Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 05, 2022

Original Research Article

Study of Immature Platelet Fraction as a Predictor of Platelet Recovery in Pediatric Dengue Patients.

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Abstract

Introduction: In dengue hemorrhagic fever, monitoring platelet counts is critical for management. Recovery is indicated by increase in platelet count. The immature platelet fraction(IPF) is a novel parameter which is an automated measure of reticulated platelets in the peripheral blood. Aim: measure the IPF in pediatric patients to predict platelet recovery.
Method: This study was done on 100 patients with dengue IgM positivity at the Department of Paediatrics, Dr. B R Ambedkar hospital, Bangalore. Dengue serology was recorded by ELISA test; with kits from PANBIO NS Antigen and Euroimmune (IgG and IgM).
Results: IPF% of patients with dengue increased from admission to day 8, before decreasing gradually to day 10 and then decreasing rapidly thereafter.
Conclusion: Counts in patients with dengue infections IPI can be used confidently to predict recovery of platelets in patients of dengue. An IP value of more than 10.0 indicates recovery of platelet count within 48 hours.
Keywords: Dengue, immature platelet count, platelet count, platelet recovery

Introduction

Dengue fever is the fastest emerging arboviral infection spread by Aedes mosquitoes with major public health consequences. It is estimated that 50 million cases of dengue fever occur worldwide annually, of whom approximately 90% are children less than five years old. About 2.5% of those affected with dengue die of the disease. According to Recent WHO 2012 guidelines Dengue is classified into Dengue +/- warning signs and Severe dengue which includes Dengue shock syndrome, respiratory distress syndrome, dengue hemorrhagic fever and organ failure. Child with fever, nausea, vomiting, rash, aches and pain positive tourniquet test is considered as probable dengue in endemic area and confirmed by NSI antigen/ IGM antibody study. The lab findings of acute DF are as follows: Total WBC is usually normal at the onset of fever: then leucopenia develops with decreasing neutrophils Platelet counts are normal. Initially Mild thrombocytopenia (100 000 to 150 000 cells/mm3) is common and about half of all DF patients have platelet count below 100 000 cells/mm3, but severe thrombocytopenia(<50 000 cells/mm3) is also found. Mild haematocrit rise (-10%) may be found. Lab features include WBC count may be normal or with predominant neutrophils in the early febrile phase. Thereafter, there is a drop in the total number of white blood cells and neutrophils, reaching a nadir towards the end of the febrile phase. The change in total white cell count ($5000 cells/mm3) and ratio of neutrophils to lymphocyte (neutrophils lymphocytes) is useful to predict the critical period of plasma leakage. This finding precedes thrombocytopenia or rising haematocrit. A sudden drop in platelet count to below 100 000

ISSN: 0975-3583, 0976-2833 VOL 13, ISSUE 05, 2022

occurs by the end of the febrile phase before the onset of shock or subsidence of fever. The level of platelet count is correlated with severity of DHF. A sudden rise in haematocrit is observed simultaneously or shortly after the drop in platelet count. Haemoconcentration or rising haematocrit by 20% from the baseline is the objective evidence of plasma leakage. Thrombocytopenia and haemoconcentration are constant findings in DHE.[1-5]

In dengue hemorrhagic fever, monitoring platelet counts is critical for management. Recovery is indicated by increase in platelet count. The immature platelet fraction(IPF) is a novel parameter which is an automated measure of reticulated platelets in the peripheral blood. These contain RNA and are larger in size, more physiologically active and analogue of red cell reticulocyte. The number of reticulated platelets reflects the rate of thrombopoiesis. The RNA of these platelets can be accurately quantified by flow cytometry using fluorescent dye like oxazine and can be identified by SYSMEX XE 2100 hematology analyser. The normal range of IPF is 1-9% mean being 4%.[4-7]

The IPF is raised in diseases where there is increased platelet destruction and consumption. It is decreased in marrow failure. The IPF% can predict the timing of platelet recovery which is 1-2 days of IPF increase. In this study we aim to measure the IPF in pediatric patients to predict platelet recovery so that unnecessary transfusion of platelets can be avoided which can lead to complications like allo immunisation, immunosuppression, transmission of infectious disease and graft vs. host disease.[6-8]

Methodology

This study was done on 100 patients with dengue IgM positivity at the Department of Paediatrics, Dr. B R Ambedkar hospital, Bangalore. Dengue serology was recorded by ELISA test; with kits from PANBIO NS Antigen and Euroimmune (IgG and IgM). These patients had follow-up at intervals ranging from 24 to 72 hours with at least two platelet count readings. The platelet count and immature platelet fraction was estimated using the fluorescent dye binding of platelet RNA on the SYSMEX XN 1000 flow cytometry (Oxazine dye 0.003%). On the PLT channel CBC was recorded simultaneously. Peripheral smears were studied in all these cases with a note on the presence of large platelets on smear.

