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Role of mean platelet volume (MPV) in diagnosing categories of thrombocytopenia

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Abstract

Introduction: Thrombocytopenia (TCP) is a common clinical problem and its etiology varies widely. Automated hematology analyzers have contributed to more accurate, precise, and faster results. Platelet indices including mean platelet volume (MPV) offer valuable information about the morphology and maturity of platelets. But MPV has not been used commonly for diagnosing the cause of TCP. Thus we undertook this study to ascertain the correlation between MPV and the cause of TCP.

Methods: 510 cases of thrombocytopenia and 500 cases of Control group with normal platelet count were included in the study. TCP was defined as platelet counts below 1.5 lacs/cumm. Hematological analysis was done on Mindray BC-3000 plus automated hematology analyzer with blood collected in K-EDTA blub. All cases were reevaluated by peripheral examination. Only those cases were included in the study which showed platelet count and platelet volume parameters with graph both in cases and control group.

Result: Group A with hyperdestruction showed increased value of MPV (10.46 fl) when compared with hypoproduction Group B (8.7 fl) and abnormal pooling Group C (8.15 fl) and with the control group (9.5 fl). All the three groups showed statistically significant difference in comparison to control. There was no significant difference between the mean platelet count between the control group and the three groups.

Conclusion: MPV is a sensitive and reliable indicator for diagnosis of thrombocytopenia due to various causes. More attention should be paid to MPV along with other platelet indices to differentiate between hyperdestructive TCP from hypoproductive and abnormal pooling TCP.

Keywords: Thrombocytopenia (TCP), Mean Platelet Volume (MPV), Platelet indices & platelet volume parameters.

Introduction

Thrombocytopenia (TCP) is a fairly common condition with diverse disorders with varying etiology. It is the most common cause of abnormal bleeding. Thrombocytopenia may be defined as a subnormal number of platelets in circulating blood.[1] It is important to know whether TCP is due to accelerated platelet destruction, decreased production or spleni pooling. The diagnosis of TCP requires bone marrow examination, platelet-associated immunoglobulin G (Paige) and reticulated platelets. These methods are either invasive &/or costly and not available routinely. Automated hematology analyzers are now routinely available in laboratories and institutes. These analyzers now provide platelet indices like mean platelet volume (MPV), platelet size deviation width (PDW), and platelet large cell ratio (P-LCR) routinely without any extra cost. But these parameters were overlooked and their clinical usefulness was not recognized in determining cause of thrombocytopenia. MPV and other indices are increased in TCP.[1,2] Many studies on these parameters have shown that they can be used to determine the cause of TCP and they have sufficient sensitivity and specificity in the diagnosis of TCP.[3,4,5,6] MPV is the average platelet volume & it provides evidence to differentiate category of TCP & may be interpreted in the same way as MCV of red blood corpuscles (RBC). We have thus undertaken this study to find the utility of MPV in diagnosing various categories of TCP.

Material and Methods

The present study was carried out from January to December 2015 in the department of pathology at Chirayu medical college and hospital, Bhopal, India. During this period 510 cases of thrombocytopenia were studied. Control group included 500 cases with normal platelet count, RBC count and WBC count. Detailed history was obtained regarding age, sex, clinical diagnosis and other hematological parameters form the case records of the patients. Hematological analysis was done on Mindray BC-3000 plus automated hematology analyzer with blood collected in K-EDTA blub within 30 minutes to 5 hours of collection. Only those cases were included in the study which showed platelet count and platelet volume parameters with graph both in cases and control group. Each case of TCP was studied by peripheral examination and cases with different results by these methods were excluded from the study. Proportion, mean and standard deviation was calculated. TCP was defined as platelet counts below 1.5 lakhs/ul. Clearance was obtained from institutional ethical committee. Data was analyzed and ANOVA test was applied as a test of significance. P value <0.001 was considered as highly significant.

Results

510 cases of TCP were studied for the present study. 318 (62.35%) were males and 192(37.65%) were females with a male to female ratio of 1.6. A slight

male preponderance was seen for the whole study and also in all age groups. Age ranged from 4 months to 87 years. Most number of cases for TCP was seen between 11-20 years accounting for 92(18.03%) cases. 75 cases (14.70%) were seen in the age group of 31-40 years. 13 % cases belonged to age group of 21-30, 41-50, 51-60 & 61-70 years. (Table 1).

