

Original Article

One Health Bulletin

Immature platelet fraction as a clinical predictor for enhanced platelet recovery in patients with dengue fever

I Ketut Agus Somia[1]✉,Cokorda Agung Wahyu Purnamasidhi[1], Dewa Ayu Fony Prema Shanti[2], Giovanca Verentzia Purnama[2], I Komang Hotra Adiputra[2]

[1]*Tropical and Infectious Diseases Division, Internal Medicine Department, Faculty of Medicine, Udayana University, Udayana University Academic Hospital, Bali 80111, Indonesia*

[2]*Faculty of Medicine, Udayana University, Bali 80111, Indonesia*

ABSTRACT

Objective: To evaluate the potential of immature platelet fraction (IPF) as a predictor of increased platelets in dengue fever patients.

Methods: A cross-sectional study was conducted. We analyzed the medical records of confirmed dengue patients who were admitted to Udayana University Academic Hospital. Pearson correlation was used to assess the correlation between increased IPF and ratio of increased platelets in patients with dengue fever.

Results: Between June 2022 and December 2022, 41 patients were included in the study. Their mean age was 45.0 ± 18.5 years, with males comprising 60.0% of the cohort. The initial mean platelet count was 107.7 × 10^3 cells/μL at baseline and increased to 128.1 × 10^3 cells/μL by the end of the observation period. The mean IPF was 1.9 ± 1.6%. A moderate positive correlation was identified between IPF levels and the subsequent increase in platelet count two days after measurement.

Conclusions: IPF reflects the rate of thrombopoiesis in patients with thrombocytopenia and serves as an indicator of recovery in dengue fever patients.

KEYWORDS: Immature platelet fraction; Dengue fever; Platelet count; Clinical predictor

1. Introduction

Dengue fever is a potentially life-threatening tropical disease caused by the dengue virus. This virus has become endemic in more than 100 countries with an annual incidence of 390 million cases worldwide, according to the World Health Organization (WHO) [1]. As a tropical country, Indonesia is one of the countries with a high rate of dengue virus infection. This disease has become a concern for the government due to its high prevalence. In 2020, a total of 103 509 cases of dengue fever were recorded, with 725 deaths reported. According to these data, the three provinces with the highest number of cases were West Java, Bali, and East Java[1,2].

Patients with dengue fever are characterized by a sudden onset of high fever. Other symptoms of dengue patients are severe joint and muscle pain, restlessness, and clammy skin. In more severe

Significance

Dengue fever's clinical progression is closely tied to platelet dynamics, yet predicting recovery remains challenging. Immature platelet fraction (IPF) is recognized as a marker for thrombopoiesis, but its role in dengue has been underexplored. This study identifies IPF as a moderate predictor for platelet recovery, enhancing our understanding of dengue management. The findings support IPF's clinical utility as an early indicator of recovery, improving patient monitoring and guiding timely interventions.

✉To whom correspondence may be addressed. E-mail: agus.somia@unud.ac.id

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2025 *One Health Bulletin* Produced by Wolters Kluwer- Medknow.

How to cite this article: Somia IKA, Purnamasidhi CAW, Shanti DAFP, Purnama GV, Adiputra IKH. Immature platelet fraction as a clinical predictor for enhanced platelet recovery in patients with dengue fever. One Health Bull 2025; 5(3): 119-123. doi: 10.4103/ohbl.ohbl_48_24

Article history: Received 30 August 2024 Revision 4 January 2025 Accepted 24 February 2025 Available online 27 February 2025

conditions, dengue fever can lead to bleeding or easy bruising. One of the distinguishing features of severe dengue is bleeding tendencies. Patients may develop petechiae (small red or purple spots under the skin), easy bruising, nosebleeds, or gum bleeding. Gastrointestinal bleeding, such as hematemesis or melena, may also occur. This feature could happen due to the disruption of the blood clotting system and the decrease in the number of platelets or commonly known as thrombocytopenia[3].

Monitoring platelet count as an indicator is critical to determine the severity of dengue[4,5]. Platelet levels often drop during the critical phase of dengue, which usually occurs 3-7 days after the onset of symptoms. Severe thrombocytopenia can also result in leakage of plasma, leading to dengue shock syndrome, which can cause organ failure. Early detection of thrombocytopenia is vital as it can signal the progression of dengue from mild to severe[1,2].

