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A COMPARATIVE STUDY OF SERUM LEVELS OF URIC ACID, C-REACTIVE PROTEIN AND SERUM URIC ACID TO CREATININE RATIO IN COPD PATIENTS AND HEALTHY POPULATION

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung condition associated with systemic inflammation and oxidative stress, which may influence metabolic markers like uric acid and C-reactive protein (CRP). Elevated serum uric acid and CRP levels, as well as the serum uric acid to creatinine ratio (SUA/Cr), have been linked to inflammatory diseases. However, their role in COPD remains unclear.

Introduction: This study aims to compare serum levels of uric acid, CRP, and the SUA/Cr ratio between COPD patients and a healthy population, investigating their potential role as biomarkers for disease severity and progression.

Methodology: A cross-sectional comparative study was conducted on 50 COPD patients and 50 healthy controls. Serum uric acid, CRP, and creatinine levels were measured, and the SUA/Cr ratio was calculated. Statistical analysis was performed to assess differences between the groups and correlations with disease severity in COPD patients.

Results: COPD patients showed significantly higher levels of serum uric acid, CRP, and SUA/Cr ratio compared to the healthy control group. A positive correlation was found between these biomarkers and the severity of COPD, indicating their potential as markers of inflammation and disease progression.

Conclusion: The study highlights that elevated serum uric acid, CRP, and SUA/Cr ratio are associated with COPD and its severity. These markers could be useful in monitoring disease progression and tailoring treatment strategies in COPD patients.

Keywords: COPD, Uric Acid, C-Reactive Protein, SUA/Cr Ratio, Biomarkers, Inflammation, Chronic Obstructive Pulmonary Disease

INTRODUCTION:

A common, treatable, and preventable disease, chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation brought on by abnormalities of the airways and/or alveoli. These abnormalities are typically the result of significant exposure to noxious particles or gases and are influenced by host factors, such as abnormal lung development. The prevalence of COPD was estimated to be 7.6%, independent of the defined diagnostic criteria. The prevalence of chronic bronchitis was estimated to be 6.4%. The prevalence of emphysema was estimated to be 1.8% [1].

COPD is undoubtedly an umbrella term, and it seems unlikely that all patients with COPD have the same underlying disease processes; thus, there is a need for differential treatment of different subgroups [2].

Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern projected to rank third in global mortality by 2020, up from sixth in 1990. COPD is characterized by persistent respiratory symptoms and airflow limitation, resulting from abnormalities in the airways and/or alveoli due to significant exposure to harmful particles or gases. The estimated global prevalence of COPD is 7.6%, with chronic bronchitis and emphysema contributing 6.4% and 1.8%, respectively. Despite its prevalence, COPD remains a heterogeneous condition, requiring tailored treatment approaches based on the different underlying disease processes.

In regions like South Asia, COPD ranks as the leading cause of premature deaths among chronic respiratory diseases. It is reported that 22-40% of COPD patients experience moderate or severe exacerbations annually, with exacerbations worsening patient outcomes. The disease is commonly associated with systemic inflammation and comorbidities, including cardiovascular disease, osteoporosis, and muscle atrophy, which significantly impair patients' quality of life.

Biomarkers like interleukin-6 (IL-6) and C-reactive protein (CRP) are elevated during COPD exacerbations and may serve as indicators for targeted treatment strategies. COPD pathogenesis involves airway alterations, such as squamous metaplasia, smooth muscle hypertrophy, and alveolar destruction. Patients with COPD often exhibit impaired lung function, systemic inflammation, and increased oxidative stress, as indicated by elevated serum uric acid levels.

Understanding the molecular processes and biomarkers involved in COPD, such as CRP and uric acid, provides a foundation for better diagnosis, treatment, and management of the disease, particularly in patients with exacerbations and comorbidities

MATERIALS & METHOD: The study protocol was evaluated by institutional ethical committee of Saifai, Etawah. Before the start of the study, written informed consent from each subject was obtained in response to fully written and verbal explanation of nature of study.

