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EVALUATION OF PLATELET INDICES IN HYPOPRODUCTIVE AND HYPERDESTRUCTIVE TYPE OF THROMBOCYTOPENIA

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Abstract

Introduction: Thrombocytopenia, defined as a platelet count below 150×10⁹/L, may result from either hypoproliferation or peripheral hyperdestruction of platelets. Differentiation between these causes traditionally requires bone marrow examination. However, advances in automated blood cell analyzers have enabled measurement of platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Plateletcrit (PCT), which may assist in evaluating thrombocytopenia.

Aim: To assess the utility of platelet indices in distinguishing between hypoproductive and hyperdestructive thrombocytopenia.

Materials and Methods: This cross-sectional study included 240 cases of thrombocytopenia, examination between January 2024 and March 2024. Patients were classified into hypoproductive (n=41) and hyperdestructive (n=199) groups. Platelet indices (MPV, PDW, PCT) and platelet counts were compared across the study groups using Student's t-test.

Results: The mean age was 38.81 years in the hypoproductive group and 39.79 years in the hyperdestructive group, with a male-to-female ratio of 1.05:1 and 1.45:1 respectively. When comparing the hypoproductive and hyperdestructive groups, only MPV showed statistically significant differences ($p \leq 0.05$). Of the platelet indices, only MPV demonstrated significant discrimination ($p = 0.02$) between the two groups.

Conclusion: MPV may serve as a useful preliminary test for distinguishing between hypoproductive and hyperdestructive thrombocytopenia, potentially reducing the need for invasive bone marrow aspiration and avoiding unnecessary platelet transfusions in patients with hyperdestructive thrombocytopenia

INTRODUCTION:

Platelets are the first line of defense that restrict blood loss caused by micro- and macrovascular damage because they aggregate and adhere to each other, preserving endothelial integrity. A platelet count of less than 150 × 109/L indicates thrombocytopenia. Thus, bleeding is a common complication of low platelet count because platelets play an important role in primary hemostasis, and it can be fatal in thrombocytopenic patients.[1,2] Thrombocytopenia is be caused by marrow hypoplasia, accelerated platelet breakdown, or splenic sequestration. The gold standard procedure for determining the reasons of thrombocytopenia is bone marrow examination, however it is invasive and costly. As a result, an alternative method should be developed as the first-line diagnostic procedure. The automated blood cell analyzer has recently enabled the assessment of the

cause of thrombocytopenia using various machine-derived parameters known as platelet indices, which include the mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), which are provided as part of a routine complete blood count.

Platelet indices are also bio-markers of platelet activation, which give diagnostic and prognostic clues in many clinical settings. MPV is a method of measuring platelet volume that determines the progenitor cells (megakaryocytes) in the bone marrow. When platelet synthesis is reduced, immature platelets become bigger and more active, and the MPV level rises, indicating greater platelet diameter, which can be utilized as a metric of platelet rate and activity. MPV, like mean corpuscular volume, measures average platelet size. [3,4,5].

PDW directly measures the variability in platelet size and reflects the heterogeneity in platelet morphology and has shown usefulness in establishing the differential diagnosis between reactive thrombocytosis and thrombocytosis associated with the myeloproliferative disease. Therefore, it helps in establishing a differential diagnosis of thrombocytopenia because of decreased production or platelet destruction.[3,4,6,7,8]PCT measures total platelet mass and is an excellent screening technique for detecting platelet quantitative abnormalities. The platelet-large cell ratio (P-LCR) is a measure of circulating bigger platelets and is used to track platelet activity. It is the ratio of bigger platelets to total platelet count, which is inversely related to platelet count but directly connected to MPV and PDW. Thus, platelet indices play an important role in distinguishing between hypo-productive and hyper-destructive thrombocytopenia. [9,10] Studies have indicated that MPV, PDW, and PCT have a good diagnostic association, which can be compared to findings from bone marrow studies. The current study seeks to determine the utility of these platelet indices (MPV, PDW, and PCT) derived from hematology analyser based on the impedance principle in distinguishing between hyper-destructive or hypoproductive causes of thrombocytopenia, for avoiding or delaying a request for bone marrow examination.

