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Original Research Article

# The Significance of Immature Platelet Fraction in the Diagnosis and Prognosis of Groups with Thrombocytopenia

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**Abstract:**

**Background and Aim:** Accelerated platelet breakdown and decreased platelet synthesis are major causes of thrombocytopenia in immune thrombocytopenic purpura (ITP). In our study, thrombocytopenia instances were classified as hypoproductive, megaloblastic, or hyperdestructive. Our study aims to assess the prevalence of IPF and its importance in various thrombocytopenic groups, with the hope that it can be used as a new emerging prognostic marker in identifying and managing such patients.

**Material and Methods:** 50 thrombocytopenia samples were collected and analysed. Based on the history and final diagnosis, all patients were classified as megaloblastic, hypoproduction, or hyperdestruction. In a k3 EDTA vacutainer, peripheral blood samples were obtained. All samples were analysed within four hours of being collected. All samples had their platelet counts and IPF% determined.

**Results:** The findings revealed that 40% of the 50 cases evaluated were men and 60% were females, with a small female preponderance. The majority of patients were between the ages of 20 and 39. In the Hyperdestructive group, 27 (93.10%) of the 50 cases exhibited increased IPF, but in the Hypoproductive group, only 01 (0.09%) of the 11 cases showed increased IPF. ITP had the highest IPF%, followed by malaria and dengue.

**Conclusion:** Immature Platelet Fraction is a straightforward non-invasive approach for calculating the proportion of reticulated platelets in peripheral blood in order to monitor megakaryocytic activity. IPF is much higher in the hyper destructive group, indicating enhanced thrombopoiesis, and its value is inversely related to platelet count in these situations.

**Keywords:** Immune Thrombocytopenic Purpura, Megaloblastic, Thrombocytopenia, Thrombotic Thrombocytopenic Purpura.



## Introduction

Thrombocytopenia is caused mostly by increased destruction/consumption of circulating platelets and decreased platelet synthesis in the bone marrow (BM). [1-4] Immune thrombocytopenic purpura (ITP), disseminated intravascular coagulation, and thrombotic thrombocytopenic purpura (TTP) are all examples of hyperdestructive and consumptive thrombocytopenia.

Hypoproductive thrombocytopenia, on the other hand, encompasses BM failure diseases such as aplastic anaemia (AA) or myelodysplastic syndromes, as well as BM infiltration owing to solid malignancy, fibrosis, or leukaemia. Chemotherapy, HIV, or CMV infection can all produce BM toxicity, which can lead to hypoproductive thrombocytopenia. In clinical practise, it is critical to separate a decrease in platelet production rate from an increase in platelet destruction rate; thus, thrombopoietic activity assessment can be helpful in correctly diagnosing the aetiology of thrombocytopenia. [5,6]

Accelerated platelet breakdown and reduced platelet generation are major causes of thrombocytopenia in ITP. The precise cause is uncertain. The global incidence of acute ITP in children ranges between 1.9 and 6.4 per 105 children per year; the estimate for adults is 3.3 per 105 adults per year. [7] Platelet Fraction (IPF) is the proportion of reticulated platelets in peripheral blood measured. The amount of reticulated platelets increases when platelet production increases and decreases when platelet production

decreases. One of the best prognostic markers for thrombocytopenic patients is non-invasive, low-cost flowcytometric assessment of reticulated platelets using an automated haematology analyzer in conjunction with blood counts. Immature Platelet Fraction (IPF), or the fraction of RPs, represents the severity of platelet damage and platelet production in bone marrow. [8,9] IPF has a normal range of 1.1-6.1%. In our study, thrombocytopenia instances were classified as hypoproductive, megaloblastic, or hyperdestructive. In the current study, the megaloblastic anaemia group is segregated from the hypoproductive group because the causes of thrombocytopenia are hypoproduction in some studies and poor thrombopoiesis in others. [10]

Our study aims to assess the prevalence of IPF and its importance in various thrombocytopenic groups, with the hope that it can be used as a new emerging prognostic marker in identifying and managing such patients.

## Material and Methods

The research was carried out over the course of a year. A total of 50 samples of thrombocytopenia were collected and analysed. Inclusion criteria: All instances with thrombocytopenia (1.5 lakh cells/l or higher) with a relevant history and investigations for final diagnosis.

