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Platelet parameters as an inflammatory marker in children

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Abstract

Introduction: Platelets which are known to play a role in inflammation change their number and shape when they are activated and this change is reflected in values of *platelet indices*. Testing for platelet parameters by reliable automated blood cell counters is inexpensive, easily accessible and routinely performed that had been recognized as a hallmark in the diagnosis of platelet activation during infection and inflammatory disorders. The aim of this study was to investigate the relationship between white blood cell count(WBC), which is known inflammatory marker and platelet count (PLT) and its parameters including mean platelet volume(MPV), platelet distribution width(PDW), plateletcrit (PCT) and platelet- large cell ratio (P-LCR) in all clinical setting of leukocytosis in children.

Methods: White blood cell counts and all platelet parameters were evaluated in 156 children with elevated white blood cell counts (group 1) and 191 children with normal white blood count (group 2) and the results of two groups were compared and statistically analysed.

Results: There is a association between WBC and platelet count but there is very low correlation exist and correlation is significant. There was a significant difference between the two groups in WBC counts, PLT counts, PCT and PDW values ($p < 0.01$), being higher in Group 1. However, there was no statistically significant difference between two groups in MPV and P-LCR values ($p > 0.05$).

Conclusion: Platelet count and PDW values are significant in infectious conditions. And no significant role of PCT, MPV and P-LCR values found in such conditions.

Keywords: Platelets, leucocytosis, *platelet indices*, children

Introduction

Platelets (PLTs) are cytoplasmic fragments of bone marrow megakaryocytes with a diameter of 3-5 μm and a volume of 4.5- 11fL. Life span of platelets is 7-10 days. They are discoid cells with no nucleus and show variability in terms of volume, intensity, age and metabolic functions. They play an important role not only in hemostasis, but also in angiogenesis, inflammation, allergic reactions and repair and renewal of tissues and contain mediators which lead to strong inflammatory response^[1]. The platelet volume is specified during formation of platelets from megakaryocytes in the bone marrow. No maturation occurs in the platelets in the circulation. Therefore, factors stimulating the bone marrow including inflammation and infection may lead to changes in the platelet volume and number^[2, 3].

Platelet indices are biomarkers of platelet activation. They may be used in detection of inflammation, in detection of the prognosis and active periods of diseases and in specifying the efficiency of treatment^[4]. Mean platelet volume (MPV) is a simple measure of platelet size that can detect abnormal function and activity of platelets. Increased MPV means more platelet activity and excessive secretion of mediators^[5, 6]. The average MPV is 7.2-11.7 fl^[7]. MPV is inversely related to platelet counts^[8]. Platelet distribution width (PDW) directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology. It is an indicator of platelet anisocytosis^[8]. The reference intervals range from 8.3-56.6%^[5]. Under physiological conditions, there is a direct relationship between MPV and PDW; both usually change in the same direction.^[9] Plateletcrit (PCT) is the volume occupied by platelets in the blood as a percentage and the normal range is 0.22-0.24%^[6]. Under physiological conditions, the amount of platelets in the blood is maintained in an equilibrium state by regeneration and elimination. PCT parallels the platelet count^[8].

Higher MPV and PDW are associated with increased risk of death, whereas the decrease in plateletcrit is associated with increased mortality risk.^[10]

Platelet large cell ratio (P-LCR) is an indicator of circulating larger platelets, which is presented as percentage. The normal range is 15-35%. It has also been used to monitor platelet activity. P-LCR is inversely related to platelet count and directly related to PDW and MPV^[8].

Traditional inflammatory markers (leukocytes, C-reactive protein) can be influenced by parameters other than infection and are slowly released^[11]. Many studies demonstrated that platelet counts and platelet parameters are strongly associated with inflammatory and infectious conditions. Only limited studies done on pediatric population. Hence we take up this study in our hospital scenario, where majority of the children are from rural background, to know whether these *platelet indices* can probably be used as an adjunct to clinical evaluation of infectious circumstances wherein there is increased white blood cell count, in pediatric population.

Materials and Methods

This study is approved by the Ethical Committee of our institution. We performed a retrospective study on the children (2-18 years of age) coming to our laboratory, government hospital, Chamarajanagara, Karnataka, between November 2018 -January 2019. Complete blood count (CBC) values were recorded, which were obtained by SYSMEX automated hematology analyzer using VCS (volume- conductivity-light scatter) technology. The analyses were carried out following daily quality control. Total 347 children were evaluated. Out of these, 156 children with elevated WBC count ($>4000/\text{mm}^3$) were called as

Group 1 and 191 subjects with normal WBC counts and the platelet parameters were included in the study as a control group (Group 2). Children under 2 years of age are excluded as platelet count upto $6 \text{ lakh}/\text{mm}^3$ is normal for that age. Children with haematological malignancies, known platelet disorders, haemolytic anaemia and children with a history of recent blood transfusions or splenectomy were excluded from the study. Children with WBC count $> 50000/\text{mm}^3$ (leukemias) are excluded from the study. Statistical analyses were performed by statistical software program SPSS for Windows version 20.0 (SPSS). Results were given as mean \pm standard deviation (SD) and minimum and maximum (min-max) values. The correlation between WBC and platelet parameters were assessed using two independent tests. Values <0.05 was considered as significant.

