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ASSESSING THE CLINICAL UTILITY OF PLATELET MORPHOMETRIC PARAMETERS IN IDENTIFYING UNDERLYING MECHANISMS OF THROMBOCYTOPENIA

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ABSTRACT:

Background: Proper management of thrombocytopenia requires a clear understanding of whether the root cause is diminished platelet synthesis or excessive breakdown. We investigated the significance of platelet indices as a non-invasive alternative to conventional diagnostics like bone marrow examination. This research aimed to assess whether Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet-Large Cell Ratio (P-LCR) can effectively differentiate between hypoproductive and hyperdestructive types of thrombocytopenia.

Methods: This study, carried out over 18 months at a tertiary care facility, prospectively and comparatively analyzed 300 patients presenting with thrombocytopenia (platelet count <150 × 10^9/L). Based on clinical, laboratory, and bone marrow findings, cases were divided into two group- hyperdestructive (n=250) and hypoproductive (n=50). An automated haematology analyzer was used to determine the platelet indices for each patient. Smear reviews were performed to rule out pseudothrombocytopenia, and cases affected by transfusion or pre-analytical delays were excluded. Data were analyzed using comparative statistics and ROC curve evaluation.

Results: Patients in the hyperdestructive group exhibited significantly higher values for MPV (11.1 ± 1.4 fL), PDW (17.8 ± 2.3%), and P-LCR (36.4 ± 5.6%) than those in the hypoproductive group (MPV 8.6 ± 1.2 fL, PDW 14.2 ± 1.9%, P-LCR 21.5 ± 4.3%), with all parameters showing strong statistical significance (p value < 0.001). Among the parameters analyzed, MPV demonstrated the greatest AUC in the ROC curve, suggesting it possesses the strongest diagnostic performance.

Conclusion: Platelet indices, particularly MPV, appear to be useful adjuncts in distinguishing between hypoproductive and hyperdestructive thrombocytopenia. When used alongside clinical and laboratory findings, these non-invasive markers may reduce dependence on bone marrow studies in selected cases.

Keywords: Thrombocytopenia, Platelet Count, Mean Platelet Volume, Platelet Distribution Width, Bone Marrow Examination, Automated Hematology Analyzer

INTRODUCTION

Thrombocytopenia, a low platelet level (less than150 × 10^9/L), is a prevalent haematological abnormality encountered across various clinical settings. Its etiologies are diverse, ranging from benign conditions to life-threatening disorders, and can broadly be categorized into two primary mechanisms: hypoproductive and hyperdestructive thrombocytopenia. [1] Based on the underlying cause, thrombocytopenia is divided into two main types. Hypoproductive thrombocytopenia occurs when the bone marrow fails to generate an adequate number of platelets, as seen in aplastic anaemia. On the other hand, hyperdestructive thrombocytopenia occurs when platelets are destroyed or consumed too rapidly in the body, a process often driven by immune responses. [2]

Traditionally, the diagnostic approach to thrombocytopenia has heavily relied on bone marrow examination to distinguish between these underlying mechanisms. Despite being the definitive diagnostic tool for identifying bone marrow pathologies, aspiration and biopsy procedures come with notable drawbacks. These procedures are invasive, costly, and come with serious risks like bleeding and infection. [3] This has led to a heightened focus on finding diagnostic alternatives that are non-invasive, economical, and widely available for the assessment of thrombocytopenia. Advancements in automated haematology analyzers have introduced the routine measurement of platelet indices, including Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet Large Cell Ratio (P-LCR), as part of complete blood count (CBC) panel. These indices provide insights into platelet morphology and production kinetics. [4] MPV provides the average platelet size, which helps us understand the dynamics of platelet production. When the body is destroying platelets too quickly (hyperdestructive states), the bone marrow responds by releasing large, immature platelets, causing a High MPV.On the other hand, when platelet production is impaired due to bone marrow dysfunction, as seen in hypoproductive conditions, the circulating platelets are generally smaller, yielding a low MPV. [5] The PDW represents a numerical assessment of platelet size diversity within a peripheral blood sample. Increased PDW values suggest a heterogeneous population of platelets, which can result from the release of both mature and immature platelets into circulation, a phenomenon commonly seen in conditions with heightened platelet destruction [6]. P-LCR indicates the proportion of platelets with greater volume, often reflecting newly produced, immature cells. A high P-LCR is therefore a key sign of increased platelet production, a typical reaction when platelets are being destroyed quickly in the bloodstream. [7]

