

# Role of Mean Platelet Volume in Dengue Fever - A Prognostic Marker

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## ABSTRACT

**Introduction:** Dengue Fever (DF) has a virus infective etiology caused by an arbovirus. This virus is spread by Aedes mosquitoes. These results in two complications such as Dengue Haemorrhagic Fever (DHF) and in its severe form Dengue Shock Syndrome (DSS) which can threaten the patient's life mainly through high vascular permeability and shock. Due to the rise in the spread of arboviral infection, medical care services are persistently struggling to improve patient management and appropriate steps going on to control vector transmission. The transfusion of platelets is indicated for the thrombocytopenic patients both as prophylaxis as well as treatment of haemorrhage. Platelet count and MPV are strongly associated with prognosis in critically ill patients. Mean platelet volume (MPV) is considered as a valuable marker in predicting the inflammatory process and disease activity. Even after the transfusion of platelets, few patients do not show the appropriate increase in platelet count.

**Aims and objectives:** 1. To assess the role of mean platelet volume in dengue fever.

2. To determine the incidence of dengue fever in various age groups.

**Materials and methods:** Platelet count and Mean platelet volume (MPV) are calculated using automated haematology analyzer.

**Results:** Out of 68 serologically diagnosed dengue cases, the maximum percentage of patients were in the age group of 20 to 40 years (47.05%) followed by 60 years and above (20.58%) with male to female ratio of 1.8:1. Majority of the patients had platelet count ranged from 20000/ $\mu$ L to 40000/ $\mu$ L (44.11%) followed by more than 60000/ $\mu$ L (25%). Patients who were critically ill (12 patients) showed MPV higher when compared to other patients.

**Conclusion:** Platelet transfusion plays important role in dengue fever yet few patients failed to improve clinically. Though many patients showed improvement in MPV value and total platelet count, few patients did not show much clinical improvement. The underlying causes for failure were bleeding manifestations and immune mediated destruction of platelets. Simply transfusion of platelets to these patients does not make the clinical improvement. Thus identifying the response of platelet transfusion by assessing the MPV value which helps the clinicians to assess the prognosis of patients,

**Keywords:** Dengue fever, Platelets, Mean platelet volume (MPV).

## INTRODUCTION

Dengue fever has become the major public health problem in our country. It is the most important arboviral infection spread by Aedes mosquitoes and is increasing all over the world and it affects nearly 2.5 billion people worldwide.

Dengue is mostly a self limiting disease which is transmitted by mosquitoes and is characterized by fever, headache, rash, joint pains, nausea and vomiting. Some infections result in Dengue Haemorrhagic Fever (DHF) and in its severe form Dengue Shock Syndrome (DSS) can threaten the patient's

life primarily through increased vascular permeability and shock. The most important manifestations in dengue fever is thrombocytopenia in acute infection. Due to an increase in the spread of this arboviral infection, medical care services are continuously striving to improve patient management and appropriate steps going on to control vector transmission. Dengue viruses cause either symptomatic infections or asymptomatic seroconversion. The dengue infection with symptomatic will have a systemic and dynamic disease. It has a big range of clinical variations which that includes both worst and asymptomatic clinical manifestations. Once the incubation period is over the dengue viruses cause the illness which begins abruptly and, in patients with moderate to severe disease. The dengue fever has three phases of disease variations – 1. febrile 2. critical and 3. recovery. [1-3]

The causes for thrombocytopenia range from idiopathic, infectious to malignancies. Infections predominantly present as febrile illness and may have associated thrombocytopenia. The low platelet count can be considered as the diagnostic marker of some common infections. The mean platelet volume (MPV) measures the activity of platelets. Thrombocytopenia is almost universally observed in dengue infection. This result from both reduced production and increased destruction of platelets. It is thought that severe thrombocytopenia correlates with disease severity and may contribute to the risk of developing haemorrhage. The Mean platelet volume (MPV) is affected by aging of platelets and varies according to the balance between production and destruction.

Platelet count and MPV are strongly associated with prognosis in critically ill patients. Mean platelet volume (MPV) is suggested as an index of inflammation, disease activity, and anti-inflammatory treatment efficacy in chronic inflammatory disorders.

The transfusion of platelets is indicated for the prophylaxis and treatment

of haemorrhage in patients with thrombocytopenia or with primary or secondary functional disorders of platelets. [4-7] The major hemorrhagic complications associated with hematological and oncological disorders can be reduced by transfusion of platelets. On the other hand, some patients fail to obtain the full advantage of platelet transfusions because they do not attain the appropriate platelet count increment following transfusion. [2,3] Hence studying the role of MPV helps in assessing the disease prognosis and further management.

#### **OBJECTIVES:**

1. To assess the role of mean platelet volume in dengue fever
2. To determine the incidence of dengue fever in various age groups.

