

Recent Developments of Dengue Haemorrhagic Fever in Indonesia

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Abstract

This library research aimed to describe the recent developments of dengue haemorrhagic fever that occur in Indonesia recently (2013). Dengue Hemorrhagic Fever (DHF) is an infectious disease and a major public health problem in Indonesia. The onset of DHF is very rapid and, within short time, causes death and It often lead to its outbreaks. Children aged < 15 years are vulnerable to DHF. WHO reported that Indonesia has the highest cases in Southeast Asia. Morbidity rate (Incidence Rate) in Indonesia in 2009 was 68.22 per 100,000 population and the mortality rate (Case Fatality Rate) was 0.89%. Jakarta Province has the highest IR, about 313.41 per 100,000 population and the highest CFR was Bangka Belitung province (4.58%). However in 2013 the IR was 45.85 per 100,000 population and CFR was 0.77%, with Bali province occupies the highest IR of 168.48 per 100,000 population and Jambi province with the highest CFR 2.82%. The number of victims and the endemic areas are increased rapidly, it is in conjunction with the mobility and population density. The highest case occurred in January-March. Some serotypes of dengue virus of type 1, 2, 3, and 4 were been isolated. Dengue virus type 2 and type 3 are the dominant serotypes, whereas type 3 is associated with the severe dengue case. Dengue eradication efforts include: Increased activities of disease and vector surveillance, early diagnosis and treatment, as well as increased efforts to eradicate dengue vector-borne diseases.

Key words: *infectious disease, dengue virus, dengue hemorrhagic fever, Indonesia.*

Based on the data obtained from all over the world it is known that Asia occupied the highest number of DHF patients each year, Southeast Asia is the region most seriously affected by DHF. Since the year of 1968-2009, WHO noted that Indonesia has the highest DHF case. The number of patients and distribution of DHF in many regions increased along with the increasing mobility and population density (Pusat Data dan Surveilans Epidemiologi, 2010).

Dengue virus belongs to Arbovirus group, which transmitted through mosquito's bite. Virology survey which conducted on DHF patients at several hospitals in Indonesia shows that the dengue virus type 3 is the most prevalent serotypes that have been isolated. In addition, dengue virus type 3 is also found in majority of patients with severe DHF or the cause of death (Soedarmo, 1999; Suroso dan Umar, 1999; Wuryadi, 1999; Kementerian Kesehatan RI, 2014).

Based on the data obtained in 1968, the DHF endemic areas in Indonesia are only found in 2 provinces and 2 cities. While in the year 2009 it has increase to 32 (97%) provinces and 382 (77%) districts/cities. There was also an increase in the number of DHF cases in the last 5 years from 2005 to 2009 and have occurred in all provinces in

Indonesia (Pusat Data dan Surveilans Epidemiologi, 2010).

One reason for the increase in HDF cases in various cities of Indonesia is that because it was not able to fully control the mosquito *Aedes aegypti*, the vector in the transmission of this disease, that lead to the extraordinary events (outbreaks) in many cities. These events are estimated to occur once every 5 years. In addition, there is no early effective detection method in order for doing the early treatment (Achmadi, 2010).

Based on the data collected by the Ministry of Health of the Republic of Indonesia regarding the pattern of 10 main diseases in among patients in 2009 it was found that DHF case is the second highest with 121,334 cases, as well as causing death as much as 898 people, with CFR about 0.74% (Pusat Data dan Informasi, 2010).

The spread of dengue disease in Indonesia is very much related to environmental conditions and people's behavior, that lead to the occurrence of disease throughout the year and attack all age groups (Kementerian Kesehatan RI, 2014).

Causes of Dengue Hemorrhagic Fever
Dengue virus is the main cause of dengue

fever, dengue hemorrhagic fever (DHF) and dengue shock syndrome it's included in group B virus Arthropod (Arbovirosis) which is now known as the genus *Flavivirus*, Family *Flaviviridae*. Dengue virus is transmitted to humans through the bite of an infected *Aedes aegypti* mosquito. There are four serotypes of dengue virus that were found in Indonesia, namely: type 1, 2, 3, and 4. Dengue virus type 2 and type 3 is the predominant serotype, where type 3 is associated with severe DHF cases. Incubation period of the disease is estimated between 1 to 4 days and viral antigen can be detected a day before fever (Soedarmo, 1999; Wuryadi, 1999; Achmadi, 2010; Guerdan, 2010).