The immature platelet fraction (IPF) is a parameter used in haematology to assess the percentage of immature platelets in a person's bloodstream. The IPF provides information about the ratio of these immature platelets to the total number of platelets in the bloodstream. A high IPF percentage suggests increased production of young platelets in response to a higher demand for platelet function, often due to ongoing bleeding, platelet destruction, or other factors[6]. However, monitoring IPF to detect the severity of dengue is still rarely done by healthcare professionals. This article explores the potential of IPF as a predictor of increased platelets in dengue fever patients.

2. Subject and methods

2.1. Study design

This study is a cross-sectional study and analyzes secondary data from 41 medical records of confirmed dengue patients who were admitted to Udayana University Academic Hospital l from June to December of 2022. This study includes epidemiological and laboratory findings, particularly platelet count and immature platelet fraction which were examined between day 3 to day 9 after the onset of symptoms.

2.2. Ethical approval

Ethical approval was released by the ethical committee of Udayana University (No: 1468/UN14.2.2.VII.14/LT/2022) This study has taken signed consent from the participants who agreed to take part in it. All subject information was maintained with strict confidentiality and used in compliance with ethical research guidelines.

2.3. Samples and data collection

2.3.1 Study subjects and sampling techniques

The study initially included all medical records of patients infected with dengue who were treated at RSUP Prof. Dr. I.G.N.G. Ngoerah from June to December 2022. The sample was selected using a consecutive sampling method, which included all patients diagnosed with dengue who received treatment during the specified time period.

2.3.2 Sample size

All patients confirmed with dengue who underwent IPF examination during the specified time period will be included as the study sample.

2.3.3 Study data collection

Eligibility was determined based on predefined inclusion and exclusion criteria. Patients aged 18-59 years with positive antigen and/or NS1 ELISA result who consented to undergo IPF count examination were selected as study subjects. From the inclusion criteria, 64 patients were identified and subsequently re-evaluated based on the predefined exclusion criteria. Patients with incomplete examination data, those who refused the examination, patients hospitalized for more than 7 days after symptom onset, patients with hematologic malignancies, HIV, or autoimmune diseases were excluded from the study. Based on these criteria, 41 medical records of confirmed dengue fever or dengue hemorrhagic fever patients were selected as the study subjects.

2.4. Diagnostic criteria

Dengue diagnosis was confirmed through positive NS1 ELISA or dengue antigen tests, with positivity determined based on specific thresholds outlined in the hospital protocol. Severe dengue was identified according to WHO criteria[2,3], which include the presence of shock, severe bleeding, or organ involvement such as liver dysfunction or fluid accumulation. The IPF was measured using flow cytometry, with values exceeding 4% considered abnormal, as per the hospital's standard protocol.

2.5. Variables and definitions

The outcome variables included the IPF and platelet count. The IPF was measured using flow cytometry in the hospital's laboratory, with abnormal values defined as greater than 4%. Platelet count was obtained from a complete blood count performed using an automated hematology analyzer, such as the Sysmex XN-1000, and reported in cells/μL.

The primary exposure variable was dengue infection, confirmed through NS1 ELISA or dengue antigen tests, with thresholds for positivity defined as NS1 >1.0 optical density (OD) and antigen

>1 000 units/mL. Predictor variables included age, recorded in years from patient medical records; sex, documented as male or female; and comorbidities, identified through medical records and defined as a binary variable (yes/no) for conditions such as diabetes, hypertension, or asthma, based on ICD-10 codes or physician's notes.

Confounders considered were age, measured in years from medical records; comorbidities, documented using ICD-10 codes or physician diagnoses; and disease severity, classified as severe or non-severe dengue according to WHO criteria, based on clinical examination and laboratory findings. Finally, effect modifiers included dengue severity, evaluated using WHO criteria, which encompass shock, bleeding, and organ involvement. The classification of disease severity was recognized as potentially influencing the interpretation of IPF and platelet counts, with severe cases often demonstrating distinct platelet dynamics.

2.6. Statistical analysis

Data were analyzed using SPSS Statistics version 25. A normality test was performed on numerical variables, with variables following a normal distribution reported as mean and standard deviation, and those with a non-normal distribution reported as median and interquartile range (Q1–Q3). Parametric analysis was conducted using Pearson correlation for normally distributed numerical data, while non-parametric analysis employed Spearman correlation for non-normal distributed data.

