## High Prevalence of Asymptomatic Dengue among Healthy Adults in Southern Malaysia: A Longitudinal Prospective Study

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Abstract : In recent decades, Malaysia has become a dengue hyper-endemic country with the co-circulation of the four-dengue virus (DENV) serotypes. The number of symptomatic dengue cases is maintaining an increasing trend since 1995 and sharply increased in 2014. The four DENV serotypes have been co-circulating since 2000, and this pattern of cyclical dominance of subtypes contributed to the development of frequent major dengue epidemics in Malaysia. Since 2012, different Malaysian state was dominated by different serotypes. The study aims to estimate the burden of asymptomatic dengue in a healthy adult population which may act as a potential source of further symptomatic dengue infection. It also aims to identify the predominant DENV serotypes which are circulating at the community level. A longitudinal prospective community-based study was conducted in the Segamat district of Johor State, southern part of Malaysia where the number of reported dengue cases has steadily increased over the last three years (2013-2015). More specifically, the study was conducted in and around of Kampung Abdullah of Sungai Segamat sub-district which was identified as a hot spot area over the period of 2013-2015. This community-based study has been conducted by Southeast Asia Community Observatory (SEACO), an ISO-certified research platform in collaboration of the Ministry of Health Malaysia and Monash University Malaysia. It was conducted from May 2015 to May 2016. In this study, 277 apparently looking healthy respondents joined who were followed up as a cohort for four times during the one-year study period. Blood was collected to detect the serological marker of dengue at each round of follow-up. Among 277, 184 respondents (66%) joined all four rounds. Half of the study respondents were at the age-group of 45-64 years, slightly more than half of the respondents (59%) were female, and the most (69%) of them were Malay; only 35% lived in urban areas. During the baseline, the study found a very high prevalence of exposure to dengue virus; 89% of the study respondents had serological evidence of previous asymptomatic dengue infection; the majority of them did not know about it as they did not develop any symptom of dengue fever; only 13% knew as they developed symptoms. At the end of the one-year study period, 19% of respondents developed recent secondary dengue infection which was also identified by the serological marker as they did not develop any symptom (asymptomatic cases). The asymptomatic dengue incidence was higher during the rainy season compared to the dry season. All four dengue serotypes were identified in the serum of the infected respondents; among them, DENV-2 was the most prominent. Further genetic analysis is going on to identify the association of HLA-B\*46 and HLA-DRB1\*08 with dengue resistance. This study provides evidence for the policymakers to be aware of asymptomatic dengue infection, to develop a useful tool for raising awareness about asymptomatic dengue infection among the general population, to monitor the community participation to strengthen the individual and community level dengue prevention and control measures when neither there is vaccine nor particular treatment for dengue.

1

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