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Original Research Article

INFLAMATORY BIOMARKERS AND LUNG FUNCTION TEST IN COPD PATIENTS EXPOSED TO TOBACCO AND BIOMASS: A COMPARATIVE STUDY

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ABSTRACT

Background: COPD is a progressive third leading cause of mortality that claims 3 million lives globally. [1] Prevalence of COPD in adult aged > 40 years is 9-10% worldwide. [2] In India, it's prevalence ranged between 6.5 – 7.6%.[3] Among the most common risk factors of chronic obstructive pulmonary disease (COPD) are tobacco smoking and biomass exposure. Tobacco induced COPD (COPD-TS) has been widely studied. However, there is limited research comparing it with biomass-induced COPD (COPD-BS) especially in terms of inflammatory biomarkers and lung function test. **Aim and Objective:** To compare the pulmonary function test result (FEV1, FVC, FEV1/FVC) in COPD patients exposed to tobacco and biomass fuel. To compare the impact of tobacco and biomass exposure on inflammatory biomarkers (IL-6, IL-8, TNF-α and CRP) between these two groups. To analyse the correlation between biomarkers and spirometry values.

Materials and Methods: This prospective cross-sectional study was conducted at the department of Pulmonary medicine, VIMSAR Burla in western Odisha from January 2024 to August 20224. Sample size (84) of either sex were examined clinically and the data were collected through "sociodemographic characteristic Questionnaire's", Biochemical estimation of CRP by Turbidimetry, IL-6, IL-8, TNF-α by ELISA and PFT by Spiro lab machine. Statistical analysis was performed with SPSS software version 21.0 (SPSS IBM corporation, Armonk. New York). The p-value< 0.05 was taken as statistically significant.

Results: A total of 84 clinically diagnosed cases of COPD patients were evaluated. Among these we found 52 number of subjects exposed to tobacco smoker COPD-TS and 32 no exposed to biomass (COPD-BS). The mean age of (COPD-TS) and (COPD-BS) were (53.18± 6.63) and (57.11± 6.77) respectively. The mean pack year of (COPD-TS) was 32.8±6.47 and mean biomass exposed (COPD-BS) hour per year was 285±84.3. The respondents mostly belong to lower economic status in both groups. The mean FEVI (L) of (COPD-BS) and the ratio percentage of FEVI (L) and FVC (L) were higher 1.41±0.26 than (COPD-TS). The level of serum inflammatory biomarkers of the study groups was higher in COPD-TS than COPD-BS group. Moreover, it was positively correlated with the FEVI (L) and highly significant at ($p<0.05$).

Conclusion: Both types of COPD are associated with high levels of systemic inflammation biomarkers. COPD-TS patients have a higher systemic

inflammatory status than the patients with COPD-BS, while exposure lead to COPD, the underlying systemic inflammatory responses and pulmonary impairment may vary i.e. higher inflammation and worse lung health in tobacco exposure may be due to its toxic nature. It might benefit some patients from anti-inflammatory treatment along with bronchodilators.
Keywords: COPD, CRP, IL-6, IL-8, TNF-α, Lung function test, Tobacco and Biomass.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death. [4] COPD is characterized by increasing airway obstruction that is not completely reversible, and it is associated with the lung's abnormal systemic inflammatory response to harmful gases. [5,6] Inflammation in the lungs enhances the growth of air gaps (emphysema), leads to the loss of alveolar attachments, and causes the thickening of airway walls. These anatomical changes result in reduced lung function and airflow restriction.

The molecular pathogenesis of COPD involves complications such as elevated levels of oxidative stress, protease–antiprotease imbalance, and genetic vulnerability.[7] Evidence on the mechanisms contributing to the risk of COPD is contradictory, with factors such as systemic inflammation, oxidative stress imbalance, hypoxia, and a sedentary lifestyle being implicated.[8,9] Cigarette smoking has been identified as the primary risk factor for the onset and progression of COPD in prior research.[10-12] Several biomarkers are crucial for the pathophysiology of COPD, but their use in tracking the disease's consequences remains unclear.

Retrospective studies have proposed a link between the development of COPD and active inflammatory markers, such as TNF-α, IL-6, IL-8, and C-reactive protein (CRP).[13-16] However, four studies,[16-19] did not find a link between CRP levels and the risk of COPD. The study by Harting et al, [19] even suggested that patients with COPD had lower serum IL-6 levels.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted at the department of Pulmonary medicine and physiology, VIMSAR Burla from January 2024 to August 2024. The study protocol was started by taking consent from the patients of the study group.

The sample technique was systematic random sampling. The aim as well as the steps of the study was clearly explained to each patient. Initial evaluation included year of exposure, socioeconomic status.

Inclusion Criteria: Newly diagnosed or known COPD patients exclusively exposed to smoke and biomass fuel.

Exclusion Criteria: Chronic lung disease (asthma, pulmonary TB, brochienctasis), Acute respiratory infection, Non-pulmonary inflammatory conditions, subject unable to perform spirometry and residing near industrial area.

