Relationship between platelet count, platelet indices, and inflammatory markers in stable and acute exacerbation of bronchiectasis patients

Burcu A. Yigitbas[a], Sibel Yurt[a], Berat Uslu[a], Celal Satici[a], Pelin Uysal[b], Ayse F. Kosar[a]

Background and objective Persistent and chronic infection is one of the reasons underlying the sustained inflammation in bronchiectasis patients, and inflammatory markers may possess important clinical implications in the follow-up. Platelets are known to have effects on inflammatory response; in addition, a negative correlation has been shown between mean platelet volume (MPV) and inflammatory disease activity. The objective of this paper is to investigate and compare the levels of platelet (PLT) count and platelet indices during stable and acute exacerbation of bronchiectasis patients.

Patients and methods Data were retrospectively collected from medical files of 63 patients (39 women) and 29 controls without bronchiectasis. Thirty patients had an acute exacerbation, and 33 were in a stable state of disease. Descriptive data, clinical, radiologic, and laboratory information were noted. The relationship between inflammatory markers and pulmonary function tests was evaluated.

Results White blood cell (WBC) count, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), and PLT count were significantly higher; however, hemoglobin level and MPV were lower during exacerbation. There was a correlation between PLT and CRP, WBC, and ESR, and a negative correlation between PLT and forced vital capacity and forced expiratory volume in 1 s. However, we found an inverse correlation between MPV and WBC, and ESR, a positive correlation between MPV and forced expiratory volume in 1 s.

Conclusion We have found that platelet indices PLT and MPV were significant in exacerbation of bronchiectasis patients compared with stable and control patients. Cell blood count, compared with CRP and other inflammatory markers, is a more practical, useful, cost-effective laboratory examination. Not just looking at the WBC, but just taking a glance at the platelet indices would be a useful and simple way to evaluate bronchiectasis patients.

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Keywords: bronchiectasis, exacerbation, inflammation, mean platelet volume, platelet count

[a]Department of Chest Diseases, Yedikule Research and Training Hospital for Chest Diseases and Chest Surgery, [b]Department of Chest Diseases, Acibadem University School of Medicine, Acibadem Atakent Hospital, Istanbul, Turkey

Correspondence to Burcu A. Yigitbas, MD, Yedikule Chest Disease Hospital Belgradkapiyolu Number 1 Zeytinburnu/Istanbul/Turkey
Tel: + 90 533 665 3549; fax: +902124090200;
e-mail: drburcuayigitbas@yahoo.com

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Introduction

Bronchiectasis is a permanent and progressive dilation of the airways as a consequence of inflammation, infection, and subsequent repair. It typically presents with chronic cough, suppurative sputum production, and airway dilation [1]. This progressive disorder of the airways is characterized by chronic infection and coexistent inflammation. Poor and insufficient treatment may lead to deterioration of pulmonary function and reduction in life expectancy [2]. Pulmonary and bronchial injury in bronchiectasis may ensource from the damage to the bronchial wall and abnormal dilation, which predisposes to poor clearance and pooling of mucus [3]. Patients are vulnerable to lower respiratory tract infections that elicit a chronic inflammatory response that subsequently causes lung damage and enhances persistent infection. This process continues as a vicious circle in which worsening of pulmonary function is accompanied with the progression of bronchiectasis. Monitorization of the condition of the patient can be made by pulmonary function tests and biochemical markers [3]. The markers in the blood may reflect the intensity of host inflammatory response in pulmonary diseases such as bronchiectasis, cystic fibrosis (CF), and community-acquired pneumonia (CAP) [4–6]. Increase in systemic markers of inflammation has been reported in even stable phases of bronchiectasis [3]. Lower socioeconomic conditions and increased colonization of the lower airway with pathogenic microorganisms may contribute to the elevation of inflammatory markers [7]. Systemic overproduction of cytokines and neutrophilic inflammation were demonstrated in bronchiectasis; however, the exact role of inflammatory markers has not been fully elucidated [8]. Persistent and chronic infection was supposed to be one of the reasons for the sustained inflammation in

