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THE IMMATURE PLATELET FRACTION; AN EARLY RECOVERY INDICATION OF THROMBOCYTOPENIA IN DENGUE FEVER

Original Research

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ABSTRACT

Background: Dengue fever is a major arboviral infection associated with significant morbidity, particularly due to thrombocytopenia, which can lead to severe complications. The immature platelet fraction (IPF%) serves as an indicator of bone marrow activity and platelet regeneration. Identifying IPF trends can help predict platelet recovery earlier than conventional platelet counts, aiding clinical decision-making and potentially reducing unnecessary platelet transfusions.

Objective: This study aimed to evaluate the role of IPF% as an early predictor of platelet recovery in dengue patients with thrombocytopenia.

Methods: A cross-sectional observational study was conducted over six months, from August 2023 to January 2024, at the Department of Medicine, CMH Rawalpindi. A total of 150 patients diagnosed with dengue, confirmed by positive NS1 antigen or IgM antibody, were enrolled. Venous blood samples (5 mL) were collected in EDTA tubes and analyzed using the Sysmex XE-2100 automated hematology analyzer. Reference IPF values were established using 50 healthy samples. Patients were categorized into two groups: Group 1 with platelet counts <20,000/µL and Group 2 with platelet counts between 20,000–60,000/µL. IPF% and platelet counts were recorded at 24, 48, and 72 hours.

Results: At 24 hours, 61 (87.1%) patients in Group 1 and 58 (72.5%) in Group 2 exhibited a rising IPF trend. By 48 hours, 64 (88.8%) in Group 1 and 60 (75.3%) in Group 2 reached peak IPF >10%. At 72 hours, 62 (96.8%) in Group 1 and 64 (80%) in Group 2 demonstrated a declining IPF trend, coinciding with platelet count recovery.

Conclusion: IPF% strongly correlates with platelet recovery in dengue-related thrombocytopenia. The declining trend of IPF serves as a potential marker for early recovery, offering a valuable clinical tool for predicting disease progression and guiding transfusion decisions.

Keywords: Dengue, hematology, immature platelet fraction, platelet count, predictive biomarker, thrombocytopenia, viral infection.

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INTRODUCTION

Dengue fever remains the most prevalent arboviral infection with significant public health implications, contributing to an estimated 390 million infections globally each year, of which approximately 96 million presents with clinical manifestations of varying severity (1). A substantial proportion of severe dengue cases progress to dengue hemorrhagic fever, occurring in 2–5% of patients and carrying an increased risk of mortality (2). Among the hallmark complications of severe dengue, thrombocytopenia is particularly concerning due to its potential to exacerbate hemorrhagic manifestations. While thrombocytopenia in dengue is primarily immune-mediated, severe cases may also involve disseminated intravascular coagulation, further complicating patient outcomes (3). Currently, no specific treatment has demonstrated a definitive clinical benefit in managing dengue-associated thrombocytopenia, making supportive care the cornerstone of treatment. Platelet recovery following transient bone marrow suppression in dengue typically occurs within ten days post-infection, although thrombocytopenia can persist beyond this period (4). Immature platelets, newly released from megakaryocytes, are larger in size, rich in RNA cytoplasm, and require approximately 24 hours to mature following bone marrow recovery (5). Given this maturation time lag, the presence of immature platelets in circulation serves as a valuable indirect marker of bone marrow activity, with their absolute count and percentage providing insight into marrow suppression and recovery dynamics (6).

Thrombocytopenia in dengue often results in a rapid decline in platelet counts, raising concerns about the need for platelet transfusion. However, unnecessary transfusions pose risks such as alloimmunization, immunosuppression, transmission of infections, and graft-versus-host disease (7). Avoiding unwarranted transfusions is particularly crucial in resource-limited settings, where blood products may not be readily available. A transfusion can be safely deferred if platelet counts are anticipated to rise, necessitating a reliable predictor of platelet recovery. The immature platelet fraction (IPF) has emerged as a promising biomarker in this regard, offering the potential to guide clinical decision-making in dengue management (8). IPF represents the proportion of immature platelets in peripheral blood, identified based on their larger size and higher RNA content, characteristics that enable their detection using advanced hematology analyzers. Measured as a percentage of the total platelet population, IPF provides an early indication of bone marrow recovery before a detectable rise in platelet count occurs. Studies have consistently demonstrated that IPF levels increase prior to platelet count recovery, suggesting its role as a valuable predictor in dengue-related thrombocytopenia (9,10).