Biochemical Analysis

Blood samples (5 mL) were collected in K3-ethylenediaminetetraacetic acid (EDTA) tubes. Samples were immediately centrifuged, and plasma aliquots were stored at −80°C until immediately before analysis. Plasma IL-6, IL-8, TNF-α levels were measured using commercially available enzyme immunoassay kits according to the manufacturers' protocols. by ELISA, CRP by Turbidimetry and PFT by Spiro lab machine. Post bronchodilator spirometry was used in this analysis.

Anthropological parameters - For Body Mass Index (BMI), weight and height of the subjects were calculated using Quetelet index as, Body weight in (kg) divided by Height (m2). Body mass index was used for defining overweight and obesity. [20]

Statistical Analysis

Recorded data were entered, checked and analysed using SPSS version 21.0 (SPSS IBM corporation, Armonk. New York). Unpaired t test was done to analyse between two variables. The p-value<0.05 was considered to be significant. The correlation between inflammatory biomarkers with functional parameters of PFT in COPD –TS and BS were analysed using Pearson's correlation coefficient. Quantitative data were expressed as a mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

RESULTS

The clinical and demographic characteristic was shown in [Table-1]. This study included two groups in which one was COPD with tobacco smoke exposure (COPD-TS, N=52) and other was COPD with biomass smoke exposure (COPD-BS, N=32). Out of which 51 (98.08%) male and 1 (1.92%) were female in (COPD-TS) where (COPD-BS) group included 4(12.5%)male and 25(87.5%) females. The mean age of (COPD-TS) and (COPD-BS) were (53.18± 6.63) and (57.11± 6.77) respectively, and the mean BMI(kg/m2) of (COPD-TS) and (COPD-BS) were (21.9± 5.5) and (24.1± 4.7) respectively. The mean pack year of (COPD-TS) was 32.8±6.47 and mean biomass exposed (COPD-BS) hour per year was 285±84.3. The respondents belong to lower economic status 20(38.46%) in (COPD-TS) and 13(40.62%) in case of (COPD-BS). The mean FEV_1(L) of (COPD-BS) was higher 1.41±0.26 than (COPD-TS)1.372±0.27, But in case of FVC (L) was maximum in case of (COPD-TS) 2.481±0.38 than

(COPD-BS)2.05±0.41 group. The ratio percentage of FEVI(L) and FVC (L) was shown greater in (COPD-BS) group58.94±12.38 than (COPD-TS) group.

Table 1: Clinical and demographic characteristics of the studied subjects

Variables	COPD –TS (N=52)	COPD –BS (N=32)	P- value
Age (yrs.)	53.18 ± 6.63	57.11±6.77	0.82
Gender Male N (%) Female N (%)	 (51)98.08% (1)1.92%	 (4)12.5% (28)87.5%	0.71
BMI(Kg/m^2) (Mean ± SD)	21.9±5.5	24.1±4.7	0.07
Pack year (yrs.)	32.8±6.47	-	NA
Hour-year	-	285±84.3	NA
Socio Economic Status N (%) Upper Upper-middle Lower-middle Upper-lower Lower	 2(3.85%) 9(17.32) 5(9.62%) 16(3.85%) 20(38.46%)	 - 2(6.25%) 8(25%) 9(28.13%) 13(40.62%)	0.013*
TYPES OF FUEL N (%) Animal dung Crop residue Mixed (Animal dung + Crop residue)	 - - -	 9(28.2%) 7(21.8%) 16(50%)	0.054
FEV$_1$(L) (Mean ± SD)	1.372±0.27	1.41±0.26	0.018*
FVC(L) (Mean ± SD)	2.481±0.38	2.05±0.41	0.07
FEV$_1$ / FVC (%) (Mean ± SD)	55.36±6.40	58.94±12.38	0.15

***p-value<0.05 was considered statistically significant, NA- not applied**

The level of serum inflammatory biomarkers of the study groups depicted in table no- 2, and we found that the mean levels of IL-6(pg/mL) 5.45±0.07, IL-8(pg/mL) 2.84±0.31, TNF-α (pg/mL) 6.89±0.05, CRP (mg/L) 4.08±1.15 in COPD-TS group was higher than COPD-BS group. All the inflammatory markers were highly significant at (p<0.05).

Table 2: Level of serum inflammatory biomarkers of the study population

Variables	COPD –TS (N=52)	COPD –BS (N=32)	P- value
IL-6 (pg/mL)	5.45±0.07	2.61±0.48	<0.05*
IL-8(pg/mL)	2.84±0.31	0.39±0.25	<0.05*
TNF-α (pg/mL)	6.89±0.05	6.21±0.08	<0.05*
CRP(mg/L)	4.08±1.15	2.66±0.79	<0.05*

***p-value<0.05 was considered statistically significant**

[Table-3] depicts the correlation among inflammatory biomarkers and functional parameters FEVI(L) in COPD -TS and COPD-BS study groups. The 'r' value of IL-6(r=0.057, p=0.001), IL-8(r=0.008, p=0.032) TNF-α (r=0.013, p=0.003) and CRP (r=0.002, p=0.041) in COPD-TS group were higher and significant at (p<0.05) as comprised to COPD-BS.

