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Comparative Study of Biochemical Markers Between COPD without CVD and COPD with CVD

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ABSTRACT:

Background:COPD is a systemic disease; it causes various comorbidities. Cardiovascular disease is also a important comorbidity due to COPD. Several biochemical parameters like plasma/serum lipid, glucose, creatinine get derange in COPD.

Aim of the study: The aim of the study was to compare the changes in biochemical parameters in COPD which causes cardiovascular disease also.

Materials and Methods: We investigated 109 confirmed COPD patients, between the age group 40 to 80 years. COPD was diagnosed by Spirometry by following GOLD guidelines.Lipid profile, blood sugar and serum creatinine were investigated among all the patients. Then to confirm the cardiovascular disease 2D echocardiography was done. Then two groups of the patients were made patients having COPD without CVD and COPD with CVD. After that we compared the lipid profile, blood sugar and serum creatinine between these groups.

Results: In this study, the number of COPD patients with moderate, severe, and very severe COPD were 39, 50, and 20, respectively.On echocardiography 57 patients had normal echocardiograph. While remaining 52 patients had cardiovascular diseases(PAH/dilated right atrium or ventricle/ LVDD/low LVEF).39 of them had severe to very COPD.On comparison of biochemical profile between COPD without PAH and COPD with PAH, dyslipidemia was found in which significant differences were found in HDL cholesterol and VLDL cholesterol,while no significant differences were found in other lipid profile test along with blood sugar and serum creatinine.

Conclusion: Our study shows a high prevalence of cardiovascular disease in COPD patients.On comparison between COPD with CVD and COPD without CVD,we found the dyslipidemia in our study. A significant statistical difference was found of HDL and VLDL cholesterol.whereas no significant difference were found at blood sugar and serum creatinine level.

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Keywords: COPD, CVD, Lipid Profile, Serum Creatinine, Blood Sugar, Triglyceride, Total Cholesterol, HDL Cholesterol, VLDL Cholesterol.

ABBREVIATIONS:

COPD: Chronic Obstructive Pulmonary disease
CVD: Cardiovascular disease
FEV1: Forced Expiratory Volume in 1 second
FVC: Forced Vital Capacity
GOLD: Global Initiative of Obstructive Lung Disease
HDL-High Density Lipoprotein
LDL-Low Density Lipoprotein
LVDD: Left ventricular diastolic dysfunction
LVEF: Left Ventricular Ejection Fraction
PAH: Pulmonary Arterial Hypertension
RA: Right Atrium
RV: Right Ventricle
TG-Triglyceride
TC-Total Cholesterol
VLDL-Very Low Density Lipoprotein

INTRODUCTION

Both Chronic obstructive pulmonary disease (COPD) and cardiovascular diseases (CVD) are major global health issues.[1,2] COPD is the 3rd leading cause of death in the world, while CVD is the 1st leading cause of death.[3]So the primary and secondary prevention of COPD, as well as CVD, are public health priorities. According to Indian health data, the death rate from COPD increased by 35.4% between 2009 and 2019.[4]According to the Economic Times, COPD kills more people than AIDS, tuberculosis, malaria, and diabetes combined. Another graving factor is that around 99.15% of the individuals had never heard the word COPD.[5]COPD is characterized by persistent respiratory symptoms and airflow limitations.[6] Cardiovascular disease is closely related to the comorbidity of COPD.[7,8]COPD patients have a major risk of CVD because COPD affects pulmonary blood vessels, right and left ventricle, leading to the development of pulmonary arterial hypertension (PAH), cor-pulmonale (COR-P).[9]CVD among COPD patients increases mortality.[10]Due to the correlation between these two diseases Sometimes it might be confused that COPD causes CVD or CVD is a cause of COPD. So a differential diagnosis between these two diseases must be required. Due to the complexity of COPD and CVD biochemical parameters like lipid profile[11,12],blood sugar[13,14], serum creatinine[15,16] get changed, which depends upon the severity of the disease.