Table 1: Age & sex distribution

Age	No of cases	Male	Female	%
< 1 year	1	1	0	0.19
1-10 year	48	35	13	9.41
11-20 year	92	63	29	18.03
21-30 year	70	48	22	13.72
31-40 year	75	39	36	14.70
41-50 year	70	51	19	13.72
51-60 year	68	37	31	13.33
61-70 year	69	31	38	13.52
71-80 year	11	9	2	2.15
81-90 year	6	4	2	1.17
91-100 year	0	0	0	0

All cases were grouped into three groups based on the predominant mechanism of thrombocytopenia. Group A – Hyperdestructive TCP, Group B – Hypoproductive TCP and Group C – Abnormal pooling. Group A constituted majority of 352 (69%) cases. This group was further subdivided into varies categories based on the clinical diagnosis(Table 2). In Group A, bacterial infections constituted the most number of cases 100 (28.40%). Cardiac cases, Dengue, malaria and renal diseases constituted 25%, 13.06%, 6.8% & 5.3% respectively. While sepsis, viral infections & pregnancy constituted 1.9% each (Table 2). All the categories in Group A had variable mean MPV with highest mean MPV in ITP (11.9±0.4) followed by dengue (10.90±0.4) and renal diseases (10.75±0.55). MPV was lowest in pregnancy (9.7±0).

Table 2: Group A= Hyper destruction of platelets (69%)

Categories	Cases	%	Mean plt count lacs/cumm	Mean MPV (fl,mean± SD)
Bacterial infections	100	28.40	0.705	10.35±2.15
Cardiac diseases	88	25	0.895	10.45±0.1
Dengue	46	13.06	0.25	10.90±0.4
Malaria	24	6.81	0.77	10.15±0.65
Renal diseases	19	5.39	1.15	10.75±0.55
Burns	14	3.97	0.615	10.16±0.2
Liver	8	2.27	0.555	10.35±0.55
diseases				
Sepsis	7	1.98	0.68	10.35±0.85
Viral infections	7	1.98	0.87	10.05±0.15
Pregnancy	5	1.42	0.725	9.7±0
Snake bite	3	0.85	0.66	10.55±0.44
ITP	2	0.56	0.26	11.9±0.4
Blood transfusion reactions	2	0.56	0.81	10.25±0.05
Miscellaneous	27	7.67	0.805	10.55±0.75
Total	352			
		Mean± SD	0.755±0.05	10.46±0.15

Group B constituted 30% of cases which included anemia 23(15.03%), aplastic anemia 3(1.96%), leukemia 42(27.45%) and solid malignancy on chemotherapy 85 cases (55.55%). In this group also MPV was variable with highest in Leukemia (12±0.8) followed by Aplastic anemia (10.45±0.95) and solid malignancies on chemotherapy (9.5±1.1)(Table 3).

Group C included 5 cases (1.42%) with splenomegaly suggesting abnormal pooling. The mean MPV was 8.15±0.35 (Table 4).

Control group included 500 cases of normal platelet counts with 280 (56%) males & 220 (44%) females. The mean platelet count in control group was 1.72±0.12 lacs/cumm, in Group A it was 0.755±0.05 lacs/cumm, in Group B- 0.468±0.09 lacs/cumm while in Group C it was 0.55±0.1 lacs/cumm.(Table 3 & 4).

Table 3: Group B= Hypoproduction of platelets (30%)

Categories	Cases	%	Mean plt count lacs/cumm	Mean MPV (fl, mean±SD)
Anemia	23	15.03	0.495	7.9±0.2
Aplastic anemia	3	1.96	0.135	10.45±0.95
leukemia	42	27.45	0.57	12±0.8
Solid malignancy on chemotherapy	85	55.55	0.675	9.5±1.1
Total	153			
		Mean±SD	0.468±0.09	8.7±0.8

Table 4: Group C = Abnormal pooling (1%)

Category	Cases	%	Mean plt count lacs/cumm	Mean MPV (fl,mean±SD)
Splenic pooling	5	1.42	0.55	8.15±0.35

Table 2, 3 & 4 shows the mean MPV for the 3 groups A, B & C. In the control group the MPV was 9.5±0.55 while in hyperdestruction group (group A) it

was 10.46±0.15, in hypoproduction group (group B) 8.7±0.8 and in Abnormal pooling group (Group C) it was 8.15±0.35. Thus it can be seen that Group A shows higher value of MPV than group B and group C.

