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Platelets count and platelets indices; mean platelet volume and plateletcrit in pediatric chronic lung disease

Iman H. Draz[1*] , Iman A. Shaheen[2] and Eman A. Youssef[2]

Abstract

Background: The lungs contribute in the final maturation of the circulating platelets, and some studies suggested that chronic lung disease (CLD) could impair circulating platelets maturation or count. Our aim was to study the validity of platelet count (PLT), mean platelet volume (MPV), and plateletcrit (PCT) as simple tools to assess chronic lung disease severity or predict its course.

Results: In 39 pediatric patients with CLD, we showed a significant rise in PLTs and PCT and a significant lower MPV when compared to normal controls (P values 0.003, 0.010, 0.004, respectively). Also, a significant positive correlation was detected between the C reactive protein (CRP) level and both the PLTs and PCT (r 0.327, 0.363 respectively) in addition to a significant reduction in MPV level in relation to the age of disease onset (P value 0.031).

Conclusion: This study disagrees with the postulation that chronic lung disease could lead to the reduction of circulating platelets and emphasizes the role of increased platelets count and decreased MPV in reflecting the inflammatory condition underlying the chronic lung disease in the pediatric age group.

Keywords: Chronic lung disease, Pediatric, Platelets count, Mean platelet volume, Plateletcrit

Background

Chronic lung diseases in children such as bronchiectasis and interstitial lung disease represent a major public health problem with limited therapeutic options [1]. The disease severity is highly variable according to the underlying condition but unfortunately, children with CLD have high overall morbidity and mortality [2]. Therefore, it is very important to find a non-invasive blood biomarker that could help in the diagnosis and predict the prognosis of ILD, it would be of more value in areas with limited resources to allow easier and earlier detection of more vulnerable patients [3].

The murine model of chronic obstructive pulmonary disease (COPD) has shown that lungs may serve as a reservoir for megakaryocytes and hematopoietic progenitor cells, where almost half of the platelets may be produced [4]. This finding sheds new light on thrombopoiesis in

mammals and raises a question of whether pulmonary platelet production takes place in the human lungs as well. If it were so, chronic pulmonary diseases that adversely affect lung tissue could affect the platelet count [5].

It was suggested that decreased mean platelet volume (MPV), one of the parameters routinely generated by blood counters, might indicate increased systemic inflammation during COPD exacerbation and that MPV could be a useful tool in the assessment of the inflammatory response [6].

Plateletcrit (PCT) provides more comprehensive data about total platelet mass because it reflects both the MPV and platelet count (PLT), where PCT is calculated by multiplying the PLT by the MPV/10^7 [7]. Platelet activation in infectious and allergic lung diseases has been well documented, platelets have been found extravascular in the lungs of patients with asthma, and in animal models of allergic lung inflammation. Previous studies demonstrated that blood leaving the lungs contained more platelets and fewer megakaryocytes than blood entering the lungs [8].

* Correspondence: imane.draz@cu.edu.eg; imane.draz@yahoo.com
[1]Pediatrics, Pediatric Pulmonology, Faculty of Medicine, Cairo University, Kasr Alainy, Street, Cairo Post Code: 11562, Egypt
Full list of author information is available at the end of the article

The aim of this study was to study changes in parameters of platelets in pediatric patients with CLD. The platelet count, MPV and PCT all represent laboratory parameters that are easy to obtain and readily available in most treatment facilities, if such elements could be applied as tools for assessment of the disease severity or to predict upcoming exacerbations or early prediction of a treatment response it would save much effort and cost.

Methods

Between September 2018 and March 2019, 121 patients with chronic lung disease presented to the pulmonary unit at the pediatric teaching hospital for follow-up. Of these, 39 subjects were recruited in this cross-sectional case-control study. Chronic respiratory diseases were defined as the presence of respiratory symptoms for 3 months or more in each of 2 consecutive years in a patient in whom other causes of such respiratory symptoms have been excluded.