The American Thoracic Society (ATS) and the Euro-pean Respiratory Society (ERS), along with the Global Initiative for Chronic Obstructive Lung Disease (GOLD), recommend spirometry

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(FEV1/FVC0.70) for the diagnosis of COPD. In the present study, the diagnosis of COPD is based on patient history, symptoms, and spirometry. COPD is diagnosed by spirometry which measures FEV1 (forced expiratory volume in 1 sec) and FVC (forced vital capacity). Cardiovascular disease confirmation is done by 2-D echocardiography. There are a limited number of studies investigating dyslipidemia in COPD patients. It is still unknown if dyslipidemia is another independent factor that could explain the increased risk of cardiovascular morbidity and mortality in COPD patients.

Rao et al reported significantly elevated low-density lipoprotein in COPD patients when compared with control but very-low-density lipoprotein, triglyceride, high-density lipoprotein, and total cholesterol were normal, and it may be due to an increased number of smokers in this group.[17]

As a result of various studies in COPD patients, it is still unclear whether COPD patients face dyslipidemia, and whether this dyslipidemia in COPD patients leads to CVD. As well as altered level of blood sugar and serum creatinine in COPD patients develop CVD. The aim of this study was to study the lipid profile, blood sugar, and serum creatinine level in COPD patients and compare these parameters with the patients who were suffering from COPD with CVD. We also looked into whether these biochemical parameters are related to the causes of CVD in COPD patients.

MATERIALS AND METHODS

A hospital-based study was done in the Department of Respiratory Medicine, SRMS Medical College Bareilly, and Department of Respiratory Medicine, Santosh Medical College Ghaziabad during the period of November 2017 to February 2020. Ethical committee approval was taken from both the medical colleges.

Sample Size: Prevalence of COPD lies between 6.5 to 7.7%. We assumed a 6.5% prevalence of COPD with a 5% absolute error and a 10% non-response rate. The estimated sample size came to be 105.

Inclusion Criteria: confirmed COPD patients of the age group of 40 to 80 years.

Exclusion Criteria: Patients suffering from pneumonia, tuberculosis, interstitial lung disease, lung carcinoma, other cancer, and HIV.

Patients were subdivided into four categories: mild, moderate, severe, and very severe COPD according to GOLD guidelines. 91 males and 18 females were included in this study. All the patients were asked about their socio-economic status, smoking habits, history of dyspnoea, duration of breathlessness, family history of respiratory disease, and diabetes mellitus with a well-defined questionnaire. Written consent has been taken from all the participants prior to the data collection. COPD was diagnosed by spirometry machine-schiller SP-1. Before performing the spirometry test, all the precautions were strictly followed by the supporting staff. With spirometry FVC (Forced vital capacity), FEV1 (Forced expiratory volume in 1st second), and FEV1/FVC ratio were measured. To confirm the cardiovascular disease, two-dimensional echocardiography was done by Siemens Acuson X-300 Premium edition.

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Collection of blood sample: Blood sample was collected using a pre-heparinized syringe by a phlebotomist.

Biochemical Test: Lipid profile, blood sugar and serum creatinine were investigated with blood sample. In the lipid profile test, triglycerides, total cholesterol and HDL cholesterol were estimated by a suitable enzymatic method. Whereas VLDL cholesterol and LDL cholesterol were found by Frieldwalds formula. Blood sugar level was detected by the glucose oxidase enzymatic method. A modified Jaffe method was used to estimate serum creatinine.

Patients Group for Study: All the study patients underwent biochemical tests (lipid profile, blood sugar and serum creatinine) and 2D echocardiography was done. Then two groups, Group 1st (COPD without CVD) and group 2nd (COPD with CVD) were prepared. After that, we compared the lipid profile, blood sugar and serum creatinine between these groups.

Statistical Analysis: A detailed statistical analysis of collected data has been done. The age and sex distribution of all patients, their body mass index (BMI), the severity of COPD, echocardiography findings, and its relation to COPD have been explained.Changes in biochemical parameters between COPD without CVD and COPD with CVD were analyzed statistically.

RESULTS

In the present study, we investigated a total of 109 patients of which 91 males and 18 females. The mean age of patients was 61.49 years. The mean BMI of all patients was 20.73 kg/m2. Based on COPD severity 39 patients were included in moderate,50 patients in severe, and 20 patients in the very severe COPD group. We had no patients with mild COPD. (Table **1**)Out of 109 patients, 85 patients (77.98%) were smokers.