Several studies have explored the usefulness of platelet indices in distinguishing the underlying causes of thrombocytopenia. Evidence suggests that patients with ITP typically exhibit elevated MPV, PDW, and P-LCR values in contrast to those with hypoproductive thrombocytopenia, such as in cases of aplastic anaemia [8]. Such evidence supports the role of platelet indices as helpful adjuncts during the preliminary workup of thrombocytopenia, with the potential to steer clinical choices and limit invasive testing.

Limitations include variability in reference ranges, influenced by factors such as age, sex, and analytical methodologies, that can affect the interpretation of these parameters. Additionally, overlapping values between different etiologies of thrombocytopenia may pose diagnostic challenges. While these platelet indices have their limitations, adding them to the diagnostic process offers clear advantages. It's a non-invasive, fast, and affordable way to assess thrombocytopenia, making it particularly beneficial in settings with limited medical infrastructure. [9] In light of their potential benefits and established limitations, the objective of the current research is to investigate whether MPV, PDW, and P-LCR can reliably differentiate between thrombocytopenia caused by decreased production and that resulting from increased destruction.

MATERIALS AND METHODS:

This study, designed as a prospective comparative investigation, was carried out from September 2024 to March 2025 and involved 300 individuals with thrombocytopenia after IEC clearance. Patients presenting to the hospital with thrombocytopenia (platelet count <150,000/mm³) and for whom bone marrow aspiration samples were received for evaluation formed the study population. Only those cases where complete clinical information, laboratory investigations, and platelet indices were available were included in the final analysis. All cases underwent detailed peripheral blood smear evaluation to exclude pseudothrombocytopenia due to platelet clumping. Such artefactual reductions in platelet counts, if noted, were excluded after smear confirmation. Moreover, recent transfusions were documented and those samples affected were excluded to avoid alteration in platelet indices.

Inclusion criteria:

- Patients of any age or sex with documented thrombocytopenia (platelet count <150 × 10⁹/L) were considered for the study.
- Availability of complete data of required platelet indices (MPV, PDW, and P-LCR).
- Availability of platelet indices including MPV, PDW, and P-LCR.
- Bone marrow aspiration submitted for evaluation with correlating clinical details.

Exclusion criteria:

- Cases where platelet indices were not reported by the hematology analyzer.
- Samples received more than three hours after collection or with clotting issues.
- Patients who received recent platelet transfusions which could influence platelet parameters.

Sample collection and laboratory evaluation:

Venous blood was collected into ethylenediaminetetraacetic acid (EDTA) tubes using aseptic techniques. All specimens were processed within three hours of phlebotomy to ensure the integrity of the

morphometric parameters. This specific time window was implemented to preclude pre-analytical artefacts, namely platelet swelling and shape distortion, which have the potential to compromise the validity of the final results.

The complete blood count (CBC), including platelet indices, was performed using an automated hematology analyzer, which reports the following platelet parameters:

- Platelet Count (PLT)
- Mean Platelet Volume (MPV): representing the average dimensions of platelets in the bloodstream
- Platelet Distribution Width (PDW): reflecting variability in platelet size.
- Platelet Large Cell Ratio (P-LCR): It quantifies the fraction of large, reticulated platelets present within circulating blood volume.

Peripheral smear review was performed for every case to validate platelet morphology and to corroborate automated findings. Additionally, data from relevant investigations including dengue NS1 and IgM/IgG serology, Widal test, sepsis markers, Quantitative Buffy Coat (QBC) for malaria, and other diagnostic workup were obtained from case records when available. All patients underwent bone marrow aspiration cytology, which was examined for megakaryocyte numbers, morphology, and marrow cellularity. Based on clinical, laboratory, and bone marrow findings, cases were stratified into two major categories:

1. Hyperdestructive thrombocytopenia: patients exhibiting adequate or increased megakaryocytes in the marrow, suggestive of peripheral destruction or consumption. These included cases of immune thrombocytopenia (ITP), sepsis, viral infections (notably dengue), and hypersplenism.
2. Hypoproductive thrombocytopenia: patients with reduced megakaryocyte numbers or suppressed hematopoiesis, indicative of impaired platelet production. Common causes included aplastic anemia, marrow suppression, and infiltration by hematological malignancies.

