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Original Research Article

Use of Platelet Indices in the Differential Diagnosis of Hypo-Productive and Hyperproductive Thrombocytopenia in Children

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Abstract

Background: Platelets are essential for maintaining the integrity of the endothelium and for controlling hemorrhages when the injury to the blood vessels occurs. A low platelet count is a common entity encountered by the general pediatrician. Pediatricians then encountered with the problem of discriminating whether the low platelet count is caused by decreased production (hypoproductive thrombocytopenia) or increased destruction (hyper-productive thrombocytopenia). *Material and Methods:* The study population consisted of thrombocytopenic patients in the period between March 2017 and March 2018. A total of one hundred eighty patients (180) both female and male were enlisted, with age ranging from 1-14 years. Two groups were made to divide these patients, hyper-productive thrombocytopenia group (n=80) and hypo-productive thrombocytopenic group (n=100). The automated cell counter with quality control and established reference ranges, was used to measure platelet count, mean platelet volume, and platelet distribution width. The sensitivity and specificity of mean platelet volume and platelet distribution width were calculated under various cutoff ranges for both thrombocytopenic conditions. *Results:* The sensitivity and specificity of platelet indices were calculated under various cut off ranges. The MPV with a cutoff of >10.6fL detects 90% of the cases of ITP while excluding 86% of the hypo-productivesituations. When the chosen cutoff for MPV is greater than 12.6fL, detection rate was 50% of the ITP cases while excluding 94% of the hypo-productive cases. *Conclusion:* Results of the present study suggest that platelet indices are significantly higher in ITP patients compared to patients withhypo-productive thrombocytopenia. Comparing the sensitivity and specificity between MVP and PDW for both groups, PDW is moresensitive to detect the ITP patient than MVP but less specific in a cutoff above the normal range.

Keywords: Platelet Indices; ITP; MPV; PDW.

Introduction

Platelets are essential for maintaining the integrity of the endothelium and for controlling hemorrhages when the injury to the blood vessels occurs. They form a plug by aggregating and adhering to each other primary hemostasis. When the injuries to the vessels are very extensive, further participation from coagulation factors to produce a fibrin plug that is firmer and more stablesecondary hemostasis. Platelet counts below 150 X 10^9L define thrombocytopenia, but they do not reveal the underlying pathology [1].

A low platelet count is a common entity encountered by the general pediatrician. Thrombocytopenia should be suspected in children with bleeding in mucous membranes or petechiae in the skin, but frequently its discovery is incidental in a complete blood count (CBC) ordered for other reasons [2-5]. Pediatricians then encountered with the problem of discriminating whether the low platelet count is caused by decreased production (hypoproductive thrombocytopenia) or increased destruction (hyper-productive thrombocytopenia) [6].

For a long time Bone marrow aspiration remained the gold standard method for evaluating the cause of thrombocytopenia. But this procedure is invasive, time-consuming as well as carry an overt risk of bleeding diathesis in critical thrombocytopenia cases.and it is not recommended as a first line diagnostic procedure and instead set aside for older patients, or patients with atypical features [1-3]. Also it a difficult test to obtain for patients who do not live near an academic center as bone marrow sampling also requires a trained hematologist to perform and interpret the results [4].

Nonpersistent and cost-effective diagnostic advancement for the assessment of thrombocytopenia are needed to better assess pediatric patients in the community. Thrombocytopenia is a decline in a platelet count of <150 x 109/L, which can occur due to a reduction in platelet syntheses such as in aplastic anemia and acute leukemia [2]. As a result of the increased destruction of normally produced platelets, other disorderssuch as immune thrombocytopenia purpura occurs [3]. The discrimination between these disorders is very important as the treatment plans differ. A group of parameters, like Platelet volume indices, are reasonably priced to measure and are derived from routine blood counts. Highly developed technology in automated blood cell analyzers has made it possible to measure different platelet indices that are, mean platelet volume (MPV) and platelet distribution width (PDW). Mean platelet volume defined as a measurement of the average size of platelets in the blood, and platelet distribution width reflects the variability in the platelet size and raises in the presence of platelet anisocytosis [4].