Exclusion criteria include platelet counts greater than 1.5 lakh/l and those lacking a complete history and final diagnosis.

Based on the history and final diagnosis, all patients were classified as megaloblastic, hypoproduction, or hyperdestruction. In a k3 EDTA vacutainer, peripheral blood samples were obtained. All samples were analysed within four hours of being collected.

All samples' platelet counts and IPF% were determined using a Sysmex XN350. IPF is diagnosed using Fluorescence Flowcytometry, which uses reticulocyte dilution fluid to stain both reticulated erythrocytes and platelets, distinguishing mature and immature platelet populations.

### Statistical investigation

The collected data was assembled and input into a spread sheet programme (Microsoft Excel 2007) before being exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). The confidence level and level of significance for all tests were set at 95% and 5%, respectively.

## Results

In the study of 50 cases, 40% were males and 60% were females, with a small female preponderance. The majority of patients were between the ages of 20 and 39 (Table 1). ITP was the most common type of case identified in those aged 20 to 39, followed by dengue and solid tumours. ITP was the most common clinical diagnosis in the study, accounting for 25% of cases, followed by dengue fever (18%) and megaloblastic anaemia (18%). Leukaemia, malaria, aplastic anaemia, and solid cancer entering the marrow were among the other diagnoses.

In the Hyperdestructive group, 27 (93.10%) of the 50 cases exhibited increased IPF, but in the Hypoproductive group, only 01 (0.09%) of the 11 cases showed increased IPF. The megaloblastic group was in the middle of the two groups, with increased IPF in four (40%) of the ten patients (Table 2). Hypoproductive, hyperdestructive, and megaloblastic groups have mean platelet levels of 21,450 cells/l, 30,500 cells/l, and 37,700 cells/l, respectively. The mean platelet count and IPF% in the megaloblastic group were considerably greater than in the hypoproductive group.

The hyperdestructive group IPF% ranged from 4.2 to 55.9%, the hypoproductive group IPF% ranged from 2.6-7.6%, and the megaloblastic group IPF% ranged from 5.8% to 31.1%. ITP had the greatest mean IPF% in the hyperdestructive group, followed by malaria. Most IPF% values fell between 10 and 20% across all groups. ITP had the highest IPF%, followed by malaria and dengue. Leukaemia had the lowest IPF%.

**Table 1: Age and Gender Distribution of all cases**

| Age (Years) | No of cases | Male | Female |
|---|---|---|---|
| <10 | 3 | 1 | 2 |
| 10-19 | 5 | 3 | 2 |
| 20-29 | 13 | 4 | 9 |
| 30-39 | 17 | 6 | 11 |
| 40-49 | 7 | 3 | 4 |
| 50-59 | 3 | 2 | 1 |
| 60-69 | 2 | 1 | 1 |
| 70 and above | 0 | 0 | 0 |
| Total | 50 | 20 | 30 |

**Table 2: Percentage of cases showing increased IPF in different groups**

| Groups | Total Cases | Cases with IPF >7 | Percentage of Total (%) |
|---|---|---|---|
| **Hyperdestructive** | 29 | 27 | 93.10 |
| **Hypoproductive** | 11 | 1 | 0.09 |
| **Megaloblastic** | 10 | 4 | 40 |

## Discussion

Although ITP can be diagnosed clinically, test confirmation is frequently required. [11] Previously, ITP was confirmed through microscopic study of bone marrow aspirates. Because bone marrow extraction is a painful procedure, flowcytometric assays were later used to jump to a final diagnosis. However, the time commitment and inconsistency of these tests restrict their utility. [12] Currently, automated measurement of reticulated platelets is employed to distinguish cases of severe thrombocytopenia from ITP. The published literature clearly demonstrated that, in the presence of thrombocytopenia, platelet RNA concentration associated directly with megakaryocytic activity. [5,13]

IPF measurements can now be performed as part of standard blood count analysis, with findings accessible at the same time. The purpose of this study was to determine the diagnostic and prognostic importance of IPF in relation to platelet counts in various thrombocytopenic patients. In the current study, 27 (93.10%) of the 50 cases in the Hyperdestructive group exhibited increased IPF, whereas only 01 (0.09%) of the 11 cases in the Hypoproductive group showed increased IPF. The megaloblastic group was in the middle of the two groups, with increased IPF in four (40%) of the fourteen cases. ITP, dengue fever, malaria, and viral diseases are all members of the hyperdestructive category. Aplastic anaemia, leukaemia, and solid malignancies with marrow infiltrations are all examples of hypoproductive diseases.

