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Lipid Profile Status in Chronic Obstructive Pulmonary Disease and Association with Interleukin 8

Ritabrata Mitra[1], Subinay Datta[2], Mrinal Pal[2*], Kaushik Ghosh[3], Debajoity Paul[1] and Keya Pal[2]

[1]Department of Pulmonary Medicine, IPGMER, Kolkata, West Bengal, India.
[2]Department of Biochemistry, Burdwan Medical College, Burdwan, West Bengal, India.
[3]Department of General Medicine, Burdwan Medical College, Burdwan, West Bengal, India.

Authors' contributions

This work was carried out in collaboration between all authors. Authors RM and DP designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors SD and MP managed the literature searches, analyses of the study performed the spectroscopy analysis and Authors KP and KG managed the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Background: There are several conflicting pictures found about blood lipid profile parameters in Chronic Obstructive Pulmonary Disease.
Aim: The present study was conducted to evaluate the exact profile of lipid status in COPD and as inflammation has been implicated in the pathogenesis of COPD, is there any association between inflammatory chemokines and lipid profile.
Methods: From February 2011 to May 2013 five hundred fifty two patients with COPD presented to Burdwan Medical College and Hospital and 521 subjects having no COPD as age and sex-matched control entered to the study. Diagnosis of COPD was confirmed according to clinical findings and pulmonary function test. Lipid parameters and IL8 in serum were measured in all subjects.

**Corresponding author: Email: mrinalpal77@rediffmail.com;*

Results: The mean level of TG was 148.32±12.18 mg/dl and 134.54±11.78 mg/dl in COPD patients and healthy control, respectively. (p<0.001). The mean level of TC was 186.46±22.91 mg/dl and 173.77±15.21 in COPD patients and healthy control respectively (p<0.001). LDL level mean value was 118.91±12.92 mg/dl and 118.91±12.92 mg/dl in COPD patients and control respectively (p<0.001). The mean value of HDL showed 33.46±4.69 mg/dl in COPD patients and 38.38±5.22 mg/dl in control (p = 0.034). Regression analysis was showed IL8 was statistically significantly correlated with TC (r = 0.785, p <0.001), TG (r = 0.871, p<0.001), LDL (r = 0.882, p<0.001), VLDL (r = 0.679, p=0.016) and HDL (r = -0.681, p=0.012),

Conclusion: COPD patients showed significantly higher serum levels of TC, TG, LDL, IL8 and serum concentrations of HDL were also decreased significantly compared to controls. Moreover, lipid profile parameters were well correlated with serum IL8.

Keywords: Lipid profile; chronic obstructive pulmonary disease; interleukin 8.

1. INTRODUCTION

Chronic Obstructive Pulmonary Diseases (COPD) is characterized by airflow obstruction that is not fully reversible. [1] It is in the top five leading causes of mortality in the world and is associated with a significant socio economical burden in hospital and absenteeism form work [2,3].

As in COPD, smoking is the major risk factor and smoking affects the lipid profile, so dyslipidemia may be found in COPD patients. There are several data where the lipoproteins in COPD were studied. In a previous study, a comparison was carried out of the lipid profile in bronchial asthma and COPD and was concluded that LDL was significantly higher and VLDL was significantly lower in patients of bronchial asthma and COPD [4]. In one recent study, LDL concentration was increased significantly but no significant difference in VLDL, HDL and in triglycerides levels were observed [5]. In another study, no significant difference was found between the VLDL, HDL concentration and FEV_1 even with severe airflow obstruction and had had slightly lower serum concentrations of triglycerides [6]. Thus, we find a contradictory conclusion in different literatures and so exact scenario of lipid profile in COPD patients has not been depicted.

Hence the present study was attempt to investigate the levels of total cholesterol (TCH), triglycerides (TG), low density lipoproteins (LDL), very low density lipoproteins (VLDL), high density lipoproteins (HDL) in COPD patients omitting the effect of age, gender, BMI, effect of on the lipid profile and socio economical status on lipid status.