Statistical analysis:

Data were analyzed using SPSS version 21.0. Baseline characteristics of the cohort were summarized with descriptive statistics, and continuous variables (MPV, PDW, P-LCR) were summarized using the mean and corresponding standard deviation. To assess differences in mean platelet indices across the hypoproductive and hyperdestructive categories, an Independent Samples t-test was performed, while Analysis of Variance (ANOVA) was utilized for multi-group comparisons. The magnitude and trend of correlation observed between platelet count and the morphometric indices were determined by calculating Pearson's correlation coefficient. The efficacy of each platelet index as a diagnostic marker was evaluated by generating ROC curves. The Area Under the Curve (AUC) was computed from each curve to serve as a metric of diagnostic accuracy. The selection of optimal cutoff points was guided by Youden's Index, for which the associated performance characteristics—namely sensitivity, specificity, PPV, and NPV—were documented. A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS:

Among the 300 participants with thrombocytopenia, 250 were identified as having a hyperdestructive etiology, while 50 were attributed to hypoproductive causes. The assessments included demographic distribution, etiology, platelet count range, and platelet indices to determine usefullness of platelet morphometric parameters in differentiating two thrombocytopenic categories.

Demographic analysis is shown in Table 1. Patients with hypoproductive thrombocytopenia demonstrated a greater average age (42.1 ± 14.3 years) compared to those with hyperdestructive thrombocytopenia (34.7 ± 12.5 years). The hyperdestructive group also contained a higher percentage of females (56.8%) than the hypoproductive group (44.0%). Across the entire study, the sex distribution showed a slight female predominance, with 54.7% female and 45.3% male participants.

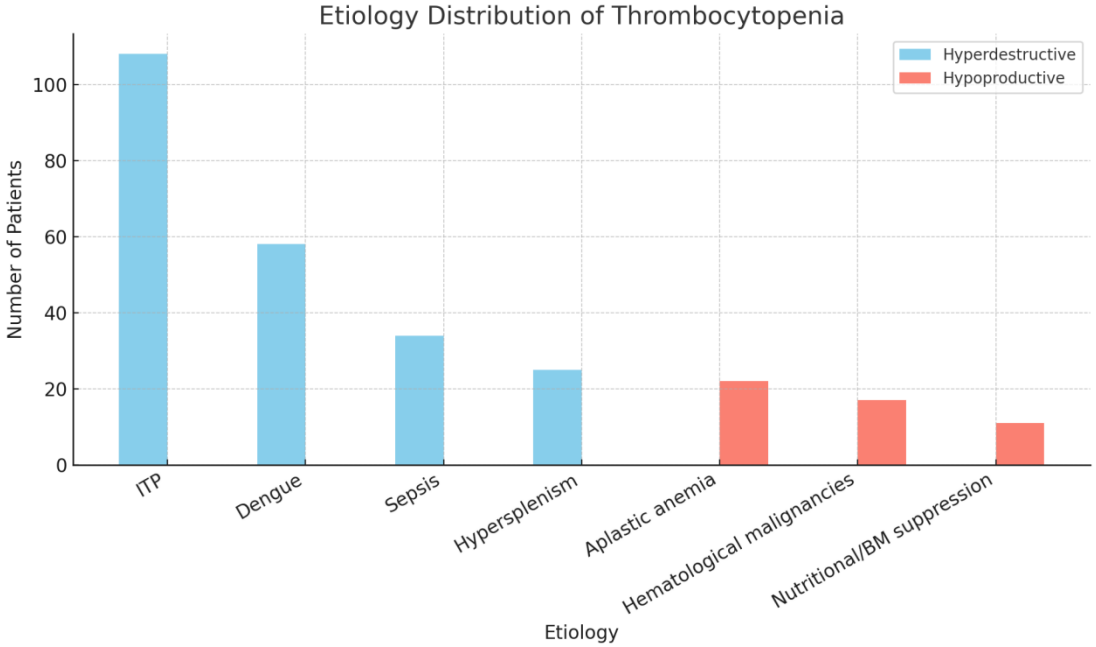
Table 1: Distribution of Demographics and Etiologies within the Thrombocytopenia Population

