

STUDY OF LIPID PROFILE AND ATHEROGENIC INDEX IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

DURAIN FATIMA^{1*}, SURYA TIWARI², PRAVIN S GOWARDIPE³, SADAWARTE SK¹

¹Assistant Professor, Department of Physiology, People's College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh, India. ²Assistant Professor, Department of Biochemistry, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India. ³Assistant Professor, Department of Physiology, Chirayu Medical College and Hospital, Bhopal, Madhya Pradesh, India. Email: drdurainfatima@gmail.com

Received: 01 September 2022, Revised and Accepted: 20 November 2022

ABSTRACT

Objectives: The present study's design investigated the lipid parameters level and atherogenic index in atherosclerosis and cardiovascular disease risk development in chronic obstructive pulmonary disease patients.

Methods: The study consists of 108 clinically diagnosed and confirmed spirometry-stable chronic obstructive pulmonary disease (COPD) patients (Mild, Moderate, and Severe), and the controls were 36 healthy individuals of the same age and sex. Blood samples were collected and the lipid profile was done. The atherogenic index of all COPD patients was calculated using the values of lipid parameters.

Results: The observation revealed that as compared to the control group, total cholesterol, triglycerides, low-density lipoproteins, and very low density lipoproteins were significantly ($p < 0.001$) raised in all the COPD sub-groups, and high-density lipoproteins levels showed significantly ($p < 0.001$) decreasing levels in all COPD groups as compared to controls. The COPD sub-group has a higher atherogenic risk ($p < 0.001$) than controls.

Conclusion: In COPD patients with dyslipidemia, there is an increased atherogenic risk, which predicts future cardiovascular risk.

Keywords: Chronic obstructive pulmonary disease, Lipid, Atherogenic index, Atherosclerosis.

© 2022 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2022v15i12.46238>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a main cause of disability and death worldwide. It is a major public health problem requiring management from the primary health-care level onward [1]. The main characteristics of COPD are irreversible, progressive, and persistent airflow limitation accompanied by shortness of breath, cough, and expectoration caused by significant exposure to air pollutants [2]. According to the World Health Organization, about 210 million people worldwide have COPD. COPD stands fifth among the major causes of death occurring due to health problems globally. COPD will achieve the third major cause of mortality in the world by 2030 [3,4].

COPD is a robust independent risk factor for ischemic heart disease and cardiovascular mortality. Atherosclerosis and cardiovascular events are the second leading cause of mortality in mild-to-moderate COPD [5]. Dyslipidemia is important because of the role of altered lipoproteins in atherogenesis and as a clinically major risk factor for cardiovascular disease (CVD). COPD patients with dyslipidemia carry a greater risk of developing ischemic heart disease [5].

Acute adverse cardiovascular events were observed during AECOPD, resulting in the rupture of atherosclerotic plaque [6]. The atherogenic index is a strong marker for predicting the risk of coronary artery disease [7]. The atherogenic index is a novel marker for atherosclerosis [8,9]. It is a logarithmically transformed ratio of molar concentrations of triglycerides (TG) to HDL-C [10-12]. With this background in mind, this study was planned to measure the lipid profile and calculation of the atherogenic index to assess the atherogenic risk in COPD patients.

METHODS

The present case-control study was conducted in Department of Physiology in collaboration with Department of Respiratory Medicine and Department of Biochemistry of Chirayu Medical College and

Hospital Bhopal. A sample size of 108 clinically diagnosed stable COPD patients from the Respiratory Department OPD and confirmed with spirometry based on post-bronchodilator FEV₁ in a patient with FEV₁/FVC <0.70, as per ATS/ERS, lung function testing were included [13] in the study. Each participant gave written informed consent. Patients with no history of exacerbations from the past 2 months are considered stable COPD cases. The patients were subdivided into three groups (36 Mild COPD, 36 Moderate COPD, and 36 Severe COPD) as per GOLD criteria [14]. A total of 36 healthy individuals of the same age and sex as controls. History of present and past illnesses relevant to the research protocol, family history, history of addiction, drug history, history of any surgery, and anthropometric measurements were included in the study. The Institutional Ethical Committee approved the study.

Inclusion criteria: COPD patients

The following criteria were included in the study:

1. Clinically diagnosed and spirometrically confirmed (as per ATS/ERS standardization) stable patients of COPD with post-bronchodilator irreversibility with FEV₁/FVC ratio <0.70 without exacerbations (2 months before the present study) and categorized as per GOLD criteria
2. Patients not receiving treatment for any known cardiovascular, metabolic, neurological, musculoskeletal, endocrinal, and respiratory disorder other than COPD.