In general, serological test for dengue serotype 1, 2, 3, and 4 indicates the presence of cross-reactions, and can cause illness with symptoms of mild to severe. However, laboratory diagnosis will only show the presence or absence of the viral infection, but can not determine the degree of the disease. That is why, it is necessary to do further tests to determine the actual degree of the disease (Silitonga, 2006).

There are various factors that lead to morbidity and mortality in patients with DHF, such as patient age, vector density, rate of spread of the dengue virus, the virus serotype prevalence and climatic conditions. In general there is no difference in the number of dengue cases in terms of gender, but lately, death caused by dengue disease is more common to occur in men than women.

Distribution of DHF Cases

Dengue hemorrhagic fever has become a public health problem in Indonesia over the last 41 years. Based on existing data, the distribution of DHF in provinces and districts/cities that are endemic had increased from 1968 to 2009. In 1968 it was only found in 2 provinces and 2 cities, while in 2009 has become 32 (97%) provinces and 382 (77%) districts/cities in Indonesia. Similarly, in the number of cases found, in 1968 was only 58 cases, but in 2009 it increases to 158.912 cases. When viewed from 2005 to 2009, it appears the number of cases fluctuated, but in general it is increasing over the years (Pusat Data dan Surveilans Epidemiologi, 2010). When compared with 2013, the distribution of DHF cases have occurred in all provinces in Indonesia with 112,511 cases. This number increased from 90,245 cases in 2012

(Kementerian Kesehatan RI, 2014).

The number of districts/cities that were infected by DHF from 2008 to 2013 increased, where in 2008 there were as many as 356 districts/cities, it increases to 412 (82.9%) in 2013. However, the number of cases declined slightly from 2012 with 417 (83.9%) districts/cities infected (Kementerian Kesehatan RI, 2014).

The distribution of DHF cases can also be seen from the time and climate changes in which the rain fall index that created bodies water which is an ideal place for mosquito breeding sites, such as bamboo, trees, tin cans, old tires, roof or gutters. Puddles will incubate the eggs and produce mosquitoes after 10-12 days. Furthermore, when the infected mosquito bites a human, the symptoms of dengue fever will occur within 4-7 days. It took about 3 weeks from the start of the rainy season until the occurrence of DHF incidence. In addition, other factors that may affect the transmission of the disease are environmental factors, urbanization, population mobility, population density and transportation (Pusat Data dan Surveilans Epidemiologi, 2010).

The incubation period of dengue virus in the mosquito is 8-12 days, followed by the development in the human body for 3-14 days, and the onset of clinical symptoms about 3-7 days (Guerdan, 2010; Pusat Data dan Informasi, 2013).

The Cases and Severeness of DHF

DHF can be mild or asymptomatic to severe. Mild or asymptomatic infection is characterized by little or no symptoms other than fever. Dengue fever is characterized by two or more of the following symptoms: pain retro-orbital/ocular, headache, rash, myalgia, arthralgia, leukopenia, and hemorrhagic symptoms. Dengue hemorrhagic fever is characterized by dengue fever with thrombocytopenia (less than 100,000 cells per m^2), and plasma leakage (increase in hematocrit > 20%) or pleural effusion, ascites, or hypoproteinemia. While dengue shock syndrome is characterized by symptoms of DHF with signs of shock, such as rapid pulse, pulse pressure is limited, and poor end organ perfusion (Guerdan, 2010).

According to Sudjana (2010), the latest 2009 guideline from the WHO, has agreed to classify the case to: (1) dengue without warning signs, (2) dengue with

warning signs, and (3) severe dengue.

The criteria for dengue with or without the danger sign are: (1) residing or travelling to DHF endemic areas, (2) fever accompanied by two of the following symptoms: nausea or vomiting, rash, aches and pains, positive tourniquet test, and leukopenia, and (3) the existence of danger signs such as abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy or weakness, liver enlargement more than 2 cm, hematocrit rise in line with the rapid decrease in blood platelet count.

