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IMPLICATIONS OF PLATELET INDICES IN EVALUATION OF THROMBOCYTOPENIA IN A TERTIARY CARE HOSPITAL

Dr. S Bhavadeep [1], Dr. Srikanth Vadlamudi [2], Dr. Addapu Dharaneedhar [3], Hima Bindhu [4], Dr. Ramya R [5]* and Dr. Vijay Kumar P [6]

[1,6] Professor, Department of Pathology, Apollo Institute of Medical Sciences and Research Chittoor.
[2,3] Assistant professor, Department of General Medicine, Apollo Institute of Medical Sciences and Research Chittoor.
[4] 3rd year MBBS, Apollo Institute of Medical Sciences and Research Chittoor.
[5] Professor, Department of Physiology, Apollo Institute of Medical Sciences and Research Chittoor. *Corresponding Author E-mail: ramyamayudhar@gmail.com

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Abstract

INTRODUCTION: Platelet count below normal values defines thrombocytopenia but do not reveal the underlying pathomechanism. Advances in automated blood cell analysers have made it possible to measure various parameters. Platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Large Cell Ratio (P-LCR), Plateletcrit (PCT) may provide some important information. Platelet indices can be derived from the platelet distribution curve obtained from impedance or optical methods. **OBJECTIVE**: In this study we aim to assess the sensitivity and specificity of these indices and set cut off values that aid in the diagnosis thrombocytopenia cause. **METHODOLOGY:** An observational cross sectional study was done in district government headquarters hospital, Chittoor in the 60 patients with thrombocytopenia who are admitted during the period of 2 months of study period. Various platelet parameters like MPV, PDW, P-LCR were studied in these patients.**CONCLUSION:** In distinguishing between the causes of thrombocytopenia that is hypo productive or hyper destructive platelet parameters play important role. These platelets indices are easily available with the help of automated haematology analysers and can be reduced the need of costly and invasive tests like bone marrow studies for evaluation of thrombocytopenia.

Keywords: Platelets, MPV, PDW, P-LCR, PCT.

INTRODUCTION

Platelets are small, granulated bodies that aggregate at the sites of vascular injury. They lack nuclei and are 2-4 microns in diameter. They normally have a half life of 4 days. The normal count of the platelets 1.5 -3.5 lakhs/ microliter. Reduction in the platelet number constitutes an important cause of generalized bleeding. A count less than 1,50,000 platelets/microliter is known as thrombocytopenia. Platelet counts the range of 20,000 – 50,000 platelets /microliter can aggravate post traumatic bleeding and platelet count less than 20,000 platelets /microliter may associate with spontaneous mucocutaneous bleeding and life threatening spontaneous intracranial hemorrhage or gastrointestinal bleeding rapidly.

Thrombocytopenia can arise as a result of multiple conditions. This can be divided into four mechanism related categories that are: a reduction in platelet production (hypo productive thrombocytopenia), increase in the platelet consumption and destruction (hyper destructive thrombocytopenia), splenic sequestration and dilution.

Hypo-productive thrombocytopenia is either specific megakaryocyte suppression as in congenital mutation of c-MPL thrombopoietin receptor, May-hegglin syndrome and drugs, chemicals and viral infections, or generalized bone marrow failures in hematological malignancy (leukemia, aplastic anemias, myeloma, myelodysplasia,

myelofibrosis), secondary to cytotoxic drugs and radiotherapy, infections (human immunodeficiency virus (HIV), cytomegalovirus(CMV), hepatitis B and C), alcohol excess and megaloblastic anemia.

Hyper-destructive thrombocytopenia is either immune as in idiopathic/ primary autoimmune (ITP), Secondary (systemic lupus erythematous, chronic lymphocytic leukemia, lymphoma), Infections (HIV, Hepatitis Band C, malaria), Drug induced (rifampicin, penicillin's, sulphonamides, Heparin, quinine), Post-transfusion purpura and Disseminated intravascular haemolysis (DIC).