Study area: Biochemistry and Respiratory Medicine department of UPUMS, Saifai, Etawah

Study of duration: one and half year

The study was involved minimum 50 COPD cases and 50 healthy individuals

Study unit: COPD patients from Respiratory Medicine Department (OPD as well as IPD), UPUMS and healthy population of Same age and sex was taken without any chronic disease.

Statistical analysis: SPSS software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis with the Windows program (26.0 version).

Following were the observations.

Table 1: Distribution of study participants (N=100)

Group	N
(COPD Patients)	50
(Healthy Individuals)	50
Total	100

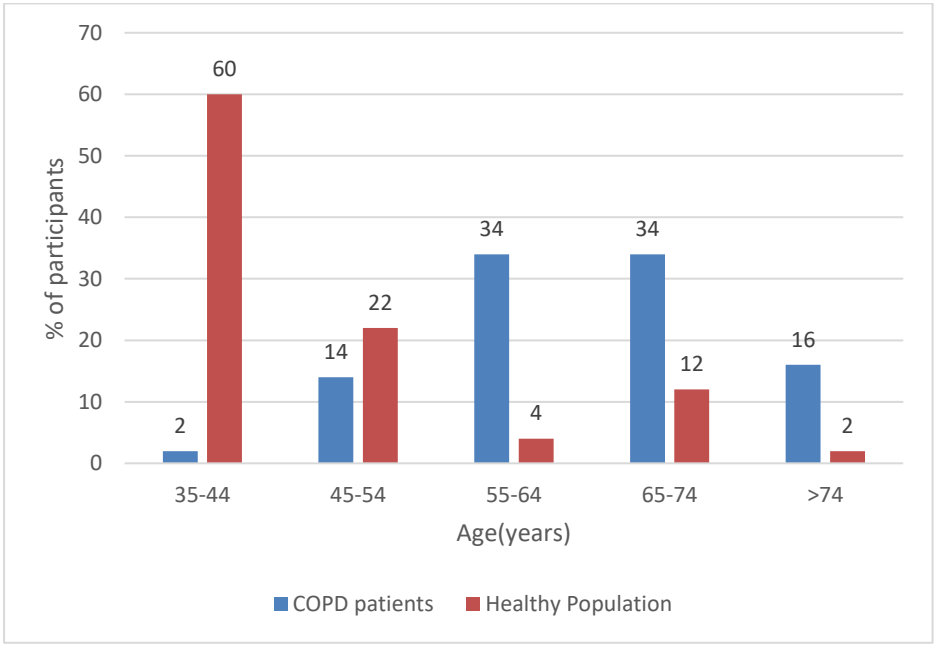
The study sample consists of an equal number of COPD patients and healthy individuals, which allows for a direct comparison between the two groups. This balanced representation may help to identify key differences in characteristics, outcome, comparative study of levels of biomarkers between COPD patients and healthy individuals.

Table -2 Distribution of the study participants based on Age and Gender (N=100)

Variables	Subgroups	COPD (n =50) Frequency (%)	Healthy Population (n=50) Frequency (%)	P value[#]
Age (years)	Mean ±SD		54.72±13.79	
	Mean ±SD	63.14±10.33	46.30±11.52	
	35-44	1(2.0%)	30(60%)	<0.001*
	45-54	7(14%)	11(22%)	
	55-64	17(34%)	2(4%)	
	65-74	17(34%)	6(12%)	
	More than or equals to 75	8(16%)	1(2%)	
Gender	Male	43(86%)	40(80%	0.424
	Female	7(14%)	10(20%)	

