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SERUM LIPID LEVELS AND BIOCHEMICAL CRITERION OF COPD PATIENTS IN RELATION TO SMOKING STATUS

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Abstract

Background: Air pollution and tobacco use are known to be associated with chronic obstructive pulmonary disease (COPD), nevertheless the former is the most investigated and implicated risk factor for the condition. One of the recognized features of this long-term lung condition is that it mostly results from persistent airway inflammation. Research suggests that smoking may have an impact on lipid metabolism since it is associated with low levels of HDL cholesterol along with elevated levels of triglycerides. Being the most prevalent aqueous antioxidant, uric acid concentration is considered to indicate the body's ability to combat oxidative stress. The purpose of our study was to determine the association of smoking status with biochemical markers and lipid profiles in COPD patients.

Methods: This prospective study was conducted at D.I Khan Medical College, there were sixty COPD patients in all, and they were split into three groups based on whether they smoked or not: non-smokers, smokers, and ex-smokers. The comprehensive demographics of the enrolled cases were documented upon obtaining informed written consent. The collected data were analyzed using SPSS 24.0.

Results: Serum urea concentrations ($p < 0.04$), smoking status (smoker, non-smoker, or ex-smoker), total serum cholesterol values ($p < 0.03$), and the total number of packs-years for the smoker/ex-smoker categories all showed low correlations with the stages of COPD ($p < 0.04$).

Conclusion: In addition to elevated low-density lipoprotein cholesterol (LDL-CHOL) or decreased blood uric acid levels, we found that smoking was associated with alterations in the lipid profiles of smokers and ex-smokers.

Keywords: Smoking status, COPD, Tobacco Consumption, Lipid Profile, Uric acid, Biochemical Parameters.

INTRODUCTION

The phrase "preventable disease" describes chronic obstructive pulmonary disorder (COPD), which is marked by changes in lung function measurements as observed on spirometry and persistent signs like cough and dyspnea. COPD is largely caused by ongoing inflammation of the airways. Although air pollution is one of the variables associated with COPD that has been most extensively investigated and implicated, smoking remains the most common risk factor. The third leading cause of death globally, COPD affects about 400 million individuals, according to the World Health Organization (WHO) [1].

Airway inflammation is an eminent cause of COPD. Oxidative stress, a byproduct of tobacco smoke is crucial for the development and exacerbation of respiratory tract inflammation. Inflammatory cytokines, which are generated as a consequence of oxidative damage and messenger RNA-mediated increased production of these inflammatory mediators, such as TNF-α, TNF-β, as well as IL-6 in type II human alveolar epithelial cells as well as IL-8 in airway cells, speed up the inflammatory reaction. This in turn encourages NF-Kb binding to DNA. [2] Systemic inflammation is another factor that influences the development of COPD, particularly impacting its progression. It can arise and persist as a result of direct or indirect pathways related to tobacco smoke exposure [3].

Tobacco or nicotine dependency is the result of long-term tobacco usage. Clinical or Para clinical methods can be used to assess nicotine dependency. The clinical evaluation is predicated on the identification of tobacco use, nicotine dependency, kind of tobacco item used, and smoking status. The number of cigarettes smoked can be used to determine a person's smoking status: non-smoker, occasional smoker, regular smoker, or former smoker. There are two methods to quantify tobacco use: the amount of cigarettes smoked in a day and the number of packs smoked annually (PY). The Fagerström nicotine dependence test is a tool for diagnosing nicotine dependence. A Para clinical assessment of tobacco dependency may be conducted using laboratory biochemical testing, which finds indicators of tobacco smoke exposure. The amount of cotinine, a nicotine metabolite that may be found in urine, blood, saliva, etc., and the quantity of carbon monoxide that is present in the exhaled air are two examples of these tests. Studies to confirm or refute self-reported abstinence most commonly use carbon monoxide in exhaled air, cotinine (a nicotine metabolism that may be measured in the plasma, saliva, urine, and hair, as well as intranasally), but also markers such as anatabine, anabazine, a substance called urinary acid (UA), and nitric oxide[4]. Uric acid, which is produced when nucleic acids degrade and after purine oxidation concludes, is another indicator of tobacco smoke exposure. Utilizing plasma, it is moved from the liver to the kidneys, where it undergoes filtration and excretion in a proportion of 70%; the remaining portion is broken down in the gastrointestinal tract. A person's uric acid levels can change with age, food, sex, genetics, activity, menopause, and other variables [5]. Because UA is the most prevalent aqueous antioxidant, it is believed to indicate the body's capability for antioxidant defense. Up to 60% of serum free radical scavenging is attributed to uric acid, and smoking induces oxidative stress [6].

