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Research Article

Comparison of the Hemagglutination Inhibition Test and IgG ELISA in Categorizing Primary and Secondary Dengue Infections Based on the Plaque Reduction Neutralization Test

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Secondary dengue infection by heterotypic serotypes is associated with severe manifestations of disease, that is, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). The World Health Organization (WHO) has recommended criteria based on the hemagglutination inhibition (HI) test to distinguish between primary and secondary dengue infections. Since the HI test has practical limitations and disadvantages, we evaluated the accuracy of WHO HI criteria and compared it with criteria based on an IgG enzyme-linked immunosorbent assay (ELISA) using a plaque reduction neutralization test (PRNT) as the gold standard. Both WHO HI criteria and IgG ELISA criteria performed strongly (16/16) in determining primary infection. However, to determine secondary infection, the IgG ELISA criteria performed better (72/73) compared to the WHO HI criteria (23/73).

1. Introduction

Dengue virus is a global concern with an increasing incidence, especially in endemic areas like Southeast Asia, South America, and the Pacific. Recent analysis, based on the geographical distribution of the disease, estimates 250–500 million infections annually, which is three times higher than the estimation from the World Health Organization (WHO) [1, 2].

Dengue virus (DENV) belongs to the family Flaviviridae, genus *Flavivirus*, which consists of four antigenically distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4). Dengue virus infection can be confirmed by virus culture, by reverse-transcription polymerase chain reaction (RT-PCR), serologically by neutralization test (gold standard), by IgM enzyme-linked immunosorbent assay (ELISA) antibodies, or by 4-fold increase of hemagglutination inhibition (HI) antibody titers between acute and convalescent specimens. HI test is more commonly used than PRNT as HI test does not need virus culture facilities and has a simpler technique [3].

Infection with any of the four serotypes can be asymptomatic or results in a wide range of clinical manifestations between dengue fever (DF), mild to severe dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) which is often fatal. Besides viral virulence and host background (immune, genetic, and nutritional), severe dengue infection is often associated with secondary infections [4]. Secondary infections, which are common in endemic areas such as Indonesia [5–8], comprised approximately 80–90% of the DHF/DSS cases. Therefore, it is important to distinguish between primary and secondary infections. The 2009 WHO