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The Correlation between Serum Levels of Progranulin and Inflammatory Markers in Patients with Chronic Obstructive Pulmonary Disease

Fatima Ali Abdulwahed Alkyoon[1] and Falah Mahdi Dananah[2]

[1,2] *University of Kufa, Faculty of medicine, Department Medical Physiology, Iraq.*

Email: fatimaalkyoon1993@gmail.com, *Falah.swadi@uokufa.edu.iq*

Abstract

Back ground: *Chronic obstructive pulmonary disease, or COPD, is an inflammatory chronic illness of the parenchyma and/or airways that is typically accompanied by increasing, irreversible dyspnea, coughing, sputum production, and/or exacerbations of respiratory symptoms. The pathological process of COPD includes bronchitis and/or emphysema; inflammation in the lungs has systemic effects as well. The most frequent causes of COPD are indoor and occupational pollution. Progranulin, or PGRN, is a precursor of pleiotropic glycosylated protein that plays a major role in wound healing, angiogenesis, neoplasia, cell development, the cell cycle, inflammation, and the modification of the autoimmune process. It is highly prevalent in a variety of cell types, including respiratory epithelial cells.* ***Objective:*** *The aim is to study relationship between serum level of PGRN and inflammatory markers in COPD patients.* ***Material and method:*** *A case control study composed of 40 patients with COPD and 45 controls, demographic characteristic, blood investigation include CRP-titer, WBC and plasma PGRN were measured and made comparison of data in cases with controls, data collected were statically analysis by SPSS .*

Result: *The study showed that, there was no significant correlation between serum progranulin level, WBC and C-Reactive Protein titer in COPD patients (P value >0.05).* ***Conclusions:*** *It was concluded that PGRN level in COPD patients don't correlate with CRP titer level or with WBC.*

Keywords: Chronic Obstructive Pulmonary Disease, Progranulin, Spirometry, C-Reactive Protein.

Article Information

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INTRUDUCTION

In 2019, chronic obstructive pulmonary disease (COPD) was third globally in terms of causes of mortality, with 3.23 million of those fatalities taking place in middle- and low-income nations. Males, individuals over 40, smokers, and former smokers had higher rates of COPD prevalence. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, the prevalence of COPD worldwide in 2019 was 10.3%.(1,5,18,24) .

Multiple types of inflammatory cells and mediators are involved in the progression of COPD, which is a complex sickness that affects the lungs and remains an inflammatory disease. Over an individual's lifetime, complex, dynamic, and cumulative interactions between genes and environment can alter normal lung development pathways and cause harm. This is the cause of it(3,8) .

Tobacco Smoking considered the most common cause of COPD (10), even though smoking is thought to be the main cause, epidemiological research revealed that 20% to 40% of COPD patients had never smoked (6), also cannabis, pipe, water pipe, cigar all consider as risk factors for COPD.(12) Genetic reasons include alpha-1 antitrypsin deficiency (AATD) (14) as an example. Pollution resulting from exposure to gas particles in the environment, whether indoors or outdoors; prior infections, such as recurrent respiratory infections primarily in the lower respiratory tract during early childhood (risk increased by two to three times); prior tuberculosis increases the risk of developing COPD (9) and increased susceptibility to pollution and reduced nutrition in low-income environments.(1)

Patients with COPD experience an altered version of their typical inflammatory response to long-term irritants such as smoke ingested from cigarettes and other particles. Although the primary origin of this modified form of inflammation remains unknown, certain research indicates that genetics might be involved (8). In inflammatory disorders including COPD and asthma, PGRN—also referred to as acrogranin or PC cell-derived growth factor (PCDGF)—plays a critical role. Its anti-inflammatory properties stem from its interaction with TNF R1/2 and inhibition of the TNF-α-TNFR1/2 signal, which prevents neutrophil degranulation. Research has indicated that elevated levels of PGRN are present in the blood of patients with COPD, possibly as a result of reduced or inhibited neutrophilic inflammation. The GRN gene encodes PGRN, which is made up of 593 amino acids and has a molecular weight of 68.5 kDa (23). Different proteinases can break down PGRN, and certain substances, including secretory leukocyte protease inhibitor (SLPI), can prevent it from having an anti-inflammatory effect. The pro-inflammatory granulins produced by PGRN degradation can counteract the anti-inflammatory effects of the protein .(21,23)

