PLATELET INDICES AS AN EARLY RESPONSE PREDICTOR TO THE FIRST-LINE THERAPY IN NEWLY DIAGNOSED IMMUNE THROMBOCYTOPENIA PURPURA

M. Arul Prakash¹, T. Balaselvi², R. Vinothkannan³, S. Govardhan⁴

¹Assistant Professor, Department of General Medicine, Madurai Medical College, Tamilnadu, India.
²Assistant Professor, Department of General Medicine, Madurai Medical College, Tamilnadu, India.
³Assistant Professor, Department of General Medicine, Madurai Medical College, Tamilnadu, India.
⁴Postgraduate, Department of Infectious Diseases, CMC, Vellore, Tamilnadu, India.

Abstract
Background: Differentiating between decreased platelet production and increased platelet destruction is crucial for accurate diagnosis of thrombocytopenia. Aim: This study aimed to evaluate the early response (within 3 weeks) predictability of platelet indices, such as mean platelet volume (MPV), immature platelet fraction (IPF), platelet larger cell ratio (PLCR), platelet distribution width (PDW), and platelet count (PCT), as first-line therapies for newly diagnosed immune thrombocytopenic purpura. Material and Methods: This prospective study, conducted over a year on 50 patients (ITP) patients, encompassed acute and regular follow-ups in a General Medicine department. Blood samples were collected in EDTA tubes and analysed for CBC within 4 h using an analyser. The study recorded patient demographics, symptoms, PLT, and MPV for diagnosis and evaluated responses based on PLT and MPV. Platelet indices were compared between responders and non-responders before and after treatment. Results: Patients were classified into responders and non-responders based on platelet count during first-line therapy. Responders exhibited a decreasing trend in mean platelet volume, immature platelet fraction, platelet larger cell ratio, platelet distribution width, and an increasing trend in plateletcrit, indicating a bone marrow response. Conversely, non-responders showed minimal changes, suggesting an inadequate bone marrow response. Higher platelet indices and lower plateletcrit values predicted early response to therapy, whereas lower platelet indices and higher plateletcrit values suggested less responsiveness, potentially necessitating second-line therapy for immune thrombocytopenic purpura. Conclusion: These findings suggest that platelet indices could serve as valuable predictors of therapeutic efficacy, potentially guiding treatment decisions and minimising the need for second-line interventions.

INTRODUCTION

Immune thrombocytopenia (ITP, also called idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura) is an acquired thrombocytopenia caused by autoantibodies against platelet antigens. It is one of the most common causes of thrombocytopenia in asymptomatic adults. It is an important cause of thrombocytopenia, presenting with bleeding manifestations or incidental thrombocytopenia identified by a complete blood count taken for other indications. ITP is the diagnosis of exclusion, and is defined as isolated thrombocytopenia (platelet count <100,000/µL) without anaemia or leukopenia and another apparent cause of thrombocytopenia. The lack of a sensitive or specific diagnostic test for ITP and many other potential causes of thrombocytopenia, some of which may be overlooked (drug-induced thrombocytopenia, hereditary thrombocytopenia), also contribute to the challenges in diagnosing ITP. The main causes of thrombocytopenia are increased destruction or consumption of circulating platelets, and decreased platelet production in the bone marrow.[1–3]
Hyperdestructive and consumptive thrombocytopenia encompass conditions such as immune thrombocytopenic purpura (ITP), disseminated intravascular coagulation, and thrombotic thrombocytopenic purpura (TTP). In contrast, hypoproliferative thrombocytopenia includes conditions of BM failure, such as aplastic anaemia or myelodysplastic syndromes, as well as BM infiltration due to solid organ tumours, fibrosis, or leukaemia. BM toxicity caused by chemotherapy, HIV, or cytomegalovirus (CMV) infection can also cause hypoproliferative thrombocytopenia.

In clinical practice, it is crucial to distinguish between a decrease in the platelet production rate and an increase in the rate of platelet destruction. Therefore, the assessment of thrombopoietic activity may be useful for correctly diagnosing the aetiology of thrombocytopenia. Assessment of thrombopoietic activity using platelet indices (MPV, IPF, P-LCR, PDW, and PCT) can help avoid unnecessary platelet transfusion in thrombocytopenic patients. Reliably predicting the natural recovery of platelets within a few days can help inform the decision of whether to perform prophylactic platelet transfusion.

**Aim**

This study aimed to evaluate the early response (within 3 weeks) predictability of platelet indices, such as mean platelet volume (MPV), immature platelet fraction (IPF), platelet larger cell ratio (P-LCR), platelet distribution width (PDW), and platelet count (PCT), to first-line therapy in newly diagnosed immune thrombocytopenic purpura.

