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Physiology

EVALUATION OF ATHEROSCLEROSIS RISK IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT **INTRODUCTION:** Chronic Obstructive pulmonary disease is considered as a risk factor for atherosclerosis and causes of morbidity and mortality worldwide due to cardiovascular disease. **OBJECTIVE:** The aim of study was investigation lipid profiles and atherosclerosis indices and their association with COPD. **MATERIAL AND METHODS:** This study enrolled 108 patients with COPD and 30 age, gender and BMI matched healthy control subjects. Atherogenic index were calculated by using the values of lipid profile. **RESULTS:** Male female ratio mild, moderate and severe COPD patients were exhibited 25(69.4%)/11(30.5%), 31(77.5%)/9(22.5%) and 20(62.5%)/12(37.5%) respectively while, control group showed 26(86.6%)/4(13.3%) (p = 0.37). The mean value of body mass index mild, moderate and severe COPD patients were 25.99±1.92, 24.79±3.86 and 27.24±4.51respectively, the control group exhibited 24.77±1.63 of BMI (p = 0.018). FVC (L) of mild, moderate and severe COPD patients were decreased significantly (2.32±0.41 to 1.91±0.38). FEV1 % predicted were also decreased significantly in mild, moderate and severe COPD patient (98.81±16.34 to 33.44± 6) while control group exhibited higher FEV1% as 93.43(p<0.001), FEV1/FVC % predicted were notably higher (63.29±14.63, 77.18±7.83 and 83.06±21.17) than those of the control group 60.32±9.81 (p<0.001). TC, LDL, VLDL and TG significantly higher and serum HDL levels were significantly lower in subjects with COPD than in control. Atherogenesis indices-atherogenic index of plasma, mild, moderate and severe COPD patients were 0.02±0.27, 0.15±0.37and 0.33±0.42respectively (p<0.001). The control group exhibited no risk. **CONCLUSION:** The study concluded that atherogenic index in mild, moderate and severe COPD subjects were significantly higher than in control subjects. Higher risk category of cardiovascular disease has identified in 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%). It is concluded that, cardiovascular risk increases in COPD patients

KEYWORDS : Atherogenesis Indices, Lipid Profiles, Cardiovascular Disease, Plasma

INTRODUCTION

Chronic obstructive pulmonary a disease is preventable and treatable disease characterized by airflow limitations that is not fully reversible. COPD is considered as a risk factor for atherosclerosis and cause of morbidity and mortality worldwide due to cardiovascular risk. Atherosclerosis and COPD are both systemic inflammatory diseases that share common risk factors/pathways and thereby may occur more frequently in the presence of each other[1]. Many studies have been identified COPD as an independent predictor of atherosclerosis[2,3]. Epidemiological studies revealed that COPD patients have various extra pulmonary comorbidities such as coronary heart disease (CHD), metabolic syndrome, and depression[4]. Few studies have explored the association of COPD, based on GOLD definition, with heart diseases.

Lung function impairment may be a risk factor for cardiovascular disease (CVD) events. The relationship between obstructive lung function impairment and heart diseases is still poorly studied on a population level[5,6]. Airflow limitation in COPD is defined as a post bronchodilator FEVI to FVC ratio < 0.70. Studied have reported reduced FEV1 nearly double risk cardiovascular mortality. Many scientists have reported COPD and cardiac comorbidities are frequently linked, they share common risk factors, pathophysiological processes, clinical signs and symptoms, and act synergistically as negative prognostic factors[7-9]. An earlier study has suggested that symptoms of chronic bronchitis predict the risk of coronary disease independently of the known major cardiovascular risk factors.

Dyslipidemia is the main underlying cause of cardiovascular disease as lipoprotein plays a crucial role in development of various cardiovascular diseases. High serum levels of lipoprotein and atherosclerosis indices have also been considered as an independent risk factor for coronary heart disease[10]. Therefore dyslipidemia is of clinical importance, so aim of our present study was to assess lipid profiles, atherosclerosis indices and cardiovascular risk percentage in COPD.

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 confermed COPD patients were included in the study and subdivided in four groups (Mild COPD 36, Moderate COPD 40, Severe COPD 32 and Control 30) 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

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 (as prescribed by treating physician) 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[11]. Triglycerides (TG) by GPO-POD method[12]. High density lipoprotein (HDL) by direct homogenous method[13]. Low density lipoprotein (LDL) by formula (LDL) = Total Cholesterol – High density lipoprotein −Triglycerides/5 and VLDL calculated by formula VLDL cholesterol = Triglyceride/5[14].

