Original Article

DOI: 10.7860/NJLM/2022/51168.2604

Pathology Section

Evaluation of Immature Platelet Fraction in Patients with Fever and Thrombocytopenia and its Clinical Utility

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ABSTRACT

Introduction: Thrombocytopenia is very common in dengue and other haematological disorders and the aetiology is multifactorial. Immature Platelet Fraction (IPF) is a novel parameter which is a measure of reticulated platelets and it reflects the rate of regeneration of platelets.

Aim: To evaluate the relationship between the IPF and platelet recovery and the consistency of its expression.

Materials and Methods: The present study was a retrospective observational study done at Institute of Pathology, Madras Medical College between November 2018 to December 2018. Total 37 patients having fever with thrombocytopenia in dengue and other haematological causes were included for analysis. The platelet count, IPF, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Plateletcrit (PCT) was evaluated at the time of admission and once in every 24 hours and plotted in excel spread sheet.

Results: About 86.4% were recovered in 24 hours after attaining the peak, 89.1% showed recovery in 24-48 hours of the rise of the IPF compared to the previous value and 94.5% recovered within 24 hours after the fall in the IPF value. It was observed that 81.8% were recovered when the IPF value ≥10% within 24-48 hours. IPF readings are able to appreciate even in low platelet count levels but the other platelet recovery parameters did not.

Conclusion: IPF is a consistent and reliable marker which can be measured even when the platelet count is low and it also predicts the platelets recovery. It is a promising marker that helps in guiding the decision towards platelet transfusion.

Keywords: Dengue, Mean platelet volume, Platelet transfusion

INTRODUCTION

Pathogenesis of thrombocytopenia is multifactorial, hence, it is difficult to diagnose and predict the recovery. The IPF is a novel parameter which is an automated measure of reticulated platelets in peripheral blood [1]. Reticulated platelets contain Ribonucleic Acid (RNA) and are newly released platelets that are larger, more physiologically active and are analog of red cell reticulocytosis [2]. The number of reticulated platelets reflects the rate of thrombopoiesis [3]. IPF level rise as bone marrow production of platelet increases and therefore, it is a measurement that provides an assessment of bone marrow platelet production from peripheral blood sample (in a similar way as a reticulocyte count provides a measure of red cell production) [2,4]. The IPF can predict the timing of platelet recovery. The mean platelet recovery time is 1-2 days from the day of IPF increase [4,5]. The normal range of IPF is between 1.1 to 6.1 [2].

Thrombocytopenia in patients with dengue may cause a steep fall in platelet count, warranting platelet transfusion. However, by monitoring the IPF value, unnecessary transfusions can be avoided since it has an increased risk of alloimmunisation, immunosuppression, transmission of infectious diseases and graft vs host disease. IPF also can be used as a predictor of platelet recovery after cytotoxic chemotherapy and peripheral blood stem cell transplantation [6]. It is also helpful in assessing the forthcoming sepsis and its recovery [7]. IPF is a good reliable, consistent clinical utility marker. It can be measured even in very low platelet count, where the other platelet recovery parameters like MPV, PDW and PCT cannot be consistently measured [8]. The aim of this study was to establish the relationship between IPF and increase in platelet count and IPF cut-off to predict platelet recovery and the consistency of the marker comparing to the other platelet recovery marker in patients with thrombocytopenia due to various causes.