While the criteria for severe dengue is characterized by plasma leakage that lead to shock, fluid accumulation with respiratory distress, severe bleeding, and severe organ disorders characterized by disturbances of consciousness, heart problems and other organs as well.

Dengue Fever and Outbreaks

DHF is a disease that has a rapid course of disease and can lead to death within a short period of time. DHF is an infectious diseases that often lead to extraordinary events (outbreaks) in Indonesia the epidemic cycle occurs every 9 to 10 years. The peak of dengue cases occur in January each year. Dengue fever mostly infects children of less than 15 years of age, but can also infects adults (Pusat Data dan Informasi, 2010).

Based on the information from Data Center and Surveillance Epidemiology of the Ministry of Health Republic of Indonesia (2010), it reported that the number of cases of DHF outbreaks fluctuated from 1998 to 2009. The highest number of extraordinary events (outbreaks) of DHF occurred in 1998 in which the number of districts/cities reported experiencing DHF outbreaks of 104 districts/cities, and outbreak cases accounted for 58% of the total reported cases of dengue. Meanwhile, in 2004, the outbreak of DHF were reported from 75 districts/cities and accounted for 9.5% of DHF cases. After 2004, the incidence and DHF cases continue to rise but reports of outbreaks and the number of districts/cities continue to decline.

Based on the data obtained from Ditjen PP & PL Ministry of Health Republic of Indonesia in 2009, the mortality rate due to outbreaks from 1998 until 2009 occurred fluctuated. The highest mortality rate in 1999 was 3.2% and in 2009 decreased to 1.82%. Mortality

caused outbreaks in 2009 increased significantly from only 0.33% in 2008, but the number of cases which reported in 2009 was lower than in 2008.

The increase and spread of dengue cases may be caused by high mobility of the population; development of urban areas; climate change such as rainfall, temperature, and humidity; vector development; changes in the density and distribution of population; behavioral factors and community participation are still lacking in the eradication of breeding place for mosquito; and other epidemiological factors (needs more research).

The Incidency Rate of DHF

Jakarta Province occupies the highest incidence rate of DHF from 2005 to 2009. When viewed from the top 5 provinces, Jakarta province occupies the highest incidence rate, followed by East Kalimantan, Bali and other provinces (Pusat Data dan Informasi, 2010). Whereas in 2013, Bali Province occupied the highest incidence rate, which is 168.48 per 100,000 population, followed by Jakarta, Yogyakarta, East Kalimantan and Central Sulawesi. The incidence rate nationwide also increase from 37.27 in 2012 to 45.85 per 100,000 population in 2013 (Kementerian Kesehatan RI, 2014).

The number of cases in Jakarta in 2009 was 313 cases per 100,000 population, it is the highest incidence rate. The province with the lowest incidence rate is East Nusa Tenggara, which was 8 cases per 100,000 population. Whereas in 2013, Bali occupies the highest number of cases as much as 6,813 and the lowest is Maluku province with 33 cases per 100,000 population (Pusat Data dan Informasi, 2010; Kementerian Kesehatan RI, 2014).

Factors causing the high incidence of DHF in Jakarta is due to population density, high population mobility and good transportation that makes the spread of the virus becomes easier and spread widely. Five provinces with the highest DHF incidence rate in Indonesia in 2009 consecutively are: Jakarta, West Kalimantan, East Kalimantan, Bali and Riau Islands (Pusat Data dan Informasi, 2010; Pusat Data dan Surveilans Epidemiologi, 2010). According to Prof. dr. Tjandra Yoga Aditama, Sp.P(K), MARS, DTM&H, DTCE (2015) head of Health Research and Development

(Balitbangkes) of the ministry of health of Indonesia that In 2014, till mid of December it was recorded that DHF patients in the 34 province of Indonesia was 71.668 people, and 641 died. This number is lower than the previous year of 2013 with 112.511 patients and 871 died.