Less is known about the usefulness of platelet indices in differentiating thrombocytopenia in children, and whether these indices are satisfactory tests for thrombocytopenia. Therefore, this study attempted to find the usefulness of mean platelet volume and platelet distribution width in discriminating among hyper-destructive thrombocytopenia and hypo-productive thrombocytopenia, evaluate the sensitivity and specificity of mean platelet volume and platelet distribution width and find cut off values in an attempt to consider the use of these indices in the initial evaluation of thrombocytopenia in pediatric patients.

Material and Methods

The study population consisted of thrombocytopenic patients in the period between March 2016 and March 2018. This observational study was conducted in a tertiary care center during the period of March 2017 to March 2018. According to Performaa detailed history and physical examination was performed. A mechanical Complete blood count including platelet count, Mean platelet volume, and platelet distribution width was documented, in addition to a bone marrow aspirate was done on each patient included in the study. Using peripheral blood smear and bone marrow aspiration/ biopsy the differentiation between hyper-productive thrombocytopenia and hypo-thrombocytopenia was confirmed. A total of one hundred eighty patients (180) bothfemale and male were enlisted, with age ranging from 1-14 years. Two groups were made to divide these patients, hyper-productive thrombocytopenia group (n=80) and hypo-productive thrombocytopenic group (n=100). Thrombocytopenia of other causes or unknown origin was excluded from this study. The automated cell counter with quality control and established reference ranges, was used to measure platelet count, mean platelet volume, and platelet distribution width. The sensitivity and specificity of mean platelet volume and platelet distribution width were calculated under various cutoff ranges for both thrombocytopenic conditions. The receiver operating characteristic (ROC) curves were obtained by plotting sensitivity against 1- specificity for the complete range of decision thresholds.

The presentation of each test was evaluated by the area below the ROC curves. This area gives the probability that a patient with the idiopathic thrombocytopenic purpura disease has a higher value of mean platelet volume and platelet distribution width in comparison to patients with other causes of thrombocytopenia. A test that entirely discriminate between the two long-suffering groups would begin in the lower left corner, go straight up to the upper left corner, and then to the upper right corner of the plot. The Data collected were analyzed using the software Statistical Package for Social Sciences (SPSS) program version 20 (IBN. Chicago, USA). Measurements of laboratory data platelet parameters of patients with thrombocytopenia in the two different hyperproductive and hyper-destructive group were statistically tested by unpaired t-test. A p-value of less than 0.05 was considered statistically significant

Results

Table 1 shows that there was significant difference MPV low, high and normal between both groups. ITP patients were highly sensitive for MPV more than 10.6 fL.

Table 2 shows that there was significant difference PDW low, high and normal between both groups. ITP patients were highly sensitive for PDW more than 16 fL.

The platelet count and platelet indices were compared between hyper-productive and hypo-productive thrombocytopenia as shown in Figure 1. It is evident from figure 1 that platelet count was significantly high low in hyper-productivethrombocytopeniacompare to hypo-productivethrombocytopenia (41.2±28.6 X 10^3 ml Vs 26.6±28.4 X 10^3 ml, p<0.001) (Figure 1).

Table 1: MPV ranges and patients distribution.

MPV Category	Thrombocytopenia aetiology		p value
	Group I (ITP)	Group II (Acute leukemia or aplastic anaemia)	
Low <6.9 fL	2	30	<0.001
High > 10.6 fL	72	14	<0.001
Normal (6.9 – 10.6 fL)	6	56	<0.001
Total	80	100	<0.001

Table 2: PDW ranges and patients distribution

PDW Category	Thrombocytopenia aetiology		p value
	ITP	Acute leukemia or aplastic anaemia	
Low <11 fL	00	10	<0.001
High > 16 fL	76	28	<0.001
Normal (11 – 16 fL)	4	52	<0.001
Total	80	100	<0.001