Materials and Methods

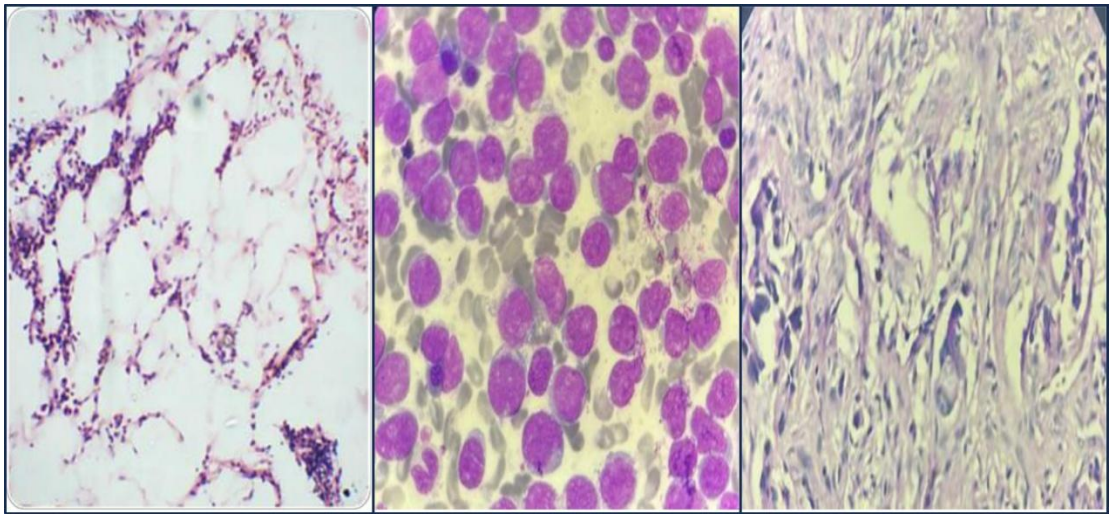
This is a hospital based cross sectional study which was done for a period of three months in clinical pathology laboratory in S.V.R.R.G.G.H , Tirupati. The study included individuals with a platelet count < 150 × 109/L, confirmed by a peripheral smear examination. The peripheral blood smears were stained with Leishmann's stain. The clinical information and demographics were obtained from case records and a case collection proforma. The study only included patients where the diagnosis was confirmed by either ancillary test or bone marrow examination. All cases of thrombocytopenia with a platelet count of less than 1,50,000/cu mm, with or without bone marrow investigations, cases with adequate clinico-hematological workup and an established clinical diagnosis, and only one sample from a single participant were considered. Pseudothrombocytopenia and patients who had undergone a blood or platelet transfusion during the previous 7 days were excluded.

Laboratory analysis

Blood samples for complete blood count (CBC) analysis were collected into 5 ml EDTA anticoagulant tubes and examined using Erba Elite 580 5-part automated hematology analyser within 2 to 4 hours of collection. This Coulter uses the impedance concept to measure RBCs and platelets. Three-level quality control samples were run twice daily. All our results were satisfactory. To rule out pseudo-thrombocytopenia and fragments of cells such as schistocytes, a Leishmann’s stained peripheral blood smear was reviewed. Based on clinical and laboratory information, the cases were broadly classified into two groups based on the cause of thrombocytopenia because of peripheral hyper-destruction (immune thrombocytopenic purpura, infections such as malaria, dengue, etc.) and a hypo-proliferative bone marrow (megaloblastic anemia, acute leukemia, aplastic anemia, myelodysplastic syndrome, multiple myeloma, marrow infiltration). In a few cases, the diagnosis was made by a bone marrow examination. An automated CBC with platelet count and indices (MPV, PWD, and PCT) was performed.

