Original Article

Clinical and laboratory evaluation of Immature Platelet Fraction for prediction of acute dengue infection

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ABSTRACT

Background: Dengue fever when there is increased platelet consumption and destruction, the immature platelet fraction (IPF) is elevated. Marrow failure results in a decrease in it. The timing of platelet recovery can be predicted by the IPF%. After an IPF rise, the platelet recovery period is one to two days. It is yet unknown what the cut-off threshold is above which platelet recovery is anticipated. The aim of this study was to evaluate IPF for platelet recovery in dengue patients.

Methods: Platelet count and immature platelet fraction (IPF) from daily blood samples of patients with dengue infection during hospitalisation and 1–4 weeks after discharge were retrospectively analysed. The levels of patients' IPF were compared with normal controls recruited from healthy children with normal platelet counts.

Results: A total of 244 EDTA blood samples were collected daily from 64 patients (45 males) with dengue infection (36 dengue fever, 28 dengue haemorrhagic fever) during hospitalisation and after discharge from the hospital. They did not receive any platelet concentrate transfusion. The median IPF among normal children was 3.6% with a 95

percentile of 9.9%. In dengue patients, an IPF of ≥10.0% after defervescence was associated with a subsequent platelet count of ≥60 × 10^9/L within 72 hours.

Conclusion: In patients with dengue infection, IPF ≥10.0% after defervescence is a predictor of subsequent platelet recovery to a haemostatic level ≥60 × 10^9/L within 72 hours.
Key words: Dengue fever, Dengue Infection, Immature Platelet Fraction, Platelet recovery.

Introduction

The arboviral virus that spreads the fastest and poses the greatest threat to public health is dengue. According to best estimates, 390 million dengue infections occur annually worldwide, with 96 million of those episodes exhibiting varied degrees of clinical severity [1]. Furthermore, the 2013 Global Burden of Dengue study revealed that there are 60 million symptomatic dengue infections year, with 10,000 or so deaths from the disease [2]. In the tropical regions where dengue sickness is most prevalent, there are currently no accessible, safe, effective and reasonably priced dengue vaccinations or targeted treatments.

In India, there were 50,000 dengue infections in 2012, including 227 fatalities, according to the ministry of health. According to the national vector-borne illnesses control programme, 988 cases were recorded from Chennai, and 5376 cases were reported from Tamilnadu. Thrombocytopenia and leucopenia are the primary haematological disorders associated with dengue [3].

There is a correlation between the severity of DHF and platelet count. The rapid decrease in platelet count is accompanied by, or soon after, a sharp increase in haemoglobin. The objective proof of plasma leakage is an increase in hemoconcentration, or an increase in hemocrit of 20% above the baseline. In DHE, hemoconcentration and thrombocytopenia are consistent findings [4–8]. Monitoring platelet counts is essential for managing dengue hemorrhagic fever. A rise in platelet count indicates recovery. The automated measurement of reticulated platelets in peripheral blood is known as the immature platelet fraction (IPF), which is a unique parameter. These are bigger, more physiologically active, and analogues of red cell reticulocytes. They also contain RNA. The quantity of reticulated platelets indicates the thrombopoiesis rate [7-10].

In illnesses when there is increased platelet consumption and destruction, the immature platelet fraction (IPF%) is elevated. Marrow failure results in a decrease in it [11]. The timing of platelet recovery can be predicted by the IPF%. After an IPF rise, the platelet recovery

period is one to two days [12,13]. It is yet unknown what the cutoff threshold is above which platelet recovery is anticipated.

An excellent, dependable, and consistent clinical utility marker is IPF. In situations where other platelet recovery metrics, such as MPV, PDW, and PCT, cannot be reliably evaluated, it can be measured even in very low platelet counts [14]. The aim of this study was to evaluate IPF in dengue patients.

Material and Methods

This study was an observational study conducted in a hospital. A study was conducted on patients who, between December 2016 and October 2018, presented to the Department of Medicine's OPD and IPD with dengue fever and thrombocytopenia. Every patient provided their informed consent before the trial started. Every patient received a thorough examination and history, and each was looked into using a proforma that was created.

Inclusion Criteria

Age around 15 years, acute undifferentiated febrile illness lasting approximately 5 days, with a recorded fever of 37.5°C and no alternative syndromic diagnosis.

Exclusion Criteria

The study excluded individuals who were pregnant, those with underlying congestive heart failure, liver failure, renal failure, diabetes mellitus, any kind of active or ongoing cancer, people infected with the HIV virus, and those with immunodeficiency.

