

## Serum high-density lipoprotein and triglycerides in patients with chronic obstructive pulmonary disease

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### Abstract:

**Background:** Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow limitation and inflammation. It is now recognized to have systemic consequences that may affect morbidity and mortality. In patients with COPD, smoking is the major risk factor which affects the lipid profile.

The objective of this study was to evaluate serum levels of high-density lipoprotein (HDL) and triglycerides (TG) in patients with COPD and compare them with healthy non-smoking controls.

**Methodology:** This study was conducted in COPD patients with age and gender matched healthy controls. Both cases and controls were evaluated to obtain relevant history and clinical data. Spirometry and fasting lipid profile were performed in cases and controls; staging of COPD was based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011 guidelines.

**Results:** Fifty one subjects diagnosed with COPD and an equal number of controls were recruited; this included 43 males and 8 females with a mean age of 57.3 years. The mean smoking index of COPD patients was 316.8. Seven (13.7%) patients had mild, 30(58.8%) had moderate, 12(23.5%) had severe and 2(3.9%) had very severe COPD.

Twelve (23.5%) patients each in the COPD and control group had elevated triglycerides; the mean level being 141.6 mg/dl in COPD patients and 136.3 mg/dl in controls. (p=0.53). Thirty one (60.7%) patients with COPD and 22(43.1%) controls had decreased HDL; mean level was 41.2mg/dl in COPD patients and 47.6mg/dl in controls. A statistically significant difference was found in serum HDL level between cases and controls. (p=0.009)

**Conclusions:** It can be concluded from this study that lipid profile derangements are common in patients with COPD compared to healthy non-smoking controls. Further, the hypothesis that COPD is a systemic disease is supported by our study.

**Keywords:** HDL; High density lipoprotein, LDL, Low density lipoprotein.

### Introduction:

Chronic obstructive pulmonary disease (COPD) is a disease characterized by airflow limitation that is not fully reversible and is a major cause of morbidity and mortality. It is considered to be the 4<sup>th</sup> leading cause of death in the world and a further increase in its prevalence and mortality is predicted in the coming decades [1]. Globally, it is expected to rise to the 3<sup>rd</sup> position as a cause of death and 5<sup>th</sup> position as a cause of disability adjusted life years (DALY'S) according to the base line projections made in Global Burden of Disease Study (GBDS) [2].

COPD is a systemic disease not only disease of lung but it affects other systems beyond the lungs. Hence, it is now considered as a systemic disease [3]. In patients with COPD a significant relationship exists between respiratory impairment and the presence of comorbid cardiovascular disease, diabetes mellitus and hypertension, respiratory impairment is more likely to have at least two of these conditions and a significantly higher risk of death and hospitalizations, especially when comorbid disease is present [4].

COPD is associated with systemic inflammation. COPD can no longer be considered a disease affecting the lungs alone. The available evidence indicates that: 1) chronic obstructive pulmonary disease has an

important systemic component; 2) clinical assessment of chronic obstructive pulmonary disease ought to take into consideration the systemic components of the disease; and the treatment of these extra pulmonary effects appears to be important in the clinical management of the disease [3].

### Mechanisms of Systemic Inflammation in COPD

**Tobacco Smoking:** Smoking induces systemic inflammation even in absence of COPD. Systemic inflammation in smokers contributes significantly to atherosclerosis. Smoking status (current or reformed) does not influence the level of systemic inflammation significantly [5,6].

**Spill over' of the Inflammatory Process:** An alternative explanation is that the inflammatory process that occurs in the lung parenchyma of these patients "spills over" into the systemic circulation and/or contributes to the priming and activation of different inflammatory cells in their transit through the pulmonary circulation [7].

The relationship between COPD, systemic inflammation and cardiovascular disease is of particular importance, since more than one-half of all patients with COPD die from cardiovascular causes [8].

In a study conducted by, Watz et al., on chronic bronchitis and COPD patients, metabolic syndrome was found in almost half of the patients having chronic bronchitis/COPD irrespective of disease stage and was associated with markers of systemic inflammation, particularly the pro-inflammatory cytokines Tumor necrosis factor- $\alpha$  (TNF-  $\alpha$ ), Interleukin (IL-6) C-reactive protein (CRP) and fibrinogen [9].

A study conducted by Karine et al., concluded that 47% of COPD patients and 21% of control participants exhibited 3 or more determinants of the metabolic syndrome.

Among the COPD patients, 61% had abdominal obesity, 63% had elevated triglycerides levels, 24% had low HDL-C levels, 13% had elevated fasting glucose levels, and 82% had raised blood pressure. Overall, 61% of men and 27% of women in the sub-group of COPD patients presented features of the metabolic syndrome (i.e., 3 or more risk factors of the metabolic syndrome).