**MATERIALS AND METHODS**

This prospective study was conducted on 50 patients with Immune thrombocytopenic purpura including those admitted with acute onset ITP and ITP patients who are on regular follow-up in the Department of General Medicine, GRH, Madurai for one year. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients. Relevant information was collected from all patients in the predesigned form. Patients were selected based on detailed history taking, clinical examination, and laboratory investigations.

**Inclusion Criteria**

Patients of both sexes, aged > 18 years, and newly diagnosed ITP were included.

**Exclusion Criteria**

Patients aged <18 years, with viral infections (HBV, HCV, HIV), H. pylori infection, drug-induced thrombocytopenia, autoimmune disorders, diabetes mellitus, thyroid disorders, renal and liver diseases, and critical illness were excluded.

**Statistical Analysis**

Data were entered and analysed using SPSS. Platelet indices were compared between responders and non-responders, both before and after treatment.

Changes in platelet indices after treatment were analysed for responders and non-responders, and the results are presented in a graphical format for visual representation.

**RESULTS**

The study included a total of 50 patients (34 being females and 16 males). Among these patients, the distribution across age groups was as follows: 18 patients were between 18 and 25 years old, accounting for 36% of the study population; 17 patients fell within the 26-35 age range, constituting 34% of the total; 9 patients were aged between 36 and 45, contributing 18% to the study; 4 patients belonged to the 46-55 age bracket, accounting for 8% of the population; and 2 patients were in the 56-65 age group, representing 4% of the total observed.

The platelet indices such as MPV, IPF, P-LCR, PDW, and PCT were observed prior to the therapy and they are termed as ‘WEEK 0’ are followed for 3 subsequent weeks and are termed as WEEK 1, WEEK 2, and WEEK 3 respectively. All these indices were compared with platelet counts, and their relationship with platelet counts was studied. The ‘RESPONDERS’ & ‘NON-RESPONDERS’ are categorised according to the criteria formulated as stated above.

Mean platelet counts of responders and non-responders during the 3-week course of therapy. In responders, the mean platelet count prior to therapy was 46,621, which increased to 74,069 after one week of therapy, further increased to 131,063 after two weeks, and eventually reached 243,844 after three weeks of therapy. Conversely, in non-responders, the mean platelet count before therapy initiation was 7,239. Following one week of therapy, this count increased to 11,807, 16,169 after two weeks, and 18,484 after three weeks of therapy. A graphical representation illustrates a consistent increase in the mean platelet count among responders throughout the duration of therapy. Conversely, non-responders exhibited a decremental response to therapy, with platelet counts not exceeding 100,000 or 30,000 following therapy, indicating a lack of significant improvement, thus categorising them as non-responders (Figure 1).

![Figure 1: Mean platelet counts of responders and non-responders during the 3 weeks course of therapy](image-url)
Mean platelet volume of responders and non-responders during the 3-week course of therapy

In responders, the mean platelet volume before therapy was 14.2, which decreased to 13.7 after one week of therapy, followed by a further reduction to 13.13 after two weeks, and ultimately declining to 11.08 after three weeks of therapy. Conversely, in non-responders, the mean platelet volume before the initiation was 10.1. Following one week of therapy, this value increased slightly to 10.15, then remained relatively stable at 10.08 after two weeks, and maintained at 10.07 after three weeks of therapy.

A graphical representation illustrates a consistent decrease in the mean platelet volume among responders throughout the therapy duration, gradually approaching normal values. Conversely, in non-responders, the mean platelet volume remained almost static and within the low-normal or below-normal range, indicating a lack of significant response from the bone marrow, which is characteristic of non-responders (Figure 2).

Immature platelet fraction of responders and non-responders during the 3-week course of therapy

In responders, the immature platelet fraction prior to therapy was 13.4, which decreased to 12.1 after one week of therapy, followed by a further reduction to 9.2 after two weeks, and ultimately declining to 5.4 after three weeks of therapy. Conversely, in the non-responders, the immature platelet fraction before therapy initiation was 1.7. Following one week of therapy, this value slightly increased to 1.3, then remained relatively stable at 1.2 after two weeks, and maintained at 1.3 after three weeks of therapy.

A graphical representation illustrates a consistent decrease in the immature platelet fraction among responders throughout the therapy duration, gradually approaching normal values. Conversely, in non-responders, the immature platelet fraction remained relatively low before and during therapy, indicating a lack of significant response from the bone marrow, which is characteristic of non-responders (Figure 3).

