Distribution of Dengue Hemorrhagic Fever (DHF) in Regards to Age and Sex in Sleman, Yogyakarta, Indonesia

Tri Wulandari Kesetyaningsih
Department of Parasitology, Faculty of Medicine and Health Sciences
Universitas Muhammadiyah Yogyakarta
Yogyakarta, Indonesia
tri_wulandari@umy.ac.id

Abstract. Dengue Hemorrhagic Fever (DHF) is a disease that has a rapid geographical spread and the number of occurrences is increasing. The disease is transmitted through the bite of *Aedes aegypti* or *Aedes albopictus* which sucks human blood during the day, so that the transmission might be related to human activities. In this sense, human activities are related to age and sex. This study aims to analyze descriptively the incidence of dengue fever based on age and sex. Secondary data in the form of data on DHF patients, including their age and sex, in the period of 2008 to 2013 were obtained from the Health Office of Sleman Regency, Yogyakarta, Indonesia. The results show: (1) the aspect of age; the number of occurrences in toddlers and children 5 to 14 years old ranged from 23.39% to 40.20% (35.68%), and the number of occurrences in patients ≥15 years old (adults) ranged from 47.90% to 66.13% (51.39%); (2) the aspect of sex; it appears that the occurrences in male patients numbering as many as 770 (52.13%) were slightly higher than for females, numbering 707 (47.87%). It is concluded that the incidence of DHF in the Sleman Regency in the period of 2008 to 2013 is higher in adults and slightly higher in males.

Keywords: dengue hemorrhagic fever, distribution, age, sex

I. INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is one of the most prominent infectious diseases in the world, because it may result in death. This disease is caused by a virus and is transmitted through mosquito bites, especially by the *Aedes aegypti* mosquito. Dengue fever spreads especially in tropical and subtropical countries where the environment is suitable for the life of the *Aedes* mosquitos. [1]

Brady et al. [2] estimates that 3.9 billion people in 128 country are at risk of getting dengue fever. In 2004 to 2010, Indonesia was the country with the highest number of dengue cases in the world after Brazil and the highest in Southeast Asia since the period of 1968 to 2009. [3] The incidence also tends to increase every year along with an increasingly wide-ranging spread. In 1968, there were 58 cases and these only occurred in Surabaya, while in 2009 there were 158,912 cases and these occurred in almost all districts and cities in 32 of the 33 provinces, except in the Maluku Province. [3] This increase may be due to rapid development and the establishment of many new urban areas.

According to Karyanti et al. (2014), [4] dengue fever in Indonesia shows a change in tendency in the age groups of patients of childhood and adulthood. Changes in the trends of these age groups have been reported since 1998. If it is associated with the fact that the incidence of dengue fever spreads along with the expansion of urban areas, then the possibility of the incidence of DHF can be related to the characteristics of urban areas.

According to Yang *et al.* (2018), [5] one characteristic of urban society is high mobility. A person's mobility can be related to their sex, especially in adulthood, because in adulthood gender can be related to roles. [6] However, this sex role may not be the same in different regions, depending on the social culture of the local community. [7], [8]

This study wants to give a scientific contribution to the trends of DHF based on age and sex, especially in Sleman Regency. Sleman Regency has an area bordering the Capital City of Yogyakarta Province, namely Yogyakarta Municipality, and is one of the endemic areas of DHF. In 2017, it had the second highest number of cases after Bantul Regency in Yogyakarta Province. In the last few years, Sleman Regency has experienced rapid changes, especially in areas bordering Yogyakarta Municipality. These changes are related to the status of DIY Province as a tourist destination and city of education. [9] The development of urban areas from the Municipality of Yogyakarta to the surrounding area, including Sleman Regency, has an impact on the number of dengue cases, which has also increased in the last decade.