Parameter	**Hyperdestructive (n = 250)**	**Hypoproductive (n = 50)**	**Total (n = 300)**
Age (mean ± SD)	34.7 ± 12.5 years	42.1 ± 14.3 years	36.0 ± 13.5
Sex			
- Male	108 (43.2%)	28 (56.0%)	136 (45.3%)
- Female	142 (56.8%)	22 (44.0%)	164 (54.7%)
Common Etiologies			

- Immune Thrombocytopenia (ITP)	108 (43.2%)	0	108
- Dengue fever	58 (23.2%)	0	58
- Sepsis-associated	34 (13.6%)	0	34
- Hypersplenism	25 (10.0%)	0	25
- Aplastic anemia	0	22 (44.0%)	22
- Hematological malignancies	0	17 (34.0%)	17
- Nutritional/BM suppression	0	11 (22.0%)	11

The most common etiologies for hyperdestructive thrombocytopenia (Figure 1) were Immune Thrombocytopenia (ITP) (43.2%), dengue fever (23.2%), sepsis-associated thrombocytopenia (13.6%), and hypersplenism (10.0%). In contrast, hypoproductive thrombocytopenia was predominantly attributed to aplastic anaemia (44.0%), haematological malignancies (34.0%), and bone marrow suppression due to nutritional deficiencies (22.0%).

Figure 1: Etiology distribution among the hyperdestructive and hypodestructive groups



Analysis of platelet count stratification revealed statistically significant differences in distribution across the two subgroups. (Table 2). A markedly higher percentage of individuals in the hypoproductive group had platelet counts under 20 × 10^9/L compared to those in the hyperdestructive group (36.0% vs. 19.2%, p = 0.002). Conversely, in the highest platelet count stratum (101–150 × 10^9/L), the hyperdestructive group contained a markedly greater percentage of patients (14.0% vs. 4.0%, p = 0.048). Statistical analysis revealed no meaningful differences between the two groups in the platelet ranges of 21–50 × 10^9/L (p = 0.591) and 51–100 × 10^9/L (p = 0.093).

As shown in Table 3, notable variations in platelet indices were observed between the two groups. A key finding was the mean platelet count, which was significantly higher in the hyperdestructive cohort (65.7 ± 31.5 × 10^9/L) in comparison with the hypoproductive cohort (42.3 ± 25.2 × 10^9/L, p < 0.001).

Table 2: Distribution according to platelet count range with p-value

Platelet Count Range (×10^9/L)	**Hyperdestructive (n = 250)**	**Hypoproductive (n = 50)**	**p-value**
< 20	48 (19.2%)	18 (36.0%)	0.002
21 – 50	95 (38.0%)	21 (42.0%)	0.591
51 – 100	72 (28.8%)	9 (18.0%)	0.093
101 – 150	35 (14.0%)	2 (4.0%)	0.048

Our analysis revealed significant elevations in all three morphometric indices for the hyperdestructive group as opposed to the hypoproductive group (p < 0.001 for all; Figure 2). The higher mean MPV (11.1

± 1.4 fL vs. 8.6 ± 1.2 fL) reflects increased platelet turnover. The increased PDW (17.8 ± 2.3% vs. 14.2 ± 1.9%) indicates greater size heterogeneity consistent with a mixed population of platelets. Finally, the elevated P-LCR (36.4 ± 5.6% vs. 21.5 ± 4.3%) points to a compensatory production of large, immature platelets in response to peripheral destruction.