Platelet larger cell ratio of responders and non-responders during the 3-week course of therapy

In responders, the platelet larger cell ratio before therapy was 40.5, which decreased to 37.4 after one week of therapy, followed by a further reduction to 34.4 after two weeks, and ultimately declining to 30.7 after three weeks of therapy. Conversely, in non-responders, the platelet larger cell ratio before therapy initiation was 14.8. Following one week of therapy, this value slightly increased to 16, then remained relatively stable at 15.4 after two weeks, and maintained at 16.17 after three weeks of therapy.

A graphical representation illustrates a consistent decrease in the platelet larger-cell ratio among responders throughout the therapy duration, gradually approaching normal values. Conversely, in non-responders, the platelet larger cell ratio remained relatively stable and low-normal or below the normal range following therapy, indicating a lack of significant response from the bone marrow, which is characteristic of non-responders (Figure 4).

Platelet distribution width of responders and non-responders during the 3-week course of therapy

In responders, the platelet distribution width prior to therapy was 14.8, which decreased to 14.3 after one week of therapy, followed by a further reduction to 14.18 after two weeks, and ultimately declining to 11.10 after three weeks of therapy. Conversely, in the non-responders, the platelet distribution width before therapy initiation was 7.3. Following one week of therapy, this value slightly decreased to 7.2, then remained relatively stable at 6.8 after two weeks.

Figure 2: Mean platelet volume of responders and non-responders during the 3-week course of therapy

Figure 3: Immature platelet fraction of responders and non-responders during the 3-week course of therapy

Figure 4: Platelet larger cell ratio of responders and non-responders during the 3-week course of therapy
weeks, and maintained at 7.2 after three weeks of therapy.

A graphical representation illustrates a consistent decrease in the platelet distribution width among responders throughout the therapy duration, gradually approaching normal values. Conversely, in non-responders, the platelet distribution width remained lower than that in responders and showed minimal variation during the course of therapy, indicating a decreased bone marrow response characteristic of non-responders (Figure 5).

![Figure 5: Platelet distribution width of responders and non-responders during the 3-week course of therapy](image)

Plateletcris of responders and non-responders during the 3-week course of therapy

In responders, the platelet count before therapy was 0.003, which increased to 0.04 after one week of therapy, followed by a further elevation to 0.09 after two weeks, and ultimately increased to 0.228 after three weeks of therapy. Conversely, in non-responders, the plateletcrit level before therapy initiation was notably higher (0.52). Following one week of therapy, this value decreased to 0.30, then slightly decreased further to 0.29 after two weeks, and remained stable at 0.3 after three weeks of therapy.

A graphical representation illustrates a consistent increase in plateletcrit among responders throughout the therapy duration, gradually approaching normal values, albeit remaining lower than the plateletcrit values of non-responders. Conversely, the plateletcrit in non-responders remained higher than that in responders before therapy and remained relatively stable even after therapy, indicating the unresponsiveness of these patients to treatment (Figure 6).

![Figure 6: plateletcrit of responders and non-responders during the 3-week course of therapy](image)

DISCUSSION

Platelet parameters are valuable indicators for monitoring therapeutic responses and predicting treatment outcomes in various medical conditions. Platelet indices are parameters that look into platelets from different angles, including MPV, IPF, P-LCR, PDW, and PCT. In this study, we investigated the dynamics of several platelet parameters in responders and non-responders to therapy for over three weeks.

The patients were classified into responders and non-responders based on platelet counts (according to the criteria) that were measured during the first-line therapy.

Following therapy, responders exhibited a progressive decrease in mean platelet volume (MPV), with values gradually approaching the normal range. In contrast, non-responders showed minimal changes in MPV levels, persistently below the normal range, indicating insufficient bone marrow response. Previous studies have also demonstrated that simple, inexpensive, and noninvasive tests, such as MPV, can effectively differentiate between hyper-destructive and hyperproductive causes of thrombocytopenia. These tests offer sufficient predictive capacity, sensitivity, and specificity, making them valuable tools for clinical practice.[8-12]

Similarly, responders demonstrate a decline in the immature platelet fraction (IPF) post-therapy, steadily approaching normal levels. Conversely, non-responders exhibited consistently lower IPF values throughout the treatment period, suggesting impaired bone marrow function. Cannavo et al. assessed the reliability of reticulated platelets, measured as the percentage of reticulated platelets (IPF%), as a diagnostic tool for thrombocytopenia pathogenesis. The results showed that the IPF% was significantly increased in patients with idiopathic thrombocytopenic purpura, suggesting its potential diagnostic value for this condition. However, elevated IPF% values were also observed in patients with acute leukaemia, indicating the need for further investigation into its role in differentiating thrombocytopenic disorders.[13]

