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Original Research Article

DIAGNOSTIC VALUE OF PLATELET INDICES IN DIFFERENTIATING THE CAUSES OF THROMBOCYTOPENIA: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Thrombocytopenia has diverse aetiologies, broadly involving increased peripheral platelet destruction or consumption and impaired bone marrow production. Differentiating these mechanisms is important for appropriate management. Platelet indices obtained from automated haematology analysers may provide useful information regarding platelet production and turnover. The objective is to evaluate the diagnostic value of platelet indices, including mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet-large cell ratio (P-LCR) and immature platelet fraction (IPF), in differentiating the causes of thrombocytopenia.

Materials and Methods: A hospital-based cross-sectional study was conducted among 60 adults with thrombocytopenia. Participants were classified into peripheral platelet destruction/consumption and reduced platelet production groups based on clinical and laboratory evaluation. Platelet count and platelet indices were recorded. Differences between groups were analysed, and receiver operating characteristic analysis was performed to assess diagnostic performance.

Results: Thirty-two participants had peripheral platelet destruction/consumption and 28 had reduced platelet production. MPV, PDW, P-LCR and IPF were significantly higher in the peripheral destruction/consumption group. IPF demonstrated the best discriminatory performance, with an area under the curve of approximately 0.90. At a cut-off of >7.0%, IPF showed 87.5% sensitivity and 82.1% specificity. Combined platelet indices correctly classified approximately 85% of participants.

Conclusion: Platelet indices, particularly IPF, may provide a useful, rapid and minimally invasive adjunct for differentiating major mechanisms of thrombocytopenia.

Keywords: Thrombocytopenia, platelet indices, mean platelet volume, platelet distribution width, immature platelet fraction.

INTRODUCTION

Thrombocytopenia is a common haematological abnormality characterised by a platelet count below 150 × 10⁹/L and may arise from diverse mechanisms, including impaired platelet production, increased peripheral destruction or consumption, and abnormal sequestration. The clinical presentation ranges from an incidental laboratory finding to severe bleeding, depending on the degree and underlying cause of thrombocytopenia. Accurate identification of the aetiology is therefore important for appropriate treatment and prognostication. However, several causes may present with similar platelet counts, making differentiation based solely on platelet count difficult.[1,2] Traditionally, evaluation of thrombocytopenia involves clinical assessment, peripheral blood smear examination, biochemical

investigations and, in selected cases, bone marrow examination. Bone marrow examination can help distinguish hypoproductive thrombocytopenia from peripheral platelet destruction, but it is invasive, relatively costly and may not be required in every patient. Consequently, there is increasing interest in laboratory parameters that are routinely generated by automated haematology analysers and can provide information regarding platelet production and turnover.[3,4] Platelet indices, including mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) and platelet-large cell ratio (P-LCR), provide quantitative information about platelet size, distribution and overall platelet mass. MPV reflects the average size of circulating platelets, while PDW reflects heterogeneity in platelet size. Larger platelets are generally younger and may indicate increased platelet production in response to peripheral platelet destruction. Studies have demonstrated that MPV, PDW and P-LCR may differ between hyperdestructive and hypoproductive forms of thrombocytopenia and may therefore assist in the initial diagnostic evaluation.[3,5] Increased MPV and PDW have particularly been reported in immune thrombocytopenia (ITP), although considerable overlap between different disorders limits their use as isolated diagnostic markers.[6] The immature platelet fraction (IPF) is a more recently utilised platelet parameter that reflects newly released platelets containing residual ribonucleic acid. It provides indirect information about thrombopoietic activity in the bone marrow. An increased IPF generally suggests preserved or enhanced platelet production, as occurs in peripheral platelet destruction or consumption, whereas lower values may indicate impaired marrow production.[1,7] Several studies have reported encouraging diagnostic performance of IPF in distinguishing hyperdestructive thrombocytopenia from hypoproductive disorders. Li et al. demonstrated substantial discriminatory ability of IPF-related parameters, while other studies have reported useful sensitivity and specificity for distinguishing ITP and bone marrow failure.[7,8] Despite these findings, platelet indices can be influenced by the underlying disease, platelet count, analyser technology and pre-analytical factors. Moreover, the diagnostic performance of individual indices may vary among different populations and clinical settings. Therefore, evaluating platelet indices collectively may provide a simple, rapid and relatively inexpensive approach to the preliminary assessment of thrombocytopenia. The present study was undertaken to assess the diagnostic value of platelet indices in differentiating the major causes of thrombocytopenia and to determine their potential utility as readily available laboratory markers in routine clinical practice.

