

Dengue Virus Serotypes of Children Diagnosed with Dengue Hemorrhagic Fever at Syarif Hidayatullah and Fatmawati General Hospital Jakarta

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Abstract--Dengue hemorrhagic fever is an infectious disease caused by dengue virus has become one of the most important viral disease worldwide. DHF is re-emerging arboviral disease of great public health importance, and it has spread to all tropical countries in the world. Pattern of dengue virus are serotypes DEN 1, DEN 2, DEN 3 and DEN 4. Previous studies have suggested that people infected with serotype DEN 3 will experience severe dengue fever, even death. Sequential infection of two serotypes leads to more severe type of disease. The aim was to know pattern of circulation Dengue serotypes at Fatmawati General Hospital and Syarif Hidayatullah Hospital, Jakarta. This study was a descriptive study with cross sectional approach to children diagnosed with DHF and DSS at Syarif Hidayatullah Hospital and Fatmawati General Hospital who hospitalized during May until November 2014. DHF diagnosed was confirmed by WHO 2011 criteria. Blood was taken for virology test by PCR to detect DEN virus. This virology test was done at laboratory of Department of Microbiology, Faculty of Medicine University of Indonesia. Of 30 DHF and DSS patients, we found 21 were positive for serotype DEN 3, six children were positive for serotype DEN 2, and one child was positive for serotype DEN 1, one child was positive for serotype DEN 4. One case was positive with mixed infected serotype that is DEN 1 and DEN 2. Patients who had DSS as many as 2 patients, were infected with mixed DEN 1 and DEN 2, and infected with DEN 3. Conclusion this study serotype DEN 3 mostly infected among DHF patients in Syarif Hidayatullah Hospital and Fatmawati General Hospital Jakarta and among them 2 patients had shock syndromes.

Keyword—Dengue Virus Serotype

I. INTRODUCTION

Dengue infection is the most rapidly spreading mosquito-borne viral disease in the world. The World Health Organization (WHO) reported that the incidence increased dramatically over the last 50 years and that dengue virus infections expanded to new countries, and from urban to rural settings. Approximately 2.5 billion people live in endemic countries of which about 1.8 billion (more than 70%) in Southeast Asia and the Western Pacific Region [1, 2].

Major dengue epidemics date back to the late 17th century. However, the start of epidemics of severe dengue began in the South-East Asia region following World War II, when conditions for mosquito-borne diseases were favorable. Dengue infections during these latter epidemics were accompanied by severe haemorrhage, shock and vascular leakage. The first recorded Dengue haemorrhagic fever (DHF) epidemic occurred in Manila, the Philippines, in 1953. Thereafter the epidemic spread quickly throughout South-East Asia and further west via India, Sri Lanka, Maldives and Pakistan, and in the east to China. Many factors are thought to be responsible for the global re-emergence of dengue fever (DF) and DHF. These include major global demographic changes and worsening of health care systems and mosquito control programs [3].

Aedes aegypti is the principal mosquito vector of dengue. Adult mosquitoes shelter indoors and bite during the daytime. They are adapted to breed around human dwellings, in water containers, vases, cans, old tires and other discarded objects. The secondary vector for dengue virus is *Aedes albopictus*, which contributes significantly to transmission in Asia and whose presence is spreading in Latin American countries. Dengue outbreaks have also been attributed to *Ae polynesiensis* and *Ae scutellaris*, but to a lesser extent [4].

Dengue viruses cause symptomatic infections or asymptomatic seroconversion. Symptomatic dengue infection is a systemic and dynamic disease. It has a wide clinical spectrum that includes both severe and non-severe clinical manifestations. After the incubation period, the illness begins abruptly and, in patients with moderate to severe disease, is followed by three phases febrile, critical and recovery [5].

Many factors influence the severity of the dengue fever. Risk factors on dengue is the immune status of the individual, strains or serotypes of the virus which infects, age of the patient, the patient's genetic background, and a secondary dengue infection. [3, 6].

Indonesia is the largest country in the region with a population of 245 million. Almost sixty per cent of the people live on the island of Java, which is most severely afflicted by

periodic outbreaks of dengue disease. However, the disease is endemic in many large cities and small towns throughout the country and has also spread to certain smaller villages, where population movement and density are high [7].

The Dengue virus is an arbovirus, from genus *Flavivirus* family *Flaviviridae*. DENV genome is composed of approximately 10,600 nt single stranded positive sense RNA containing a single open reading frame (ORF) that is flanked by 2 un-translated regions (UTRs) at the 5' and 3' ends. DENV virion is composed of 3 structural proteins; a core protein (C), a membrane protein (M), an envelope (E) protein and 7 non-structural proteins. There are 4 distinct serotypes of DENV, known as DENV-1, DENV-2, DENV-3, and DENV-4. The amino acid differences of DENVs have been implicated in the pathogenesis of DHF. Each serotype provides specific lifetime immunity, but only a short term cross-immunity. All serotypes can cause severe and fatal disease [8, 9].

In Indonesia, serotype DEN-3 is dominant, and it is assumed this serotype causes severe clinical manifestations in patients [3, 9].

In this study, we want to know the type of DENV circulating in Syarif Hidayatullah and Fatmawati Hospital.

