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Original Research Paper

Medical Science

CARDIOVASCULAR RISK ASSESSMENT IN PATIENT WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT Coronary artery disease (CAD) is the epidemic of modern civilization in which dyslipidemia contributes significantly to its pathogenesis. Over the last few decades, several risk factors have been found to be associated with CAD like smoking, age, sex, hypertension etc. The aim of present study was exploration of lipid profiles and atherosclerosis indices; atherogenic index, castelli risk index, atherogenic coefficient and their association with Chronic Obstructive pulmonary disease (COPD). COPD is considered as a risk factor for atherosclerosis and causes of morbidity and mortality worldwide due to cardiovascular disease. This study enrolled 108 patients with COPD and 30 age, gender and BMI matched healthy control subjects. Atherogenic indices were calculated by using the values of lipid profile. FVC (L) and FEV1 % predicted were decreased significantly in mild, moderateand severe COPD patient than those of control group.FEV1/FVC % predicted were notably higher in mild, moderate and severe as compared to control group.TC, LDL, VLDL and TG significantly higher and serum HDL levels were significantly lower in COPD than those of control. Atherogenic Indices; Atherogenicindex of plasma, Castelli risk index; CRI, CRII and Atherogenic coefficient were also increase in mild, moderate and severe COPD patients.The control group exhibited no risk. The present study concluded that AIP, CR-I, CR-II and AC considered to be better predictors than conventional lipid parameters for early detection of CVDs in COPD patients. These calculated fractions of atherogenic indices can provide a better value for the determination of cardiovascular diseases risk in the areas where resources and techniques are limited.

KEYWORDS : Atherogenic indices, Lipid Profiles, cardiovascular disease, Smoking

INTRODUCTION

It is now well established that cardiovascular disease contributes significantly to both morbidity and mortality in COPD. Understanding modifiable risk factors for CVD such as smoking, hypertension, diabetes, overweight, and high cholesterol can help to prevent and reduce disease burden. Dyslipidemia is defined as elevated plasma concentration of lipids (triglyceride and total cholesterol) and their related blood-transporting lipoproteins: HDL cholesterol, LDL cholesterol, and VLDL cholesterol.[1,2] Lipid ratios like AIP, CRI, CRII and AC could be used for identifying individuals at higher risk of cardiovascular disease in Indian population in the clinical setting especially when the absolute values of individual lipoproteins seem normal and in individuals with elevated triglyceride concentrations.[3] Many scientists have reported COPD and cardiac co morbidities are frequently linked, they share common risk factors, pathophysiological processes, clinical signs and symptoms, and act synergistically as negative prognostic factors.[4, 5,6] The Present study implemented the relationship of Atherogenic index of plasma, Castelli risk index; CRI, CRII and AC among COPD in order to highlight that lipid profile and atherogenic indices is the early predictor for CVDs. Byperforming this study, we can detect the early cases among COPD and provide advices such as lifestyle changes, increased physical activity, healthy dietand effective drug management.

MATERIAL AND METHODS

Study setup

The present study was conducted in Department of Physiology in collaboration with Dept. of Respiratory Medicine and Biochemistry of Chirayu Medical College and Hospital Bhopal, a tertiary care hospital in Central India. The study was approved by the ethical committee of Chirayu Medical College and Hospital Bhopal (Approval No- ECR/502/Inst/MP/2013/RR-2017). The biochemical investigations were done in Biochemistry laboratory of Central Research Lab of Chirayu Hospital Bhopal.

Study design: Case control study

Sample Size

A sample size of 108 clinically diagnosed and spirometrically confirmed COPD patients (Mild COPD 36, Moderate COPD 40 and Severe COPD 32) and 30 controls were included in the study according to severity as per GOLD criteria.

INCLUSION AND EXCLUSION CRITERIA

Subjects of both genders, age 40 to 60 years were included in the present study. Clinically diagnosed and spirometrically confirmed patients of COPD who gave written voluntary consent to participate in the study. Subjects with Post bronchodilator irreversibility with FEV1/FVC ratio less than 70% were included. COPD patients not on hypolipidemic drugs and steroids. Patients not receiving treatment for any known metabolic, neurological, muscolo skeletal and endocrinal disorder were also included. Patient not willing to give consent were excluded. Patients suffering from respiratory disease other than COPD, any neurological, endocrinal and musculo skeletal disorder to the extent that may affect respiratory functions as confirmed by treating physician were also excluded.

