



OPEN Risk of dengue virus infection according to serostatus in individuals from dengue endemic areas of Mexico

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The variability in the host immune response directed against dengue virus (DENV) has demonstrated the need to understand the immune response associated with protection in incident infection. The objective was to estimate the association between serostatus and the risk of incident DENV infection. We used a prospective study from 2014 to 2016 in the localities of Axochiapan and Tepalcingo, Morelos, Mexico. We recruited 966 participants, of which, according to their infection history registered were categorized in four groups. To accomplish the objectives of this study, we selected to 400 participants older than 5 years of age were followed for 2.5 years. Blood samples were taken every 6 months to measure serological status and infection by ELISA. In individuals with at least two previous infections the risk of new infection was lower compared to a seronegative group (hazard ratio adjusted 0.49, 95% CI 0.24–0.96), adjusted for age and locality. Therefore, individuals who have been exposed two times or more to a DENV infection have a lower risk of re-infection, thus showing the role of cross-immunity and its association with protection.

Dengue is a viral disease transmitted by *Aedes* mosquitoes and is considered a public health problem worldwide¹. The clinical spectrum of infection by any of the four serotypes of dengue virus (DENV) is wide because it may present as an asymptomatic infection, a symptomatic infection or sometimes a lethal infection².

In 2014, 40% of the world's population was at risk of being infected, with the number estimated as between 50 and 100 million infections per year by any of the four serotypes (DENV-1 to DENV-4)³. However, Bhatt et al. estimated that the number of infections in the world is three times higher than that reported by the World Health Organization (WHO), with 294 million unapparent infections (95% CI 217–392) and 96 million apparent infections (95% CI 217–392)⁴.

The maintenance of disease transmission in tropical and subtropical countries depends on demographic factors as well as altitude, temperature, and humidity. Additionally, the immunity generated in the population against several DENV serotypes and the evolution of the virus itself are considered factors influencing transmission, contributing to periodicity in the onset of dengue cases⁵.

Humoral immunity may increase the risk of showing the severe form of dengue, as suggested by several studies performed in Thailand, Indonesia, and Cuba that estimated titers of neutralizing antibodies related to protection and evaluated the association between the presence of preexisting neutralizing antibodies and severe cases^{6,7,8}.

On the other hand, several findings have been observed that conflict with the enhancement theory of the immune response. For example, in Peru, febrile cases reported in the postsecondary infection group compared to the primary and secondary infection groups dropped significantly by 93% for DENV-3, and 64% for DENV-4, showing that preexisting cross-reactive antibodies may decrease the risk of infection^{9,10}.

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