Specific types of lipids found in cells are crucial for many functions of the cell, such as energy supply, membrane integrity, and signaling functions including cell division, metabolism, and activation of apoptosis. The pathophysiology of COPD is correlated to lipid dysregulation, according to a growing body of research. Reduced lung function and a higher risk of COPD morbidity are associated with obesity with elevated triglyceride and cholesterol contents [7]. Statin usage was linked to a 52% decrease in COPD mortality and a 38% reduction in overall mortality (95% CI 0.52 to 0.73), according to a meta-analysis [8]. Furthermore, phospholipid, which is made up of two tails of fatty acids that are hydrophobic and a hydrophilic head, plays a vital role in cell membrane formation. The bulk of pulmonary surfactants is composed mostly of phospholipids, and the specific makeup and concentration of each phospholipid is a crucial component of the surfactant's functionality. The surfactants exhibit greater resistance to high pressures produced at the interface of air and liquid of the mammalian lung when there is more phosphatidylcholine (PC)16:0/16:0 enhancement inside them. Patients with COPD also have recognized decreases in total surfactant phospholipids, which may be related to pulmonary function.[9]

Based on the theories of systemic inflammation, aging, and lung function degradation, the coexistence of COPD and MetS was first studied.[10,11] Additionally, certain pathogenic theories have recently been proposed based on MetS's clinical features. The innate immune system can be triggered by hyperlipidemia and fatty acid-induced inflammation. Second, subepithelial fibrosis and airway smooth muscle hyperplasia are caused by higher levels of leptin and decreased levels of adiponectin in abdominal obesity. Finally, changes to the mechanical and functional properties of the smooth muscle of the airways may result from insulin resistance and hyperglycemia. Breathing hyperresponsiveness and airway blockage are the results of these processes.[12]
The purpose of this study was to find the association of smoking status with biochemical markers and lipid profiles in COPD patients.

MATERIALS AND METHODS

This prospective study was conducted at D.I Khan Medical College for a period of January 2022-December 2023 and comprised 60 patients. Patients who met the eligibility requirements for the GOLD criteria for COPD diagnosis signed an informed consent form, and could comprehend and follow research instructions were included in this investigation. Patients who did not meet the aforementioned requirements refused to sign an informed consent form, were unable to comprehend the study's protocol, experienced unsteady chronic or acute medical conditions (psychiatric, cardiovascular, etc.), had neuro-motor retardation, were pregnant, or receiving treatment with statins, allopurinol, or colchicine were all excluded.
A combination of anamnestic and clinical data, health records, or current symptoms were used to diagnose COPD, in compliance with criteria issued by the Global Institute for Research over chronic obstructive pulmonary disease (GOLD) [14]. Lung function tests were used to validate it when the volume of forced expiratory flow in one second (FEV1)/forced pulmonary capacity (FVC) < 0.70 was evaluated using a spirometric ratio. The patients were divided into four groups based on the FEV1 value, which indicated the degree to which the airflow restriction: GOLD I stage was defined as FEV1 value below 80 percent, GOLD II stage as FEV1 value between 50 and eighty percent, GOLD III stage as FEV1 value between 30 as well as 50%, and GOLD IV stage as FEV1 value less than 30%.
B2 agonists were used to treat COPD in each study participant in addition to traditional bronchodilators or inhaled corticosteroids.
Based on their smoking status, the patients were split into three groups: daily smokers, non-smokers, or ex-smokers. Patients with a lifetime cigar smoking total of more than 100 were included in the smoker group. Patients in the ex-smoker group had given up smoking for at least six months before the assessment.
Descriptive data in the form of a typical basis, and deviation from the mean, median, and range were provided for smokers, non-smokers, and ex-smokers. The Spearman's ranked correlation coefficient was used to measure the degree of relationship between biochemical indicators linked to smokers and non-smokers.