[#]Chi square test/ fisher exact test

Figure 1: Distribution of study participants based on Age groups



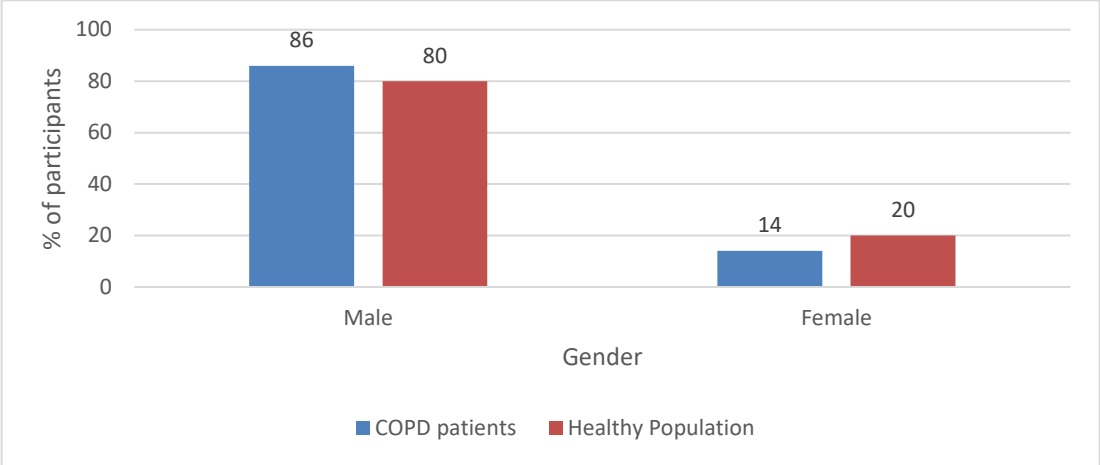


Figure 2: Distribution of study participants based on Gender

Table no- 2 describes the mean age of the total study participants was 54.72±13.79. The mean age of COPD patients was 63.14±10.33 years compared to 46.30± 11.52 years among healthy individuals.

The age distribution shows that individuals in the 55-64 age groups are affected by COPD accounting for 34% of the COPD groups compared to only 4% in the healthy population. In age groups of 35-44 years, 2.0% were COPD patients and 60% were healthy population. In age groups of 45-54 years, 14.0% were COPD patients and 22% were healthy population. In age groups of 65-74 years, 34.0% were COPD patients and 12% were healthy population. In age groups of >74 years, 16% were COPD patients and 2% were healthy population.

Table 3- Estimation of level of uric acid (mg/dl) in COPD patients

Variable	Patients of COPD	
Uric acid (mg/dl)	Mean	SD
	4.88	1.73

Table no-3 depicts the mean level of uric acid in patients with COPD was 4.88 with standard deviation of 1.73.

Table 4- Estimation of level of uric acid in Healthy population

Variable	Healthy population	
Uric acid (mg/dl)	Mean	SD
	5.58	1.39

Table no-4 depicts the mean level of uric acid in the healthy population was 5.58 with standard deviation of 1.39.

Table 5- Estimation of level of CRP in COPD patients

Variable	Patients of COPD	
CRP (mg/l)	Mean	SD
	72.23	71.09

Table no-5 depicts the mean level of CRP in patients with COPD was 72.23 with a standard deviation of 71.09.

Table 6- Estimation of level of CRP in Healthy population

Variable	Healthy population	
CRP (mg/dl)	Mean	SD
	3.73	3.18

Table no -6 depicts the mean level of CRP in the healthy population 3.73 with a standard deviation of 3.18.

Table 7- Estimation of level of S. Creatinine in COPD patients

Variable	Patients of COPD	
Creatinine (mg/dl)	Mean	SD
	1.14	0.74

Table no -7 depicts the mean level of Creatinine in COPD patients was 1.14, with Standard deviation of 0.74.

Table 8- Estimation of level of S. Creatinine in Healthy population

Variable	Healthy population	
Creatinine (mg/dl)	Mean	SD
	0.88	0.17

Table no-8 depicts the mean level of Creatinine in the healthy population 0.88, with Standard deviation of 0.17.

Table 9- Estimation of Uric acid /creatinine ratio in COPD patients

Variable	Patients of COPD	
Uric acid /creatinine (mg/g)	Mean	SD
	4.93	1.91

Table no-9, depicts the mean Uric acid/Creatinine ratio in COPD patients was 4.93, with Standard deviation of 1.91.