The patients group constituted 23 (58.9%) males and 16 (41.0%) females, their ages ranged from 2 to 13 years with a mean of 6.9 ± 3.41 years, they were then compared with a group of 40 healthy control subjects with matched age and sex distribution randomly chosen from the general clinic, the normal control group constituted 18 (45%) males and 22 (55 %) females, their ages ranged from 1.5 to 13 years with a mean of 6.1 ± 3.05 years. Patients were then stratified into two groups: interstitial lung disease (n = 20) and non-cystic fibrosis (CF) bronchiectasis (n = 19) based on high-resolution computed topography (HRCT) findings.

Exclusion criteria included any associated disorders that may affect the platelet count as kidney failure, auto-immune diseases, diabetes, malignancies, chronic liver disease, and patients with prior treatment with anti-coagulant. Both groups were enrolled in the study after obtaining informed consent from the patients' legal guardians and the approval of the institutional ethical committee. Confidentiality of the data was guaranteed in handling the database according to the revised Helsinki Declaration of biomedical ethics [9].

Blood count was performed using an automated hematology analyzer "XN-1000 Sysmex" which measures blood count parameters including total leucocytic count (TLC), red blood cells (RBCs) count, RBCs mean corpuscular volume (MCV), platelet count, and mean platelet volume (MPV) by direct current detection method, blood film scanning of individual cases was done to exclude any analytical errors. Plateletcrit was calculated by multiplying MPV and platelet count to assess the functioning platelet mass. Erythrocyte sedimentation rate (ESR) was measured using the Westergren tube method for both groups, C-reactive protein (CRP) was quantitatively measured by the automated Beckman coulter AU 480 chemistry analyzer with cut off value 5 mg/L.

Data analysis

Data were analyzed using the statistical package for the Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). Data was summarized using mean, standard deviation, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Kruskal-Wallis and Mann-Whitney tests [10]. Correlations between quantitative variables were done using the Spearman correlation coefficient [11]. P values less than 0.05 were considered statistically significant.

Results

The current study revealed that pediatric patients with CLD had significantly higher platelet count when compared to the normal control group (P values 0.003), we also showed a significant decrease in the MPV among the patients group when compared to the normal control group (P values 0.004), the plateletcrit was significantly higher when compared to the normal group (P value 0.010). ESR and CRP were significantly higher in the diseased group (P values 0.00) (Table 1). When the patients' group was further divided into interstitial lung disease and non-CF bronchiectasis then compared to the normal group, the MPV was significantly lower in both patients' subgroups (P values 0.007, 0.048 respectively); however, there was no statistically significant difference between the 2 patients' subgroups regarding the MPV nor the PCT. (Table 2).

Platelet count, MPV, and plateletcrit where studied among the CLD group and compared to different parameters including age, age of onset, oxygen saturation, hemoglobin concentration, TLC, ESR, CRP, presence of fever, and changing pattern of chronic cough, sputum, or dyspnea. On comparing the platelet parameters (platelet count, MPV, and PCT) against other parameters, significant negative correlation existed between the MPV and age (P value 0.015, r – 0.388), also significant negative correlation existed between the MPV and age of start of illness (P value 0.031, r – 0.346). Significant negative correlation existed between the platelet count and hemoglobin concentration (P value 0.032, r – 0.343). Significant positive correlation existed between the platelet count and PCT in relation to the CRP (P value 0.042, r 0.327 and P value 0.023, r 0.363 respectively) (Tables 3 and 4)

There was no statistically significant difference on correlating the platelet parameters (platelet count, MPV and PCT) among patients who presented with fever, changing pattern of chronic cough, sputum, or dyspnea and those who did not present with those symptoms,

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Table 1 Comparison between cases and controls regarding CBC findings and other labs

