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General Medicine

AN OBSERVATIONAL STUDY TO COMPARE LIPID PROFILE STATUS IN STABLE COPD PATIENTS AND ITS CORRELATION WITH COPD RELATED FACTORS

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ABSTRACT **CONTEXT:** COPD is a progressive disease associated with systemic inflammatory response, which may lead to extra pulmonary manifestations. This study observed the lipid profile changes in COPD patients and it is correlated with various parameters.

AIMS AND OBJECTIVES: To study the lipid profile status in stable COPD patients its correlation with other COPD factors.

STUDY DESIGN observational study

MATERIALS AND METHODS The study was conducted on 100 clinically stable COPD patients attended medicine OPD of Government Rajaji Hospital & Madurai Medical College during the study period from April 2017 to August 2017. 50 matched persons were taken as controls. Serum lipid profile and spirometry was performed in them.

RESULT: There were 87 Males & 13 Females cases.Total cholesterol (p=0.006) and LDL (p=0.001) was significantly increased and the HDL was significantly decreased in relation with increasing in COPD stages. (p= 0.02).

CONCLUSION: Periodic monitoring of lipid profile is advised in COPD patients.

KEYWORDS : COPD, lipid profile, Dyslipidaemia

INTRODUCTION

COPD (Chronic obstructive pulmonary disease) is a progressive disease associated with systemic inflammatory response, which may lead to extra pulmonary manifestations in the majority of patients with a negative impact on overall prognosis of the disease. (1, 2) Despite therapeutic developments in the past few years, COPD is a leading cause of morbidity and mortality.

COPD co-morbidities, defined as other chronic medical conditions associated with COPD, contribute significantly to poor health outcomes. (3) The co- morbidities associated with COPD are cardiovascular diseases (CVD) like, Ischemic heart disease(22%), Cerebro vascular disease (14%), Heart failure (39%),Pulmonary hypertension, Arrhythmias (12-14%), Hypertension (40 -60%), **Dyslipidaemia**, Type 2 diabetes mellitus, Coagulopathy, Polycythaemia, Anaemia, Skeletal muscle dysfunction (32%), Osteoporosis, Depression (20 – 60%), Obstructive sleep apnoea, GERD (30 – 60%), Renal dysfunction , Lung cancer , Pneumonia. (3, 4, 5, 6)

COPD is projected to be the 3rd leading cause of death in the world by 2030, and the 7th as a burden of disease. (4) COPD prevalence is about 4-5% in India. (10, 11) The prevalence of COPD in non-smokers is about 25 – 45 % among total COPD cases in India. (12) Dyslipidaemia has also been observed in other pulmonary diseases likeAsthma, Cystic fibrosis. (7)

Most of the increased mortality associated with COPD is due tocardiovascular diseases. Dyslipidaemia is one of the major risk factor forIschemic Heart disease (IHD) in COPD.

Dyslipidaemia is clinically important because of role of lipoproteins inatherogenesis and it plays a crucial role in development of various cardiovascular diseases and DM type 2. Smoking is strongly implicated in thermogenesis and smoking is one ofthe major risk factors for development of dyslipidaemia.

Nicotine in Cigarette smoke increases atherogenic LDL via acceleratedtransfer of HDL and impaired clearance of LDL , resulting in deposition of LDLin arterial wall.Dyslipidaemia is one of the risk factors for cardiovascular morbidity andmortality particularly IHD, and many authors from India and abroad reportedvarying results.

No such studies could be found in COPD patients in Tamilnadu. Thepresent study is planned to study the lipid profile status in stable COPD patientsand to correlate it with COPD related and other factors.

MATERIALS AND METHODS:

STUDY POPULATION:

The study was conducted on 100 clinically stable COPD patients attended general medical OP and Thoracic medicine OPD of Government Rajaji Hospital & Madurai Medical College during the study period from April 2017 to August 2017. 50 age, sex, socioeconomic status matched persons came to medicine OPD were taken as controls. Serum lipid profile was performed in the patients and the controls. Spirometry was done in patients.

INCLUSION CRITERIA:

Stable COPD patients

EXCLUSION CRITERIA:

Patients with Hypertension ,
Diabetes Mellitus and other systemic illness not related to COPD
Alcoholics
Tuberculosis
Thyroid disorders
Rheumatological disorders like RA, SLE etc.
Patients on systemic steroids & lipid lowering agents.
Patients with familial dyslipidaemias
Patient with COPD exacerbation within 6weeks

ETHICAL COMMITTEE APPROVAL: Obtained.

STUDY PROTOCOL:

A previously designed proforma will be used to collect the demographic and clinical details of the patients. Detailed history pertaining to present illness as well as a thorough history regarding other disease conditions were obtained. Each patient was enquired about previous drug intake for Hypertension, Diabetic and cardiac illness.