Table 10- Estimation of Uric acid /creatinine ratio in Healthy population

Variable	Healthy population	
Uric acid /creatinine (mg/g)	Mean	SD
	6.45	1.87

Table no-10, depicts the mean Uric acid/Creatinine ratio in the healthy population was 6.45 with Standard deviation of 1.87.

Table11 – Association of the study participants on the bases of the level of Serum Uric acid, CRP and creatinine.

Variables	Subgroups	COPD (n =50) Frequency (%)	Healthy Population (n=50) Frequency (%)	P value#
S. uric acid[1]	Low	8(16%)	1(2%)	0.014*
	normal	35(70%)	46(92%)	
	Raised	7(14%)	3(6%)	
S. CRP[2]	Normal	4(8%)	39(78%)	<0.001*
	Raised	46(92%)	11(22%)	
S. creatinine[3]	Low	7(14%)	4(8%)	0.001*
	normal	28(56%)	44(88%)	
	Raised	15(30%)	2(4%)	

[1] normal: male 3.5-7.2mg/dl; female 2.6-6.0mg/dl

[2]normal value 0-6mg/l

[3]normal value: male 0.7-1.2mg/dl, female 0.5-0.9mg/dl

[#]Chi-square test/ Fisher exact test

(Reference ranges are taken from the literature of "Biosystems Diagnostics Pvt Ltd, EN ISO 13485 Standard Certified Co" & Tietz Textbook of clinical chemistry and Molecular diagnosis, 4th ed. Burtis CA, Ashwood ER, Burns DE. WB Saunders Co, 2005)