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bronchiectasis [9,10]. Hodge *et al.* reported that proinflammatory T cells with systemic cytotoxicity are increased in children with bronchiectasis, and this finding was supposed to be related to adaptive immune response, as well as a more severe disease. Systemic inflammatory changes associated with chronic lung disease have been associated with the spillover of lymphocytes [11]. Increased proinflammatory cells are detected in the peripheral blood of both adults with chronic lung diseases and children with bronchiectasis [2,11]. Platelets are traditionally recognized for hemostasis; however, increasing number of studies show that these rather ubiquitous blood components are potent immune modulators and effectors. Platelets have been shown to directly recognize, sequester, and kill pathogens, to activate and recruit leukocytes to sites of infection and inflammation [12]. In addition, platelets are known to have effects on inflammatory response; in particular, changes in platelet (PLT) count during bacterial infections are thought to be associated with the severity and mortality of the infection. The increase in PLT count has been reported to be correlated with the severity of tuberculosis and acute-phase reactants; it has been shown that platelet and platelet indices can be used to define activation of tuberculosis [12–14]. Mean platelet volume (MPV) has been shown to correlate with the function and activation of platelets; besides, an inverse correlation between inflammatory disease activity such as inflammatory intestinal diseases, rheumatoid arthritis, and MPV has been shown [15,16]. However, there are scarce data of MPV and PLT count showing correlation in bronchiectasis patients in stable and exacerbation phase in adults. Systemic inflammation as reflected in increased blood neutrophils and plasma cytokines has been shown in bronchiectasis patients. This inflammatory process was found to be somewhat related to the severity of the disease and bacterial colonization [8]. The objective of the current study is to evaluate and to investigate the levels of PLT count and platelet indices in patients with stable and exacerbation phase of bronchiectasis.

Patients and methods

Study design

This retrospective study was carried out in the Chest Diseases Department of our institution following the approval of the local Institutional Review Board (10 02 2015/81). Data were extracted from the medical files of patients diagnosed and treated for bronchiectasis between January 2014 and December 2014. Diagnosis of bronchiectasis was established on detailed history and physical examination findings. Radiologic data were provided by chest radiography and high-resolution computed tomography. Criteria for inclusion in the study were a diagnosis of bronchiectasis on findings from high-resolution computed tomography [17]. Diagnosis and assessment of bronchiectasis patients were carried out according to British Thoracic Society guidelines [18]. Patients with clinical, radiological, and laboratory tests suggesting CF and bronchiectasis due to tuberculosis sequelae, and patients using anticoagulant and antiplatelet drugs and parenteral or oral corticosteroids were excluded from the study. Control group was selected from healthy individuals. Patients were grouped as the exacerbation group, the stable group, and the control group. Bronchiectasis exacerbation was defined as deterioration in three or more of the following key symptoms for at least 48 h: cough; sputum volume and/or consistency; sputum purulence; breathlessness and/or exercise tolerance; fatigue and/or malaise; hemoptysis and a clinician determines that a change in bronchiectasis treatment [19].

Outcome parameters

Baseline descriptive information, results of blood tests including complete blood count, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), sputum culture, and antibiotics, as well as pulmonary function tests were recorded. Clinical information involving type and duration of symptoms, previous history of therapeutic embolization, surgery, hospitalization, and exacerbation in the previous year linked with bronchiectasis, and comorbidities were noted. Evaluation of pulmonary function tests was based on forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), and FEV_1/FVC ratio.

Statistical analysis

Normal distribution of data was tested with Kolmogorov–Smirnov test. Parametric tests were applied to data with normal distribution, and nonparametric tests were applied to data of questionably normal distribution. Correlation between parameters with normal distribution was assessed by Pearson's test, whereas Spearman's ρ-test was used for variables that do not have normal distribution. Quantitative variables are expressed as mean, SD, median, interquartile range, minimum, and maximum values. The confidence interval was set at 95% and statistical significance was assumed for P values less than 0.05. Categorical variables were compared using Pearson's χ^2 and Fisher's exact tests. Evaluation of groups with and without normal distribution was made by independent samples t-test and Mann–Whitney U-test, respectively.

Results

Our series comprised 71 patients (39 women, 54.9%) with a mean age of 47.7±15.9 (15–76) years. Number of patients in stable and acute exacerbation states of bronchiectasis were 33 (46.5%) and 38 (53.3%), respectively. The mean age of the exacerbation group was 52.88±16.25; however, the mean age of the stable group was 43.24±14.33 ($P<0.05$). Foreseeing that this age mismatch would alter our results, we then performed age adjustment. Our series eventually comprised 63 patients (39 women) and 29 controls (13 women) with a mean age of 50.73 ±15.46 years in the exacerbation group, 46.00±12.43 years in the stable group, and 51.10±15.97 years in the control group ($P=0.298$). Baseline data demonstrating demographic and clinical information are shown in Table 1. Number of patients in stable and acute exacerbation states of bronchiectasis were 30 (32.3%) and 38 (36.6%) and controls 29 (31.2%), respectively. There was no difference between two groups regardless of sex, smoking, and education status, as well as BMI. Married patients were found to be more in the stable group (28/29, $P=0.02$).

