Infection with dengue virus results in a wide spectrum of clinical manifestation, ranging from asymptomatic infection to dengue hemorrhagic fever. Both experimental and observational studies have focused on identifying the reasons for this variability in disease outcome and on ways to anticipate when a dengue infection may result in severe disease. These studies have indicated that excessive activation of the immune response during a dengue infection may lead to a cascade of cytokine production known as a cytokine storm, that ultimately leads to a risk of hemorrhage. We developed a within-host mathematical model of dengue infection that links viral and immunological dynamics to the risk of developing severe disease. The model includes the role of the innate immune response in limiting viral infection and in contributing to disease, as well as both the enhancing and protective roles of the adaptive immune response. We show that the model is consistent with known risk factors for developing severe disease, and reproduces the relationship between known markers of disease severity and the risk of developing severe disease. We then use the model to shed light on why these relationships might exist and in what ways these markers might be limited in their predictive power. (Received January 21, 2014)