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Brief Article

Lipid profile patterns in chronic obstructive pulmonary disease and its correlation with the severity of disease

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Abstract

This cross-sectional study was conducted to determine the serum lipid profiles in chronic obstructive pulmonary disease (COPD) patients and its correlation with the severity of COPD in the Department of Respiratory Medicine at Bangabandhu Sheikh Mujib Medical University. A total of 100 spirometric-confirmed cases of COPD were included. Fasting blood samples for lipid profiles were collected. To identify the association between severity of COPD with lipid profiles Pearson's correlation was used. Further multiple linear regression was done to identify the relation. The mean (standard deviation) age of the patients was 59.0 (10.7)years. The ratio of males and females was 19:1. The mean forced expiratory volume (liters) in 1 second (FEV1) was 55.1 (18.1). Most of the patients had stage II (48%) and stage III (36%) airflow obstruction. Plasma level of total cholesterol and triglyceride tend to increase, statistically non-significant, with stages of COPD. However, the association of plasma lipids becomes statistically significant with FEV1 when the effects of age, BMI, pack-year smoking, duration of illness are accounted in multiple linear regression analysis.

Keywords: Chronic obstructive pulmonary disease, lipid profile, Correlation

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is increasingly considered a multisystem disease characterized by both pulmonary and systemic inflammation[1]. In COPD, pulmonary inflammation occurs due to the lungs' unusual inflammatory response to deleterious gasses and particles[2]. The prevalence of this disease is growing because of the increased prevalence of smoking as well as the population aging in several countries. The prevalence of COPD in Bangladesh is between 10.3% to 13.5 %, higher among rural than urban, and in males than females[3,4].

COPD is now documented to have significant systemic concerns that may affect morbidity and mortality. COPD often co-exists with several comorbidities that may sway the prognosis of the disease[5]. As in COPD, smoking is the major risk factor and smoking affects the lipid profile, so abnormal lipid profiles may be observed in COPD patients. Various reasons like smoking, aging, and using drugs such as steroids cause a deranged lipid profile among COPD patients. A study by Lucas showed that the prevalence of abnormal lipid profiles in COPD and the control group was 48.3% and 31.7% respectively[6].

Dyslipidemia may contribute to the higher mortality rates in COPD[7]. However, the prevalence and consequences of dyslipidemia in COPD are still conflicting. Significantly higher levels of triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), and lower levels of high-density lipoprotein

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Highlights

1. **Plasma level of total cholesterol and triglyceride tend to increase, statistically non-significant, with stages of COPD.**
2. **Plasma lipids are the determinants of FEV1 when the effects of age, BMI, pack-year smoking, duration of illness are accounted.**

(HDL) had been reported in COPD patients. However, their impact on disease outcomes had not been uniformly demonstrated[1,8-10]. This study aimed to explore the levels of total TC, TG, LDL, and HDL in chronic obstructive pulmonary disease patients and their correlation with the severity of the disease.

METHODS

This cross-sectional study was conducted between 27.02.2019 to 30.09.2019 on the inpatients and outpatients attending the Department of Respiratory Medicine at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. We estimated the sample size using the z^2pq/d^2 formula. Considering the prevalence[6] (p) 0.483 and margin of error (d) 10% the sample size was 96. Finally, a total of 100 COPD patients were included in this study.

The diagnosis of COPD was carried out by spirometry following the GOLD guidelines (post-bronchodilator Forced expiratory volume in 1st second/ forced vital capacity ratio less than 0.7). The patients were categorized into four stages based on severity according to the GOLD guidelines. Stage I: force expiratory volume in 1 second (FEV1) ≥ 80% predicted, stage II (50% ≤ FEV1 < 80% predicted), stage III (30% ≤ FEV1 < 50% predicted), stage IV (FEV1 < 30% predicted). Spirometry was done on a computerized spirometer (Heliox). Spirometry was performed when the patients were clinically stable and the patients were asked to abstain overnight from oral and inhaled bronchodilators as per ATS/ERS guidelines. Before performing spirometry written informed consent was taken from patients or respondents. After baseline spirometry, 200µg of inhaled salbutamol was administered via metered-dose inhaled and the test was repeated after 15 minutes. The computerized spirometry gives age, sex, weight, and height-matched predicted and test values. The best of the three attempts was selected. Among these FEV1 and FEV1/FVC ratios were analyzed and categorized as per GOLD staging. The exclusion criteria were known cases of pre-existing other lung diseases, patients on lipid-lowering drugs, seriously ill patients, inability to properly perform spirometry, and the presence of congenital or valvular cardiomyopathy or familial hyperlipidemias.

