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Original Research Article

Utility of immature platelet fraction to predict platelet recovery in dengue patients having thrombocytopenia

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ABSTRACT

Background: Dengue is one of the most common viral and probably also the most common important arbovirus infections in the world. Thrombocytopenia in patients with dengue may cause a steep fall in platelet count, warrant for platelet transfusion. However, unnecessary transfusions are best avoided due to heightened risk from alloimmunization, immunosuppression, transmission of infectious diseases and graft-vs.-host disease. This brings us to the issue of how we can reliably predict the rise in the platelet count. IPF count holds great promise of being this predictor. The aim of this study was to establish the relationship between IPF and increase in platelet count in patients with dengue who suffer from thrombocytopenia.
Methods: This is a hospital based observational descriptive study done in November 2017 to August 2019 on all the dengue patients who were positive for NS1 antigen or IgM antibody or both and treated at Mahatma Gandhi Medical College and Hospital, Jaipur. The values of platelet and IPF were retrieved for day 1st, 3rd, 5th and 7th day of admission. Association between values of IPF and significant clinical change in platelet values during the subsequent 48 hrs is done. A sensitivity analysis was carried out to ascertain the cut-off of IPF on the corresponding days which yielded increase in platelet values of over 20,000 in the subsequent 48 hrs.
Results: There is statistically significant ($P<0.01$) improvement in platelet values within 48 hrs when the IPF is more than 6.1%.
Conclusions: IPF is an additional parameter to predict platelet recovery, so that prophylactic platelet transfusion can be deferred and also the hazards associated with it.

Keywords: Dengue, Platelets, Immature platelet fraction, Platelet transfusion

INTRODUCTION

Dengue is a mosquito-borne infection caused by four distinct serotypes of an arbovirus i.e. dengue virus. These four distinct serotypes of dengue virus viz. DEN -1, DEN-2, DEN-3 and DEN -4 are closely related. Symptoms start after an incubation period of 3 to 7 days and follow three phases- an initial febrile phase, a critical phase around the time of defervescence, and a spontaneous recovery phase.[1]

Dengue is the result of complex interactions among host, vector and virus that are influenced by climatic factors. In virus development, temperature plays important role, so study of different climatic regions may be useful in understanding spatio-temporal variations in dengue risk.

The major pathophysiological hallmark of dengue is plasma leakage as a result of increased vascular permeability. Following this leakage, hypovolemic shock occurs as a consequence of a critical plasma volume loss. Constant haematological abnormalities occurring in

dengue include bone marrow suppression, leucopenia and thrombocytopenia.

An enhanced immune response of the host to a secondary dengue virus infection is a feature of DHF and leads to many consequences. These immune mechanisms are complement activation, immune complex formation, increased histamine release and a massive release of many cytokines into the circulation leading to shock, vasculopathy, thrombopathy and disseminated intravascular coagulation (DIC). The mechanisms of bleeding in DHF are multiple like vasculopathy, thrombopathy and DIC. Thrombopathy consists of thrombocytopenia and platelet dysfunction.[2]

The immature platelet fraction (IPF) is measured in an automated measure of reticulated platelets in peripheral blood. Reticulated platelets are newly released platelets that contain RNA and are larger, more physiologically active and are the analog of the red cell reticulocyte.[3]

The number of reticulated platelets reflects the rate of thrombopoiesis.[4] IPF levels rise when bone marrow production of platelets increases, and therefore, its measurement provides an assessment of bone marrow platelet production from a peripheral blood sample, in a similar way as a reticulocyte count provides a measure of red cell production.[3,5]

Thrombocytopenia in patients with dengue may cause a steep fall in platelet count, warrant for platelet transfusion. The IPF% can predict the timing of platelet recovery. The platelet recovery time is 1-2 days of IPF increase.[6,7] The cut off value above which platelet recovery is expected is yet to be validated. The IPF is identified by Sysmex XN1000 hematology analyser in the reticulocyte channel using a fluorescent dye and carefully designed gating system and counted by a special software termed IPF master.[8]

The aim of this study was to establish the relationship between IPF and increase in platelet count in patients with dengue who suffer from thrombocytopenia.

Aim and objectives

Aim and objectives were to find out relation between Platelet counts, Immature platelet fraction (IPF) in dengue seropositive patients. Evaluate and use the quantification of IPF to predict recovery in cases of thrombocytopenia arising due to platelet destruction seen in cases of dengue.

METHODS

This is an observational, descriptive study done at the department of pathology, Mahatma Gandhi Medical College and Hospital, Jaipur where information were collected from records for the period from November 2017 to August 2019. This study is approved by Institutional Ethics Committee. The study population includes all the dengue patients who were positive for NS1 antigen or IgM antibody or both and treated at Mahatma Gandhi Medical college and Hospital, Jaipur.

