A Study of Platelet Parameters as a Novel Marker of Severity of Inflammation in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death worldwide, characterised by both systemic as well as pulmonary inflammation. During an acute exacerbation, the inflammatory pathways are unregulated to a greater extent and may also precipitate a critical cardiovascular event. Platelet parameters like platelet count, Mean platelet volume (MPV) and platelet distribution width (PDW) are markers of platelet activation and also has been associated with various inflammatory conditions.

Aim of the Study: To find out the role of Platelet Parameters in COPD and to establish the relationship between the severity of COPD with the Platelet Parameters and to find out whether the platelet parameters can be a useful prognostic tool that will help the therapeutic target in COPD.

Material and Methods: Forty COPD patients who visited Pulmonary Medicine OPD during the study period, were included in the study. COPD patients were diagnosed by spirometry and classified according to the GOLD's criteria. The results of the Spirometry was compared with the different platelet parameters like platelet count, mean platelet volume and platelet distribution width to establish the probable role of platelets in the severity of COPD.

Result and Conclusion: It was concluded from the study that as the disease worsens, the number of platelets increase and this result is associated with spirometric parameters. The MPV and PDW also increased with the severity of disease in patients with COPD. So, the platelet parameters can be used as a simple, quick, tool to predict the severity in COPD patient and help in predicting the prognosis of the disease.

Key Words: COPD, Spirometry, Platelet parameters, MPV, PDW

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is estimated to affect greater than 5% of the adults and with a progressively rising rate of morbidity and mortality¹². As it is estimated, COPD will be the third leading cause of death worldwide by 2020³⁴. COPD is a great financial burden upon health systems, primarily because of its acute exacerbations which require hospitalization⁵. COPD is mainly characterized by restricted airflow, which is a result of inflammation as well as the remodelling of the airways⁶. COPD is characterised by both systemic as well as pulmonary inflammation. During an acute exacerbation, the inflammatory pathways are unregulated to a greater extent and may also precipitate acute cardiovascular events. COPD is also associated with low-grade systemic inflammation as obvious from increased total leucocyte count, acute phase proteins like C-reactive protein (CRP), and inflammatory...
cytokines. Platelet parameters like platelet count, Mean platelet volume (MPV) and platelet distribution width (PDW) are markers of platelet activation. Increased MPV is associated with many vascular diseases, like peripheral, cerebrovascular disease, and coronary artery disease. Biljak et al. reported elevated platelet count and decreased MPV in COPD patients. In contrast, Cui et al. stated that a high MPV predicts impaired pulmonary and cardiac function in elderly COPD patients. However, only a few studies have been done showing the relationship between MPV and the severity of COPD. Hence our study aimed to establish the role of platelet parameters in patients of COPD and to find the correlation of various platelet parameters with the severity of COPD. We also intended to find out if it could be used as a prognostic tool in future.

**AIMS AND OBJECTIVES**

1. The study aimed to find out the role of Platelet Parameters in COPD and to establish the relationship between the severity of COPD with the Platelet Parameters.
2. To find out whether the platelet parameters can be a useful prognostic tool that will help the therapeutic target in COPD.

**MATERIAL AND METHODS**

The study was undertaken in the Department of Physiology of IMS and SUM Hospital, Bhubaneswar. Forty COPD patients who visited the Pulmonary Medicine OPD during the study period were included in the study. COPD patients were diagnosed according to the GOLD’s criteria. Approval from the institutional ethic committee (IEC) was obtained, and written informed consent was taken from patients who participated in the study. Patients with other acute and chronic lung diseases, Haematological disorders, patients with any other chronic inflammatory condition or Cancer patients on Long term Oxygen Therapy were excluded from the study.

In all the patients included in the study group, the following investigations were done in addition to the routine investigations:

- platelet count, mean platelet volume and platelet distribution width.
- Pulmonary Function Tests
- Chest X-Ray

The result of various tests was recorded independently of one another. A detailed medical history was obtained, and a detail physical examination was performed. Physical examination was followed by spirometry.

COPD was diagnosed on the basis of clinical examination (chronic and progressive dyspnea, cough, and sputum production) and also spirometry findings (FEV1/FVC (forced vital capacity) <0.70 after use of bronchodilation).

The Spirometry results (Lung Function Test) was used to define the severity of disease as per the Global Initiative for Chronic Obstructive Lung Disease classification (GOLD criteria).

- **Stage I (mild)-GOLD 1** - FEV1/FVC <70% and FEV1 ≥80% predicted;
- **Stage II (moderate)-GOLD 2** - FEV1/FVC <70% and 50% ≤FEV1 <80% predicted;
- **Stage III (severe)-GOLD 3** - FEV1/FVC <70% and 30% ≤FEV1 <50% predicted;
- **Stage IV (very severe)-GOLD 4** - FEV1/FEVC <70% and FEF25 <30% predicted.

For our study, the first three categories were taken into consideration.

**Biochemical Analysis of Blood Samples**

The blood sample was collected in the morning following an overnight fast. Ethylenediaminetetraacetic acid tubes were used to avoid platelet swelling. MPV and PDW was estimated within 30 minutes after sampling by an automated blood cell counter (Sysmex XE 2100, Kobe, Japan). The results of the Spirometry was compared with the different platelet parameters like platelet count, mean platelet volume and platelet distribution width to establish the probable role of platelets in the severity of COPD.

