IJPRP

Indian Journal of Pathology: Research and Practice
Volume 9 Number 2 (Part I), May – August 2020
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.9220.8

Original Research Article

Role of Immature Platelet Fraction in Diagnosis and Prognosis of Thrombocytopenic Groups

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How to cite this article:

Meghana Akula, P Lakshmi Anusha, Krishna Reddy CH. Role of Immature Platelet Fraction in Diagnosis and Prognosis of Thrombocytopenic Groups. Indian J Pathol Res Pract 2020;9(2 Part I):49–53.

Abstract

Background: Thrombocytopenia is defined as a decrease in peripheral blood platelet count less than 150,000 cells/µL. Immature Platelet Fraction (IPF) is simple non-invasive procedure to measure percentage of reticulated platelets in peripheral blood. Our study aimed at measuring the IPF percentage and evaluating its significance in hyperdestructive, hypoproductive and megaloblastic thrombocytopenic groups.

Methods: In present study a total of 73 cases of thrombocytopenia were studied, which included 43 cases of hyperdestruction, 16 cases of hypoproduction and 14 cases of megaloblastic group. IPF% along with complete blood counts was estimated for all samples using Sysmex XN350. Cases not meeting the required criteria were excluded from study.

Results: Of 73 patients, 56% were females and 44% were males. ITP was the most common clinical diagnosis in the study with 27% of cases followed by dengue and megaloblastic anaemia with 19% each. Out of 43 cases of Hyperdestructive group, 41 (95.3%) cases showed increased IPF in comparison to Hypoproductive group, in which only 01 (0.06%) case out of 16 cases showed increased IPF. Megaloblastic group were in between the both groups showing increased IPF in 06 (42.8%) cases of total 14 cases.

Conclusion: Since bone marrow examination is invasive and expensive, platelet indices such as PDW, MPV and P-LCR lack significant sensitivity and specificity, Immature Platelet Fraction can be used as a simple non-invasive procedure for estimating the reticulated platelets percentage in peripheral blood to monitor the megakaryocytic activity.

Keywords: Immature Platelet Fraction; Megaloblastic Anemia; Reticulated Platelets; Thrombocytopenia.

Introduction

Thrombocytopenia is defined as a decrease in peripheral blood platelet count less than 150,000 cells/µL. Thrombocytopenia results broadly due to decreased marrow production, increased platelet destruction and sequestration in spleen.[1] The etiology being multifactorial can be infective, nutritional, congenital, drug induced, immunological and others. Reticulated platelets (RPs) are newly released platelets which are larger and more reactive than mature platelets and contain RNA.[2] They are the platelet analogue of red cell reticulocyte, hence termed reticulated platelets. Immature Platelet Fraction (IPF) is measurement of percentage of reticulated platelets in peripheral blood. The number of reticulated platelets reflects the rate of thrombopoiesis, increasing when platelet production rises and decreasing when production falls. Non-invasive, inexpensive flowcytometric

measurement of reticulated platelets through automated haematology analyser along with blood counts is one of the best prognostic marker for evaluating thrombocytopenic patients. Immature Platelet Fraction (IPF), the percentage of RPs reflects the severity of damage to platelets and the generation of platelets in bone marrow.[3,4] The normal range of IPF is 1.1–6.1%. Thrombocytopenia cases in our study are divided into hypoproductive, megaloblastic and hyperdestructive groups. Megaloblastic group are separated from hypoproductive group in present study as causes for thrombocytopenia is megaloblastic anaemia has been postulated as hypoproduction in some studies and as ineffective thrombopoiesis in others.[5] Our study aimed at measuring the IPF percentage and evaluating its significance in different thrombocytopenic groups, which can be used as a new emerging prognostic marker in diagnosing and managing such patients.

Subjects and Methods

The study was conducted over a period of six months from September 2018 to February 2019. A total of 73 cases of thrombocytopenia samples were collected and studied.

Inclusion criteria: All cases with thrombocytopenia i.e. <1.5 lakh cells/µl with relevant history and investigations for final diagnosis.

Exclusion criteria: Platelet counts >1.5 lakh/µl and cases without proper history and final diagnosis.

All cases were categorised into megaloblastic, hypoproduction and hyperdestruction based on history and final diagnosis. Peripheral blood samples were collected in k3 EDTA vacutainer. All samples were analysed within 4 hours of sample collection. The platelet counts and IPF% were measured for all samples using Sysmex XN350. Determination of IPF is with fluorescence flowcytometry using reticulocyte diluting fluid which stains both reticulated erythrocytes and platelets, thus differentiating mature and immature platelet populations.