Table 3: Correlation of inflammatory biomarkers with functional parameters FEVI(L) in COPD -TS and COPD-BS study groups

Parameters	COPD-TS ('r' -value)	COPD-BS (' r' –value)	P-value
IL-6 (pg/mL)	0.057	0.093	0.0001*
IL -8(pg/mL)	0.008	0.036	0.032*
TNF-α (pg/mL)	0.013	0.102	0.003*
CRP(mg/L)	0.002	0.057	0.041*

DISCUSSIONS

The incidence of COPD varies significantly by country, region, age, sex, and epidemiology. In European, Asian, and North American countries, the incidence ranges from 1.40% to 8.92%. This highlights that COPD has become a major chronic non-infectious disease significantly affecting human health in the 21st century. [21]

Our study included 84 COPD patients, who were thoroughly investigated. The findings revealed that males are more exposed to tobacco (COPD-TS) than females, while females are more exposed to biomass smoke (COPD-BS). Notably, most respondents from both groups (COPD-TS and COPD-BS) belonged to a low socioeconomic status. Similar findings have been reported by other researchers, indicating an association between socioeconomic status and COPD. [22-24]

In India, females, particularly in rural areas, are often involved in cooking where biomass is used as fuel. Biomass smoke contains numerous pollutants

and is known to pose health hazards.[25] Exposure to indoor air pollution from biomass fuel combustion causes various diseases in developing countries, such as Acute Respiratory Infections (ARI), Otitis media (Middle Ear Infection), COPD, Lung cancer, Asthma, Cancer of the nasopharynx and larynx, Tuberculosis, and eye diseases like Cataract and blindness.[7] Thus, biomass smoke exposure (BS) has been proposed as a significant risk factor for these diseases, especially among non-smokers.[26,27]

Our study found that mean lung function test results were higher in COPD-TS patients than in COPD-BS patients. Although cigarette smoke exposure is the primary risk factor for COPD development, biomass smoke exposure is considered an additional risk factor, leading to reductions in lung function parameters (FEV_1, FVC, and FEV_1/FVC) [28]. COPD-BS patients tend to have a slower decline in forced expiratory volume in 1 second (FEV_1) and a different distribution of phenotypes than COPD-TS patients.[29,30] Researchers have reported that biomass smoke-induced COPD is associated with a slower decline in FEV_1, a different distribution of phenotypes,[29-32] higher pigment deposition and fibrosis in the lungs, thicker pulmonary arterial intima, and reduced emphysema compared to tobacco-exposed patients (COPD-TS).[33]

In our findings, levels of inflammatory markers such as IL-6, IL-8, TNF, and CRP were slightly higher in COPD-TS patients than in COPD-BS patients. Similar results were also found by Golpe et al. (2017),[34] Mehera et al. (2012),[35] and Solleiro-Villavicencio et al. (2015) [36]. It is well known that IL-6 and IL-8 may play a role in the pathophysiology of atherosclerosis and are linked to an increased risk of death in COPD.[37] These markers could contribute to the development of inflammatory sites within the injured vascular walls of the lungs.[38] Golpe et al. (2017) suggest that COPD-TS patients may be more susceptible to cardiovascular comorbidity than COPD-BS patients. This theory is supported by a recent preliminary investigation that found a higher frequency of ischemic heart disease in T-COPD patients. [34]

CRP is an acute phase protein secreted by the liver, serving as a sensitive biomarker for tissue damage and systemic inflammation. It is unaltered by hormones, immunosuppressants, or anti-inflammatory medications and is more informative when there is a bacterial infection in the respiratory tract. [39] However, this study contrasts with two other studies reporting similar CRP levels in COPD-TS and COPD-BS patients. [34,40] This discrepancy may be explained by the different techniques used in CRP quantification (ELISA and immunoturbidimetry) and the characteristics of the study populations. Our study is supported by Gan et al. (2024), [41] which suggested that reduced lung function is associated with increased levels of systemic inflammatory markers, with important pathophysiological and therapeutic implications for patients with stable COPD.

CONCLUSION

From the results of our study, it can be concluded that inflammatory biomarkers are elevated in both types of COPD patients. However, the increase is more pronounced in COPD-TS (tobacco smoke-exposed) patients than in COPD-BS (biomass smoke-exposed) patients. Additionally, COPD-TS patients exhibit worse lung health.

By combining pulmonary function tests (PFT) with inflammatory biomarkers, physicians may gain a detailed understanding of disease severity and progression. This approach could aid in the early detection and precise monitoring of COPD patients.

Further large-scale studies are needed to identify clinical phenotypes, monitor therapeutic responses, and define potential sex differences in the biological response to biomass and tobacco smoke. Additionally, further studies needed to investigate the potential disparities in the systemic consequences of both types of fumes.

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Conflicts of interest: There are no conflicts of interest.

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