

## Diagnostic Implication and Utility of Platelet Indices in Differentiating Hypoproduktive and Hyperdestruktive Thrombocytopenia

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### Abstract:

#### Aims and Objective :

-To evaluate the variation in platelet indices in establishing clinical correlation in patients presenting with thrombocytopenia.

- To study the relationship of platelet indices with respect to the underlying mechanism of thrombocytopenia.

**Materials & Methods:** This was a hospital-based cross-sectional study for a period of 3 months (from January 2019 to March 2019) on patients with thrombocytopenia, conducted at CIMS & H, LUCKNOW. Platelet count, Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV) and relevant clinical details of the thrombocytopenic patients were collected and tested for statistical significance by unpaired-t test.

Benesphera Avantor 5-part Automated Hematology Analyser was used to assess platelet indices.

**Results:** This study included 70 patients of thrombocytopenia who were classified into hypoproduktive (13 cases) and hyperdestruktive (57 cases). The mean platelet count in hypoproduktion group is  $0.71 \pm 0.50$  and in hyperdestruktion group is  $1.03 \pm 0.31$  with a

P value of 0.003. The mean MPV in hypoproduktion group is  $9.02 \pm 1.08$  and in hyperdestruktion group is  $13.60 \pm 1.74$  with a P value of 0.0001. The mean PDW in hypoproduktion group is  $17.17 \pm 2.12$  and in hyperdestruktion group is  $17.42 \pm 1.01$  with a

P value of 0.53. The mean PCT in hypoproduktion group is  $0.45 \pm 0.44$  and in hyperdestruktion group is  $1.16 \pm 0.48$  with a P value of 0.0001.

**Conclusion:** During evaluation of thrombocytopenic patients, it is essential to identify the etiology, whether it is due to hypoproduktion or hyperdestruktion which will have impact on the management.

Mean platelet volume may provide useful information in discriminating the hypoproduktive and hyperdestruktive thrombocytopenia. Interpretation of platelet indices can help the thrombocytopenic patients in the initial management and can avoid invasive investigations.

**Keywords:** Thrombocytopenia, Platelet indices, Mean Platelet Volume, Plateletcrit, Platelet Distribution Width.

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Date of Submission: 16-08-2019

Date of Acceptance: 31-08-2019

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### I. Introduction

With improvement in the technologies, advancement occurs in all field including medicine.

Thrombocytopenia is a significant finding in hospitalized patients which may be often missed if platelet parameters are not evaluated routinely. Platelet counts below 1.5 Lacs/cumm define thrombocytopenia, but they do not reveal the underlying pathology.<sup>[1]</sup> During evaluation of these patients, it is essential to identify the etiology, whether it is due to hypoproduktion or hyperdestruktion which will have impact on the proper management of the patients.

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 carries an overt risk of bleeding diathesis in critical thrombocytopenia cases. Serology (For infectious diseases), Platelet associated Immunoglobulin G (PAIgG) and Molecular markers for Disseminated Intravascular coagulation (DIC) are used in evaluating thrombocytopenic patients which are relatively costly.<sup>[2]</sup> Previously platelet count was the only vital information available about this small blood element.

But recently, with availability of Automated Blood Cell Analyzers new indices related to platelet count are also being estimated. Most important parameters among them are plateletcrit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW). Platelet activation leads to changes in platelet shape with

increase in platelet swelling leading to an increase in MPV and PDW. Determinations of platelet size are traditionally made by microscopic measurements of platelet diameters, a method which is not readily available in routine daily practice. The automated cell counter, however, provides an MPV on each whole blood sample that is processed, which makes possible the study of platelet size in a great variety of clinical conditions.<sup>[3]</sup> Recent years studies have come up to explore the utility of these parameters in routine clinical practice.

This study attempts to find the usefulness of these platelet indices in the initial evaluation of patients with thrombocytopenia by assessing their variation in different clinical scenarios and to assess their sensitivity and specificity.