Among controls, 32% of participants showed abdominal obesity, 32% elevated triglycerides, 15% had low HDL C levels, 12% elevated fasting glucose levels, and 59% raised blood pressure. Overall, 20% of men and 21% of women in the control group presented 3 or more risk markers of the metabolic syndrome [10].

An epidemiological study conducted in China showed the characteristic of central obesity (34.1 versus 33.1%) and raised blood pressure (56.7 versus 53.4%) were more common in individuals with airflow obstruction than in those with normal lung function, the opposite was seen for raised fasting glucose level (34.3 versus 36.9%), raised triglyceride level (29.6 versus 33.4%) and reduced HDL-cholesterol level (15.9 versus 16.6%) [9].

The pattern of dyslipidemia in COPD has not been well characterized. Chronic obstructive pulmonary disease as a cardiovascular risk factor result of a case-control study (CONSISTE study) showed COPD subjects had the highest prevalence of IHD (12.5% vs. 4.7%) when compared to controls. Dyslipidemia was found in 48.3% of COPD patients and 31.7% among controls [11].

A study in a tertiary care hospital in South India revealed that the mean LDL among COPD patients was  $114.89 \pm 19.61$  (mg/dl) against the control group who had a mean LDL of  $96.22 \pm 19.96$  (mg/dl) which was statistically significant ( $P < 0.05$ ) [12].

### Materials and Methods:

This was a prospective observational cross sectional study which was carried out on Chronic Obstructive Pulmonary Disease patients and healthy controls. The study was conducted at the MS Ramaiah Medical College and Hospital, Bangluru, India. ethical committee approval and consent from the study subjects was obtained.

### Inclusion Criteria

1. Patients diagnosed with COPD based on GOLD guidelines, on history, clinical examination, and pulmonary function test ( $FEV_1/FVC < 0.7$ ).
2. Healthy controls

### Exclusion Criteria

1. Presence of asthma or other chronic respiratory diseases.
2. Presence of malignancy or serious comorbidities that would prevent the study completion.
3. Patients with active pulmonary tuberculosis
4. Patients with acute exacerbation of COPD requiring ICU admission.

**Study Methods:** Both cases and controls were interviewed to obtain relevant data. Based on inclusion and exclusion criteria, about 51 cases of chronic obstructive pulmonary disease patients were compared with an equal number of healthy controls. Global initiative for chronic obstructive pulmonary disease (GOLD) guidelines was used for diagnosing COPD [5].

After taking a history and performing relevant clinical and laboratory evaluations, the following parameters were compiled in a structured clinical proforma:

Clinical history and demographic data, Weight, height, BMI (wt in kg/ht in meter<sup>2</sup>), spirometry report, serum triglyceride level and serum high density lipoprotein).

Spirometry was done on a computerized spirometer (Spirobank G). The test was performed when patients were clinically stable. Spirometry was performed before and after post-bronchodilator short acting  $\beta$ -agonist.

Sample size was 102, calculated using N-master software with 51 cases and 51 controls.

**Statistical Analysis:** All quantitative variables in the present study such as age, hypertriglyceridemia, low HDL were summarized in terms of descriptive statistics such as mean, standard deviation, median and range. All the qualitative variables were expressed in terms of frequencies and proportions. Student T test/Mann-Whitney test were used as indicated to compare the difference between the mean values in cases and controls. Chi-square test was used to find the association between the serum HDL, Serum LDL and COPD. P value  $< 0.05$  was considered to statistically significant. SPSS Version 20 software was used for statistical analysis.

### Results:

**Demographic and Anthropometric Features:** The present study was done on 51 cases of COPD and an equal number of age and sex matched healthy controls. The mean age was 57.3 years in cases and 57.4 years in controls. Among each group there were forty three (84.3 %) males and eight (15.7 %) females. The mean BMI in COPD patients was  $24 \pm 5.32$  kg/sq.m

compared to  $22.59 \pm 4$  kg/sq.m in controls. ( $p=0.120$ ). Among cases, 4(7.8%) cases had BMI  $<18.5$ , 22(43.1%) had normal BMI (18.5-23), 11(21.6%) had BMI 23-25, 8 (15.6%) had BMI 25-30 and 6(11.8%) had BMI $>30$ . The mean waist circumference among patients was  $92.63 \pm 8.1$ cm and  $90.22 \pm 7.78$  cm in controls. ( $p= 0.128$ ) Among these parameters, waist

circumference of  $\geq 102$  cm or in male subjects and  $\geq 88$  cm in female subjects was considered as one of the defining features for metabolic syndrome according to the NCEP ATP III criteria. All the demographic and anthropometric parameters are depicted in Table 1.