Data Collection

The study included 108; mild 36, moderate 40 and severe 32 COPD patients comprise the case group. Their data with respect to history; history of present and past illness relevant to research protocol, family history, history of addiction, Drug history, past history of any surgery. Anthropometric measurements; weight, height, body mass index were included. The control group includes 30 healthy volunteers visiting the hospital with patient or caretakers during the period.

Pulmonary Function Test and Data Interpretation

The spirometry was done using RMS Helios 702 electronic portable PC based spirometer and following parameters were recorded: Forced Vital Capacity (FVC) (L) Forced expiratory volume (FEV) 1% predicted and FEV1/FVC % predicted. All the

patients were subjected to pre and post bronchodilator spirometric evaluation and were staged as per Global Initiative of Chronic Obstructive Lung Disease (GOLD criteria 2018). According to the severity of airflow limitation based on post-bronchodilator FEV1, patients were classified and parameters recorded as Mild COPD (FEV1>80% of predicted),Moderate COPD (FEV1 50-80% of predicted), Severe COPD (FEV1 30-50% of predicted).

Lipid profile

Under aseptic conditions 2 ml sample of venous blood were collected from subjects in the morning at least 12 hours after the last meal by venipuncture in plain tubes. The samples were allowed to clot at room temperature for at least 30 minutes, then centrifuged at 2500 rpm for 15 minutes at room temperature and plasma is transferred to fresh polypropylene tube and were stored below -20°C. Before performing the assay, samples were brought to room temperature (18 -25°C) and mixed gently. Estimation of lipid profile was done by commercially available kit (COBAS INTEGRA 400/400 plus) using ROCHE COBAS INTEGRA 400 plus analyzer and following parameters were recorded: Total cholesterol (TC) by enzymatic end point CHOD-POD method, [7] Triglycerides (TG) by GPO-POD method,[8] High density lipoprotein (HDL) by direct homogenous method,[9] Low density lipoprotein (LDL) by formula (LDL) = Total Cholesterol – High density lipoprotein –Triglycerides/5 and VLDL calculated by formula VLDL cholesterol = Triglyceride/5.[10]

Calculation of atherogenic index

Atherogenic index has been exhibited to be a strong marker for predicting the risk of Coronary artery disease. The atherogenic index of all COPD patients was calculated using the values of lipid parameters according to the following formulae: Atherogenic Index for Plasma (AIP) = log triglyceride/ high-density lipoprotein cholesterol, Castelli's Risk Index (CRI-I) = TC/HDLc, Castelli's Risk Index (CRI-II) = LDLc/HDLc and Atherogenic Coefficient (AC) = (TC–HDLc)/HDLc with the concentrations in mg/dL.[11,12]

STATISTICAL ANALYSIS

The data is presented as mean± SD. The results obtained were statistically analyzed using GraphPad Prism 5 software (UK). Statistical tests performed were ANOVA. The results were considered significant when the *p*-value was less than 0.005.

RESULTS AND DISCUSSION

In the present study, mild 36, moderate 40, severe 32 COPD and healthy controls 30 were included. Higher risk category of cardiovascular disease has identified COPD subjects; mild 8 (22%), moderate 15(37.5%) and severe 17(53.12%). Lower risk exhibited in COPD subjects; mild 28(77.7%), Moderate 25(62.5%) and severe 15(46.8%). The cases are outlined in table 1. The study subjects had a mean age of mild, moderate and severe were 50.03, 49.38 and 50.53 years respectively, in COPD group and 52.23 years in control group ($p=0.693$). In the current investigation male female ratio mild, moderate and severe COPD patient were exhibited 25:11, 31:9 and 10:6 ($p= 0.37$). It has been reported the COPD is a male governing disease; prevalence of the disease may be high in males because of more smoking in this gender.[13] In the recent study mean value of body mass index mild, moderate and severe COPD patients were 25.99±1.92, 24.79±3.86 and 27.24±4.51 respectively, the control group exhibited 24.77±1.63 of BMI ($p = 0.018$). In the present work smoking status were significantly increased in the COPD group; mild, moderate and severe 20(55.5%), 23(57.5%) and 22(68.7%) respectively ($p<0.001$), as cigarette consumption in cases than control subjects 12(40 %) ($p=0.47$), these results are in collaboration with the extensive work of Jindal et al.[14] where they reported cholesterol, triglycerides, and plasma β-lipoprotein concentration are elevated, and HDL cholesterol is lowered in smokers as compared to non-smokers.

