

# Utility of Platelet Count and Platelet Indices in the Evaluation of Thrombocytopenia

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## ABSTRACT

### BACKGROUND

Thrombocytopenia is defined as a low platelet count, less than 150000 / microlitre which is attributed to a variety of haematological and pathological disorders. It can result from four different mechanisms like hypoproduction, hyperdestruction, abnormal platelet distribution and dilutional loss. The type of mechanism leading to thrombocytopenia can be determined with the help of platelet count and platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (Pct). We wanted to study the utility of platelet count and platelet indices in the evaluation of thrombocytopenia, evaluate platelet indices as a diagnostic tool in differentiating various types of thrombocytopenia and correlate platelet indices with bone marrow findings.

### METHODS

This was a prospective observational study done in a teaching medical college in India over a period of two years from June 2017 to May 2019. The patients were divided into two groups as hyperdestructive and hypoproducer related thrombocytopenia. The platelet count and platelet indices were determined in a five part haematology autoanalyzer and were compared with suitable controls. Findings were correlated with Bone marrow examination for exact aetiology.

### RESULTS

A total of 60 patients was considered for the study, of which 21 belonged to hyperdestructive thrombocytopenia and 39 belonged to hypoproducer group. All 21 cases in the former group were of immune mediated thrombocytopenia (ITP). MPV  $11.51 \pm 1.97$  was significantly higher in hyperdestructive thrombocytopenia as compared to hypoproducer thrombocytopenia wherein it was  $8.34 \pm 2$ . PDW was also more in the former group as compared to latter and showed a mean value of  $16.67 \pm 1.03$  and  $14.68 \pm 2.29$  respectively. The difference in Pct was insignificant in determining the cause of thrombocytopenia between the groups.

### CONCLUSIONS

Platelet indices give valuable preliminary information as to the type of thrombocytopenia, i.e. hyperdestructive or hypoproducer type. This will guide in patient management decisions and may obviate the need for bone marrow examination in at least some patients. Also platelet indices do not need extra blood sample and do not incur additional cost.

### KEYWORDS

Hyperdestructive, Hypoproducer Thrombocytopenia, Platelet Indices, Bone Marrow, ITP

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## BACKGROUND

Thrombocytopenia is defined as low platelet count less than 150000 / microlitre which is attributed to variety of haematological and pathological disorders.<sup>1</sup> It can result from four different mechanisms like hypoproduative thrombocytopenia, hyperdestructive thrombocytopenia, abnormal platelet distribution and dilutional loss. The type of mechanism leading to thrombocytopenia can be determined with the help of platelet count and platelet indices such as mean platelet volume, platelet distribution width and plateletcrit.<sup>2</sup>

### Mean Platelet Volume (MPV)

MPV is the average size of platelet cells in the blood, it indicates that bone marrow is manufacturing platelets normally. Normal MPV ranges are approximately 6.8 to 10 fl. The analyser computes  $MPV (fl) = \text{plateletcrit} \times 100 / \text{platelet count} \times 10^9 / L$ .

### Platelet Distribution Width (PDW)

It represents the degree of heterogeneity of platelets, a measure of platelet anisocytosis.<sup>3</sup>

### Plateletcrit (Pct)

$Pct (\%) = MPV \times \text{platelet count}$ .

It is the product of the MPV and platelet count and by analogy with the haematocrit may be seen as an indication of circulating platelets in a unit volume of blood.<sup>3</sup> Thrombocytopenia is divided into four broad groups based on various mechanisms and they are: a reduction in platelet production (hypo-productive), increased platelet destruction (hyperdestructive), abnormal platelet distribution and dilutional loss.<sup>4</sup>

Hypoproduative thrombocytopenia may be either due to specific megakaryocyte suppression as in congenital mutation of thrombopoietin receptor, May-Hegglin syndrome, Wiscott-Aldrich syndrome, drugs, chemicals and viral infections, or due to generalized bone marrow failures as in haematological malignancies. Hyper-destructive thrombocytopenia is caused by Immune mechanisms as in idiopathic / primary autoimmune (ITP), Secondary (SLE, CLL, Lymphomas), infections (viral or parasitic), drug induced, post-transfusion purpura and disseminated intravascular haemolysis. Abnormal distribution of platelets occurs in splenomegaly and dilutional thrombocytopenia in massive blood transfusion.<sup>4</sup>

Platelet activation leads to swelling and changes in the platelet shape, thereby increasing the MPV and PDW. The determination of platelet count and platelet indices is made from the automated electronic Coulter machine. This study attempts to find the usefulness of platelet indices in the evaluation of thrombocytopenia and whether the platelet indices can point towards a preliminary diagnosis.