This study aims to evaluate the clinical utility of IPF% in predicting platelet count recovery among dengue patients with thrombocytopenia. By establishing its predictive value, this research seeks to mitigate unnecessary platelet transfusions, thereby minimizing associated risks and optimizing resource utilization in healthcare settings. Given the constraints of limited medical resources, particularly in endemic regions, this study also underscores the economic implications of reducing avoidable transfusions, ultimately contributing to more efficient dengue management strategies.

METHODS

The study was a prospective observational investigation conducted at the Combined Military Hospital (CMH), Rawalpindi, Pakistan, from August 2023 to January 2024, following ethical approval from the hospital's ethical review board. The study aimed to assess the role of the immature platelet fraction (IPF%) in predicting platelet recovery among patients diagnosed with dengue. A total of 150 patients aged 18–80 years were enrolled, with the sample size determined using the EPI Open Calculator. The diagnosis of dengue was confirmed through the detection of dengue non-structural antigen 1 (NS1) and/or dengue-specific IgM antibodies. Patients were admitted from the time of presentation to the hospital until the resolution of symptoms. Written informed consent was obtained from all participants after being briefed about the study objectives. Among the enrolled patients, 95 (63.3%) were male, and 55 (36.6%) were female. To standardize comparisons, patients were categorized into two groups based on platelet count: Group 1 included those with a platelet count of less than 20,000/µL, while Group 2 comprised those with platelet counts ranging from 20,000/µL to 60,000/µL. The classification was strictly based on platelet count rather than clinical severity, ensuring that all patients within each group had similar baseline platelet parameters for a uniform assessment of platelet recovery dynamics.

A 5 mL venous blood sample was collected from each participant using an ethylenediaminetetraacetic acid (EDTA) tube. Samples were stored at 4–8°C and subsequently warmed to 20–25°C for 20–25 minutes before analysis. The Sysmex XE-2100 automated hematology

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analyzer was utilized for IPF measurement. The system employs a semiconductor diode laser beam with fluorescent staining to differentiate between mature and immature platelets based on RNA content and cell volume. To establish a reference range for IPF, blood samples from 50 healthy individuals undergoing routine complete blood count testing were analyzed. Reproducibility was assessed by analyzing three distinct samples: one with normal IPF and normal platelet count, another with high platelet count and low IPF, and a third with high IPF. The sample with high IPF was repeatedly analyzed seven times to evaluate measurement consistency. Stability was assessed using three samples with normal IPF and normal platelet counts and three with low platelet counts and high IPF. All patients underwent serial monitoring of IPF% and platelet count at 24-hour, 48-hour, and 72-hour intervals to track platelet recovery trends. The IPF values observed in the study ranged from 2% to 5%. This time-based approach allowed for the identification of early predictors of platelet recovery, which could aid in optimizing clinical decision-making, particularly in determining the necessity of platelet transfusions. The methodology ensures a robust assessment of IPF as a predictor of platelet recovery in dengue patients with thrombocytopenia. By focusing on platelet count-based classification rather than clinical severity, this study provides a more objective framework for evaluating bone marrow activity and platelet regeneration trends over time.

RESULTS

A total of 150 patients were included in the study, of whom 95 (63.3%) were male and 55 (36.6%) were female. Patients were categorized based on platelet count into two groups: Group 1 included 70 (46.6%) patients with platelet counts <20,000/µL, and Group 2 included 80 (53.3%) patients with platelet counts between 20,000/µL and 60,000/µL. Immature platelet fraction (IPF%) was measured and ranged between 2% and 5% at baseline. All patients were observed at 24, 48, and 72 hours for IPF percentage and platelet count assessment. Three key IPF trends were noted during the study: an initial rise in IPF, a peak where IPF exceeded 10%, and a subsequent decline. In Group 1, at the 24-hour mark, 61 (87.1%) patients showed an increasing IPF trend with a mean platelet count of 15,000/µL. At 48 hours, 64 (88.8%) patients had an IPF peak exceeding 10%, and the mean platelet count rose to 25,000/µL. By 72 hours, 62 (96.8%) patients with previously peaked IPF exhibited a declining trend, with platelet counts surpassing 70,000/µL. Similarly, in Group 2, at 24 hours, 58 (72.5%) patients had an increasing IPF trend with an average platelet count of 35,000/µL. By 48 hours, 60 (75.3%) patients had peaked IPF levels exceeding 10%, and platelet counts increased to 44,000/µL. At 72 hours, IPF began to decline in 64 (80%) patients, with platelet counts rising to 90,000/µL. The decline in IPF was more pronounced in Group 1, correlating with a more substantial increase in platelet count compared to Group 2. A significant association was observed between IPF trends and platelet recovery, indicating that the fall in IPF corresponded with thrombocytopenia resolution.