Table: 1 Cardiovascular disease risk percentage in COPD Patient.

Cardiovascular disease Risk %			
Risk category	Higher risk	Mild	08(22%)
		Moderate	15(37.5%)
		Severe	17(53.12%)
	Lower risk	Mild	28(77.7%)
		Moderate	25(62.5%)
		Severe	15(46.8%)

Pulmonary Function Test

In mild COPD patient FVC (L),forced expiratory volume (FEV1) % predicted were exhibited 2.32±0.41and 98.81± 16.34($p<0.001$). While FEV1/FVC% predicted were notably higher (63.29±14.63) ($p<0.001$).In moderate COPD patient, FVC (L), FEV1% predicted were exposed 2.42±0.63 and 63.77±7.68 respectively ($p<0.001$). Although, FEV1/FVC% predicted were notably elevated 77.18±7.83 ($p<0.001$).In severe COPD patient, FVC (L), FEV1% predicted were exposed 1.91±0.38 and 33.44± 6 respectively ($p<0.001$). While, FEV1/FVC% predicted were notably increased83.06±21.17 ($p<0.001$). The control group FVC (L), FEV1 % predicted and FEV1/FVC% predicted exhibited 3.13±0.61, 93.43±18.41and 60.32±9.81 respectively (**Figure1**).

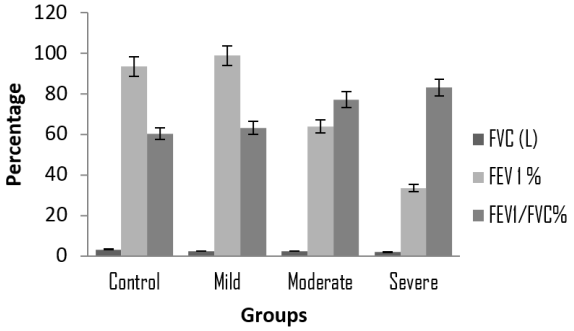

Figure:1 Pulmonary Function Testchronic obstructive pulmonary disease patients and control Group. Values are expressed as Mean±SD (Standard deviation), *p*value ≤ 0.05 is considered statistically significant.

Similar data have been reported by Sharma *et al.* [15] where they had studied that forced vital capacity and atherosclerosis risk assessment in patients with chronic obstructive pulmonary disease.Many researchers have proved that a moderately reduced FEV1, an independent risk factor for CVD, is associated with an increasedincidence of heart failure in older and middle-aged individuals.[16, 17, 18] Previous findings confirmed lower FEV1/FVC % wasassociated with higher risk for COPD exacerbations.[19,20]

Lipid Profile

In this section of experiment, total cholesterol (TC) concentration wereincreased in mild (191.72±27.96), moderate (207.08±46.32) and severe (220.34±61.44) COPD patients ascompared to control group (171.11±18.11) ($p=0.044$). HDL cholesterolwere decreased, in mild (60.11±18.67), moderate (55.95±24.03) and severe (44.78±21.39) ($p=0.013$) COPD patient. While, LDL cholesterol were increased mild (105.57±37.47), moderate (118.39±55.24) and severe (131.14±58.91) COPD cases as compared to control group (83.41±28.14) ($p=0.126$) **(Figure 2)**. Very Low density lipoprotein cholesterol (VLDL) enhanced in mild (26.04±8.55), moderate (32.62±15.83) and severe (45.90±25.38) COPD patients significantly as, compared to control (26.31±7.13) ($p<0.001$). Triglyceride (TG) concentration were also significantly augmented in mild (130.19±42.77), moderate (163.70±74.34) and severe

(222.12±116.18) COPD patients as compared to control (118.22±31.48) ($p<0.001$) **(Figure 2).**

The present findings increase concentration of TC, LDL, VLDL, TG and decrease values of HDL are also in collaboration with the extensive work of Tautu et al. [21] where they reported cardiovascular risk factors and their use for an accurate cardiovascular risk assessment. No significant differences in the lipid profile concentrations and even with severe airflow obstruction had a little lower serum concentrations of triglycerides.[22] Begum et al [23] exhibited that all lipid parameters including TC, HDL, LDL and TG raised in COPD patients. Similarly, the present findings that the higher concentration of TC, LDL, VLDL, TG and decrease values of HDL are also in agreement with those of Millan et al. [24] who have reported the lipoprotein ratios, physiological significance and clinical usefulness in cardiovascular prevention.