Parameters	Cases(n = 39)	Controls(n = 40)	P value
HB			
Range	8.5–15.2	8.6–14.8	
Mean ± SD	11.6 ± 1.3	11.8 ± 1.5	0.518
TLC			
Range	4.6–24	3.9–14.2	
Mean ± SD	11.2 ± 4.9	7.9 ± 2.8	*0.001*
PLTS			
Range	154–819	123–438	
Mean ± SD	394.8 ± 175.6	278.2 ± 85.8	*0.003*
MPV			
Range	7.60–10	8.10–10.0	
Mean ± SD	8.68 ± 0.57	9.07 ± 0.54	*0.004*
PCT			
Range	0.122–2.20	0.123–3.227	
Mean ± SD	0.396 ± 0.339	0.324 ± 0.477	*0.010*
HCT			
Range	25.5–45.6	29 – 43	
Mean ± SD	34.8 ± 4	36.6 ± 3.4	*0.031*
ESR			
Range	12–70	2 – 22	
Mean ± SD	38.3 ± 16.3	10.8 ± 4.4	*0.000*
CRP			
Elevated	29 (72.5%)	0 (0)	*0.000*
Normal values	11 (27.5%)	40 (100)	

P P value,*HB* hemoglobin, *TLC* total leucocyte count, *PLT* platelets, *MPV* mean platelets volume, *PCT* plateletcrit, *HCT* hematocrit, *ESR* erythrocyte sedimentation rate *CRP* C-reactive protein
Italic is significant

also no significant correlation existed between the previously mentioned platelet parameters and degree of oxygen saturation among the patients group.

Discussion

Recent studies on murine models have shown that maturation of platelets takes place, to some extent in the lungs, this raises the possibility that chronic lung diseases could affect platelet maturation or count [4]. Chronic lung

Table 2 *P* value for the comparison between interstitial lung disease group, non-CF bronchiectasis group, and normal control group

	MPV	Pltcrit
Interstitial lung disease vs non-CF bronchiectasis	0.566	0.720
Interstitial lung disease vs controls	0.007	0.021
Non-CF bronchiectasis vs controls	0.048	0.063

MPV mean platelets volume, *PCT* plateletcrit

disease carries many challenges for the patients and their caregivers, such as having an unpredictable clinical course, absence of a definitive treatment, restriction of activities whether due to the disease or the medications as well as later psychosocial effects [2]. Our study found a significant rise in platelet count in the patients group when compared against the normal control group, this comes in agreement with the study by Maclay et al. [12] which may be attributed to hypoxemia, underlying inflammation, and oxidative stress, although it disagrees with results obtained by Skoczyński et al. [13] both studies however were carried on adult COPD patients.

In agreement with our current study, the number of platelets in the COPD patients was inversely associated with the hemoglobin level [13]. The cause of anemia in COPD is related to certain pro-inflammatory markers, at least a component of the anemia is attributable to inflammation (anemia of chronic disease) [14].

CLD is associated with low-grade systemic inflammation, activation of circulating inflammatory cells, and increased levels of inflammatory cytokines. This is postulated to explain the significant rise in both CRP and ESR among the patients group when compared to the normal control. We also found a significant reduction in the MPV among patients, and when the patients' group was subdivided into Interstitial lung disease and non-CF bronchiectasis both subgroups still had a significantly lower MPV when compared to the normal control but not when compared to each other. Low levels of MPV are associated with high-grade inflammatory diseases and reverse in the course of anti-inflammatory therapy [15].

Mean platelet volume (MPV) is one of the parameters routinely generated by blood counters; it reflects the platelet production rate and stimulation. An inverse correlation between MPV and disease activity was demonstrated in inflammatory bowel diseases, rheumatoid arthritis, and ankylosing spondylitis [16]. Other studies have demonstrated elevated MPV values in COPD patients [17]. In 2016, Agapakis and *coauthors* concluded that MPV may be an inflammatory marker and could be a useful tool to detect patients with an increased risk of exacerbation as the mean platelet volume levels were significantly decreased in the exacerbation period in a study carried on adult COPD patients [18].