On echocardiography 57 patients (52.29%) were not having any cardiovascular disease, 52 patients (47.71%) had pulmonary arterial hypertension (PAH), 33 patients (30.28%) had dilated right atrium/right ventricle, 25 patients had (22.94%) left ventricular diastolic dysfunction followed by 24 patients (22.02%) with low left ventricular ejection fraction.

Patients included in moderate COPD 33.33 % had PAH, 10.25% had dilated RA/RV,7.69% had LVDD and low LVEF. While patients included in the severe COPD group 44% had PAH, 28% had dilated RA/RV and 16% had LVDD and low LVEF. Patients included in very severe COPD groups 85% had PAH, 75% had dilated RA/RV,70 % had left ventricular diastolic dysfunction and 65% had low LVEF.As the severity of COPD increases from moderate to severe, findings of cardiovascular disease significantly increase. (Table-2)

Major CVD findings in our study was pulmonary arterial hypertension (n=52). The mean age of patients having PAH was 64.77±9.50 whereas the mean age of patients without PAH 58.49±9.52. Mean BMI of patients having PAH 20.76±3.36 whereas mean BMI of patients without PAH 20.71±4.81. (Table3)

COPD refers to a group of diseases that cause airflow blockage and breathing related disorder.COPD is also considered as a systemic disease because it affects entire body rather than a single organ, therefore COPD causes various comorbidities. Among the COPD patients several

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biochemical parameters get altered. Biochemical parameters change in COPD which is also related to CVD. Atherosclerosis is most common among CVD patients. This occurs due to the alteration in lipid profile. In the present study, when we compare the lipid profile between two groups with or without CVD, serum triglyceride among the COPD without PAH was 65.86 ±27.63, while COPD with PAH is 85.90±45.22. Serum triglyceride value is comparatively high in PAH patients, but it is statistically insignificant. (Table4)

The same finding is there in total cholesterol, its values are in COPD without PAH was 170.70 ± 22.89, while COPD with PAH was 195.96±33.22. Total cholesterol level was comparatively high in COPD with CVD patients, but this is statistically insignificant. The same findings found in the case of LDL cholesterol, COPD without PAH 108.99 ±21.54 while COPD with PAH is 132.45 ± 31.51. LDL cholesterol value was comparatively high in COPD patients with PAH, but this is statistically insignificant. While in the case of HDL cholesterol (good cholesterol) its value should be lower in healthy individuals. In the present study COPD without PAH, HDL value was 48.54 ±5.55, while in COPD with PAH is 46.33±4.41,HDL cholesterol value found to be statistically significant. VLDL cholesterol in COPD without PAH was 13.17 ±5.53,while in COPD with PAH patients17.18±9.04, VLDL cholesterol values found to be statistically significant. Blood sugar level among COPD without PAH was 131.67 ± 43.39, while inCOPD with PAH was 135.15±40.79.Blood sugar level found to be statistically insignificant. Serum creatinine level in COPD without PAH was 1.154 ± 0.53 and in COPD with PAH was 1.26±0.72. Serum creatinine level in between COPD without PAH and COPD with PAH was statistically insignificant.

Table 1: COPD patient distribution

COPD stages according to GOLD criteria			**No of Patients**	
Grade	**FEV1/FVC(%of predicted)**	**COPD severity**	**Nos**	**%**
GOLD 1	≥80	Mild	0	0
GOLD 2	50-79	Moderate	39	35.78
GOLD 3	30-49	Severe	50	45.87
GOLD 4	< 30	Very severe	20	18.35

Table 2: Comparison between severity of COPD and cardiac changes

Cardiac Changes		**Moderate COPD(39)**	**Severe COPD(50)**	**Very Severe COPD (20)**	**Statistical analysis**
Pulmonary arterial hypertension (PAH)	**No**	26	28	3	$\chi2$=14.6548p=0.000657
	Yes	13	22	17	
Dilated right atrium/ventricle	**No**	35	36	5	$\chi2$=26.4785p<0.00001
	Yes	4	14	15	
Left ventricular diastolic	**No**	36	42	6	$\chi2$=31.5515p<0.00001