**Statistical Analysis**

The statistical analysis was done using SPSS 20. The quantitative data were summarized with Mean ± standard deviation and documented. Correlation between ages of different groups such as mild, moderate and severe was calculated using chi-square test, and the difference in the proportion of cases with varying levels of MPV in both groups and the various other clinical parameters like FVC, FEV1, FEV1/FVC, PDW and platelet count were analysed using ANOVA.

**RESULTS**

A total of 40 Chronic Obstructive Pulmonary Disease were studied for platelet parameters and pulmonary function test. After analysis, the following results were obtained. All test results were significant at P<0.05, and P<0.001 was considered highly significant. In our study, we found a significant increase in MPV, PDW and platelet count with an increase in the severity of COPD.
OBSERVATION

Table 1: Demographic characteristics of COPD patients

| Variables                  | Study group (COPD Patients) | Mild COPD Stage I (mean ± SD) | Moderate COPD stage II (mean ±SD) | Severe COPD Stage III (mean ± SD) | P-value |
|---------------------------|----------------------------|------------------------------|-----------------------------------|----------------------------------|---------|
| Number                    | 40                         | 10                           | 20                                | 10                               |         |
| Age in years              | 44±9.8                     | 39.0±8.39                    | 46.95±15.61                      | 47.0±13.61                       | P<0.3   |
| Sex (male/female)         | 23/17                      | 5/5                          | 11/9                              | 7/3                              | P< 0.7  |

Table 2: Spirometric findings of different study groups

| Variables                  | Mild COPD Stage I (mean±SD) | Moderate COPD stage II (mean±SD) | Severe COPD Stage III (mean±SD) | P-value |
|---------------------------|-----------------------------|----------------------------------|---------------------------------|---------|
| FEV1 (% predicted)        | 84.40±7.39                  | 62.72±9.15                       | 37.96±4.83                      | P<0.001 |
| FVC (% predicted)         | 99.00±20.90                 | 72.48±14.28                     | 47.94±6.03                      | P<0.001 |
| FEV1/FVC (%) (mean±SD)    | 65.48±3.09                  | 66.11±5.68                      | 64.15±3.53                      | P<0.563 |

Table 3: Platelet Parameters in different study groups

| Variables                  | Mild COPD (mean±SD)         | Moderate COPD (mean±SD)         | Severe COPD (mean±SD)           | P-value |
|---------------------------|-----------------------------|---------------------------------|---------------------------------|---------|
| Platelet count (x10⁹/litre)| 267.4±32.38                 | 342.9±68.26                     | 484.8±19.54                     | P<0.001 |
| Mean platelet volume (MPV)in fl | 8.46±0.23                | 9.19±0.12                       | 9.82±0.15                      | P<0.001 |
| Platelet Distribution Width (PDW) in % | 11.18±0.44                    | 12.81±0.21                     | 13.89±0.31                      | P<0.001 |

Figure 1: Mean Platelet Volume in the study groups.

Figure 2: Mean Platelet Distribution Width in the study groups.
DISCUSSION

COPD is a progressive disease along with chronic inflammation. It presents with an acute increase in severity of the disease, which may be due to several factors like air pollution, occupational exposure, age and genetic susceptibility. Stable COPD is associated with low-grade systemic inflammation which can be concluded from increasing levels of blood leucocytes and acute phase proteins\(^{15,16}\). As indicated from earlier studies, it is suggestive that the lung function impairment in COPD is strongly associated with impaired cardiovascular functions and deaths related to the cardiovascular system\(^{17}\). In addition to it, COPD and atherosclerosis frequently coexist and have some combined risk factors like age and also smoking. Inflammation is considered as the leading cause of progression of COPD and atherosclerosis. Platelets are considered to be responsible for atherogenesis, atherothrombosis and inflammation. According to recent studies, it has been found that an increase in arginase activity in case of platelets indicates altered metabolism of Nitric oxide and an increase in platelet activity seen in COPD\(^{18}\). It was also reported that patients of COPD had higher level of soluble P Selectin, a marker of platelet hyperreactivity\(^{19}\). Some studies indicate the inverse relations between MPV and disease activity in rheumatoid arthritis, inflammatory bowel disease, and ankylosing spondylitis\(^{20,21}\). MPV is referred to as a ‘marker of inflammation’, is found to be elevated in patients who are at risk of atherothrombotic disease. MPV and PDW reflect the platelets size and the rate of production of platelets in the bone marrow, and it can be used as an indicator of activation of platelet and the severity of inflammation.

In our study, we have found that the platelet count increases significantly as the severity of COPD increases. There was also a significant increase in MPV and PDW with increasing severity of the disease. However, the association between Mean platelet Volume and COPD is still unclear. Some studies have shown that patients with Stable COPD have an increased level of MPV compared to those in the control groups\(^{22}\) whereas according to another report it was found that this association of increased mean platelet volume in COPD patients was not significant statistically\(^{23}\). The controversial statements may be a result of the inability to rule out confounding factors like body mass index, use of specific medication, Obesity, smoking status etc.\(^{24}\). Onder et al\(^{24}\) studied the relationship between hypoxia and thrombocytes in patients of COPD, and they concluded that MPV values were higher in hypoxic patients with COPD as compared to non-hypoxic participants and controls. Biljak et al.\(^{14}\) found that patients with stable COPD patients had a significantly higher level of PLT count and decreased MPV in comparison to healthy controls.

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