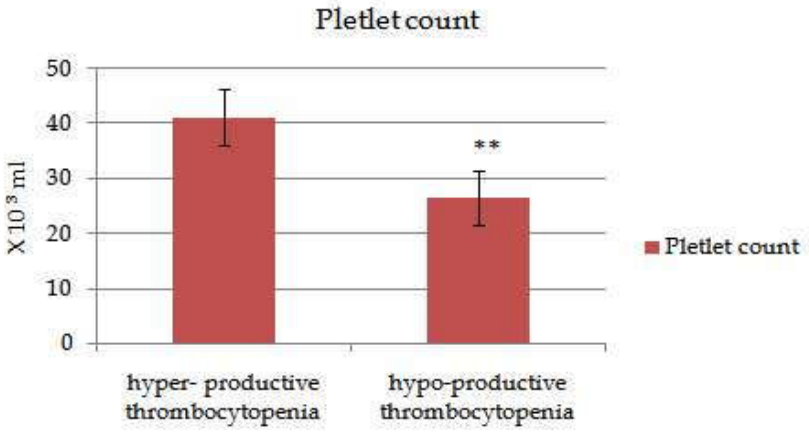

Fig. 1: Platelet count in both groups.

Figure 2 shows that MPV fL was significantly low in hyper-productive thrombocytopenia in comparison of hypo-productive thrombocytopenia. (7.9±2.2 fL V s12.8±2.6 fL, p<0.001)

It is evident from figure 3 that PDW fL was significantly low in hyper-productive thrombocytopenia in comparison of hypo-productive thrombocytopenia. (13.43±3.2 fL Vs 20.12±3.8 fL, p<0.001)

The sensitivity and specificity of platelet indices were calculated under various cut off ranges. The MPVwith a cutoff of >10.6 fL detects 90% of the cases of ITP while excluding 86% of the hypo-productive situations. When the chosen cutoff for MPV is greater than 12.6fL, detection rate was 50% of the ITPcases while excluding 94% of the hypo-productive cases. (Table 3).

The PDW with a cutoff of 16fL detects 95% of the cases of ITP while excluding 80% of hypo-productive thrombocytopenic patients. When the chosen cutoff for PDW is greater than 20fL, detection rate is only 40% of the cases of ITP while excluding 97% of the hypo-productive conditions. The selected ranges for MPV and PDW were 10.6 and 16 respectively. Under these cut-off ranges, plateletindices especially PDW showed favourable sensitivity and specificity (Table 4).

Table 3: Sensitivity and specificity for diagnosis of ITP and AA or AL under various cutoff ranges of MPV

Aetiology of thrombocytopenia	MPV value	Sn%	Sp%	PPV	NPV
Hyper-productive Thrombocytopenia (ITP)	>12.8	50	94	88	72.3
	>11.8	60	94	89.6	77
	>10.8	90	86	83.7	91.4
Hypo-productive Thrombocytopenia (AA or AML)	≤ 10.8	86	90	91.4	83.7
	<8.8	64	92.5	91.4	62.7
	<6.8	28	97.5	93.3	48

Table 4: Sensitivity and specificity for diagnosis of ITP and AA or AL under various cutoff ranges of PDW.

Aetiology of thrombocytopenia	PDW value	Sn%	Sp%	PPV	NPV
Hyper-productive Thrombocytopenia (ITP)	>22	40	98	94	34.6
	>20	75	92	88.6	82
	>18	98	80	80.4	95.6
Hypo-productive Thrombocytopenia (AA or AML)	≤ 18	80	95	95.6	78.8
	<16	66	97.5	96.8	68.8
	<12	38	100	100	50.4

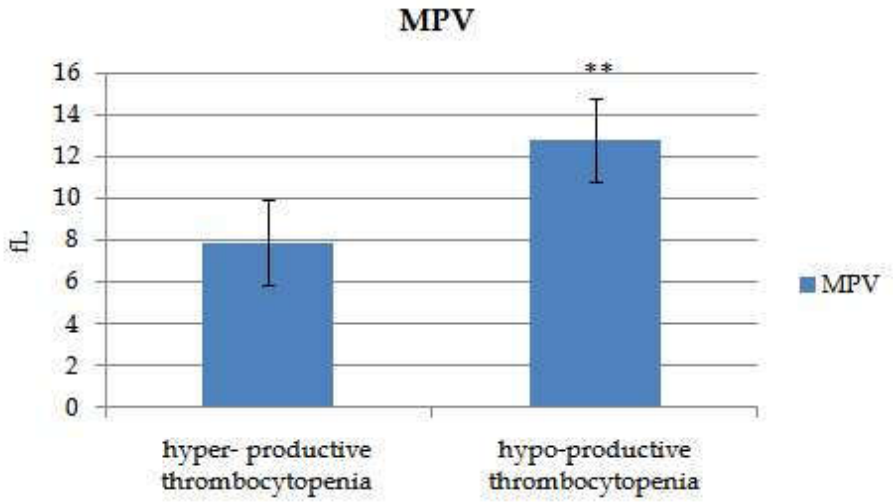

Fig. 2: comparison of MPV in both groups.