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), with the concentrations in mg/dL[15,16].

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

The demographic characteristics, pulmonary function parameters of groups (COPD), mild 36, moderate 40, severe 32 and healthy controls 30. 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(69.4%)/11(30.5%), 31(77.5%)/9(22.5%) and 20(62.5%)/12(37.5%) respectively while, control group showed 26(86.6%)/4(13.3%). (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[17].

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 **(Table 1).** Smoking is a very important risk factor for COPD, cholesterol, triglycerides, and plasma β-lipoprotein concentration are elevated, and HDL cholesterol is lowered in smokers as compared to non-smokers[18].

Table: 1 General parameter of chronic obstructive pulmonary disease patientsand control Group.

Parameters	Control	Mild COPD	Moderate COPD	Severe COPD	P value
Age	52.23±4.81	50.03±5.78	49.38±5.49	50.53±6	0.693
Male	26(86.6%)	25(69.4%)	31(77.5%)	20(62.5%)	0.37
Female	4(13.3%)	11(30.5%)	9(22.5%)	12(37.5%)	
BMI	24.77±1.63	25.99±1.92	24.79±3.86	27.24±4.51	0.018
Smoker	12(40%)	20(55.5%)	23(57.5%)	22(68.7%)	0.47
Non Smoker	18(60%)	16(44.4%)	17(42.5%)	10(31.2%)	

In the present investigation we found that forced vital capacity (L) of mild, moderate and severe COPD patient were decreased significantly 2.32±0.41, 2.42±0.63 and 1.91±0.38 respectively as compare to control group 3.13±0.61 (p<0.001) **(Table 2)**. The data of the present findings showed that forced vital capacity (L) decreased significantly in COPD patient are in full corroboration with the detailed work of Kang et al[19], who have studied the impact of low forced vital capacity on behavior restrictions in a population with airflow obstruction. Similar data have been reported by Sharma et al[20], where they had studied that forced vital capacity and atherosclerosis risk assessment in patients with chronic obstructive pulmonary disease.

In the present investigation forced expiratory volume (FEV1) % predicted were also decreased significantly in mild, moderate and severe COPD patient (98.81±16.34,1to 33.44± 6) while control group exhibited higher FEV1% as 93.43±18.41 (p<0.001)**(Table 2)**. The present findings suggested that forced expiratory volume (FEV1)% predicted decreased significantly, these are well supported by earlier classic work of Bikov[21], who reported that FEV1 is a stronger mortality predictor in patients with moderate COPD increased risk for cardiovascular disease. Many researchers have proved that a moderately reduced FEV1, an indepen-dent risk factor for CVD, is associated with an increasedincidence of heart failure in older and middle-aged individuals[22-24].

In the present work FEV1/FVC % predicted were notably higher (63.29±14.63, 77.18±7.83 and 83.06±21.17) than those of the control group 60.32±9.81 (p<0.001), and the differences were not statistically significant **(Table 2).** The present data of the findings have proved that FEV1/FVC % predicted notably higher these data are in full validation with the work of Fragoso et al[25] who have reported the ratio of FEV1 to FVC as a basis for establishing chronic obstructive pulmonary disease. Previous findings confirmed lower FEV1/FVC % wasassociated with higher risk for COPD exacerbations[26,27].

Table: 2 Pulmonary Function Testchronic obstructive pulmonary disease patients and control Group.

Parameters	Control	Mild COPD	Moderate COPD	Severe COPD	P value
FVC (L)	3.13±0.61	2.32±0.41	2.42±0.63	1.91±0.38	<0.001
FEV 1 % (predicted)	93.43± 18.41	98.81± 16.34	63.77± 7.68	33.44± 6	<0.001
FEV1/FVC% (predicted)	60.32± 9.81	63.29± 14.63	77.18± 7.83	83.06± 21.17	<0.001

Dyslipidemia is considered to be one of the most important risk factors for the development of atherogenesis and to assess the CV risk. Increased low density lipoprotein (LDL) cholesterol levels and decreased High density lipoprotein (HDL) cholesterol levels are indicative of an atherogenic lipid pattern [28].

In this section of experiment, total cholesterol (TC) concentration of mild, moderate and severe COPD patients were exhibited 191.72±27.96, 207.08±46.32 and 220.34±61.44 (p=0.044) respectively, which is higher than control group (171.11±18.11). HDL decreased 60.11±18.67, 55.95±24.03 and 44.78±21.39 (p=0.013) respectivelyin mild, moderate and severe COPD Patient. While, LDL were increased mild, moderate and severe COPD cases 105.57±37.47, 118.39±55.24and 131.14±58.91 (p=0.126) respectively, as compared to control group (83.41±28.14) **(Table 3)**.