The patient's details were retrieved from the hospital in patient management system. The platelet counts and IPF were retrieved from Sysmex XN1000 hematology analyzer. The values of platelet and IPF were available for day 1st, 3rd, 5th and 7th day of admission for each patient.

The patients were grouped into 5 categories according to their platelet count on the day of the admission.[2]

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

A platelet count value of<1,50,000 was considered as thrombocytopenia. For this study a change in platelet value more than 20,000 count in 48 hrs was considered as a clinically significant change. For the IPF a value>6.1% was considered as a high IPF value. Descriptive analysis was initially performed. This was followed by associating between high values of IPF and significant clinical change in platelet values during the subsequent 48 hrs.

This analysis was carried only in the thrombocytopenics. Further a sensitivity analysis was carried out for observations of platelet count below 1.5 lakhs for all patients (n=140) for Day 1,3 and 5 and ascertained the cut-off of IPF on the corresponding days which yielded increase in platelet values of over 20,000 in the subsequent 48 hrs.

RESULTS

A total of 140 subjects were studied. Dengue was more common in 20-29 years of age group. The patients who had thrombocytopenia on day 1 were 116 (82.85%). (Figure 1) Among them 20 (14.3%)were of no risk category and 96 (68.57%) were in the risk group. These 96 patients are grouped into risk categories. 50% were in the low risk, 11.4% in the moderate risk and 7.1% in the high risk groups. On day 3, 5 and 7 the risk categories improved with 53.57% (42.6% low, 8.6% moderate, 2.14% high), 35.71% (31.42% low, 2.9% moderate, 1.42% high) and 17.85% (17.14% low, 0.7% moderate, 0% high) respectively.

Number of patients with low IPF i.e.≤6.1%, on day 1 was 44 (31.4%), on day 3 was 50 (35.7%), on day 5 was 59 (42.1%) and on day 7 was 69 (49.3%). Number of patients with high IPF i.e.>6.1%, on day 1 was 96 (68.6%), on day 3 was 90 (64.3%), on day 5 was 81 (57.6%) and on day 7 was 71 (50.7%) (Figure 2).

Change in number of patients with low and high IPF% on day 3, 5 and 7 was statically significant ($p<0.05$).

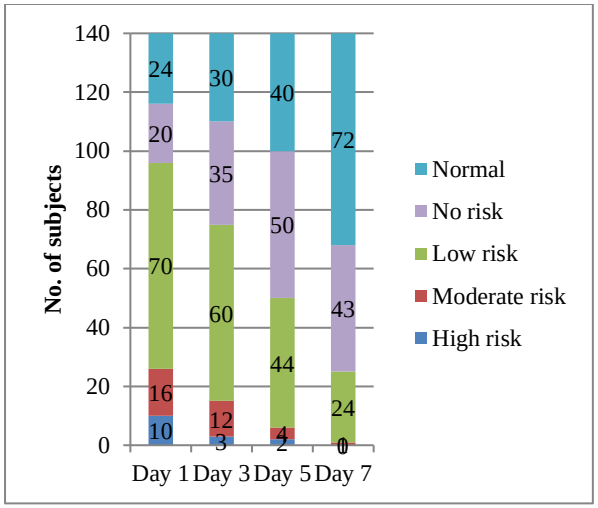

Figure 1: Platelet level categories on various days in risk group.

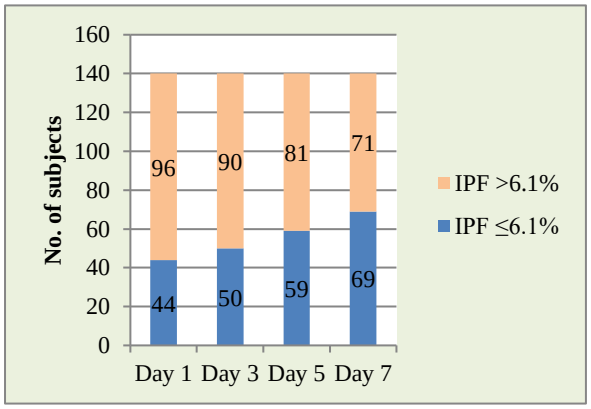

Figure 2: Immature platelet fraction level categories on various days in risk group.

Total patients with low IPF i.e.≤6.1% was 44 in which 6 (13.6%) shows improvement in platelets (>20,000) on day 3 but 38 (86.4%) patients not showed improvement in platelet count.