## II. Aims and Objective

- To evaluate the variation in platelet indices in establishing clinical correlation in patients presenting with thrombocytopenia.
- To study the relationship of platelet indices with respect to the underlying mechanism of thrombocytopenia.

## III. Materials & Methods:

This was a hospital-based cross-sectional study for a period of 3 months (from January 2019 to March 2019) on patients with thrombocytopenia, conducted at CIMS & H,LUCKNOW. Platelet count, Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV) and relevant clinical details of the thrombocytopenic patients were collected and tested for statistical significance by unpaired-t test.

Benesphera Avantor 5-part Automated Hematology Analyser was used to assess platelet indices.

Correlation with routine peripheral smear findings of the respective cases was done.

Relevant clinical details and available investigations including serological results of the patients were included.

### Inclusion criteria:

All adult Patients aged >18 years of both sexes with a platelet count of less than 1.5 Lacs/cumm.

### Exclusion criteria:

- 1) Patients aged less than 18 years &
- 2) Patient on antiplatelet drugs and other medications causing thrombocytopenia were excluded.

### Statistical analysis:

The results are presented in mean±SD. The Unpaired t-test was used for comparisons. The receiving operating curve (ROC) analysis was carried out. The area under curve (AUC) with its 95% confidence interval (CI) was calculated. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NP) with its 95%CI was calculated. The p-value < 0.05 was considered statistically significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

## IV. Results

This study included 70 patients of thrombocytopenia who were classified into hypoproliferative ( 13 cases) and hyperdestructive ( 57 cases). The distribution of cases in each subgroup and comparison of the distribution with similar studies were shown in table 1. The mean platelet count in hypoproliferation group is  $0.71 \pm 0.50$  and in hyperdestruction group is  $1.03 \pm 0.31$  with a P value of 0.003. The mean MPV in hypoproliferation group is  $9.02 \pm 1.08$  and in hyperdestruction group is  $13.60 \pm 1.74$  with a P value of 0.0001. The mean PDW in hypoproliferation group is  $17.17 \pm 2.12$  and in hyperdestruction group is  $17.42 \pm 1.01$  with a P value of 0.53. The mean PCT in hypoproliferation group is  $0.45 \pm 0.44$  and in hyperdestruction group is  $1.16 \pm 0.48$  with a P value of 0.0001. Mean Values of different platelet indices and P-value in hyperdestruction immune thrombocytopenia and hypodestruction thrombocytopenia were shown in table 2.

**Table 1 :** The distribution of thrombocytopenia cases in each subgroup and comparison of the distribution with similar studies.

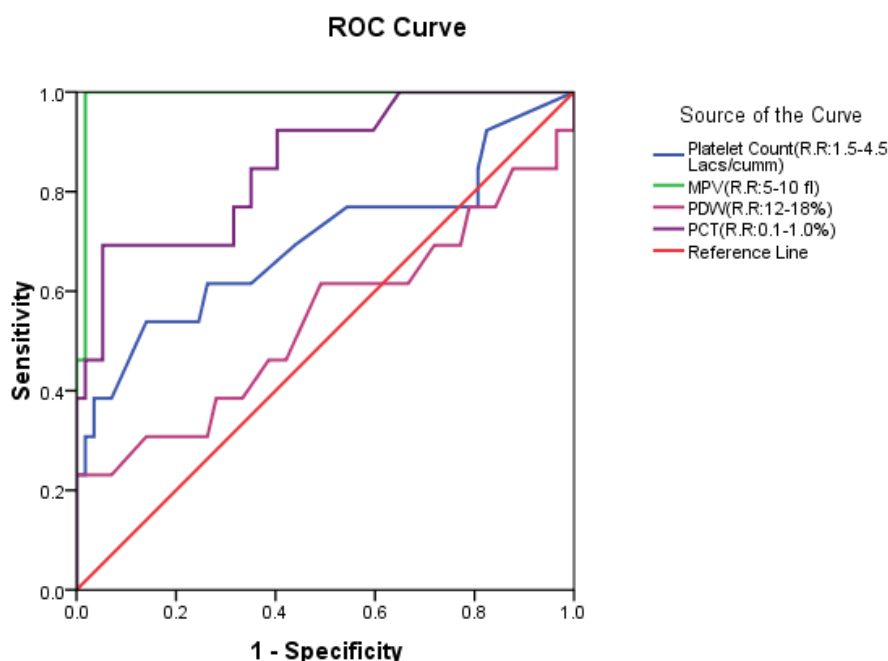
Etiologies	Katti et al <sup>[23]</sup> Total cases (%)	Parveen et al <sup>[24]</sup> Total cases (%)	Present study Total cases (%)
<b>HYPODESTRUCTION</b>			
Megaloblastic Anaemia	08(8%)	11	12
Leukemia & MDS	06	02	01
Aplastic Anaemia	-	-	-
Others	-	13	-
<b>HYPERDESTRUCTION</b>			
ITP	04	3	-
Dengue	29	26	25
Malaria	24	8	16

