Original Research Article

Role of platelet indices in the evaluation of thrombocytopenia

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Abstract

Background: Thrombocytopenia is defined as decrease in the count of platelets in circulating blood, so any alteration in count or function of platelets is potentially life-threatening. Evaluation of thrombocytopenia's via platelet indices is safe and rapid procedure due to wide use of automated cell counters. In literature, there are few studies done on utilization of platelet indices in patients with thrombocytopenia due to accelerated destruction, thrombocytosis and in normal platelet count. This study is carried out to evaluate platelet indices in patients with thrombocytopenia(immune/non-immune/miscellaneous) and its role in decrease platelet productions and in accelerated platelet destruction.**Materials and methods:** This is a observational type of descriptive study done over a period of one year from April 2019 to March 2020. In this study, a total of 150 cases were evaluated with 75 healthy people in control group and 75 patients with thrombocytopenia in the study group. Assessment of complete blood count, Mean platelet volume (MPV), platelet distribution width(PDW), platelet large cell ratio (PLCR) and platelet large cell count (PLCC) was done on Beckman Coulter hematology analyser. In both control and study group, clinical features, platelet counts and platelet indices were analysed. The study group was further divided into hypo-proliferative and destructive thrombocytopenia sub-group depending on clinical and laboratory diagnosis and bone marrow studies in available cases. **Result**: The study group were further divided into hypoproliferative group and destructive group. Thrombocytopenia due to accelerated destruction includes 32 cases, whereas thrombocytopenia due to decreased production includes 34 cases in which megaloblastic group has 22 cases and non-megaloblastic group has 12 cases respectively. A total of 09 cases couldn't be included in either groups and hence placed in miscellaneous group. The platelet count was not significantly different statistically between destructive and hypo-proliferative categories **(p value =0.586).**. Statistical comparison of the three platelet volume indices among various categories of thrombocytopenia was analysed. The MPV, PDW, PLCR and PLCC were significantly higher in megaloblastic group as compared to non-megaloblastic hypo-proliferative thrombocytopenia. Also, PDW was significantly lower in non-megaloblastic group as compared to both megaloblastic as well as destructive thrombocytopenia**. Conclusion:** Platelet indices in particular MPV and PLCR can discriminate hyper-destructive from hypo-productive thrombocytopenia. PDW can differentiate non-megaloblastic hypo-proliferative category from both the destructive and megaloblastic category of thrombocytopenia.

Keywords:thrombocytopenia,platelets

Introduction

Thrombocytopenia is defined as decrease in the count of platelets in circulating blood. Platelet count below 150,000/cmm after excluding pre-analytical and post- analytical errors is considered as thrombocytopenia. The main role of platelets is to maintain primary hemostasis, so any alteration in count or function of platelets is potentially life-threatening. The decrease in count may be due to inadequate production of platelets in the bone marrow(hypo-proliferative thrombocytopenias), or increase destruction in peripheral blood circulation(destructive thrombocytopenias). Hence evaluation of platelet is important and mandatory in every case of thrombocytopenia's for correct diagnosis and treatment. This can be done by automated cell counters, peripheral smear examination, bone marrow studies and platelet indices. The evaluation of thrombocytopenia via bone marrow studies is a debated topic as it is invasive and non-conclusive in many cases except in cases of atypical presentation of immune thrombocytopenia's. However evaluation of thrombocytopenia's via platelet indices is safe and rapid procedure due to wide use of automated cell counters. In literature, there are few studies done on utilization of platelet indices in patients with thrombocytopenia due to accelerated destruction, thrombocytosis and in normal platelet count. Hence a systemic review analysis is required to study effective role of non-invasive platelet indices in hypo-productive and destructive thrombocytopenias. This study is carried out to evaluate platelet indices in patients with thrombocytopenia (immune/non-immune/miscellaneous) and its role to assess decrease platelet productions and in accelerated platelet destruction.

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Materials and methods

This is a observational type of descriptive study done over a period of one year from April 2019 to March 2020. In this study, a total of 150 cases were evaluated which included 75 healthy people with normal platelet count in control group and 75 patients with thrombocytopenia in the study group. A 2ml of venous blood was collected in EDTA(ethylene diamine tetracetic acid) anticoagulant tube from antecubital vein and all whole-blood counts were assayed within 2 hours of sample collection. Microscopic examination of a peripheral blood film stained with Leishman stain was done wherever necessary. Assessment of complete blood count, Mean platelet volume (MPV),

platelet distribution width(PDW), platelet large cell ratio (PLCR) and platelet large cell count (PLCC) was done on Beckman Coulter hematology analyser. In both control and study group, clinical features, platelet counts and platelet indices were analysed. The study group was further divided into hypo-proliferative and destructive thrombocytopenia sub-group depending on clinical and laboratory diagnosis and bone marrow studies in available cases.