There was no significant difference in symptom duration, symptom frequency, dominant symptom, and comorbidities between groups.

There was a significant difference in exacerbation rate in the previous year between groups (2.70±2.17 in the exacerbation group, 1.47±1.31 in the stable group, $P=0.007$); in relation to exacerbation, hospitalization in the previous year and operations due to bronchiectasis were not significantly different between groups.

Notably, CRP, white blood cell (WBC), PLT levels, and ESR were higher in patients with acute exacerbation ($P=0.000, 0.000, 0.014, 0.000$, respectively), as shown in Table 2. In contrast, hemoglobin (HB) and MPV levels were lower in patients during exacerbation ($P=0.013$, 0.000, respectively).

Table 1 Patient demographics and clinical determinants and comorbidities adjusted for age

Variables	Exacerbation ($n=30$)	Stable ($n=33$)	Control ($n=29$)	P value
Age	50.73±15.46	46.00±12.43	51.10±15.97	0.298
Sex				
Male	8 (20.0)	16 (40.0)	16 (55.2)	0.092
Female	21 (40.4)	18 (34.6)	13 (44.8)	
Education				
Elementary	15 (48.4)	16 (51.6)	–	0.77
High school and university	10 (52.6)	9 (47.4)	–	
Marital status				
Single	7 (87.5)	1 (12.5)	–	0.02*
Married	19 (40.4)	28 (59.6)	–	
Smoking status				
Smoker	7 (31.8)	15 (68.2)	–	0.062
Nonsmoker	20 (57.1)	15 (42.9)	–	
Cigarette package/year	6.67±13.65	9.87±14.39	–	0.394
BMI	24.37±4.65	23.47±3.03	–	0.365
Symptom duration	10.13±10.08	6.48±7.16	–	0.101
Symptom frequency				
Every week	21 (52.5)	19 (47.5)	–	0.244
Once/twice a month	9 (37.5)	15 (62.5)	–	
Dominant symptom				
Dyspnea/wheeze	12 (44.4)	15 (55.6)	–	0.739
Cough/sputum	18 (48.6)	19 (51.4)	–	
Exacerbation in the previous year	2.70±2.17	1.47±1.31	–	0.007*
Hospitalization in the previous year	1.07±1.96	0.09±0.29	–	0.174
Operation due to bronchiectasis	2 (100)	0 (0)	–	0.216
Comorbidities (n)				
DM	1/30	1/34	3/29	0.887
HT	4/30	2/34	2/29	0.376
CRF	1/30	0/34	0/29	0.338
CHD	0/30	1/34	0/29	0.251
Psoriasis	0/30	1/34	0/29	0.251

Continuous data are expressed as mean±SD for normal distribution and categorical data are expressed as n (%); CHD, chronic heart disease; CRF, chronic renal failure; DM, diabetes mellitus; HT, hypertension; $^{**}P<0.05$, statistical significance. *P values to emphasize significancy.

Table 2 Relationship between exacerbation, stable, and control groups regarding biochemical and spirometric variables adjusted by age

Variables	Exacerbation (*n*=30) (mean±SD)	Stable (*n*=33) (mean±SD)	Control (*n*=29) (mean±SD)	*P* value
Biochemical				
CRP	80.83±88.99	6.75±6.05	2.29±2.03	**0.000**
WBC	15.21±5.66	8.21±1.93	8.2±1.57	**0.000**
HB	12.60±1.67	13.83±1.61	13.24±1.60	**0.013**
PLT	307.10±100.71	254.76±64.35	247.06±88.70	**0.014**
PCT	0.25±0.08	0.22±0.55	0.24±0.73	0.316
MPV	8.14±1.08	8.82±1.09	10.12±1.03	**0.000**
PDW	15.30±2.15	15.99±0.87	12.27±2.31	**0.000**
ESR	49.35±25.22	17.53±11.31	–	**0.000**
Spirometry				
FVC (ml)	1.71±0.72	2.57±0.94	–	**0.000**
FVC (%)	55±23.30	72.24±16.60	–	**0.001**
FEV_1 (ml)	1.17±0.59	2.13±0.88	–	**0.000**
FEV_1 (%)	45±24.55	71.25±20.94	–	**0.000**
FEV_1/FVC (%)	65.40±13.46	77.88±11.56	–	**0.000**

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HB, hemoglobin; MPV, mean platelet volume; PLT, platelet; PCT, platelet crit; PDW, platelet distribution width; PDW, platelet distribution width; WBC, white blood cell; Significance is shown as bold.