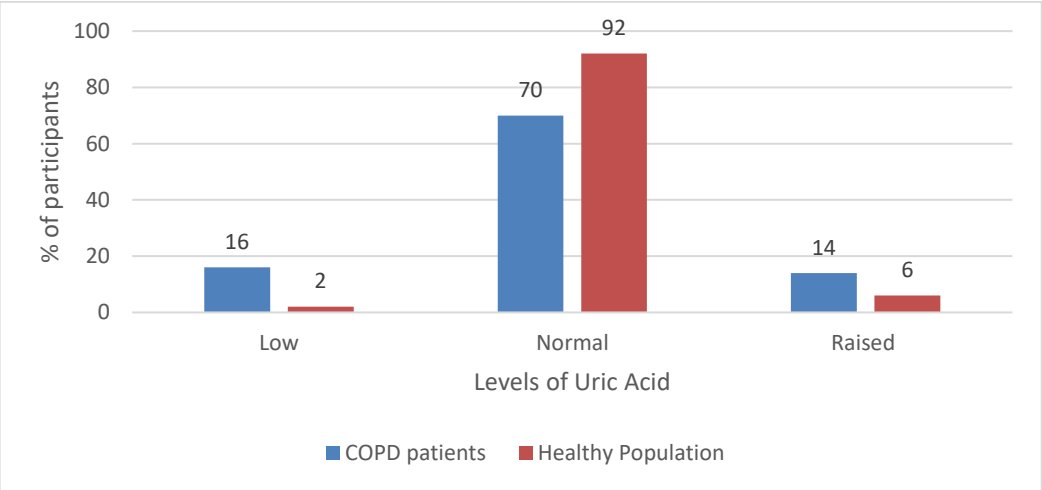


Figure 3: Distribution of study participants based on their S. Uric acid levels

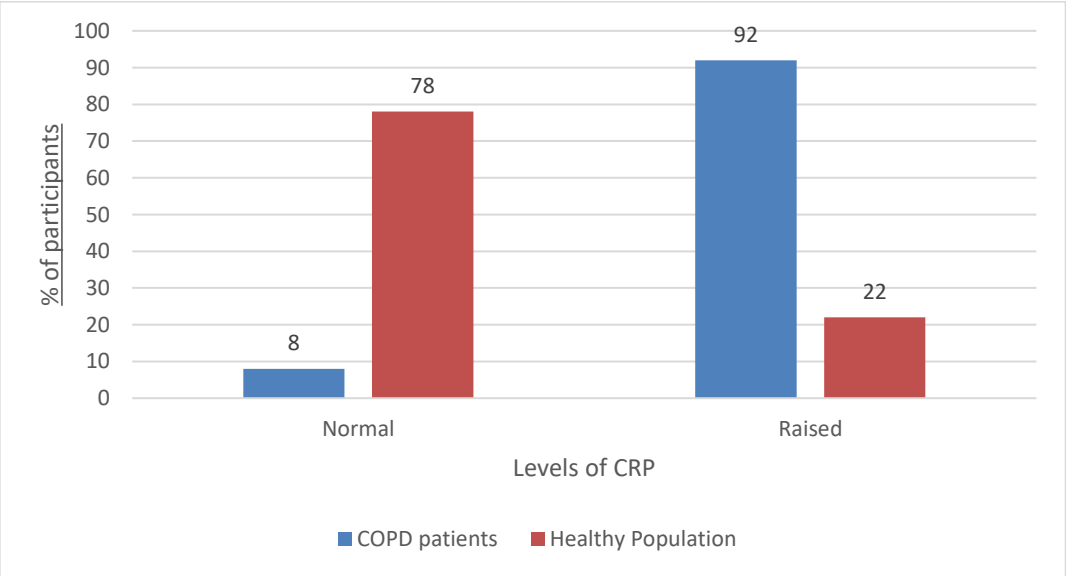


Figure 4: Distribution of study participants based on their S. CRP levels

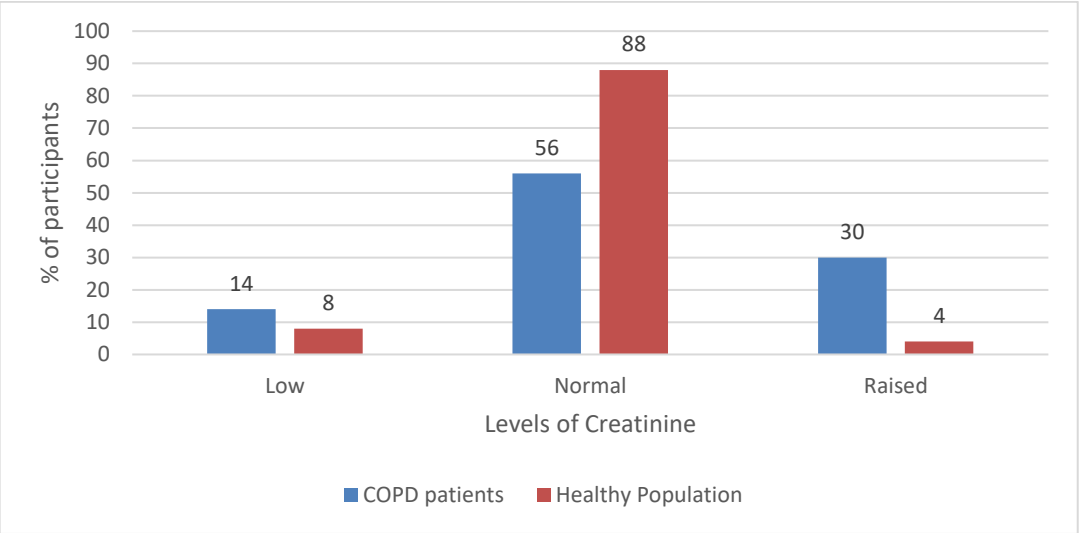


Figure 5: Distribution of study participants based on their S. creatinine levels

Serum uric acid levels in COPD patients showed that 16% of the population had lower levels, 70% had normal levels, and 14% had higher levels. Among the population of healthy individuals, 2% had lower serum uric acid levels, 92% had normal levels, and 6% had higher levels.

92% of the COPD patients had elevated CRP levels, whereas just 8% had normal values. Three-quarters (78%) of the healthy individuals had normal CRP levels, while 22 % had elevated levels.

Serum creatinine levels in COPD patients showed that 14% of the population had lower levels, 56% had normal levels, and 30% had higher levels. Of the persons in good health, 8% had serum creatinine levels that were below normal, 88% had normal levels, and 4% had elevated levels.