The primary objective of the analysis was to evaluate the correlation between increased IPF and platelet count in dengue patients. A significance level of $P<0.01$ was set for all analyses. To control for potential confounding bias, we adjusted for variables such as age, sex, and comorbidities (*e.g.* diabetes and hypertension) using multivariate regression analysis. This ensures that observed associations between IPF and platelet count are not confounded by these factors. Additionally, to address selection bias, consecutive sampling was used to include all eligible patients who met the inclusion criteria during the study period. Patients with incomplete data or contraindications for IPF testing were excluded from the study. To minimize information bias, data were collected from reliable sources, including standardized laboratory tests (NS1 ELISA, *etc.*). All laboratory tests were conducted following established protocols, which ensured consistency and accuracy in the data collected.

3. Results

We observed 41 patients diagnosed with dengue fever who were tested with antigen and/or NS1 test. Based on the 41 medical records of confirmed dengue fever patients presented in Table 1, 60.9% were male and 39.1% were female. The average age of subjects in this study was 45.0 ± 18.5 years with the age range 21-40 years accounting for 51.2% of the participants. The remaining patients were in the following age ranges : 41-60 years (29.3%), 61-80 years (14.6%), and over 81 years (4.9%). A total of 8 (19.5%) patients received blood transfusions during treatment due to thrombocytopenia and plasma leakage.

The patient's platelet count and IPF (%) were measured during hospitalization, with symptom onset ranging from three to nine days after fever onset. The platelet count showed a downward trend from the first day until the fifth day of illness, and an upward trend afterwards. The initial mean platelet count was 107.7×10^3 cell/μL and the final mean platelet count was 128.1×10^3 cell/μL (Figure 1). The average IPF was 1.9 ± 1.6%. The IPF peaked on the fourth and eighth days of illness, with an upward trend observed from the fifth to the eighth day. The highest IPF recorded was 7.1% on the eighth day, while the lowest was 0.2% on the sixth day (Figure 2).

Correlation of IPF% and ratio of platelet increases were measured using pearson correlation analysis. We found a moderate positive correlation between IPF and increased platelets two days after measurement. This finding shows that after the peak of the IPF, the platelet count will increase two to three days later and vice versa for the IPF value. Based on statistical testing, results were significant (Table 2).

Table 1. Patients characteristics.

Variables	n=41*
Age group, years	
Mean ± SD	45.0 ± 18.5
21 – 40	21 (51.2)
41 – 60	12 (29.3)
61 – 80	6 (14.6)
⩾ 81	2 (4.9)
Sex	
Male	25 (60.9)
Female	16 (39.1)
Severity of dengue	
Non-severe	29 (70.7)
Severe	12 (29.3)
Plasma leakage	
Yes	8 (19.5)
No	33 (80.5)
Outcome after admission	
Recovered	41 (100.0)
Not recovered	-

Data were expressed as n (%) unless otherwise specified.

Table 2. Correlation of IPF and platelet counts over three days.

	Platelet count (Day 1)	Platelet count (Day 2)	Platelet count (Day 3)	P*
Platelet count (Day 1)			1	0.05
Platelet count (Day 2)		1	0.31	0.01
Platelet count (Day 3)	1	0.32	0.35	0.01

*Correlation is significant at the 0.01 level (2-tailed).

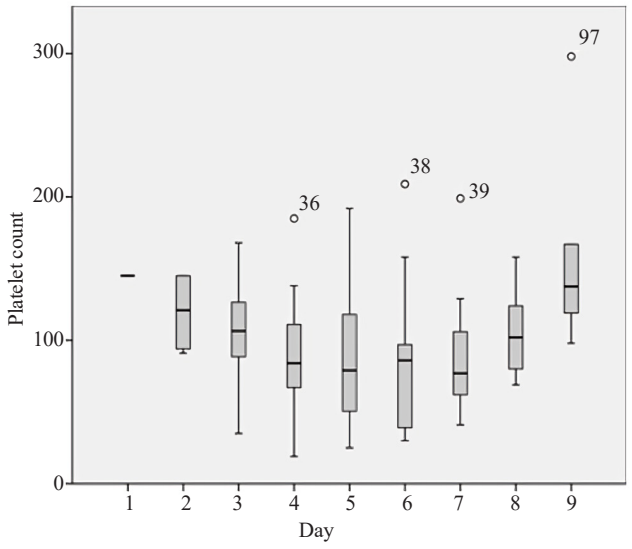


Figure 1. Time course of platelet count (cell/µL).

