Analysis of Dengue Infection Severity among Ethnics in Surabaya, Indonesia

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Abstract

Background: Dengue infection prevalence remains high in tropical countries, including Indonesia, whereas the government had struggled to overcome the disease. Indonesia has very diverse ethnicities living across the archipelago, there might be a wide variety of susceptibility and severity.

Objective: This research was aimed to analyse ethnicity as a risk factor for dengue infection severity in Surabaya, Indonesia.

Design and Methods: This research observed Dengue Hemorrhage Fever (DHF) or Dengue Fever (DF) patients aged over 12 years, who were hospitalized in three private hospitals in Surabaya. Data collection was conducted from March 20, 2013 to May 20, 2013 with a sample size of 95 patients. Ethnicity, dengue infection severity, clinical findings, and relevant laboratory information data were obtained. This was a cross-sectional study design with consecutive sampling. All data were analysed using SPSS 17.00 software. The statistical analysis was performed at a significance level of p-value <0.005 using the chi-square test.

Results: The majority of patients who suffered from severe dengue infection based on WHO classification and bleeding symptoms were Chinese patients (82.1%). The laboratory results pointed out Chinese patients had the highest hemoglobin concentration (15.62 ± 1.70 %), highest PCV (44.90 ± 4.23 g/dl), and the lowest platelets (31.42 ± 22.05 x 103μl). There were significant dengue infection severity difference (p=0.015), hemoglobin increase (p=0.004), PCV (0.024), and platelets (p=0.006) between Chinese, Javanese, and other ethnicities.

Conclusion: Chinese ethnic had the highest risk of suffering severe dengue infection in Surabaya.

Keywords: dengue infection severity; ethnicity; Indonesia; Chinese; Javanese

Introduction

Dengue Hemorrhagic Fever (DHF) and Dengue Fever (DF) prevalence remain high in the tropical countries, include Indonesia. By 2008, the spread of DHF reached ± 69 countries in Southeast Asia, Western Pacific and the USA. The number of cases increases from 479,848 in 1990-1999 to 1,656,870 in 2000-2008 worldwide.[1] In Indonesia the incidents of DHF and DF in Indonesia reached 51 per 100,000 in 2007 with the Case Fatally Rate (CFR) 1.8% and in 2009 reached 66.48 per 100,000 with the CFR 0.89%.[2] All sub-districts in Surabaya have become dengue endemic areas, the data from 2007 to 2011 are 113; 75.6; 78.43; 116; 36.22 per 100,000 while CFR are 0.7%; 0.46%; 0.26%; 0.4% and

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0.69% respectively.[3]

Interaction of host-agent-environment affects the disease. Previous studies showed that the factors from host that could affect the manifestation of the disease are race/ethnic, sex, age, nutrition status, secondary infection and immune response.[4]

Ethnic or race might determine the manifestation of dengue. The Chinese who live in Singapore were found higher in attack rate of DHF than the Malay and the Indian.[5] A study in Brazil showed that African people are more protective than the whites toward dengue virus. Indonesia is a country with diverse ethnicities and cultures, there might be a wide variety of susceptibility to dengue infection.[6] In Indonesia, the Javanese is the largest ethnic group, the second is the Sundanese (15.51%), the third is the Malay, Batak and Madurese contribute 3.70%, 3.58% and 3.03%, respectively. There are another 10 ethnic groups, each contributing between 1.2% and 3.0%, with the Chinese as the lowest (1.20%) in this group.[7]

Manifestation of dengue infection varies which is characterized by bleeding symptoms and leakage of plasma, measured by Hematocrit (Hct) or Packed Cell Volume (PCV), hemoglobin and trobocytes depletion. DHF according to WHO (2011) is classified into 4 grades and added with expanded dengue syndrome.[1]

Finding out the description of the dengue infection severity based on the ethnicity could be used as a basis to create an effective model of prevention and management of the dengue infection. The model is created based on the ethnicity as its approach, thus the result is expected to be more effective and could indirectly help reducing the number of patients and death rate due to dengue infection in Indonesia, especially in Surabaya.

This study aims at analyzing the severity of dengue infection based on the ethnicity in Surabaya; Javanese, Chinese and other group ethnics.

Methods

The study was analytic observational with a cross sectional design. The sample was IgM and/or IgG dengue positive DHF/DF patients. With inclusion criterias were: not in a state of suffering from other severe infections and aged above 12 years old. Patients were hospitalised at 3 private hospitals in Surabaya between March 20th until May 20th 2013. Total sample was 95. Independent variable was ethnicity, while dependent variable was DHF severity based on WHO criteria in 2011.

Immnochromatography dengue strip test, PanBio™ duo cassete, was used to confirm the diagnosis with dengue IgM and IgG. Data of Hb, PCV and platelets were analyzed by the hospitals using hematology analyzer tool, products from Sysmex™ and Celltac™.