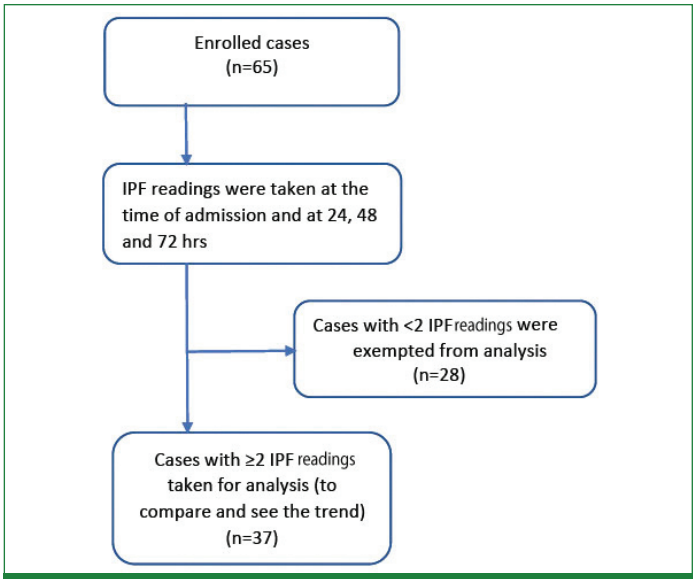
MATERIALS AND METHODS

This was a retrospective observational study conducted at Institute of Pathology, Rajiv Gandhi Government General Hospital and Madras Medical College, Chennai, Tamil Nadu, India, between November 2018 to December 2018. Data was analysed on October 2020. The consent was not obtained since it was done as routine patients clinical care and not done as a separate research mode. History taking, clinical examination and peripheral blood smear study (for manual platelet counting) was done for all patients.

Inclusion criteria: Dengue Immunoglobulin M (IgM) serology positive patients with fever and thrombocytopenia and patients with fever and thrombocytopenia of other causes were included in the study.

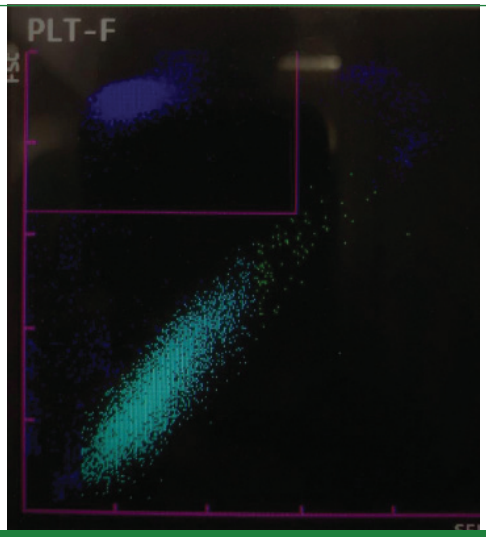
Exclusion criteria: Patients with idiopathic thrombocytopenia and chemotherapy induced thrombocytopenia were excluded.

Total 65 cases were enrolled in this study and 37 cases were taken into analysis explained in the flowchart [Table/Fig-1].



[Table/Fig-1]: Flowchart explains the recruitment and analysis protocol.

Sample collection: Two mL of venous blood sample was collected daily from the patients using K2 Ethylenediaminetetraacetic acid (EDTA) containing purple top tubes. The samples were kept in the refrigerated under 2-8°C until the use for analysis. All samples were analysed within two hours of collection. The platelet count, MPV, PDW, PCT and IPF were analysed using XN1000 Sysmex (Japan) fully automated analyser. The platelet count and IPF was estimated using florescent dye binding of platelet RNA on the Sysmex XN 1000 by flowcytometry on the PLT-F channel [Table/Fig-2]. Platelet count less than 1.5 lacs/mm^3 was considered as thrombocytopenia. Rise in the IPF value >6.1 was considered as increased IPF and ≥10 was considered as peak IPF value. Platelet count and IPF follow-up was done at intervals ranging from 24-72 hours with atleast two readings. To calculate recovery time on a single data point of IPF with a cut off value of ≥10% is considered in this study.



[Table/Fig-2]: Image of IPF-F reading in XN1000 Sysmex (Japan) fully automated analyser.

STATISTICAL ANALYSIS

Data was plotted in the Excel spread sheet and the analysis of relationship between platelet count and IPF, platelet count and IPF cut-off value, IPF and other platelet recovery parameters were done.

RESULTS

Total 37 patients associated with fever and thrombocytopenia were analysed. Among them, dengue IgM serology were positive in 15 cases and negative in 22 cases. On the day of admission, the platelet counts ranged from 3000-1,00,000 cells/cumm. IPF was monitored everyday along with platelet count and peripheral blood smear. Two IPF readings were taken in 14 patients upto 24 hours and three readings were taken in 15 patients within 48 hours and four readings were taken in eight cases within 72 hours.