Figure 2: Analysis of platelet indices between study groups

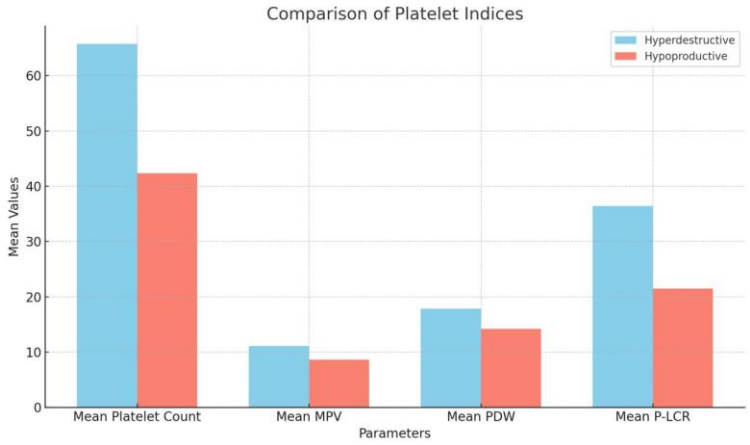
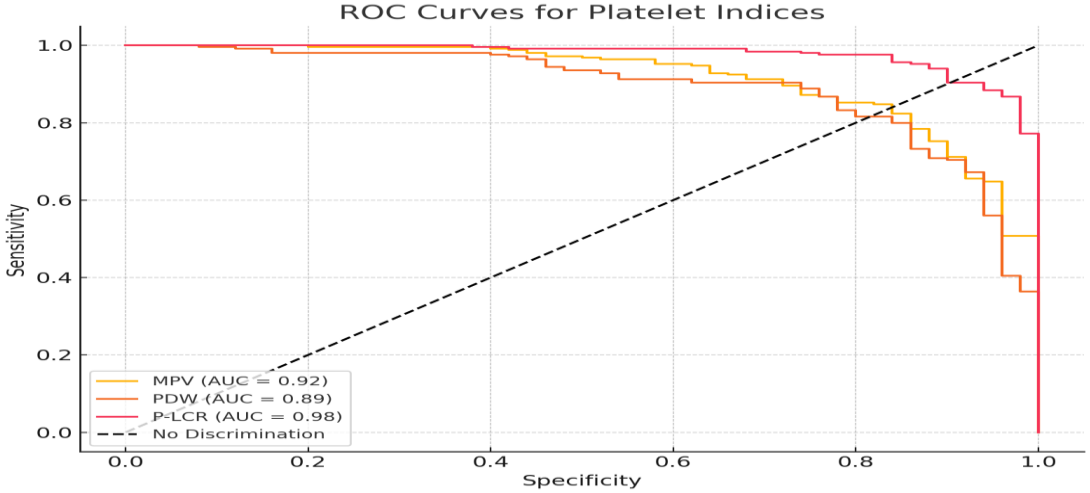


Table 3: Differential Analysis of Platelet Parameters in Hyperdestructive and Hypoproductive Thrombocytopenia

Parameter	**Hyperdestructive (n = 250)**	**Hypoproductive (n = 50)**	**p-value**
Mean Platelet Count (×10⁹/L)	65.7 ± 31.5	42.3 ± 25.2	< 0.001
Mean MPV (fL)	11.1 ± 1.4	8.6 ± 1.2	< 0.001
Mean PDW (%)	17.8 ± 2.3	14.2 ± 1.9	< 0.001
Mean P-LCR (%)	36.4 ± 5.6	21.5 ± 4.3	< 0.001

A comparative analysis revealed significant differences in platelet count, MPV, PDW, and P-LCR across the hyperdestructive and hypoproductive groups ($p < 0.001$ for all), confirming their diagnostic potential. To quantify and rank this potential, Receiver Operating Characteristic (ROC) curve analysis was performed. The resulting Area Under the Curve (AUC) values indicated that P-LCR had the highest diagnostic accuracy (AUC = 0.98), followed by MPV (AUC = 0.92) and PDW (AUC = 0.89). Based on these findings, P-LCR is suggested to be the most powerful discriminator between the two thrombocytopenic etiologies.