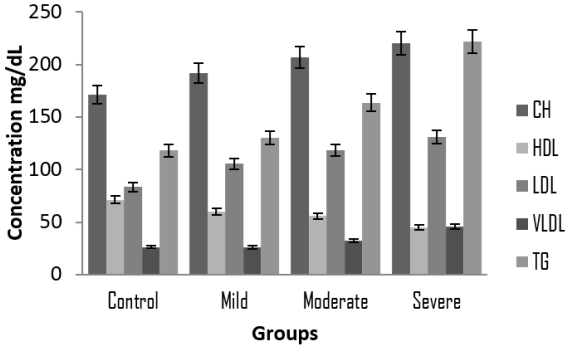

Figure: 2 Lipid profiles of chronic obstructive pulmonary disease patientsand control Group. Values are expressed as Mean±SD (Standard deviation), pvalue ≤ 0.05 is considered statistically significant.

Atherogenesis Indices

The present research work of experiment, atherogenesis indices; atherogenic index of plasma (AIP) were also elevated in mild (0.02±0.27), moderate (0.15±0.37) and severe (0.33±0.42) COPD patients ($p<0.001$). The control group exhibited no risk. Castelli's Risk Index; CR-I of mild (3.91±2.46), moderate (5.22±3.90) and severe (6.84±4.72) COPD patients wereelevated significantly those of control group (2.32±1.11) ($p=0.007$). Although, CR-II were also increase mild (2.34±1.99), moderate (3.36±3.06) and severe (4.35±3.38) COPD as compared to control 1.34±1.23 ($p=0.017$). Atherogenic coefficient (AC) were exhibitedin mild (2.86±2.46), moderate (4.25±3.87) and severe (5.73±4.60) COPD patients as compared to control (1.81±1.48) ($p=0.008$). The study concluded that atherogenic indices in mild, moderate and severe COPD were significantly higher than control **(Figure 3).**

The present findings proved serum atherogenic indices; AIP, castelli's risk index; CR-I and CR-II and AC were significantly higher and serum high-density lipoprotein levels were significantly higher in subjects with COPD than in control subjects can be correlated with the findings of Sasikala and Goswami, [25] who reported the Castelli risk index-1 and atherogenic coefficient are better predictors of cardiometabolic risk in patients with hypothyroidism. The present study found that there was a significant increase atherogenesis indices of CRI-I and CRI-II, AC and AIP ($p<0.001$) in patients with COPD compared to controls, which is in accordance with study done by Khan et al. [26] who studied the lipid profile in thyroid dysfunction. The present findings of the experiment were full agreement with previous study, it was reported that CRI-I and II are predictive of AIP as well as AC and therefore are likely to be related in their ability to pinpoint patients with risk of CVD.[27]

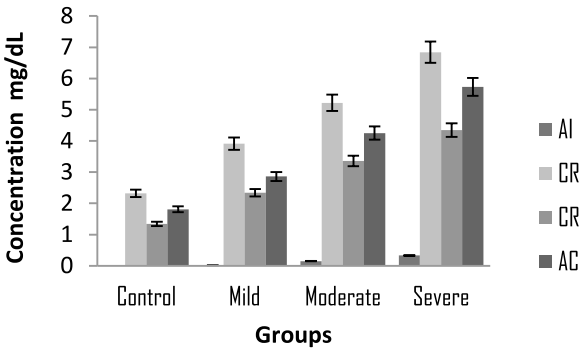

Figure: 3 Atherogenic index, Castelli's Risk Indices (CR-I, CRII) and Atherogenic Coefficient (AC) of chronic obstructive pulmonary disease patients and control Group. Values are expressed as Mean±SD (Standard deviation), pvalue ≤ 0.05 is considered statistically significant.

CONCLUSION

Coronary artery disease is the epidemic of modern civilization in which dyslipidemia contributes significantly to its pathogenesis. We aimed to investigate the plasma levels of lipid parameters, atherogenic indices on development of atherosclerosis and cardiovascular disease risk percentage in chronic obstructive pulmonary disease. The present study suggested that pulmonary function test, lipid profile, Atherogenic Indices; Atherogenic index of plasma, Castelli risk index and Atherogenic coefficient might be diagnostic tool subject with higher risk of cardiovascular disease and helpful for its effective and early drug management.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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