A thorough clinical examination and essential biochemical investigation was done.

STATISTICAL ANALYSIS: The data collected in the study was formulated into a master chart in Microsoft Office excel and statistical analysis was done with help of computer using statistical software package SPSS V.17 for Windows.

Using this software, frequencies, range, mean, standard deviation and percentages were calculated.

RESULTS:

The study results were as follows:

There were 87 Males and 13 Females. Mean age of the patients was 57.38 Years. Controls were 40 males and 10 females.

There were 34 smoker and 38 Ex-smoker Males. 51.38 % Males were heavy smokers. All females were non-smoker.

67 % of patients had >5 years of TDI. Mean TDI was 9.2Years.

Majority of patients (51%) had normal BMI. Mean BMI was 19.07kg /m2.

54%, 26 %, 3 % patients belonged to moderate, severe, very severe stage of COPD respectively. None of the females had very severe COPD.

Majority of patients (88%) had Grade 1 & 2 Dyspnea (MMRC Scale)
Majority (79%) of patients had ≤1 exacerbation in the last one year. 79.31% among males, 76.92% among females had ≤1 exacerbation in the last one year.

5%, 33.2%, 52.4%, 4.8% patients had ≥ 2 exacerbations in the last year belonged to Mild, Moderate, Severe, Very severe stages of COPD respectively. More number of patients had ≥ 2 exacerbations in the last year,as the severity of COPD increases.

Lipid profile status comparison with various COPD related factors in thepresent study

a) Mean lipid profile value of study subjects:

Mean Total cholesterol was 153.1 ± 45.8 mg/dl
Mean Triglyceride was 98.5 ± 58.2mg/dl.
Mean HDL was 45.4 ± 17.7mg/dl.
Mean VLDL was 19.7 ± 11.6mg/dl.
Mean LDL was 93.0 ± 32.5 mg/dl.

b) Even though all mean lipid values were higher in females than males, there was no statistical significance.

c) Change in lipid parameters were not related to change in age of COPD patients.

d) BMI had positive correlation with increase in mean VLDL

Table No: 1 Comparison of lipid parameters with COPD Stages

Lipid Profile	COPD Severity				P value
	Mild	Moderate	Severe	Very Severe	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
TC	143.5 ± 27.1	143.8 ± 44.9	172.0 ± 50.1	210.3 ± 21.9	0.006
TG	90.0 ± 57.4	100.7 ± 67.4	99.8 ± 37.8	95.3 ± 47.1	0.930
HDL	56.5 ± 18.3	46.7 ± 18.6	36.1 ± 10.9	39.6 ± 2.8	0.002
VLDL	18.1 ± 11.4	20.2 ± 13.5	19.8 ± 7.6	19.0 ± 9.4	0.940
LDL	87. 2 ± 27.6	84.6 ± 30.2	110.6 ± 32.6	125.0 ± 29.5	0.001

e) Progress in COPD stages was associated with significant reduction in HDL. (p =0.02) and TC and LDL were higher in stage 4 compared to other COPD stages.

Table No: 2 Comparison of lipid profile with Dyspnea Grading

Lipid Profile	Dyspnoea MMRC Scale				P value
	I	II	III	IV	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
TC	141.4 ± 40.2	144.7 ± 33.0	221.6 ± 39.0	244.0 ± 28.9	<0.001
TG	90.0 ± 61.0	100.7 ± 55.4	122.1 ± 55.4	130.3 ± 53.2	0.335
HDL	48.8 ± 22.3	42.2 ± 11.1	46.1 ± 15.4	34.0 ± 4.5	0.230
VLDL	18.0 ± 12.2	20.1 ± 11.0	24.4 ± 11.0	25.7 ± 10.7	0.350
LDL	84.1 ± 26.8	97.2 ± 34.0	104.5 ± 39.9	140.3 ± 2.0	0.007

f) As Dyspnea grade increased, there was elevation of both mean Total cholesterol (p=0.001) & mean LDL (P=0.007).

g) As the number of exacerbations per year increased, there was a significant increase in mean total cholesterol (P=0.005), mean TG (p=0.04) and mean LDL (p=0.001)

Table No: 3 Comparison of Lipid profile with TDI in years

Lipid Profile	Total Duration of Illness (in years)			P value
	≤ 5	6-10	>10	
	Mean ± SD	Mean ± SD	Mean ± SD	
TC	145.8 ± 44.5	154.9 ± 37.5	158.5 ± 55.0	0.515
TG	79.7 ± 37.4	119.4 ± 75.7	95.0 ± 47.0	0.016
HDL	46.6 ± 20.2	44.3 ± 13.7	45.5 ± 19.3	0.871
VLDL	15.9 ± 7.4	23.9 ± 15.2	19.0 ± 9.3	0.016
LDL	88.2 ± 30.4	92.4 ± 30.5	98.6 ± 36.5	0.435

h) The change in atherogenic lipid parameters (HDL, LDL) were not related to increase in TDI except significant increase in mean TG (P=0.01) with increase in TDI.

i) There was no significant difference in lipid profile related to smoking status.

j) There was no significant alteration in lipid parameters with relation to treatment with Inhaled β2 agonists and inhaled Corticosteroids.

k) There was significant decrease in HDL with treatment of oral β2 agonists.