Figure 4: ROC analysis of platelet parameters for etiological classification of thrombocytopenia



DISCUSSION:

Thrombocytopenia, a condition defined by a diminished platelet count, stems from numerous etiologies that are principally categorized based on their underlying mechanism: hypoproductive, involving insufficient platelet synthesis, and hyperdestructive, entailing accelerated platelet clearance.
Differentiating between these two categories is crucial for guiding appropriate clinical management. Conventional diagnostic evaluation has historically relied upon invasive procedures, such as bone marrow examination. In contrast, advancements in automated hematology analyzers permit the routine measurement of platelet indices (MPV, PDW, and P-LCR), which are potential non-invasive aids for this diagnostic differentiation. [10] The analysis revealed notable disparities in platelet indices across the study groups. In particular, individuals with hyperdestructive thrombocytopenia exhibited significantly elevated mean values of MPV, PDW, and P-LCR compared to those diagnosed with hypoproductive thrombocytopenia. These results corroborate the findings of previous studies and underscore the potential of these indices as diagnostic markers. [11,12]
MPV represents the calculated average size of platelets found in the bloodstream. Larger platelets are typically younger and more reactive, often released in response to increased peripheral destruction.In our study group, we found a clear difference in average MPV. A notable increase in mean MPV was observed in the hyperdestructive group (11.1 ± 1.4 fL) relative to the hypoproductive group (8.6 ± 1.2 fL). Numbenjapon et al. observed a comparable trend, establishing an MPV cut-off of ≥8.8 fL to diagnose hyperdestructive thrombocytopenia, with a sensitivity of 77% and specificity of 89%. [13] Similarly, Bhat et al. reported a mean MPV of 9.56 ± 1.34 fL in hyperdestructive cases, significantly higher than 8.45 ± 1.30 fL observed in hypoproductive cases. [14] By measuring the variability in platelet volume, the PDW provides a direct assessment of the heterogeneity inherent in the platelet population. An increased PDW suggests a mix of young and old platelets, often seen in conditions with heightened platelet turnover. Our analysis revealed a statistically significant elevation in PDW for the hyperdestructive cohort (17.8 ± 2.3%) in comparison with the hypoproductive cohort (14.2 ± 1.9%). This result supports the work of Jeon K et al., which similarly identified increased PDW as a feature of destructive thrombocytopenia. [15] The P-LCR parameter quantifies the proportion of platelets within the peripheral blood that exceed a volume threshold of 12 fL.
Elevated P-LCR values are indicative of increased thrombopoiesis, often as a compensatory mechanism for peripheral destruction. In the present study, the hyperdestructive group demonstrated a significantly higher mean P-LCR (36.4 ± 5.6%) than the hypoproductive group (21.5 ± 4.3%). A comparable increase in P-LCR among patients with destructive thrombocytopenia was also documented by Arshad et al., supporting the present results, thereby underscoring its utility in the differential diagnosis of this condition. [16] Furthermore, a study by Celik et al. highlighted the prognostic significance of P-LCR in myelodysplastic syndromes, with lower P-LCR associated with worse overall survival. [17]
Receiver Operating Characteristic (ROC) curve analysis in our study underscored MPV as the most effective discriminator between thrombocytopenia types. This finding is consistent with previous research, including the work of Obuchowskiet al., which similarly underscored the diagnostic utility of MPV in differentiating thrombocytopenic etiologies. Consequently, the routine incorporation of platelet indices such as MPV, PDW, and P-LCR into complete blood count panel offers an economical and non-invasive approach for the initial evaluation of thrombocytopenia, potentially reducing the clinical requirement for invasive procedures like bone marrow biopsy. [18]
While our findings support the utility of platelet indices in differentiating thrombocytopenia types, certain limitations must be acknowledged. Factors such as anticoagulant type, sample handling, and analyzer variability can influence measurements . Moreover, while these indices provide valuable insights, they should complement, not replace, comprehensive clinical assessments and other diagnostic modalities.

CONCLUSION:

To conclude, this study highlights the clinical utility of platelet indices, especially MPV in distinguishing the underlying causes of thrombocytopenia. The integration of these parameters into standard hematological evaluations has the potential to augment diagnostic accuracy and better inform clinical management. Nevertheless, additional extensive studies involving larger populations are necessary to confirm and generalize these observations and to establish universally accepted, standardized cutoff values for routine clinical application.

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