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dysfunction	**Yes**	3	8	14	
Low left ventricular ejection fraction (<55%)	**No**	36	42	7	$\chi 2=27.2352 p<0.00001$
	Yes	3	8	13	

Table 3: Distribution of patients age,male female ratio and age

Groups	Age(years) (mean ±SD)	Male: female ratio	BMI (mean ±SD)
COPD without PAH (n=57)	58.49±9.52	47:10	20.71±4.81
COPD with PAH (n=52)	64.77±9.50	44:8	20.76±3.36

Table 4: Comparison of biochemical parameters

Biochemical parameters	COPD patient (mean ±std deviation)		t-test values
	COPD without PAH (n=57)	COPD with PAH (n=52)	
Triglyceride	65.86 ±27.63	85.90±45.22	0.073 Non-Significant
Total cholesterol	170.70 ± 22.89	195.96±33.22	1.495Non-Significant
LDL cholesterol	108.99 ±21.54	132.45±31.51	2.067 Non Significant
HDL cholesterol	48.54 ±5.55	46.33±4.41	0.022 Significant
VLDL cholesterol	13.17 ±5.53	17.18±9.04	0.007 Significant
Blood Sugar	131.67 ± 43.39	135.15±40.79	0.666 Non-Significant
Serum creatinine	1.154 ± 0.53	1.26±0.72	0.39Non-Significant

DISCUSSION

COPD is a chronic lung disease of the elderly group that usually affects people after the 4th decade of life.[18]According to the Economic Times Health World report published in October 2019, COPD is the world's third leading cause, and more than 90% of people are unaware of it.[5]Smoking prevalence is very high among COPD patients. There is a wide variation in smoking prevalence between males and females. The prevalence of smoking is much greater in men than in women**.** COPD is the result of cumulative exposure for decades. Often, the prevalence of COPD is directly related to the prevalence of tobacco smoking, although, in many countries, outdoor, occupational, and indoor air pollution (resulting from burning of wood and other biomass fuel) are major COPD risk factors. Cigarette smoking is clearly the single most important identifiable etiological factor in COPD. In the present study, among the 109 COPD patients, 92 patients (84.40%) were smokers. Susan et al reported the same as our study, about 85% of people with COPD develop the disease because of cigarette smoking.[19]Age is a risk factor for COPD.As age advances, FEV1 declines, and other risk factors add to the disease process.[20]As well, in COPD patients, cardiovascular disease findings increase with age also. There are various cardiac manifestations due to COPD. These infestations aggravate COPD, increasing morbidity and mortality among COPD patients. The findings of cardiovascular