Table 12- Association of study participants based on predisposing risk factors(N=100)

Variables	Subgroups	COPD (n =50) Frequency (%)	Healthy Population (n=50) Frequency (%)	P value[#]
Smoking	Yes	35(70)	13(26)	<0.001*
	No	15(30)	37(74)	
Pack/year (smokers, N= 48)	Mean ±SD	20.99 ±7.99	1.87±0.70	-

[#]Chi-square test/ Fisher exact test

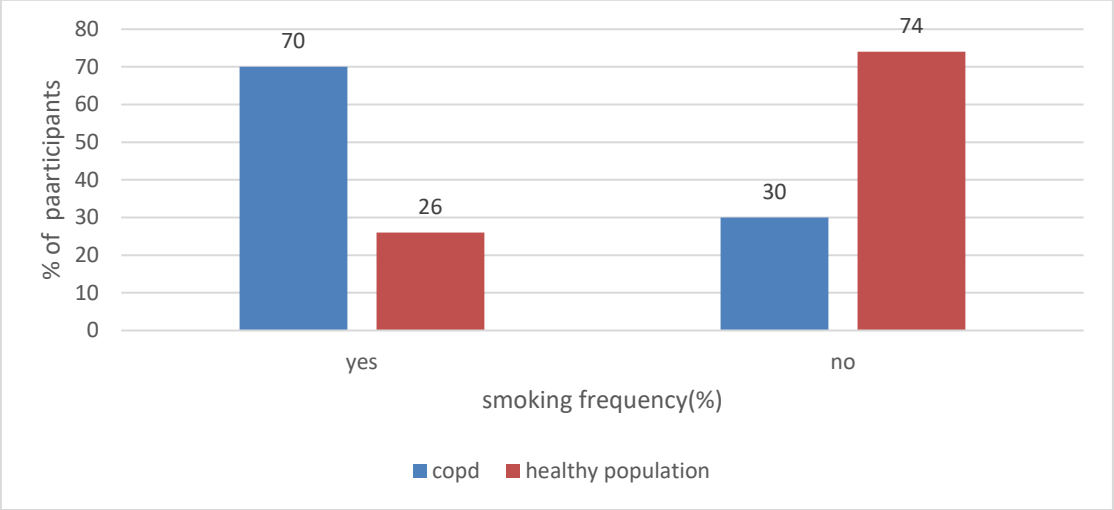


Figure 6: Distribution of study participants based on their predisposing risk factors.

In the COPD subgroup, 70% of participants were smokers, while 30% were non-smokers. In the Healthy population subgroup, 26% of participants were smokers, while 74% were non-smokers.

The mean pack/year for smokers in the COPD subgroup was 20.99 ± 7.99. The mean pack/year for smokers in the Healthy population subgroup was 1.87 ± 0.70.

Table 13- Grades of severity on basis of pulmonary function test in COPD patients and healthy individuals (based on post-bronchodilator FEV1)

Variables	Grades	Severity	COPD /patients Frequency (%)	Healthy individuals (%)	P value#
FEV1		Normal	15(30)	37(74)	<0.001*
	1	Mild	16(32)	13(26)	
	2	Moderate	19(38)	00	

No participants were found in 3 (severe) &4 (very severe) category based on FEV1 in this study, so, these two categories were omitted from table.