Statistical analysis

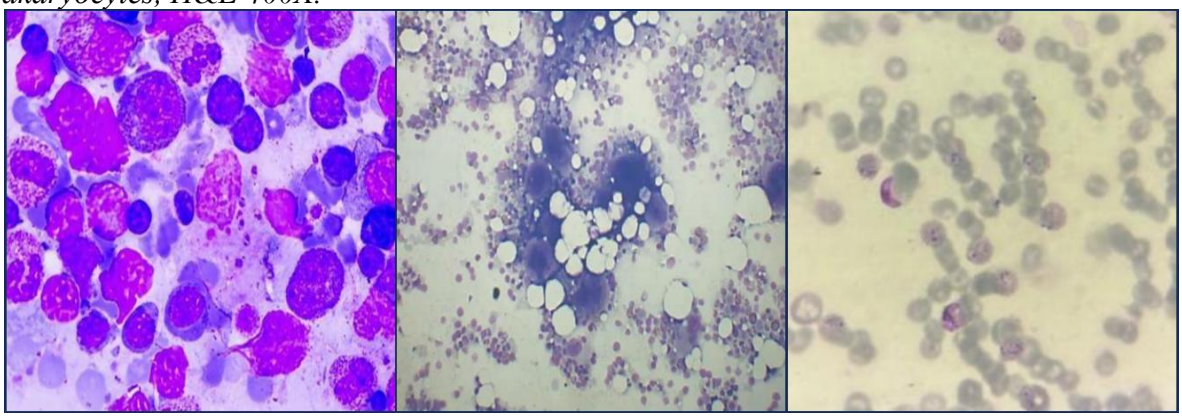
The data were statistically analyzed using SPSS version 21. The descriptive variables were reported as frequencies and percentages. The correlation test was used to determine the relationship between continuous variables. The Student t-test was performed to compare the two groups. P-values < 0.05 were considered statistically significant.



A\ B C

Figure 1: Hypoproliferative type of thrombocytopenia *:**A-**Hypoplastic marrow seen in Aplastic anemia, H&E 40X **B-** Packed marrow with blast cells in acute lymphoblastic leukemia, Leishman stain,1000X*

***C-**Lung adenocarcinoma metastasis in bone marrow biopsy causing decreased proliferation of megakaryocytes, H&E 400X.*



A B C

***Figure 2: Hyperdestructive type of thrombocytopenias**:**A-** L. D bodies seen in marrow in case of Leshmania**B-**proliferation of megakaryocytes in ITP**. C-** Gamatocytes and ring forms seen in RBC, PS in case of malaria falciparum.Leishman stain ,1000X,400X,1000X.*

Results

In the present study, a total of 240 cases were studied and the age range of patients was between 0 and 80 yr. The mean age of the patients was 38.81 and 39.79, respectively in hyperdestructive and hypoproductive groups. Among 240cases, 199 cases were sorted as hyperdestructive thrombocytopenia with male to female ratio 1.45:1.Fig -1 shows images of few examples of hypoproductive type of thrombocytopenia. In hypoproductive thrombocytopenia group there is slight male preponderance with male to female ratio 1.05:1 as shown in Table-1. Images of hyperdestructive type of thrombocytopenia are shown in Fig-2.

Causes of thrombocytopenia with their frequencies, mean values of platelet count, MPV, PDW and PCT in both hypoproductive and hyperdestructive types are depicted in [Table-2].
The comparison of mean values of platelet count, MPV, PDW and PCT between both the groups are shown in [Table-3] When platelet parameters of hypoproductive cases were compared with hyperdestructive cases only MPV showed significant ($p \leq 0.05$) correlation. Among the three platelet indices, only MPV showed significant correlation among both the groups.