**Table 1: Demographic and anthropometric parameters**

Parameter	Cases (n=51)	Controls (n=51)
Age (years)	$57.29 \pm 8.97$	$57.37 \pm 8.88$
Male: Female	43(84.3 %) /8(15.7 %)	43(84.3 %) /8(15.7 %)
Smokers	43(84.3 %)	0
BMI (kg/m <sup>2</sup> )	$24.05 \pm 5.32$	$22.59 \pm 4.01$
Waist circumference (cm)	$92.63 \pm 8.10$	$90.22 \pm 7.78$

#### Smoking Status and Exposure to Biomass Fuel:

Among cases, 43 male patients (84.3%) gave a history of smoking. This included 31(72%) patients who smoked cigarettes and 13(30%) who smoked beedis. Thirty patients were ex-smokers 30 (69.7%) and 13 (30.3%) were current smokers (depicted in Table 2).

All 8 female patients included in the study were non-smokers but had a history of exposure to biomass fuel. All controls were non-smokers and did not have any underlying pulmonary or systemic illness.

#### Laboratory Investigations

**Spirometry:** Among subjects in the COPD group, 7 (13.7%) patients had mild, 30 (58.8%) had moderate, 12 (23.5%) had severe and 2(3.9%) had very severe COPD. Mean spirometric values recorded in cases and controls are shown in Table 3. Categorization of COPD (according to GOLD guidelines) is depicted in Table 4 and Fig. 1.

**Table 2: Smoking status of study subjects**

b	Cases		Controls	
	No	%	No	%
Non smoker	8	15.7	51	100.0
Current smoker	13	25.5	0	0.0
Ex-smoker	30	58.8	0	0.0
Total	51	100.0	51	100.0

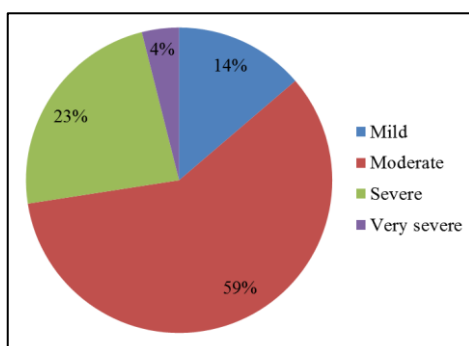
It was found that majority of the smokers had history of smoking more than 10 beedis/cigarette per day with a mean smoking index of 316.8. and mean pack years (of smoking) of 11. These indices which indicate the frequency of smoking have been shown in Table 2.

**Table 3: Spirometry values in COPD patients and controls**

	Cases	Controls	P value
FEV1/FVC	$57.92 \pm 8.87$	$82.12 \pm 5.58$	$<0.001^{**}$
FEV1	$57.71 \pm 17.03$	$100.90 \pm 12.4$	$<0.001^{**}$
FVC	$79.75 \pm 18.24$	$103.31 \pm 12.87$	$<0.001^{**}$

**Table 4: GOLD stage and spirometry values in COPD patients**

	Gold staging			
	Mild (n-7)	Moderate (n-30)	Severe (n-12)	Very severe (n-2)
FEV1/FVC	$63.93 \pm 3.32$	$59.59 \pm 8.58$	$51.63 \pm 8.36$	$50.60 \pm 6.51$
FEV1	$84.14 \pm 2.67$	$60.77 \pm 10.64$	$39.75 \pm 4.69$	$27.00 \pm 0.00$
FVC	$99.43 \pm 5.16$	$84.07 \pm 12.90$	$63.92 \pm 14.64$	$41.00 \pm 2.83$



**Fig. 1: GOLD stage among COPD patients**

**Biochemical Investigations:** The mean values of Fasting Blood Sugar (FBS), High density lipoprotein (HDL) and Triglyceride (TG) in cases and controls have been detailed in the table 5. Twelve (23.5%) patients each in the COPD and control group had elevated triglycerides; the mean level being 141.6 mg/dl in COPD patients and 136.3 mg/dl in controls. Thirty one (60.7%) patients with COPD and 22 (43.1%) controls had decreased HDL; mean level was 41.2mg/dl in COPD patients and 47.6mg/dl in controls. A statistically significant difference was found in serum

HDL level between cases and controls (depicted in Table 6 and Fig. 2 and 3)