The mainstay in evaluation of these patients of thrombocytopenia lies in the identification of the cause, whether hyperdestructive or hypo productive, based on which the management will differ. Bone marrow aspiration or biopsy still remains the primary investigation in such cases. The main limitation of the bone marrow evaluation is its invasive procedures with risk of bleeding diatheses in cases of severe thrombocytopenia. [1] Therefore, it is not recommended as first line diagnostic procedure. Of late, the automated blood analysers (Mindray) as made it possible to assess the cause of thrombocytopenia through various machine derived parameters called platelet indices, which include the mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT), which are provided as a part of routine complete blood count. These parameters form a preliminary, non-invasive mode of evaluating the cause for thrombocytopenia. [2]

Platelet indices are also bio markers of platelet activation, which give diagnostic and prognostic clues in many clinical settings. MPV is the mode of measured platelet volume and determines the progenitor cell (megakaryocytes) in the bone marrow. When platelet production is decreased, young platelets become enlarged and more active, so the MPV level increases, which indicate the increased platelet diameter, which can be used a marker of platelet rate and platelet activation. Therefore, MPV is the parameter that measures the average platelet size as the mean corpuscular volume does for red blood cells (RBCs). [3-5] 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. [3,4,6-8] PCT is a measure of total platelet mass and is an effective screening tool for detecting platelet quantitative abnormality. Platelet-large cell ratio (P-LCR) is an indicator of circulating larger platelets and used to monitor platelet activity. It is the ratio of larger platelets to total platelet count, and it is inversely related to platelet count and directly related to MPV and PDW. Therefore, platelet indices have a significant role in discrimination between hypo productive and hyper destructive thrombocytopenia. [9,10]

Studies have shown that MPV, PDW, and P-LCR have a good diagnostic correlation which can compare to findings from the study of the bone marrow. The present study attempts to find the usefulness of these indices (MPV, PDW and PCT) derived from the machine on the principle of impedance in discriminating between hyper destructive or hypo productive causes of thrombocytopenia and to assess their sensitivity and specificity and thereby help in avoiding or at least delaying a request for bone marrow examination.

Aım And Objectıves

The purpose of this study is to evaluate the cut-off values for the MPV, PDW, PCT, and P-LCR indices in order to determine their sensitivity and specificity in aiding in the diagnosis of thrombocytopenia.

METHODOLOGY

1. **Study Type**: An observational cross sectional study.
2. **Study Centre:** District government headquarters hospital – Chittoor.
3. **Study Population:** The patients with thrombocytopenia who are admitted in the government hospital in the period of 2 months of research.
4. **Inclusion Criteria:** The patient with thrombocytopenia the age of above 20 years admitted in the government hospital Chittoor during the study period.
5. **Exclusion Criteria:**
    - Patients of age below 20 year to avoid age related changes in platelet indices.
    - Those suffering from myelodysplastic syndrome. (MDS)
    - Individuals suffering from autoimmune conditions like juvenile rheumatoid arthritis, vitiligo, systemic lupus erythematosus (SLE), Type 1 diabetes mellitus (DM), and anti-platelet medications that cause thrombocytopenia.
    - Those utilizing antiplatelet medications and those with thrombocytopenia-causing medications.
6. **Sample size:** 104 patients.
7. **Study period:** September 2023 to November 2023.

Statıstıcal Analysıs

Data was entered in to Microsoft Excel and analysis was done by using IBM Statistical Package for the Social Sciences (SPSS) version 21 (IBM Corp., Armonk, NY, USA). Categorical variables were presented in proportions and percentage and continuous data was presented in mean and standard deviation (SD) or as median and interquartile ranges depending on the normality of the data, after testing normality of the data by using Shapiro-wilk normality test. Associations between categorical variables were tested using chi-square test and continuous variables were tested using t-test. For all the comparisons probability value of less than 0.05 will be considered statistically significant.

Observatıon And Results

Table 1: Gender distribution of Thrombocytopenia patients

Gender	Number	Percentage (%)
Male	62	59.6%
Female	42	40.4%
Total	104	100%

Out of 104 thrombocytopenia patients studied, 62 (59.6%) were male and remaining 42 (40.4%) were female.