Table1: Demographic Data

Variable	Count	Percentage (%)
Total Patients	150	100
Male	95	63.3
Female	55	36.6
Group 1 (<20,000 Platelets)	70	46.6
Group 2 (20,000-60,000 Platelets)	80	53.3

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Table 2: Increase in IPF in group 1 and 2 at 24, 48 and 72 hours

IPF (24 hrs.)	**Groups**		**p-value**
	Group 1 (<20,000 platelets)	Group 2 (20,000-60,000 platelets)	
<5%	9	22	0.027
5-10%	61	58	
IPF (48 hrs.)			
<10%	6	20	0.008
>10%	64	60	
IPF (72 hrs.)			
<10%	68	64	0.001
>10%	2	16	

Table 3: Increase in platelet count in group 1 and 2 at 24, 48 and 72 hours

Platelet count (24 hrs.)	**Groups**		**p-value**
	Group 1 (<20,000 platelets)	Group 2 (20,000-60,000 platelets)	
<20,000	70	22	0.000
20,000-40,000	0	58	
Platelet count (48 hrs.)			
<20,000	6	0	0.000
20,000-40,000	64	20	
40,000-60,000	0	60	
Platelet count (72 hrs.)			
<20,000	2	0	0.05
20,000-40,000	6	16	
40,000-60,000	62	64	

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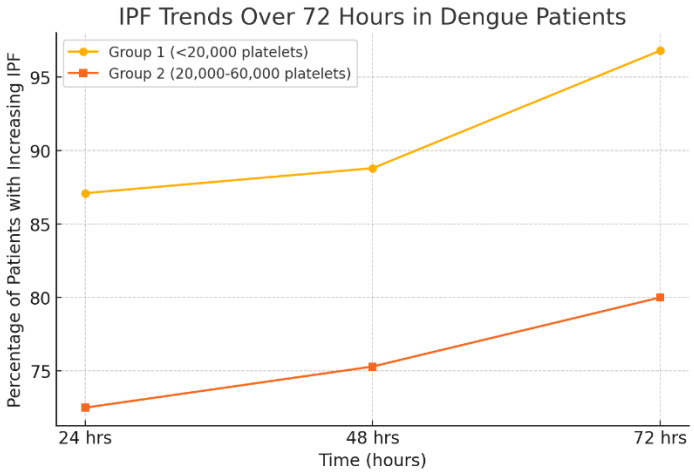