Results:

In the total, 200 cases of dengue included, 30 had severe dengue. The mean age of the subjects was 43 years [SD 4.6]. More number of males [63%] were there in the study group as compared to females [37%].

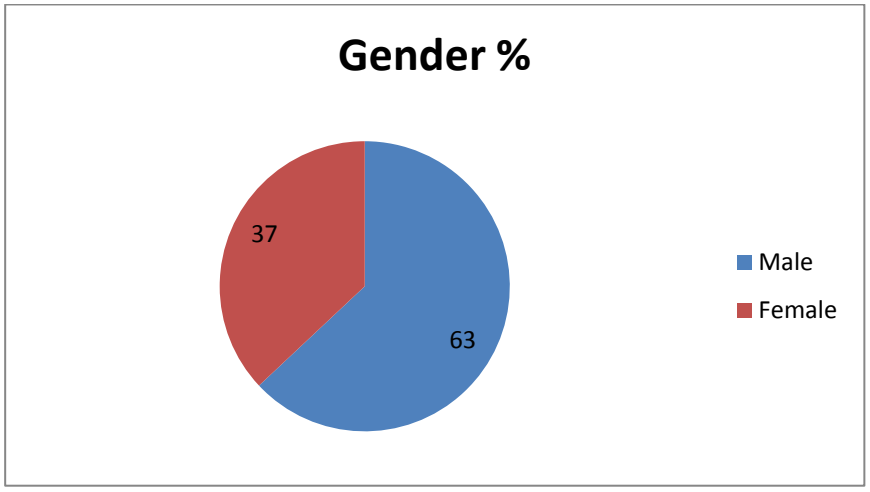

Figure 1: Showing gender distribution

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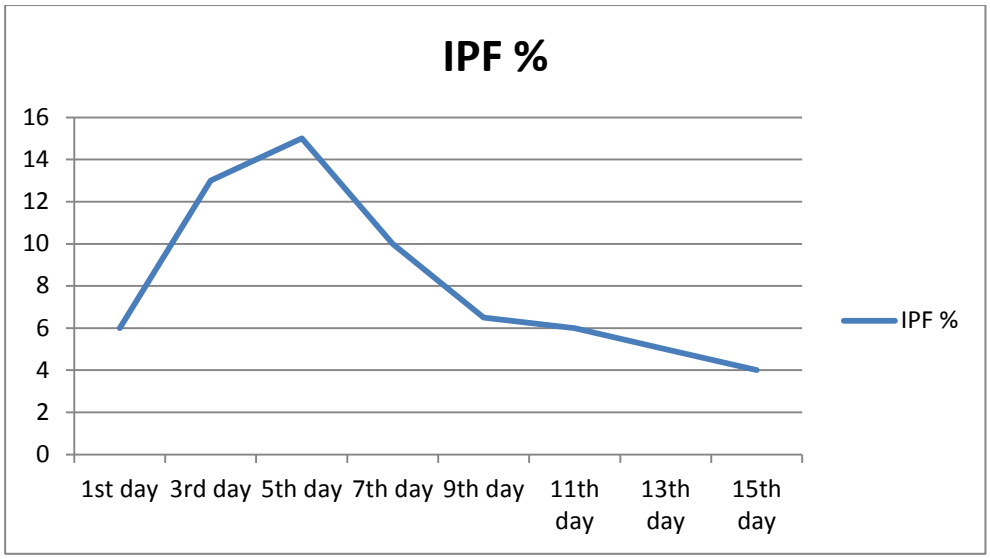

