The Effect of FcγRIIA Polymorphisms on Dengue Outbreak Severity

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The mosquito-borne flavivirus, Dengue virus (DENV), and the subsequent Dengue Disease, affect an estimated 390 million people worldwide. The four known serotypes—DENV-1, DENV-2, DENV-3, DENV-4—are pathogenic resulting in different clinical characteristics: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) or Dengue Shock Syndrome (DSS). Homotypic infection from one of these distinct serotypes does not result in reinfection, however, heterotypic infection is thought to progress to a more severe form of disease, DHF/DSS. Reinfection with a second serotype is aided by a process known as antibody dependent enhancement (ADE) with the FcγRIIA receptor protein being most well-known receptor for this phenomenon. In this work we develop a system of ordinary differential equations to analyze the impact of FcγRIIA polymorphisms on the dynamics of a Dengue outbreak. We use data collected from a local population in Tempe, Arizona to determine the genotypic distribution for the FcγRIIA receptor and to explore the impact of population's genetic variation on the DENV disease dynamics. Through numerical simulation of the model we show that increased rates of reinfection with DHF/DSS due to genetic variation allows the virus to have a greater impact on disease outcome, compared to a genetically homogeneous population. These susceptible populations may have higher death rates and overall cases counts. Our results have the potential to guide both preventive measures and post-exposure treatment in populations at higher risk due to their genetic variability during DENV outbreaks.