In this study, IPF ≥10 was reached in 23 cases and IPF value <10 in 14 cases. The relationship of the IPF count to platelet recovery by looking at different points in time/time points is as follows:

When IPF reached its peak value;

When IPF showed a rising trend;

When IPF showed a falling trend;

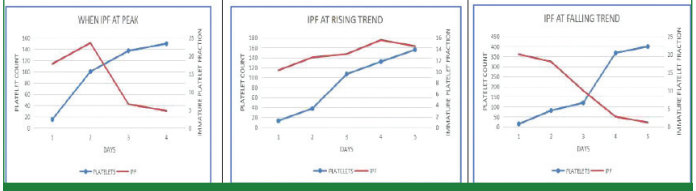
When IPF crossed 10%;

[Table/Fig-3] illustrates the relationship of platelet with IPF at its peak, rising trend and falling trend. Peak refers to the maximum IPF value reached while monitoring IPF on daily basis. The time required to start recovering after IPF reached its peak value was then calculated. It is observed that 86.4% was recovered within 24 hours, 94.5% were recovered in 48 hours and remaining in 72 hours. Rising/falling trend was defined as an increase or decrease respectively, in IPF by more or less than 10% (cut-off value of IPF) from its previous value. Present study demonstrated that 89.1% (33 cases) showed recovery

DAYS	1	2	3	4
PLT	15	100	137	150
IPF	17.8	23.6	6.6	4.7

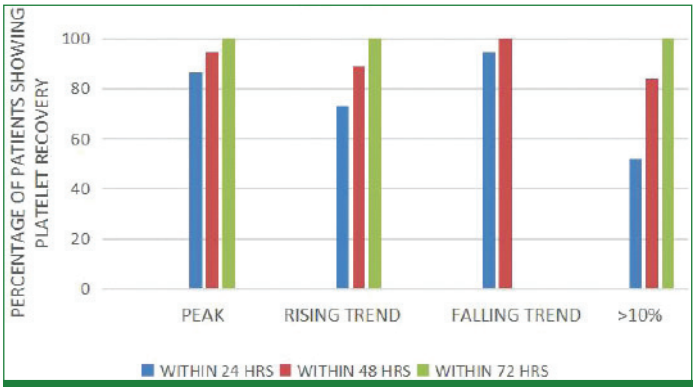
DAYS	1	2	3	4	5
PLT	13	38	107	132	156
IPF	10.2	12.5	13.1	15.6	14.1

DAYS	1	2	3	4	5
PLT	14	81	120	368	400
IPF	20.1	18	10	2.8	1.2



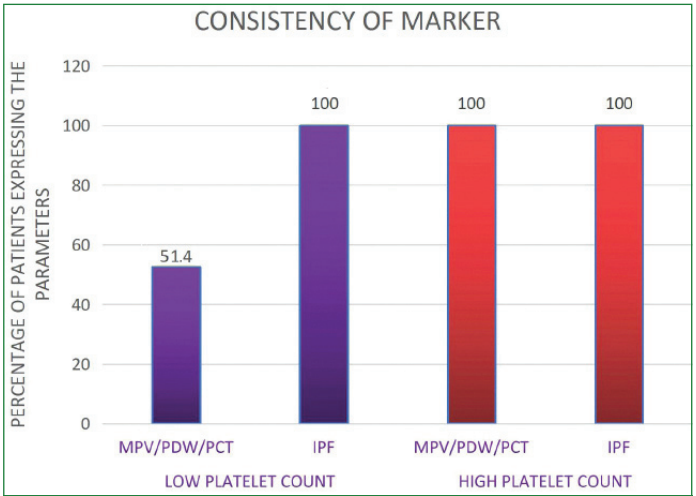
[Table/Fig-3]: Relationship of platelet with IPF at its peak, rising trend and falling trend.

within 24-48 hours of the rise and 94.5% showed a recovery within 24 hours of fall. The recovery time was also calculated on a single data point with a cut-off value of ≥10% and found that 81.8% of the patients showed platelet recovery within 24-48 hours if the IPF was more than 10% [Table/Fig-4].



[Table/Fig-4]: Percentage of patients showing platelet recovery at different time points.