We wanted to study the utility of platelet count and platelet indices in evaluation of thrombocytopenia, evaluate platelet indices as a diagnostic tool in differentiating various types of thrombocytopenia and correlate platelet indices with bone marrow findings.

## METHODS

This was a prospective observational and case control study carried out in the haematology division of the Department of Pathology, at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, over a period of two years from June 2017 to May 2019. The study did not have any ethical issues. Written informed consent was taken from all the study subjects.

In the present study, the patients of thrombocytopenia were studied for their age-related aetiology and platelet volume parameters (MPV, PDW and Pct) obtained with automated blood cell counter for their clinical significance. Controls were normal healthy patients who came for routine master health check-up.

All patients with thrombocytopenia and pancytopenia were included in the study. Patients with pseudothrombocytopenia, patients who had received platelet transfusion in the last ten days and patients with coagulation disorders were excluded from the study.

Patients were categorised into two groups based on the aetiologies of thrombocytopenia as Group I (hyperdestructive thrombocytopenia) and Group II (hypoproduative thrombocytopenia). They were considered to have hyperdestructive if they had one or more clinical conditions like ITP and hypoproduative like in patients with megaloblastic anaemia, leukaemia and lymphoma.

Complete blood counts were performed on automated haematology five-part cell analyser (Mindray-5303 blood cell counter) using 2 ml of EDTA anticoagulated blood. The platelet count, the MPV, PDW and Pct as given by the automated blood cell counter were noted in all cases. In all cases, low platelet counts were confirmed by repeat analysis in the cell counter and by microscopic correlation with a Leishman-stained peripheral blood smear study and manual counting of the corresponding sample. As an ancillary part of the study, we carried out microscopic evaluation of the platelet size and abnormality in Leishman-stained peripheral blood films. The area selected for microscopic examination was the body part of the smear near the tail end where RBCs are in monolayer and their margins are just touching to each other. Bone marrow aspiration study (and biopsy wherever required) were done for all the sixty cases and the findings were noted.

The mean platelet parameters in hyperdestructive thrombocytopenia and hypoproduative thrombocytopenia were calculated and compared. The medical record files of these patients were retrieved from the Hospital Information System (HIS) for the determination of provisional or associated diagnosis made by their primary physicians. Data was entered into excel sheets and percentages, ratios, mean values and standard deviations were calculated.

**RESULTS**

A total of 60 patients were studied. In the present study, patients of thrombocytopenia with a platelet counts of less than 1,50,000 were studied for their aetiology in relation to age and for the platelet parameters as obtained by automated blood cell counter in order to assess if the platelet parameters (MPV, PDW and Pct) can help in differentiating hyperdestructive and hypoproductive thrombocytopenia.

| Age Range (in Years) | No. of Cases | Percentage (%) |
|----------------------|--------------|----------------|
| 11 to 20             | 6            | 10 %           |
| 21 to 30             | 6            | 10 %           |
| 31 to 40             | 14           | 23.3 %         |
| 41 to 50             | 18           | 30 %           |
| 51 to 60             | 9            | 15 %           |
| 61 to 70             | 7            | 11.6 %         |
| <b>Total</b>         | <b>60</b>    | <b>100 %</b>   |

**Table 1. Age Distribution in Hyperdestructive and Hypoproductive Case Groups**

The above table shows the maximum number of cases in the age group of 41 - 50 (30 %) followed by age group between 31 - 40 (23.3 %).

**Mean Age in the Groups**

In hyperdestructive thrombocytopenia group, the mean age and the standard deviation (Mean ± SD) were 45.33 ± 13.92 years. In hypoproductive thrombocytopenia group, the mean age and the standard deviation (Mean ± SD) were 40.51 ± 14.91 years. The combined mean age and SD for all the patients was 42.2 ± 14.63 years.

