

LETTER TO THE EDITOR

Mean platelet volume increased in children with asthma

To the Editor,

Asthma is a chronic respiratory disease which is characterized by recurrent attacks of cough, wheezing, dyspnea, and variable expiratory airflow limitation. Asthma is a worldwide problem with an estimated 300 million affected individuals. Inflammation in asthma involves several inflammatory cells. Inflammatory cells such as eosinophils and/or neutrophils are defined well in the asthmatic airway (1). Platelets primarily involve in prevention of bleeding. Besides, they may also involve in various processes as secretion of proinflammatory, anti-inflammatory, and angiogenic factors, and collection of leukocytes and progenitor cells at areas of vascular damage and inflammation. Platelets play a role in allergic reactions that are inflammatory processes. Both intact platelets and platelet-released inflammatory mediators play crucial roles in the sustained inflammatory response of many allergic diseases. The platelet counts and platelet-activating markers in the plasma were significantly altered after exposure to an allergen in patients suffering from allergic inflammatory reactions. Platelet activation is necessary to transform arachidonic acid into lipid mediators which exacerbates the allergic response such as thromboxane A₂ (TXA₂), cysteinyl leukotrienes, and lipoxins (2). Platelet activation was demonstrated in asthmatic patients (3, 4). Experimental evidence demonstrated that platelets had a role in each stage of asthma pathogenesis in development of bronchoconstriction, airway inflammation, airway remodeling, and bronchial hyper-responsiveness (5). Platelets' volume increase when platelets become activated. Mean platelet volume (MPV) is one of the parameters in routine complete blood count test and shows the average volume of platelets in the circulation. MPV is one marker of platelet activation. In previous studies; relation between mean platelet volume changes and different diseases such as acute pyelonephritis had been shown (6). We have limited information about MPV in asthmatic patients (7, 8). In our country, in the study of Tuncel et al., they found no difference in terms of MPV among asthmatic patients during asymptomatic periods and exacerbations and control group (7). A new study on adults showed that decreased mean platelet volume was associated with stable and exacerbated asthma (8). In our study, we aimed to evaluate MPV and to assess its relationship with clinical parameters in children with stable and exacerbated asthma.

Six hundred and thirteen children with asthma, followed up in the pediatric allergy and immunology department of a public hospital of obstetrics and pediatrics, were included in the study. Patients were evaluated retrospectively between September 2012 and August 2014. Two hundred and nineteen children with no evidence of allergic disease (i.e., asthma, allergic rhinitis, and eczema) were included in the control group. 162 patients in the patient group were evaluated during exacerbation and classified as exacerbation group separately. Patients who have had an acute/chronic infection (except for exacerbation) and patients with any other systemic disease such as

hepatic, renal, cardiovascular diseases, diabetes mellitus, cancer, and systemic inflammatory disorders were excluded. In addition, stable asthmatic patients with anemia/polycythemia, leukopenia/leukocytosis, and thrombocytopenia/thrombocytosis in complete blood count analysis were excluded from the study. A detailed allergic history, including the age, a familial atopy history, and exposure to cigarette smoke were recorded. Familial atopy was accepted as positive when having allergic disease in first degree relatives (parents and siblings). The diagnosis of asthma was evaluated according to the GINA guidelines (1). Skin prick tests were performed using the same antigens ((*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*, grasses mix, cereals pollen mix, trees mix, weed mix, *Alternaria alternaria*, cockroaches, cat dander, and dog dander (Stallergenes SA, 92160 Antony, France) for all patients. The immunoglobulin (Ig) E levels and complete blood count were measured. The study was approved by the Zeynep Kamil Woman's and Children's Diseases Training and Research Hospital Ethics committee, and an oral consent was obtained from all subjects and/or their parents.

Results were given as either mean $\pm$ standard deviation (SD) or as mean $\pm$ standard deviation (median) according to the distribution. Student's t-test was used for the comparison of normally distributed variables. Chi-square, Mann-Whitney U-test, and Kruskal-Wallis tests were used for non-normally distributed variables. Pearson's correlation test was used for the correlation analyses of continuous variables. Paired samples t-test was used to compare the change of MPV during exacerbation and stable period. $p < 0.05$ was considered as significant.