After 9 to 12 hours of overnight fasting, 5 ml venous blood samples were drawn in the morning before breakfast from the COPD patients to measure TC, TG, LDL, and HDL. The total cholesterol, HDL, and triglycerides were directly analyzed by using standard enzymatic techniques in the biochemistry Lab, BSMMU. LDL cholesterol was calculated by using the Friedewalds equation.

Statistical analysis was carried out based on IBM SPSS Statistics (version 26.0, RRID: SCR_019096). Sex, occupation and stages of COPD were expressed in frequency and percentage. Age, BMI, pack year of smoking, duration of illness, FEV in 1 second and lipid profiles were expressed in mean and standard deviation. To identify the relation between severity of COPD with lipid profiles Pearson's correlation was used after that a linear regression model adjusted with age, body mass index, pack year of smoking, duration of illness were used to determine the associated factors of FEV1. A value of $P< 0.05$ was considered statistically significant for all tests. Before the commencement of this study, the thesis protocol (BSMMU/2019/2056) was approved by the Institutional Review Board of BSMMU.

RESULTS

A total of 100 spirometric-confirmed COPD patients were included in our study. The mean (standard deviation) age of presentation was 59.0 (10.7) years. 34% and 32% of the patients were between 60 to 69 years and 50 to 59 years. Most of the participants were male (95%). Among the occupation, 29 out of 100 were businessmen followed by 23% were cultivators. In this study, the mean (standard deviation) BMI, duration of illness, and pack year of smoking of the study subjects were 20.3 (3.9), 10.8 (6.6), and 26.7 (15.3) respectively. The mean TC, TG, LDL, and HDL were 167.3 (42.4), 121.7 (51.9), 102.0 (35.6), and 40.1 (9.9) mg/dL correspondingly. Among the stage of COPD, most patients were in stage II (48%) followed by stage III (36%). 9% and 7% were in stage I and stage IV respectively **(Table 1)**.

TABLE 1 Background characteristics of study subjects in 95 male and 5 female patients with chronic obstructive pulmonary disease

Variables	Mean	Standard deviation
Age (years)	59	10.7
Body mass index (kg/m²)	20.3	3.9
Pack-year of smoking	26.7	15.3
Duration of illness (days)	10.8	6.6
Forced expiratory volume in 1 sec (liters)	55.1	18.1
Lipid profile (mg/dL)		
Total cholesterol	167.3	42.4
Triglycerides	121.7	51.9
Low-density lipoprotein cholesterol	102	35.6
High-density lipoprotein cholesterol	40.1	9.9

The level of total cholesterol increases with the stage of COPD. However, this result was not statistically significant (P<0.05) **(Table 2)**. None of the lipid variables were correlated with FEV1. However, the association of plasma lipids becomes statistically significant with FEV1 when the effects of age, BMI, pack-year smoking, duration of illness were taken in to account in multiple linear regression analysis **(Table 3)**.

COPD is a male predominant disease and smoking is a major risk factor. In our study male to female ratio was 19:1. Similar observation has been reported by Soriano[11], andvan Haren Willems[12]. In the present study, the interquartile range of duration of Illness was 10.8 ± 6.6 years and the smoking pack year was 23.3 ± 10.6 years. This finding was similar to the study done by Seemungal[13]. Cigarette smokers, either active or passive or past smokers, have a higher prevalence of respiratory symptoms, lung functional abnormalities, a greater annual rate of decline of FEV1, and greater COPD exacerbation and mortality[14].

The relationship between smoking and lipid profile is well recognized. Smoking is associated with increased cholesterol, triglyceride, and LDL cholesterol and decreased HDL cholesterol[15]. Though smoking is a risk factor for COPD, the lipid profile has not yet been well characterized in COPD patients. It is not known, whether an abnormal lipid profile in COPD is an independent risk factor for higher morbidity and mortality[16,17].

TABLE 2 Mean (standard deviation) lipid levels in four stages of chronic obstructive pulmonary disease

Lipid Profile (mg/dL)	Stage I (n=9)	Stage II (n=48)	Stage III (n=36)	Stage IV (n=7)	P*
Total cholesterol	175.6 (53.8)	170.8 (42.9)	161.8 (39.8)	160.7 (41.7)	0.70
Triglycerides	162.2 (49.9)	119.8 (52.8)	117.0 (39.5)	117.0 (85.2)	0.09
Low-density lipoprotein cholesterol	99.3 (31.1)	104.1 (37.6)	99.1 (35.4)	106.5 (33.8)	0.91
High-density lipoprotein cholesterol	38.2 (9.4)	41.5 (9.2)	39.1 (10.9)	38.0 (11.2)	0.60

*Analysis of variance

DISCUSSION

In our study lipid profile of COPD patients and its correlation with different stages of COPD was demonstrated. COPD is a chronic, progressive and irreversible pulmonary disease that commonly affects the aged population more than 40 years of age. With increasing age, the function of the lung decline, and various comorbidities may increase the disease progression. The mean age of the participants was 59.0 ± 10.7 years. 34 out of 100 (34%) patients and 32 out of 100 (32%) patients were between 60 to 69 years and 50 to 59 years. This finding is similar to the study done in India[1,3,10].