**Gender Wise Distribution in Hyperdestructive and Hypoproductive Thrombocytopenia**

In the hyperdestructive group there were 15 (71.4 %) males and 6 (28.5 %) females.

| Platelet Count   | Hyperdestructive Thrombocytopenia | Hypoproductive Thrombocytopenia | Total             |
|------------------|-----------------------------------|---------------------------------|-------------------|
| 8000 to 30000    | 8 (13.3 %)                        | 8 (13.3 %)                      | 16 (26.6 %)       |
| 31000 to 60000   | 8 (13.3 %)                        | 9 (15 %)                        | 17 (28.3 %)       |
| 61000 to 90000   | 5 (8.3 %)                         | 7 (11.67 %)                     | 12 (20 %)         |
| 91000 to 120000  | -                                 | 4 (6.6 %)                       | 4 (6.6 %)         |
| 120000 to 150000 | -                                 | 11 (18.3 %)                     | 11 (18.3 %)       |
| <b>Total</b>     | <b>21 (35 %)</b>                  | <b>39 (65 %)</b>                | <b>60 (100 %)</b> |

**Table 2. Distribution of Platelet Count in Hyperdestructive and Hypoproductive Thrombocytopenia**

In the hypodestructive group there were 21 (53.8 %) males and 18 (46.1 %) female patients. Male: female ratio was 2.5:1 and 1.1:1 in hyperdestructive thrombocytopenia and hypoproductive thrombocytopenia respectively.

The above table shows a greater decrease in platelet count in hyperdestructive thrombocytopenia. Aetiology-wise distribution of cases in hyperdestructive thrombocytopenia:

All the 21 (100 %) cases were of immune mediated thrombocytopenia (ITP) aetiology.

| Diagnosis             | No. of Cases (n) | Percentage (%) |
|-----------------------|------------------|----------------|
| Megaloblastic anaemia | 32               | 82.2 %         |
| Acute leukemia        | 04               | 10.2 %         |
| Lymphoma              | 01               | 2.5 %          |
| Post chemotherapy     | 01               | 2.5 %          |
| CML                   | 01               | 2.5 %          |
| <b>Total</b>          | <b>39</b>        | <b>100 %</b>   |

**Table 3. Aetiology Wise Distribution of Cases in Hypoproductive Thrombocytopenia**

Megaloblastic anaemia with 32 (82.2 %) cases was the commonest cause of hypoproductive thrombocytopenia.

|  | Hyperdestructive Thrombocytopenia | Cases        | Controls | P Value |
|--|-----------------------------------|--------------|----------|---------|
| Platelet count (mean ± S.D. × 10 <sup>3</sup> / l) | 43.5 ± 20.9                       | 238 ± 55.2   | 0.00001  |         |
| MPV (fl) (mean ± S.D.)                             | 11.51 ± 1.97                      | 9.75 ± 0.81  | 0.00078  |         |
| PDW (fl) (mean ± S.D.)                             | 16.67 ± 1.03                      | 15.69 ± 0.34 | 0.0002   |         |
| Pct (%) (mean ± S.D.)                              | 0.05 ± 0.04                       | 0.23 ± 0.06  | 0.00001  |         |

**Table 4. Standard Deviation for Platelet Count, MPV, PDW and Pct in Hyperproductive Thrombocytopenia Cases and Controls**

The above table shows high mean values in hyperdestructive cases than controls. P value shows high significance (< 0.00001).

|  | Hypoproductive Thrombocytopenia | Cases        | Controls | P Value |
|--|---------------------------------|--------------|----------|---------|
| Platelet count (mean ± S.D. × 10 <sup>3</sup> / l) | 77.25 ± 44.02                   | 240 ± 59.63  | 0.00001  |         |
| MPV (fl) (mean ± S.D.)                             | 8.34 ± 2.03                     | 9.67 ± 1.10  | 0.0010   |         |
| PDW (fl) (mean ± S.D.)                             | 14.68 ± 2.29                    | 15.74 ± 0.59 | 0.2502   |         |
| Pct (%) (mean ± S.D.)                              | 0.11 ± 0.12                     | 0.22 ± 0.06  | 0.00002  |         |