Based on the information from Data Center and the Surveillance Epidemiology Ministry of Health Republic of Indonesia (2010) it is known that the increasing number of highrisk provinces and subject to change from year to year where in 2007 all provinces in Java and Bali belong to high risk area, but in 2009 there was a change in which other provinces in Kalimantan, the West, East and Central Kalimantan turned into a high risk area. The incidence rate is considered high risk if the incidence rate is more than 55 per 100,000, moderate risk 20-55 per 100,000 population, and low risk are with less than 20 per 100,000 population.

In reviewing the incidence rate from 2008 to 2013 it was shown that the numbers fluctuate, where in 2008 the incidence rate is 59.02, and it increases in 2009, then decline in 2011, but rise again in 2013 to 45.85 per 100,000 population (Kementerian Kesehatan RI, 2014).

If the dengue cases are viewed by age group, then there was a shift in the case since the year 1993-2009. In 1993-1998 DHF cases were dominant in the age group of less than 15 years, whereas in 1999-2009 it shifted to age group of 15 years or older. Based on these data, it can be stated that the transmission of dengue disease occurs not only at home but also in schools and workplaces, and even many who are infected are in their productive age (Pusat Data dan Informasi, 2010; Pusat Data dan Surveilans Epidemiologi, 2010). The distribution of cases can also be seen by sex or gender. Based on data released by the Data Center and Surveillance Epidemiology (2010) it showed that in 2008, based on gender, male patients were as many as 10,463 people (53.78%) and women 8,991 people (46.23%) . Although the number of patients is found more in men than women, but the percentage is almost the same, therefore it can be stated that the distribution of dengue disease is not related to gender.

Mortality Rate (Case Fatality Rate) of DHF

Case Fatality Rate (CFR) in 2009

increased compared to the previous year. Based on data obtained from the Data Center and Information (2010), in 2009 there were 158,912 cases with the number of death of 1,420 people. It shows that the number of DHF incidence rate is 68.22 per 100,000 population and the CFR of 0.89%. While in 2008 the incidence rate of 59.02 per 100,000 population and the CFR of 0.86%. Although the CFR in 2009 is higher than in 2008, but there is a downward trend in the CFR from 2005 to 2008. However, in 2013 it decreased to 0.77% with the number of cases of death as many as 871 people (Kementerian Kesehatan RI, 2014).

The province with the highest CRF in 2009 was Bangka Belitung, which reached 4.58%, followed by Bengkulu of 3.08%, and Gorontalo of 2.2%. While the lowest CFR was found in the province of West Sulawesi, but no death case, and DKI Jakarta Province of 0.11%. Whereas in 2013, the highest number of deaths occurred in the province of Jambi by 2.82% (Kementerian Kesehatan RI, 2014). Nationally, the peak occurrence of cases in 2009 was in January to March, then declined after July and reached its lowest point in September. However, it rose slightly in November and December (Pusat Data dan Informasi, 2010).

In 2013 there were three provinces with fatality rate of more than 2%, Jambi, Bangka Belitung and East Nusa Tenggara. These three provinces were included in the high CFR category, therefore it is necessary to improve of the quality of health services and human resources, including diagnostic and management support facilities for DHF patients (Kementerian Kesehatan RI, 2014).

Based on the data from Sourced Animals for Disease Control (P2B2) in 2010 the number of cases of DHF in Indonesia are about 150,000 cases where the number of deaths are around 1,317 people. The number of death in 2010 put Indonesia as the highest cases of dengue hemorrhagic fever in ASEAN (Kompas Online, 2011). Most dengue cases in Indonesia are found in big cities such as Jakarta, Surabaya and Bandung.

Control of Dengue Fever

DHF is transmitted by mosquito as the vector, so one way to control this disease can be carried out by mosquito nest eradication (PSN). The implementation of control can be

