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Use of Immature Platelet Fraction as a Prognostic Marker in Dengue Fever

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ABSTRACT

Objective: To investigate the relationship between immature platelet fraction and poor short-term prognosis in dengue fever patients.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Pakistan Air Force Hospital, Islamabad Pakistan, from Oct to Dec 2022.
Methodology: In this study, a total of 300 cases had a confirmed diagnosis of dengue fever and were admitted to the hospital. An immature platelet fraction was performed on all the patients on the fifth day of febrile illness. All the patients were monitored closely by the treating team at 24, 48, and 72 hours for the presence of thrombocytopenia on the complete blood picture or other clinical complications of dengue fever.
Results: In the study, the median age of patients with dengue fever was 36(IQR-42) years. Out of 350 patients, 239(68.2%) were males, while 111(31.8%) were females. 282(80.5%) patients had a good prognosis, while 68(19.5%) did not have a good prognosis and showed clinical or haematological manifestations. On the fifth day of illness, 279(79.7%) had an IPF of >10%, whereas 71(20.3%) had an IPF of <10%. A statistical test revealed that IPF of less than 10% had a statistically significant association with poor prognosis in patients treated for dengue fever (p-value<0.001).
Conclusion: The immature platelet fraction was found to be less than 10% in a considerable number of patients. In the first week of illness, a decreased immature platelet fraction was found to be associated with the presence of thrombocytopenia and other clinical complications among patients managed for dengue fever.

Keywords: Dengue fever; Immature platelet fraction; Prognostic marker.

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INTRODUCTION

Dengue fever is a disease of lower and middle-income countries that has been an epidemic in our part of the world almost every year for the last decade.[1] Recent studies have shown that in most patients, it is limited to febrile illness, but in some cases, it may cause serious morbidity or even mortality.[2] Despite guidelines in place for evaluation and treatment of this illness, a considerable number of patients either suffer from complications or die with dengue fever.[3]

Fever, myalgias, lethargy, fatigue, sore throat, abdominal symptoms, and rash may occur as symptoms during the course of illness in patients suffering from dengue fever.[4] Platelet count and function may both be affected in a few patients, leading to severe and life-threatening complications.[5] Most of the patients who die or suffer serious life-threatening consequences actually have hemorrhagic complications secondary to platelet-related disorders.[6]

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In clinical practice, a variety of platelet-related indices have been used to predict the outcome of underlying infective or immune-mediated conditions. The immature platelet fraction is a new marker used to differentiate among various reasons for deceased platelets found in the blood of patients suffering from different types of disorders.[7] Wayez *et al*. revealed that an IPF of more than 8% was associated with a quick recovery in platelet count.[8] Dadu *et al*. revealed that IPF of more than 10% predicted a good outcome, especially platelet recovery, in patients suffering from dengue fever. They pointed out that this platelet index has the potential to become an important marker for clinical teams managing patients with dengue fever.[9]

For the last few years, dengue fever has been one of the main concerns of all of our country's health-regulating bodies. A lot of emphasis is placed on primary prevention and control of spread via mosquitoes, but thousands of people still get this disease, which is managed at primary, secondary, and tertiary care health facilities. A recent local study published in

this regard showed alarming figures related to the incidence of this disease and the mortality and morbidity caused by it in different parts of Pakistan.[10] Because our health resources are limited, patients' levels of care should be prioritised based on severity or suspected severity. This can be done if we have adequate knowledge of clinical risk factors and relevant laboratory markers. We planned this study with the rationale to look for an association between immature platelet fraction and poor short-term prognosis in patients managed for dengue fever at PAF Hospital, Islamabad Pakistan.

METHODOLOGY

The comparative cross-sectional study was conducted at the General Medicine Department of PAF Hospital, Islamabad Pakistan, from October to December 2022, after Hospital Ethical Committee approval (ltr no. IH/76077/5/TRG). Sample size was calculated using the WHO sample size calculator in two groups. Group-I had a good prognosis (57.3%), while Group-II had a poor prognosis (11.4%).[11] We used a non-probability consecutive sampling technique to collect a sample of dengue patients who had been admitted to the unit. Patients with dengue fever with a good and bad prognosis were divided into two study groups.

Inclusion Criteria: Patients of either gender, aged 18–60 years diagnosed with dengue fever and admitted to PAF Hospital Islamabad were included.

Exclusion Criteria: Patients labelled as pyrexia of unknown origin or any diagnosed comorbid infection or cause of fever in addition to dengue fever, those who were on steroids or any other medications that could have affected the platelet count or precipitated bleeding, patients with diagnosed bleeding disorders, malignant hemato-vascular system conditions, or any other part of the body were excluded.

The study included all patients with confirmed dengue fever who were admitted to the dengue ward based on clinical and laboratory findings by the consultant medical specialist. All the baseline investigations were performed with serial platelet levels from the Armed Forces Institute of Pathology (AFIP). On the fifth day of febrile illness, an immature platelet fraction was obtained from AFIP using the standard method, under the supervision of a consultant Haematologist. Patients were then followed up at 24, 48, and 72 hours after IPF was performed for both laboratory and clinical parameters. Trends of a fall in platelet count and any systemic complications of dengue fever were observed and noted for all the patients. Patients were classified as having a poor prognosis if they had a decrease in platelet count from any systemic complication.[12]

In the statistical analysis, SPSS version 23.0 was used. The median (IQR) was calculated for the patients' ages. For patients with IPF <10% and any systemic complications, frequency and percentage were calculated. Chi-square test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

