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Pathology

UNDERSTANDING THE ROLE OF PLATELET INDICES IN VARIOUS CLINICAL CONDITIONS OF THROMBOCYTOPENIA

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ABSTRACT **Background**: Thrombocytopenia is caused by decreased production, increased consumption, and sequestration of platelets. Bone marrow aspiration remained gold standard method for thrombocytopenia evaluation. Being invasive, time-consuming it's less favorable. Now with advent of autoanalyzers, it's easy to measure platelet count and indices: Mean platelet volume, Plateletcrit, platelet distribution width. Present study aim is to explore platelet indices utility and correlation with platelet count in thrombocytopenia thus helping in patient treatment. **Materials &methods:** The study was conducted on total 150 patients attending a tertiary hospital in Karnataka for 3 months. All EDTA blood samples received for complete blood count in lab were processed within 1 hour in Sysmex XP-100 analyzer. Patients above 18 years age with platelet count <1.5 lakhs were included in study. Platelet count, MPV, PDW, PCT values collected from CBC sheet and documented. Peripheral smear findings, relevant clinical information and serological investigations were included in study.**Results:** 120 belonged to hyperdestructive; rest 30 belonged to hypoproductive group. Mean platelet count obtained in hyperdestructive group is 77.8±36.0; in hypoproductive group is 71.9±36.2 with P value of 0.58. MPV in hyperdestructive group is 12.5±0.8 ; in hypoproductive group is 10.11±1.4 with significant P value of 0.05. Mean PDW in hyperdestructive group is 18.0±4.0 ; in hypoproductive group is 17.2±4.8 with P value of 0.6. Mean PCT in hyperdestructive group is 0.08±0.01 ; in hypoproductive group is 0.07±0.02 with P value of 0.2. **Conclusion:** Platelet count and indices MPV, PDW, PCT are useful parameters in differentiating hyperdestructive from hypoproductive thrombocytopenia causes and help in treatment plan.

KEYWORDS : thrombocytopenia, platelet indices, plateletcrit, MPV, PDW, PCT

INTRODUCTION:

RBCs, WBCs, platelets are formed elements of blood. Their counts get altered in various diseases, so estimation of their count is an important hematological investigation. Platelets play a pivotal role in hemostasis in formation of platelet plug at sites of vascular injury followed by activation of coagulation factors to form stable fibrin clot. Thrombocytopenia is defined as reduction in peripheral blood platelet count below lower limit of normal ie. 1.5 lakhs/µl. It may occur due to decreased production, increased consumption or increased sequestration of platelets. Hypoproductive thrombocytopenia result from bone marrow failure due to aplastic anemia, megaloblastic anemia, bone marrow infiltration with lymphoma/leukemia/myeloma, myelodysplasia, chemotherapy or radiation induced. Hyperdestructive thrombocytopenia causes are ITP (idiopathic thrombocytopenic purpura), infectionsdengue/ malaria/filariasis, septicemia,chronic liver disorder, DIC (disseminated intravascular coagulation),TTP (thrombotic thrombocytopenic purpura), HUS (hemolytic uremic syndrome),microangiopathic hemolytic anemia, giant hemangiomas.

Thrombocytopenia is not a disease entity but a significant finding resulting from many disease processes in most hospitalized patients. In all these cases it's important to identify the underlying cause whether hypoproduction or hyperdestruction of platelets. Initially bone marrow aspiration remained gold standard method for evaluation of thrombocytopenia cases. [(1)]But the procedure is invasive, time-consuming and carries risk of infection spread and bleeding diathesis. Now with recent advent of autoanalyzers, it's easy to measure platelet count & platelet indices MPV (mean platelet volume), PCT (plateletcrit), PDW (platelet distribution width).[(2)]Also because of platelets tendency to form aggregates and potential overlap with red blood cells, platelet count is quite important to correlate with peripheral smear.[(3)]

Platelet volume is a marker of platelet function and activity. Platelet activation brings about changes in platelet shape resulting in platelet swelling, causing increase in MPV. It indicates bone marrow activity, high MPV indicate increase megakaryocytic activity. Low MPV seen in marrow suppression. Platelets with increased count and different sizes pseudopodia possibly affect PDW. PDW is a marker of platelet anisocytosis. PCT is a reliable marker of platelet biomass.[(4)] Thus these platelet indices are important in analyzing cause for platelet abnormalities and help in treatment purpose. Though these platelet indices are easily available, they are not much reported due to lack of standardization. [(5)]The aim of this study is to explore the utility of these platelet indices and understanding their role in correlation with platelet count in various clinical conditions of thrombocytopenia and help in patient treatment management.

MATERIALS AND METHODS:

This cross-sectional study was conducted on a total of 150 patients attending a tertiary hospital in Karnataka for a period of 3 months after taking approval from Institutional Review committee. All EDTA blood samples received for blood count in lab were processed within 1 hour in Sysmex XP-100 analyzer. Quality control of analyzer was followed according to manufacturer's instructions.