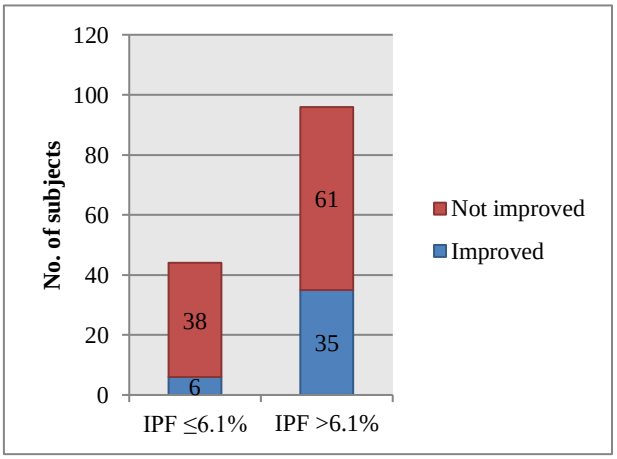

Figure 3: Change in platelet count from day 1 to 3 in relation to IPF on day 1.

Total patients with high IPF i.e.>6.1% was 96 in which 35 (36.5%) shows improvement in platelets (>20,000) on day 3 but 61 (63.5%) patients not showed improvement in platelet count.

The difference of the improvement of platelet between patients of low and high IPF on day 3 is statically significant (P<0.05) (Figure 3).

There was significant correlation between day 1 IPF % and change in platelet count from day 1 to day 3 (P<0.05) (Figure 4).

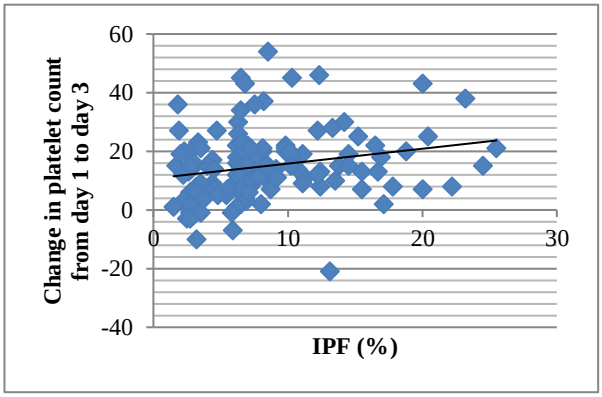

Figure 4: Correlation between day 1 IPF % and change in platelet count from day 1 to day 3.

A sensitivity of IPF test to predict platelet improvement on day 3, 5 and 7 was 85.37%, 82.41% and 77.42% respectively (Table 1).

Table 1: Diagnostic parameters of day 1 IPF (cutoff-6.1%) for predicting improvement in platelet count (>20,000/cumm) on different follow up days.

Parameters	Day 3	Day 5	Day 7
Sensitivity	85.37%	82.41%	77.42%
Specificity	38.38%	78.13%	100%
PPV	36.46%	92.71%	100%
NPV	86.36%	56.82%	36.36%
Accuracy	52.14%	81.43%	80%

DISCUSSION

In recent years, IPF become a reliable future guide for decisions concerning platelet transfusions. Earlier studies show that there is a direct correlation between increases in base IPF levels and corresponding increases in platelet count. The time lag between increased IPF levels and corresponding increases in platelet count appears to be around 24–48 hr in patients with dengue. Therefore, for monitoring thrombocytopenia in patients with dengue, measurement of IPF should be considered as routine practice.

Dengue was more common between 20-29 years (42.9%) in the present study. A study done by Febe R Suman et al

reported more patients below 5 years whereas Pakistan study group reported it to be common in adults.[9,10,11] In the present study thrombocytopenia was noted in 116 patients (82.85%) on day 1 of admission.

Immature platelets are reticulated platelets, presence of which show the thrombopoietic activity of the marrow. This is similar to reticulocytes which predict erythropoietic activity. The immature platelets are measured as percentage of platelets or absolute counts. Sarah et al reported IPF as an indicator of thrombopoietic state where Briggs et al concluded that recovery from thrombocytopenia in chemotheraphy and transplant patients was preceded by increase in IPF%.[12,13]

The IPF is identified by flow cytometery technique using a nucleic acid specific dye in the reticulocyte/platelet optical channel. This application is available in the XN1000 automated blood cell counter with upgraded software.

In our study, the reference range of IPF was 0.9-5.4% considered as per manufacturer's information. In our study we found 36.5% of patients with high IPF showed change in risk category within 2 days and 56.2% within 4 days and 7.3% within 6 days while study done by Febe R Suman et al found 55.9% of patients with high IPF showed change in risk category within 2 days and 24.75% within 4 days and 15% within 6 days.[9]

There is statistically significant (P<0.05) improvement in platelet values within 48 hours when the IPF is more than 6.1%. The IPF values were also on the rising trend from day1 to day 5 (Figure 5).

