



ASSOCIATION OF LIPID PROFILE IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

Respiratory Medicine

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by persistent respiratory symptoms and airflow limitation. From an epidemiological perspective, COPD is currently the fourth leading cause of death worldwide, with a huge economic and social burden. Studies investigating lipid profile in chronic obstructive pulmonary disease (COPD) are limited in number with inconsistent results. **Aims and Objective:** The aim of this study was to investigate lipid parameters in the serum of stable COPD patients and their relationship to disease severity, smoking, comorbidities, and treatment. **Materials and Method:** The study included 75 COPD patients and 50 controls. Triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were assessed. Non-HDL-C (NHC), Atherogenic Coefficient (AC), TG/HDL-C, Plasma Atherogenic Index (AIP), Castelli Risk Index I and II (CRI-I, CRI-II) As well as the monocyte-to-HDL ratio (MHR) was calculated. HDL-C and MHR are elevated, while other lipid parameters and indices are decreased, in COPD patients compared with healthy individuals. **Results:** Smoking did not affect lipid parameters. However, lipid profiles were only altered in more severe disease stages. AC, CRI-I, and CRI-II were positively correlated with pulmonary function parameters in COPD patients and negatively correlated with COPD multicomponent indices (ADO, BODEx, and DOSE). The combined model including CRI-II, C-reactive protein, fibrinogen, and leukocytes showed excellent diagnostic performance and correctly classified 72% of the study participants with an AUC of 0.800 (0.742–0.849), $P < 0.001$. Bronchodilator monotherapy and statins had opposite effects on TC, LDL-C, and NHC, while TG, TG/HDL-C, and AIP were elevated in COPD patients with cardiovascular disease. **Conclusion:** Lipid imbalances are present in COPD and appear to develop late as the disease progresses. Further studies are needed to elucidate the underlying mechanisms of dyslipidemia.

KEYWORDS

Chronic, Obstructive, Pulmonary, Disease, Epidemiological, Lipid Profiles, Dyslipidemia

INTRODUCTION

COPD often co-exists with other comorbidities that may impact prognosis of the disease [1]. Among these, Cardio-vascular events are the leading cause of morbidity and mortality in COPD. A greater than twofold risk is reported for cardiovascular-related hospitalization and mortality in patients with COPD compared with those without COPD [2].

Dyslipidemia is considered as the major risk factor for cardiovascular disease (CVD) and may contribute to the higher mortality rates in COPD associated with CVD [3].

However, the prevalence and consequences of dyslipidemia in COPD is still unclear. Some, but not all studies have demonstrated altered lipid levels in COPD. Significantly higher levels of TG, cholesterol, LDL and lower levels of HDL have been reported in COPD patients; however, their impact on disease outcomes has not been uniformly demonstrated [4].

Hence an attempt was made here to explore and document the extent of dyslipidemia in an Indian cohort of COPD patients.

Aims and Objective

The aim of this study was to investigate lipid parameters in the serum of stable COPD patients and their relationship to disease severity, smoking, comorbidities, and treatment.

MATERIALS AND METHOD

The study included 75 COPD patients and 50 controls. Triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were assessed. Non-HDL-C (NHC), Atherogenic Coefficient (AC), TG/HDL-C, Plasma Atherogenic Index (AIP), Castelli Risk Index I and II (CRI-I, CRI-II) As well as the monocyte-to-HDL ratio (MHR) was calculated. HDL-C and MHR are elevated, while other lipid parameters and indices are decreased, in COPD patients compared with healthy individuals.

RESULTS

Detailed baseline demographic and clinical characteristics of the study

population are presented in Table 1. The study was carried out in 125 stable patients diagnosed with COPD. Based on FEV1, patients were characterized as moderately severe (FEV1 50-80%), severe (FEV1 30-50%) and very severe (FEV1 < 30%). PFT variables of recruited subjects are shown in Table 2. Mean levels of mid upper arm circumference and sum of four skin fold thickness were increasing significantly with the severity of COPD.

Table 1: Demographics and clinical characteristics of the study population.