Table 2: Age distribution of Thrombocytopenia patients

Age Category	Number (n = 104)	Percentage (%)
11 to 20 years	12	11.5%
21 to 30 years	26	25%
31 to 40 years	20	19.2%
41 to 50 years	19	18.3%
51 to 60 years	13	12.5%
61 to 70 years	9	8.7%
71 to 80 years	5	4.8%

Out of 104 thrombocytopenia patients studied, most of the cases reported between the age group of 21 to 30 years [n=26; 25%], followed by 31 to 40 years [n=20; 19.2%], 41 to 50 years [n=19; 18.3%], 51 to 60 years [n=13; 12.5%], 11 to 20 years [n=12; 11.5%], 61 to 70 years [n=9; 8.7%], and 71 to 80 years [n=5; 4.8%]. Mean age of the patients was 40.5 ± 16.66 years and ranges between 14 years to 80 years.

Table 3: Severity of thrombocytopenia among study participants

Severity of thrombocytopenia	Number (n = 104)	Percentage (%)
Mild (≥100 to <150 x 10^9/L)	9	8.7%
Moderate (>50 to <100 x 10^9/L)	65	62.5%
Severe (≤50 x 10^9/L)	30	28.8%

Out of 104 thrombocytopenia patients studied, around 9 (8.7%) patients had mild thrombocytopenia with a thrombocyte count between ≥100 to <150 x 10^9/L, 65 (62.5%) patients had moderate thrombocytopenia with a thrombocyte count between >50 to <100 x 10^9/L, and remaining 30 (28.8%) patients had severe thrombocytopenia with a thrombocyte count ≤50 x 10^9/L. Mean thrombocyte count of patients was 68.6 x 10^9/L, and ranges between 18 to 150 x 10^9/L.

Table 4: Association of severity of thrombocytopenia with Mean Platelet Value

Severity of thrombocytopenia	Mean Platelet Value (MPV)		p-value
	Mean	SD	
Mild	9.73	1.37	0.159; NS
Moderate	9.81	1.09	
Severe	9.35	0.89	

SD = Standard deviation; NS = Not Significant

Mean platelet value for mild thrombocytopenia patients was 9.73 ± 1.37 fL, for moderate thrombocytopenia patients was 9.81 ± 1.09 fL, and for severe thrombocytopenia patients was 9.35 ± 0.89 fL. The difference in MPV values between groups was not significant.

Table 5: Association of severity of thrombocytopenia with Platelet Distribution Width (PDW)

Severity of thrombocytopenia	Platelet Distribution Width		p-value
	Mean	SD	
Mild	16.2	1.41	0.115; NS
Moderate	14.4	3.16	
Severe	15.5	3.04	

SD = Standard deviation; NS = Not Significant

Mean platelet distribution width for mild thrombocytopenia patients was 16.2 ± 1.41 fL, for moderate thrombocytopenia patients was 14.4 ± 3.16 fL, and for severe thrombocytopenia patients was 15.5 ± 3.04 fL. The difference in PDW between groups was not significant.

Table 6: Association of severity of thrombocytopenia with Platelet-crit (PCT)

Severity of thrombocytopenia	Platelet-crit (PCT)		p-value
	Median	Inter-quartile range (IQR)	
Mild	0.117	0.093 – 0.123	<0.001; S
Moderate	0.075	0.066 – 0.088	
Severe	0.034	0.025 – 0.041	

S = Significant

As the platelet-crit is not distributed normally, values were presented in median and inter-quartile ranges and association was tested using Kruskal-Wallis test. Median platelet-crit of mild thrombocytopenia patients was 0.117% (IQR: 0.093% – 0.123%), for moderate thrombocytopenia patients was 0.075% (IQR: 0.066% – 0.088%), and for severe thrombocytopenia patients was 0.034% (IQR: 0.025% – 0.41%). The difference in platelet-crit between groups was significant and significantly higher in mild thrombocytopenia patients than moderate and severe thrombocytopenia patients.