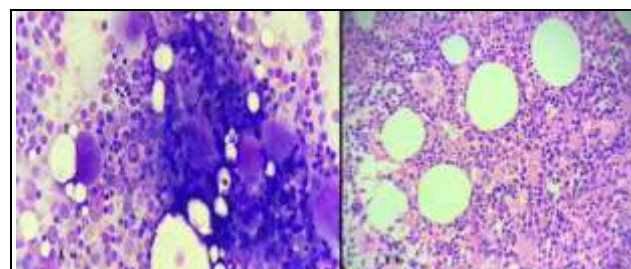
**Table 5. Standard Deviation for Platelet Count, MPV, PDW and Pct of Hypoproductive Thrombocytopenia Cases and Controls**

On comparing the platelet parameters (MPV, PDW and Pct) in the two groups of thrombocytopenia (cases and controls) lower mean MPV, PDW and Pct were seen in hypodestructive thrombocytopenia

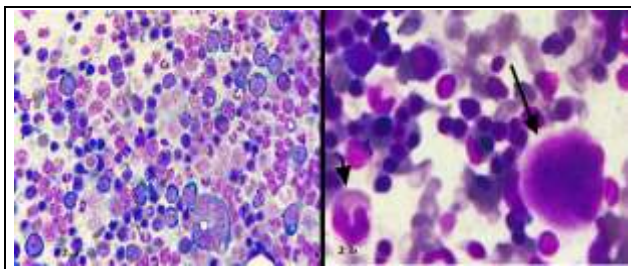
| Cause             | TP  | FP | TN | FN | Sensitivity | Specificity |        |
|-------------------|-----|----|----|----|-------------|-------------|--------|
| Hyper-Destructive | MPV | 17 | 04 | 18 | 03          | 85.0 %      | 81.8 % |
|                   | PDW | 6  | 15 | 21 | 0           | 100 %       | 58.3 % |
|                   | Pct | 1  | 20 | 2  | 21          | 4.5 %       | 9.0 %  |
| Hypo-Productive   | MPV | 11 | 28 | 39 | 0           | 100 %       | 58.2 % |
|                   | PDW | 33 | 06 | 38 | 1           | 97.0 %      | 86.3 % |
|                   | Pct | 5  | 34 | 0  | 39          | 11.3 %      | 0.00 % |

**Table 6. Sensitivity and Specificity of MPV in Hyperdestructive and Hypoproductive Thrombocytopenia**

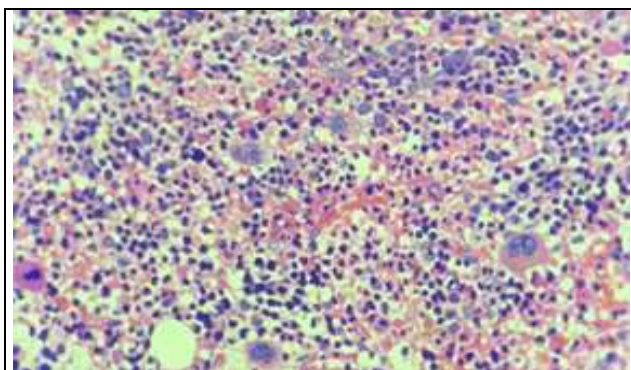
TP: True Positive, FP: False Positive, TN: True Negative, FN: False Negative



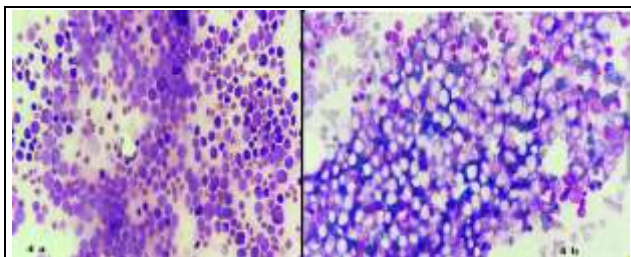
**Figure 1. a: Megakaryocyte Hyperplasia (ITP) (Leishman Stain, 400X) and 1 b: Bone Marrow Biopsy in a Case of ITP (H & E; 400X)**



**Figure 2. a: Bone Marrow Aspiration Showing Megaloblasts with Erythroid Hyperplasia (Leishman Stain, 40X) and 2 b: Dyspoietic Megakaryocyte (Arrow) and a Giant Band form (Giant Head) in a Case of Megaloblastic Anaemia (Leishman Stain, 100X)**