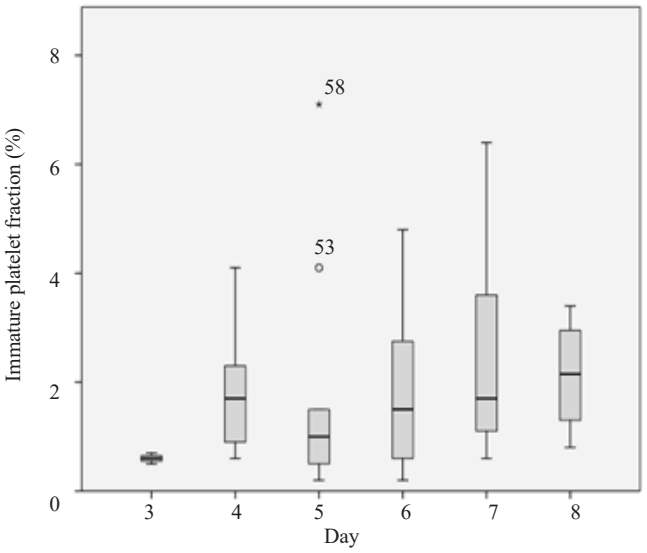


Figure 2. Time course of immature platelet fraction(%).

4. Discussion

Treatment of severe dengue infections depends on proper fluid management and effective bleeding control to maintain vital organ functions. Local interventions and platelet concentrate transfusions are necessary to correct haemostasis in cases of excessive bleeding. The main strategy in treating this condition is strict observation and monitoring. Most patients will be discharged from the hospital once the fever subsides and the appetite returns. However, at this stage, the platelet count may not have fully returned to normal.

In general, platelets will spontaneously return to normal within 7-10 days after the peak of the fever[7]. IPF can reflect the rate of thrombopoiesis in patients with thrombocytopenia as well as an indicator of patient recovery[8,9]. In addition, IPF has been used as a marker for determining the etiology of thrombocytopenia, whether due to excessive platelet destruction or decreased production of platelets in the bone marrow[8].

In this study, IPF was measured as a predictor of thrombocyte rise in the following days. We found a moderate positive correlation between IPF and increased platelet counts two and three days after IPF% peak. This finding shows how IPF can be used as a predictor of platelet increase in patients with dengue infection. In diagnosing thrombocytopenia, the use of IPF can help in distinguishing between peripheral thrombotic damage, marked by an increase in IPF, and active thrombopoiesis from hypoplastic bone marrow with decreased thrombopoiesis. A cutoff value of >5.95% with a sensitivity of 88.0% and specificity of 75.9% indicates that a patient's thrombocytopenia is caused by excessive platelet destruction[8]. Similar results were also found by Jung *et al.*, Abe *et al.*, and Sakuragi *et al.* who threshold values of 7.7%, 6.15%, and 7.3% respectively[10–12].

In study by Jeon *et al.* found that IPF was a predictive marker for thrombocyte recovery[13]. The study noted that in patients with severe thrombocytopenia, platelet counts recovered to >40.0 × 10^9/L 3 to 4 days after the IPF dropped from its peak. In another study by van der Linden *et al.*, it was presented that IPF could be used as a predictor of thrombocyte recovery within two days using a cut off value of 5.3%[14]. The study by Chuansumrit *et al.* revealed that the level of IPF with a value >10% will be followed by the thrombocyte recovery to the hemostatic level within 72 hours[7]. The results are similar to the study conducted by Dadu *et al.* which stated that when a patient with dengue fever reaches the IPF value of >10%, it was found that 93.5% of patients will have recovery within 24-48 hours[15]. Similarly, the study carried out by Suman F *et al.* found that 28 patients with a dengue infection showed the recovery of the platelets within 48 hours when IPF was >10.6%[16].

5. Conclusions

In this study, we identified that IPF has the potential to serve as a predictive marker for platelet count recovery, which typically occurs two to three days after the peak IPF value. This finding indicates that IPF% can be utilized as a predictor of platelet increase in patients with dengue infection. Additionally, IPF has been used as a marker to determine the etiology of thrombocytopenia, whether it is caused by excessive platelet destruction or decreased platelet production in the bone marrow, as observed in patients with dengue infection. These findings suggest that IPF can be utilized as an additional predictive tool to monitor platelet recovery and identify the etiology of thrombocytopenia. However, it is important to note that recovery from dengue infection is not solely determined by platelet count. The restoration of platelet levels is merely one of the indicators of the recovery phase in dengue.