#### **MATERIALS AND METHODS**

The EDTA blood samples of pre transfusion values of patients with dengue fever having thrombocytopenia were taken. The platelet count and mean platelet volume were calculated over a period of 24 months. Within 1 hour following platelet transfusion, parameters such as platelet count and mean platelet volume are evaluated. Post transfusion parameters are compared with Pre transfusion parameters. The values of Platelet count and MPV are calculated by, Automated hematology analyzer (HORIBA, ABX Pentra DF 120)

#### **RESULTS**

Out of 68 serologically diagnosed dengue cases, the maximum percentage of patients were in the age group from 20 to 40 years (47.05%) followed by 60 years and above (20.58%) and minimum percentage of patients were in the age group of 40 to 60 years (14.7%) with male to female ratio of 1.8:1 (Figure 1 and 2). Majority of the patients before transfusion had platelet count range from 20000/ $\mu$ L to 40000/ $\mu$ L (44.11%) and minimum number of patients had platelet count in the range of 41000/ $\mu$ L to 60000/ $\mu$ L (14.7%) (Figure 3). The post transfusion platelet count showed

increment with each unit of transfusion except for 12 cases in which the increment was very minimal which led to bleeding manifestations. The number of platelets in each unit ranges from  $0.4$  to  $1.8 \times 10^{11}$  in PRP-PC method. Considering each unit should contain minimum of  $4 \times 10^{10}$  platelets, response to platelet transfusion can be found by platelet count increment and mean platelet volume (MPV). Patients with bleeding manifestations who are critically ill had  $MPV > 11.5$  (17.5%) (Table 2&3) when compared to other patients without bleeding manifestations.

**Table 1: MPV values in pre and post transfusion**

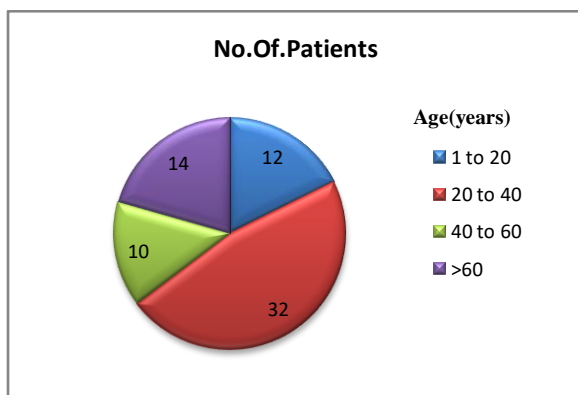
Platelet counts	Pretransfusion MPV(mean)	Posttransfusion MPV(mean)
1000 to 20000	11.5	11.5
21000 to 40000	11.4	11.3
41000 to 60000	11.3	10.5
> 60000	11.0	9.5

**Table 2: Patients showing mean MPV variation**

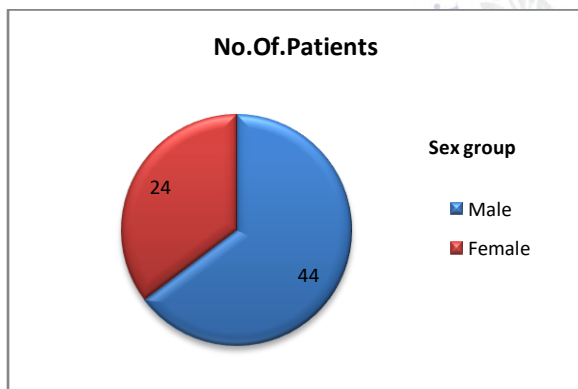
Mean platelet volume	No.of patients
MPV > 11.5	12
MPV < 11.5	56

**Table 3: Disease severity:**

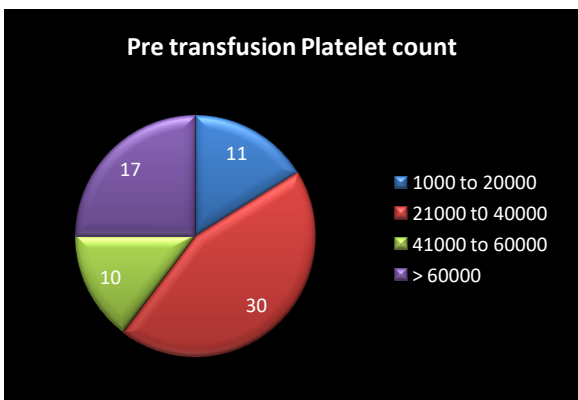
Disease	No. of patients
Dengue with bleeding manifestations	12
Dengue fever	56



**Figure 1: Age distribution of Patients with Dengue fever**



**Figure 2: Sex Distribution of Patients with Dengue fever**



**Figure 3: Range of Pre transfusion Platelet count**

## DISCUSSION

Dengue is an infectious disease causing morbidity and mortality in humans which is caused by dengue virus (DENV), a human arboviruses of family Flaviviridae, transmitted by mosquitoes of genus Aedes. Almost 4 serotypes in dengue viruses; DENV 1, DENV 2, DENV 3, DENV 4. These 4 serotypes are similar in their antigenicity, but varies adequately to determine their cross-protection from few months after infection by any one of them. Once infected with any one serotype gives immunity to the entire life for that particular serotype. Man and mosquito are reservoirs of infection. [1,2,6-9] Transovarian transmission has made the control more complicated. Primary infection in non immune persons normally causes Dengue fever. Subsequent dengue infection by different serotype causes more severe illness like DHF/DSS.