Statistical data analysis

Statistical analysis was done by using SPSS software(version 20.0). Data were spread on excel sheet, calculated statistical parameters like mean and standard deviation. For Qualitative data analysis, Chi square test was applied for statistical significance. For Quantitative data analysis, t-test was applied for statistical significance. If p value was <0.05, it was considered as statistically significant.

Results

A total of 150 cases which consist of 75 healthy controls and 75thrombocytopenic patients were reviewed in this study.

In control group, maximum cases were in age group of 25-35 years, ranging from 12 years to oldest case of 60 years. Male to female ratio was 1.2:1 in this group. Whereas, in thrombocytopenic group maximum cases were between 30-40 years, ranging from 08 years to 65 years age group with male to female ratio was 1.14:1. The various etiological factors leading to thrombocytopenia is tabulated in table-1.

The study group were further divided into hypo-proliferative group and destructive group. Thrombocytopenia due to accelerated destruction includes 32 cases, whereas thrombocytopenia due to decreased production includes 34 cases in which megaloblastic group has 22 cases and non-megaloblastic group has 12 cases respectively. A total of 09 cases couldn't be included in either groups and hence placed in miscellaneous group.

Table 1: Distribution of Thrombocytopenia cases based on pathogenetic mechanism

Thrombocytopenia's				Total
Destructive thrombocytopenia	Hypo-proliferative thrombocytopenia		Miscellaneous	
	Megaloblastic group	Non-megaloblastic group		
Immune thrombocytopenia Viral hepatitis Dengue fever Malaria,Kala-Azar	Megaloblastic anemia	Acute leukemia Aplastic anemia Chronic lymphocytic leukemia	Septic shock Acute Pancreatitis Snake venom Hypersplenism	
32	22	12	09	75

The platelet counts in various groups are summarized in Table 2. The peripheral smears showing thrombocytopenia are illustrated in Figures-1 and bone marrow findings in Figure-2. The platelet count was not significantly different statistically between destructive and hypo-proliferative categories **(p value =0.586).**.

Table 2 : Platelet count distribution in control and study group

Group (n)	Platelet count ($x10^9$/l) mean±SD
Control group (75)	278.4±19.43
Destructive thrombocytopenia (32)	42.1±12.22
Hypoproliferative: megaloblastic group(22)	47.5±14.77
Hypoproliferative: non-megaloblastic group (12)	52.4±24.22
Miscellaneous (09)	56.2±18.66

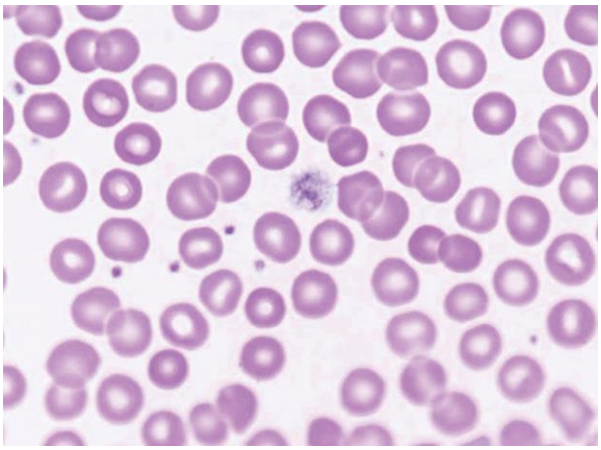

Fig 1: Peripheral smear showing thrombocytopenia with large platelets (Leishman's stain, ×40).