Exclusion criteria: COPD patient

The following criteria were excluded from the study:

1. Patients suffering from a respiratory disease other than COPD, any cardiovascular, neurological, endocrinal, and musculoskeletal disorders to the extent that may affect respiratory functions as confirmed by the treating physician
2. Patients belonged to very severe COPD
3. Patients on hypolipidemic drugs.

Table 1: Baseline characteristics of the study population

Variables	Control group (n=36) (Mean±SD)	Mild COPD group (n=36) (Mean±SD)	Moderate COPD group (n=36) (Mean±SD)	Severe COPD group (n=36) (Mean±SD)
Age (years)	52.23±4.81	50.02±5.78	49.37±5.48	50.53±5.99
Height	178.41±6.87	178.44±6.81	177.85±6.86	178.50±6.42
Weight	62.48±8.45	62.13±10.48	64.05±10.46	58.00±10.59
BMI (kg/m ²)	24.77±1.63	25.99±1.92	24.70±3.79	26.85±4.72
Pulse	84.59±10.48	84.00±11.10	83.85±8.05	81.59±9.68
RR	12.59±2.05	14.41±2.29	15.72±3.32	18.21±3.96
SBP	115.02±4.00	128.61±9.90	129.95±8.47	132.52±8.95
DBP	75.70±4.03	83.66±6.22	83.70±5.44	81.78±15.66

COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Lipid parameters in the study population

Lipid parameters (mg/dl)	Controls n=36 (mean±SD)	MILD COPD group n=36 (mean±SD)	Moderate COPD group n=36 (mean±SD)	Severe COPD group n=36 (mean±SD)	p-value
Total Cholesterol	171.11±18.11	191.72±27.96	207.07±46.32	220.34±61.44	<0.001
Triglycerides	118.22±31.48	130.19±42.77	163.70±74.34	222.12±116.18	<0.001
High-density lipoprotein	71.22±11.13	60.11±18.67	55.95±24.03	44.78±21.39	<0.001
Low-density lipoprotein	83.41±16.14	105.57±37.47	118.39±55.24	131.14±58.91	<0.001
Very low-density lipoprotein	26.31±7.13	26.04±8.55	32.62±15.83	45.90±25.38	<0.001

COPD: Chronic obstructive pulmonary disease

Table 3: Atherogenic index in the study population

Study groups	Atherogenic index (Mean±SD)	p-value
Control (n=36)	-0.09±0.09	p=0.26
Mild COPD (n=36)	0.02±0.27	<0.001
Moderate COPD (n=36)	0.15±0.37	
Severe COPD (n=36)	0.33±0.42	

COPD: Chronic obstructive pulmonary disease

Observations in Table 2 revealed that as compared to the control group, TC, TG, LDLs, and very low-density lipoproteins were raised in all the COPD sub-groups (p<0.001) as compared to controls. HDLs levels (p<0.001) showed decreased levels with increased disease severity compared to controls.

Table 3 showed all the COPD subgroups had a higher atherogenic risk (p<0.001) compared to controls. The COPD sub-group had a higher atherogenic risk (p<0.001) compared to the control group.

DISCUSSION

Characterization of COPD not only by the airflow limitation and abnormal chronic inflammatory responses of the lung tissue but serious systemic consequences and coexisting diseases such as CVD, metabolic syndrome, diabetes mellitus, and psychological disorders [22-25]. Recent evidence suggests that alteration in major lipid metabolic pathways contributes to the pathogenesis of lung disease, including COPD [26-28]. Lipids play a major role in host inflammatory response by generating lipid mediators that regulate inflammation [29].

The observations of the present study revealed that all the lipid fractions in mild, moderate, and severe COPD raised as compared to the control group. The values of HDL cholesterol in mild COPD, moderate COPD, and severe COPD showed a decreasing trend with increasing severity of COPD compared to the control group (p≤0.001). The present study's findings agreed with the study conducted by Markelic *et al.* [30] and Jha *et al.* [31]. Both COPD and CVD share common risk factors and pathological processes. The most critical risk factor identified for both conditions is smoking, environmental pollution, a sedentary lifestyle, and the coexistence of non-communicable diseases such as diabetes and hypertension.

Lung function impairment might be a risk factor for cardiovascular ailment (CVD) events. Studies have reported reduced FEV1 nearly double the risk of cardiovascular mortality [33,34].