Parameters	Moderate COPD (n = 35)	Severe COPD (n = 52)	Very severe COPD (n = 38)	p value
Age (years)	57.7 ± 12.01	59.9 ± 9.8	56.6 ± 8.9	0.28
Smoking index	120.0 (30.0 - 3000.0)	304.0 (20.00 - 2000.0)	312.0 (117.0 - 3000.0)	0.62
Exercise capacity				
6-minute walk test (meters)	424.9 ± 118.9	334.7 ± 121.02	322.1 ± 89.98	0.001*
Anthropometry				
BMI (kg/m ²)	22.1 ± 4.9	21.1 ± 3.78	20.4 ± 4.1	0.22
Mid upper arm circumference (cms)	25.1 ± 3.5	24.5 ± 3.4	23.03 ± 3.14	0.006*
Sum of four skin fold thickness (mm)	42.2 (17.0 - 133.0)	48.9 (11.0 - 75.0)	31.8 (30.0 - 90.0)	0.02*
Waist/Hip ratio	0.90 ± 0.08			

All values expressed as Mean ± SD or Median (min - max); *: Statistically significant.

Table 2: Spirometry variables in subjects recruited in the study.

Pulmonary function test				
Variable	Moderate COPD	Severe COPD	Very severe COPD	p value
FEV1 (l)	62.4 ± 10.6	39.2 ± 5.2	27.5 ± 12.7	0.001*

FVC (l)	74.8 ± 16.1	57.2 ± 9.9	45.6 ± 14.7	0.001*
FEV1/FVC (%)	87.8 ± 15.4	72.3 ± 11.1	62.2 ± 13.1	0.001*
PEFR (l)	30.0 (9.0 - 108.0)	20.0 (11.0 - 50.0)	12.0 (0.0 - 46.0)	0.001*
MEF25-75 (l/s)	48.0 (9.0 - 94.0)	26.5 (10.0 - 56.0)	19.0 (7.0 - 93.0)	0.001*

*: Statistically significant.

Lipid Profile In Study Population

Concentration of total cholesterol (TC), LDL, HDL, VLDL and TG in moderate, severe and very severe COPD patients are shown in Table 3. None of the lipid was found significantly different among three groups of COPD patients. These are depicted in Figure 1 and Figure 2.

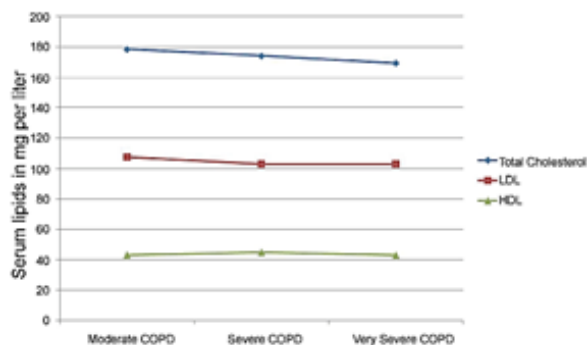


Figure 1: Distribution of total cholesterol, LDL and HDL levels amongst patients with respect to severity of COPD.

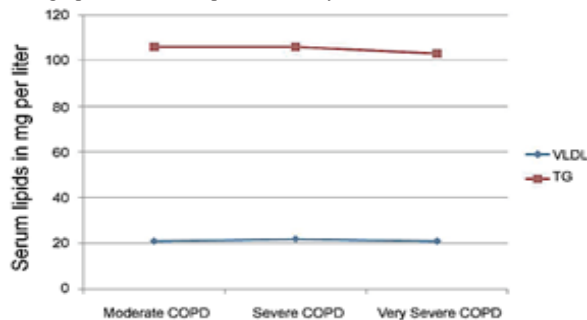


Figure 2: Distribution of VLDL and TG levels amongst patients with respect to severity of COPD.

Table 3: Lipid profile in study population.

Parameters	Moderate (n = 35)	Severe (n = 52)	Very severe (n = 38)	p value
T. Cholesterol (mg/l)	178.5 ± 34.5	174.2 ± 36.4	169.4 ± 34.1	NS
LDL (mg/l)	107.5 ± 34.5	103.0 ± 33.7	103.1 ± 35.6	NS
HDL (mg/l)	43.2 ± 5.3	44.9 ± 8.4	43.1 ± 9.5	NS
VLDL (mg/l)	21.0 (11.0 - 112.0)	21.9 (2.0 - 177.0)	21.0 (10.0 - 80.0)	NS
TG (mg/l)	106.0 (55.0 - 418.0)	106.0 (36.0 - 353.0)	103.0 (52.0 - 295.0)	NS

NS: Not statistically significant.