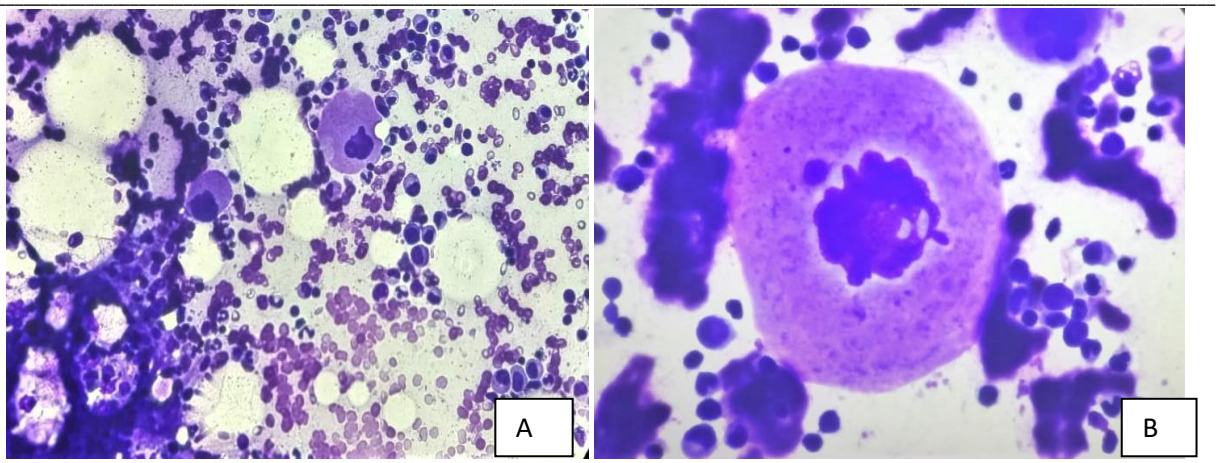

Fig 2:A: Hypogranular hypolobated megakaryocytes in bone marrow aspirate. (MGG 400 X) **B:Emperiopolesis in megakaryocytes. (MGG 1000 X)**

Platelet indices were then compared in the study and control group(table-3). Platelet indices includes mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (PLCR) and platelet large cell count (PLCC). There was significant difference in hypo-proliferative categories, especially in non-megaloblastic group when compared with control group. No significant difference was found between destructive thrombocytopenia and control group. Statistical comparison of the three platelet volume indices among various categories of thrombocytopenia was analysed. The MPV, PDW, PLCR and PLCC were significantly higher in megaloblastic group as compared to non-megaloblastic hypo-proliferative thrombocytopenia. Also, PDW was significantly lower in non-megaloblastic group as compared to both megaloblastic as well as destructive thrombocytopenia(figure-3 and figure-4).

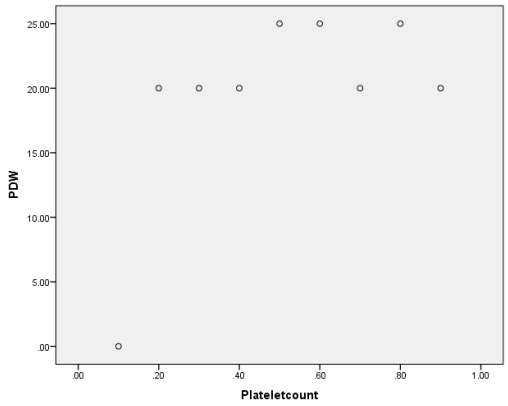

Fig 3 : Hyperdestruction cases - Correlation between platelet count and platelet distribution width. Foot notes inverse r = −0.954p= 0.092

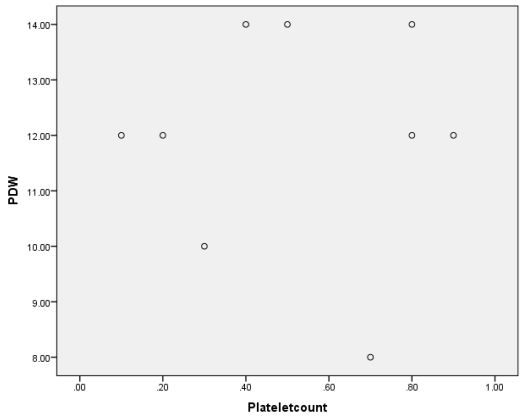

Fig 4: Hypoproduction cases - Correlation between platelet count and platelet distribution width. Foot notes linear r = 0.962p > 0.0001

Table 3 : Comparison of platelet indices between control and study group.

Groups	Platelet Indices			
	MPV(mean± SD)	PDW(mean± SD)	P-LCR(mean± SD)	P-LCC(mean± SD)
Control group(75)	10.51±2.33	13.72±2.11	31.66± .477	73.53±19.22
Destructive thrombocytopenia(32)	10.41 ± 2.13 (p=0.657)	14.354± 1.65 (p=0.076)	27.64±3.77 (p=0.331)	17.42±2.76 (p<0.0001)*
Hypo-proliferative: megaloblastic group(22)	11.58 ± 1.43 (p=0.012)*	15.48±1.78 (p=0.043)*	34.08± 4.52 (p=0.089)	20.81±3.76 (p<0.0001)*
Hypo-proliferative: non-megaloblastic group (12)	9.44± 1.6 (p=0.043)*	11.09± 2.11 (p=0.023)*	22.84± 3.77 (p=0.041)*	17.91±2.98 (p<0.0001)*

MPV -mean platelet volume; PDW -platelet distribution width; PLCR - platelet large cell ratio; PLCC- platelet large cell count. *The p values are after Student's t- test, on comparison with control group.

Discussion

Platelets play an important role in normal hemostasis,thrombosis and in various bleeding disorders[1].Hence, quantitative alterations and qualitative defects in platelets leads to thrombocytopenia which cause great morbidity and mortality. There are various etiopathological factors causing thrombocytopenia which can be broadly classified due to either peripheral destruction(destructive thrombocytopenia)or inadequate production(hypo-proliferative thrombocytopenia)[1].