The limitation of this study is the limited sample size, which may reduce the representativeness of the findings for a broader population and limit the generalizability of the results to different

clinical scenarios. We recommend that future studies include larger sample sizes and perform daily IPF measurements to establish a definitive cut-off point for IPF in relation to subsequent platelet count increases. Such research could enhance the reliability of IPF as a predictive marker in clinical practice.

Conflict of interest statement

The authors claim there is no conflict of interest.

Funding

This study receives no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Somia IKA and Purnamasidhi CAW designed the study, data collection, manuscript writing, and manuscript review. Shanti DAFP, Purnama GV, and Adiputra IKH contributed to analyze the study, manuscript wring and manuscript editing. All authors approved the final version of the manuscript and agree to be accountable for the accuracy and integrity of the work.

References

[1]World Health Organization. 2024. *Dengue and severe dengue*. Available online from: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue. [Accessed on 6 June 2024].

[2] Kementerian Kesehatan Republik. *Data DBD Indonesia. In Data Kesehatan Republik Indonesia*. Jakarta: Kementerian Kesehatan Republik Indonesia; **2021**; 30.

[3] Schaefer TJ, Panda PK, Wolford RW. *Dengue Fever*. In: StatPearls [Online]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430732/. [Accessed on 13 June 2024].

[4] Wahidannisa R, Muslim M, Arsyad M. Gambaran trombosit pada penderita demam berdarah dengue di rumah sakit brigjen H. Hasan basry kandangan februari dan maret 2015. *ERGASTERIO* 2016; **3**(2):1-10.

[5] Losada PX, DeLaura I, Narváez CF. Dengue virus and platelets: From the biology to the clinic. *Viral Immunol* 2022; **35**(5): 349-358.

[6] Saidah F, Sjakti HA. Peran pemeriksaan immature platelet fraction dalam imun trombositopenia. *Sari Pediatr* 2018; **20**(3): 190.

[7] Chuansumrit A, Apiwattanakul N, Sirachainan N, Paisooksantivatana K, Athipongarporn A, Tangbubpha N, et al. The use of immature platelet fraction to predict time to platelet recovery in patients with dengue infection. *Paediatr Int Child Health* 2020; **40**(2): 124-128.

[8] Goel G, Semwal S, Khare A, Joshi D, Amerneni CK, Pakhare A, et al. Immature platelet fraction: Its clinical utility in thrombocytopenia patients. *J Lab Physicians* 2021; **13**(3): 214-218.

[9] Rauber P, Lammert F, Grotemeyer K, Appenrodt B. Immature platelet fraction and thrombopoietin in patients with liver cirrhosis: A cohort study. *PLoS One* 2018; **13**(2): e0192271.

[10]Jung H, Jeon HK, Kim HJ, Kim SH. Immature platelet fraction: Establishment of a reference interval and diagnostic measure for thrombocytopenia. *Korean J Lab Med* 2010; **30**(5): 451-459.

[11]Sakuragi M, Hayashi S, Maruyama M, Kiyokawa T, Nagamine K, Fujita J, et al. Immature platelet fraction (IPF) as a predictive value for thrombopoietic recovery after allogeneic stem cell transplantation. *Int J Hematol* 2018; **107**(3): 320-326.

[12]Abe Y, Wada H, Tomatsu H, Sakaguchi A, Nishioka J, Yabu Y, et al. A simple technique to determine thrombopoiesis in thrombocytopenic patients using immature platelet fraction (IPF). *Blood* 2004; **104**(11): 3941.

[13]Jeon K, Kim M, Lee J, Lee JS, Kim HS, Kang HJ, et al. Immature platelet fraction: A useful marker for identifying the cause of thrombocytopenia and predicting platelet recovery. *Medicine (Baltimore)* 2020; **99**(7): e19096.

[14]Van der Linden N, Klinkenberg LJJ, Meex SJR, Beckers EAM, de Wit NCJ, Prinzen L. Immature platelet fraction measured on the sysmex XN hemocytometer predicts thrombopoietic recovery after autologous stem cell transplantation. *Eur J Haematol* 2014; **93**(2): 150-156.

[15]Dadu T, Sehgal K, Joshi M, Khodaiji S. Evaluation of the immature platelet fraction as an indicator of platelet recovery in dengue patients. *Int J Lab Hematol* 2014; **36**(5): 499-504.

[16]Suman F, Dcruze L, Rajendran R, Varadarajan S. Dengue: Platelet and immature platelet dynamics a study done at a tertiary care centre from south india. *IJRTSAT* 2014; **3**(1): 6-21

Publisher's note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Edited by Liang TC, Qi Y