Proinflammatory cytokines such as CRP, tumor necrosis factor-α, and interleukin-6 are increased in COPD and contribute to the generation of oxidative stress with subsequent platelet activation and also MPV reduction [19]. Moreover, the previous hypothesis is supported by the significantly higher CRP and ESR among the patients' group compared to the normal control group. In our study, the MPV levels had a significant negative correlation with elevated CRP, as the higher CRP values are associated with lower

Table 3 Comparison between cases and controls; platelets count, MPV, and plateletcrit findings in relation to other parameters

N (39)		PLTS	MPV	PCT
Age in years	Correlation coefficient	0.070	0.388	0.033
	P value	0.670	0.015	0.840
Age of start of illness in years	Correlation coefficient	0.050	0.346	0.032
	P value	0.764	0.031	0.846
SO2	Correlation coefficient	0.063	0.139	0.075
	P value	0.704	0.397	0.650
HB (g/dL)	Correlation coefficient	0.343	0.065	0.233
	P value	0.032	0.696	0.154
TLC	Correlation coefficient	0.042	0.082	0.010
	P value	0.798	0.622	0.952
ESR	Correlation coefficient	0.158	0.168	0.062
	P value	0.336	0.307	0.705
CRP	Correlation coefficient	0.327	0.164	0.363
	P value	0.042	0.317	0.023

MPV, this comes in agreement with the findings of Agapakis et al. [18] However, this finding does not agree with the results obtained by Kalemci et al. [20] were they reported a significant increase in MPV with increasing severity of adult COPD yet, in agreement with the current study they reported an increase in platelets count and subsequently PCT with increased severity of adult COPD.

Plateletcrit represents the actual platelet mass as it constitutes the percentage of the volume that platelets occupy in blood, it normally ranges around 0.2% blood volume. For such an important role and variable functions to be concentrated in this small volume, this makes the research of variations in platelets number and volume of big value [8].

Conclusion

To our best knowledge, this is the first study to target the pediatric age group and study the relation of chronic respiratory diseases and simple indices of platelet parameters. Also to our best knowledge, this is the first study of the relation of platelet count, MPV, and PCT with oxygen saturation, fever, change in the pattern of cough, sputum, or dyspnea as indicators of exacerbation; however, the study did not find any significant relation between those mentioned parameters.

More valuable data could be obtained by performing the study on a larger scale, and following up the patients for longer periods to assess the fluctuation in the platelet count and indices in relation to different clinical aspects of the disease.

Table 4 Comparison between cases and controls; platelets count, MPV, and plateletcrit findings in relation to changing pattern of chronic cough and fever

	Changing pattern of chronic cough, sputum, or dyspnea										
	Yes					No					P value
	Mean	Standard deviation	Median	Minimum	Maximum	Mean	Standard deviation	Median	Minimum	Maximum	
PLTS	405.72	192.38	344.00	154.00	819.00	363.30	130.47	370.00	193.00	523.00	0.740
MPV	8.76	0.60	8.80	7.60	10.00	8.44	0.42	8.40	7.90	9.00	0.098
PCT	3579.29	1798.75	3080.00	1216.60	7698.60	5051.04	6066.01	3474.80	1659.80	22041.00	0.887
	Fever										
	Yes					No					P value
	Mean	Standard deviation	Median	Minimum	Maximum	Mean	Standard deviation	Median	Minimum	Maximum	
PLTS	420.94	217.93	328.00	168.00	819.00	374.68	141.84	400.00	154.00	600.00	0.685
MPV	8.81	0.68	9.10	7.60	10.00	8.58	0.47	8.65	7.70	9.30	0.172
PCT	3757.55	2086.31	2853.60	1545.60	7698.60	4110.52	4180.63	3474.80	1216.60	22041.00	0.878

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Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate
The study was approved by the Cairo University Ethical Committee ref. number I-031016. Participation was subject to the verbal informed consent of caregivers.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Pediatrics, Pediatric Pulmonology, Faculty of Medicine, Cairo University, Kasr Alainy, Street, Cairo Post Code: 11562, Egypt. [2]Clinical and Chemical Pathology, Faculty of Medicine, Cairo University, Kasr Alainy, Street, Cairo Post Code: 11562, Egypt.

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