**Figure 3. Bone Marrow Biopsy in a Case of Megaloblastic Anaemia Showing Bony Trabeculae with Intervening Bone Marrow Elements with Erythroid Hyperplasia (H & E stain, 100X)**



**Figure 4. a: Bone Marrow Aspiration in a Case of AML Showing Blasts (Leishman Stain, 100X) and 4 b: Bone Marrow Imprint in a Case of AML Showing Predominantly Blasts (Giemsa Stain, 100X)**

This study also calculated the sensitivity and specificity of diagnosis of hyperdestructive and hypoproduative thrombocytopenia by comparing with the control group of patients. The variables for calculation for sensitivity and specificity was calculated by categorizing patients into true positive, true negative, false positive and false negative.

The p value for platelet parameters between the two groups: For platelet counts it was 0.00017, for MPV it was 0.00001, for PDW it was 0.00002 and was significant. For Pct it was 0.01755 and statistically not significant.

## DISCUSSION

Blood platelets are highly complex, anucleate cells derived from bone marrow megakaryocytes. In the present days, platelets have emerged as remarkable cells that possess the capacity to contract and secrete biologically active substances when stimulated appropriately.<sup>5</sup>

A well-prepared peripheral blood film provides basic information about the platelet number, size, distribution, and structure. Presence of artefact can cause misdiagnosis. Automated cell counters provide precise values and are being increasingly used in developed and developing countries.

In the present study, thrombocytopenia was studied for different types of aetiology by way of platelet parameters as obtained by automated blood cell counter and was assessed for their utility in the differential diagnosis of hyperdestructive and hypoproduative thrombocytopenia and was correlated by bone marrow examination findings.

The youngest patient was an 11-year-old and oldest patient was a 70-year-old. The maximum number of cases of 18 patients was seen in the age group of 41 - 50 years which accounts for 30 % of patients. Next followed by 14 cases in the age group of 31 - 40 years which accounted for 23.3 %. (Table 1)

In the present study, the mean age in hyperdestructive and hypodestructive thrombocytopenia was  $45.33 \pm 13.92$  and  $40.51 \pm 14.91$  years respectively. In Rajalakshmi et al<sup>6</sup> study, the mean age in hyperdestructive cases was 49.1 and in hypoproduative thrombocytopenia it was 72.3 years. In our study, the gender distribution in hyperdestructive thrombocytopenia was 2.5:1 which was more than double when compared to females, similar findings were seen in studies by Rajalakshmi et al<sup>6</sup> who observed male predominance with male: female ratio of 1.5:1. The gender distribution of male to female ratio in hypoproduative thrombocytopenia was 1.2:1.

The least platelet count seen in hyperdestructive thrombocytopenia was 8000 / microl with most (16 / 21) of the cases showing less platelet count between 8000 - 60000 / microl. The mean platelet count in hyperdestructive age group and in Controls was  $43.5 \pm 20.9$  and  $228 \times 10^3 \pm 55.2$  respectively, which showed a p value of 0.00001 which is statistically highly significant. This signifies that hyperdestructive thrombocytopenia is more severe in nature.

The platelet count in hypoproduative thrombocytopenia was between 120000 - 150000 / microl in most (11 / 39) cases which was significantly higher than the platelet count in hyperdestructive thrombocytopenia. Mean platelet count in hypodestructive thrombocytopenia was  $77.5 \times 10 \pm 44.02$ . It was observed that thrombocytopenia in hyperdestructive group is more marked as compared to hypoproduative group. (Table 2)

Present study showed immune thrombocytopenic purpura to be the cause for all the cases in hyperdestructive group. Similar findings were seen in Khaleed et al<sup>4</sup> and Numbenjapon et al<sup>7</sup> studies, Baig et al<sup>8</sup> wherein it was 100 % and 52 % respectively. A bone marrow examination can provide important information about the aetiology of thrombocytopenia. However, it is a painful and invasive procedure. Hence, the evaluation of platelet indices may guide in distinguishing the possible causes of thrombocytopenia, without directly going for the bone marrow procedure.<sup>8</sup> It is important to evaluate whether thrombocytopenia is a result of hyperdestruction of platelets or due to hypoproduction of platelets. Of the total 60 cases

of thrombocytopenia studied, hypoproliferative thrombocytopenia (65 % cases) was more common than hyperdestructive type. Similar observations were noted by various workers.<sup>1, 7, 8</sup> This has evoked much interest in platelet indices and many studies have suggested that MPV, PDW and PCT can be used as markers for the early diagnosis and categorization of thrombocytopenia to evaluate the activity of bone marrow in disorders of platelets.