Aim and objectives: The present study aimed to evaluate the diagnostic value of platelet indices, including mean platelet volume, platelet distribution width, plateletcrit, platelet-large cell ratio and immature platelet fraction, in patients with thrombocytopenia and to determine their ability to differentiate thrombocytopenia caused by peripheral platelet destruction or consumption from thrombocytopenia resulting from impaired bone marrow production.

MATERIALS AND METHODS

Study design: A hospital-based cross-sectional study.

Study participants: A total of 60 Patients of either sex who were diagnosed with thrombocytopenia, defined as a platelet count below 150 × 10^9/L, were included. Participants were subsequently categorised according to the final clinical and laboratory diagnosis into groups representing peripheral platelet destruction or consumption and reduced platelet production. The diagnostic classification was based on clinical history, physical examination, complete blood count, peripheral blood smear, biochemical investigations and other relevant investigations as indicated. The approach was based on the recognised utility of platelet production-related parameters in differentiating hypoproductive from hyperdestructive thrombocytopenia.[9,10]

Inclusion criteria

Patients aged 18 years and above with a platelet count below 150 × 10^9/L were included. Patients in whom a definitive clinical diagnosis of the underlying cause of thrombocytopenia could be established were considered eligible for analysis.

Exclusion criteria

Patients with pseudothrombocytopenia, platelet transfusion within the preceding seven days, pregnancy, known inherited platelet disorders and those receiving drugs known to significantly alter platelet production or function were excluded. Patients with inadequate blood samples, clotted samples or samples showing significant pre-analytical errors were also excluded.

Methodology: Venous blood samples were collected under aseptic precautions into tubes containing ethylenediaminetetraacetic acid (EDTA). Complete blood counts were performed using an automated haematology analyser. The platelet count and platelet indices, including mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet-large cell ratio (P-LCR) and, where available, immature platelet fraction (IPF), were recorded. IPF was assessed using the automated fluorescence-based platelet analysis provided by the haematology analyser. IPF represented the proportion of newly released platelets and was considered an indicator of marrow thrombopoietic activity.[9,11] Peripheral blood smears were examined to confirm the automated platelet count, assess platelet morphology and identify abnormal circulating cells or platelet clumping. Relevant biochemical, microbiological, radiological and bone marrow investigations were reviewed whenever clinically indicated to establish the underlying cause.

Study variables: The primary study variables were platelet count, MPV, PDW, PCT, P-LCR and IPF. Demographic characteristics, clinical diagnosis and relevant laboratory findings were also recorded. Platelet indices were compared between thrombocytopenia due to increased peripheral destruction or consumption and thrombocytopenia associated with reduced platelet production.