II. METHODS

A. Research Design

This research is descriptive, and uses secondary data in the form of data on DHF patients, including their age and sex, in the period of 2008 to 2013 in four sub-districts of eight DHF endemic areas in Sleman Regency. Sub-district selection is determined based on trends in the incidence of dengue fever from 2008 to 2013. Observed sub-districts are Gamping, Depok, Godean and Sleman. Gamping represents an endemic area of DHF with a high number of cases every year. Depok Sub-district represents endemic areas with a high number of cases which are declining. Godean Sub-district represents an endemic area with a moderate number of cases which is increasing. Sleman Sub-district represents an endemic area with a moderate number of cases which are relatively stable.

B. Data Collection

The data was obtained from the Health Office of Sleman Regency, Yogyakarta, Indonesia. Patient data is grouped by age, that is 0-4 years; 5-14 years; and ≥15 years.
as well as by sex. The analysis is descriptive of the changes of the number of dengue cases from time to time during the period of 2013 to 2018, based on the variables of age and gender.

III. RESULT

The results of preliminary observations from secondary data at Sleman Regency Health Office show that the number of DHF cases from 2008 to 2013 are 2,292 in the entire Sleman Regency.

A. Occurrence of Dengue Fever

The distribution of DHF cases from 2008 to 2013 is shown in Figure 1. It shows that several regions can be grouped based on the number of dengue cases each year. The groups are: (1) areas with a high number of occurrences, namely Gamping, Depok and Kalasan; (2) regions with a moderate number of occurrences, namely Mlati, Ngaglik, Godean, Ngemplak, Sleman; and (3) areas with a low number of occurrences, namely Prambanan, Berbah, Seyegan, Minggir, Moyudan, Turi, Tempel, Pakem, and Cangkringan.

Of the three groups of endemic regions, there are five types of endemic areas based on the trend of occurrences, namely: (1) Highly endemic with relatively high numbers of occurrence (> 50 / 100,000); (2) Highly endemic with occurrences likely to decrease; (3) Moderately endemic (20-50 / 100,000) with occurrences likely to increase; (4) Moderately stable endemic; and (5) Low or sporadically endemic (<20 / 100,000). Figure 2 illustrates the fluctuations in the incidence of dengue fever in the period of 2008 to 2013.

Figure 1. Number of DHF occurrences per sub-district in Sleman Regency in 2008 to 2013

B. Distribution Based on Age

The distribution of dengue occurrences based on age in five sub-districts in the study area in Sleman Regency from 2008 to 2013 is presented in Table 1. It shows that there were no significant changes regarding the percentage of occurrences in each age group. The results show occurrences in the age group of children under five and children 5 to 14 years range from 23.39% to 40.20% (35.68%), and the occurrences in the adult age group ≥ 15 years range from 47.90% to 66.13% (51.39%).

Table 1. Distribution of DHF occurrences based on age groups in Sleman Regency between 2008 and 2013

| Age          | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|--------------|------|------|------|------|------|------|
|              | n    | n    | n    | n    | n    | n    |
| 0 - 4        |      |      |      |      |      |      |
|              | n (%)| n (%)| n (%)| n (%)| n (%)| n (%)|
| 5 - 14       | 47   | (14.07) | (10.63) | (12.50) | (12.26) | (10.48) | (15.17) |
| ≥ 15         | (38.02) | (40.20) | (33.20) | (33.96) | (23.39) | (23.39) | (36.24) |
| 0 - 4        | (49.4) | (51.2) | (56.3) | (46.2) | (45.9) | (56.5) |
| 5 - 14       | (50.6) | (48.8) | (43.7) | (53.8) | (54.0) | (43.5) |

C. Distribution by Sex

The accumulation of dengue occurrences in Gamping, Godean, Depok, Sleman and Pakem Sub-districts from 2008 to 2013 in terms of sex is shown in Table 2. It seems that there is a slight difference between the 770 male patients (52.13%) and 707 women (47.87%), with more occurrences in the male group (Table 2). For occurrences in each individual year, there are no significant differences between male and female patients.