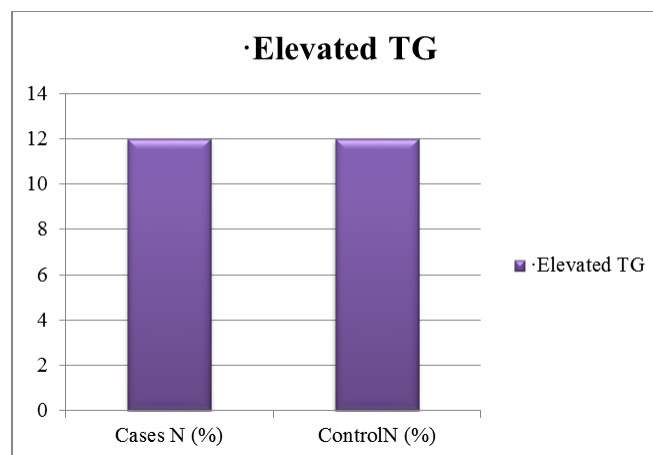
**Table 5: Biochemical parameters in cases and controls**

Mean of serum TG and HDL

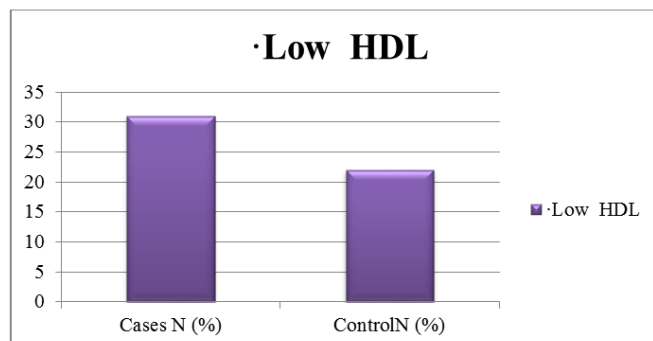
	Cases	Controls	P value
TG (mg/dl)	141.61±51.05	136.35±31.79	0.534
HDL (mg/dl)	41.22±11.73	47.61±12.35	0.009**
FBS (mg/dl)	95.04±11.820	92.88±15.213	0.426

**Table 6: Lipid parameters**

Lipid parameters	Cases N (%)	Control N (%)	P - value
1. Elevated TG	12(23.5%)	12(23.5%)	1.000
2. Low HDL	31(60.8%)	22(43.1%)	0.074+



**Fig. 2:**



**Fig. 3:**

Spirometry values like mean of FEV1 was compared with mean of HDL AND LDL showed that low FEV1 value is in consistent with low HDL and

high triglycerides the details of which is depicted in the Table 7 and Fig. 4 and 5.

**Table 7: Comparison of mean of FEV1 vs serum HDL and TG**

	Cases Mean± SD mg/dl	Control Mean± SD mg/dl	P value
FEV1	57.71 ± 17.029	100.90 ± 12.402	(p-value <0.05)
HDL	41.22 ± 11.79	47.61 ± 12.35	(p-value =0.009)
LDL	141.61 ± 51.04	136.35 ± 31.8	(p-value =0.534)

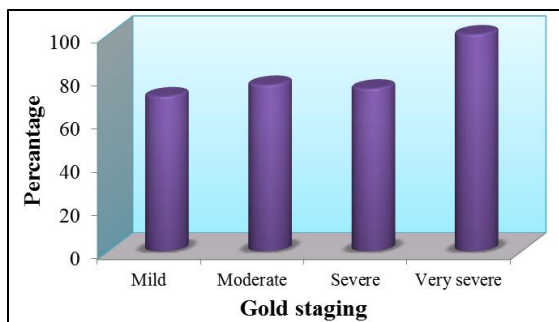


Fig. 4: Increase level of TG in various gold stage

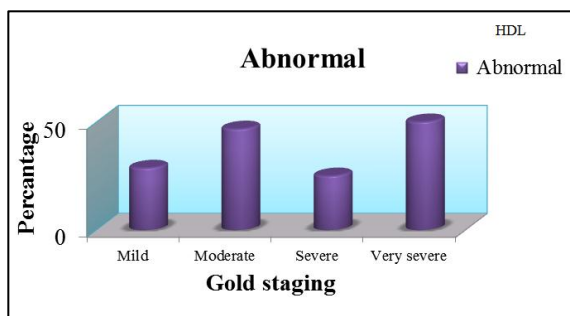


Fig. 5: Increase level of HDL in various GOLD stage

### Discussion:

Our study was a cross-sectional study conducted on 51 COPD subjects and an equal number of matched controls screened for serum high density lipoprotein and triglycerides. Our study exhibited significant level of HDL component of metabolic syndrome with 31 (60.7%) patients having low HDL level as compared to 22(43.1%) controls which was statistically significant. ( $p=0.009$ ). This is in concordance with various studies [9,11].