Every patient had a 3 ml venous blood sample taken, which was promptly sent to the lab. The detection of the NS1 antigen and anti-dengue immunoglobulin IgM and IgG was performed in accordance with manufacturer instructions using a commercially available strip test (SD Bio line Dengue Duo). The fully automated XN1000 Sysmex (Japan) analyzer was used to examine the platelet count, MPV, PDW, PCT, and IPF. Using fluorescent dye binding of platelet RNA on the Sysmex XN 1000 by flowcytometry on the PLT-F channel, the platelet count and IPF were determined.

The patients were grouped into 5 categories according to their platelet count on the day of the admission [15].

High risk < 20,000/c.mm

Moderate > 20,000 – 40,000/c.mm

Low risk > 40,000 – 1,00,000/c.mm

No risk > 1,00,000 – 1,50,000/c.mm

Normal > 1.5 lakhs / c.mm

Statistical analysis

The link between platelet count and IPF, platelet count and IPF cut-off value, IPF, and other platelet recovery parameters was analysed after the data was plotted in an Excel sheet.

RESULT

The study included 148 suspected instances of dengue; 120 of those cases were proven to be dengue, while the remaining 28 cases were classified as non-dengue. Twenty-one of the dengue cases that were confirmed were considered serious cases. In the study group, there were 42 women (35%) and 78 men (65%). The mean IPF of the cases was 8.3% (SD± 6.4%), while the mean platelet count was 46.8 × 10^3 /µL (SD ± 298 × 10^3 /µL).

The current study's mean IPF was 10.9%, with a minimum of 2.6% and a maximum of 26.9% observed. A common finding in dengue and other platelet diseases is thrombocytopenia. Thrombocytopenia in dengue is caused by a variety of factors, including early, transitory bone marrow suppression and megakaryocyte destruction.

Of them, 85 (70.83%) were in the risk group and 35 (29.1%) were not in any risk category. Risk criteria are used to categorise these 120 patients. There were three risk categories: low risk (32.94%), moderate risk (42.35%), and high risk (24.70%).

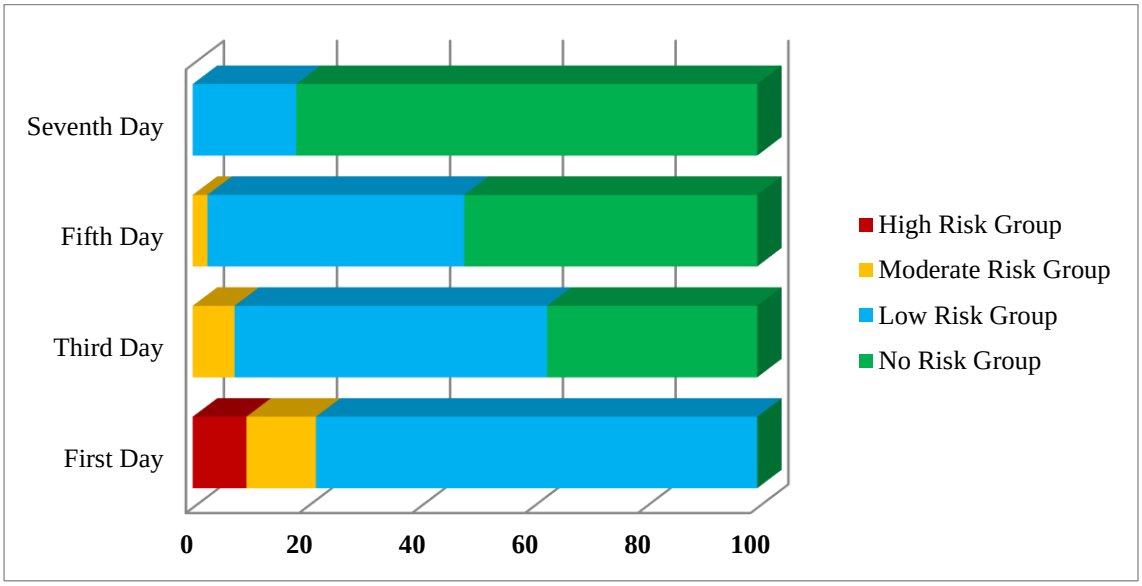

Figure 1: Platelet categories on various days in Dengue patients

Patients with dengue had a lower platelet count at admission and continued to do so until days 8 and 9 following the onset of fever. From day 10 forward, the platelet count rose towards normal levels. From the time of admission to day 6, the IPF% of dengue patients grew. From that point on, it decreased progressively until day 8, at which point it rapidly decreased. IPF% was significantly greater and the platelet count of patients with severe dengue was significantly lower on days 5–7 (P=0.0348 on day 5, P=0.0087 on day 6, and P=0.059 on day 7).