Table 2. The distribution of dengue occurrences based on sex in Sleman Regency between 2008 and 2013

| Sex          | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 |
|--------------|------|------|------|------|------|------|
|              | n    | n    | n    | n    | n    | n    |
|              | (%)  | (%)  | (%)  | (%)  | (%)  | (%)  |
| Male         | 165  | 154  | 144  | 49   | 57   | 201  |
| Female       | (49.4) | (51.2) | (56.3) | (46.2) | (45.9) | (56.5) |
|              | (50.6) | (48.8) | (43.7) | (53.8) | (54.0) | (43.5) |

IV. DISCUSSION

Dengue Fever in Sleman Regency. The Special Province of Yogyakarta (DIY) ranks seventh for dengue cases nationally in 2014, with an incidence rate (IR) of 54.39 per 100,000 population, which is higher than the national IR of 39.8 per 100,000. [10] In 2013, Sleman Regency was an endemic area with the third highest number of cases in DIY Province after Yogyakarta Municipality and Bantul Regency, with an IR of 95.99 per 100,000 residents. Out of the 17 sub-districts in Sleman Regency, there are eight endemic DHF sub-districts which have high numbers of cases each year. These eight DHF endemic sub-districts include Depok, Gamping, Godean, Mlati, Kalasan, Sleman, Ngaglik and Ngemplak. Of the eight sub-districts of the endemic areas, four sub-districts were taken as samples for this study, namely Depok, Gamping, Godean and Sleman.
A. Distribution of Dengue Incidence Based on Age of Patient

From a sample of 1,477 dengue patients in four research locations or sub-districts recorded at the Sleman Regency Health Office between 2008 and 2013, it was found that the incidence distribution is higher in adult ≥15 years with a score of 51.39%. The shift in occurrences in the age group of patients from toddlers and children to the adult age group also occurred nationally in Indonesia since 1998. [3],[4] The increase in the percentage of DHF patients in adulthood is possibly related to the pathogenesis of viral infections and to one's mobility.

The change in the group of patients from children to the adult age group is likely due to a typical phenomenon in secondary infection. If the infectious virus serotype differs from the primary infection, it will result in more severe clinical symptoms. [11] It is known that there are 4 types of dengue virus serotypes, namely DEN-1, DEN-2, DEN-3 and DEN-4. This theory of the emergence of more severe clinical symptoms in secondary infections is known as the ‘immune enhancement hypothesis’.

According to Guzman et al. (2013),[12] secondary infections with different types of serotypes, besides creating antibodies, will also increase viral proliferation in lymphocytes so that the number of viruses will increase. Even viremia in secondary infections can reach more than five times that of the primary infection. [13] This increasing number of viruses will trigger the occurrence of antigen-antibody complexes, which will continue to be active in the complement system. Activation of the complement system will result in increased permeability of blood vessels, which will increase plasma permeation from the blood vessels and will clinically aggravate the manifestations. Fatalities may occur due to hypovolemic shock. [12]

In relation to the age of the patient, it is estimated that infection in the adult age group (≥15 years) is a secondary infection because they have already been infected with the primary infection during childhood. Clinical symptoms of the dengue virus primary infection are usually mild [14] and do not always develop into DHF, but this depends on the virulence of the type of DEN virus that infects the patient and on the condition of the patient's immunity. [15] Of the 4 types of dengue virus serotypes, DEN-2 serotypes [16],[17] and DEN-3 serotypes [17] have quite high virulence compared to DEN-1 and DEN-4 serotypes. However, viral virulence may be different for different regions. For example, in Indonesia, serial studies of the types of viruses associated with clinical severity indicate that DEN-3 viruses are related to the severity of dengue infection, in this case the mortality rate,[13],[18] whereas in Cuba, clinical severity and fatal cases in the 1981 dengue epidemic was connected to DEN-2 serotypes. [19]

In terms of the pattern of transmission, dengue infection in children and toddlers is estimated to occur at home because they are more active in the house or around the house during the day, including sleeping during the day, playing games or watching television.[20] Dengue fever occurs through active blood-sucking of Aedes mosquitoes during the day, especially in the morning (08.00-10.00 a.m) and in the afternoon (14.00-16.00 p.m).[21] This causes the incidence of DHF in children to be more limited in the spread and number of infections.