To know the statistical significance, Z Test was applied on all groups and also the control group. In all groups the values were highly significant (P<0.0001) when compared with control group and also among the three groups. (Table 5). There was no significant variation in the mean platelet counts among the three groups.

Table 5: Statistical significance

Group A Vs Control	Z = 8.57 (p<0.0001)
Group B Vs Control	Z = 17.005(p<0.0001)
Group C Vs Control	Z = 46.63 (p<0.0001)
Group B Vs Group A	Z = 15.98(p< 0.0001)
Group C Vs Group A	Z = 22.80 (p< 0.0001)
Group B Vs group C	Z = 12.86 (P< 0.0001)
(P<0.0001 is extremely significant)	

Discussion

Thrombocytopenia (TCP) can be due to hyperdestruction of platelets, hypoproduction of platelets or abnormal spleenic pooling. Platelet destruction may result from both intracorpuscular defects and extracorpuscular abnormalities. One of the major causes of increased destruction of platelets is by immunological mechanism in which antibodies against platelets cause their premature destruction. Hypoproduction of platelets may be due to bone marrow suppression like aplastic anemia, leukemias, infiltration by malignancy, chemotherapy and irradiation. Abnormal pooling or abnormal in vivo distribution of an essentially normal total platelet mass may also produce thrombocytopenia. This type of TCP is seen in various disorders associated with splenomegaly.[1,2].

Bone marrow (BM) examination is the gold standard test in discriminating between the types of thrombocytopenia. However, this procedure is invasive and not necessary as first-line diagnostic procedure. Other tests like reticulated platelets and PAIgG can be used but PAIgG and bone marrow aspiration was not recommended as a diagnostic measure in recent guidelines (British Committee for

Standards in Haematology General Haematology Task Force,2003).[3,5,7] Thus a simple, inexpensive and non-invasive method needs to be evaluated for the differential diagnosis of thrombocytopenia.

MPV has evoked much interest of all the platelet indices and many studies have suggested that MPV and other platelet indices are potentially useful markers for the early diagnosis and categorization of TCP and can play a role in the rapid evaluation of bone marrow activity of patients with platelet-associated disorders. These studies have yielded variable results.[6,7,8,9,10] Mean platelet volume (MPV) is a platelet index that has been available since the 1970s. Since then, other indices of plateletshave been introduced, including platelet volume distribution width (PDW), plateletcrit (PCT), and platelet large cell ratio (PLCR).[11] While MCV for red cells have been widely accepted and used for anemia classification,platelet indices have not been routinely used by clinicians and their clinical usefulness has been elusive. With the widespread availability of automated hematology analyzers platelet parameters are now routinely available and thus can be applied in the clinical setting.

In our study bacterial infections constituted the majority of cases for TCP (28.40%) followed by cardiac diseases(25%) and solid malignancies on chemotherapy (55.55%). While Alam M et al found malaria (43.2%) and other infections as major causes for TCP,[12] Ross C et al found anemia(38.2%) as the major cause of TCP followed by ITP(10.9%).[13] Solid malignancy on chemotherapy and leukemia constituted a higher percentage of cases in our study when compared with other studies.[4,14] This difference is due to the fact that this hospital caters more to oncology patients.