Various etiological factors causing destructive thrombocytopenia includes idiopathic thrombocytopenia, malaria, kala-azar, dengue fever etc[2].

The causative agents in hypo-proliferative thrombocytopenia sub-group includes aplastic anemia,acute leukemias and chronic lymphocytic leukemias(with marrow infiltration)[3].

To identify causes and sub-classify thrombocytopenia as hyper-destructive or hypo-productive, simple, inexpensive and non-invasive tests like platelet indices have been reported with sufficient predictive capacity, sensitivity and specificity[4].Platelet indices are biomarkers of platelet activation. Platelet indices (PI) includes mean platelet volume (MPV), platelet distribution width (PDW), Platelet – Large cell ratio (P-LCR), Platelet- Large cell coefficient (P-LCC). These platelet indices are a group of derived platelet parameters obtained from automated complete blood count hematology analysers[5]. Recent studies suggests that platelet indices help in extensive clinical investigations focusing on the diagnostic and prognostic values in a variety of settings in a cost effective manner[6].

The platelets volume in peripheral blood circulation is heterogeneous and varied differences in its structures and metabolic functions. Mean platelet volume(MPV) is a measure of platelet volume, which reflects change in either platelet stimulation or rate of platelet production[7]. Typically, the average MPV is 7.2–11.7 fl in healthy subjects. MPV is determined from megakaryocytes in bone marrow. When platelet production is decreased, young platelets become bigger and more active, and increase in MPV levels. Basically, Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation.MPV changes are complex, and are not only related to the platelet count, but also related to the method of laboratory analysis used[8].

Platelet distribution width(PDW) is a measure of platelet heterogeneity. The heterogeneity is considered to be due to aging of platelets or due to heterogeneous demarcation of megakaryocytes. Platelet large cell ratio(PLCR) is themeasure of larger platelet which emphasis on the fact that platelet volume indices vary with the platelet count[9].Few studies have shown increase in MPV in destructive thrombocytopenia as compared to those with hypo-proliferative thrombocytopenia. Also it has been found that the PDW and PLCR are higher in destructive thrombocytopenia than in hypo-proliferative thrombocytopenia. A recent study concluded that MPV and PDW indices had a high sensitivity, specificity, positive and negative predictive values for the diagnosis of ITP[10]. In our study MPV, PDW and PLCR were increased in destructive thrombocytopenia as compared to the non-megaloblastic hypo-proliferative group. However the difference was significant only in PDW[11].It is observed that MPV and PDW variation is directly proportional to platelet count in hypoproduction and inversely proportional in hyper destructive categories[12].

Recent studies showed that platelet indices like MPV is increased in myocardial infarction and cerebro-vascular accidents. It is widely used surrogate marker of platelet function and shown as sign of inflammation in various conditions like ulcerative colitis, Crohn's disease, rheumatoid arthritis, chronic renal and liver disease, hepatitis B, pre-eclampsia, metabolic syndromes like diabetes mellitus and nonalcoholic fatty liver[13]. Errors in hematology analysers to be kept in mind while evaluating platelet indices. When there is abnormal distribution of platelets or fragments of RBCs and blasts, the analyzer may not display the values of platelet indices; thus, interpreting the result from the histogram and reviewing the smear could be necessary. Relatively the smaller sample size and limited disease categories in particular in hyper destructive thrombocytopenia group may limit application of this finding in broader patient groups. Further studies on the evaluation of megakaryocytic alteration and their contribution to thrombocytopenia can provide growing knowledge to the pathogenesis of numerous hematopoietic disorders that may identify broader clinical applications of the newer strategies to regulate platelet count and functioning [14].

Conclusion

In conclusion platelet indices in particular MPV and PLCR can discriminate hyper-destructive from hypo-productive thrombocytopenia and give the haemato-pathologist an initial hint about the possible mechanism of thrombocytopenia. On the basis of our results, we recommend the division of hypo-proliferative thrombocytopenia further into megaloblastic and non-megaloblastic categories. Platelet distribution width can differentiate non-megaloblastic hypo-proliferative category from both the destructive and megaloblastic category of thrombocytopenia.This helps in preventing patients particularly of immune thrombocytopenia from undergoing unnecessary, invasive bone marrow aspiration or prevent undesirable platelet transfusion. Further studies comparing impedance and impedance with optical method and inclusion of more types of hyper-destructive thrombocytopenia may enable us to use these indices for broader patient groups. Cut off values need to be established on the given laboratory setup and place for the indices to be used as a discriminating tool for thrombocytopenia.

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