For this study, a total of 350 patients admitted to the hospital for management of dengue fever were recruited. The median age of patients with dengue fever included in the study was 36(42) years. Out of 350 patients, 239(68.2%) were males, while 111(31.8%) were females. Table-I shows the social and demographic characteristics of patients with dengue fever. 282(80.5%) patients had a good prognosis, while 68(19.5%) did not have a good prognosis and showed clinical or haematological manifestations. On the fifth day of illness, 279(79.7%) had an IPF of >10%, whereas 71(20.3%) had an IPF of <10%. Thrombocytopenia, affecting 19(5.4%) of our study participants, was the most common complication, followed by abdominal pain (2.5%) and vomiting (2.5%). Out of the total study

Table-I: Characteristics of Patients with Dengue Fever (n=350)

Study parameters	n(%)
Age (years)	
Median (IQR)	36(42) years
Gender	
Male	239(68.2%)
Female	111(31.8%)
Immature platelet fraction	
>10%	279(79.7%)
<10%	71(20.3%)
Comorbid illnesses	
No	293(83.7%)
Yes	57(16.3%)
Complications faced by the target population	
Thrombocytopenia	19(5.4%)
Pain abdomen	09(2.5%)
Vomiting	09(2.5%)
Petechial hemorrhages	09(2.5%)
Internal hematomas	05(1.4%)
Bleeding from gums	04(1.1%)
Bleeding per rectum	03(0.8%)
Bleeding in vomiting	03(0.8%)
Hematuria	02(0.5%)
Prolong bleeding from minor wounds	02(0.5%)
Dengue shock syndrome	02(0.5%)
Others	04(1.1%)

participants, 02 patients (0.5%) suffered from dengue shock syndrome.

For comparison purposes, two groups were made. Group-I had patients with a good prognosis of 280(80.5%), while Group-II had patients with a poor prognosis of 68(19.5%). Statistical analysis revealed that an immature platelet fraction of less than 10% was statistically significantly higher in the group of patients with poor prognosis as compared to the gr-oup of patients with good prognosis (p-value<0.001). Other variables studied were not statistically different in both groups (p-value>0.05) (Table-II).

Table-II: Relationship of Variables Including Immature Platelet Fraction with Presence of Poor Prognosis (n=350)

	Good Prognosis	Poor Prognosis	*p*-value
Age			
40 year or less	152(53.9%)	37(54.4%)	0.939
>40 years	130(46.1%)	31(45.6%)	
Gender			
Male	187(66.3%)	52(76.4%)	0.099
Female	95(33.7%)	16(23.6%)	
Presence of comorbid illnesses			
No	233(82.6%)	60(88.2%)	0.621
Diabetes mellitus	38(13.5%)	06(8.8%)	
Hypertension	05(1.7%)	01(1.4%)	
Ischemic heart disease	03(1.1%)	01(1.4%)	
Rheumatoid arthritis	03(1.1%)	00(0%)	
Immature platelet fraction			
>10%	270(95.7%)	09(13.2%)	<0.001
<10%	12(4.3%)	59(86.8%)	

DISCUSSION

A lower immature platelet fraction was associated with complications in the first week of febrile illness among patients managed for dengue fever in our hospital. From August to November, dengue fever has been prevalent in our part of the world, and a huge number of patients suffer from it. Researchers and clinicians have been working hard to identify risk factors linked to complications in these patients.[13] They have also been working on laboratory investigation patterns that could be associated with poor outcomes or prognosis in order to pick high-risk patients early and manage them aggressively.[14] We designed this study with the goal of looking for an association between immature platelet fraction and a poor short-term prognosis in patients treated with dengue fever.

In 2021, Yasuda *et al*.[15] conducted a study from Japan regarding the role of immature platelet fraction in predicting the course of illness among patients suffering from dengue fever. They highlighted that this new platelet index is quite useful in predicting the severity of illness. Our study had similar findings, and it was found that a decreased immature platelet fraction was associated with severe symptoms and thrombocytopenia among these patients. After this parameter was tested, we closely monitored the patients for three days. According to Looi *et al*. (2021), dengue fever progression was correlated with immature platelet function.[16] It was concluded that IPF done on days 3-5 of illness was significantly associated with severe forms of illness, and its use in predicting the course of illness was advocated. In our analysis, the immature platelet fraction was found to be less than 10% in a considerable number of patients. In the first week of illness, a decreased immature platelet fraction was found to be associated with the presence of thrombocytopenia and other clinical complications among patients managed for dengue fever.

A study from Thailand was published with the objective of looking for the role of immature platelet fraction in predicting the time to recovery of platelet count in patients managed for dengue fever. After defervescence, it was discovered that IPF ≥10.0% emerged as a predictor of subsequent platelet recovery to a normal level.[17] We studied both clinical and laboratory parameters and found that IPF ≥10.0% was associated with both a good laboratory and clinical response among dengue fever patients.

In 2022, a prospective study was published in which the authors attempted to determine the predictive value of IPF regarding the early and smooth recovery of patients from dengue fever. They used a cutoff of 7.15% on days 2 or 3 and found it to be sensitive and specific in predicting smooth recovery.[18] We studied a cutoff of 10% at day 5 of illness and found it to be associated with good clinical and laboratory parameters recovery.

LIMITATION OF STUDY

Multiple factors could lead to complications and may be associated with a poor outcome; therefore, it cannot be concluded that decreased immature platelet fraction was the main cause of the poor prognosis in patients suffering from dengue fever. This study was only conducted on admitted patients, so it could not accurately reflect the actual burden of the problem.

CONCLUSION

The immature platelet fraction was found to be less than 10% in a considerable number of patients. In the first

week of illness, a decreased immature platelet fraction was found to be associated with the presence of thrombocytopenia and other clinical complications among patients managed for dengue fever.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AH & AN: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MTY & UQ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FAS & SU: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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