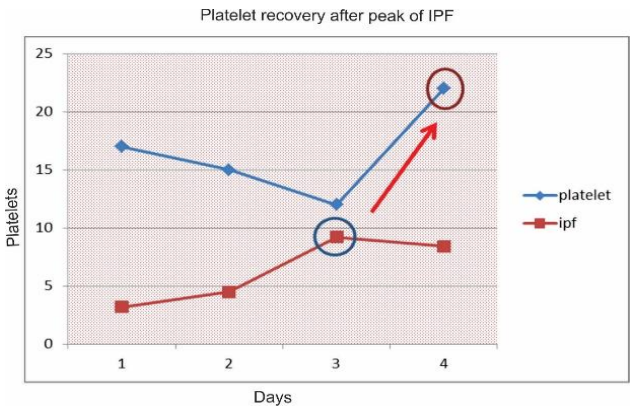

Figure 5: Platelet recovery after peak of IPF.

It was observed that 36.5% patients showed recovery within 48 hrs, 92.7% patients within 96 hrs and 100% patients after 6 day of the peak of IPF.

In our study PPV of 36.46%, 92.71% and 100% on day 3, 5 and 7 respectively indicates that if the IPF value is more than 6.1%, there is 36.46%, 92.71% and 100% chance of platelet recovery on day 3,5 and 7 respectively. The immature platelet fraction (%IPF) is a new parameter which is an automated measure of reticulated platelets in peripheral blood. In our study, the reference range was found to be 0.9-5.4%, which is similar to a reference range derived by Briggs of 1.1-6.1%.

CONCLUSION

Dengue epidemic calls for platelet transfusion, sometimes inappropriate also. Careful clinical watch and monitoring platelet count may help to group the patients under risk of category. IPF become a reliable future guide for decisions concerning platelet transfusions.

There appears to be a direct correlation between increases in base IPF levels and corresponding increases in platelet count, so that prophylactic platelet transfusion can be deferred and also the hazards associated with it. Therefore, for monitoring and evaluate thrombocytopenia in patients with dengue, measurement of IPF should be considered as routine practice.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Simmons CP, Farrar JJ, Nguyen vV, Wills B. Current Concepts. N Engl J Med 2012; 366:1423-32.
2. Srichaikul T, Nimmannitya S Haematology in dengue and dengue haemorrhagic fever.Baillieres Best Pract Res Clin Haematol. 2000;13(2):261-76.
3. Briggs C, Hart D, Kunka S, Oguni S, Machin S. Immature platelet fraction measurement: a future guide to platelet transfusion requirement after haematopoietic stem cell transplantation. Transfus Med 2006;16:101–9.
4. Briggs C. Quality counts: new parameters in blood cell counting. Int J Lab Hematol 2010;31:277–97.
5. Lemes A, Molero J, Lopez P, Martin P,Luzardo H, Martin R, Garcia GD, De la Iglesia S, Jimenez S. Immature platelet fraction (IPF) utility in follow up patients receiving chemotherapy. Haematologica 2007;92:425–8.
6. Saigo K, Sakota Y, Masuda Y, Matsunaga K, Takenokuchi M, Nishimura K et al. Automatic detection of immature platelets for decision making regarding platelet transfusion indications. Transfus Apher Sci, 2008;38(2):127-32.
7. Dadu, T, Sehgal K, Joshi M, Khodaiji, S. Evaluation of the immature platelet fraction as an indicator of platelet recovery in dengue patients. Internat J Lab Hematol. 2013.
8. Carol B, Ian L, Punamar K. Performance evaluation of the Sysmex haematology XN modular system. J Clin Pathol, 2012;0:1-7.
9. Febe R Suman, Lawrence D'Cruze. Dengue: platelet and immature platelet dynamics a study done at a

tertiary care centre from South India. Int J Rec Trend Sci Tech. 2014;12(1):620-3.
10. Francisca RF, Guerreiro A, Romelia PG, Marin HP, Daniella M.L.IVOCB Dengue: Profile of haematological and biochemical dynamics. Rev. Bras Haematol, 2012;34:1-10.
11. Irfan A, Fayyaz AM, Aamir H, Shahida ARS. Dengue fever; cliniciopathologic correlations and their associations with poor outcome. Professional Med J. 2011;18:57-63.
12. Sara JB, Bethau P, Mare F, Lemke KP, Peter AS. Platelet production and platelet destruction assessing mechanisms of treatment effect in immune thrombocytopenia (ITP). Blood, 2010;11:321-98.
13. Hinzmann R. The clinical significance of themeasurement of immature platelets. Sysmex lab info. 2005.

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