Chronic Liver Disease	3	20	09
Sepsis	4	6	02
DIC	2	-	-
Others	19	31	05
Total	100	120	70

**Table-2:** Comparison of platelet indices between hypoproliferative thrombocytopenia and hyperdestructive thrombocytopenia

Platelet indices	Hypoproliferative (n=13)	Hyperdestructive (n=57)	p-value <sup>1</sup>
Platelet count	0.71±0.50	1.03±0.31	0.003*
MPV	9.02±1.08	13.60±1.74	0.0001*
PDW	17.17±2.12	17.42±1.01	0.53
PCT	0.45±0.44	1.16±0.48	0.0001*

<sup>1</sup>Unpaired t-test, \*Significant



Diagonal segments are produced by ties.

**Fig.1:** ROC Curve Showing Sensitivity And Specificity Of Platelet Indices In Differentiating hypoproliferative thrombocytopenia From hyperdestructive Thrombocytopenia

**Table-3:** Predictive values of platelet indices in differentiating hypoproliferative thrombocytopenia from hyperdestructive thrombocytopenia

Predictive values, % (95%CI)	Platelet count ≤0.80	MPV ≤10.0	PDW ≤18.0	PCT ≤0.75
Sensitivity	53.8 (26.7-80.9)	100.0 (100.0-100.0)	69.2 (44.1-94.3)	69.2 (44.1-94.3)
Specificity	75.4 (64.3-86.6)	98.2 (94.8-101.7)	26.3 (14.9-37.7)	71.9 (60.3-83.6)
PPV	33.3 (13.2-53.5)	92.9 (79.4-106.3)	17.6 (7.2-28.1)	36.0 (17.2-54.8)
NPV	87.8 (78.6-96.9)	100.0 (100.0-100.0)	78.9 (60.6-97.3)	91.1 (82.8-99.4)
AUC (95%CI)	0.69 (0.51-0.88)	0.99 (0.87-1.01)	0.54 (0.33-0.74)	0.85 (0.73-0.97)

### V. Discussion

Platelet indices include Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV). Though these parameters have been available from the routinely used blood cell counters in the laboratory, their exact role in application to clinical diagnosis has still not been fully established.<sup>[4]</sup>

Measurement of platelet indices in automated analysers has many advantages over manual estimation, as it is very simple, quick and inexpensive test which also eliminates the observer bias.<sup>[5, 6]</sup> Further in manual method, a delay between collection of blood and smear preparation, may change the platelet morphology and also artefactual increase in platelet diameter can occur because of increased adhesiveness with flattening of the platelets on the smears.<sup>[7]</sup>

Numbenjapon et al<sup>[8]</sup> found that MPV was significantly higher in hyperdestruction group compared to hypoproliferative thrombocytopenia. In hyper destructive thrombocytopenia, bone marrow compensates actively for the platelet loss and start releasing young larger platelets (“left shift”) which tend to decrease in size during its 7-10 days life span.<sup>[9]</sup> In our study also we found a significant low ( $9.02 \pm 1.08$ ) mean MPV in the hypoproliferative group than in the hyperdestruction group ( $13.60 \pm 1.74$ ).