The present study revealed that mean MPV was significantly higher in hyper destructive group (Group A) as compared to hypoproductive group (Group B), abnormal pooling (Group C) and control group. Numbenjapon et al[5] also evaluate MPV in discriminating hyperdestructive from hypoproductive thrombocytopenia and found that a cut-off MPV value of 7.9fl would have a sensitivity of 82.3% and a specificity of 92.5% and concluded that MPV is a reliable diagnostic test to differentiate between these two conditions. Similarly Kaito et al,[3] Ntaios et al[6] Khaleel et al[8] and shah et al[14] also reported that MPV was higher in ITP patients when compared with hypoproductive thrombocytopenic patients, which reflected an increase in the production rate and they established cut off values ranging from 9 fl to greater than 11 fl. According to Elsewefy et al[2] and Sridhar et al[4] these differences in the cut off value could be due to difference in selection of patients and the difference in the type of hematology analyzer used as older automated analyzers, which could have been used in these studies, cannot discriminate platelets from other similarly sized particles such as fragmented red or white blood cells, cell debris, and immune complexes.The high MPV in platelet destruction could be explained by the fact that newly produced platelets are larger than circulating platelets, which tend to decrease in size with age in the circulation similar to reticulocytes with increased mean volume. As a result, in patients with thrombocytopenia secondary to peripheral destruction the MPV is increased, reflecting active bone marrow compensation with release of young platelets.[5,8]

Although the above studies found MPV reliable in differentiating the categories of TCP, Elsewefy et al[2] and Borkataky et al[15] found no significant difference in the MPV between the destructive thrombocytopenia group and the control group or the hypoproductive thrombocytopenia group. Borkataky et al also demonstrated that platelet distribution width (PDW) has discriminating property to determine the etiology of thrombocytopenia. Khanna R et al[9] and Xu RL et al[10] also mentions that MPV have low sensitivity and specificity to predict the presence of bone marrow diseases in thrombocytopenic patients. The present study has its limitations as we did not analyze other platelet indices like PDW & P-LCR other than MPV. This was done intently as we wanted to test only MPV as a discriminating factor since this factor has been put to test by researchers in the recent years. Further studies by combining the platelet indices may provide promising results.

Some studies suggest that it is not always possible to record platelet indices in severe TCP and in the presence of red cell fragmentation, a platelet histogram cannot be adequately drawn, and the indices cannot be recorded.[3,4,8] Babu E and Basu D also mentioned the difficulties in getting these parameters and discarded those cases lacking these parameters.[16] We avoided this problem by discarding cases without indices and histogram and selected only those cases which had platelet indices and provided a histogram. In control group all cases had showed values and histogram.

The mean platelet volume (MPV) reflects the average platelet size and platelet function better than the platelet count itself. Young platelets are larger than old platelets. Increased number of young platelets indicates increased platelet production. In fact, the MPV is inversely proportional to the degree of platelet maturity.[11] Larger platelets are functionally, metabolically, and enzymatically more active than smaller ones.[17] Nelson et al in their study mentioned that, patients with thrombocytopenia due to loss or destruction of platelets have larger platelets, whether the loss is due to infection, hemorrhage, or immune destruction and when thrombocytopenia was due to lack of production, the platelet volume was similar to that seen in patients with normal blood cell counts.[18] In our study the mean MPV in hyperdestructive group was significantly higher than in hypoproductive group and abnormal pooling group. The difference between these values was highly significant statistically(Table 5). Vinholt PJ et al in their review article observed that MPV can aid in diagnosing the cause of thrombocytopenia, but a clear cut-off cannot yet be provided, while Islam S et al concludes that MPV along with other indices could help to distinguish hyper-destructive thrombocytopenia and hypo-productive thrombocytopenia very easily and it is also cost effective.[20] Though the present study included all age groups, study by Aponte-Barrios NH et al in pediatric age group found that MPV can distinguish between thrombocytopenia due to an increase in the destruction of platelet and thrombocytopenia due to a reduction in platelet production.[21]

Conclusion

The widespread availability of automated hematology analyzers in hospitals and laboratories now permit accurate measurement of MPV and other indices. Although bone marrow examination remains the gold standard for TCP, MPV is definitely a useful and reliable test to differentiate between hyperdestructive TCP form the hypoproductive and abnormal pooling TCP. The results of our study for differentiating cause of TCP are statistically significant. More attention should be paid to these indices for causes of TCP. MPV should be combined with other platelet indices for more accurate results and further studies with combining these indices will definitely provide promising results.

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