Results

Based on the ethnicity, most of patients identified themselves as Javanese (42.1%), while Chinese and other ethnic groups occupy almost the same (Table 1). Majority of patient suffered from severe category of DHF (62.1%). Laboratory data showed that Hb increase, platelets and leucocyte count decrease were severe in the most patients, 51.6%, 61.1%, 58.9%, respectively (Table 2).

Based on the bleeding symptoms that, in this study, are categorized into 3: severe (hematemesis, melena, epistaxis), moderate (*echimose*, spontaneous *petechia*) and mild (positive RL without bleedings), the study showed that severe and moderate bleedings are more commonly found among Chinese patients than Javanese and other group ethnics. The symptoms of mild bleedings are mostly found in among Javanese patients.

Table 3 showed that Chinese patients had highest mean of Hb and PVC and lowest mean of platelets compared to others. While other ethnic groups category showed lowest mean of leucocytes compared to Javanese and Chinese.

Chi-square statistical test shows that there are differences in the severity of dengue infection based on those indicators, except for leucocytes decrease, between Chinese, Javanese and other ethnic groups. (Table 4)

Table 1. Characteristic of patients

Variable	N (%)
Sex	
- Male	52 (54.7)
- Female	43 (45.3)
Age	
- Adolescence (12-16 years)	21 (22.1)
- Young adult (17-25 years)	32 (33.7)
- Midle age (26-45 years)	36 (37.9)
- Older adult (>45 years)	6 (6.3)
Ethnic	
- Chinese	28 (29.5)
- Javanese	40 (42.1)
- Others / mixed	27 (28.4)

Table 2. The diagnosis of dengue infection severity

The diagnosis of dengue infection severity	N (%)
• WHO criteria for DHF (2011)	
- Mild (DF & DHF grade I)	36 (37.9)
- Severe (DHF grade II, III, IV and DHF exp.)	59 (62.1)
• bleeding symptoms	
- Mild	36 (37.9)
- Moderate	46 (48.4)
- Severe	13 (13.7)
• PCV/haematocrite increase	
- Mild	49 (51.6)
- Severe	46 (48.4)
• Hb increase	
- Mild	46 (48.4)
- Severe	49 (51.6)
• Platelet decrease	
- Mild	37 (38.9)
- Severe	58 (61.1)
• Leucocytes decrease	
- Mild	39 (41.1)
- Severe	56 (58.9)

Laboratory (PCV, Hb, platelets, and leucocyte) were classified into two categories, mild and severe. Mild was when the laboratorial result is below the mean of all patients' results while severe was when the result is higher than the overall patients' results.

Table 3. Laboratory examination

Laboratory examination	Mean ± SD
• Highest PCV - Chinese - Javanese - other ethnics	44.06 ± 4.87 % 44.90 ± 4.23 % 43.27 ± 4.17 % 44.37 ± 6.28 %
• Highest Hemoglobin (Hb) - Chinese - Javanese - Other ethnics	15.14 ± 1.75 g/dl 15.62 ± 1.70 g/dl 14.62 ± 1.45 g/dl 15.44 ± 2.05g/dl
• Lowest Platelets - Chinese - Javanese - other ethnics	41,540 ± 27,940 /µl 31,420 ± 22,050 /µl 52,980 ± 29,790 /µl 35,110 ± 25,120 /µl
• Lowest Leucocytes - Chinese - Javanese - other ethnics	2,930 ± 1,360 /µl 2,810 ± 1,490 /µl 2,890 ± 1,150 /µl 2,120 ± 1,540 /µl

Table 4. Comparison of dengue infection severity based on ethnicity

Comparison of dengue infection severity based on ethnicity	P value
Severity based on WHO dengue classification and ethnicity	0.015
Severity based on hemoconcentration of Hb increase and ethnicity	0.004
Severity based on PCV/haematocrite increase and ethnicity	0.024
Severity based on platelets decrease and ethnicity	0.006
Severity based on leucocyte decrease and ethnicity	0.493

Discussion

Characteristics of Patients with Dengue Fever

Sex

Ratio of DHF/DF patients over the age of 12 years between male and female was slightly higher in male (54.7%). The finding also similiar with another research on dengue infections at Hasan Sadikin Hospital, Bandung, where the percentage of male patients was 50.7%.8 Another study conducted in Singapore showed that the ratio of male:female was 1.9:1, whereas in India was 1:0.57, respectively.5 These conditions might indicate that the proportion of DHF/DF incidents between men and women were almost equal.

