

*Short Communication*

## Platelets: Indicator of inflammation in COPD

Gulfidan Cakmak<sup>1\*</sup>, Zuhai Aydan Saglam<sup>1</sup>, Tayyibe Saler<sup>1</sup>, Mustafa Yenigun<sup>1</sup>, Esra Ataoglu<sup>1</sup>, Levent Umit Temiz<sup>1</sup> and Tuncalp Demir<sup>2</sup>

<sup>1</sup>4th Clinic of Internal Medicine, Haseki Training and Research Hospital, Haseki Millet Caddesi, Aksaray-Istanbul, Turkey.

<sup>2</sup>Istanbul University Medical Faculty of Cerrahpasa, Department of Respiratory Medicine. Cerrahpasa-Istanbul, Turkey.

Accepted 07 May 2019

COPD is a disease presenting with pulmonary inflammation as well as a systemic one. The present study was conducted to see if platelet count may be accepted as an indicator of systemic inflammation other than erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). 964 smoker patients without any concomitant disease were divided into groups as COPD and non-COPD according to spirometric values. Physical examination, posteroanterior chest x-rays and blood samples were determined. Patients with COPD had higher ESR, CRP levels and platelet count than the group without COPD. According to spirometric parameters, as the severity of the disease increased, platelet counts also revealed a statistically significant increase. We conclude that the increase in the number of platelets may be an indicator of severity of the disease and systemic inflammation in patients with COPD.

**Key words:** Platelet, inflammation, COPD.

### INTRODUCTION

The importance of systemic inflammation in pathogenesis of COPD is recently emphasized. Neutrophils have an important role in systemic inflammation; they take place in releasing cytokines and activation of many cells. Among these cells, thrombocytes are of importance since they cause thrombosis, pulmonary embolism and pulmonary hypertension when activated and help the progression of the disease. As the indicator of systemic inflammation, levels of TNF- $\alpha$ , IL-8 and IL-6 are measured frequently ((Kojima et al., 2005; Gunnar, et al., 2006; Bansal et al., 2002; Global Initiative for Chronic Obstructive Lung Disease et al., 2004). Measurement of these parameters is not cheap and feasible in every health center. However, it is easy and cheap to achieve platelet count in every center, yet it is underestimated and not investigated sufficiently. According to our results we suggest platelet count to be a feasible indicator of systemic inflammation.

### MATERIALS AND METHODS

964 patients (Female: 233; Male: 731) presenting to our outpatient clinic of pulmonary disease in Haseki Training and Research Hospital between years 2004-2005 who had a history of smoking at least 10 pcks/yr and stable clinical condition were included in the study. The patients were excluded in case of a thoracic, abdominal or eye

surgery within last three months; they were hospitalized because of a cardiac problem, a gastrointestinal bleeding as well as obesity, active tuberculosis, pregnancy, lactation, a neurologic or psychiatric disorder and cooperation failure. None of the patients presented any symptom of infection and rheumatologic or hematologic disease.

The study was approved by the ethical committee of the hospital. After providing an informed consent, the patients underwent a physical examination and chest radiographies were provided. Blood samples were obtained for ESR, CRP, leukocyte and platelet counts. Sedimentation rate was measured by Linear device with Westegen method. CRP was measured by Dade Behring with nephelometric method and 24 parameters of blood count was assessed by full automatic blood counter, ADVIA 120. The number of platelets were measured mechanically with Bayer Advia 120 Hematology and Trinity Biotec Amax 400.

Spirometry was performed with Jaeger 4.0 Master scope device. Following 6-8 times of forced expiration, highest three values with a difference of maximum 150 ml were recorded and the highest one was accepted as the result. After the patients received 200 mcg of salbutamol and rested at a sitting position for 20 min, the test was repeated. All of the tests were performed while the patients were sitting erect with a nose clip applied. The individuals who had FEV<sub>1</sub>/FVC values less than 70% were diagnosed as COPD according to GOLD 2004 guidelines. The individuals with and without COPD were compared according to ESR, CRP, leukocyte and platelet numbers. The assessments were made by Chi-Square, Student's t test, Mann Whitney-U test, Pearson-Spearman correlation, One-way ANOVA, Tukey's HSD and Kruskal Wallis tests.