RESULTS

There were 51 (85%) males and 9 (15%) females among all COPD cases. The mean age of the cases was 61.14±12.53 years and the mean BMI was 25.5±3.27 kg/m^2. The majority of participants, 42 (70%), were from urban areas, while 18 (30%) had rural residency. Comorbidities like HTN, DM, and obesity were identified. (Table 1)

Table 1: Demographical Characteristics of cases:

Variables	Frequency	Percentage
Gender		
Male	51	85
Female	9	15

Mean age (years)	61.14±12.53	
Mean BMI (kg/m^2)	25.5±3.27	
Residency		
Urban	42	70
Rural	18	30
Comorbidities		
HTN	25	41.7
DM	19	31.7
Obesity	16	26.7

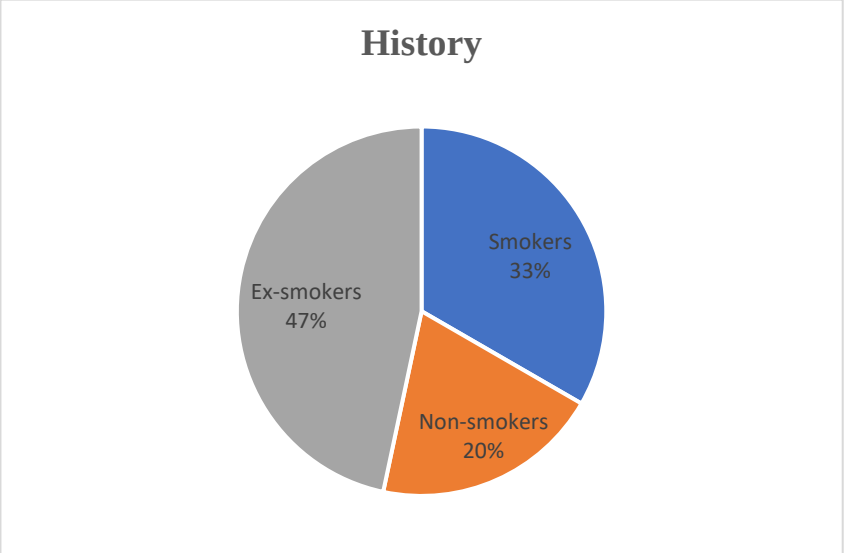


Figure 1: Smoking history among all cases

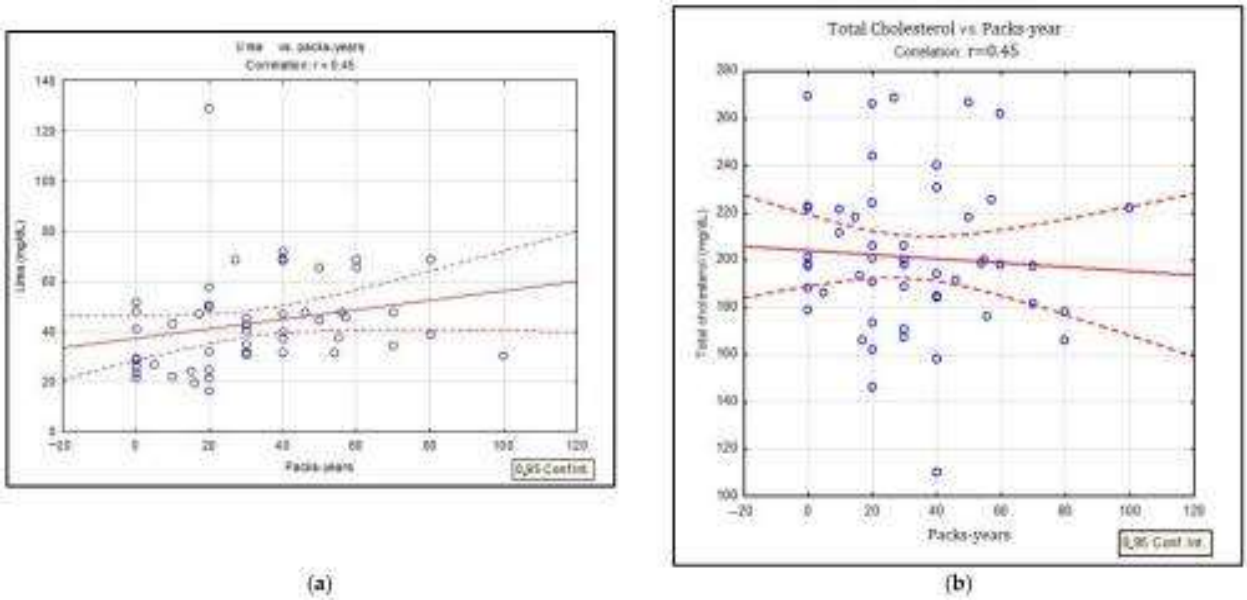
There were 20 smokers, 12 were non-smokers and 28 were ex-smokers. (Figure-1)
With biochemical markers, there was statistical significance was observed among nonsmokers and ex-smokers with smokers with a p-value <0.04. (table 2)

Table 2: Levels of Biochemical markers in COPD cases:

Variables	Non-smokers	Smokers	Ex-smokers
HDL	52.3	49.6	51.7
LDL	98.5	107.2	112.7
Lipids	347.9	372.5	361.3
Total Cholesterol	182.4	201.1	199.7
Triglycerides	108.5	103.7	105.6
Glucose	106.8	108.3	111.3
Uric acid	5.90	5.60	5.82
Urea	33.6	50.3	43.7
Creatinine	0.76	0.83	0.78

Serum uric acid concentrations (pˆ0.04), the level of smoking (smoker/non-smoker/ex-smoker) and total cholesterol in the blood values (p <0.03), and the total number of packs-years among the smoker/ex-smoker categories (p <0.04) all show low correlations with the stages of COPD. (Figure 2)

Figure 2: There is a linear association between PY (packs-years) and urea (a), PY (packs-years) and cholesterol (b), and COPD stage and uric acid (c).