IPF was considerably higher in the hyperdestructive group compared to the hypoproductive and megaloblastic groups in our investigation, which was consistent with studies by Pons et al and Naz et al. [15,16]. One instance from dengue and one from viral aetiology exhibited lower IPF in the hyperdestructive group. The cause for such a low IPF score could be related to the disease being in its latter stages or in its early stages. Thrombocytopenia is a well-known sign in malaria, and it is usually caused by platelet loss in the peripheral circulation. [16] Our findings are consistent with earlier research. Adly et al demonstrated that the median IPF was significantly higher in patients with thrombocytopenia due to increased peripheral platelet destruction than in those with thrombocytopenia due to decreased platelet production, and that the IPF could be a highly sensitive and specific marker for the diagnosis of ITP. [17] Strauss et al discovered that the IPF is a good marker for thrombocytopenia caused by defective platelet production, whereas the AIPC (representing the immature platelet count) may be useful for distinguishing acute ITP from thrombocytopenia in children with newly diagnosed acute lymphocytic leukaemia. [2] However, most previous research only examined patients with thrombocytopenia who had different underlying causes, rather than comparing all patients to healthy people.

Both inefficient thrombopoiesis and hypoproduction have been hypothesized as mechanisms for thrombocytopenia in megaloblastic anaemia. In our study 40% cases of megaloblastic group showed increased IPF, which is significantly higher when compared to hypoproductive group, suggesting that mechanism other than hypoproduction for thrombocytopenia, hence they are to be separated from hypoproductive group. Megaloblastic anemia is very common among Indian population due to dietary habits. [18,19] Studies on IPF% and platelet indices in megaloblastic group are few, some studies postulated that platelet indices were significantly higher in megaloblastic group compared non megaloblastic hypoproductive group. [20] In megaloblastic anemia due to pancytopenia, at times it difficult to differentiate leukemia or myelodysplasia based on bone marrow findings, in such case platelet indices, IPF%, red cell indices might be helpful prior to induction of chemotherapy. [21] Several studies like our study have provided adequate evidence suggesting that IPF% can be useful in the diagnosis, predicting the course of disease and as treatment indications for platelet transfusions in thrombocytopenic patients especially in hyperdestructice cases. Apart from thrombocytopenia cases the role of IPF as a platelets recovery marker in hematopoietic stem cell transplant recipients and as an indirect biomarker of poor prognosis in myelodysplastic syndrome with karyotypic abnormalities was studied. [22,23] Linden et al showed that IPF could be used as a predictor of platelet recovery within 2 days using a cut-off of 5.3% in patients receiving autologous stem cell transplantation. [1] Abe et al showed that the IPF was significantly higher in patients with ITP and in those who completed chemotherapy (ie, during the recovery

phase) significantly lower during the nadir phase post-chemotherapy, and within normal range in patients with incomplete ITP remission and in those with AA. [5] In contrast, Greene et al showed that the absolute immature platelet counts, but not their fractions, are more suitable for differentiating thrombocytopenias such as ITP and TTP. [24] Hong et al showed that the AIPC ratio was a useful variable to confirm TTP diagnosis and to monitor clinical response using an arbitrary cut-off value of 3. [25] Further studies of the role of age, sex, and platelet count in matched study populations with different etiologies of thrombocytopenia are required to validate our findings.

## Conclusion

Immature Platelet Fraction is a straightforward and noninvasive method used to estimate the percentage of reticulated platelets in the peripheral blood. It is used to monitor the activity of megakaryocytes. The incidence of idiopathic pulmonary fibrosis (IPF) is notably higher in the hyperdestructive group, suggesting an elevated production of platelets in these individuals. Furthermore, the value of IPF is negatively related to the platelet count. The hypoproductive group did not exhibit any increase in IPF, indicating a drop in production. The Megaloblastic thrombocytopenia group has to be distinguished from hypoproductive groups due to the much greater IPF% (Immature Platelet Fraction), mean IPF%, and mean platelet counts. Further investigation in this area is necessary.

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