Very Low density lipoprotein (VLDL) augmented in mild, moderate and severe COPD patients 26.04±8.55, 32.62±15.83and45.90±25.38 (p<0.001) respectively as, compare to control (26.31±7.13). Triglyceride (TG) concentration were also significantly increased in mild, moderate and severe COPD patients, 130.19±42.77, 163.70±74.34and 222.12±116.18 (p<0.001) respectively as compare to control (118.22±31.48) **(Table 3).** Atherogenesis indices-atherogenic index of plasma, mild, moderate and severe COPD patients were 0.02±0.27, 0.15±0.37and 0.33±0.42 respectively (p<0.001). The control group exhibited no risk. The study concluded that atherogenic index mild, moderate and severe COPD subjects were significantly higher than in control subjects **(Table 3).**

The present findings proved serum TC, LDL, VLDL, TG and atherogenic index like were significantly higher and serum high-density lipoprotein levels were significantly lower in subjects with COPD than in control subjects can be correlated with the findings of Acay et al[29], who reported the atherogenic index as a predictor of atherosclerosis. The present findings of TC, LDL, VLDL, TG, atherogenic index and decrease values of HDL are also in corroboration with the extensive work of Tautu et al[30], where they reported cardiovascular risk factors and their use for an accurate cardiovascular risk assessment. Similarly, the present findings that the higher concentration of TC, LDL, VLDL, TG, atherogenic index and decrease values of HDL are also in agreement with those of Millan et

al[31] who have reported the lipoprotein ratios, physiological significance and clinical usefulness in cardiovascular prevention. No significant differences in the lipid profile concentrations and even with severe airflow obstruction, had a little lower serum concentrations of triglycerides[32]. Begum et al[33] exhibited that all lipid parameters including TC, HDL, LDL and TG are raised in COPD patients. The present findings have also suggested TC, LDL, VLDL, TG and atherogenic index were significantly higher and serum high-density lipoprotein levels were significantly lower in subjects with COPD, which is in contrast with the detailed work of Rao et al[17], who reported that serum of lipid parameters are not different from healthy controls.

Table: 3 Lipid profiles of chronic obstructive pulmonary disease patientsand control Group.

Parameters	Control	Mild COPD	Moderate COPD	Severe COPD	P value
TC	171.11±18.11	191.72±27.96	207.08±46.32	220.34±61.44	0.044
HDL	71.22±11.13	60.11±18.67	55.95±24.03	44.78±21.39	0.013
LDL	83.41±28.14	105.57±37.47	118.39±55.24	131.14±58.91	0.126
VLDL	26.31±7.13	26.04±8.55	32.62±15.83	45.90±25.38	<0.001
TG	118.22±31.48	130.19±42.77	163.70±74.34	222.12±116.18	<0.001
AI	No risk	0.02±0.27	0.15±0.37	0.33±0.42	<0.001

Higher risk category of cardiovascular disease has identified in 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%). It is concluded that, Cardiovascular Risk increase in Patients with Chronic Obstructive Pulmonary Disease. The present findings confirmed that higher risk and lower risk category of cardiovascular disease has identified COPD subjects. It can be correlated to the findings of Sharma et al[20] which has explored atherosclerosis risk assessment in patients with chronic obstructive pulmonary disease.

CONCLUSION

Cigarette smoking, biomass fuel, occupational exposure all cause local lung inflammation from where the local inflammatory mediators are spilled over into systemic circulation producing various systemic effects including dyslipidaemia. Dyslipidaemia is associated with increase in COPD exacerbations and risk of cardiovascular mortality.Atherosclerosis and COPD are very common disorders that may influence each other and leading causes of the morbidity and mortality which may affect the lipid profile. We aimed to investigate the of the plasma levels of lipid parameters and atherogenic index on development of atherosclerosis in subjects with COPD. In present investigation high TC, LDL, VLDL, TG, atherogenic index of plasma and low HDL was observed. It is concluded that positive correlation between atherogenic index of plasma and cardiovascular disease risk percentage in COPD Patient, suggesting that atherogenic index can be used as early predictors of cardiovascular disease risk in COPD patients, it might be useful for the early treatment of cardiovascular disorders.

CONFLICT OF INTERESTS

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

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