Table 7: Association of severity of thrombocytopenia with Platelet Large Cell Ratio (P-LCR)

Severity of thrombocytopenia	Platelet Large Cell Ratio (P-LCR)		p-value
	Mean	SD	
Mild	24.4	6.53	0.128; NS
Moderate	26.5	6.21	
Severe	23.8	5.60	

SD = Standard deviation; NS = Not Significant

Mean platelet large cell ratio for mild thrombocytopenia patients was 24.4 ± 6.53%, for moderate thrombocytopenia patients was 26.5 ± 6.21%, and for severe thrombocytopenia patients was 23.8 ± 5.60%. The difference in platelet large cell ratio between groups was not significant.

Table 8: Association of Gender with severity of Thrombocytopenia

Gender	Thrombocytopenia			p-value
	Mild	Moderate	Severe	
Male	7 (11.3%)	38 (61.3%)	17 (27.4%)	0.502; NS
Female	2 (4.8%)	27 (64.2%)	13 (31%)	
Total	9 (8.7%)	65 (62.5%)	30 (28.8%)	

NS = Not Significant

Out of 62 male thrombocytopenia patients studied, 7 (11.3%) patients had mild thrombocytopenia, 38 (61.3%) patients had moderate thrombocytopenia and remaining 17 (27.4%) patients had severe thrombocytopenia. On the other hand out of 41 female thrombocytopenia patients studied, 2 (4.8%) patients had mild thrombocytopenia, 27 (64.2%) patients had moderate thrombocytopenia and remaining 13 (31%) patients had severe thrombocytopenia. The association between gender and severity of thrombocytopenia was not significant.

Table 9: Association of Age with severity of Thrombocytopenia

Age category	Thrombocytopenia			p-value
	Mild	Moderate	Severe	
11 to 30 years	3 (7.9%)	25 (65.8%)	10 (26.3%)	0.748; NS
31 to 50 years	3 (7.7%)	24 (61.5%)	12 (30.8%)	
51 to 70 years	2 (9.1%)	14 (63.6%)	6 (27.3%)	
>70 years	1 (20%)	2 (40%)	2 (40%)	
Total	9 (8.7%)	65 (62.5%)	30 (28.8%)	

NS = Not Significant

Out of 38 thrombocytopenia patients with age between 11 to 30 years, 3 (7.9%) patients had mild thrombocytopenia, 25 (65.8%) patients had moderate thrombocytopenia and remaining 10 (26.3%) patients had severe thrombocytopenia. In 39 thrombocytopenia patients with age between 31 to 50 years, 3 (7.7%) patients had mild thrombocytopenia, 24 (61.5%) patients had moderate thrombocytopenia and remaining 12 (30.8%) patients had severe thrombocytopenia. In 22 thrombocytopenia patients with age between 51 to 70 years, 2 (9.1%) patients had mild thrombocytopenia, 14 (63.6%) patients had moderate thrombocytopenia and remaining 6 (27.3%) patients had severe thrombocytopenia. In 5 thrombocytopenia patients with age above 70 years, one (20%) patient had mild thrombocytopenia, 2 (40%) patients had moderate thrombocytopenia and remaining 2 (40%) patients had severe thrombocytopenia. The association between age categories and severity of thrombocytopenia was not significant.

DISCUSSION

Thrombocytopenia may result from aberrant splenic pooling, hypoproduction, or hyperdestruction of platelets. There is a chance that both intracorpuscular and extracorpuscular anomalies. Among the main reasons why platelet deterioration has increased include immunological process whereby antibodies are produced against platelets are the reason of their early demise. Platelet hypoproduction could be caused by bone marrow suppression, such as leukemias, aplastic anemia, cancerous invasion, chemotherapy, and exposure to radiation. Unusual in vivo or aberrant pooling dispersion of the overall platelet mass, which is nearly normal, may result in thrombocytopenia as well. This particular thrombocytopenia is observed in a number of illnesses linked to Splenomegaly. [11, 12] In order to achieve initial hemostasis, platelets are essential. An automated hematology analyzer can now determine platelet indices including MPV, PCT, and PDW by the help of recent technological advancements. [13]