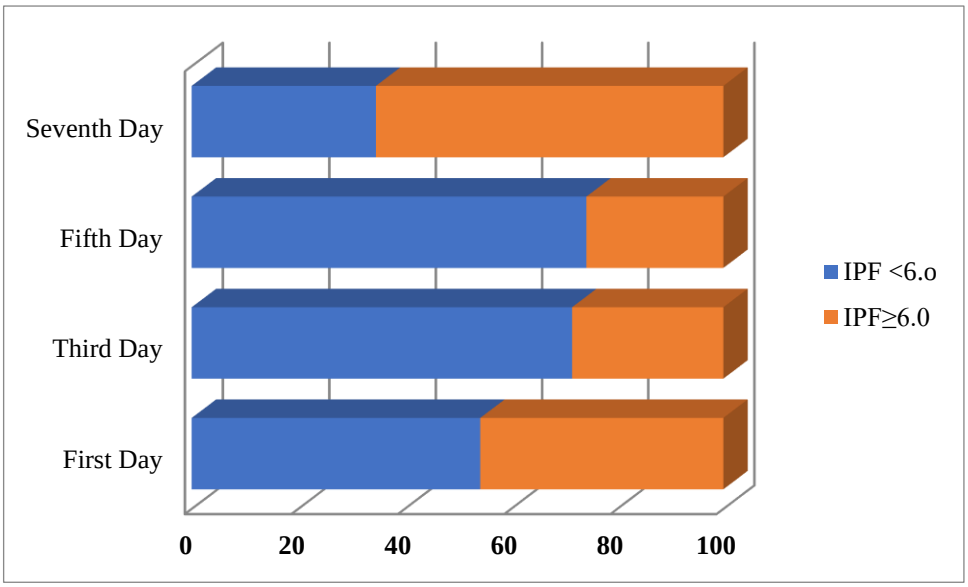

Figure 2: IPF Level on various days in Dengue patients

Similar to the platelet count, the reticulocyte count declined from day 1 to day 3, then increased from day 4 to day 7. On days three and four, there was no significant difference in the absolute reticulocyte count between individuals with severe dengue and those without; however, on day five, there was a significant difference. Similar to the reticulocyte absolute count, the ratio of reticulocyte counts to total erythrocytes (RET%) exhibited similar trend (p=0.651 on day 3; p=0.382 on day 4; and p=0.0065 on day 5).

Table No.1: Day wise improvement according to risk categories

Risk	**Day 3**	**Day 5**	**Day 7**
Low Risk	07 (25%)	13 (46.42%)	08 (28.57%)
Moderate Risk	16 (44.44%)	13 (36.11%)	07 (19.44%)
High Risk	02 (9.52%)	06 (28.57%)	13 (61.90%)

