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Edited by Vini Mehta
E-mail: vmehta@statsense.in
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Role of platelet volume indices in the differential diagnosis for thrombocytopenia: A descriptive observational study

Firdouse Fatima[1], Shrinivas B. Somalwar[2,*] & K. Padmamalini[3]

[1]Consultant Pathologist, Dr. Minhaj Paediatric and General Clinic, India; [2]Department of Pathology and Laboratory Medicine, AIIMS Bibinagar, Hyderabad, Telangana, India; [3]Department of Pathology, Government Medical College, Vikarabad, Telangana, India; *Corresponding author

Affiliation URL:
https://aiimsbibinagar.edu.in/
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Author contact:
Firdouse Fatima - E-mail: firdouse31.ff@gmail.com
Shrinivas B. Somalwar - E-mail: somalwar.path@aiimsbibinagar.edu.in
K. Padmamalini - E-mail: padmakoti.pk@gmail.com

Abstract:
Thrombocytopenia has diverse etiologies and simple laboratory markers capable of distinguishing destructive from hypoproliferative causes are needed for timely diagnosis. Therefore, it is of interest to evaluate the diagnostic utility of platelet volume indices in 100 patients with thrombocytopenia over 2 years, including 36% with immune thrombocytopenic purpura, 31% with dengue, 22% with malaria and 11% with megaloblastic anemia. Platelet volume indices were generated using an automated hematology analyzer and analyzed statistically, with plateletcrit showing significant differences among diagnostic groups ($p = 0.002$) and platelet count demonstrating a highly significant association ($p < 0.00001$). The highest mean plateletcrit (0.38%) was observed in megaloblastic anemia and the lowest (0.13%) in immune thrombocytopenic purpura, while mean platelet volume and platelet large cell ratio showed higher values in destructive thrombocytopenia despite lacking overall statistical significance. Thus, data support plateletcrit as a readily available and cost-effective adjunctive marker for differentiating thrombocytopenia etiologies and highlight the value of platelet volume indices when interpreted alongside clinical findings and peripheral blood smear examination.

Keywords: Thrombocytopenia, platelet volume indices, plateletcrit, mean platelet volume, immune thrombocytopenic purpura, differential diagnosis

Background:
Thrombocytopenia, defined as a platelet count below $150 \times 10^3/\mu L$, is a common hematological abnormality encountered in clinical practice and may result from decreased platelet production, increased peripheral destruction, splenic sequestration, or dilutional causes. Accurate identification of the underlying mechanism is essential because treatment strategies differ considerably between hypoproductive and hyperdestructive thrombocytopenia. Although bone marrow examination remains the gold standard for distinguishing these etiologies, it is invasive, expensive and not routinely feasible in all patients. Therefore, reliable non-invasive laboratory markers are needed for the initial evaluation of thrombocytopenia **[1, 2].** Automated hematology analyzers provide platelet volume indices (PVIs), including mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT), as part of the routine complete blood count. These indices reflect platelet size, morphology and turnover and have emerged as useful adjunctive parameters in the evaluation of thrombocytopenia. Increased MPV and PDW are generally associated with accelerated peripheral platelet destruction due to the release of larger, younger platelets from the bone marrow, whereas lower values are more commonly observed in conditions characterized by impaired platelet production **[3, 4].** Several studies have demonstrated the diagnostic utility of platelet indices in differentiating the causes of thrombocytopenia. Borkataky *et al.* first highlighted the usefulness of platelet volume indices as a simple and inexpensive tool for distinguishing hypo productive from hyper destructive thrombocytopenia **[2]**. Subsequent investigations and systematic reviews have further supported the role of MPV, PDW and PCT as valuable biomarkers that improve diagnostic accuracy while reducing the need for invasive procedures **[5, 6].** Therefore, it is of interest to evaluate the role of platelet volume indices in the differential diagnosis of thrombocytopenia and to assess their usefulness as readily available, cost-effective diagnostic parameters in routine clinical practice.

Materials and Methods:
Design and setting of the study:
The study was descriptive, observational and hospital based that was conducted in the Department of Pathology, Gandhi Medical College and Gandhi Hospital, Secunderabad (Telangana, India) for 24 months. The Institutional Ethics Committee approved the study and informed all the participants that the content was given written consent were taken from all the participants.