Age

Group of 26-45 years old (37.9%) was higher than any other groups. Some studies in Latin America and Southeast Asia in the early 1980 showed that many dengue cases were suffered in older adult. In Singapore, the mortality alteration of dengue infection occurred at the older age, proved by the case of death in 1982 which 50% higher among > 15 years old (the age group of 15-34). In Bangladesh, the proportion of hospitalized dengue infection patients aged 18-33 years old was higher than any other age groups (82%).5 In Malaysia, dengue cases were suffered more in 13-35 years old people since 1982.9

Diagnosis of Dengue Infection Severity

According to WHO criteria for DHF, the most hospitalized patients were categorized as DHF grade II rather than DHF grade I, Dengue Fever or Dengue Shock Syndrome.1 This facts happened due to spontaneous bleeding symptoms on DHF grade II, which were not shown on grade I or dengue fever. Many of dengue fever patients usually not to go to hospitals because the symptoms are milder than DHF. This situation is also similar to a study in Iran that showed the highest inpatient case was DHF II (92%).10

The study of prognostic indicators of dengue infection severity showed a significant relationship between the value of PCV, platelets and leukocytes to the severity of dengue infection.11 In addition, a meta-analysis study showed that thrombocytopenia

and PVC hemoconcentration were strongly associated with DSS.12 Moreover, another study found a significant relationship between dengue severity with thrombocytopenia (p: 0.002) and leukocytes (p: 0.067). The results of this study indicate that the severity of Hb, PCV, platelets and leukocytes is almost the same as shown by the percentage data from mild, moderate to severe.13

Based on the severity of bleeding symptoms, Chinese were suffered more serious bleeding symptoms compared to other ethnic groups. Based on the severity of Hb, PCV hemoconcentration and trombositopenia, Chinese have more severe symptoms as well. This condition showed that Chinese were more susceptible to severe clinical symptoms when they are infected by dengue compared to Javanese or other ethnics. The results of this study are similar to study conducted in Cuba showed the DHF/DSS ratio risk for the whites:blacks:mixed-race = 5.5:1:1.8, and also there was a tendency that a certain ethnicity become more susceptible than other ethnic groups.14 Chinese genetically have lighter skin color compared to Javanese, consequently they have more severe clinical symptoms. In addition, study in Singapore found the attack rate of Chinese was higher than Malay and Indian ethnic.5

The Differences of Dengue Infection Severity Based on Ethnicity

The ethnicity was mostly Javanese, eventhough the study was conducted in hospitals near Chinatown and area where the Arabian or Madurese live together. It happens as the larger number of Javanese descent (83.68%) lives in Surabaya compared to other ethnics, 7.5% Madurese, 7.25% Chinese, 2.04% Arabian and the rest is for other ethnic groups.

Based on Chi-square analysis, there was a significant difference of dengue infection severity between those 3 ethnic groups. Therefore, the difference of ethnicity can lead to the difference of infection response, which means there is a tendency of greater genetic difference in controlling the immune response in different ethnic groups compared to the same ethnic groups.

There were several studies discussing about the relation between genetic and the response to dengue infection; including HLA, HPA, vitamin D receptor,

etc. According to HL. Blum, someone's health status is influenced by the environment, genetic (heredity), and lifestyle as well as health services. The theory stated that the genetic is one factor contributing to health status.

This study showed different severity of dengue infection in different ethnicity. Ethnicity is a unique human population that differ from another due to frequency of particular gene and in its development are some variations in both genetic and phenotypic variation. There were some previous studies that showed differences of dengue infection severity between phenotypes whites, blacks or mixed-races. One of them showed that the whites have more risk than the colored ones. Those researches had same results with this study which is suggesting that Chinese is clinically more affected than Javanese or other ethnic.14 Another research conducted in Cuba showed that the percentage of DHF II and III in adults patients were 81% whites, 13% Caucasians-mixed and 6% blacks respectively. The mortality case was found in whites 77%, colored 14% and blacks 9%. These conditions happened due to a stronger specific immune response of whites to dengue virus, hence cytokine increased that led to more severe clinical manifestation.15

Study in Cuba showed that factor of varying severity of dengue infection in different ethnics due to the personalized immunological reaction, more specifically T-lymphocytes activation and cytokines. On the other hand, the polymorphism of human leukocyte antigene (HLA) region which encode specific protein roled in immune response. The variation of HLA has been known in several viral diseases, such as delayed progression of HIV and Hepatitis B carriage. Furthermore, T cell receptor which is directly response to dengue virus antigen might be vary in number distributed between different ethnics. The last is the role of monocytes expressing FCγ receptor which is main target of dengue infection antigen forming dengue virus-dengue antibodies immune complex.16 Beside the serotype of dengue virus also determine the severity of the disease.17

Conclusion

Chinese suffered the most severe dengue infection compared to Javanese and other ethnic groups. It is essential, when health professionals deal with dengue infected patients, to obtain information regarding the exact origin and ethnicity of the patient. Previous studies revealed that each ethnicity has different susceptibility on dengue virus. Thus, on this point forward doctor are going to treat Chinese patients of DHF / DF more intensively and to arrange a new procedure that increases the doctors' awareness in dealing with Chinese patients with dengue infections.

This paper also underlines the importance of preventing dengue infection by giving environmental intervention to reduce mosquito breeding sites, especially in Chinatowns.

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