Ntaios et al<sup>[10]</sup> found an increased MPV and PDW in Immune Thrombocytopenic Purpura (ITP). Kaito et al<sup>[2]</sup> similarly found a significant increase in MPV and PDW in ITP than in Aplastic anemia. Similarly few studies found a high PDW can also result in hyper destructive thrombocytopenia because of the release of heterogenous population of platelets which vary in their size (anisocytosis).<sup>[11, 12]</sup> Both MPV and PDW are reliable tests in hyperdestructive thrombocytopenia and considered as tests of 100% sensitivity and specificity for the diagnosis of ITP.<sup>[13,14]</sup> But in contrast, Tomito et al<sup>[15]</sup> found a low MPV in hyperdestructive thrombocytopenia and Nakadate H et al<sup>[16]</sup> and Baynes RD et al<sup>[17]</sup> found no significant difference in the MPV and PDW between the hyperdestructive and hypoproliferative thrombocytopenia. Bashir AB et al<sup>[18]</sup> found significant differences in the MPV, PDW and PLT in patients with dengue infection and they suggested that these parameters can be used as probable indicators for dengue in endemic area. He also found a MPV <9 fl and high PDW >13fl had a considerable sensitivity for dengue fever.

PCT is a representation of volume percent of platelets and its value is not altered by severity of thrombocytopenia of either hypoproliferative or hyperdestructive etiology.

Shah et al<sup>[19]</sup> found that increase in PDW and MPV. They also found increase in MPV in Ischemic heart disease patients.

In our study we did not find any significant difference in PDW between the two subgroups. But Shah et al<sup>[20]</sup> and Borkatakya et al<sup>[6]</sup> found a higher PDW in hyperdestructive thrombocytopenia when compared to hypoproliferative thrombocytopenia. Kaito et al<sup>[13]</sup> suggested that a PDW value of more than 17 fl and Ntaios et al<sup>[14]</sup> suggested a value between 15 and 17 fl discriminate these two subgroups. But Xu et al<sup>[21]</sup> found a contrasting result of higher PDW values in the hypoproliferative thrombocytopenia and attributed this as a result of significant dysplasia of hematopoiesis in the bone marrow in the hypoproliferative group. The major disadvantage in these retrospective studies is that some had a smaller study population and other confounding factors that influenced the platelet volume. Further the cut off values suggested by these studies have not been validated.<sup>[22, 23]</sup>

**Limitation of the study:** The sample size in our study is small and further we had a limited number of cases 13 (18.6%) in the hypoproliferative category. This may limit its application when applied to a larger patient community.

## VI. Conclusion

During evaluation of thrombocytopenic patients, it is essential to identify the etiology, whether it is due to hypoproliferative or hyperdestruction which will have impact on the management. Mean platelet volume may provide useful information in discriminating the hypoproliferative and hyperdestructive thrombocytopenia. MPV is an accurate, reliable & easily obtained platelet parameter which is helpful in diagnosing the basic etiology of thrombocytopenia. Platelet indices show inverse relationship with platelet count as they are increased in hyperdestructive type & show linear relationship in hypoproliferative type. Interpretation of platelet indices can help the thrombocytopenic patients in the initial management and can avoid invasive investigations like bone marrow aspiration and unnecessary platelet transfusion. Further studies with large number of cases in each subgroups are needed to explore the role of this useful platelet index in thrombocytopenia and also to find the diagnostic role of platelet indices in various other diseases.

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Dr. Shashwat Vidyadhar. “Diagnostic Implication and Utility of Platelet Indices in Differentiating Hypoproliferative and Hyperdestructive Thrombocytopenia.” *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 18, no. 8, 2019, pp 07-11.