

Distribution of Dengue Virus Serotype in Tangerang, Indonesia

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Abstract: Dengue is an acute systemic viral infection transmitted by *Aedes aegypti* mosquitoes that is a public health burden in Indonesia with the increasing number of cases, especially during epidemics. Therefore, this study was investigating the prevalence of dengue infection and their serotype pattern in Tangerang, Indonesia. During 9 months-period (July 2011-March 2012), a prospective study of epidemiological and laboratory test based on rapid screening test for NS-1 antigen and confirmatory DENV has been conducted for these cases. Of the 84 samples, 62/84 (73.8%) show positive in dengue cases and 47/82 (57.3%) positive for DENV. DENV-1 was found to be the most common serotype 19/82 (23.2%) followed by DENV-3 17/82 (20.7%), DENV-2 16/82 (19.5%) and DENV-4 7/82 (8.5%) respectively. Out of 47 confirmed dengue infection there were 10/47 (21.3%) infected by two serotype of dengue viruses. Of these, 8/10 (80%) were proved to be secondary infection. The commonest clinical presentations were fever, nausea/vomiting/abdominal discomfort, myalgia and headache. At the time this study was conducted, Tangerang province, Indonesia had become a dengue endemic area with all four DENV circulates. The dominance of DENV-1 was the highest followed by DENV-3, 2 and 4. The occurrence of multi-serotype dengue viruses had a role in the incidence of concurrent DENV infection cases.

Key words: DENV, serotype, concurrent, secondary infection, Indonesia

INTRODUCTION

Dengue is a systemic viral infection caused by all four Dengue Virus (DENV-1-4) which belong to the flaviviridae family. Transmission of this virus by *Aedes aegypti* mosquitoes occurs worldwide, especially in subtropical and tropical countries with an estimated 50-100 million cases yearly (Simmons *et al.*, 2012; Bhatt *et al.*, 2013). In developing countries such as Indonesia, the burden of dengue has impact in human suffering, lack of health services and massive social and economic losses (Suaya *et al.*, 2009). Concomitant with the dengue cases has significantly increased in recent years globally; the average number of these cases in Indonesia was 129,435 for the period 2004-2010. Even in 2013 there was an outbreak with 112,511 infections reported in Indonesia and the number of deaths were 871.

The pattern of DENV spreading is closely related with high density of mosquitoes which is appearing in similar result of sequences among the host and vector (Mammen *et al.*, 2008). In cases of severe dengue, the differences of DENV serotypes pattern varies in many various countries such as DENV-2 became the primary cause in Cuba, Thailand, Malaysia and DENV-3 for Indonesia (Rico *et al.*, 1997; Guzman *et al.*, 2010). At present, information of dengue virus serotype in adult

dengue infection in in the province of Tangerang, Indonesia is limited. Keeping this mind, our research was defining the prevalence of DENV and their pattern in one of the urban area in Indonesia.

MATERIALS AND METHODS

Patients: A prospective study was conducted in four primary health care centre and one hospital located in Tangerang, Indonesia from July 2011-March 2012 after receiving permission from the institutional ethical committee, Faculty of Community Health, University of Indonesia (032/H2.F10/PPM.00/2011). The eligible participants were adult patients (age 15-60 year-old) which has lasted for ≤ 72 h. The clinical data consisting of symptoms such as headache, nausea/vomiting/abdominal pain, retro-orbital pain, myalgia, arthralgia, skin rash, spontaneous bleeding and positive tourniquet test were analyzed. The definite dengue diagnosis was based on the presence of 2/more clinical symptoms, positive RT-PCR and/or NS-1 antigen detection results accompanied by either positive and/or negative IgM/IgG antidengue antibody.

Laboratory methods: Paired anticoagulated blood samples were collected from eligible patients during the first

visit. Complete blood count was performed by an automated haemocytometer (Sysmex®, Japan). All serum samples collected were tested for:

- NS-1 antigen, IgM and IgG antidengue antibodies detection by Dengue duo (Standard Diagnostic Inc®, Korea)
- DENV identification with Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) as defined by Lanciotti *et al.* (1992) for the detection of non-dengue viruses such as Japanese Encephalitis Virus (JEV), Chikungunya Virus (CV) and other flavivirus based on in-house protocol developed by Microbiology Department, Faculty of Medicine, University of Indonesia

RESULTS AND DISCUSSION

A total of 84 participants were enrolled and 62 (73.8%) participants were confirmed as having dengue illness. The early clinical and haematological presentations are shown in Table 1. RT-PCR was performed on 82 participants, of whom 47 (57.3%) had positive result of DENV. Half (23.2%) of these participants had DENV-1 serotype followed by 17 (20.7%) DENV-3, 16 (19.5%) DENV-2 and the least was DENV-4 in 7 (8.5%). Of 47 confirmed laboratory dengue infection, 10 (21.3%) had co-infection with two DENV serotypes (Table 2). The remaining 8/10 (80%) were positive for co-infection, also classified as having secondary infection in our analysis.