There was no difference between the groups with regard to gender and age. Mean MPV was 8.21 ± 0.81 fL (5.3–11.3) in the study group and 7.95 ± 1.05 (5.6–12.6) in the control group. The difference was statistically significant ($p = 0.004$). Platelet count was significantly higher in asthmatic children compared to controls ($p = 0.008$). The demographic features, MPV, and platelet counts of the study population are shown in Table 1.

One hundred and sixty-two of the patient group were evaluated during exacerbation, and their complete blood count and CRP levels were assessed. Patients were classified into 3 groups as stable asthmatics (group I), exacerbated asthmatics (group II), and control group (group III). No statistically significant difference was present between groups in terms of gender and age ($p > 0.05$) (Table 2). In terms of MPV in the pairwise comparison of the groups, while there were statistically significant differences between Group I and Group II and between Group I and Group III, there was no significant difference between Group II and Group III. In terms of the mean number of platelets, there were significant differences between Group I and Group III and between Group II and Group III, there was no significant differences between Group I and Group II (Table 2).

Table 1 Comparison of sociodemographic features and mean platelet volume between patients and control groups

	Study group (n = 613)	Control group (n = 219)	p
Gender (n)			
Male/female	352/261	114/105	0.178*
Age (years)			
Mean±standart deviation	6.3 ± 2.8	6.1 ± 1.7	0.141**
Minimum–maximum (median)	3–17.7 (6.5)	3–18 (6.4)	
Mean platelet volume (fL)			
Mean±standart deviation	8.21 ± 0.8	7.95 ± 1.1	0.004**
Minimum–maximum (median)	5.3–11.3 (8.2)	5.6–12.6 (7.9)	
Platelet counts ($\times 10^3/\mu\text{L}$)			
Mean±standart deviation	331.3 ± 73.6	305.5 ± 74.9	0.008***
Minimum–maximum	150–500	150–470	

*chi-square test; **Mann–Whitney *U*-test; ***Student's *t*-test.

Table 2 Comparison of sociodemographic features and laboratory parameters between patients with stable asthma (Group I), acute asthma exacerbation (Group II), and healthy controls (group III)

Parameters	Stable asthma (n = 451)	Exacerbated asthma (n = 162)	Healthy controls (n = 219)	p			
				All	I–II	I–III	II–III
Gender (n)							
Male/female	266/185	86/76	114/105	0.168*	0.196*	0.097*	0.917*
Age (years)	6.3 ± 2.8	6.1 ± 2.5	6.1 ± 1.7	0.290**	0.455***	0.162***	0.257***
Mean platelet volume (fL)	8.21 ± 0.8	7.89 ± 0.9	7.95 ± 1.1	0.003**	0.004***	0.006***	0.567****
Platelet counts ($\times 10^3/\mu\text{L}$)	331.2 ± 71.6	329.6 ± 87.4	305.5 ± 74.9	0.008**	0.344***	0.006****	0.005****

*chi-square; **Kruskal–Wallis test; ***Mann–Whitney *U*-test; ****Student's *t*-test.

The presence of familial atopy, smoking exposure, the number of exacerbations in previous years, the number of hospitalizations, eosinophilia, and IgE levels were not significantly different between Group I and Group II ($p > 0.05$). Patients in Group II had a significantly higher presence of atopy compared with Group I (respectively, 61.1%, 49.3%; $p = 0.010$). There was not a significant correlation between MPV and the number of exacerbations in previous years, the number of hospitalizations, number of eosinophils, and IgE levels. There was not found any significant difference between MPV and sensitivity to allergens.

Increase in CRP level was detected in 130 of 162 patients (80.2%) during exacerbation. There was a weak negative correlation between the number of leukocytes and platelets with MPV during exacerbation (respectively, $r = -0.181$ $p = 0.019$, $r = -0.21$ $p = 0.007$). While mean MPV level of 162 patients in exacerbated asthmatics group was 8.20 ± 0.9 fL in stable period, it was measured as 7.89 ± 0.9 fL during exacerbation. Change in MPV levels in stable period and exacerbation period was statistically significant ($p = 0.002$).

CRP levels of 32 patients whom are part of the exacerbation group were normal (<0.5 mg/dl). There was a positive correlation between CRP levels and MPV in these patients ($r = 0.400$ $p = 0.023$).