The inflammatory process, systemic inflammation, smoking status, and ischemic heart disease may all contribute to the elevated CRP levels observed in COPD patients. Elevation of CRP has been associated with myocardial infarction, unstable angina, stroke, and sudden coronary mortality.(20,25,28)

The white blood cell (WBC) is regarded as a key element of immunity. It plays a role in defense against infections and shielding the body from diseases. The five types of WBC are neutrophils, basophils, eosinophils, lymphocytes, and monocytes. Abnormalities in the count of WBC can indicate a number of diseases, including inflammation, allergies, bacterial, fungal, and viral infections, leukemia, and lymphoma.

PATIENTS AND METHODS

40 COPD patients (26 men and 14 women) who met inclusion criteria and were not excluded from exclusion criteria were gathered from Al-Sader Teaching Hospital in Al-Najaf city between January and August of 2023.

Forty-five healthy individuals, sixteen men and twenty-nine women, were included in the study. They were selected at random from the general community, free of COPD, and possessed normal pulmonary function tests as determined by spirometry. After being informed about the purpose of the study, the methods of the research, the spirometry test, and the blood draw, participants gave their verbal agreement. Those with COPD who were over 35, stable at diagnosis (13), and had not previously received treatment with long-acting beta-agonis, anti-inflammatory medications, or oral corticosteroids were included in the study (11,15). Exclusion criteria include renal or hepatic failure, inflammatory bowel disease, connective tissue disorders, cancer within the previous five years, and chronic illnesses that cause systemic inflammation .(17)

Methods

Each participant gave a five-milliliter venous blood sample, which was placed in a gel tube. Serum progranulin was measured using the Human PGRN ELISA Kit (Elabscience/USA), and CRP was measured for each participant using the Human CRP ELISA Kit (Elabscience/USA), all in accordance with the precise manufacturing source's protocol and WBC blood investigation.

STATISTICAL ANALYSIS

The data for the study were analyzed using the Statistical Package for the Social Sciences (SPSS 23.0 for Windows), and the results showed descriptive statistics as mean±SD, frequency, and percentage. For categorical variables, chi-square tests were used to compare groups, and for nonparametric data, the Mann-Whitney U-test was employed. For normally distributed data, Pearson's correlation coefficient was employed, with a significance threshold of $p < 0.05$.

RESULT

The current study included a total of 85 participants (40 COPD patients and 45 as a control). Two thirds of COPD group were male against one third of the control group. The analysis of data showed that there was significant statistical difference in the mean Plasma progranulin levels between the COPD and the control group (table-2 and figure1). The results concluded that there was no significant correlation between the mean progranulin level and the mean levels of the inflammatory markers of the COPD group and also of the control group ($p>0.05$) as shown in table3 below.

Table NO.1: Demographic characteristics of the COPD and control group.

Characteristics		Patients n=40	Control n=45	P value
Age (years)	Below 45	13 (32.5) %	27 (60) %	0.06
	45-54	13 (32.5)	8 (17.7)	
	55-64	7 (17.5)	7 (15.6)	
	65 and above	7 (17.5)	3 (6.7)	
Gender	Male	26 (65)	16 (35.6)	**0.007**
	Female	14 (35)	29 (64.4)	

Table NO.2: Comparison of progranulin level between patient and control.

Variable		mean±SD	P value
Plasma progranulin level (ng/ml)	Patients	230.52±189.01	**0.006**
	Control	114.19±68.41	

Figure NO.1: Plasma progranulin levels in COPD and control group.