In previous study conducted in other regions or countries provide that clinical features in gastrointestinal problems only seen in 10.2-48.9% of cases (Basuki *et al.*, 2010; Thai *et al.*, 2010; Dumas *et al.*, 2013). Here we showed that during study periode, nausea/vomiting/abdominal pain was found in almost all participants. These complaints were due to increasing of the gastrointestinal mucosal permeability, congestion of the gall bladder or the release of mediators such as histamine/serotonin (Zulkarnain, 2004). Unfortunately, our study did not implement an ultrasound exam that could detect the presence of gastrointestinal symptoms.

The most prevalent serotype in this study was DENV-1 which was compatible with prior study in China or Surabaya, other province in Indonesia (Jiang *et al.*, 2012; Yamanaka *et al.*, 2011). A prior study from other province in Indonesia gained difference results which DENV-2 was the predominance serotype (Nusa *et al.*, 2014). However, phylogenetic analysis based on enveloped gene sequence revealed the similarity of genotype dispersion which closely associated to endemic viruses circulated earlier. This difference was mainly

Table 1: Clinical and haematological presentations among participants

Characteristics ¹	DENV positive (n = 47)	Definite dengue illness (n = 62)
Demographic information		
Age (years)	29.57±10.50	30.33±10.68
Female	26 (55.31)	41 (66.13)
Male	21 (44.69)	21 (33.87)
Clinical presentations		
Fever	47 (100)	62 (100)
Nausea/vomiting/ abdominal pain	41 (87.23)	52 (83.87)
Retro-orbita pain	6 (12.76)	12 (19.35)
Myalgia	30 (63.83)	41 (66.12)
Arthralgia	17 (36.17)	24 (38.70)
Headache	38 (80.85)	49 (79.02)
Positive tourniquet test	4 (8.51)	7 (11.29)
Spontaneous bleeding	9 (19.14)	14 (22.58)
Haematological results		
Hemoglobin (g dL ⁻¹)	13.48±2.10	13.37±2.03
Hematocrit (%)	39.68±5.83	39.42±5.52
total WBC count (mm ³)	4845±3081	4899±2966
Platelet count (mm ³)	143942±67791	138188±63455
Lymphocytes count (%)	30.59±15.37	30.10±15.13
Monocytes count (%)	9.97±4.63	10.07±4.70

¹Data presented as n (%) or mean±standard deviation

Table 2: Distribution of dengue serotype

RT-PCR result	n (%)
Dengue virus serotype¹	
DENV-1	19/82 (23.2)
DENV-2	16/82 (19.5)
DENV-3	17/82 (20.7)
DENV-4	7/82 (8.5)
CV	1/31 (3.2)
JEV	0/3 (0)
Other flaviviruses	3/35 (7.9)

¹DENV co-infections: 4/10 (40%) with DENV-2 and 3; 2/10 (20%) with DENV-1 and 2; 2/10 (20%) with DENV-1 and 3; 1/10 (10%) with DENV-1 and 4 and 1/10 (10%) with DENV-3 and 4

consequence of human mobilization or migration, high vector index and virulence of dengue viruses (Nusa *et al.*, 2014; Xu *et al.*, 2006). Like wise, the occurrence of four dengue virus serotype (DENV-1 to DENV-4) has been reported in endemic area such as subtropical and tropical countries (Simmons *et al.*, 2012; Bhatt *et al.*, 2013), this circumstances was also found in Tangerang province.

Concurrent infections of multiple dengue virus serotypes in patients have been quite widely reported in many endemic countries in China, South East Asia, Brazil and India (Jiang *et al.*, 2012; Yamanaka *et al.*, 2011; Nusa *et al.*, 2014; Lardo *et al.*, 2016; Araujo *et al.*, 2006; Vinodkumar *et al.*, 2013). It is estimated as one of the enhance factor in high cases of dengue, therefore the hyperendemicity have a role on the incidence of co-circulation of multiple DENV (Lardo *et al.*, 2016). However, these present study noted that no participants were catagorized in severe dengue. These results were similar with other study conducted by Araujo *et al.* (2006) that pointed co-circulation DENV-2 and DENV-3 had no responsible for severe manifestation. Unlike these

reports, other studies observed that many of co-infection cases had more severe illness (Lardo *et al.*, 2016; Vinodkumar *et al.*, 2013). In a relatively similar study, Lardo *et al.* (2016) reported concurrent infection by dengue viruses serotype 2 and 3 yielded severe clinical manifestation. In an earlier study conducted in Bangkok found that no significant correlation between dengue serotypes and clinical manifestation of illness (Fried *et al.*, 2010). These finding was supported by others study that declared primary or secondary dengue infection and a specific DENV serotype were not related with clinical symptoms and severity of dengue illness (Dussart *et al.*, 2012; Fahri *et al.*, 2013).

CONCLUSION

At the time this study was conducted, Tangerang province, Indonesia had become a dengue endemic area with all four DENV circulates. The dominance of DENV-1 was the highest followed by DENV-3, 2 and 4. The occurrence of multi-serotype dengue viruses had a role in the incidence of co-infection cases.

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