The atherogenic index has to be a strong marker for predicting the risk of coronary artery disease [7]. The present study showed that the COPD sub-group had higher atherogenic risk (p≤0.001) than controls. Similar findings were also reported by Sharma *et al.* [35] Markelic *et al.* [30]. They also found statistically significant difference in AIP between GOLD Stage 4 patients (-0.182±0.254) and in controls (-0.005±0.269)

Inclusion criteria: Controls

1. Healthy asymptomatic individuals with no history of chronic respiratory, endocrinal, metabolic, cardiovascular, neurological, and musculoskeletal disorders
2. Spirometric parameters within normal limits as per ATS/ERS standardization [13] and GOLD criteria [14] (FEV1 and FVC above 80% predicted and FEV1/FVC ratio above 0.70).

METHODS

Under aseptic precautions, after obtaining the voluntary written consent of the subjects, 3 mL of blood was collected from the peripheral vein after overnight fasting. The sample was transferred to a plane vial and allowed to clot for 15 min. Centrifugation at 3000 rpm for 10 min separates the serum. Serum was used for estimation of the lipid profile by commercially available kit (COBAS INTEGRA 400/400 plus) using ROCHE COBAS INTEGRA 400 plus analyzer. The following parameters were recorded -total cholesterol (TC) - by enzymatic end point CHOD-POD method [15], TG - by GPO-POD method [16], high-density lipoprotein (HDL) - by direct homogenous method [17], low-density lipoprotein (LDL) - by Freidwald formula [18] [LDL = TC - HDL - (TG/5)], and VLDL-calculated by formula [19] VLDL cholesterol = Triglyceride/5.

Calculation of atherogenic risk - by the formula [12,20,21] $\text{Log}_{10} (\text{TG}/\text{HDL-C})$.

RESULTS

Table 1 displays the demographic and clinical characteristics of the subjects. It includes mean values of age, height, weight, BMI, pulse, respiratory rate, systolic, and diastolic blood pressure in the mild, moderate, and severe COPD group and control group.

($p=0.003$).

CONCLUSION

The observations suggest that lipid abnormality coexists with COPD making these patients more vulnerable to cardiovascular risk. The atherogenic index of plasma is a critical index used for cardiac risk estimation. This index is considered a more useful diagnostic aid than the estimation of lipid parameters alone. Calculating atherogenic risk in COPD patients may prove valuable for improving the quality of life and preventing future extrapulmonary morbidity and mortality.

AUTHORS CONTRIBUTIONS

Dr. S.K. Sadawarte and Dr. Durain Fatima were involved in the study's design and data collection and helped to draft the manuscript. Dr. Surya Tiwari and Dr. Pravin S. Gowardipe were involved in the statistical analysis and manuscript writing. All the authors have read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHORS FUNDING

None.