### RESULTS

452 individuals were included in the group of patients

\*Corresponding author. E-mail: [gulfidan70@gmail.com](mailto:gulfidan70@gmail.com)

**Table 1.** The characteristics of the participants with and without COPD.

	COPD (n=512)	Without COPD (n=452)	p
Age	49.70±13.03	59.82±30.03	p<0.001
Smoking(pck/yr)	31.68±51.86	42.66±29.78	p<0.001
ESR(mm/hr)	24.67±6.87	27.07±8.12	p<0.001
CRP	4.62±2.09	5.50±2.83	p<0.001
Leukocyte count (/mm <sup>3</sup> )	8346.59±2163.62	8345.02±2294.63	p=0.991
Platelet count(/mm <sup>3</sup> )	260210.76±74162.65	279303.25±67540.46	p<0.047
FEV <sub>1</sub> /FVC(%)	80.26±41.10	55.93±9.54	p<0.001

**Table 2.** The characteristics of COPD patients according to the stage of the disease.

	Stage 1	Stage 2	Stage 3	p
Age	50.33±13.01	55.74±13.24	64.91±11.47	p<0.0001
Smoking(pck/yr)	31.47±52.73	38.90±26.97	48.01±30.11	p<0.0001
ESR(mm/hr)	23.16±6.65	28.50±8.00	27.32±7.31	p<0.0001
CRP	4.19±2.15	6.04±2.86	5.29±2.57	p<0.0001
Leukocyte count (/mm <sup>3</sup> )	8554.24±6570.80	9353.82±16741.96	10335.37±19014.34	p=0.333
Platelet count(/mm <sup>3</sup> )	252856.04±69715.40	264638.94±85545	298081.34±252358.33	p<0.0001
FVC	3905.26±910.25	2979.33±791.15	2379.48±565.68	p<0.0001
FVC%	108.41±14.99	83.48±14.92	66.69±13.08	p<0.0001
FEV <sub>1</sub>	2989.82±785.17	1892.53±478.30	1188.13±270.00	p<0.0001
FEV <sub>1</sub> %	100.89±14.72	65.52±8.66	41.67±5.47	p<0.0001
FEV <sub>1</sub> /FVC	69.27±7.70	64.19±10.89	51.54±12.43	p<0.0001
FEF <sub>25-75</sub>	5466.42±1830.03	2852.41±1313.27	1306.94±647.86	p<0.0001
FEF <sub>25-75</sub> %	82.52±21.71	44.13±20.64	22.37±25.03	p<0.0001

with COPD according to GOLD criteria and 512 in the control group. The number of male patients (average age: 59.82 ± 30.03 years) with COPD was significantly higher than control group (average age: 49.70 ± 13.03 years) (Table 1).

In COPD group, average age and smoking rates were higher while spirometric parameters were lower as expected. ESR and CRP levels were significantly higher in COPD group (p<0.001). Leukocyte numbers were higher than control group but the difference was not statistically significant. The platelet count was also significantly higher in COPD group than control group (p<0.001). In COPD patients, as the disease worsened, ESR, CRP, platelet and leukocyte counts increased. While the increase in ESR, CRP levels and platelet numbers was statistically significant, the increase in leukocyte numbers did not show any significance (Table 2).

## DISCUSSION

COPD is a chronic inflammatory and progressive disease presenting with acute exacerbations in which several environmental factors like air pollution, occupational exposure and subjective factors like age and genetic susceptibility are important (Aronsson et al., 2005; Kojima et al., 2005; Enright et al., 2003; Gunnar, et al., 2006; Bansal

et al., 2002; Global Initiative for Chronic Obstructive Lung Disease et al., 2004; Hidekazu et al., 2005; Giovanni et al., 2000; Jaen et al., 2003; Menezes et al., 2005). There is both respiratory and systemic inflammation in COPD (Global Initiative for Chronic Obstructive Lung Disease et al., 2004). Expression of adhesion molecules, secretion of platelet activator factor, prostaglandins, leukotrienes and cytokins from airway epithelial cells are important in inflammation (Global Initiative for Chronic Obstructive Lung Disease et al., 2004; Mannino, 2002). Neutrophils cause activation and dysfunction of platelets.