Our study exhibited high mean LDL level  $141.61 \pm 51.04$  in COPD patients as compare to control  $136.35 \pm 31.8$  which is in concordance with various studies [11,12].

A study conducted by Karine et al., has concluded that 24% had low HDL-C levels [9]. The CONSISTE study showed that COPD subjects had the highest prevalence of IHD (12.5% vs. 4.7%) when compared to controls. Dyslipidemia was found in 48.3% of COPD patients and 31.7% among controls [11].

An epidemiological study conducted in China showed results that metabolic syndrome (22.6 versus 19.8%), central obesity (34.1 versus 33.1%) and raised blood pressure (56.7 versus 53.4%) were more common in individuals with airflow obstruction than in those with normal lung function, the opposite was seen for raised fasting glucose level (34.3 versus 36.9%), raised triglyceride level (29.6 versus 33.4%) and reduced HDL-cholesterol level (15.9 versus 16.6%) [9].

Our study exhibited 31 (60.7%) patients having low HDL level as compared to 22(43.1%) controls which was statistically significant. ( $p=0.009$ ). This is in concordance with various studies [9,11]

An Indian study conducted by Anup et al., has showed low levels of HDL in COPD patients than in control group with mean HDL level of  $49.28 \pm 2.784$  and in control  $51.52 \pm 3.845$   $N=27$  [13]. Another Indian study conducted by Niranjana et al., also showed low HDL level in COPD patients than in control group with mean of  $39.7 \pm 12.47$  in cases and  $44.57 \pm 8.57$  in controls which is consistent with results of our study [14].

In our study, twelve (23.5%) patients each in the COPD and control group had elevated triglycerides; the mean level being 141.6 mg/dl in COPD patients and 136.3 mg/dl in controls. ( $p=0.53$ ) which was not in concordance with studies showing prevalence of high triglyceride level in COPD patient than in control groups [9,11,14].

A study conducted by Karine et al., concluded that 63% of the COPD patients and 32% of controls had elevated triglycerides [10].

**Age and Gender Distribution:** In our study, mean age cases and controls was 57.3 years with a male to female ratio of 5.3:1. Higher proportion of males compared to females could be attributed to increased frequency of smoking among males and exposure to various dusts and allergens at the workplace.

**Smoking Status:** In our study, all male 43(84.3%) cases were smokers and all 8(15.7%) female cases were non-smokers with history of exposure to biomass fuel. Among smokers majority were 31(72%) cigarettes smokers than 13(30%) who smoked beedis with a mean smoking index of 316.8. and mean pack years (of smoking) of 11.

As mentioned in earlier studies, smoking is an important contributory factor for systemic inflammation and its consequences in COPD [13,15,16]. Some of these studies have been reviewed below.

Fabbri et al., and Lone et al., suggest that the term 'Chronic Systemic Inflammatory Syndrome' (comprising age >40 years, smoking for >10 pack-years, symptoms and abnormal lung function compatible with COPD, chronic heart failure, metabolic syndrome, and increased CRP) be added to the diagnosis of COPD [17,18].

Smoking induces systemic inflammation even in absence of COPD. Systemic inflammation in smokers contributes significantly to atherosclerosis [5,6]. Smoking triggers a local inflammatory response in lungs and it also causes systemic inflammation that results in comorbidities like cardiovascular or metabolic disorders [15].

It has been observed in ECLIPSE study that comorbidities were significantly higher in patients with COPD than in smokers and never smokers. COPD patients had more pack years of smoking than smokers with normal lung function and among subjects males were more exposed to smoking than females. They also showed that 'pack years' was the best available measure to quantify smoking status [18].

**Association with Diabetes Mellitus and HTN:** Ten (62.5%) patients had combination of hypertension, increased TG, and low HDL was found more frequent 4(40%). Six (37.5%) patients had 4 parameters of metabolic syndrome

Six (37.5%) patients had combination of parameters DM, hypertension, low HDL, and increased WC was found more common in this group of patients 4 (66.6%).

### Conclusions:

Lipid profile derangements are more common in COPD patients than in general populations and smoking is a major risk factor for development of COPD and systemic inflammation. It is also concluded that COPD is systemic diseases associated more commonly with diabetes, hypertension, lipid profile derangement, osteoporosis, psychological manifestations and osteoporosis. Early detection and treatment of dyslipidaemia in COPD can prevent development of complications like cardiovascular and cerebrovascular disease. Efforts should be made at educating patients and physicians about the screening for dyslipidaemia and other systemic manifestation of COPD.

**Conflicts of Interest:** None declared

**Acknowledgements:** None

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