In our study, we found that mean MPV level was higher in asthmatic children than control. Mean platelet volume is a

reflection of platelet size, and it has been shown to correlate with platelet function and activation. A higher MPV value is indicator of increased platelet activity and thus more intense inflammation (2). We mentioned above that platelet activation was necessary for the formation of various mediators which have played a role in allergic reactions and platelet activation existed in asthma (2–4). In addition, experimental evidence demonstrated that platelets had a role in each stage of asthma pathogenesis (5). We suggested that asthma was a chronic inflammatory disorder, and increased MPV values may have been associated with asthma. In accordance with our hypothesis, we found a high mean MPV level in asthmatic children in our study. However, previous studies which evaluated MPV in asthmatics had reported different results. Tuncel et al. (7) compared MPV levels of 100 asthmatic children aged between 2.5 and 16 years in exacerbation period and asymptomatic period and of 49 healthy children. Comparison of MPV values in asthmatic patients both in an acute asthmatic attack ($p = 0.434$) and asymptomatic period and healthy controls had no statistically significant difference ($p = 0.110$). They suggested that studies with larger number of patients were needed to evaluate the role of MPV in asthma. We believe that our study reflects real life better as it covers more children from a wider age range. In a recent study, Sun et al. (8) compared MPV values of 85 adult patients with asthma in exacerbation and stable period and MPV values of the control group. They detected that patients with exacerbated asthma had lower MPV compared to patients with

stable asthma and control subjects and the MPV was reduced in patients with stable asthma compared to control subjects. Our results may not be compatible with this study as it was conducted in adults and with fewer patients.

In our study, we found that platelet counts in asthmatic children were significantly higher than control. The results of the studies about the number of platelets in asthmatics are inconsistent in the literature. Kowal et al. (4) demonstrated that platelet count decreased in allergic asthma patients during allergen challenge with *Dermatophagoides pteronyssinus*. Nastalek et al. (9) reported that the platelet counts were higher in patients with atopic dermatitis and asthma compared to the control. In the study of Tuncel et al. (7), platelet counts in asthmatic children both during an asthmatic exacerbation and during the asymptomatic period were higher than healthy control group. But these differences were not statistically significant. While acute exposure to allergens leads to a decrease in the platelet count, a chronic allergen exposure may lead to an increase in platelet count. This discrepancy may be due to megakaryopoiesis stimulation in bone marrow with chronic allergen exposure.

Mean MPV in asymptomatic period was higher than exacerbated asthma and healthy control groups. There was no difference between exacerbated asthma and control group. Mean MPV values decreased during asthma exacerbation, and this reduction was statistically significant. There are limited data about MPV change during asthma exacerbation. Tuncel et al. (7) found no difference between these three groups in terms of mean MPV in their study. Sun et al. (8) reported lower mean MPV values in exacerbated asthma compared to stable period and control groups. These differences between the studies may be due to differences in age groups and number of population of these studies.

While mean MPV values in asthmatic children were significantly higher than controls, we expected a further rise in the mean MPV value during the acute asthma exacerbation. However, in our study, we found a decrease in the mean MPV values during the acute asthma exacerbation contrary to our expectations. This situation can have several causes.

Firstly, effects of acute and chronic allergen exposure on platelets may be different. Secondly, it may be occur due to accompanying pneumonia during asthma exacerbation. There was increase in CRP levels as 80% during the asthma exacerbation of our cases. Karadag-Oncel et al. (10) was evaluated MPV values in 196 children with community-acquired pneumonia. They found that mean MPV values in children with community-acquired pneumonia were significantly lower compared to controls group. It is hard to define how many cases had comorbid pneumonia as our study was retrospective. As most of our cases during exacerbation had high CRP levels and as we did not include cases with any kind of inflammatory disease in our study, it points out an accompanying infection. We assume that the decrease in mean MPV levels was due to these reasons.

The limitation of our study is not to evaluate the tests that are related with platelet activation such as the measurement of TXA2 metabolites and platelet-derived growth factor. This investigation could not be carried out because our study was performed retrospectively. Despite this limitation, our study is important because it assesses the relationship among platelet count, MPV, and asthma in such a large population in childhood.

As a result, mean MPV level and platelet counts were higher in asthmatic children than control. Mean MPV in asymptomatic period was higher than exacerbated asthma and healthy control groups. MPV was decreased during the exacerbation probably due to concurrent infection. There was a positive correlation between CRP and MPV in patients whose CRP levels were normal in asthma exacerbation. All these results suggest that platelets are being activated in asthma.

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