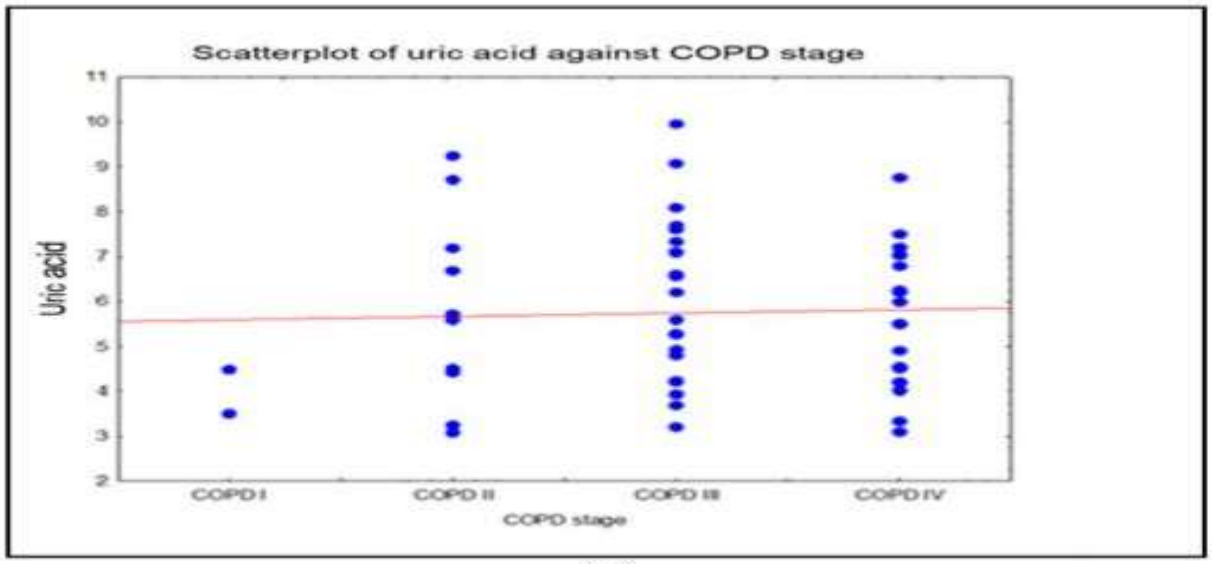
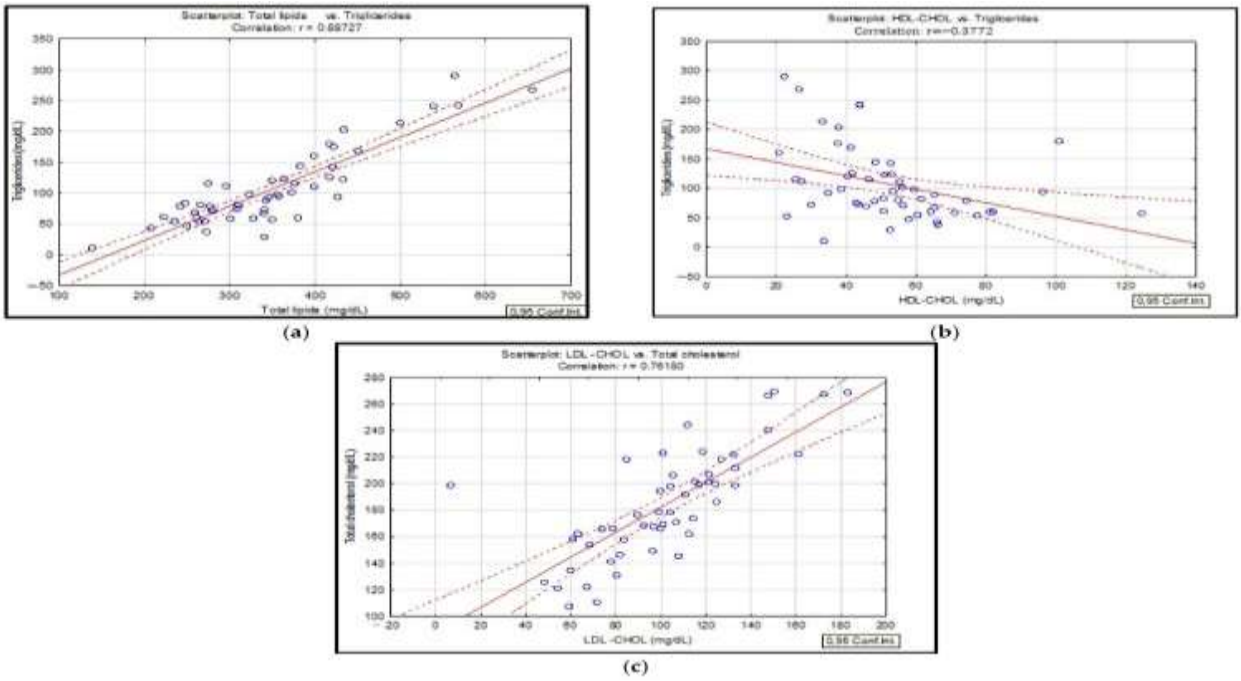


Figure 3: Triglycerides and total lipids (a); triglycerides and HDL-CHOL (b); and LDL-CHOL and total cholesterol (c) in COPD patients were analyzed using linear regression.