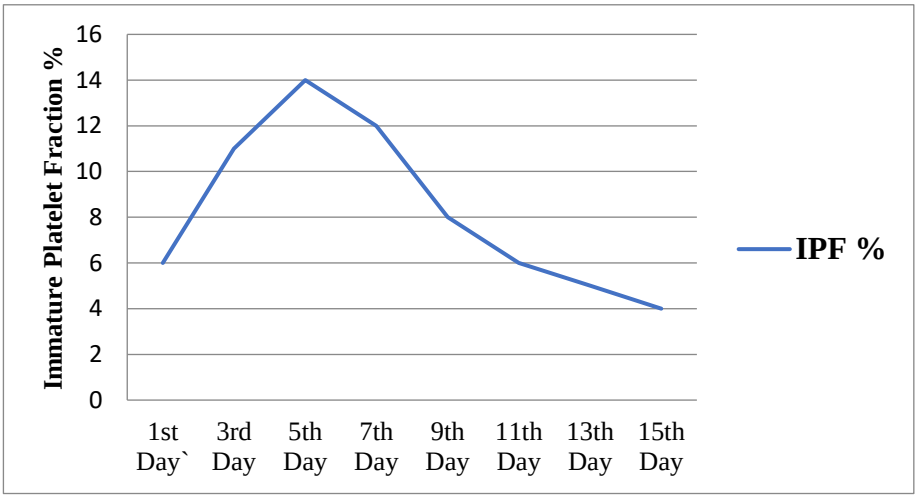

Figure 3: Trends of mean IPF% of study group

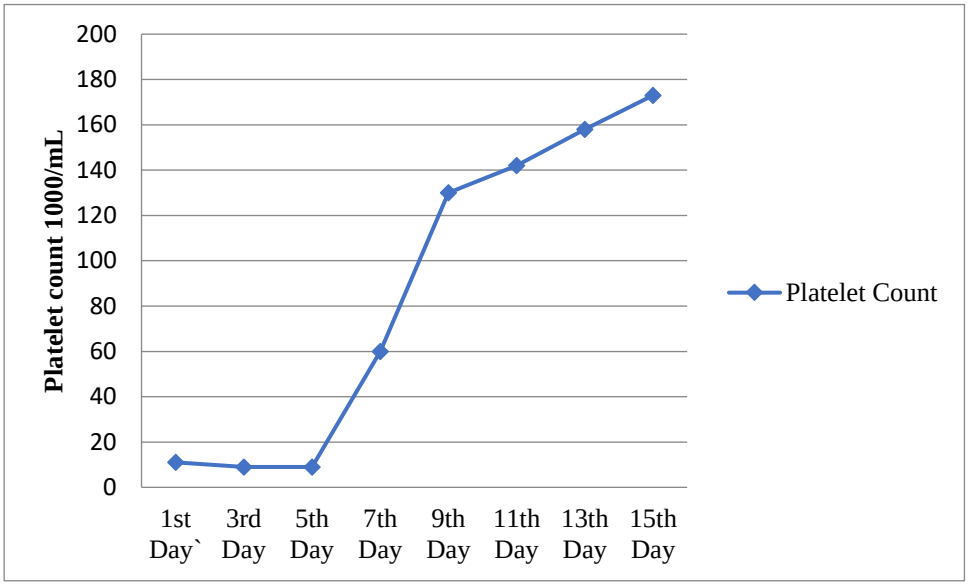

Figure 4: Trends of mean Platelets count

Discussion

An automated measurement of reticulated platelets in peripheral blood is the new IPF parameter. The IPF value typically falls between 1.1 and 6.1 [16]. A doctor can use IPF to forecast a patient's platelet recovery from dengue and prevent needless platelet transfusion [17]. Males (65%) were more frequently impacted in this study; comparable findings were published from Delhi in 2006 [18]. In contrast to our research, a Brazilian study found that more female patients were isolated [19]. IPF% rose for longer than three days before platelet recovery, indicating that it may be a useful indicator for predicting how patients with dengue will respond in terms of platelet count; Studies by Dadu et al., 2014 [20], Kumar et al., 2016

[21], and Chuansumrit et al., 2020 [22] produced findings that were comparable to these. While Francisia F et al [24] only noticed on the eleventh day8,11, Ahmed S et al [23] had discovered platelet growth on the seventh day. This suggests that it's critical to keep an eye on the platelet count for at least a week following admission.

Day 1 to Day 5 saw an increase in the IPF levels as well. Between days five and seven, there is a downward trend. The reason for this is that before platelet recovery, the IPF rises from 1-2 days to 3-7 days [25, 26]. 54.2% of patients with high IPF in this study drift their risk category within three days of onset of fever, followed by 26.7% in five days and 15.4% in seven days. Patients with IPF < 6.3% had platelet recovery in 10.2% of cases. These changes might be because of lower IPF level than normal levels, or it could be because IPF fall of before platelet recovery. In 3.1% of cases, there was minor improvement in patients having significant IPF level. This could result from use of antibiotics or sepsis.

An automated method of measuring reticulated platelets in peripheral blood is called Immature Platelet Fraction (IPF). In current study, we observed that 83.5% patients had IPF level more than 10% and only 16.8% patients had IPF below 10% when the IPF was correlated with the platelet counts on third day and fifth day. A noteworthy positive association was discovered, which is comparable to the research presented by Dadu et al. in 2014. We followed the WHO's recovery standards, which called for a platelet count cut off value of 50,000/cumm to be reached before platelets could be recovered. Patients were considered to have recovered if their platelet count was greater than 50,000/cumm on the second or third day of presentation. These individuals can be released from the hospital since their hemodynamics is stable [27].

CONCLUSION

Even in cases of low platelet counts, immature platelet fraction (IPF) consistently indicates platelet recovery. When it comes to helping make decisions about platelet infusions for thrombocytopenia, IPF is a dependable and promising metric. In dengue patients, there appears to be a 24-48-hour time lag between an increased IPF value and a commensurate increase in platelets; in patients with thrombocytopenia from other causes, there appears to be a 24-72-hour time lag. As a result, thrombocytopenia patients should routinely have their IPF value measured when they are being evaluated and monitored.

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