The diagnosis of ITP is usually one of exclusion, requiring other causes of thrombocytopenia to be ruled out. Peripheral blood smear shows decreased platelet count with normal RBC and WBC. The bone marrow aspirate shows increased megakaryocytes and greatly diminished platelet production in the marrow. Further bone marrow has increased number of megakaryocytes per field which are hypolobated and small. Some megakaryocytes may also show vacuolations. Almost all the cases of ITP showed young, immature, more rounded, less polyploid megakaryocytes and very few mature platelet-producing megakaryocytes on morphology in the present study. (Figure 1a and 1b)

In the present study, 39 cases of hypoproliferative thrombocytopenia were noted of which, 32 cases were of megaloblastic anaemia (82.05 %), 4 cases of acute leukaemia (10.26 %), 1 case of lymphoma (2.56 %), 1 case of post chemotherapy (2.56 %) and 1 case was of Chronic myeloid leukemia / CML (2.56 %). (Table 3). Megaloblastic anaemia often presents as pancytopenia with accompanying low platelet counts. In a study by Shailaja et al from southern India, megaloblastic anaemia contributed to 39 % cases of pancytopenia.<sup>9</sup> In megaloblastic anaemia, bone marrow examination shows hypercellularity with increased erythropoiesis, with M : E ratio around 1:1). There is erythropoietic shift to left, more immature cells, with increase in proerythroblasts and basophilic erythroblasts. Megakaryocytes are usually larger with hyperlobated nuclei. Mature granulopoietic cells show hypersegmented nuclei. Giant metamyelocytes are also present.<sup>6</sup> Same findings were seen in our cases also. Ineffective thrombopoiesis has been proposed as a mechanism, where marrow shows normal to increased megakaryocytes. The findings of normal, increased and decreased megakaryocytes in our study support the hypothesis of both hypoproduction and ineffective thrombopoiesis in the causation of thrombocytopenia in megaloblastic anaemia. It is attributed this to bone marrow suppression and significant inhibition of nucleic acid synthesis in the megakaryocytes leading to hypolobated forms and dysplastic forms. (Figure 2a 2b and 3)

There were four (10.2 %) cases of acute leukemia. There was one (2.5 %) case of hypoproliferative thrombocytopenia due to Non-Hodgkin's lymphoma that had spread to bone marrow.

Mean platelet volume (MPV) index has been available since the 1970s. Recently other indices are also available, including platelet volume distribution width (PDW), plateletcrit (Pct), and platelet large cell ratio (PLCR).

MPV is the average size of platelets in the blood, it indicates the bone marrow is manufacturing platelets normally. While MCV for red cells is widely accepted and used for classifying anaemia; platelet indices have not been

routinely used by clinicians and their clinical usefulness has remained elusive.

The mean MPV was  $11.51 \pm 1.97$  and was more in hyper destructive group in comparison to control groups which was  $9.75 \pm 0.81$ . P value was significantly higher with 0.00001. The hypoproliferative group showed a mean of  $8.34 \pm 2.03$  which was significantly lower than hyperdestructive thrombocytopenia group of patients. The sensitivity and specificity of MPV to differentiate between types of thrombocytopenia was 80.9 % and 85.7 % respectively.

Numbenjapon et al<sup>7</sup> also evaluated MPV in discriminating hyperdestructive from hypoproliferative 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. Islam et al<sup>10</sup> and Kaito et al<sup>11</sup> showed a cut-off value of 8.4 - 12fl. Similarly, Khaleed et al<sup>4</sup>, Kaito et al<sup>11</sup>, Ntaios et al<sup>12</sup> and Shah et al<sup>13</sup> also reported an increased MPV in ITP patients when compared to hypoproliferative low platelets patients, signifying increased platelet production and they established cut off values ranging from 9 fl to greater than 11 fl.