Patients above 18 years age of either gender with platelet count <1.5 lakhs were included in the study after taking patient consent. Infants and children less than 12 years age, with platelet count >1.5 lakhs & those on anti-platelet drugs were excluded. Request forms without clinical details or repeated blood samples from same patients were excluded. Following platelet parameters: Platelet count, MPV, PDW, PCT of thrombocytopenic patients were collected from CBC sheet and documented. Peripheral smear findings of respective cases were collected. Relevant clinical information and serological investigations were also included in study.

Statistical Analysis:

All data collected were analyzed using SPSS. *P* value less than equal to 0.05 was considered significant.

RESULTS:

The present study included 150 patients of thrombocytopenia which was further subdivided into hyperdestructive and hypoproductive cases. In the hyperdestructive group we had 120 cases and in hypoproductive group we had 30 cases. Fig 1, 2 and Table 1 shows the distribution of the number of cases in each etiological subgroup and comparison with other studies. Table 2 shows the mean values of all platelet indices and *P* value in both hyperdestructive and hypoproductive group. The mean platelet count obtained in this study in hyperdestructive group is 77.8±36.0& in hypoproductive group is 71.9±36.2 with *P* value of 0.58. The mean MPV obtained in hyperdestructive group is 12.5±0.8 and in hypoproductive group is 10.11±1.4 with significant *P* value of 0.05. The mean PDW obtained in hyperdestructive group is 18.0±4.0 and in hypoproductive group is 17.2±4.8 with *P* value of 0.6. The mean PCT obtained in hyperdestructive group is 0.08±0.01 and in hypoproductive group is 0.07±0.02 with *P* value of 0.2.

DISCUSSION:

Platelets are anucleate cells that are derived from megakaryocytes. They play a crucial role in stoppage of bleeding by helping in clotting process. When the platelet count falls below 1.5 lakhs/µl, it is called thrombocytopenia. Thrombocytopenia can be due to increased destruction of platelets or impaired production of platelets or even abnormal pooling of platelets in spleen.

Normally a peripheral blood smear is required for evaluation of platelet count, size, structure, distribution under the microscope. But automated hematology analyzers with recent technology advancement have made it easy to produce & record platelet count along with platelet indices: MPV, PDW, and PCT. [2]As all the thrombocytopenia cases doesn't require an invasive bone marrow aspiration or biopsy study , these platelet parameters will help in explaining the underlying mechanism of thrombocytopenia. Present study is done with the aim to explore the utility of these platelet indices and understanding their role in correlation with platelet count in various clinical conditions of thrombocytopenia; help in patient treatment.

One of the important platelet parameters MPV has been a widely studied parameter in literature. It reflects the size, activity and function of platelets.[6,7] Normal range of MPV is 7.5-11.5 fl. It is increased when thrombocytopenia occurs due to peripheral platelet destruction (since platelet production is stimulated with release of large platelets in circulation) and is normal or low when thrombocytopenia is due to impaired platelet production. Increased shedding of platelets from megakaryocytes is indicated by raised level of MPV. Because of wide physiological variation in MPV, platelet size is a difficult parameter to quantitate accurately. Giant platelets are seen in May-Hegglin anomaly, Bernard Soulier syndrome, ITP, myelodysplastic syndrome, myeloproliferative neoplasms, splenectomy, hyposplenism etc. Small platelets are seen in aplastic anemia, Wiskott-Aldrich syndrome, storage pool disorders, thrombocytopenia absent radii syndrome.[8]

PDW is an indication of variation in size of platelets, increases with platelet anisocytosis. Normal range is 9-14 fl. PDW is said to be specific marker of platelet activation.[9]Activation of platelets brings about morphological alteration, pseudopodia formation thus affecting PDW. Hence high PDW noticed in accelerated hyperdestructive thrombocytopenia cases because of heterogenous platelet population.[10]Platelets in a unit volume of blood are indicated by PCT.[11]

In our study a total of 120 hyperdestructive and 30 hypoproductive thrombocytopenia cases were analyzed. MPV was found to be higher for hyperdestructive group than hypoproductive group with a significant p value of 0.05. Nelson et al and Numbenjaponet al also reported similar findings of higher MPV in hyperdestructive thrombocytopenia cases and stated that in hyperdestructive thrombocytopenia, bone marrow compensate for the platelet loss actively with release of young large platelets. [12,13]Similar findings were also reported by Baig MA et al, Parveen et al, Narasimhulu et al.[1,14,15]

With regard to PDW in our study, it was higher in hyperdestructive group than hypoproductive group. Ntaios et al reported an increased MPV and PDW in ITP cases. [16]Shah et al and Borkataky et al also reported higher PDW in ITP cases compared to AML and non-megaloblastic hypoproliferative cases.[17,18]Ntaios et al also stated PDW cut off value between15-17 fl with 100% sensitivity, specificity.[16]Similarly Kaito et al also reported increased MPV, PDW in ITP than aplastic anemia. Also Kaito et al stated PDW cut off value more than 17fl to distinguish ITP from hypoproductive thrombocytopenia.[2] But Xu et al reported different results in his study that MPV and PDW do not have enough predictive efficiency to diagnose bone marrow failure in thrombocytopenic patients..[19] The major disadvantage of these retrospective studies is small study population and confounding factors that affect platelet volume plus the prospective invalidation of the cut-off values.PCT is not altered much by severity of thrombocytopenia of either hyperdestructive or hypoproductive group because in healthy patients platelet mass is regulated to keep it constant[20]

