

# Risk of Bleeding in Dengue: Making Predictions is Difficult Especially about the Future

Ashit V Hegde 

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Platelet counts are the only parameter diligently monitored by patients suffering from dengue and unfortunately by many physicians as well. There is a widespread belief both among the lay public and among several physicians that thrombocytopenia leading to severe bleeding is the most dreaded complication of dengue. There is therefore a spate of alternative remedies which claim to increase the platelet count, the most popular of which of course is the papaya leaf extract. Patients with moderate thrombocytopenia are unnecessarily admitted to the ICU for "observation" and even worse, often receive needless platelet transfusions.

The pathogenesis of thrombocytopenia in dengue is complicated.<sup>1,2</sup> Bone marrow suppression contributes to the low platelet count. There are several mechanisms that cause peripheral destruction of the platelets, viz. an activated complement cascade, phagocytosis, and antibody-mediated lysis. Platelet dysfunction is also present.

Nevertheless, several studies suggest that the risk of bleeding in patients with dengue does not co-relate with platelet counts.<sup>3-5</sup> These studies have also proposed that there is an increased risk of complications in patients who receive prophylactic platelet transfusions. Platelets play a small role in the development of bleeding in dengue. Coagulopathy and direct vascular damage are also important factors.<sup>6,7</sup>

The study by Priya et al.<sup>8</sup> in this issue of the *IJCCM* adds to the body of evidence that there is no correlation between platelet counts and the risk of "Clinically significant bleeding (CSB)" in patients with dengue. This study also suggested that a raised PTT (> 40) was a strong predictor of CSB. This is in line with the theory that coagulopathy due to a decrease in coagulation factors contributes to bleeding in dengue. An increased SOFA score was also a predictor of CSB in this study. It is only logical that an increased severity of disease is associated with a higher risk of bleeding. Fever was the third parameter associated with an increased risk of bleeding in this study, High fever is known to impact platelet function and aggressive control of fever might be one of the strategies to reduce the risk of bleeding (this needs to be proven however).

The authors have devised a predictive score using these 3 parameters which could identify patients at risk of CSB. The definition of "Clinically significant bleeding" in this study was however a bit liberal because even minor bleeding was included in the definition. A modification of the predictive score that could predict patients at risk of more severe bleeding (Grade 3 and 4) might be more useful clinically.

At present the clinical significance of the observations made by Priya et al. is limited. Studies that examine the value of close

Department of Medicine and Critical Care, P. D. Hinduja Hospital, Mumbai, Maharashtra, India

**Corresponding Author:** Ashit V Hegde, Department of Medicine and Critical Care, P. D. Hinduja Hospital, Mumbai, Maharashtra, India, Phone: +91 22 24462250, e-mail: ahegde1957@gmail.com

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observation in an ICU or of prophylactic administration of blood products (not necessarily platelets) to patients deemed to be at high risk of bleeding (based on the predictive score) need to be conducted.

It is also reassuring to note that only 38 of 9,817 (0.4%) hospitalized cases of dengue had CSB. The percentage of patients with grade 3 and 4 bleeding is therefore even lower.

Bleeding is, therefore, not the major cause of mortality in dengue. Severe capillary leak causing intravascular volume depletion is the most important complication of dengue. Myocarditis, hepatitis, encephalitis, and Secondary HLH may also occasionally contribute to mortality and morbidity.

Physicians should therefore focus on identifying those patients who are at high risk of developing severe capillary leak because early intervention in these patients can clearly prevent progression to more severe disease. The warning signs proposed by the WHO are good indicators of progression to severe disease.<sup>9</sup>

"It is difficult to make predictions, especially about the future." is a quote attributed to many people, from the physicist Niels Bohr to legendary baseball player Yogi Berra.

On the basis of the observations made by Priya et al., the following quote may be modified "It is not so difficult to make predictions, especially about the future. risk of bleeding in dengue". But until we have more studies, so what?

## ORCID

Ashit V Hegde  <https://orcid.org/0000-0003-4342-122X>

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