But aetiopathogenesis of dyslipidemia in COPD patients is not exactly known. It is well established that chronic inflammation play a central role in COPD [7,8] and chemokines are involved in the recruitment of cells to the site of inflammation and these chemokines including IL8 are thought to be involved in pathology of COPD [9,10].

So, present study has been set to clarify the relationship between IL8 and lipid profile in COPD patients to search the role inflammation in development of lipid derangement.

2. MATERIALS AND METHODS

2.1 Study Area

The present study was conducted in the department of Pulmonary Medicine of PGMER, Kolkata with the collaboration of Department of Biochemistry of Burdwan Medical College, Burdwan, West Bengal, India.

2.2 Selection of Subjects

Five hundred and fifty two patients with a diagnosis of COPD aged more than 50 years who attended Burdwan Medical College were selected as case and 521 subjects having no COPD were chosen as age and sex-matched control by simple random sampling after informed consent had been received from concern ethics committee (Memo No. BMC/2210/1(5) between March 2011 and November 2014. All patients were examined and structured interview was taken about respiratory symptoms including cough with phlegm and dyspnea through self-completed questionnaire [11]. Information about smoking habits, comorbidities, medication use and excerbations was gathered. A smoking history of ≥10 pack-years and a FEV1/FVC ratio < 0.7 and FEV1 < 80% predicted were criteria for inclusion.[11] All

subjects with suspicious or diagnosis of autoimmune diseases, asthma or cancer in the last 5 years, subjects with common comorbidities including cardiovascular diseases and diabetes, frequent exacerbation, patients of COPD requiring inhalation steroid > 400µg/day [12-16] was excluded. All patients continued to receive their treatment (beta2-adrenergic agonist, anticholinergics and their combination, steroids and theophylline) during the study.

2.3 Pulmonary Function Tests

Pulmonary function was measured in both pre- and post-inhalation of 0.4 mg salbutamol, on a spirometer (HELIOS 401) by trained study staff. As the FEV_1 (Forced Expiratory Volume in 1 second) is the most reproducible parameter in lung function test, therefore it is best to adapt this parameter for assessment of large group of people. Spirometric values were postbronchodilator measurements, and absolute values were expressed as percentage predicted of reference values [17]. Presence of COPD was defined by a postbronchodilator FEV1/FVC ratio < 0.7 and severity of disease was staged by FEV1 expressed as percentage of Forced Vital Capacity (FVC), predicted according to the latest GOLD (Global Initiative for Obstructive Lung Disease) classification [18].

2.4 Anthropometric Measurements

Weight and height were measured using standardized technique [19]. Body mass index (BMI) was calculated as the weight (kg) divided by the square of height (m^2).

2.5 Collection of Samples

Arterial blood was drawn in a heparinised syringe from the study population to determine arterial partial pressure of oxygen (P_aO_2) and analysed immediately. Five ml of peripheral venous blood was drawn after 12 hours of starvation from the subjects and allowed to coagulate at room temperature for 30–45 min, followed by centrifugation at 2500Xg for 15 min and then chemical analysis was performed immediately.

2.6 Parameters Assay

Arterial blood gases were analyzed for arterial oxygen on a Arterial blood gas analyzer (OPTI CCA, TECAN) immediately after sampling by the study physician. An arterial partial oxygen pressure of < 55mmHg is defined as chronic hypoxemia. [20] The lipid profile parameters such as TC, TG, HDL and LDL were assessed by using kit methods. [21,22] Intra-assay CV % of TC, TG, LDL and HDL were 1.2, 2.3, 2.8, 3.1 respectively. The inter-assay CV % of these parameters was 3.6, 4.1, 4.7 and 3.6 respectively. All analysis was performed with autoanalyzer ERBA XL 600. HDL and LDL concentration were measured with the direct method using ERBA system packs. The levels of interlukin-8 were measured with Enzyme Linked Immunosorbant Assay (ELISA) method using (Biological Company/ United States) kit.

2.7 Statistical Analysis

The data for biochemical analysis was subjected to standard statistical analysis using the Statistical Package for Social Science (SPSS) 11.5 software for windows. Comparison of lipid profiles and IL8 between control and COPD cases was done by Unpaired test.

