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Platelet Distribution Width – Platelet Indices for Determining the Causes of Thrombocytopenia

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ABSTRACT

Background and aim: Thrombocytopenia (TCP) is low platelets count. It can result from defective platelet production or due to increased platelet breakdown. The platelet number alone does not give a complete picture of platelet maturity and function. The platelet indices have become a subject of intensive study in recent years to find the causes of TCP. The platelet parameters are widely available as part of full blood count with no extra cost. Mean platelet volume (MPV) and platelet distribution width (PDW) are useful parameters in evaluating disorders of platelets. This study was undertaken to evaluate the effectiveness of PDW in diagnosing causes of TCP. **Material and methods:** Six hundred fifty cases of TCP and 500 individuals of control group with normal platelet count were included in the study. TCP was defined as platelet count below 1.5 lacs/mm^3. Hematological analysis was done on Sysmex XT-1800i automated hematology analyzer. Platelet counts of all the cases were rechecked by peripheral smear examination. Only those cases that had sufficient clinico-hematological work up and the causes of TCP had been reliably established were included in the study. **Results:** Hyperdestructive and abnormal pooling group constituted majority of the cases (446 [68.6%]), while hypoproductive group constituted 204 (31.4%) cases. The mean PDW was significantly higher in hyperdestructive group when compared with hypoproductive group and control group. The difference was statistically significant. **Conclusion:** PDW provides plenty of clinical information about the causes and pathophysiology of TCP and can be helpful to distinguish hyperdestructive from hypoproductive TCP.

Keywords: Thrombocytopenia, platelet indices, platelet distribution width, mean platelet volume

Thrombocytopenia (TCP) is not a disease entity by itself, but a finding that may result from a number of disease processes. There is subnormal number of platelets in the circulating blood and it is one of the most common causes of abnormal bleeding. Low platelet counts can have varied causes that can be grouped in three major categories as decreased production, increased destruction and splenic sequestration/abnormal pooling. Variation in the size, especially, large platelets, is seen on peripheral smear. This varying size of platelets was suggested to help in deciding the category of TCP long back. With the advancements in automated hematology analyzers, new platelet parameters are available, resulting in greater precision and faster processing of specimens. Some of these parameters include platelet indices: Plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW). However, despite being routinely available, these indices are generally considered as not interpretable and are rarely used by laboratories and physicians.

Clinically, platelet volume measurements have long been of interest to researchers concerned with platelet production. MPV correlates with platelet function and activation, whether measured as aggregation, thromboxane synthesis, beta-thromboglobulin release, procoagulant function or adhesion molecule expression.

There is evidence supporting that PCT, rather than platelet counts, predicts the risk of bleeding in patients with TCP. PDW is a quantitative assessment of platelet size and volume and is of limited usefulness in distinguishing between reactive thrombocytosis and essential TCP. PDW is increased in the presence of platelet anisocytosis.

MPV and PDW are increased in TCP. PDW represents the degree of heterogeneity of platelets. The changes

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in PDW may be the result of recruitment of multiple ploidy classes of megakaryocytes. Each ploidy class contributes a set of platelets with different MPV. Several 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.

Osselaer et al, in their study, observed that PDW is certainly an important but forgotten platelet parameter. Hence, we have undertaken this study to ascertain the value of this forgotten parameter, PDW, in distinguishing various categories of TCP.

MATERIAL AND METHODS

Thrombocytopenia was defined as platelet count <1.5 lacs/mm^3. Blood was collected in K-EDTA vacutainer and analysis was done by the Sysmex XT-1800i automated hematology analyzer within 2-6 hours of collection. Platelet count and platelet volume parameters of all the samples were noted. Each case of TCP was reassessed by peripheral smear examination and also by manual method, if necessary. Cases with discrepancy in counts by different methods were excluded from the study. Only the cases with sufficient clinical and hematological work-up were included in the study. The statistical data was finally analyzed by SPSS software.

RESULTS

Total 650 cases of TCP were studied for the present study. Out of these, 416 (64%) were males and 234 (36%) were females with a male-to-female ratio of 1.78:1. A slight male preponderance was seen for the whole study and also in all age groups. Age ranged from 8 months to 84 years.