The highest incidence of DHF occurs in the adult age group (≥ 15 years), when [22] transmission occurs while actively working or studying in school. Transmission outside the house is likely to cause the spread of dengue fever more rapidly, because the mobility of the productive age group is higher. Some studies that link the incidence of DHF with human mobility include that of, [23] which state that someone who has high mobility will increase the possibility of infection by 9.29 times compared to people with low mobility. De Silva (2016) [24] proves that with spatiotemporal analysis, population mobility from and to endemic areas can expand the spread of dengue fever to the surrounding area.

Another possibility that causes a shift in the age group of DHF patients from childhood to adulthood is the presence of a genetic mutation of the DEN virus.[25] Changes in the genetic properties of viruses can affect viral virulence.[26] However, research on the genetic mutation of the DEN virus in relation to clinical symptoms is still very limited. The limited number of perfect animal models as a means of in-vivo research to study the pathogenesis of viral infections causes obstacles in understanding the role of the DEN virus in the incidence of DHF. The ideal experimental animals used for dengue immunology research, although imperfect, are primates. The use of experimental animals of this type is very expensive and access is very limited. Research on dengue immunology is currently aimed more at studying the antibody-dependence enhancement (ADE) phenomenon and vaccine development. [27]

From the discussion above, it can be concluded that the distribution of the incidence of DHF in the adult age group is higher, possibly because: (1) the infection is a secondary infection; (2) if the infection occurs in adults, the spread will be easier and wider because the mobility of adults is higher than that of children.

B. Distribution of Dengue Incidence by Sex

The results of this study indicate that there is a tendency for dengue incidence in men to be higher (52.13%) than in women (47.87%). Data at the national level in 2008 also showed a tendency for incidence in male patients to be higher (53.78%) than for women (46.23%). [3] Studies in several countries in Southeast Asia with different cultures and socio-economic levels, namely Laos, the Philippines, Singapore, Malaysia and Sri Lanka, also showed similar results. Occurrences in male DHF adult patients (≥15 years) were higher than in women, which ranged between 54.4% and 61.8%. [28] Studies in Singapore prove that the incidence of dengue fever in adult men is related to weekend breaks, while in women it is not. It is estimated that dengue infection in Singapore occurs through activities outside the house related to vacations, not activities in the house or at work. [29]

Research on the distribution of dengue incidence in regards to sex in children is still not consistent. Some information shows that in the age group of children (1-14 years), girls tend to suffer more from DHF than boys. According to Permatasari et al., [15] girls aged one to 14 years have a possibility of dengue infection that is 3.33 times greater.
The higher number of DHF patients being girls may be related to two things, namely hormonal factors and nutritional status. According to Permatasari et al., [15] girls have low estrogen levels so that leptin in the body is also low. Leptin is a hormone that functions to regulate body weight. Low leptin in the body causes the weight of girls to be low and thus they are more susceptible to disease. [31] also proves that the weight and nutritional status of female toddlers is lower than that of males. Low nutritional status causes low immune response both on a humoral and on a cellular level, so that it is likely to be more susceptible to infection, including dengue virus infection. [32] However, the relationship between nutritional status and DHF infection was denied by Hung et al.,[33] Marón et al.,[34] and Trang et al. [35] According to Hung et al.,[33] there is no relationship between gender and nutritional status, and the intensity of dengue primary infection. Data in Thailand also shows a difference, namely that the number of DHF patients being boys is higher than girls. [36] Thus, studies are still needed on the vulnerability of children to dengue disease, especially those related to their sex.

From the discussion above, it can be concluded that from the aspect of sex, in adults (≥15 years), the incidence in men tends to be higher than that of women. This is likely related to higher male mobility when compared to women. Whereas in children (<15 years old), sex and the incidence of dengue fever are still being debated.

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