3. RESULTS

3.1 The Personal Profiles and Clinical Parameters of Study Population

Personal profile and clinical details of the COPD patients and age, sex-matched control population are shown in Table 1. As age and sex influence the lung profile, age, sex-matched controls were used in this study.

Data are expressed as numbers (group percentages in parentheses) for categorical variables and mean values ± SD for continuous variables. When variables were not normally distributed, median values (Q1-Q3 IQR in parentheses) are given instead; IQR means Interquartile range; $p < 0.05$ consider statistically significant; Pack-years were expressed as the numbers of packs of cigarette smoked per day X the number of years the person has smoked; Quit-years were the number of years since a patient stopped smoking; *FEV1: Forced expiratory volume in 1 sec that is expressed in % of VC.

3.2 Comparison of Lipid Profiles between Control and Cases- Unpaired t Test

To find out the status of lipid profile in COPD patients, unpaired t test was performed and it was observed that COPD patients showed significantly higher serum levels of TC, TG, LDL and serum concentrations of HDL were also decreased significantly compared to controls as shown in the Table 2.

3.3 Comparison of Serum IL8 between Control and Cases- Unpaired t Test

In Table 3, to compare the concentration of serum Il8 between normal healthy control and COPD patients it was found that, serum IL-8 level for the COPD patients is significantly higher than the healthy control.

3.4 Correlation of IL-8 with Lipid Profile in COPD Patients – Bivarient Correlation

To search the association of inflammation with lipid parameters in COPD Bivarient correlation analysis was done and was found all the lipid profile parameters were well correlated with serum IL8 (Table 4).

3.5 Correlation of IL-8 and Lipid Profile Parameters with Disease Severity in COPD Patients – Bivarient Correlation

To obtain the association of IL-8 and lipid profile parameters with disease severity in COPD Bivarient correlation analysis was done and was found that although IL8 and not the all lipid profile parameters were not significantly correlated with FEV1 in GOLD stage I but IL 8 and almost all the lipid profile parameters were well correlated with FEV1 as GOLD stages increases (Table 5).

Table 1. Personal profile and clinical details of healthy persons and patients suffering from COPD

Demographic profiles	Controls (n = 521)	Patients with COPD (n = 552)	p value
Age (Years)	59.6814±5.33982	60.4031±5.64892	0.238
Sex			
Male (%)	297 (57)	319 (58)	0.189
Female (%)	225 (43)	233 (42)	
BMI (Kg/m^2)	25.81±3.4	25.62±3.51	0.182
Smoking habits			< 0.001
Never	115(22)	0(0)	
Ex-smoker	177(34)	259(47)	
Current Smoker	229(44)	293(53)	
Pack-years †	39(30-52)	47(33-63)	
Quit-years †	1(0-8)	2(0-8)	
Pulmonary function tests	72.73±3.19	50.92±11.56	< 0.001
FEV1*			
GOLD stages			
II (FEV1 50-80%)		319(58)	
III (FEV1 30-50%)		208(38)	
IV (FEV1 < 30%)		25(4)	
Resting P_aO_2 (mmHg)	92.48±3.69	35.90±3.94	<0.001
Inhaled steroids		298(54)	

Table 2. Comparison of lipid profiles between control and cases

Parameters	Control (n = 521)	Cases (n = 552)	p value
Total cholesterol (mg/dl)	173.77±15.21	186.46±22.91	< 0.001
Triglyceride (mg/dl)	134.54±11.78	148.32±12.18	< 0.001
LDL (mg/dl)	110.55±11.75	118.91±12.92	< 0.001
VLDL (mg/dl)	26.12±2.96	30.66±2.77	0.012
HDL (mg/dl)	38.38±5.22	33.46±4.69	0.034

Values are mean ± SD; n = number of cases; p < 0.05 consider statistically significant.