#Chi-square test/ Fisher exact test

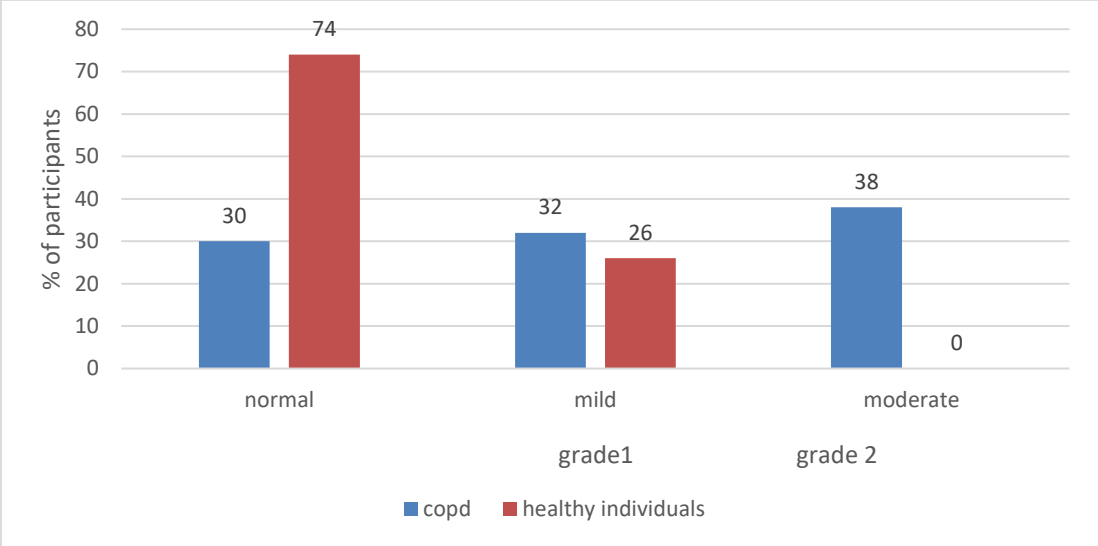


Figure 7: Distribution of COPD patients based on their Grades of Severity of airflow obstruction.

The distribution of COPD patients based on grades and severity of airflow obstruction (based on post-bronchodilator FEV1) is as follows: - Mild COPD: 16 patients (32%) - Moderate COPD: 19 patients (38%) The P value provided in the table is <0.001, indicating a statistically significant difference in the distribution of COPD patients between the mild and moderate severity categories based on post-bronchodilator FEV1 values.

Discussion

COPD is a common, preventable and treatable disease, but extensive under-diagnosis and misdiagnosis leads to patients receiving no treatment or incorrect treatment. Appropriate and early diagnosis of COPD can have a very significant public-health impact. By comparing these biomarkers between COPD patients and healthy individuals, the study may help identify potential markers for disease severity, prognosis and treatment response in COPD.

Age distribution - The present study revealed that mean age of the COPD patients was 63.14±10.23 years compared to 46.30±11.52 years of the healthy population. Approximately two-thirds (68%) of the COPD patients were aged between 54-74 years, showing preponderance of COPD in this age groups. This observation was similar to the Nagihan Durmus Kocak et al.(2016) [24], which predicts the mean age of COPD patients was 65±10 years.

Significance of age - The difference is statically significant with a p-value of <0.001, indicating a clear age difference between the two groups. Among the patients with COPD, major age groups were aged between 54-74 years. C.REHERISON et al.(2009)[1] in his study, patients over 40 years of age, in particularly those aged between 40-64 years.

Significance of Gender- In our study, 86% (43) of COPD patients were male and 14% (7) were female. This observation is similar to Nagihan Durmus Kocak etal.(2016) [24], in which 92 males and 18 females. The difference is statistically insignificant with a p-value of <0.424.

Significance of abnormal Serum uric acid levels in COPD patients- Serum uric acid values clearly show that people with COPD are more likely than the general population to have elevated levels (14% vs. 6%). The Serum Uric Acid level was estimated in both COPD patients and healthy individuals. The mean value in COPD patients was (4.88±1.73) and in healthy individuals was (5.88±1.39). The difference between both study groups was statistically significant (P < 0.014*). Nagihan Durmus Kocak et al.(2016) [24], in their study found that s. uric acid level is higher in the patients' group than the control groups, as given (34±24.9 vs 13.6±17.8, p<0.001). This study suggests that, people with COPD may have higher serum uric acid levels more frequently, suggesting a possible connection between inflammation and oxidative stress.