Data analysis: The collected data were entered into a Microsoft Excel spreadsheet and analysed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on the distribution of data. Categorical variables were presented as frequencies and percentages. Differences in platelet indices between diagnostic groups were assessed using appropriate parametric or non-parametric tests. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic performance of individual platelet indices in differentiating the major mechanisms of thrombocytopenia. The area under the ROC curve, sensitivity, specificity and optimal cut-off values were calculated. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 60 participants with thrombocytopenia were included in the study. Based on the clinical and laboratory assessment, 32 (53.3%) participants were classified as having peripheral platelet destruction/consumption, while 28 (46.7%) had reduced platelet production. The platelet indices showed appreciable differences between the two groups, particularly MPV, PDW, P-LCR and IPF, in keeping with the concept that increased platelet turnover is associated with larger and more immature circulating platelets. The mean age of the study population was approximately 44.7 years. Males constituted 58.3% of the participants. The mean platelet count was lower in the peripheral destruction/consumption group than in the reduced-production group [Table 1]. Among the identified causes, immune thrombocytopenia was the most frequent diagnosis, accounting for 25.0% of participants, followed by megaloblastic anaemia (16.7%) and dengue-associated thrombocytopenia (13.3%) [Table 2]. MPV, PDW, P-LCR and IPF were significantly higher in participants with peripheral platelet destruction/consumption compared with those having reduced platelet production. The difference was particularly prominent for IPF. These findings were broadly consistent with previous observations that IPF and platelet volume parameters increase with enhanced peripheral platelet turnover [Table 3]. ROC analysis demonstrated that IPF had the highest diagnostic performance, with an approximate AUC of 0.90, followed by P-LCR, MPV and PDW. An IPF value above 7.0% showed 87.5% sensitivity and 82.1% specificity for identifying thrombocytopenia associated with peripheral destruction or consumption. The strong discriminatory performance of IPF was consistent with published evidence demonstrating its usefulness in distinguishing increased platelet destruction from reduced marrow production [Table 4]. When the platelet indices were interpreted collectively, 51 of the 60 participants (85.0%) were correctly classified according to the underlying mechanism of thrombocytopenia. The findings suggested that platelet indices, particularly IPF, when interpreted alongside MPV, PDW and P-LCR, could provide useful supportive information for differentiating peripheral platelet destruction from impaired platelet production. Similar diagnostic utility of platelet indices has been reported in previous studies [Table 5].

Table 1: Demographic data of the participants (n=60)

Characteristic	Peripheral destruction/consumption (n=32)	Reduced platelet production (n=28)	Total (n=60)
Age, years (mean ± SD)	41.6 ± 15.2	48.3 ± 16.8	44.7 ± 16.1
Male, n (%)	19 (59.4)	16 (57.1)	35 (58.3)
Female, n (%)	13 (40.6)	12 (42.9)	25 (41.7)
Platelet count, ×10⁹/L	61.4 ± 28.7	74.8 ± 31.6	67.7 ± 30.4

Table 2: Distribution of underlying causes of thrombocytopenia

Cause	Number (n)	Percentage (%)
Immune thrombocytopenia	15	25.0
Dengue-associated thrombocytopenia	8	13.3
Sepsis/consumptive thrombocytopenia	5	8.3
Liver disease/hypersplenism	4	6.7
Megaloblastic anaemia	10	16.7
Aplastic/hypoplastic marrow disorders	7	11.7
Acute leukaemia/marrow infiltration	6	10.0
Chemotherapy/drug-associated marrow suppression	5	8.3
Total	60	100

Table 3: Comparison of platelet indices between diagnostic groups

Platelet parameter	Peripheral destruction/consumption (n=32)	Reduced production (n=28)	p-value
MPV (fL)	11.3 ± 1.4	9.1 ± 1.3	<0.001
PDW (fL)	17.8 ± 1.6	15.9 ± 1.5	<0.001

PCT (%)	0.069 ± 0.031	0.075 ± 0.035	0.48
P-LCR (%)	39.6 ± 8.7	27.8 ± 7.4	<0.001
IPF (%)	12.1 ± 4.9	5.2 ± 2.1	<0.001

Table 4: Diagnostic performance of platelet indices for identifying peripheral platelet destruction/consumption

Parameter	Optimal cut-off	Sensitivity (%)	Specificity (%)	AUC
MPV	>10.2 fL	78.1	75.0	0.82
PDW	>16.8 fL	75.0	71.4	0.79
P-LCR	>32.0%	81.3	78.6	0.84
IPF	>7.0%	87.5	82.1	0.90

Table 5: Diagnostic performance of platelet indices for identifying peripheral platelet destruction/consumption

Diagnostic category	Correctly classified, n (%)	Misclassified, n (%)
Peripheral destruction/consumption	28 (87.5)	4 (12.5)
Reduced platelet production	23 (82.1)	5 (17.9)
Overall diagnostic agreement	51 (85.0)	9 (15.0)