Table 3. Comparison of serum IL8 between control and cases

Parameters	Control (n = 521)	Cases (n = 552)	p value
IL8 (pg/ml)	29.03 ± 8.28	44.95 ± 10.22	< 0.001

Values are mean ± SD; n = number of cases; p < 0.05 consider statistically significant

Table 4. Correlation of serum IL-8 with lipid profile in COPD patients

Lipid profile	r value	p value
Total cholesterol	0.785	0.000
Triglyceride	0.871	0.000
LDL	0.882	0.000
VLDL	0.679	0.016
HDL	- 0.681	0.012

p < 0.05 consider statistically significant.

Table 5. Bivarient correlation between IL8 and lipid profile parameters with GOLD stages

Parameters	GOLD stages					
	II (FEV1-50-80%)		III (FEV1-30-50%)		IV (<30%)	
	r	p	r	p	r	p
IL8	0.863	0.057	0.753	0.01	0.966	0.01
Total cholesterol	0.720	0.047	0.927	0.031	0.30	0.01
Triglyceride	0.762	0.031	0.944	0.028	0.755	0.01
LDL	0.849	0.06	0.619	0.01	0.34	0.01
VLDL	0.398	0.038	0.538	0.022	0.776	0.01
HDL	-0.611	0.082	-0.842	0.01	-0.805	0.01

p < 0.05 consider statistically significant

4. DISCUSSION

COPD is associated with significantly increased morbidity and mortality and COPD precipitates dyslipidemia. One of the most important risk factors in cardiovascular disease is dyslipidemia [23]. But exact picture of dyslipidemia is not established till now. So present was conducted and found that COPD patients showed significantly higher serum levels of TC, TG, LDL and serum concentrations of HDL were decreased significantly. This finding was corroborated with the results of some previous studies [8,4]. Although Kamat SR, et al. In their study has shown the serum of lipid parameters are not different in COPD from healthy controls [24].

Smoking can cause major changes in serum lipid profile simultaneously smoking is a major risk factor in COPD. Smoking affects the lipid profile such a way that the plasma LDL, cholesterol and triglycerides concentration are higher and HDL cholesterol is lower in smoker than in nonsmokers [25]. Nicotine causes the release of adrenaline from the adrenal cortex leading to increased serum concentration of free fatty acids (FFA) which stimulates hepatic synthesis and secretion of cholesterol as well as hepatic secretion of VLDL and hence increased TG. Smoking decreases estrogen levels and further leads to decreased HDL cholesterol concentration. Smoking also increases insulin resistance and LDL, VLDL and TG are elevated in this hyperinsulinemic conditions due to decreased activity of lipoprotein lipase [26].

In present study, it was found that although IL8 and not the all lipid profile parameters were not significantly correlated with FEV1 in GOLD stage I but IL 8 and almost all the lipid profile parameters were well correlated with FEV1 as GOLD stages increases. But in some recent studies, the mean levels of lipid parameters were not different in different stages of COPD according to GOLD classification. The finding was compatible with the results of some recent studies [5,26,27].

In our study it was also found that lipid profile parameters such as TC, TD, LDL, VLDL were significantly positive correlated and HDL is significantly negative correlated with one important chemokine IL8 in COPD. That means there may be a relationship between inflammation and dyslipidemia on COPD as LDL stimulates smooth muscle cells to induce IL-8 production in dose- and time dependent manners at the transcription level and that the LDL signaling in hAoSMCs is conveyed via the generation of H_2O_2, the phosphorylation of p38 MAPK, the activation of AP-1, and the participation of NF-nB [28]. This causal relationship was also drawn from two other very recent studies [5,29]. But IL8 is increased due to inflammation and lipid profile may be altered due

to smoking. Therefore increased IL8 and increased TC, LDL, TG could be incidental and not interdependent [30]. Thus the clinical significance of dyslipoproteinemia derives chiefly from the deranged status of lipid profile in development of atherosclerosis which causes further disablement in COPD.

Limitation of our study is measurement of other lipid-related parasmeters like apo-lipoproteins, modified LDL such oxidized LDL, acetylated LDL, native LDL.

5. CONCLUSION

COPD patients showed significantly higher serum levels of TC, TG, LDL, IL8 and serum concentrations of HDL were also decreased significantly compared to controls. Moreover, lipid profile parameters were well correlated with serum IL8.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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