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disease increase with the severity of COPD.[21]In the present study population, pulmonary arterial hypertension has been a major finding. One possible reason for this high prevalence of pulmonary hypertension could be selection bias that favored ordering echocardiograms in patients with clinical features of pulmonary hypertension. The findings of our study appear to be like previous studies in respect of PAH, which increases with the severity of COPD.[22]In the present study, PAH was found in 52 patients (47.70%).The mean age of COPD patients without PAH is 58.49, while those with PAH are 64.77. It shows that the incidence of cardiovascular disease increases with age among COPD patients. It is reviewed in another study also by Ann D Morgan et al.[23]In the present study, there is no change in BMI among the patients with or without CVD. CVD in COPD does not differentiate between males and females. COPD is an umbrella term that represents airflow blockage and breathing-related disorders.[24]COPD is also classified as a systemic disease because it affects the entire body rather than just one organ. As a result, COPD causes a variety of comorbidities.[25]Common comorbidities described in association with COPD are pulmonary infections, skeletal muscle abnormalities, hypertension, diabetes, cancer, pulmonary vascular disease.[26,27]Chronic conditions of these diseases affect the health of COPD patients.[28]Due to various comorbidities among COPD patients, several biochemical parameters get altered. Biochemical parameters change in COPD, which is also related to CVD. Atherosclerosis is the most common among CVD patients. This occurs due to the alteration in lipid profile. In the present study, when we compared the lipid profile between two COPD groups with or without CVD, serum triglyceride among the COPD without PAH was 65.86 ±27.63, while COPD with PAH was 85.90±45.22. Serum triglyceride value is comparatively high in COPD with PAH patients, but it is statistically insignificant. The same is true for total cholesterol, which was 170.70 ±22.89 in COPD without PAH and 195.96±33.22 in COPD with PAH. Total cholesterol level was comparatively high in COPD with CVD patients, but this is statistically insignificant. The same findings were found in the case of LDL cholesterol, COPD without PAH is 108.99 ±21.54 while COPD with PAH is 132.45 ± 31.51. LDL cholesterol value was comparatively high in COPD patients with PAH, but this is statistically insignificant. While in the case of HDL cholesterol (good cholesterol), its value should be low in healthy individuals. The HDL cholesterol value in COPD without PAH was 48.54± 5.55 in the current study, while it was 46.33± 4.41 in COPD with PAH. This difference was observed to be statistically significant. VLDL cholesterol in COPD without PAH was 13.17 ±5.53, while in COPD with PAH patients 17.18 ± 9.04, VLDL cholesterol values were found to be statistically significant. The blood sugar level in COPD without PAH was 131.67± 43.39, while it was 135.15±40.79 in COPD with PAH. Blood sugar levels were found to be statistically insignificant. Serum creatinine level in COPD without PAH was 1.154 ± 0.53 and in COPD with PAH was 1.26±0.72. Serum creatinine level in between COPD without PAH and COPD with PAH was statistically insignificant. (Table:4)As a result of our study, on comparison of lipid profile between two groups (COPD without CVD and COPD with CVD), we found significant changes in HDL cholesterol and VLDL cholesterol between these groups. Whereas triglyceride, total cholesterol, and LDL cholesterol values were found not to be significant.The majority of studies show that HDL cholesterol (the basic

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representative of lipid profile parameters) is low in COPD and cardiac patients.[29-31]Dyslipidemia is probably one important factor for COPD as well as CVD. Patients with COPD generally encounter cardiovascular complications. The lipid profile is usually acknowledged as a good predictor of cardiovascular disease. Treatment for dyslipidemia is important in both cases. Because the decreased level of HDL in patients is also the cause of atherosclerosis. To reduce the chances of dyslipidemia, people should be on a healthy diet and smoking must be restricted. Mitra, et al. found a significantly abnormal lipid profile in all COPD patients.[32]Our study was compatible with some previous studies. There are wide variations in lipid profile levels in COPD patients. Overall,dyslipidemia in COPD and its association with the severity of COPD remains uncertain. Serum creatinine and blood sugar level values are not found to be significant between these two groups. (Table:4)In a cohort study, Chung-Yu et al reported that COPD patients have a 1.61 times higher risk of developing renal disease than those without COPD.[33]It might happen that in our study we did not include the glomerular filtration rate to assess kidney function. And one possible reason is that our sample size is small in comparison to this case-cohort study by Chung-Yu Chen.In the present study, no significant difference was found in blood sugar level between COPD with PAH and COPD without PAH, but other studies say that high blood sugar levels constitute important comorbidities that have a negative impact on lung function, the reason behind these remains identified. It might be possible that hyperglycemia leads to directly altered lung function by glycosylation of connective tissue, increased muscle weakness, and /or inflammation. In this regard, several studies have demonstrated that pulmonary function tests are significantly decreased in subjects with high blood sugar levels in comparison to healthy control.[34-36]

CONCLUSION

In COPD there is narrowing in the airways. Airways narrowing affects cardiac function. So the cardiovascular disease is one of the comorbidity of COPD. Our study shows a high prevalence of cardiovascular disease in COPD patients. In this study, we evaluated the serum level of glucose, lipid profile, and creatinine. We found dyslipidemia in our study. A significant difference in HDL cholesterol and VLDL cholesterol found between the COPD without CVD and COPD with CVD groups. Decreased level of HDL cholesterol in COPD patients with a degree of bronchial obstruction causes atherosclerosis. No significant difference was found in blood sugar and serum creatinine level between the above-mentioned groups.

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