DISCUSSION

Thrombocytopenia is encountered frequently in clinical practice and may result from impaired platelet production, increased peripheral destruction or consumption, or sequestration. Differentiating these mechanisms is clinically important because management differs considerably. In the present study, platelet indices were evaluated in 60 patients with thrombocytopenia, of whom 32 had peripheral platelet destruction/consumption and 28 had reduced platelet production. The findings demonstrated significantly higher mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR) and immature platelet fraction (IPF) in the peripheral destruction/consumption group. The mean MPV was significantly higher among patients with peripheral platelet destruction than among those with reduced platelet production. This finding can be explained by increased thrombopoietic activity following accelerated peripheral platelet loss. Newly released platelets are generally larger than mature circulating platelets, resulting in an increased MPV when marrow compensation is preserved. A previous comparative study reported significantly higher MPV in hyperdestructive thrombocytopenia and demonstrated that platelet indices could assist in differentiating hyperdestructive from hypoproductive disorders.[12] Similarly, a study evaluating platelet indices in thrombocytopenia reported higher MPV, PDW and plateletcrit in hyperdestructive cases, supporting the findings of the present study.[13] PDW was also significantly increased in the peripheral destruction/consumption group. PDW reflects variability in platelet size and may increase when circulating platelets comprise populations of different ages and sizes. Kaito et al. previously demonstrated that PDW, MPV and P-LCR were useful in differentiating immune thrombocytopenia from aplastic anaemia, with PDW and P-LCR showing particularly good discriminatory capacity.[14]

The increased P-LCR observed in the present study further supported the presence of a larger platelet population in patients with increased platelet turnover. Similar observations have indicated that P-LCR is increased in destructive thrombocytopenia and may provide additional information beyond the platelet count.[15] The most prominent finding in the present study was the significantly higher IPF in the peripheral destruction/consumption group. IPF represents newly released platelets containing residual RNA and therefore provides an indirect assessment of marrow thrombopoietic activity. The mean IPF was approximately 12.1% in the peripheral destruction/consumption group compared with 5.2% in the reduced-production group. These findings are consistent with an Indian study in which IPF was substantially higher in patients with increased platelet destruction than in those with decreased platelet production.[16] Another study also demonstrated that IPF had the highest discriminatory performance among several platelet parameters and could distinguish hyperdestructive/consumptive thrombocytopenia from hypoproductive thrombocytopenia.[17] In the present study, ROC analysis showed that IPF had the highest diagnostic performance, with an AUC of approximately 0.90, followed by P-LCR, MPV and PDW. The observed IPF cut-off of >7.0% provided 87.5% sensitivity and 82.1% specificity. These values are comparable with previous investigations, although reported cut-offs vary according to analyser, population and study design. An investigation of IPF in immune thrombocytopenia reported an AUC of 0.97 and demonstrated high sensitivity and specificity at a cut-off of 6.3%.[18] Such differences emphasise the importance of establishing analyser-specific and population-specific reference values rather than applying a universal threshold. The distribution of underlying causes in the present study also reflected the heterogeneous nature of thrombocytopenia. Immune thrombocytopenia was the commonest diagnosis, followed by megaloblastic anaemia and dengue-associated thrombocytopenia. Platelet indices may be particularly useful in such settings because automated analysers provide these parameters alongside the routine complete blood count without requiring additional invasive procedures. Studies in dengue have also demonstrated that platelet indices can provide useful information regarding platelet kinetics and disease

behaviour.[19,20] The overall diagnostic agreement of 85.0% obtained using combined platelet indices was encouraging. However, platelet indices should not be interpreted as standalone diagnostic tests. Analytical differences between haematology analysers, sample handling, platelet clumping and underlying inflammatory or infectious conditions may influence their values. Recent literature has also highlighted methodological variability as an important limitation in interpreting platelet indices.[21] Therefore, these parameters should complement clinical assessment, peripheral smear examination and other relevant investigations. IPF, P-LCR, MPV and PDW, can serve as useful, inexpensive and readily available supportive markers for differentiating peripheral platelet destruction from impaired platelet production. Their incorporation into routine evaluation may reduce the need for invasive investigations in selected patients, although larger prospective studies are required to validate diagnostic cut-offs.

CONCLUSION

Platelet indices, particularly immature platelet fraction, MPV, PDW and P-LCR, demonstrated significant differences between peripheral platelet destruction and reduced platelet production. Their combined assessment provided useful diagnostic discrimination and may serve as a simple, rapid and minimally invasive adjunct to conventional investigations in the evaluation of thrombocytopenia.

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