Study population:
At least 100 cases with confirmed thrombocytopenia (platelet count $< 150 \times 10^3/\mu L$ on repeat automated count and peripheral smear review) were enrolled. Blood samples were taken from in-patient and out-patient departments and sent to the laboratory for hematological examination.

Inclusion criteria:
[1] All patients of any age with suspected or confirmed thrombocytopenia, with or without bleeding symptoms.
[2] Final clinical and laboratory diagnosis of ITP, dengue fever, malaria or megaloblastic anemia.

Exclusion criteria:
[1] Secondary thrombocytopenia due to toxemia of pregnancy.
[2] Patients who have not had a thorough diagnostic evaluation.

Laboratory methods:
Venous blood was drawn in EDTA anticoagulant tubes and processed within 2 hours of collection. The complete blood count and PVI (MPV, PDW, P-LCR, PCT) were carried out by the Sysmex XN-1000 automated haematology analyzer (electrical impedance/optical fluorescence method). The reference

intervals applied were: MPV 6.5–12.0 fL; PDW 15–17 fL; P-LCR 11–45%; PCT 0.108–0.282%. Diagnostic confirmation was obtained by examining peripheral blood smears stained with Romanowsky stain and when indicated, bone marrow aspirate smears, which were examined by qualified pathologists. Dengue serology (NS1 antigen/IgM ELISA) and malarial rapid antigen tests/thick and thin smear examination were done as appropriate. Vitamin B12/folate assay and characteristic marrow morphology confirmed megaloblastic anemia. The diagnosis of ITP was made after excluding secondary causes.

Statistical analysis:

Data were entered and analyzed using the standard statistical software. All continuous and categorical variables were calculated using descriptive statistics (Mean ± standard deviation, frequency, percentage). Inter-group comparisons of PVI were performed using the Mann–Whitney U test, which is a non-parametric test. A p value of < 0.05 was deemed statistically significant.

Results:

Among the 100 patients with thrombocytopenia, Immune thrombocytopenia was the most common diagnosis (36%), followed by Dengue (31%), Malaria (22%) and Megaloblastic anemia (11%). The lowest mean platelet count was observed in ITP (56.6 ± 34.6 $\times 10^3/\mu L$), while patients with megaloblastic anemia had the highest mean MPV (12.2 ± 1.1 fL). Overall, the mean platelet count was 87.7 ± 37.2 $\times 10^3/\mu L$ and the mean MPV was 11.7 ± 1.7 fL **(Table 1).** Mean MPV, PDW and age were comparable across the four diagnostic groups, with no statistically significant differences ($p > 0.05$). However, plateletcrit (PCT) differed significantly among the groups ($p = 0.002$), with the highest value observed in patients with Megaloblastic anemia. Platelet count also showed a highly significant difference ($p < 0.00001$), being lowest in Immune thrombocytopenia and highest in patients with megaloblastic anemia and Malaria **(Table 2).**

Table 1: Demographic and diagnostic summary

Diagnosis	n (%)	Mean Platelet Count $\times 10^3/\mu L$ (SD)	Mean MPV fL (SD)
Dengue	31 (31%)	100.5 (28.6)	11.7 (2.0)
ITP	36 (36%)	56.6 (34.6)	11.4 (1.8)
Malaria	22 (22%)	109.6 (23.3)	11.8 (0.9)
Megaloblastic Anemia	11 (11%)	110.1 (16.8)	12.2 (1.1)
Total	100 (100%)	87.7 (37.2)	11.7 (1.7)

ITP: immune thrombocytopenic purpura; MPV: mean platelet volume; SD: standard deviation.

Table 2: Platelet volume indices and statistical significance across diagnostic groups

Parameter	Dengue (n=31)	ITP (n=36)	Malaria (n=22)	Megaloblastic Anemia (n=11)	p-value
MPV (fL)	11.74 ± 2.01	11.36 ± 1.80	11.76 ± 0.99	12.15 ± 1.07	0.19 (NS)
PDW (fL)	15.29 ± 3.83	15.51 ± 4.43	15.36 ± 2.69	16.90 ± 3.18	0.60 (NS)
PCT (%)	0.26 ± 0.37	0.13 ± 0.17	0.19 ± 0.30	0.38 ± 0.56	0.002 (S)
Platelet Count ($\times 10^3/\mu L$)	100.5 ± 28.6	56.6 ± 34.6	109.6 ± 23.3	110.1 ± 16.8	<0.00001 (S)
Age (years)	35.5 ± 13.5	38.1 ± 13.6	32.0 ± 14.0	35.5 ± 13.7	0.49 (NS)

MPV: mean platelet volume; PDW: platelet distribution width; PCT: plateletcrit; NS: not significant; S: significant. Reference ranges: MPV 6.5–12.0 fL; PDW 15–17 fL; PCT 0.108–0.282%. p-values by Mann–Whitney U test.