The main presentations/ manifestations of the DHF/DSS are sudden development of shock, capillary leakage, bleeding manifestations/thrombocytopenia occurring at the time of defervescence of fever. Expert groups in various countries such as from South-East Asia, Latin America and at WHO headquarters in Geneva, Switzerland in 2008 agreed that: “dengue infection is considered one disease entity but with different clinical presentations and often with unpredictable clinical evolution and outcome”; the classification into levels of severity has a high potential for being of practical use in

the clinicians' decision as to where and how intensively the patient should be observed and treated in more consistent reporting in the national and international surveillance system, and as an end-point measure in dengue vaccine and drug trials. [1,2,8-11] Pathogenesis of dengue fever is not made out exactly but it is suggested that it is mediated through soluble mediators, complement activation and cytokines that are responsible for various manifestations. Thrombocytopenia is considered as an indicator of clinical severity, as per criteria by WHO. The pathogenesis of thrombocytopenia in dengue infection is not fully identified and may be multifactorial. The most important factor considered to be causing destruction of platelets is immune-mediated attack. [2,4,9,10] The possible pathogenesis of thrombocytopenia in dengue are; 1. The bone marrow progenitor cells is the main target of dengue infection in which it inhibits their function to lessen the proliferative capacity of hematopoietic cells which can induce hypoplasia of the bone marrow during the acute phase of the disease. 2. This leads to thrombocytopenia by consumption of platelets due to disseminated intravascular coagulation (DIC), destruction of platelets due to rapid apoptosis, lysis by the complement system and by the involvement of antiplatelet antibodies. The antibodies seen in dengue infection are against dengue virus non structural protein 1 (NS1) which exhibits cross-reactivity with endothelial cells and human platelets, which causes damage to platelets and endothelial cells leading to inflammatory activation. The dengue guidelines as per WHO 2009 does not prefer the usage of platelet transfusions prophylactically, whereas the 2011 regional WHO guidelines for South East Asia suggest prophylactic platelets may be considered in those with a platelet count less than  $10 \times 10^9/L$ . Some countries in which dengue are endemic supports the usage of platelet transfusions prophylactically to prevent haemorrhage in patients with thrombocytopenia. However platelet

transfusions are economically high, potentially dangerous and their usage in dengue fever absolutely lacks an evidence basis. [8,10,11,12]

The MPV is measured by a machine called automated analyzer, it is routinely available in the inpatient and outpatient setting at a relatively low cost. The normal range of MPV is 7.5 - 11.5 fL. Platelet size can be considered as a potential marker of platelet reactivity. Larger platelets are metabolically and enzymatically more active and have greater prothrombotic potential. The increased volume of platelets (MPV) is associated with other markers of platelet activity, including high platelet aggregation, increased synthesis of thromboxanes, release of  $\beta$ -thromboglobulin and increased expression of adhesion molecules.

If MPV is decreased, it is called microthrombocytes and it indicates the disorders such as aplastic anemia, Wiskott-Aldrich Syndrome, thrombocytopenia absent radii (TAR) syndrome and storage pool disease. If MPV is increased, it is called macrothrombocytes and it indicates the disorders such as idiopathic thrombocytopenic purpura, Bernard Soulier disease, May-Hegglin anomaly, greater risk of heart attacks and stroke with increased platelet activation. [13-17]

In our study the assessment of disease prognosis is done by pre and post transfusion platelet count and MPV. The patients with bleeding manifestations and critically ill patients have high MPV value and lower platelet count when compared to other dengue patients, this is in correlation with in Khan et al. in their study 22 patients (53.6%) were non responders among the treatment group and the platelet count increment is lower in critically ill patients. The possible causes of non responders are immune mediated attack causing destruction to platelets leading to thrombocytopenia. [18-20] The high MPV and low platelet count were seen in patients having dengue fever with bleeding manifestations when compared to patients without bleeding

manifestations. Also the patients with lower platelet counts may have higher degree of immune mediated destruction of platelets that lead to poor response to platelet transfusion. In the study of Lye et al, there was a lack of efficacy of platelet concentrate transfusion. [19-21] The number of platelets in each unit ranges from 0.4 to 1.8 x 10<sup>11</sup> in PRP-PC method.

## CONCLUSION

All platelet transfusion to thrombocytopenic patients in case of dengue fever does not show improvement in their clinical condition. So, assessing the platelet transfusion response helps the clinicians to go with better treatment. Thus identifying the response by assessing the MPV value helps the patients to assess their prognosis. Assessing the efficacy of platelet transfusion in these patients provide a useful data in transfusion therapy and in the clinical outcome of the patients. Hence, the Mean platelet volume is the key factor which acts an indicator of disease prognosis.

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