The high MPV in platelet destruction is attributed to increase in circulating new younger and larger platelets showing that bone marrow is active.<sup>14</sup> Larger platelets are functionally, metabolically, and enzymatically more active than smaller ones.

Nelson et al<sup>15</sup> in their study observed that patients with destructive thrombocytopenia had larger platelets, and those with hypoproliferative type had platelet volume similar to patients with normal blood cell counts. In our study the mean MPV in hyperdestructive group was significantly higher than in hypoproliferative group. The difference between these values was statistically highly significant.

However, the reported mean MPV values are 8.1 fl and 9.8 fl in the UK study, 7.2 fl and 8.8 fl in the Taiwan and 7.3 fl and 8.62 fl in the Indian study in hypoproliferative and hyperdestructive patients, respectively.

The differences could be due to use of different types of automated haematology analysers. Kaito et al<sup>11</sup> had used Sysmex-XE2100 analyser and observed a mean MPV of 10.2 fl for aplastic anaemia patients and 12.2 fl for cases of ITP. Ntaios et al<sup>12</sup> also used Sysmex-XE2100 automated analyser in their study and they observed that the higher values of the platelet indices as compared to other studies can be attributed to a difference in haematology analysers.

Another explanation for the differences in the cut-off values of MPV in different studies can be the difference in the type of the haematological analyser used, as older automated analysers, 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. Moreover, they do not count large or giant platelets because they cannot be differentiated from red blood cells. Furthermore, many papers in the literature have shown that MPV is dependent on a number of variables, including the time of analysis after venipuncture, the anticoagulant used, the specimen storage temperature, and counter technologies.

Another possibility is a real authentic difference in the platelet indices among people from different geographic locations. Hong et al studied platelet indices in healthy Chinese adults using Sysmex XT 2100 from different areas and observed variations between regions. The MPV varied from  $10.30 \pm 0.80$  to  $12.36 \pm 1.34$ .<sup>16</sup>

**PDW**

The present study showed higher mean PDW in hyperdestructive thrombocytopenia than in hypoproductive thrombocytopenia which was  $16.67 \pm 1.03$  fl and  $14.68 \pm 2.29$  fl, respectively. The sensitivity and specificity of PDW for hyperdestructive study group was at 100 % and 58.33 % respectively and also showed a high significant p value of 0.0002 when compared to that of the hypoproductive thrombocytopenia study group.

The p value was also highly significant in hypoproductive thrombocytopenia. A few studies found that 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). Shah et al<sup>13</sup> found a higher PDW in hyperdestructive thrombocytopenia when compared to hypoproductive thrombocytopenia. Kaito et al<sup>11</sup> suggested that a PDW value of more than 17 fl and Ntaios et al<sup>12</sup> suggested a value between 15 and 17 fl discriminate these two subgroups. Various other authors like Khaleed et al,<sup>4</sup> Kaito et al,<sup>11</sup> Ntaios et al<sup>12</sup> and Shah et al<sup>13</sup> also reported a higher PDW in ITP patients as compared to hypoproductive thrombocytopenic patients. Negash et al<sup>17</sup> also observed in a similar study that all platelet indices were significantly higher in ITP patients (n=33) than in hypoproductive thrombocytopenic patients (n = 50).

The high PDW in hyperdestruction is due to younger platelets which are larger. As the active bone marrow sends out new platelets into circulation, the PDW increases. According to Islam et al<sup>10</sup> the PDW cut of value of < 14fl has 86.67 % sensitivity and 93.3 % of specificity and with PDW cut-off value of > 15fl, the sensitivity and specificity were 100 % and 83 % respectively.

According to Elsewefy et al<sup>2</sup> these differences in the cut off value could be due to difference in selection of patients and the difference in the type of haematology analyser used as older automated analysers, 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. Patients with Acute lymphoblastic leukemia (ALL) often present with pancytopenia or bicytopenia but may sometimes have normal peripheral blood cell counts. The platelet series is the earliest and the most consistently decreased series in ALL cases at the time of diagnosis and even at the time of relapse.<sup>4</sup> Symptoms and signs in ALL are generally consequences of bone marrow failure or due to infiltration of medullary or extramedullary sites by leukemia.<sup>2</sup> Decreased platelet counts are often seen at the time of diagnosis (median:  $48 - 52 \times 10^9 / L$ ), and megakaryocytes are decreased or absent.