To reveal the inflammation in lungs, bronchial lavage, sputum and bronchial mucosa biopsy samples were searched for inflammatory cells and cytokins. These inflammation markers are almost everytime present in the airway wall and sputum of the smoker COPD patients whose findings belong to stage 1-3 (Aronsson et al., 2005; Willemse et al., 2005; Soriano 2002). ESR, CRP, leukocyte count, TNF- $\alpha$ , IL-8 and IL-6 levels are accepted as important indicators of the systemic inflammation in COPD (Global Initiative for Chronic Obstructive Lung Disease et al., 2004; Mannino, 2002; Willemse et al., 2005). In our study, ESR, CRP levels and platelet counts are measured and found to be significantly higher in COPD group than control group. A negative correlation was determined between these parameters and spirometric va-

riables.

In conclusion, we found that as the disease worsens, the number of platelets increase and this result is associated with spirometric parameters. To the best of our knowledge, this is the first report suggesting that platelet number may also be an indicator of systemic inflammation in patients with COPD.

All of the authors declare that they do not have any conflict of interest in this study.

## REFERENCES

- Aronsson ME, Pehrsson K, Nilsson JA, Nilsson PM, Löfdahl CG (2005). Mortality in GOLD stages of COPD and its dependence on symptoms of chronic bronchitis. *Respiratory Res.* 98:1-9.
- Bansal R, Lata H, Goel A, Madhur Y (2002). Association of Increased Platelet Volume in Patients of Chronic Obstructive Pulmonary Disease: Clin. Implication. *JACM.* 3:169-172.
- Enright PL, Kaminsky D (2003). Strategies for screening for Chronic Obstructive Pulmonary Disease. *Respir Care.* 48(12):1194-1201.
- Giovanni V, Marzia P, Francesco P, Francesco DP, Sandra B, Laura C, Carlo G (2000). Prevalence of Airways Obstruction in a General Population. *Chest.* 117:339-345.
- Global Initiative for Chronic Obstructive Lung Disease (2004). Global Strategy for Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Executive Summary
- Gunnar G, Thorarinn G, Eva L, Runa H, Charlotte SU, Eva B, Markku MN, Tiina A, Per B, Christer J (2006). Mortality in COPD patients discharged from hospital: the role of treatment and comorbidity. *Respirat. Res.* 7:109-118.
- Hidekazu T, Wataru H, Tsukasa S, Takashi S, Tetsuzo S (2005). Prevalence of chronic obstructive pulmonary disease in Japanese people on medical check-up. *Tohoku J. Exp. Med.* 207: 41-50.
- Jaen Diaz JI, De Castro Mesa C, Gontan G, Salamanca MJ, Lopez de Castro F (2003). Prevalence of Chronic Obstructive Pulmonary Disease and Risk Factors in Smokers and Ex-Smokers. *Arch Bronconeumol.* 39(12):554-558.
- Kojima S, Sakakibara H, Motani S, Hirose K, Mizuno F, Ito M, Hashimoto S (2005). Effects of Smoking and Age on COPD in Japan. *J. Epidemiol.* 15(4):150-155.
- Mannino MD (2002). Epidemiology, Prevalence, Morbidity and Mortality, and Disease Heterogeneity. *Chest.* 121(5):121-126.
- Menezes AMB, Jardim JR, Perez-Padilla R, Camelier A, Rosa F, Nascimento O, Hallal PC (2005). Prevalence of chronic obstructive pulmonary disease and associated factors: the PLATINO Study in São Paulo, Brazil. *Cad. Saude Publica, Rio de Janeiro.* 21(5):1565-1573.
- Soriano JB, Vestbo J, Pride NB, Kiri V, Maden C, Maier WC (2002). Survival in COPD patients after regular use of fluticasone propionate and salmeterol in general practice. *Eur. Resp. J.* 20:819-825.
- Willemse BW, Hacken N, Rutgers B, Postma DS, Timens W (2005). Association of current smoking with airway inflammation in chronic obstructive pulmonary disease and asymptomatic smokers. *Respiratory Res.* 38(6):28-38.