Primary dengue virus infections during infancy produce a higher incidence of dengue hemorrhagic fever (DHF) compared to primary infection in older children and adults. The current hypothesis for this phenomenon is that passively acquired maternal anti-dengue antibodies mediate enhancement of viral infection in these infants. We are conducting a prospective study of dengue virus infections during infancy to directly measure pre-illness anti-dengue humoral and cellular immune responses and their association with clinical protection or disease severity. We have approximately 4,000 mother-infant pairs enrolled in the study in San Pablo, Laguna, Philippines. During surveillance for acute febrile illnesses during the 2007 rainy season, we identified 40 infants with acute dengue virus infections. The vast majority were dengue virus type 3 infections. We will present our preliminary data on pre-illness anti-dengue humoral immune responses, viremia, and disease severity in this cohort. The findings from this study will have implications for dengue vaccine development and testing.