done through local sociocultural approach method of COMBI (Communication for Behavioral Impact). This method was introduced in 2004, and has been implemented in several cities in 2007, South Jakarta, East Jakarta, Padang and Yogyakarta. In 2008 in 5 cities, South Jakarta, Bandung, Tangerang, Semarang and Surabaya. And in 2009 was held in the city of Bogor, Bekasi, Depok, Batam and Mataram. Eradication of mosquito nest by COMBI method is one of the priority activities in the program of the departemen of health in future (Pusat Data dan Informasi, 2010; Pusat Data dan Surveilans Epidemiologi, 2010). In the effort to control DHF, one of the indicators that was used is the free larvae number. When compared to the free larvae rate in 2005-2009, there was an increase which began in 2005-2008, but reduced in 2009. The free larvae rate in 2008 was around 86% and fluctuated until the year 2012. The free larvae rate in 2012 increased from the year 2011, that is from 76.2% to 79.3%. The success of mosquito nest eradication can be measured through the number of free larvae. The transmission of DHF can be prevented or reduced if free larvae rate is equal or more than 95%. However until 2013 the free larvae rate nationally has not yet reach the target (Pusat Data dan Surveilans Epidemiologi, 2010; Pusat Data dan Informasi, 2013; Kementerian Kesehatan RI, 2014).

Controlling dengue can be done by increasing disease and vector surveillance activities; early diagnosis and early treatment; and to improve the eradication of the vector through the eradication of mosquito breeding and larva survey periodically (Pusat Data dan Informasi, 2010 dan 2013).

DHF Vector Control

One way of preventing DHF is through vector control. Currently research has been carried out to find the right vaccine to prevent DHF, but it has not reached the expected results.

According to Sukowati (2010), environmental management can be used as a control measure to reduce the mosquito vector habitat and population. The success of this depends on environmental management in the community, cross-sectoral, policy holders and non-governmental organizations through the partnership program. The success of environmental management in order to control mosquitoes has been shown by

Purwokerto, a town in Central Java.

Mosquito control can also be done through biological control, such as bacteria, larvae-eating fish and the Cyclops (Copepod). Some biological agents have been used to control the mosquito larvae population. Betta fish have been used in the city of Palembang to control mosquito larvae of *Aedes Aegypti* and proved to be quite effective. But until now, this biological control still has not widely used and sustain by the community. Therefore, it takes the role of local governments and stakeholders to provide support and counseling so that people or community can protect themselves and their families from the transmission of DHF (Sukowati, 2010). Eradication of mosquito breeding area can be done through fumigation with insecticide in the two cycles in which the first cycle all the mosquitoes will die, but not eradicating the larvae. As new mosquito hatched, the second spraying, performed 1 week after, will eradicate surviving mosquitoes. The effectiveness of this cycle can be detected through examination of periodic wiggler (Pusat Data dan Informasi, 2013).

The most popular controlling processes today are chemically control. The use of insecticides in the DHF vector control can be beneficial and can also be detrimental. Obviously, the use of insecticides on target, dose, time and scope will be able to control the DHF vector, as well as to minimize negative impacts on the environment.

Recently, based from the data from the Department of Health of Yogyakarta shows that in the last 10 years the occurrence of DHF is increasing. In relation to this, the faculty of medicine of UGM through its activity "Eliminate Dengue Project" (EDP) is developing a method called *Wolbachia*. *Wolbachia* is a natural bacteria that is injected into the eggs of *Aedes aegypti*. This bacteria will then reduce that ability of this mosquito to transmit dengue virus to human. This bacteria can not live in human. Research showed that this bacteria can reduced the replication of this dengue to about 80% to 90%. (Bisnis Online, 2015)

Conclusion

Dengue hemorrhagic fever is still a major public health problem in Indonesia today. DHF is caused by dengue virus which belongs to the group B virus Arthropod (Arbovirosis) with four serotypes have been

isolated in Indonesia, namely: type 1, 2, 3, and 4.

DHF mostly infects children aged less than 15 years. DHF is transmitted to humans through the bite of an infected *Aedes Aegypti*. Epidemic cycle occurs every 9 to 10 years where the peak increase in DHF cases occurred in January-March.

Number of patients and wide distribution area increases along with the increasing mobility and population density. The incidence rate (IR) in Indonesia in 2009 was 68.22 per 100,000 population and mortality rate (CFR) of 0.89%. Whereas in 2013 where IR = 45.85 per 100,000 population and CRF = 0.77%. Bali province occupies the highest IR of 168.48 per 100,000 population and Jambi Province with the highest CFR 2.82%.

Efforts to eradicate DHF include: improving disease surveillance activities and vectors, early diagnosis and treatment, as well as increasing efforts to combat dengue vector.

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