Table-1 socio-demographic characteristics of patients and controls

Variable	**Number(n)**	**Sex**	
		Male	**Female**
Hypo-productive	41	21	20
Hyper-destructive	199	118	81
Total	240	139	101

Table-2- Causes of thrombocytopenia under each group with frequency and mean values of

Hypoproductive cases	Number of cases(%)	Plateletcount (mean±SD) (×109)	MPV(mean ±SD)(fl)	PDW(mean ±SD)(fl)	PCT(mean ±SD)%
Acute leukemia	16(66.6)	50.5 ± 32.7	9.93±1.34	13.8 ± 3.85	0.09 ± 0.15
Aplastic/hypoplastic marrow	7(6.25)	62.0 ± 32.9	11.0 ± 1.28	17.3 ± 3.20	0.08 ± 0.03
MDS	5(2.91)	45,600 ± 32,098	11.0 ± 1.51	17.5 ± 5.22	0.05 ± 0.03
Megaloblastic anemia	5(2.91)	57.2±18.5	9.90 ± 0.92	12.8 ± 3.62	0.06 ± 0.02
Myelofibrosis	3(1.25)	21,333 ± 577	10.7 ± 0.72	17.3 ± 4.59	0.02 ± 0.01
Multiple myeloma	2(0.83)	102,000 ± 15,556	8.25 ± 0.78	9.40 ± 0.01	0.08 ± 0.01
Lymphoma	2(0.83)	95,000 ± 57,983	8.95 ± 0.91	12.4 ± 2.76	0.09 ± 0.06
Metastatic cancer	1(0.48)	14 ,000 ± NaN	8.90 ± NaN	11.0 ± NaN	0.01 ± NaN
TOTAL	41				
Hyper destructive cases					
Dengue	67(27.9)	57,258 ± 27,587	10.4 ± 1.11	14.5 ± 3.64	0.07 ± 0.08
Liver failure	42(17.5)	62,268 ± 23,240	10.0 ± 1.12	14.1 ± 3.73	0.06 ± 0.02
Sepsis	31(12.9)	65,404 ± 37,192	10.5 ± 1.11	14.7 ± 3.86	0.07 ± 0.03
Malaria	23(9.58)	51,826 ± 31,223	10.2 ± 1.35	15.0 ± 5.00	0.06 ± 0.03

CKD	15(6.25)	56,800	± 34,256	10.1 ± 1.07	14.1 ± 3.78	0.06 ± 0.04
ITP	11(4.58)	71,000	± 33,094	10.0 ± 2.05	13.3 ± 3.97	0.07 ± 0.03
HELLP syndrome	6(2.5)	84,500	± 13,278	10.1 ± 0.48	15.8 ± 2.84	0.06 ± 0.03
Thalassemia	3(1.25)	56,000	± 50,478	10.0 ± 0.10	15.0 ± 4.00	0.04 ± 0.02
Leishmaniasis	1(0.48)	14,500	± NaN	8.70 ± NaN	11.10 ± NaN	0.03 ± NaN
TOTAL	199					

Table-3 comparison of mean platelet count and mean platelet indices between hypoproductive, hyper-destructive, and healthy controls

Variables	**Hypo-productive**	**Hyper-destructive**	**P value**
Platelet count	57807.69±34935.39	59594.72±29739.98	0.77
MPV (fl)	9.68±1.25	10.25±1.11	0.016
PCT (%)	0.08±0.12	0.06±0.05	0.22
PDW (fl)	13.06±3.60	14.42±3.79	0.08

Values are presented as mean±SD. Data were analyzed using Student's t-test. SD - standard deviation. MPV - mean platelet volume, PCT- plateletcrit, PDW - platelet distribution width'

DISCUSSION

One of the prevalent findings in various illness states is thrombocytopenia. The primary cause of this is essentially either diminished or compromised bone marrow. Either as a result of enhanced splenic sequestration, peripheral rapid degradation, or production. One It is challenging to determine the cause of the platelet count decline clinically. [1] In the past, bone marrow examinations, reticulated platelets, and platelet-associated IgG have been used to assess the cause of thrombocytopenia; however, these methods are expensive, intrusive, and not readily accessible. Numerous studies have recently evaluated the cause of thrombocytopenia using a variety of platelet indicators.