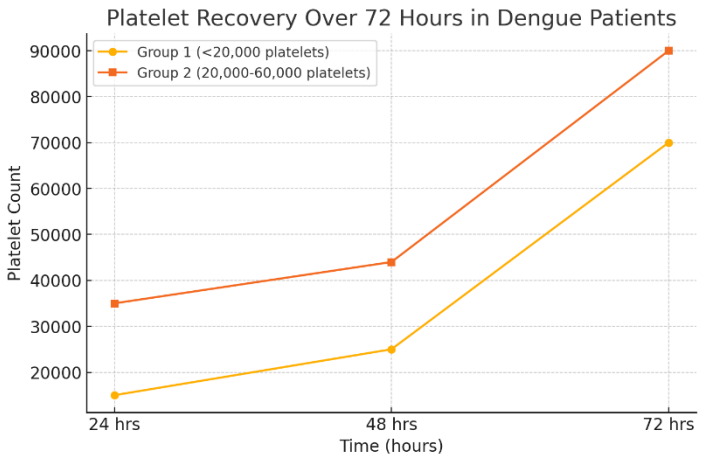

DISCUSSION

Dengue fever is a mosquito-borne viral infection with a significant global disease burden. Thrombocytopenia is a hallmark of dengue, posing a substantial risk for hemorrhagic complications and severe disease outcomes. The disease progression involves an initial viremic phase followed by a host immune response, during which plasma leakage occurs, coinciding with a decrease in platelet and white blood cell counts. The platelet count is widely monitored as a key biomarker to guide clinical management, particularly in differentiating between the critical and recovery phases of the illness (11). Although there is no specific antiviral treatment for dengue, early supportive interventions have significantly reduced mortality rates to less than 1% (12). Identifying reliable early indicators of platelet recovery is crucial to optimizing patient management, preventing unnecessary platelet transfusions, and reducing healthcare costs (13). The immature platelet fraction (IPF) has gained attention as a biomarker of bone marrow activity and platelet regeneration. Studies have demonstrated that IPF levels rise early in dengue patients and peak before platelet count recovery, making it a promising indicator of disease progression and recovery (14). Evidence suggests that in severe dengue cases, IPF remains elevated between days 3 and 5 of illness before falling as platelet counts begin to rise (15). A study has shown that IPF% was significantly increased in patients with severe dengue compared to those with non-severe disease, reinforcing its potential as an early recovery marker (16). The observed increase in IPF is likely a compensatory response to platelet destruction, similar to mechanisms seen in immune thrombocytopenic purpura, or may reflect a rebound effect from transient bone marrow suppression induced by the dengue virus (17).

The clinical implications of IPF as an early recovery indicator are substantial. An earlier prediction of platelet recovery could facilitate timely discharge, minimize hospital-acquired infections, and reduce unnecessary platelet transfusions (18). Studies have established that IPF peaks ahead of platelet count recovery, with a majority of patients demonstrating significant platelet increase within 24 to 48 hours of IPF peaking. This reinforces the prognostic value of IPF in guiding platelet transfusion decisions and tailoring treatment strategies to individual patient needs (19). Another study found that IPF values in dengue patients during hospital admission were significantly higher than in healthy individuals, with most patients reaching peak IPF early in their hospital stay, further supporting its role as an early predictor of platelet recovery (20). In this study, 150 patients were analyzed, with 95 males and 55 females. Patients were divided into two groups based on platelet count, with 70 patients in Group 1 (<20,000/µL) and 80 in Group 2 (20,000–60,000/µL). The findings revealed that Group 1 exhibited a more rapid increase in IPF, reaching peak levels earlier than Group 2, with 88.8% of patients in Group 1 crossing the 10% IPF threshold compared to 75.3% in Group 2. By 72 hours, IPF had fallen in 96.8% of Group 1 patients, correlating with a significant rise in platelet count above 70,000/µL. In contrast, 80% of Group 2 patients showed a decline in IPF at 72 hours. These findings reinforce the utility of IPF as a predictive marker for platelet recovery, particularly in patients with severe thrombocytopenia. The greater and more rapid fall in IPF in Group 1 aligns with the more pronounced platelet count recovery, highlighting the potential of IPF to guide clinical decision-making in severe dengue cases.

Despite the promising findings, this study has limitations. It was conducted in a single center with a relatively small sample size, limiting the generalizability of the results. Additionally, the observation period was confined to 72 hours, and extending the follow-up duration

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could provide further insights into the long-term trends of IPF and platelet recovery. A multicenter study involving a larger and more diverse patient population would be necessary to validate these findings and develop standardized clinical guidelines. Nevertheless, this study provides strong evidence supporting the role of IPF in dengue management, reinforcing its potential as a predictive biomarker for thrombocytopenia recovery and a valuable tool in optimizing patient care.

No conflicts of interest were reported in this study.

CONCLUSION

The findings of this study underscore the significant prognostic value of the immature platelet fraction (IPF%) in assessing thrombocytopenia recovery in severe dengue. The dynamic trends of IPF, including its rise and subsequent decline, provide critical insight into the early stages of platelet regeneration, offering a more reliable indicator of recovery than platelet count alone. Its clinical utility extends beyond predicting disease progression, as it serves as a valuable tool for optimizing patient management, minimizing unnecessary platelet transfusions, and aiding in timely discharge decisions. By integrating IPF% into routine dengue management, healthcare providers can enhance treatment strategies, ultimately improving patient outcomes and resource utilization in dengue-endemic regions.

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