All cases were segregated into two groups based on the predominant underlying mechanism of TCP: Group A – Hyperdestructive TCP, Group B – Hypo-productive TCP. Group A constituted majority of the cases 446 (68.6%). This group was further subdivided into various categories based on the clinical diagnosis (Table 1). In Group A, bacterial infections accounted for the maximum number of cases, i.e., 114 (25.56%). All the categories in Group A had variable mean PDW with highest mean PDW in pregnancy (17.15 ± 1.05), while PDW was lowest in cardiac diseases (15.15 ± 0.5). Highest mean MPV was seen in cases of immune thrombocytopenia (ITP) (11.95 ± 0.45) and lowest (9.7 ± 0.3) seen in pregnancy (Table 1).

Group B constituted 204 (31.4%) cases. In this group also, PDW was variable with highest in aplastic anemia (13.6 ± 0.3) and lowest in leukemia (11.65 ± 0.85). Cases of leukemia showed the highest mean MPV (12 ± 0.8) while lowest mean MPV (7.9 ± 0.2) was seen in patients of megaloblastic anemia (Table 2).

Control group included 500 cases of normal platelet counts with 280 (56%) males and 220 (44%) females. The mean platelet count in control group was 1.72 ± 0.12 lacs/mm^3. In Group B, 0.105 lacs/mm^3 was the lowest platelet count, seen in patients of aplastic anemia, in Group B (Tables 1 and 2).

Table 1. Group A - Hyperdestruction of Platelets 446 (68.6%)

Categories	No. of cases	Percentage (%)	Mean platelet count/mm^3	Mean MPV (fl) (mean ± SD)	Mean PDW (fl) (mean ± SD)
Bacterial infections	114	25.56054	0.710	10.30 ± 2.1	15.34 ± 1.5
Cardiac diseases	92	20.6278	0.896	10.45 ± 0.1	15.15 ± 0.5
Renal diseases	64	14.34978	1.110	10.70 ± 0.52	15.65 ± 0.35
Liver diseases	43	9.641256	0.625	10.42 ± 0.52	16.13 ± 0.08
Dengue	40	8.96861	0.224	10.92 ± 0.4	17 ± 0.14
Malaria	25	5.605381	0.785	10.22 ± 0.60	15.50 ± 0.05
Pregnancy	15	3.363229	0.740	9.7 ± 0.3	17.15 ± 1.05
Viral infections	12	2.690583	0.910	10.05 ± 0.15	16.10 ± 0.15
ITP	08	1.793722	0.256	11.95 ± 0.45	15.86 ± 0.14
Sepsis	06	1.345291	0.645	10.28 ± 0.82	16.14 ± 0.26
Blood transfusion	02	0.44843	0.840	10.20 ± 0.05	16.4 ± 0.1
Miscellaneous	25	5.605381	0.825	10.50 ± 0.70	15.55 ± 0.25
Mean ± SD			0.713 ± 0.24	10.47 ± 0.54	15.99 ± 0.59

Table 2. Group B - Hypoproduction of Platelets 204 (31.4%)

Categories	No. of cases	Percentage (%)	Mean platelet count/mm^3	Mean MPV (fl) (mean ± SD)	Mean PDW (fl) (mean ± SD)
Solid malignancy	110	53.9215686	0.615	9.55 ± 1.05	12.55 ± 0.15
Leukemia	65	31.8627451	0.256	12 ± 0.8	11.65 ± 0.85
Megaloblastic anemia	21	10.2941176	0.455	7.9 ± 0.2	12.95 ± 0.15
Aplastic anemia	8	3.92156863	0.105	10.45 ± 0.85	13.6 ± 0.3
Mean ± SD			0.357 ± 0.19	9.97 ± 1.48	12.69 ± 0.71

DISCUSSION

Thrombocytopenia is quantitative reduction in the platelet count and can be due to increased peripheral destruction, inadequate production or abnormal pooling. A confident assessment of mechanism cannot be made in individual cases on clinical grounds. Platelet indices are the measurements made on peripheral blood platelets and include MPV, PDW and platelet-large cell ratio (P-LCR). These parameters can be easily obtained from routine automated hematology analyzers but their role in application to clinical diagnosis is yet to be established. Measurement of platelet indices in automated analyzers has many advantages over manual estimation. It is simple, quick and inexpensive and it also eliminates the inter- and intraobserver bias. Moreover, in the manual method, the delay between collection of blood and smear preparation may change platelet morphology and cause artefactual increase in platelet diameter, due to increased adhesiveness with flattening of the platelets on the smears.

Platelet volume is a marker of platelet function and activation. In very general terms, increased MPV might be expected in "regenerative" TCP, i.e., that caused by increased peripheral loss, destruction or utilization of platelets and accompanied by increased production of platelets by marrow (megakaryocytic hyperplasia).