Indicators of platelets are widely accessible because these results are computed by the majority of automated haematology analyzers. In thrombocytopenia patients, we examined three platelet parameters—MPV, PDW, and PCT—to determine their significance, if any, in explaining the mechanism of low platelet count and to compare these results with other studies.

In the present study, hyperdestructive type (66.7%) of thrombocytopenia was more common than hypoproductive type (33.3%), similar to Parveen S and Vimal M, Reddy RS et al., Gulati I et al., [13,14,15], but in contrast to studies done by Xu RL et al[12], who reported hypoproductive type to be more common in their studies.

The mean age of hypoproductive type was 38.81 years and hyperdestructive type was 39.71 years which was similar to studies done by Rajashekar RB et al.,and Norrasethada L et al., who reported slightly higher means in hyperdestructive type than hypoproductive type [16,17].

The overall male to female ratio of all 240 cases was 1.37:1 with mild male predominance similar to Reddy RS et al., and Gulati I et al., studies [14,15]. The hyperdestructive thrombocytopenia was more common in males with male to female ratio of 1.45:1 similar to Xu RL et al., [12], Rajashekar RB et al., and Norrasethada L et al., [16,17] but in contrast with Elsewefy DA et al [11].

Among hypoproductive also noted a slight male predominance with male to female ratio of 1.05:1 similar to Xu RL et al. [12], and Norrasethada L et al., in validation set [12,17] but in contrast to Rajashekar RB et al., and Norrasethada L et al., in training set [16,17]

The mean platelet count was significantly higher in hyperdestructive group compared to hypoproductive with p=0.77 showing no significance similar to Elsewefy DA et al, Parveen S and Vimal M, Norrasethada L et al., and Kaito K et al., studies [11,13,17,3] but in contrast to Xu RL et al[12]., study (0.003).
The mean MPV was significantly higher in hyperdestructive type when compared to hypoproductive type (p=0.016) similar to studies done by Elsewefy DA et al., Parveen S and Vimal M, Xu RL et al., Norrasethada L et al., and Kaito K et al., [11,13,17,3]. In contrast, Nakadate H et al.,[18] reported no significant difference in MPV values between hyperdestructive type and hypoproductive type of thrombocytopenia. In hyperdestructive thrombocytopenias the bone marrow compensates by aggressively releasing larger, younger platelets, known as left shift. These platelets over the next 7-10 days shrinks and their life span is reduced.[13,19].
Using different automated haematology analyzers resulted in varying mean MPV values across studies. In most of the studies, the mean MPV was greater in hyperdestructive group than in hypoproductive thrombocytopenia [13-15].

In this study, mean PDW (0.22) and mean PCT(0.08) did not show any significance between hypoproductive and hyperdestructive groups similar to Elsewefy DA et al., Parveen S and Vimal M, Reddy RS et al., and Nakadate H et al., [11,13,14,18]. In contrast, Mowafy NM et al., reported positive correlation between PDW in Immune Thrombocytopenic Purpura (ITP) and non-ITP cases [20].
Additional studies are necessary to evaluate MPV in more specific diagnostic categories that are relevant to everyday clinical settings—such as patients who present with normal hemoglobin levels, no evidence of leukemic blasts, and normal white blood cell counts [3]. With the advent of advanced hematology analyzers employing different technologies—such as electrical impedance, optical light scatter, and fluorescent staining—it is important to assess each system separately. Establishing MPV cut-off values specific to each method will help enhance its reliability and usefulness in clinical decision-making.

Conclusion

MPV (Mean Platelet Volume) can be a helpful initial test in differentiating between hypoproductive and hyperdestructive thrombocytopenia. Utilizing MPV may reduce the need for invasive procedures such as bone marrow aspiration and help prevent unnecessary platelet transfusions in patients with hyperdestructive thrombocytopenia. It offers a non-invasive approach that could assist in patient evaluation and management. However, more research is required to determine a standardized MPV cut-off value specific to different haematology analysers. Establishing such benchmarks would enhance its clinical usefulness and support better decision-making while avoiding avoidable interventions.

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