There is controversy regarding the performance and assessment of spirometry findings which sometimes increases bias in the study findings. We could not remove the bias but rather minimize the risk of bias. To minimize the bias in our study, we used the spirometer (Heliox) at our laboratory and the same procedure for all the participants. In the current study, most of the patients were in stage II 48% followed by stage III 36%. 9% and 7% were in stage I and stage IV respectively. Mean cholesterol, TG, LDL, and HDL were within the normal limit. Lipid profile levels with the severity of COPD showed that the mean difference of Cholesterol, TG, LDL, and HDL with 4 stages of COPD was not statistically significant (P>0.05). A similar finding was found by Jain[1]. But our investigation finding was

TABLE 3 Determinants of forced expiratory volume in 1 second as obtained by multiple linear regression (n=100)

Variables	Beta coefficients	Standard error	t	*P**
Age (years)	-0.1	0.2	-0.9	0.39
Body mass index (Kg/m²)	1.3	0.4	3.2	0.00
Pack-year smoking	0.2	0.1	1.8	0.08
Duration of illness (years)	0.8	0.3	3	0.00
Total cholesterol(mg/dL)	0.9	0.3	3.6	0.00
Low-density lipoprotein cholesterol (mg/dL)	-0.9	0.3	-3.6	0.00
High-density lipoprotein cholesterol (mg/dL)	-0.9	0.3	-2.7	0.01
Triglycerides (mg/dL)	-0.1	0.1	-2	0.05

*Adjusted R square is 26.3%

contradictory to the study by Mitra[5]. Mitra described that lipid profile parameters were positively correlated and HDL is negatively correlated with interleukin-8 in COPD. That means there was a relationship between inflammation and dyslipidemia in COPD.

Over many years, the Friedewald equation has proven to be a useful and affordable tool for estimating LDL. As it is estimated rather than directly measured so there are many circumstances in which the estimation is erroneous, particularly during the high TG. The LDL calculation is erroneous when triglyceride exceeds 400 mg/dL and the underestimating of LDL starts at triglyceride levels as low as 150 mg/dL[18]. The mean TG and LDL levels in our study were low 121.7 ± 51.9 and 102.0 ± 35.6 respectively. Although the low levels of TG and LDL were exceptional, however, the exact cause is not known.

In our study correlation of COPD and its severity with cholesterol, TG, LDL, and HDL were compared. However, no statistically significant correlation was established. Our study was similar to the previous study[10,19]. But contradictory to Mitra[5], and Xuan[20]. A meta-analysis showed that the use of hypolipemic agents like statin, gender, body mass index, lifestyle, smoking, and severity of disease might be the contributing factors for dyslipidemia in COPD patients[20]. The possible explanation for the development of dyslipidemia in COPD was systemic inflammation, physical inactivity, use of corticosteroids, and oxidative stress due to smoking.

Limitation

Due to the fund and time limitation, we calculated the sample size considering the large margin of error (10%). However, using an ideal margin of error of 5% the sample size will be 384. In addition, the subjects were recruited purposively. Because of small sample size the mean lipid profile level found unstable specially stage I and IV.

Conclusion

Plasma level of total cholesterol and triglyrides tend to increase, statistically non-significant, with stages of COPD. However, the association of plasma lipids becomes statistically significant when the effects of age, BMI, pack-year smoking, duration of illness are account in multiple linear regression analysis. Further studies with a representative large number of samples are required for a conclusive result.

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Author contributions

- Conception and design: GCS, SKP, RC, SA
- Acquisition, analysis, and interpretation of data: GCS, SKP, SCP, SI
- Manuscript drafting and revising it critically: GCS, DD, CA, SARAC, MAR[4], AKMMH, MAR[1]
- Approval of the final version of the manuscript: GCS, SKP, AKMMH, MAR[1]
- Guarantor of accuracy and integrity of the work: GCS

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

Ethical approval was taken from IRB, BSMMU (BSMMU/2019/2056).

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