PCT, derived from platelet count and MPV, and PDW, derived from direct flow cytometric measurement of platelet cell volume, are less documented for their clinical roles.

The present study was carried out with the objective of studying platelet parameters in various clinical cases. We targeted 650 cases of TCP and their clinical features, platelet count and platelet parameters - MPV and PDW - were studied. Though we studied 1,000 cases of TCP, platelet parameters were given by cell counter in 650 cases. Analysis of the parameters was done in these 650 cases only and that constituted 65% of all. In control group, the same parameters were given in all 400 cases. In 350 (35%) cases, the platelet parameters were not given by the cell counter and in these cases, the platelet histogram showed deviation from the normal bell-shaped curve, leading to no output of values for platelet indices. This is a major limitation for platelet volume parameter studies in TCP and similar findings have been quoted by studies. All the cases were grouped according to most predominant mechanism.

We divided our study cases into two major groups on the basis of the predominant mechanism as Group A (Accelerated platelet destruction and pooling) and Group B (Impaired platelet production).

Group A - In hyperdestructive causes of TCP, marrow compensates actively for platelet loss. They release young platelets which are larger in size. There is a decrease in size during its 7-10 days life span. This group is constituted by disorders like immune and nonimmune cases of ITP, microbial infections, drugs, systemic lupus erythematosus (SLE) and neonatal TCP. Majority of our cases belonged to Group A (68.6%), suggesting the mechanism of accelerated destruction. We also included cardiac, renal, gestational TCP, neonatal TCP, post-transfusion cases and TCPs with shock and some other miscellaneous conditions in this group. The group had mild-to-moderate TCP except for the ITP category, which presented with relatively severe TCP.

The platelet count decreases proportionally and inversely to increasing spleen size. Approximately a third of total platelet mass is normally sequestered in spleen. Commonly, platelet counts of 50,000-70,000/mm^3 have been found in individuals with cirrhosis and associated splenomegaly. Our study accounted 9.6% cases in this group, with congestive splenomegaly suggesting abnormal platelet pooling with mean platelet count of 62,500.

Group B - There are several disorders with TCP secondary to inadequate platelet production from the

marrow such as chemotherapy for solid malignancies, acute leukemia, megaloblastic and aplastic anemia. Our study constituted 31.4% cases in this group, which included few dimorphic anemia in megaloblastic anemia. This category of patients had relatively moderate-to-severe TCP as compared to previous category.

The mean PDW in the present study for Group A was higher than that of control group, while value for Group B was similar to that of control group. Nelson et al noticed that patients with TCP due to loss or destruction of platelets have larger platelets, whether the loss is due to infection, hemorrhage or immune destruction. When TCP was due to lack of production, the platelet volume was similar to that seen in patients with normal blood cell counts. Babu et al noticed increased platelet heterogeneity in all TCP groups.

In normal subjects, MPV has an inverse, nonlinear relation with platelet count, while platelet volume heterogeneity has a direct, nonlinear relation with MPV. In comparison to the reference range established for normal subjects, patients with chronic lymphocytic leukemia, atherosclerotic heart disease, diabetes mellitus and chronic undifferentiated schizophrenia have been shown to have normal platelet volume mean and heterogeneity. Patients treated with cytotoxic chemotherapy for acute nonlymphocytic leukemia, patients with megaloblastic anemia and patients with aplastic anemia have been noted to have abnormally small platelets with increased heterogeneity. Patients with chronic myelogenous leukemia seem to have abnormally large platelets with increased heterogeneity.

Borkataky et al noticed high mean PDW values except for nonmegaloblastic subgroup of impaired production. Platelet size is heterogeneous even in normal persons. Its heterogeneity is; however, increased in patients with ITP, sepsis, disseminated intravascular coagulation (DIC), myocardial infarction and diabetes mellitus (accelerated destruction). The heterogeneity of platelet volume is considered to be due to aging of platelets or due to heterogeneous demarcation of megakaryocytes.

SUMMARY AND CONCLUSIONS

Platelet distribution width is an important index in platelet parameters. PDW, along with other platelet indices, can give valuable information regarding the mechanism of platelet destruction. Increased variation in PDW indicates greater platelet heterogeneity along with destruction and splenic pooling. PDW varies inversely with platelet count. Further large studies with large number of cases in each subgroup are needed to explore the role of platelet indices in TCP and also to find the diagnostic role of platelet indices in various other diseases. The parameter P-LCR also needs to be worked upon to see for subtle changes, if any, and whether it could be explained by the mechanism of destruction of platelets.

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