Results

Out of 73 cases studied 44% were males and 56% were females with slight female preponderance. Majority of patients belonged to 21–40 years age group (Table 1). Predominant cases observed between 21–40 years were ITP followed by dengue and solid malignancies. ITP (Fig. 1) was the most common clinical diagnosis in the study with 27% of cases followed by dengue and megaloblastic anaemia with 19% each. Other diagnoses included leukemia, malaria, aplastic anaemia and solid malignancy infiltrating the marrow (Fig. 3).

Table 1: Age and sex distribution of all cases.

Age	No. of Cases	Male	Female
<10yrs	6	2	4
11–20 yrs	8	5	3
21–30 yrs	19	8	11
31–40 yrs	23	8	15
41–50 yrs	10	4	6
51–60 yrs	4	3	1
61–70 yrs	1	2	3
> 70 yrs	–	–	–
Total	73	32	41

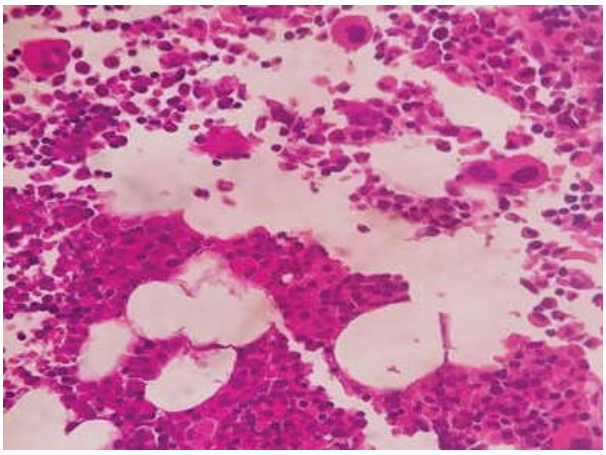

Fig. 1: Bone marrow biopsy showing megakaryocytic hyperplasia in ITP.

Out of 43 cases of Hyperdestructive group, 41 (95.3%) cases showed increased IPF in comparison to Hypoproductive group, in which only 01 (0.06%) case out of 16 cases showed increased IPF. Megaloblastic group were in between the both groups showing increased IPF in 06 (42.8%) cases of total 14 cases (Table 2). The mean platelet values of hypoproductive, hyperdestructive and megaloblastic groups are 21,250 cells/µl, 30,150 cells/µl and 37,200 cells/µ respectively. In megaloblastic group the mean platelet count and IPF% were significantly higher compared to hypoproductive group.

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

Groups	Total Cases	Cases with IPF >7	Percentage of Total
Hyperdestructive	43	41	95.3%
Hypoproductive	16	01	0.06%
Megaloblastic	14	06	42.8%

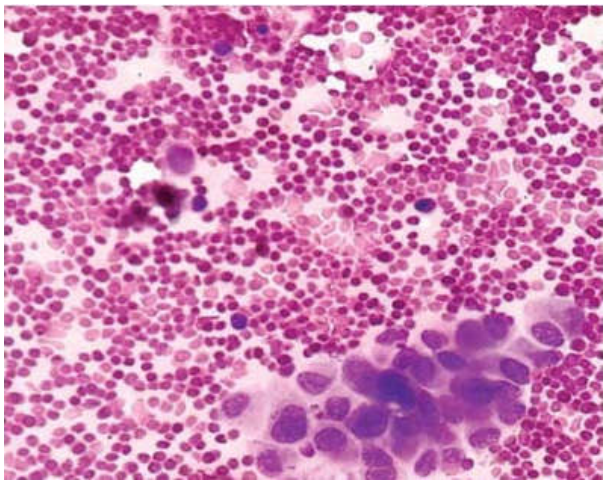

Fig. 2: Bone marrow aspiration smear showing metastatic deposits.

Hyperdestructive group IPF% ranged from 4.4–56.4%, Hypoproductive group IPF% varied between 2.8–7.4%, whereas megaloblastic group IPF% was ranging from 5.3%–30.7%. In hyperdestructive group, highest mean IPF% was seen in ITP (32.7%) followed by malaria (24.5%). In megaloblastic group mean IPF% was 18%. Among all groups most values of IPF% were falling between 10–20%. Maximum IPF% was seen in ITP (56.4%) followed by malaria (40.1%) and dengue (35.1%). Least IPF% was observed in leukaemia (2.8%) (Table 3). Highest IPF% was observed between 8,000–20,000/µl platelet counts.