Significance of abnormal Serum-CRP levels in COPD patients- Serum CRP levels were estimated in both COPD patients and healthy individuals. The mean value in COPD patients was (72.23±71.09) and in healthy individuals was (3.73±3.18). The analysis of CRP levels reveals a statistically significant (P < 0.001*), difference between COPD patients and healthy individuals, with a higher frequency of raised CRP levels observed in COPD patients (92% vs. 22%).

This association underscores the role of systemic inflammation in COPD and highlights CRP as a potential biomarker for disease severity and progression. Chin-wang Hsu et al.2020 [(10)], in their study, found that COPD patients with pneumonia have significantly higher blood CRP levels compared to patients with AECOPD.

Significance of abnormal Serum Creatinine levels in COPD patients- Serum creatinine levels were estimated in both COPD patients and healthy individuals. The mean value in COPD patients was (1.14±0.74) and in healthy individuals was (0.88±0.17). The difference between these two study groups was statistically significant ($P < 0.001$*). Regarding serum creatinine levels, the data indicate that COPD patients exhibit raised creatinine levels compared to the healthy population (30% vs. 4%). In contrast, the death rate at one year was considerably higher ($p = 0.003$) among patients with low pre-admission creatinine, where 62.5% of patients had died, compared to 30.49% mortality in patients with a normal or higher creatinine value, according to a study by Abdul B. Afzal et al.(2022) [(43)].

Comparison of Uric acid/Creatinine Ratio: - Compared to the healthy population (6.45 mg/g), the mean uric acid/creatinine ratio (4.93 mg/g) is lower in COPD patients. In contrast with Nagihan Durmus Kocak et al.(2016) [(24)] s. uric acid levels were higher in patients with COPD compared to healthy controls.

Significance of smoking and pack/year in COPD patients- The statistics show a substantial difference in smoking status between patients with COPD and healthy individuals, with a greater percentage of smokers in the COPD group (70% vs. 26%). This finding underscores the well-established link between smoking and the development of COPD, as smoking is a major risk factor for the disease. The statistically significant p-value (<0.001) further supports the strong association between smoking and COPD. A study conducted by, Nagihan Durmus Kocak et al.(2016) [(24)] discovered that the patients' groups had more smocking packs/year than control groups (34±24.9 vs 13.6±17.8, $p<0.001$).

Significance of FEV1 in COPD patients- The data reveal that among COPD patients, the majority fall into the moderate category (38%), followed by mild (32%) and normal (30%). In contrast, healthy individuals predominantly have normal airflow (74%), with a smaller proportion classified as mild (26%). The statistically significant p-value (<0.001) indicates a significant difference in the distribution of airflow obstruction grades between COPD patients and healthy individuals. Notably, it has been reported that in almost 75% of patients older than 65 years old diagnosed with mild COPD using the GOLD criteria, the measured FEV1/FVC values are within the normal range for healthy age-related and race-matched controls as found in S.Kakavas et.al[(58)].

Conclusion -

- Age stratification showed a significant difference in our study with a higher prevalence of COPD in the 54-74 (years) of age group.
- Gender showed a significant difference, with the prevalence of COPD being higher in males than females.
- In conclusion, the distribution of COPD severity categories among patients differs significantly from that of healthy individuals.
- It may be inferred from my study's findings that uric acid, creatinine, and CRP levels are significantly correlated.
- In my study, the levels of CRP and Creatinine were raised in COPD patients as well as found to be higher among COPD patients compared to healthy populations.
- COPD patients exhibit a significantly lower mean Uric acid/Creatinine ratio compared to healthy individuals.
- COPD patients exhibit a significantly lower mean uric acid level compared to healthy individuals but percentage of the COPD patients were higher which have higher value of uric acid than healthy individuals.
- The majority of COPD patients fall into the moderate category, indicating a higher level of disease severity compared to the healthy population.

CONFLICT OF INTEREST: The authors declare that there are no conflicts of interest.

SOURCE OF FUNDING: The study received no external funding.

CONSENT: Written informed consent has been obtained from all participants in accordance with international or university standards and is maintained by the authors.

ETHICAL APPROVAL: Ethical approval was granted in compliance with international or university standards, and the written approval is preserved by the authors.

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