**Plateletcrit**

Pct is a representation of volume percent of platelets and its value is not altered by severity of thrombocytopenia of either hypoproductive or hyperdestructive aetiology. In our study, the mean Pct in hyperdestructive group was  $0.05 \pm 0.04$ . The mean Pct in hypoproductive group which was  $0.11 \pm 0.12$ . The P value was 0.01755 which was not significant. Most of our patients fell into normal range which was not helpful in differentiating hyperdestructive and hypoproductive thrombocytopenia. Similar findings were observed by Kaito et al<sup>11</sup> and Khanna et al.<sup>17</sup> Elsewefy et al<sup>2</sup> in their study observed that the P-LCR index was significantly higher in patients with ITP compared to the control group and significantly lower in patients with myeloid insufficiency compared to the control group. We observed that PCT could not be taken as a diagnostic criterion for differentiating thrombocytopenic aetiology.

| Study                          | Type of Thrombocytopenia | Mean Platelet Count | Mean MPV    | Mean PDW    | P Value  |
|--------------------------------|--------------------------|---------------------|-------------|-------------|----------|
| Khaleed et al <sup>4</sup>     | Hyperdestructive         | 39                  | 12.33       | 15.61       | 0.000    |
|                                |                          | ±                   | ±           | ±           |          |
|                                | 15.3                     | 0.4                 | 0.7         |             |          |
|                                | 64.23                    | 10.08               | 13.83       |             |          |
| Rajalakshmi et al <sup>6</sup> | Hypoproductive           | ±                   | ±           | ±           | 0.0001   |
|                                |                          | 34.6                | 1.8         | 1.7         |          |
|                                | 61.4                     | 12.1                | 16.69       |             |          |
|                                | ±                        | ±                   | ±           |             |          |
| Islam et al <sup>10</sup>      | Hyperdestructive         | 0.31                | 1.1         | 13.5        | < 0.001  |
|                                |                          | ±                   | ±           | ±           |          |
|                                | 48.2 ± 0.3               | 11.8 ± 1.9          | 11.85 ± 1.9 |             |          |
|                                | 30.46 ± 14.1             | 12.0 ± 11.2         | 18.07 ± 2.5 |             |          |
| Parveen et al <sup>18</sup>    | Hypoproductive           | 38.73               | 9.75        | 11.75       | < 0.001  |
|                                |                          | ±                   | ±           | ±           |          |
|                                | 15.99                    | 1.1                 | 2.1         |             |          |
|                                | 79.6 ± 36.3              | 12.3 ± 0.9          | 19.3 ± 4.2  |             |          |
| Present Study                  | Hyperdestructive         | 75.9 ± 36.4         | 10.17 ± 1.3 | 19.7 ± 5.3  | < 0.0001 |
|                                |                          | 43.5 ± 20.9         | 11.5 ± 11.9 | 16.67 ± 1.0 |          |
|                                | 77.25 ± 44.0             | 8.34 ± 2.0          | 14.68 ± 2.2 |             |          |
|                                | ±                        | ±                   | ±           |             |          |

**Table 7. Comparison with Other Studies**

When compared to other similar studies the present study showed a mean platelet count of  $43.5 \pm 20.9$  in hyperdestructive and  $77.25 \pm 44.02$  in hypoproductive thrombocytopenia, respectively. MPV was  $11.5 \pm 11.97$  and  $8.34 \pm 2.03$  in hyperdestructive and hypoproductive thrombocytopenia. PDW was  $16.67 \pm 1.03$  and  $14.68 \pm 2.29$  in hyperdestructive and hypoproductive thrombocytopenia, respectively.

**CONCLUSIONS**

Platelet indices such as MPV, PDW show prominent increase in hyperdestructive type of thrombocytopenia and are accompanied usually by markedly low platelet counts, whereas, hypoproductive thrombocytopenia does not show marked increase in MPV or PDW and usually does not have severe thrombocytopenia. The plateletcrit does not show any variation in either of the thrombocytopenias. Platelet indices provide useful preliminary information about the type of thrombocytopenia even before bone marrow reports arrive. Also they neither need additional blood sample or additional time and do not incur any extra expense as they can be performed during routine blood cell counting.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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