FEV_1, FVC, and FEV_1/FVC ratio were decreased in the exacerbation group (*P*=0.000, 0.000, 0.000, respectively).

None of the stable group patients had exacerbation symptoms; the most detected pathogen was *Pseudomonas aeruginosa* (6/30) in the exacerbation group. Prescribed antibiotics are listed in Table 3.

As shown in Table 4, PLT was positively correlated with CRP (*r*=0.258, *P*=0.016), WBC (*r*=0.343, *P*=0,001), and ESR (*r*=0.408, *P*=0.001), whereas a significant negative correlation was found between PLT and HB (*r*=-0.268, *P*=0.009), MPV (*r*=-0.388, *P*=0.000), FVC (*r*=-0.440, *P*=0.000), FEV_1 (*r*=-0.447, *P*=0.000), and FEV_1/FVC (*r*=-0.112, *P*=0.380). However, MPV is negatively correlated with CRP (*r*=-0.322, *P*=0.002), WBC (*r*=-0.348, *P*=0.001), and PLT (*r*=-0.388, *P*=0.000), and positively correlated with HB (*r*=0.244, *P*=0.018), FVC (*r*=0.229, *P*=0.071), FEV_1 (*r*=0.279, *P*=0.027), and FEV_1/FVC (*r*=0.092, *P*=0.472).

Discussion

Bronchiectasis is the pathological bronchial dilatation usually linked with mucosal thickening and impaired secretion clearance, leading to accumulation of secretion, chronic suppurative cough, and pulmonary function loss associated with chronic inflammation [18]. The goal of treatment turns to empirical treatments to eliminate infective exacerbations and reduce the progression of disease [19–21]. Both local and systemic inflammatory markers have been used to monitor disease activity during exacerbation and stable phases of bronchiectasis. Wilson *et al.* [3] suggested that bronchiectasis patients had elevated systemic markers of inflammation even at their stable phase. Not only levels of CRP, ESR, and IgA were increased, but also WBC, neutrophil count, CRP, and ESR were positively correlated with bronchiectasis. Thus, some markers of inflammation may be correlated closely with the extent of disease, whereas some of them may be linked more closely with the deterioration of lung function [3]. The role of MPV as an indicator of platelet function has been investigated in association with several inflammatory disorders such as CF [22], ulcerative colitis [15], rheumatoid arthritis [16], familial Mediterranean fever [23], CAP, sepsis [24,25], and tuberculosis [26]. Besides, reactive thrombocytosis in tuberculosis has been shown to be correlated with acute-phase reactants and severity of the disease [27,28]. Our study indicated that HB level and PDW were lower, whereas PLT count, CRP, WBC, and ESR levels were higher during the exacerbation. Similar to these findings, Koc *et al.* [29] reported that PLT count was high in patients with bronchiectasis when compared with nonsmokers (*P*<0.001) and smokers (*P*<0.008), and differ from this study by the finding that MPV levels were insignificant between all groups. Uysal *et al.* [30] reported that there was no significant difference between MPV values of nonexacerbation period and control group (*P*>0.05). MPVs during acute exacerbation were significantly lower when compared with the values of nonexacerbation period and controls (*P*=0.02 and 0.01, respectively). MPV and PLT counts

(r=−0.502, P=0.01), as well as leukocyte count and HB levels, were inversely correlated with each other in the exacerbation period (r=−439, P=0.00) in children with bronchiectasis [30]. In this study, we found significant difference regarding MPV and PLT count between exacerbation and stable group (P=0.000 and 0.014, respectively). Moreover, in a study by Karadag-Oncel *et al.* [31], 196 patients were diagnosed with CAP during the study period, aged 1–18 years, and this study indicated that MPV value was significantly higher in hospitalized CAP patients compared with outpatients (7.32±0.71 vs. 6.83±0.5 fl; P=0.012); besides, patients with CAP had lower MPV values than their healthy counterparts (7.1±0.68 vs. 8.31±1.2 fl; P<0.001). On the contrary, this study found that MPV values were significantly lower than healthy controls (8.14±1.08 vs. 10.12±1.03, P=0.000). There was agreement with the results of Ali [32] who reported that, regarding MPV, a highly significant statistical correlation was observed among the studied groups, with a significant decrease in acute exacerbation chronic obstructive pulmonary disease patients and chronic lung disease, compared with stable chronic obstructive pulmonary disease patients who had lower levels than the control volunteers (P<0.00), and HB levels were increased among patients in the exacerbation group compared with the stable group, who showed higher ratios compared with controls, and this was not significant (P=0.346 and 0.451, respectively).