Maximum IPF value was 26.9% and minimum value was 2%. The maximum IPF value was 26.9%, seen in non dengue patients. Among the dengue serology positive patients, the highest IPF value was 20.1%. The mean IPF value is generally higher in non dengue thrombocytopenic patients than dengue serology positive patients. The IPF value was expressed in all patients with whatever the platelet value the patients had, but the other platelet recovery markers like MPV, PDW and PCT were not expressed in all low platelet count cases i.e., 51.4% (19 cases) of all the studied cases [Table/Fig-5].



[Table/Fig-5]: Percentage of recordings of IPF vs other platelet recovery markers in low and high platelet.

DISCUSSION

The IPF is a new parameter which is an automated measure of reticulated platelets in peripheral blood. The normal range of the IPF value is 1.1 to 6.1 [2]. In present study, the mean IPF was 11.67%, minimum IPF measured was 2% and maximum was 26.9%. Thrombocytopenia is a usual finding associated with dengue and other platelet disorders. In dengue, the reason for thrombocytopenia is multifactorial, which includes early transient bone marrow suppression with damage to megakaryocytes [9],

haemophagocytosis [10,11], and platelet aggregation to endothelial cells targeted by dengue fever viruses [12]. Usually, a prophylactic platelet transfusion is given when the platelet count is less than 20,000 cells/cumm in asymptomatic patients. There are no guidelines available when to transfuse platelets in an asymptomatic patient. However, according to World Health Organisation (WHO), it should be noted that prophylactic platelet transfusion for severe thrombocytopenia in otherwise haemodynamically stable patient have been shown to be ineffective and not necessary [13]. IPF can be used by the physician to predict the recovery of platelets in patients with dengue so as to avoid unnecessary platelet transfusion.

Present study showed that after reaching the peak IPF value, 86.4% were recovered in 24 hours, 94.5% were recovered in 48 hours and the rest at 72 hours. Present study found a delay in recovery of platelets in patients with negative dengue serology. Dadu T et al., studied 32 dengue only patients with thrombocytopenia and showed that 84.3% patients were recovered in 24 hours and the rest within 24 to 48 hours [1]. Present study also found that the IPF starts going up (rising trend), where 89.1% cases had recovery of platelets within 24-48 hours. After reaching the peak value, IPF started falling on the next day. This fall in the IPF was a strong predictor of an impending rise in platelets. So, if the platelets have not started recovering then the time lag for recovery of platelets in such cases was 24 to 48 hours. It was observed that 94.5% showed recovery within 24 hours of the fall. Based on the single time point IPF cut-off value of 10% and found that 81.8% patients showed platelet recovery within 24-48 hours if the value was ≥10%. But Dadu T et al., showed 93.75% showed recovery within 24-48 hours of the rise and 100% recovery within 24 hours of the fall and 93.75% showed recovery within 24 hours if the IPF was >10% (cut-off value).

The other parameters used to assess platelet regeneration in thrombocytopenia are MPV, PDW and PCT. In present study, 51.4% of patients with low platelet count did not show these parameters but the IPF value was expressed in all patients with low platelet count. Similarly, Bhat R and Pai S showed 36.8% of patients with low platelet count had a missing credit of these markers whereas IPF was expressed consistently in all cases [8].

Limitation(s)

Aetiology of non dengue cause were not made out. Only limited number of studies were available to compare. Prospective studies with large sample size are required, many numbers of studies are warranted in dengue and other indications are required for the study.

CONCLUSION(S)

Immature Platelet Fraction (IPF) is a consistent marker of platelet recovery even in low platelet count. IPF is reliable and promising parameter in guiding the decisions related with platelet transfusions in thrombocytopenia. The time lag between increased IPF value and the corresponding increase in platelet appears to be around 24-48 hours in dengue patients and around 24-72 hours in patients with thrombocytopenia due to other causes. Therefore, measuring IPF value should be in routine in the evaluation and monitoring of patients with thrombocytopenia.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 03, 2021
- Manual Googling: Nov 07, 2021
- iThenticate Software: Nov 23, 2021 (11%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jul 02, 2021**
Date of Peer Review: **Jul 24, 2021**
Date of Acceptance: **Nov 07, 2021**
Date of Publishing: **Apr 01, 2022**