Results

Totally (including Group 1 and Group 2 children), 347 complete blood counts were analysed. The mean age of subjects was 11.88 ± 6.647 years for group 1 and 11.37 ± 6.505 years for group 2. There were not statistically significant differences between two groups with respect to age. The statistical evaluation of WBC, PLT, MPV, PDW, PCT and P_LCR values of the two groups is given in Table 1. There was a significant difference between these two groups in WBC counts, PLT counts and PDW values ($p < 0.05$). However, there was no statistically significant difference between two groups in PCT, MPV and P-LCR values ($p > 0.05$). On the other hand, there were statistically significant, but weak correlation between the WBC and platelet counts in group 1 ($p < 0.05$) and no correlation between WBC and platelet count in group 2 ($p > 0.05$) (Figure 1, Figure 2).

Table 1: Statistical evaluation of both the groups

	Group	N	Mean	Std. Deviation	Sig. (2-tailed)	95% Confidence Interval of the Difference	
						Lower	Upper
WBC_count	1	156	14.6581	5.16234	.000	6.12538	7.75496
	2	191	7.7179	2.23967	.000	6.06481	7.81554
Platelet_count	1	156	3.3525	1.02211	.003	.10291	.48220
	2	191	3.0599	.77285	.003	.09745	.48765
PCT	1	156	.5560	3.01852	.173	-.13125	.72781
	2	191	.2577	.05316	.219	-.17918	.77574
PDW	1	156	10.3679	1.76365	.001	-1.99614	-4.7760
	2	191	11.6048	4.54944	.001	-1.94225	-.53149
MPV	1	156	9.7308	2.61469	.557	-.28146	.52174
	2	191	9.6106	.96080	.587	-.31498	.55526
P_LCR	1	156	21.1167	6.95695	.069	-2.80301	.10336
	2	191	22.4665	6.75486	.069	-2.80763	.10798

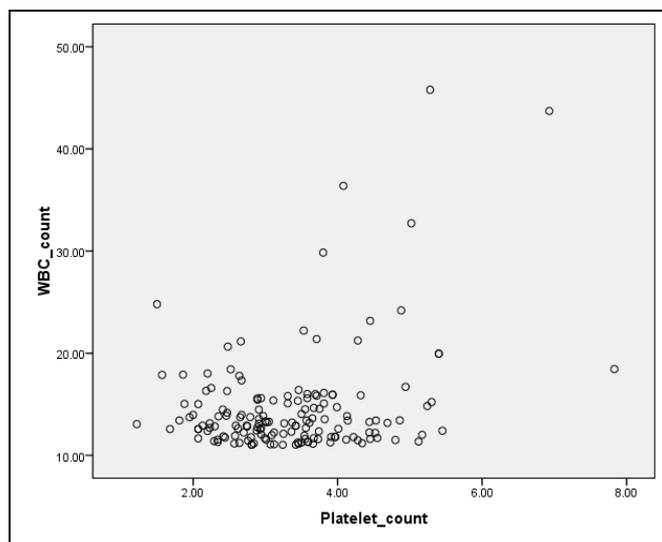


Fig 1: The scatter plot of PLT counts and WBC counts in group 1 (WBC counts higher than upper limit of reference range)

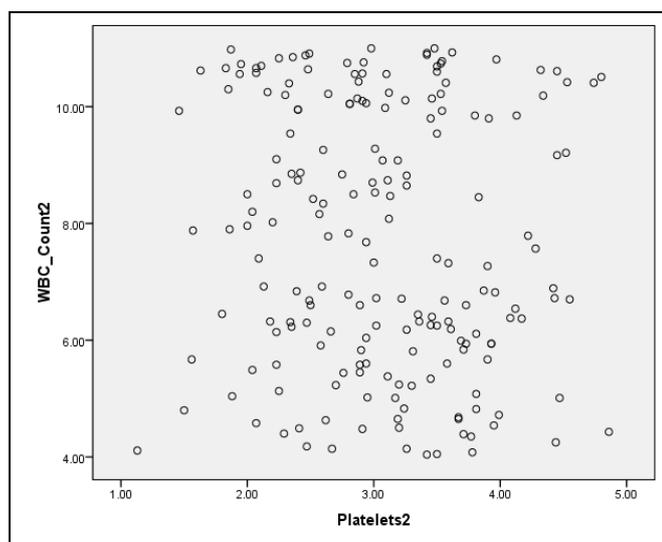


Fig 2: The scatter plot of PLT counts and WBC counts in group 2 (WBC counts within reference range)

Discussion

Platelet parameters have been one of the fastest and easiest tests to verify platelet function with the development of the new automated complete blood count (CBC) analyzers. This study was aimed to demonstrate whether *platelet indices* in children can probably be used as an adjunct to inflammatory marker like leucocytosis in infectious circumstances. Many studies demonstrated that PLT counts and PLT parameters are strongly associated with inflammatory and infectious conditions [7].