Table 3 Exacerbation symptoms, pathogens detected, and antibiotics for treatment

Variables	Exacerbation group	Stable group	*P* value
Acute exacerbation (*n*)			
Increased sputum	28/30	0/34	**0.00**
Increased cough	28/30	0/34	**0.00**
Increased dyspnea	24/30	0/34	**0.00**
Hemoptysis	6/30	0/34	**0.001**
Increased respiratory rate	10/30	0/34	**0.00**
Leukocytosis	10/30	0/34	**0.00**
Fever	7/30	0/34	**0.00**
Newly onset infiltration	14/30	0/34	**0.00**
Pathogens detected			
Acinetobacter spp.	1/30	0/34	–
Escherichia coli	3/30	0/34	–
Haemophilus influenzae	1/30	0/34	–
Klebsiella pneumoniae	2/30	0/34	–
Pseudomonas aeruginosa	6/30	3/34	–
Staphylococcus aureus	0/30	0/34	–
Serratia marcescens	1/30	0/34	–
No pathogen	11/30	0/34	–
Antibiotics			
Amoxicillin	1/30	–	–
Fluoroquinolone	4/30	–	–
Second-generation cephalosporins	1/30	–	–
Third-generation cephalosporins	4/30	–	–
Meropenem	1/30	–	–
Piperacillin tazobactam	1/30	–	–
Amoxicillin +fluoroquinolone	1/30	–	–
Third-generation cephalosporins +fluoroquinolone	3/30	–	–
Third-generation cephalosporins +lincosamine	1/30	–	–

Significance is shown as bold.

Foreseeing the progression of the disease and taking the essential precautions can be possible with a detailed analysis of these inflammatory markers. Wilson *et al.* [3] suggested that some of the inflammatory markers were elevated and correlated with the extent of disease and poor lung function. In this study, there was a negative significant correlation between PLT and HB, MPV, FVC, FEV_1, and FEV_1/FVC ratio but a positive significant correlation between PLT and both CRP and WBC. Our results have shown that results of pulmonary function tests such as FVC and FEV_1 seem to be sensitive markers for inflammation. Helmy *et al.* [33] found that MPV values were significantly lower in patients of acute exacerbation than in smokers and controls (both, P<0.001); also, a positive correlation was found between MPV and FEV_1, CRP, and total leukocytic count in total sample. Similarly, this study showed that MPV was negatively correlated with CRP, WBC, and PLT, but positively correlated with HB,

Table 4 Correlations between platelets, mean platelet volume, and inflammatory markers

	CRP	WBC	HB	MPV	PLT	ESR	FVC	FEV_1	FEV_1/FVC
PLT									
r	0.258	0.343	−0.268	−0.388	1	0.408	−0.440	−0.447	−0.112
P value	**0.016**	**0.001**	**0.009**	**0.000**		**0.001**	**0.000**	**0.000**	0.380
MPV									
r	−0.322	−0.388	0.244	1	−0.388	−0.374	0.229	0.279	0.092
P value	**0.002**	**0.000**	**0.018**		**0.000**	**0.004**	0.071	**0.027**	0.472

Data are presented as the Pearson correlation coefficient and *P* value; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HB, hemoglobin; MPV, mean platelet volume; PLT, platelet; WBC, white blood cell; Significance is shown as bold.

FVC, FEV_1, and FEV_1/FVC ratio. In agreement with the present study results, Guan *et al*. [34] reported that patients elucidated statistically significant reduction in FVC and FEV_1 during bronchiectasis exacerbations.

These findings imply that an interpretation of components of complete blood count may provide important implications for follow-up and treatment of patients with bronchiectasis. Further prospective, controlled trials on larger series are warranted to explain the implications and clinical relevance of inflammatory markers in bronchiectasis. Main limitations of the present study include small sample size, retrospective design, and lack of a convalescence group. Moreover, the complex interaction of inflammatory markers with genetic, environmental, and metabolic factors must be remembered during interpretation of our results. Further controlled, randomized trials on larger series are warranted to draw more accurate conclusions on the inflammatory process in the pathophysiology of bronchiectasis.

Conclusion

Results of the present study demonstrated that inflammatory markers may provide important clues for bronchiectasis patients. An integrated analysis of inflammatory markers in conjunction with clinical, radiological, and microbiological data may be useful for guidance of treatment and follow-up strategy. A simple, cost-effective way by cell blood count analysis can be helpful to determine patients' exacerbation state.

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Conflicts of interest

There are no conflicts of interest.

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