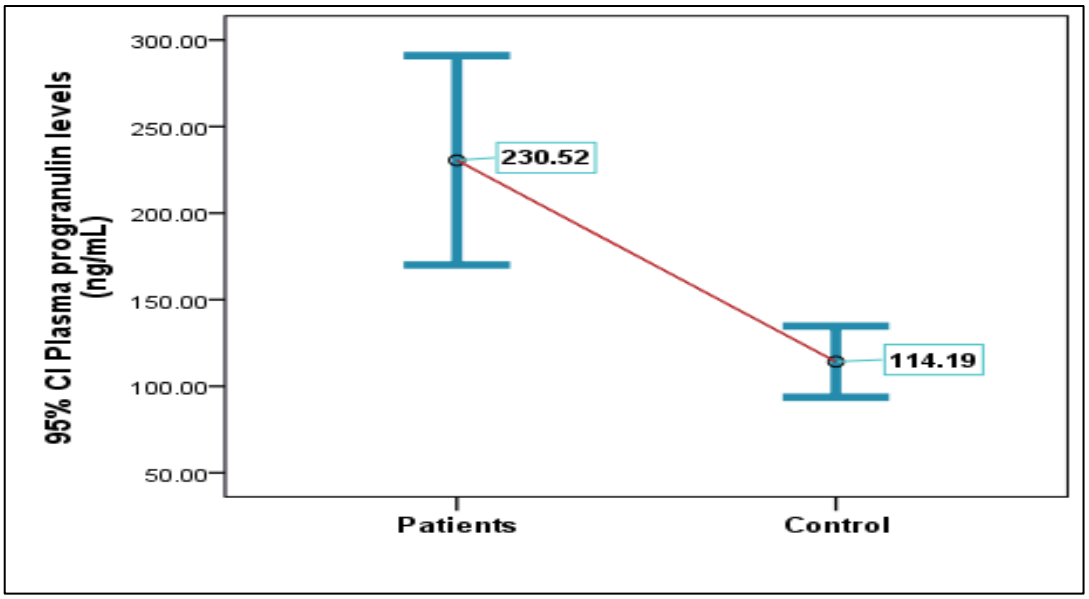

Table NO.3: Correlations between progranulin level and inflammatory markers.

Variables	Patients		Control	
	Pearson Correlation (r)	P value	Pearson Correlation (r)	P value
WBC	0.099	0.542	-0.047	0.758
CRP	0.023	0.889	-0.090	0.557

DISCUSSION

This study involved 40 COPD patient (patient group) and 45 non-COPD subjects. There is no difference in age between patients and controls P value (0.06) ,the age consider as risk factor for developing of COPD due to either the lung function decline with increase age or due to increase time of exposures to the other causes such as tobacco smoking ,air pollution and occupational pollution during the life (1),this consistent with other studies(12) ,65% of the patients in this study were males ,this consistent with study of (18). Systemic review composed of more than 150 previous study ,that found prevalence of COPD was larger in males than females but the difference in prevalence between males and females in developed countries and high income countries was not significant statistically, this appear due to environmental factors and behavioral factors , genetic factors and prevalence of smoking high in men all these causes lead to difference in prevalence of COPD between genders, the diagnosis of COPD in developing countries still higher in males than females, but because of increase in smoking among females and working in males occupations that have risk of develop COPD due to pollution(3),but in other research (4). that found no difference in prevalence of COPD between men and women. (18), explain in high income countries prevalence of COPD higher in females than males, due increase exposure to tobacco smoking and found females have more susceptibility to harmful effect of tobacco smoking due to smaller size of lung in female so become more susceptible to oxidative stress .(22)

This study showed a significant difference in progranulin level between cases of COPD and controls (230.52±189.01 vs 114.19±68.41 , P value 0.006) ,which is similar to finding of other study which found that progranulin level higher in stable COPD than controls(10)..Also shows that there is no significant association between progranulin level and inflammatory markers in patients and controls, which differs from the finding by a study of (10) found that progranulin correlated positively to CRP and ratio of neutrophil/lymphocyte . (26) found that there is no significant association between progranulin level and white blood cells count. This study shows that there is no significant association between progranulin level and inflammatory markers in patients and controls may be due to small sample size and there is similarity between cases and controls in age,smoking habit,past medical history and the cases we take them in stable stage for at least one month prior to examination and they are 99% of them in GOLD 2 stage.

CONCLUSIONS

We concluded for this study that elevated levels of PGRN are linked to COPD and are no significant association with inflammatory markers.

RECOMMENDATION

we recommended further studies with larger sample size for clarify the effect of PGRN on the severity of COPD and inflammatory markers.

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