In our study, among all the *platelet indices*, platelet count and PDW values were significantly correlated ($p < 0.05$) with increased WBC count in group 1 individuals when compared to group 2 with normal WBC count. Other parameters like PCT, MPV and P-LCR values were not correlated significantly ($p > 0.05$). In a similar study by Ozturk N *et al.* [12] they found that the PLT counts and PCT values significantly increased in patients with leucocytosis when compared with the control group with normal WBC count. In addition, they have found that MPV and PDW values were not significantly different in both groups.

Mean platelet volume (MPV) has been evaluated in many conditions in the literature. However, studies have frequently shown controversial results. Tuncel *et al.* [13] compared the MPV values between patients who had asthma attack and healthy individuals and found no significant difference between the two groups. Sun *et al.* [14] found MPV to be lower in patients with asthma compared to the healthy group. Ergul AB *et al.* [15] found platelet count to be statistically significantly higher but MPV value was lower in the patients with acute bronchiolitis compared to healthy children.

Even the studies done on chronic inflammatory conditions like pulmonary tuberculosis also showed controversial results. While Gunloughlu G *et al.* [16] reported that the use of MPV as an inflammation marker and a negative acute-phase reactant in PTB does not seem to be reliable, study by Lee MY *et al.* [17] found MPV can be an inflammatory marker to determine the disease activity in TB patients. In yet another study by Sahin F *et al.* [18] indicates that reactive thrombocytosis and higher PCT and PDW develop frequently in PTB. Our study also showed no role of MPV in inflammatory conditions.

There are many other studies done on role of MPV like in inflammatory and infectious conditions of liver such as Hepatitis A, Hepatitis B and Hepatitis C by Akin F *et al.* [19], Ekiz F *et al.* [20] and Pumak T *et al.* [21] respectively. They all reported that MPV levels are increased in those conditions. Akin F *et al.* [19] also observed that MPV levels were significantly higher and WBC counts were significantly lower in children with Hepatitis A when compared to healthy children indicating that MPV can act as a better inflammatory marker than WBC count in such conditions.

Obesity accounts for a low-graded inflammatory process with an increase in platelet numbers and the incidence of thrombosis. This is a serious predisposing factor particularly in cardiovascular (CVS) disease. The underlying mechanism is due to the increase in the circulating interleukin-6 (IL-6) secreted from adipose tissue. IL-6 is an important indicator of proliferation of megakaryocytes and megakaryopoiesis. Studies have shown higher platelet numbers and MPV parameters in obese adults than normal population [22]. Although, not statistically significant, study by Ozsu E *et al.* [23] on obesity in children, showed that MPV increased with obesity and insulin resistance and concluded that MPV in combination with the platelet count can be potentially be used to identify the at-risk patients and monitored through adulthood.

Diabetes has been proved to be a prothrombotic condition. Type 1 and type 2 diabetes have platelet hyperactivity, dysfunction and changed morphology which lead to thrombus formation, microvascular embolization and play a key role in acute coronary events and other thromboembolic diseases. Studies have determined higher MPV in individuals with both T1DM and T2DM, and these changes have been linked to metabolic control [24]. Venkatesh *et al.* [25] and Ersoy *et al.* [26], all determined a significant increase in MPV values in subjects with childhood T1DM compared to a control group. But Korkamaz O *et al.* [24] determined no statistically significant difference in MPV values between children with T1DM and the control group. Indices of platelet morphology such as MPV, PDW, PCT and PLT were similar in children with T1DM and in healthy controls. Tekin *et al.* [27] and Zayed KMS *et al.* [28] had reported

thrombocytosis and elevated MPV & PDW in patients with UTI in comparison to healthy controls.

Bilici *et al.* [29] and Erdem *et al.* [30] have suggested that the MPV was significantly lower in the acute appendicitis group compared to the control group at childhood and adult patients, respectively. Unlike these studies, Yilmaz Y *et al.* [31] has reported that MPV has no diagnostic value in pediatric acute appendicitis cases.

The study done by Elmoneim *et al.* [11] on critically ill children showed increase in MPV in sepsis. This observation is similar to studies done by Dastugue *et al.* [32] who reported rise in MPV in patients with shock and also study by Lelei VDJ *et al.* [33], showed higher MPV values in patients with sepsis, indicating that monitoring of MPV can help in risk stratification of critically ill children. Sriram SM *et al.* [34] reported that PCT, MPV, PDW and platelet count showed statistically significant relation in children with sepsis when compared to controls.

These findings show that a linkage of PLT indices is present not only in simple but also in severe infections, and these indices can thus be used for daily clinical practice.

Conclusion

The present study is the first of its kind in Chamarajanagar district. This study showed that platelet count and platelet distribution width values were significantly high in simple infectious and inflammatory conditions in children but there is no correlation with plateletcrit, MPV and P-LCR values. The correlation is low as the sample size is less. There are controversial results with regard to platelet parameters in many studies done on both adult and pediatric population. And very few similar studies done on children. Hence we need more such studies to come up on role of *platelet indices* on various clinical conditions in children for the employment of these indices in routine clinical practice in adjunct to other inflammatory markers.

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