CONCLUSION:

Platelet count and indices MPV, PDW, PCT are simple easy to obtain parameters on routine basis at no extra cost. Thus interpretation of these parameters will help to avoid unnecessary invasive bone marrow procedures or platelet transfusion in thrombocytopenic patients. In our study high MPV, PDW were documented in hyperdestructive thrombocytopenia cases. These parameters will help to provide useful information in differentiating hyperdestructive from hypoproductive thrombocytopenic cases and help in deciding treatment plan. However large scale studies have to be undertaken to further prove defining role of these indices in various diseases along with standardization.

Acknowledgement:
Nil

Figure 1:

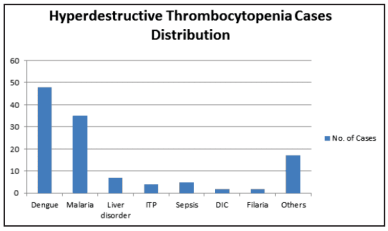

Figure 2:

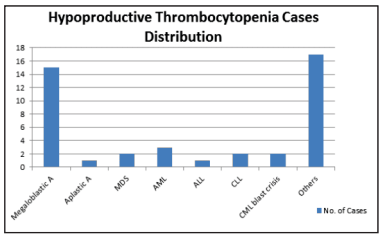

Figure 3: Photomicrograph 40X of a giant platelet

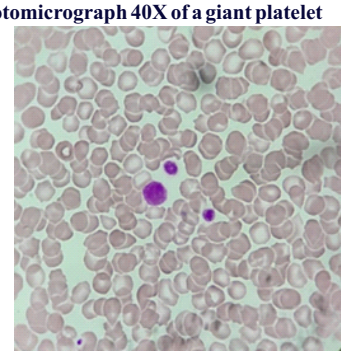

Table 1: Distribution of thrombocytopenia cases in each subgroup & comparison with other studies

Etiology	Present Study	Katti et al	Numbenjapon et al
HYPERDESTRUCTIVE	120 cases	85 cases	64 cases
Dengue	48 (40%)	29 (34%)	-
Malaria	35 (29%)	24 (28%)	-
Chronic liver disease	07 (6%)	03 (4%)	-
ITP	04 (3%)	04 (5%)	53(83%)
Sepsis	05 (4%)	04 (5%)	09(14%)
DIC	02 (2%)	02 (2%)	-
Filariasis	02 (2%)	-	-
Others	17 (14%)	19 (22%)	02(3%)
HYPOPRODUCTIVE	30 cases	15 cases	38 cases
Megaloblastic Anemia	15 (50%)	8 (53%)	-
Aplastic Anemia	01 (3%)	-	12(31%)
MDS	02 (7%)	01(7%)	04(11%)
AML	03 (10%)	01(7%)	18(47%)
CML(Blast crisis)	02 (7%)	02(13%)	-
ALL	01 (3%)	-	04(11%)
CLL	02 (7%)	03(20%)	-
Others	04 (13%)	-	-

Table 2: Mean value of Platelet Indices in both Hyperdestructive & Hypoproductive group

Platelet Indices	Hyperdestructive	Hypoproductive	P Value
Platelet count (meanSD) (x109/L)	77.8±36.0	71.9±36.2	0.58

MPV (mean± SD) (fl)	12.5±0.8	10.11±1.4	0.05
PDW (mean± SD)(fl)	18.0±4.0	17.2±4.8	0.6
PCT (mean± SD)(%)	0.08±0.01	0.07±0.02	0.2

Table 3: Comparison of Platelet Indices in both Hyperdestructive & Hypoproductive group with other studies

Platelet indices	Baig MA et al	Parveen et al	Narasimhulu et al	Present study
HYPERDESTRUCTIVE CASES				
MPV (mean± SD) (fl)	11.6±2.25	12.3±0.9	12.4±0.9	12.5±0.8
PDW (mean± SD) (fl)	15.16±1.36	19.3±4.2	20.4±5.6	18.0±4.0
PCT (mean± SD) (%)	0.09±0.14	0.08±0.1	0.08±0.01	0.08±0.01
HYPOPRODUCTIVE CASES				
MPV (mean± SD) (fl)	8.5±1.27	10.17±1.3	8.14±1.2	10.11±1.4
PDW (mean± SD) (fl)	14.10±1.15	19.7±5.4	18.6±1.2	17.2±4.8
PCT (mean± SD) (%)	0.08±0.12	0.06±0.03	0.06±0.01	0.07±0.02

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