One such metric that provides a measure of platelet size and, indirectly, activity is MPV. In a healthy individual, the MPV typically ranges from 8.4 to 12.1 fL. Greater MPV is indicative of larger platelets, which are more metabolically and enzymatically active than smaller platelets. [14] The degree of cell heterogeneity is represented by PDWs such as Red cell distribution width. Research on PDW and MPV has demonstrated a high degree of specificity and sensitivity in the diagnosis of thrombocytopenia. [15, 16] PDW typically falls between 8.3 and 14.0 fL. The predicted PDW values are impacted by platelet activation, which results in an increase in the quantity and size of pseudopodia. [14] P-LCR is an additional platelet activity marker that calculates the proportion of all circulating platelets larger than 12 fL in volume. Usually, it falls between 15% and 35%. [17] The platelet count, or PCT, is a

measurement of the amount of blood that platelets occupy. It is expressed as a percentage, with a typical range of 0.22–0.24%. [18]

Automation has disadvantages of its own, as demonstrated by routine work where the device does not always record the platelet indices. Situations with red cell fragmentation, EDTA-induced pseudo thrombocytopenia, and severe thrombocytopenia are often observed circumstances that cause these issues. It is impossible to draw a platelet histogram and record indices under these circumstances. As a result, their application may be restricted in some situations. [14] A review of 45 publications on platelet indices conducted in 2020 by Pogorzelska et al. [17] revealed that the calibrations of analyzers and the various techniques used in hematology analyzers (optical, impedance) do affect the results of measurements, underscoring the necessity of standardization in platelet indices measurement. It is not necessary to employ bone marrow testing as the first-line diagnostic method for thrombocytopenia because it is an intrusive procedure. Together with the platelet counts, the full blood counts produced by the automated analyzer values for platelet indices are also provided. [19]The synthesis and activation of platelets influence these platelet indicators. Therefore, in order to begin therapy as soon as possible, platelet indices can be utilized to classify the source of the thrombocytopenia.

In our study Out of 104 thrombocytopenia patients studied, 62 (59.6%) were male and remaining 42 (40.4%) were female similar to Francis et al,. showing predominance of male population (80/126). Most of the cases reported between the age group of 21 to 30 years [n=26; 25%], followed by 31 to 40 years [n=20; 19.2%], >40 years [n= 58; 55.8%] where the mean age of the patients was 40.5 ± 16.66 years and ranges between 14 years to 80 years. Around 9 (8.7%) patients had mild thrombocytopenia with a thrombocyte count between ≥100 to <150 x 10^9/L, 65 (62.5%) patients had moderate thrombocytopenia with a thrombocyte count between >50 to <100 x 10^9/L, and remaining 30 (28.8%) patients had severe thrombocytopenia with a thrombocyte count ≤50 x 10^9/L.

In view of Mean Platelet Value (MPV), Platelet Distribution Width (PDW) and Platelet Large Cell Ratio (P-LCR), we found in our study that there was no significant with thrombocytopenia. Comparably to patients with moderate and severe thrombocytopenia, there was a significant (<0.001) difference in plateletcrit across the groups for mild thrombocytopenia patients, similarly vani mittal et al,. shows relationship of plateletcrit with thrombocytopenia shows a direct relationship which was also significant. [20] Giovanetti et al,. [21] Wiwanitkit et al,. [22] Adibi et al.[23] Naina et al,. [24] demonstrate that plateletcrit aids in the differentiation of thrombocytopenia.

CONCLUSION

Platelet indices could be useful in postponing or preventing needless, invasive bone marrow testing. A more useful metric that can be used to distinguish between the hyper-destructive and hypo-productive causes of thrombocytopenia is plateletcrit, which is statistically significant. Because platelet indices are similar to RBC indices and can be used to determine the likely pathophysiology of thrombocytopenia, clinicians should investigate them in all cases of thrombocytopenia. Thus, platelet indices such as plateletcrit, which were obtained from hematology analysers in this study, serve as a reliable diagnostic tool for thrombocytopenia cases.

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