Figure 2: Line diagram showing immature platelet fraction

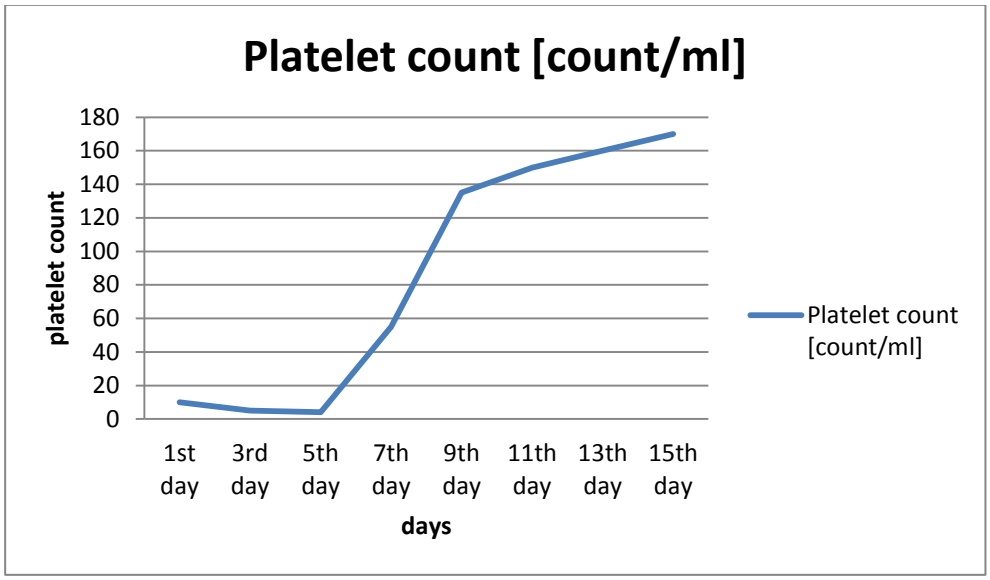

Figure 3: Line diagram showing platelet count

IPF% and platelet count of patients with dengue are displayed for the time course from the onset of fever until day 15.

The platelet count of patients with dengue decreased from admission to day 5, and remained low until day 7 and day 8 after onset of fever, thereafter platelet count increased from day 9 onwards towards normal values. IPF% of patients with dengue increased from admission to day 8, before decreasing gradually to day 10 and then decreasing rapidly thereafter.
Platelet count and IPF% were compared between patients with non-severe dengue and patients with severe dengue on day 3, day 4, day 5 and day 6. Compared with patients with non-severe dengue, the platelet count of patients with severe dengue was significantly lower and IPF% was significantly higher on days 3–5 (P=0.0275 on day 3; P=0.0012 on day 4; P=0.014 on day 5).

Reticulocyte count decreased from days 2 to 5, and then increased from days 5 to 10 in a trend similar to that of platelet count. The difference in absolute reticulocyte count of patients with severe dengue and patients with non-severe dengue was not significant on day 3 or day

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4, but was significant on day 5. The ratio of reticulocyte count to total erythrocytes (RET %) showed the same behaviour as reticulocyte absolute count (P=0.338 on day 3; P=0.392 on day 4; P=0.0043 on day 5).

Discussion:

This study in 100 patients with confirmed dengue showed that the increasing trend of IPF% was concomitant with progressive thrombocytopenia in the first week of illness, and thereafter, the trends of these two parameters were reversed, supporting the results of previous studies.

Considering the platelets count, majority of our patients 98.11% had their platelet counts less than 50000/ cu.mm and only 1.88% cases presented with platelet counts above 50000/cu.mm. The complex mechanism of thrombocytopenia remains controversial. Various mechanisms have been proposed like direct bone marrow suppression by the virus; anti-dengue antibody-mediated platelet destruction, peripheral consumption of platelets and isolated replication of virus in the platelet [13]. The release of high levels of platelet activating factor may induce platelet consumption and enhance adhesiveness of endothelial cells resulting in thrombocytopenia [14]. Thrombocytopenia can also be due to increased peripheral destruction, inadequate production or abnormal pooling.[9]

Immature Platelet Fraction (IPF) is an automated measure of reticulated platelets in peripheral blood. In our study, we observed that 84.91% patients had IPF more than 10% and only 15 % patients had IPF below 10%. When the IPF was correlated with the platelet counts on day 2 and day 3, a significant positive correlation was found, similar to the study shown by Dadu, et al[10]., 2014. The recovery criteria taken by us was in accordance with WHO, where a platelet count cut off value of 50000/cumm was taken for platelets recovery. Those patients whose platelet count reached more than 50000/ cumm either on the second or third day of presentation were said to have recovered. These patients are haemodynamically stable and can be discharged from hospital.[11]

Bashir et al[12] 2015, Anuradha et a1[l3]., 2014, Navya, et al[14]., 2016 and Mukker, et al[15]., 2018 [17,18,11,19] They also observed low value of mean platelet volume (MPV) with low platelet count. Navya, et al[14] 2016 in their study group of 100 patients, saw a mean MPV of <9 fl in 72% of patients. A mean MPV of <9 fl indicates bone marrow suppression. Thus postulating transient bone marrow suppression by dengue virus as one of the mechanisms of thrombocytopenia in patients of dengue fever [11].

Conclusion:

Platelets counts started rising after the IPF touched 10.0% with a quick recovery from a falling trend. IPF shows a strong co-relation with a recovery of platelet. Counts in patients with dengue infections IPI can be used confidently to predict recovery of platelets in patients of dengue. An IP value of more than 10.0 indicates recovery of platelet count within 48 hours.

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