Total cholesterol (TC), LDL, HDL, VLDL and TG levels were correlated with anthropometric measurements in all COPD patients. No component of the lipoproteins except Triglyceride was significantly correlated with anthropometric measures (Table 4).

Table 4: Anthropometric Correlation with serum Triglycerides.

Parameters	p value	Correlation coefficient
BMI (kg/m ²)	0.003*	0.26
Waist Hip ratio	0.51	-0.09
Sum of four skinfold thickness (mm)	0.06	0.21
MUAC (cm)	0.003*	0.03

*: Statistically significant.

The triglyceride levels were significantly correlated with BMI (p = 0.003), sum of 4 skinfold thickness (P = 0.06) and mid upper arm

circumference (p = 0.003). No significant correlation was found between triglyceride level and waist hip ratio.

DISCUSSION

In this cross-sectional observational study, we analyzed the lipid profile in COPD patients with varying degree of severity. It was observed that all components of lipid profile were within the normal predicted upper level. In addition, we did not find any statistical difference in total cholesterol (TC), LDL, VLDL, HDL and TG between mild, moderate and severe COPD. However, Triglyceride levels were significantly correlated with Body Mass Index (BMI) and Mid Upper Arm Circumference (MUAC). Increase in BMI and MUAC may increase triglyceride levels in COPD patients.

Patients with COPD generally encounter cardiovascular complications. Lipid profile is usually acknowledged as a good predictor for cardiovascular disease. Mitra, et al. found significantly high serum levels of all lipoproteins TC, TG, LDL in COPD cases than controls. HDL levels were also significantly decreased in cases than controls [8]. Our findings were compatible with a number of previously held studies. Attaran D, et al. evaluated the serum lipid profile in chemical warfare patients with COPD and found statistical difference in cholesterol and triglyceride levels between patients and controls but none of the lipid parameter showed any correlation with severity of airflow limitation assessed by FEV1 [9]. Similar results were reported in other studies [10]. Conversely, Beti Zafirova-Ivanovska and colleagues reported that hypercholesterolemia in COPD patients significantly increases with disease severity [11]. Overall, a definitive demonstration of dyslipidemia in COPD and its association with disease severity remains uncertain.

It is notable, however, that most previous reports show lipid profile within normal range. However, lipid levels were elevated in COPD compared to controls but were not abnormally high. These observations enforced us to think that etiological factors for COPD might contribute for cardiovascular complications in patients with COPD. Cigarette smoking is markedly the most important etiological factor for COPD [12] accordingly we found considerably high smoking index in very severe COPD patients. A number of studies have also been reported discussing role of smoking in causing dyslipidemia [13]. Smoking is a contributor for the development of COPD as well as for dyslipidemia.

The 6MWT is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests [14]. Similar to previous studies, we found that the 6MWD of our subjects reduced significantly with worsening disease severity. This may have important implications on activities of daily living.

Anthropometric measurements are very useful to understand any disease so that role of nutrition can be ascertained in disease etiology and its management. Malnutrition is common in COPD and associated with poor exercise tolerance and higher morbidity and mortality. Sum of four skin fold thickness (SUM) and Mid Upper Arm Circumference (MUAC) are significantly lower in very severe COPD patients. COPD patients with lung deficit function require more energy to compensate their reduced lung function. Majority of their total energy expenditure is attributed to lungs for its efficient working. Body fat equally participates in energy production leading to lesser fat accumulation.

CONCLUSION

To conclude, our study suggests cardiovascular problems are not enhanced with disease worsening. We did not find any correlation between COPD disease severity and lipoproteins, but more comprehensive studies are required to get accurate results. As statin treatment in COPD patients reduced mortality rates, there must be integrated pathway linking COPD with cardiovascular problems. More work is needed to uncover the causative mechanism of cardiovascular disease in COPD.

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