Regarding the platelet larger cell ratio (PLCR), responders experienced a decrease following therapy, with values gradually declining each week. In contrast, non-responders displayed relatively static PLCR levels, remaining low-normal or below the normal range post-therapy, indicative of an inadequate bone marrow response. The platelet distribution width (PDW) followed a similar trend, with responders demonstrating a reduction in PDW values post-therapy, gradually nearing normal levels. In contrast, non-responders maintained PDW levels lower than responders, with minimal changes observed during treatment, further suggesting a compromised bone marrow response.
Kaito et al. investigated the diagnostic utility of MPV, PDW, and platelet-large cell ratio (P-LCR) in immune thrombocytopenia (ITP). They found that an MPV greater than 11 femtoliters (fl) demonstrated improved sensitivity (87.2%) and specificity (80.0%) in diagnosing ITP.[10] In addition, Negash et al. observed a significant negative correlation between platelet count and platelet indices in patients with ITP, which appears to be driven primarily by acute ITP cases, characterised by a mean platelet count of 12.8 × 109/L and mean values of 16.6 fl for MPV, 19 fl for PDW, and 51.5% for MPV, PDW, and P-LCR, respectively. These findings suggest that platelet indices, especially MPV and P-LCR, may offer improved discriminatory or predictive capacity for ITP, particularly during the initial assessment and diagnosis of patients with thrombocytopenia.[14]

In our study, plateletcrit (PCT) values showed divergent patterns between responders and non-responders. Responders exhibited increasing PCT levels post-therapy, although they remained lower than non-responders. Conversely, non-responders displayed higher PCT levels prior to therapy, which persisted or exhibited minimal change post-therapy, indicating a lack of therapeutic response. In responders, the variability in platelet indices can be attributed to the presence of microthrombocytes due to autoantibodies and adequate megakaryocytes resulting from an effective bone marrow response. Conversely, non-responders demonstrated lower variability in platelet indices, reflecting inadequate bone marrow function. Tang et al., reported that platelet indices, such as MPV, PCT, and PDW, potentially reflect megakaryopoietic activity in ITP. Analysis of their diagnostic performance using receiver-operating characteristic curves revealed higher MPV and lower PCT in ITP compared to myelodysplasia and controls, alongside lower platelet distribution width than myelodysplasia, but higher than controls. The correlation between MPV and megakaryocyte quantities suggests their potential as reliable markers for diagnosing ITP, with combined testing of MPV and PCT enhancing the diagnostic sensitivity.[12]

Overall, higher MPV, IPF, PLCR, and PDW values coupled with lower PCT values may signify a favourable response to first-line therapy in newly diagnosed immune thrombocytopenic purpura (ITP). Conversely, lower MPV, IPF, PLCR, and PDW values along with higher PCT values may indicate diminished responsiveness to first-line therapy and the potential need for second-line treatment strategies. Overall, our findings underscore the utility of platelet parameters as potential biomarkers for monitoring therapeutic response. The observed differences between responders and non-responders highlight the importance of personalised treatment approaches based on individual platelet profiles. Further studies are warranted to validate these findings and explore their implications in clinical practice.

**CONCLUSION**

In conclusion, our study highlights the dynamic changes in platelet indices following therapy in responders compared to non-responders. Responders exhibited a gradual normalisation of platelet volume, immature platelet fraction, platelet larger cell ratio, platelet distribution width, and plateletcrit, reflecting an adequate bone marrow response. Conversely, non-responders showed static or minimal changes in these indices, indicating an inadequate bone marrow response. These findings underscore the potential utility of platelet indices as early predictors of therapeutic response in immune thrombocytopenic purpura, aid in treatment decision making, and possibly reduce the need for second-line therapies.

**Limitations**

The relatively small sample size and limited disease categories, particularly in the thrombocytopenia group, may restrict the applicability of these findings to other patient groups. Furthermore, the limitations of our study include the necessity for a larger sample size to establish statistical significance, exclusion of splenic sequestration as a cause of thrombocytopenia, and lack of bone marrow examination in cases of dengue and malaria, which could have provided additional insights.

**REFERENCES**


9. Bowles KM, Cooke LJ, Richards EM, Baglin TP. Platelet size has diagnostic predictive value in patients with