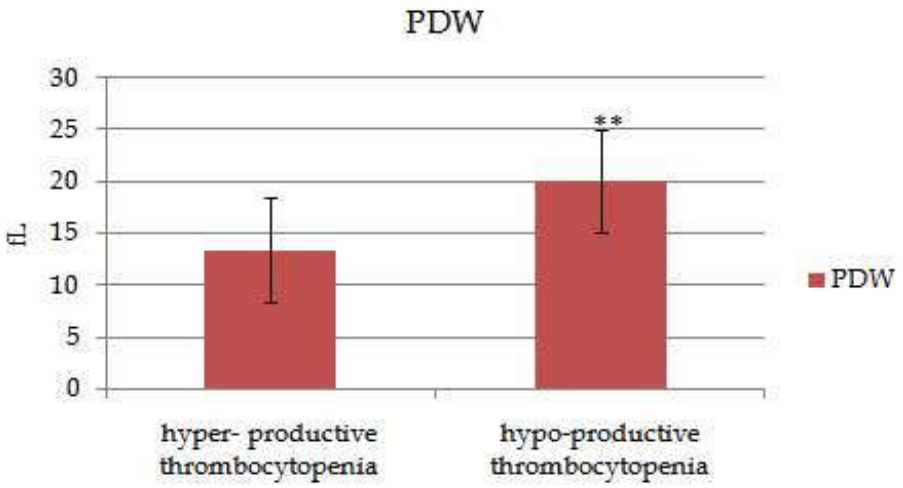

Fig. 3: Comparison of PDW in both groups.

Discussion

Clinical findings may be helpful in evaluating thrombocytopenia is not solely to be sensitive enough to the vast majority of hyper-productive state as in ITP; moreover, it should be precise enough to fundamentally rule out hypo-productive cases, such as acute leukemia or aplastic anemia. Further, it is one of the important aspects to explore whether the thrombocytopenia is caused by increased platelet destruction or decreased production.

Diagnosis of aplastic anemia

Bone marrow test is used for the diagnosis of aplastic anemia; however, no consensus agreement has been made for its inevitability for ITP diagnosis as it is an invasive and cost affecting test [5]. Therefore, a non-invasive, easier approach and cost effective test is needed for the assessment of platelet disorders in thrombocytopenia patients especially children [6].

Findings of the present study showed that platelet indices were significantly higher in ITP patients in comparison of hypo-productive thrombocytopenia patients. Moreover, results revealed that calculated MPV with a cutoff of >10fL detects 90% of the patients of ITP and excluding 86% of the hypo-productive situations. While PDW with acutoff of >16fL was able to detect 95% of the ITP conditions and excluding 80% of the hypo-productive patients. That is why these indices may be effective in differentiating between these two types of thrombocytopenia. These findings are consistent with the previous findings of Borkataky et al. [7] and Katio et al. [8] as they reported similar effective use of platelet indices in differentiating diagnosis of hyper-productive and hyp-productive thrombocytopenia.

Similarly, Alsweedan et al. [9], Woong et al[10] and Ntaios et al.[11] observed in their studies that platelet indices were effective in distinguishing thehypo-productive thrombocytopenia from hyper-productive stage in adult patients.

Results of the current study suggest that the specificity and sensitivity of platelet indices significantly enabled the diagnosis hyper-producing thrombocytopenia stage of ITP.

Further, it has been recorded in the present study that ROC curves of MPV and PDW were shifted to the upper left which indicate the prompt diagnosis of ITP as the area under the curve was large which specify ITP disorder. Therefore, it correctly classified both types of thrombocytopenia. These findings are in agreement with the findings of the earlier study of Kaito et al. [7] as they reported deviation from the mean size and mean volume of platelet have great sensitivity and specificity which effectively establish the diagnosis of immune thrombocytopenia and PDW. Moreover, these are trustworthy marker for the differential diagnosis of hyper-productive thrombocytopenia from hypo-productive thrombocytopenia in adult patients.