DISCUSSION:

The study was conducted on 100 clinically stable COPD patients and 50controls attending general medical OP and Thoracic medicine OPD of Government Rajaji Hospital & Madurai Medical College to assess the lipid profile status and to correlate it with COPD related factors like severity of COPD, BMI, TDI, Exacerbation, Smoking status. Cases were strictly selected as per the criteria.

In the present study, all mean lipid values were higher in females than males and there were not statistically significant. R W Dal negro et al (2015) found that the prevalence of dyslipidemia in COPD is more among females than males. Fekete and Mosler (1987) reported that triglycerides were significantly lower in COPD females, the other parameters were almost equal in both the gender. In present study, it is not significant statistically.

In the present study, there was no significant change in atherogenic (HDL, LDL) lipid parameters with increase in TDI. This may be possible due to the severity of systemic inflammation of COPD increases, as the duration of illness increases.

In the present study, there was no significant change in atherogenic (HDL, LDL) lipid parameters with increase in TDI. There was significant increase in mean TG (P=0.01) with increase in TDI. It was found that with increase in BMI, there was increase in mean total cholesterol, mean triglycerides, mean LDL and reduction in mean HDL levels. But these are not statistically significant.

Decreased Ventilatory function (FVC, FEV1) were likely to develop Dyslipidemia. In the present study, there was significant Total cholesterol (p=0.006) and LDL (p=0.001) elevation and significant HDL reduction in relation with increase in COPD stages but Don D. and S.F Paul showed that severe airflow obstruction had slightly lower concentration of triglycerides.According to Niranjan et al (13) &Attaran et al , mean levels of lipid parameters were not different in different stages of COPD according to GOLD classification.

In the present study, there was significant elevation of both Total cholesterol & LDL with increase in Dyspnea grade. Manglano JD et al (2016) also found that COPD patients with dyslipidemia had more dyspnea grade but Tisi GM et al(1981) reported that increased HDL in COPD patients and hypothesized that the increased work of breathing might constitute a chronic exercise stimulus for the respiratory muscles, resulting in an increase in HDL levels. Although possible, it is doubtful that respiratory muscles have such a systemic impact.

In this study, there was no significant change in mean value of lipid parameters with treatment of ICS. Calverley P M et al (2007) found

that Inhaled corticosteroids (ICS) commonly used in COPD at doses Up to 1000mcg fluticasone per day for years) are associated with initial systemic effects including atherogenicdyslipidaemia but Yuvaz et alalso has shown that HDL level increases in children with asthma who use inhaled steroids. The Mechanism of effect was not clear.

In the present study, reason for no change in lipid parameters with ICScould be due to none of our patients had high dose inhaled steroid as mentionedin Calverley et al study.

In 1997, Floren CH et al , found that increased HDL cholesterol wasdue to drugs like Bambuterol (Inhaled β2-adrenergicagonist) and concluded thatBambuterol increases HDL synthesis in the liver and intestinal wall. In 2003,BaharUlubap et al, Studied lipid profile in COPD patients and concluded that the increased HDL levels might be related to the drugs used by patients. Tisiet al, suggested that the effects of some drugs, such as B2 agonists, might beresponsible for an increased level of HDL in COPD patients.in contrast, in thepresent study, there was significant reduction of HDL with the treatment of OralB2 agonists.

In the present study, there was a significant increase in mean totalcholesterol (P=0.005), mean TG (p=0.04) and mean LDL (p=0.001) withincreased frequency of exacerbations in last one year. Enrico MC et al (2011) showed that serum levels of triglycerides directly relate to the frequency andduration of exacerbation in COPD population. According to Kupeli et al, COPD patients with Dyslipidemia had more exacerbations. Statins are associatedwith a reduction in death rate by 36% and 30% decrease in risk of COPDexacerbation. Systemic inflammation increases during COPD exacerbations withan elevation of oxidative stress, plasma fibrinogen and serum IL -6 levels,suggesting that COPD exacerbations can increase dyslipidemia.

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.

So these patients should be regularly screened for dyslipidemia and started treatment with hypolipidemic drugs in time to reduce the cardiovascular morbidity and mortality.

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