REFERENCES

- Jindal SK, Gupta D, Aggarwal AN. Guidelines for the management of chronic obstructive pulmonary disease in India: A guide for physician (2003). *Indian J Chest Dis Allied Sci* 2004;46:137-93.
- Van Iwaarden F, Welmers B, Verhoef J, Haagsman HP, Van Golde LM. Pulmonary surfactant protein A enhances the host-defense mechanism of rat alveolar macrophages. *Am J Respir Cell Mol Biol* 1990;12:91-8.
- Mannino DM, Buist AS. Global burden of COPD: Risk factors, prevalence, and future trends. *Lancet* 2007;370:765-73.
- Decramer M, Janssens W, Miravittles M. Chronic obstructive pulmonary disease. *Lancet* 2012;379:1341-51.
- MacLay JD, MacNee W. Cardiovascular disease in COPD: Mechanisms. *Chest* 2013;143:798-807.
- Sin DD, Man SF. Why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular diseases? The potential role of systemic inflammation in chronic obstructive pulmonary disease. *Circulation* 2003;107:1514-9.
- Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, et al. Assessment of coronary artery disease by cardiac computed tomography: A scientific statement from the American Heart Association committee on cardiovascular imaging and intervention, council on cardiovascular radiology and intervention, and a committee on cardiac imaging, council on clinical cardiology. *Circulation* 2006;114:1761-91.
- Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* 2004;291:210-5.
- Pletcher MJ, Tice JA, Pignone M, Browner WS. Using the coronary artery calcium score to predict coronary heart disease events: A systematic review and meta-analysis. *Arch Intern Med* 2004;164:1285-92.
- Niroumand S, Khajedaluae M, Khadem-Rezaiyan M, Abrishami M, Juya M, Khodae G, et al. Atherogenic index of plasma (AIP): A marker of cardiovascular disease. *Med J Islam Repub Iran* 2015;29:240.
- Shen S, Lu Y, Qi H, Li F, Shen Z, Wu L, et al. Association between ideal cardiovascular health and the atherogenic index of plasma. *Medicine (Baltimore)* 2016;95:e3866.
- Dobiášová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: Correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). *Clin Biochem* 2001;34:583-8.
- European Respiratory Society. ATS COPD Guidelines European Respiratory Society. Switzerland: European Respiratory Society; 2005.
- Global Initiative for Chronic Obstructive Lung Disease: Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease 2018 Report.
- Allian CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of Total serum cholesterol 1974;20:470-5.
- Werner M, Gabrielson DG, Eastman J. Ultramicro determination of serum triglyceride by bioluminescent assay. *Clin Chem* 1981;27:268-71.
- Burstein M, Scholnick HR, Morfin R. Rapid method for isolation of lipoproteins from human serum by precipitation with polyanions. *J Lipid Res* 1970;11:583-95.
- Knopfholz J, Disserol CC, Pierin AJ, Schirr FL, Streisky L, Takito LL, et al. Validation of the friedewald formula in patients with metabolic syndrome. *Cholesterol* 2014;2014:261878.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without the use of the preparative ultracentrifuge. *Clin Chem* 1972;18:499-502.
- Frohlich J, Dobiášová M. Fractional esterification rate of cholesterol and ratio of triglycerides to HDL-cholesterol are powerful predictors of positive findings on coronary angiography. *Clin Chem* 2003;49:1873-80.
- Dobiasova M. Atherogenic index of plasma [log (triglycerides/HDL-cholesterol)]: theoretical and practical implications. *Clin Chem* 2004;50:1113-5.
- Fabbri LM, Luppi F, Beghe' B, Rabe KF. Complex chronic comorbidities of COPD. *Eur Respir J* 2008;31:204-12.
- Roversi S, Roversi P, Spadafora G, Rossi R, Fabbri LM. Coronary artery disease concomitant with chronic obstructive pulmonary disease. *Eur J Clin Invest* 2014;44:93-102.
- Corbi G, Bianco A, Turchiarelli V, Cellurale M, Fatica F, Daniele A, et al. Potential mechanisms linking atherosclerosis and increased cardiovascular risk in COPD: Focus on sirtuins. *Int J Mol Sci* 2013;14:12696-713.
- Bellocchia M, Masoero M, Ciuffreda A, Croce S, Vaudano A, Torchio R, et al. Predictors of cardiovascular disease in asthma and chronic obstructive pulmonary disease. *Multidiscip Respir Med* 2013;8:58.
- Alvarado A, Arce I. Metabolic functions of the Lung, disorders and associated pathologies. *J Clin Med Res* 2016;8:689-700.
- Lamonaca P, Prinzi G, Kisialiou A, Cardaci V, Fini M, Russo P. Metabolic disorder in chronic obstructive pulmonary disease (COPD) patients: Towards a personalized approach using marine drug derivatives. *Mar Drugs* 2017;15:81.
- Kilk K, Aug A, Ottas A, Soomets U, Altraja S, Altraja A. Phenotyping of chronic obstructive pulmonary disease based on the integration of metabolomes and clinical characteristics. *Int J Mol Sci* 2018;19:666.
- Yedgar S, Krinsky M, Cohen Y, Flower RJ. Treatment of inflammatory diseases by selective eicosanoid inhibition: A double-edged sword? *Trends Pharmacol Sci* 2007;28:459-64.
- Markelic I, Hlapcic I, Rogic D, Rako I, Samarzija M, Popovic-Grle S, et al. Lipid profile and atherogenic indices in patients with stable chronic obstructive pulmonary disease. *Nutr Metab Cardiovasc Dis* 2021;31:153e161.
- Kumar JR, Mahajan S, Mehta D, Ambad RS, Koundal P. Lipid profile in patients with COPD: A cross-sectional study. *Int J Med Biomed Stud* 2020;4:121-6.
- Andréa S, Conde B, Fragosoc E, Boléo-Tomé JP, Areias V, Cardoso J. COPD and cardiovascular disease. *Pulmonology* 2019;25:168-76.
- Eriksson B, Lindberg A, Müllerova H, Rönmark E, Lundbäck B. Association of heart diseases with COPD and restrictive lung function—results from a population survey. *Respir Med* 2013;107:98-106.
- Johnston AK, Mannino DM, Hagan GW, Davis KJ, Kir VA. Relationship between lung function impairment and incidence or recurrence of a cardiovascular event in a middle-aged cohort. *Thorax* 2008;63:599-605.
- Sharma H, Kapur P, Jalali KR, Dubey K. Atherosclerosis risk assessment in patients with chronic obstructive pulmonary disease: A case-control study. *Ther Clin Risk Manag* 2019;15:1061-71.