen RC, Sharrett AR, *et al* — Associations between lipoprotein(a) levels and cardiovascular outcomes in black and white subjects: the Atherosclerosis Risk in Communities (ARIC) Study. *Circulation* 2012; **125:** 241-9.
15 Erqou S, Kaptoge S, Perry PL, Di Angelantonio E, Thompson A, White IR, *et al* — Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. *JAMA* 2009; 302: 412-23.