Findings of the present study have shown sensitivity and specificity of PDW were significantly sensitive for detecting ITP in comparison of sensitivity and specificity of MPV in thrombocytopenia patients. However, this specificity was lesser in a cut off more than normal range (>16). Moreover, determination of differential

diagnosis can be stratify by clinician as ITP is unlikely to be found in thrombocytopenia patients having sensitivity and specificity of PDW in normal range (11-16): whereas, highly decreased incidence may be found with sensitivity and specificity of PDW below normal range (<11).

This can be valuable tool for the general pediatrician in stratifying the severity of disease in thrombocytopenic patients and more efficiently referring patients for further work-up.

It is important to be aware that some limitations are encountered in our study. 1) In severe thrombocytopenia and in the presence of red cell fragmentation, a platelet histogram cannot be adequately drawn, and the indices cannot be recorded 2) Although automated cell counters are fairly accurate in determining platelet count, the possibility of instrumental artifacts at low platelet count cannot be ruled out.

Conclusion

Results of the present study suggest that platelet indices are significantly higher in ITP patients compared to patients with hypo-productive thrombocytopenia. Comparing the sensitivity and specificity between MVP and PDW for both groups, PDW is more sensitive to detect the ITP patient than MVP but less specific in a cutoff above the normal range.

Platelet volume indices can differentiate with some certainty ITP from AL and AA which may help pediatricians to avoid the invasive bone marrow aspiration, which needs the assistance of a haematologist for diagnosis and result interpretation.

References

1. Strauß G, Vollert C, von Stackelberg A, Weimann A, Gaedicke G, Schulze H. Immature platelet count: A simple parameter for distinguishing thrombocytopenia in pediatric acute lymphocytic leukemia from immune thrombocytopenia. Pediatr Blood Cancer. 2011 Oct 1;57(4):641–7.
2. Lanzkowsky P. Chapter 12 - Disorders of Platelets. In: Lanzkowsky P, editor. Manual of Pediatric Hematology and Oncology. 5th edition San Diego: Academic Press; 2011.pp.321–77. http://doi.org/dj4bfc.
3. Monteagudo E, Fernández-Delgado R, Sastre A, Toll T, Llort A, Molina J, et al. Protocol for the study and treatment of immune thrombocytopenic purpura (ITP). ITP-2010. AnPediatr (Barc). 2011;74:414.e1-8.
4. Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115:168-86. http://doi.org/bwdf3s.
5. Consolini DM. Thrombocytopenia in infants and children. Pediatr Rev. 2011;32:135-51.
6. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113:2386-93.
7. Borkataky S., Jain, R., Gupta, R., Singh, S., Krishan, G., Gupta K. and Kudesia M. Role of platelet indices in the differential diagnosis of thrombocytopenia: a simple and inexpensive method. Hematology. 2009;4(3):182-186.
8. Katio, K., Otsubo, H., Usui, N., Yoshida, M., Tanno, J., Kurihara, E., Matsumoto, K., Hirata, R. and Kurihara, E. Platelet size deviation width, platelet large cell ratio, and mean platelet volume have sufficient sensitivity and specificity in the diagnosis of immune thrombocytopenia. Br J Haematol. 2005;28(5):698-702.
9. Alsweedan, S., Al-Shurman, A. and Mahmoud, A. Diagnostic value of platelet indices in children with leukemia. J of Pediatric hematology/oncology. 2010;30(12):953-55.
10. Woong, S. and Think-You, K. Mean platelet volume and platelet distribution width are useful in the differential diagnosis of aplastic anemia and idiopathic thrombocytopenic purpura. Clinical Chemistry and Laboratory Medicine. 2010;48(11):1675-76.
11. Ntaios, G., Papadopoulos, A., Chatinikolaou, A., Saouli, Z., Karalazou, P., Kaiafa, G., Girtovitis, F., Kontonias, Z., Savopoulous, C., Hatzitolios, A. and Alexiou-Daniel, S. Increased values of mean platelet volume and platelet size deviation width may provide a safe positive diagnosis of idiopathic thrombocytopenic purpura. ActaHaematol. 2008; 119:173-77.