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Detection Of Asymptomatic Dengue Infection Executive Summary

[Adapted from the report by ROS AZIAH MOHD RASHID]

Background

Dengue fever is an important mosquito-borne human viral disease globally caused by the infections of four dengue virus serotypes (DENV 1-4). The incidence of dengue has increased 30-fold in the past 50 years. Presentations of dengue range from asymptomatic, mild febrile illness to life-threatening conditions including severe bleeding, organ dysfunction, and shock. It has been estimated that dengue resulted in 58.4 million symptomatic cases and was responsible for 1.14 million disability-adjusted life-years in 2013. The estimated population at risk of DENV infection worldwide is around 3.97 billion people. It has been a known fact that the majority of DENV infections are clinically inapparent. Transient dengue viremia can occur either in symptomatic cases before onset of clinical illness or in people with inapparent infection.

Detection of asymptomatic dengue infection is difficult and challenging. While symptomatic dengue can be clinically suspected and then the confirmatory laboratory diagnosis can provide definite diagnosis, there is no clinical clue for asymptomatic infection. Detection of asymptomatic dengue infection is therefore based on laboratory diagnosis. The currently used diagnostic test for dengue infection can be divided into virologic/ molecular based [virus Isolation (cell culture), nucleic acid hybridization, reverse transcriptase –polymerase reaction (RT-PCR)], antigen based (NS1) and serologic based [haemaglutination-inhibition (HAI), Enzyme linked immunosorbent immunoassay (ELISA) and plaque reduction neutralization test (PRNT)]. Since viremia occurs for only a short period (one to two days before onset of symptom and up to five to seven days after onset of symptom), the virologic/ molecular/ antigen based are applicable only in symptomatic infection. Therefore, serologic methods to detect rising in dengue antibody in asymptomatic persons are more convenient.

It is claimed that the burden of asymptomatic dengue infection is high and it may play a role in dengue transmission. Apart from that, methods for detecting asymptomatic infection [including the diagnostic tests used and blood sampling] depend on the objectives, budgets, the level of accuracy needed and the feasibility.

This technology review was requested by Head of Vector Borne Disease Sector, Disease Control Division, Ministry of Health to look into evidence on asymptomatic dengue infection in terms of its' burden, detection and transmission.

Objective/aim

The objective of this technology review was to evaluate the effectiveness, costimplication, safety and organisational issues of detecting asymptomatic dengue infection.

Results and conclusions

A total of 143 records were identified through the Ovid interface and PubMed, and two were identified from other sources (references of retrieved articles). There were 19 full text articles included in this review comprised of two diagnostic accuracy studies, four cohort studies and 13 cross sectional studies. The studies were conducted in Vietnam, Thailand, China, Saudi Arabia, Pakistan, India, Malaysia, Taiwan and Singapore.

There was very limited diagnostic accuracy studies retrieved for detecting asymptomatic dengue infection. The accuracy of NS1 in detecting asymptomatic dengue infection could not be determined due to limited number of study (one study) with limited sample size (17 individuals). Indirect ELISA was reported to

have accuracy of 83% in detecting symptomatic and asymptomatic dengue infection compared to gold standard test ($PRNT_{50}$). Serology test involving ELISA were frequently used in incidence and seroprevalence studies of asymptomatic dengue infection.

Generally, the incidence of asymptomatic dengue infection was found to be higher compared to symptomatic dengue infection. Inapparent to symptomatic (I:S) ratio ranged from 0.9:1 to 2.5:1. However, viral load or viraemia level in asymptomatic patients was found to be lower compared to symptomatic patients.

Very limited evidence retrieved to suggest that several factors such as symptomatic dengue incidence and dengue serotype circulation affects the incidence of inapparent and symptomatic dengue infection among school children.

There was also very limited evidence retrieved to suggest that asymptomatic and pre-symptomatic DENV-infected people were more infectious to mosquitoes compared to symptomatic people. However, there was no retrievable evidence on transmission of dengue virus from mosquitoes to human among asymptomatic infection.

There was no evidence retrieved on the cost-effectiveness, safety and organisational issues on detection of asymptomatic dengue infection.

Methods

Electronic databases were searched through the Ovid interface: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946 to Present, EBM Reviews - Cochrane Central Register of Controlled Trials - December 2018, EBM Reviews - Cochrane Database of Systematic Reviews - 2005 to December 2018, EBM Reviews - Health Technology Assessment – 4th Quarter 2018, EBM Reviews – NHS Economic Evaluation Database 4th Quarter 2018. Searches were also run in PubMed database and U.S. Food and Drug Administration (USFDA) website. Google and Google Scholar was also used to search for additional web-based materials and information. Additional articles were identified from reviewing the references of retrieved articles. Last search was conducted on 13th January 2019.