II. METHODS

This study was a descriptive study with cross sectional approach to children diagnosed with DHF and DSS at Syarif Hidayatullah Hospital and Fatmawati General Hospital who hospitalized during May until November 2014. DHF diagnosed was confirmed by WHO 2011 criteria. Blood was taken for virology test by PCR to detect DEN virus. This virology test was done at laboratory of Department of Microbiology, Faculty of Medicine University of Indonesia.

With the Inclusion criteria: Patients with dengue fever or dengue hemorrhagic fever (DHF) according to WHO criteria, aged under 14 years, hospitalized in Syarif Hidayatullah and Fatmawati Hospital, provided that a parent or guardian gave informed consent.

The study was approved by the Syarif Hidayatullah University Medical Research Ethics Committee. Blood samples were obtained from each patient in the study. Acute-phase blood samples (2–3 mL) were obtained at admission to the hospital (day 3 to day 7 after the onset of fever). Serum was separated as quickly as possible, and serum samples were store 70 C. NS-1, IgG dan IgM Dengue were examined with Elisa, and detection of dengue virus with PCR.

Detection of molecular-based detection of viral genetic material using the PCR method is the gold standard for diagnosis of dengue infection. The isolation of the virus, using the PCR method is easier, cheaper, faster and more sensitive. PCR methods are generally divided into two i.e. the conventional method and the method of real time PCR. Isolation of viral RNA from serum by using the QIA amp viral RNA kit commercials mini kit (Qiagen). Isolation of RNA is done in a special room, use the Security Cabinet BSC class I.

III. RESULT

A. Characteristic Patients

In the period May to November 2014 found 40 patients treated in Syarif Hidayatullah and Fatmawati Hospital. Of the 40 patients only 30 patients who meet the criteria for inclusion in this study.

TABLE I. THE CHARACTERISTICS OF THE SUBJECTS OF THE STUDY 30 N

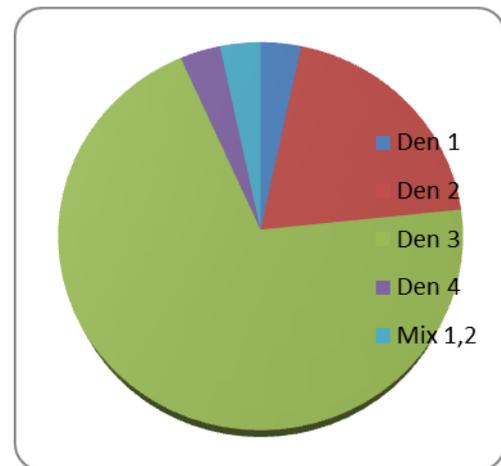
The characteristics of the		N (%)
Gender	boys	17 (56,67)
	girls	13 (43,33)
Age	0-5 years	3 (10)
	6-10 years	15 (50)
	11-14 years	12 (40)
Nutritional status	Good nutritional status	29 (96,67)
	Overweight	1 (3,33)

The subjects of the study consists of 30 children, with 17 (56.67%) boys, and 13 (43.33%) girls. Based on age, subject at domination by children from 6-10 years as many 15 children (50%), the next age group 11-14 years 12 (40%), and 1-5 year as many 3 children (10%). Nutritional status in most of the 29 (96%) are good nutritional status.

B. Degree of Dengue (According to WHO)

On this research we obtained 22 of 30 children who have an experienced DHF grade 1, six children with DHF grade 2, two children with DHF grade 3.

C. Den V



In this research were dominated by DENV 3 as much as 21 children, followed by six children infected DENV 2. In this research we found mixed infected DENV 1 and DENV 2 in one child.

IV. DISCUSSION

Dengue hemorrhagic fever is primarily disease of children under 15 years in hyper endemic areas. This study showed that DHF is more frequent to be found in

children aged 6-10 years. The result was consistent with that reported by Karyanti, Harris, and Sukri.^(1,10,11)

Boys and girls ratio was nearly equal in our study. The result was consistent with that reported by Dewi, Sukri, Narayanan, Gayatri [5, 11, 12, 13].

Almost children have good nutritional status. Kalayanarooj has concluded that nutritional status has no correlation with severe cases and shock [14].

In this research we found twenty two children were diagnosed DHF grade 1. Only two children diagnosed with DHF grade 3 or DSS. In the WHO guidelines, DHF is also classified according to severity. Grade I is defined as fever and non-specific constitutional signs and symptoms; the only haemorrhagic manifestation is a positive TT and/or easy bruising. Grade II is the same as grade I but includes spontaneous bleeding, usually in the form of skin or other haemorrhages. Grade III is circulatory failure manifested by a rapid, weak pulse and narrowing of the pulse pressure or hypotension, with the presence of cold, clammy skin and restlessness. Grade IV is profound shock with undetectable blood pressure or pulse. Grades III and IV define DSS [8].

DENV 3 dominated found in this research, and we found to mixed serology in one child.

The outbreak trend of DHF in the country has become irregular, with a high inter-epidemic background. All dengue serotypes are circulating, although severe disease is predominantly attributed to DENV-3 [3].

Epidemic outbreaks of DHF occurring every 8–10 years have also been reported in other countries, and might be the result of cross-protective immunity. DENV-4 was responsible for this epidemic pattern in Thailand which has an immunological cross-reaction with DENV-1 and, possibly, with other serotypes [1].

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