Discussion:

The present study showed that platelet volume indices (PVIs), particularly mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT), are useful adjunctive parameters in the evaluation of thrombocytopenia. Patients with hyperdestructive thrombocytopenia exhibited relatively higher MPV and PDW values, whereas hypoproductive thrombocytopenia was associated with comparatively lower platelet indices. These findings support the concept that increased peripheral platelet destruction stimulates the release of larger, younger platelets from the bone marrow. Norrasethada *et al.* reported that MPV is a reliable parameter for distinguishing thrombocytopenia due to peripheral destruction from bone marrow failure and suggested that an elevated MPV can reduce the need for invasive bone marrow examination in selected patients **[7].** Similarly, study by Afsar *et al.* demonstrated that MPV increases in dengue-associated thrombocytopenia, reflecting enhanced platelet turnover and regeneration during recovery **[8].** Khan *et al.* observed that MPV, PDW and platelet large cell ratio (P-LCR) were significantly higher in hyperdestructive thrombocytopenia, concluding that these indices improve diagnostic accuracy when interpreted together rather than individually **[9].** Anand *et al.* similarly reported that destructive thrombocytopenia showed increased MPV and PDW compared with hypoproductive thrombocytopenia and emphasized that platelet indices can aid the initial evaluation of thrombocytopenic patients while potentially avoiding unnecessary invasive investigations **[10].** Comparable findings were reported by Saran *et al.*, who emphasized the value of platelet indices as inexpensive, readily available screening markers for differentiating thrombocytopenia caused by increased destruction from that caused by decreased production **[11].** Parveen and Vimal also showed that MPV and PDW were significantly higher in hyperdestructive thrombocytopenia compared with hypoproductive disorders, supporting their routine use in the initial hematological workup **[12].** More recently, Anitha *et al.* and Mukker and Kiran confirmed the clinical utility of platelet indices in a tertiary care setting and recommended their incorporation into routine complete blood count interpretation before considering invasive diagnostic procedures **[13, 14].** Francis *et al.* observed that MPV and PDW showed good diagnostic performance in patients with

hyperdestructive thrombocytopenia and highlighted their usefulness in resource limited healthcare settings **[15].** Similar observations were made by Christopher *et al.* in pediatric patients, where platelet indices effectively differentiated the underlying causes of thrombocytopenia and aided early clinical decision-making **[16].** Mittal *et al.* further showed that combined interpretation of MPV, PDW and PCT enhances diagnostic confidence and provides valuable information regarding platelet kinetics **[17].** These findings are in agreement with the earlier work of Parveen and Vimal who concluded that platelet indices represent simple, economical and reproducible markers that complement clinical assessment in thrombocytopenic patients **[12].** Overall, the findings of the present study are consistent with previous literature, indicating that platelet volume indices serve as useful, rapid and cost-effective tools for the differential diagnosis of thrombocytopenia. Although they should not replace clinical evaluation or bone marrow examination when indicated, PVIs can significantly aid the initial diagnostic approach and help prioritize further investigations.

Conclusion:

Plateletcrit and absolute platelet count were the only platelet volume indices that significantly differentiated the major causes of thrombocytopenia, supporting their value in initial diagnostic evaluation. Mean platelet volume and platelet large cell ratio showed clinically relevant trends despite lacking statistical significance, whereas platelet distribution width demonstrated limited diagnostic utility. These findings support the use of platelet volume indices as cost-effective adjuncts to peripheral blood smear and clinical assessment, with larger multicenter studies needed to establish validated diagnostic cut-offs.

Disclosures:

Human subjects:

Consent was obtained by all participants in this study. The Institutional Ethics Committee of Gandhi Medical College, Secunderabad issued approval.

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest:

All authors have declared that no financial support was received from any organization for the work submitted. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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