Table 3: Minimum and Maximum IPF% among different clinical diagnosis.

Diagnosis	No of Cases	IPF%	
		Min	Max
Dengue	14	4.4	35.1
Malaria	7	8.0	40.1
ITP	20	9.1	56.4
Viral infections	2	5.7	7.4
Megaloblastic anaemia	14	5.3	30.7
Aplastic anaemia	4	5.5	6
Leukemia	9	2.8	7.4
Solid malignancy	3	5.1	5.9

Discussion

Immature Platelet Fraction expressed in percentage is a measure of circulating reticulated platelets, which are young platelets with RNA. Thrombocytopenia being a sign is to be evaluated to find out the underlying cause for effective management. Best method to find the megakaryocytic activity is bone marrow examination. Since bone marrow examination is invasive and expensive, the usefulness of platelet indices such as PDW, MPV and P-LCR estimated by the automated analysers are investigated in various studies.[5–10] Since all the indices have less sensitivity and specificity a new parameter was needed to access the bone marrow megakaryocytic activity. Immature Platelet Fraction is a simple non-invasive procedure to monitor the megakaryocytic activity. It is a relatively new parameter which can potentially be used to assess the rate of thrombopoiesis which could in turn be used to assess the prognosis of a thrombocytopenic state.[11] The IPF measurement can now be performed as part of the routine blood count analysis and the results are available at the same time. The present study was done to access the diagnostic and prognostic significance of IPF in relation to platelet counts in different thrombocytopenic patients. In present study, out of 43 cases of Hyperdestructive group, 41 (95.3%) cases showed increased IPF in comparison to Hypoproductive group, in which only 01 (0.06%) case out of 16 cases showed increased IPF. Megaloblastic group were in between the both groups showing increased IPF in 06 (42.8%) cases of total 14 cases. Hyperdestructive group includes ITP, dengue, malaria and viral infections. The hypoproductive group includes aplastic anemia, leukemia, and solid malignancy with marrow infiltrations. In our study IPF was significantly higher in hyperdestructive group (95%) compared to hypoproductive (0.06%) and megaloblastic group (42.8%), which was in concordance with studies by Pons et al and Naz et al.[12,13] Two case which showed reduced IPF in hyperdestructive group include one from dengue and one from viral etiology. The reason for such low IPF could be due to end stage or early stage of disease. Thrombocytopenia is established finding in malaria and is usually due to peripheral destruction of platelets.[14] In our study all cases of ITP, malaria and majority cases of dengue showed higher IPF, which signifies common underlying mechanism in all these cases is increased destruction of platelets. In present study significant inverse correlation between IPF% and platelet count; lower the platelet counts, the higher the IPF% was seen in hyperdestruction group, similar findings were observed by Dadu et al, Briggs et al and Pons et al.[3,11,12,15] In megaloblastic anaemia both ineffective thrombopoiesis and hypoproduction has been proposed as the mechanism for cause of thrombocytopenia. In our study 43% 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.[16,17] 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.[18] Hence more studies are required for evaluating role of IPF in megaloblastic group before coming to needful conclusion. 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.[19] In our study only one case from hypodestructive group showed higher IPF, which was a case of leukemia. 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[20] and as an indirect biomarker of poor prognosis in myelodysplastic syndrome with karyotypic abnormalities[21] was studied.

Conclusion

Immature Platelet Fraction is a simple non-invasive procedure for estimating the reticulated platelets percentage in peripheral blood to monitor the megakaryocytic activity. IPF is significantly higher in hyperdestructive group indicating increased thrombopoiesis in such cases and its value is inversely proportional to platelet count. Hypoproductive group showed no increase in IPF suggesting decreased production. Megaloblastic thrombocytopenia group is to be separated from hypoproductive groups, as IPF%, mean IPF% and mean platelet counts were significantly higher and further study on this area is required. Since bone marrow examination is invasive and expensive and platelet indices such as PDW, MPV and P-LCR lack significant sensitivity and specificity, IPF as a relatively new parameter can potentially be used as a diagnostic and prognostic maker for assessing the rate of thrombopoiesis in thrombocytopenic patients.

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