Statistically significant Pearson correlation coefficients were found by analyzing the correlation matrices for the three cohorts under investigation smokers, non-smokers, and ex-smokers. Upon assessing the lipid profile, noteworthy statistical associations were noted between the total lipid values and the triglyceride principles ($r = 0.85$, $p < 0.05$), the LDL-CHOL concentrations, and the serum total cholesterol levels ($r = 0.75$, p ς 0.05), and the serum triglyceride values and HDL-CHOL ($r = 0.35$, p ę 0.05). (Figure 3)



DISCUSSION

Reliability in non-invasive biomarker diagnosis and treatment is becoming more and more important as COPD becomes more common. Obtaining blood biomarkers for this purpose is reasonably straightforward and non-invasive.[13] The most well-characterized and often used blood biomarkers in clinical practice are blood eosinophils.[14] The blood eosinophil count and COPD have a weak link (R2 = 0.35), according to recent studies, and the presence of hypertension and age have a major impact on this correlation. Some research indicates that a patient's eosinophil level may be lowered by the amount of germs present. Furthermore, the ECLIPSE cohort[15] evaluated 34 blood indicators in total. Only three of these 34 biomarkers—surfactant protein D, fibrinogen, and CC-16—were determined to be stable indicators of baseline disease progression with a low correlation coefficient[16].

Shen et al. (2019) proposed a correlation between elevated blood levels of oxidized low-density lipoprotein (ox-LDL) and lung function, inflammatory processes, and oxidative stress in individuals with COPD. The primary pathogenic factor causing COPD is cigarette smoking.[17] Yamaguchi et al. 2005 [18] discovered that compared to non-smokers, smokers had considerably reduced levels of vitamin E and significantly greater levels of thiobarbituric acid-reactive compounds and 8-hydroxydeoxyguanosine. An LDL subfraction test revealed a rise in oxidatively damaged LDL, which was manifested as greater LDL-2 and decreased LDL-1 levels. Our findings agree with the findings of these investigations as well.

The present investigation revealed the non-normal distribution of the lipidic profile parameters, and the statistical findings indicate significant associations, particularly about total cholesterol, triglycerides, total lipids, and low-density lipoprotein. The emergence of dyslipidemia in individuals with COPD may be caused by oxidative stress and smoking, according to recent research on abnormalities in lipid metabolism. Nevertheless, these claims have limits concerning body mass index (BMI), gender, smoking intensity, and the severity of the condition [19]. Moreover, studies have shown a connection between smoking and an atherogenic lipid profile, which may exacerbate oxidative stress. There is a higher chance of elevated blood levels of triglycerides and total cholesterol when smoking, in any of its forms [20].

The alterations in the lipid profile of COPD patients have several causes at this time. Systemic inflammation is a significant component that is linked to higher blood triglycerides and lower HDL-CHOL. According to the study's findings, smokers had lower HDL-CHOL and higher LDL-CHOL levels. The usage of drugs based on β-2 agonists, which are suggested for the treatment of COPD, is the most likely reason for the aberrant HDL-CHOL levels. [21 With] this study, no significant correlations

were found between the dosage of β-2 agonist and HDL-CHOL levels. Meanwhile, research on COPD patients revealed that corticosteroids had a considerable impact on plasma lipid levels, particularly in those who have exacerbations [22].

There have been few researches that address the connection between smoking and serum creatinine levels. It has been shown that those who smoke often [23], as well as those with different renal disorders and hypertension, have higher blood creatinine levels. Researchers Dülger et al. 2002 examined renal function in smokers who were either active or passive. They found that active smokers had substantially higher creatinine levels ($p < 0.01$), suggesting that passive smoking can still have an impact on the kidneys, particularly on glomerular function [24]. A modest number of studies have been published in the literature that demonstrate how smoking increases the risk of mild renal impairment, proteinuria, and moderate hyperfiltration, especially in older adults and males. Even in persons who don't seem to have kidney disease, smoking typically harms renal function; however, the negative effects of smoking on the kidneys are more noticeable in patients who have different kidney illnesses as well as in hypertensive individuals[25].

CONCLUSION

In addition to elevated low-density lipoprotein cholesterol (LDL-CHOL) or decreased blood uric acid levels, we found that smoking was linked to alterations in the lipid profiles of smokers and ex-smokers.

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