ABSTRACT

**Background**: Dengue is an endemic vector borne disease in tropical and subtropical area, including Indonesia. Even several areas experienced dengue outbreak, with high number of cases. The study was conducted to describe clinical and laboratory profile in hospitalized patient with dengue infections during 2016 outbreak in Banyumas Regency, Indonesia.

**Material and Method**: A descriptive study was carried out in clinical and laboratory profile from Banyumas Regency Health Office data. 463 patient were included in this study due to the complete information.

**Results**: Fever, limp and nausea were the major presenting symptoms of the patients. 59.6% of patients were without thrombocytopenia. DHF was the major cases among the patients with 84.55 % and most of them categorized as secondary infection (48.1%).

**Conclusion**: Most of the patients during outbreak experienced a severe clinical manifestations, probably due to the secondary infection based on serology test.

**Key words**: dengue, outbreak, clinical profile, laboratory
1.0 Introduction

Dengue is a vector-borne disease that continues to be a health problem particularly in tropics regions. The spread of disease distribution continues to expand to sub tropical countries due to the expansion of *Aedes albopictus* mosquitoes [1]. The major vector of Dengue Virus (DENV) infection is still *Aedes aegypti* mosquitoes, which also transmit other diseases such as Chikungunya, Zika, Mayaro and yellow fever viruses [2-4]. The disease is caused by dengue virus consisting of 5 serotypes, DENV-1, 2, 3, 4 and 5 [5,6]. Its clinical manifestations range from asymptomatic to serious symptoms such as Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)[7].

Dengue is highly endemic in Indonesia and still become one of the main health problems in this country since it was detected in the cities of Jakarta and Surabaya in 1968 [8]. Although the case fatality rate (CFR) of DENV infection is declining but reports illustrated that among countries in Southeast Asia, Indonesia has the highest economic burden of dengue [9,10]. About 45% of the total dengue disease burden in the Southeast region is happened in Indonesia [11]. The shifting age pattern from young children to older age groups observed from 1999 onwards [12]. Four of the DENV (DENV-1,2,3,4) serotypes are circulating in Indonesia, with the tendency of DENV-3 related to more severe clinical manifestations [12,13]. The spread of this disease is often associated with population mobility, urbanization, global warming, rainfall, slum areas, socioeconomic etc [14]. The epidemiology of dengue is dynamic following the change in the human host, the dengue virus and Aedes mosquitoes bionomics [15,16]. Changing dengue epidemiological trends have affected in a shift in the disease burden from children to the adult population, sex differences and expansion to rural areas [17]. The change also may occurred in clinical symptoms of dengue fever. Several studies believed that the severity of disease is associated with the type of serotype dengue virus. Dengue outbreak could be showing symptoms and severity that are different from the usual events. Indeed, It is interesting to analyse the clinical manifestation of DENV infection during dengue outbreak. Several studies show a change in symptoms during dengue outbreak [18,19]

The clinical manifestation of dengue in outbreak condition could be different in disease severity [20]. It is interesting to find out the clinical profile of dengue patients during outbreak. The aim of this study is to analyse clinical symptoms and laboratory manifestations of hospitalized patients with DENV infection during outbreak in Banyumas Regency, central Java Indonesia. We believe that this information would be beneficial to dengue treatment and management.

2.0. MATERIAL AND METHODS

2.1 Ethical statement

This study was carried out with ethical approval from Ministry of National Education, Faculty of Medicine University of Jenderal Soedirman (Ref : 145/KEPK/VII/2016).

Wijayanti et al, 2018 184
2.2 Study area

The study area in Banyumas Regency, located in the southwest of Central Java Province, Indonesia. Coordinates for this location are as follows: 108° 39' 17" - 109° 27' 15" East longitude, and 7° 15' 05" - 7° 37' 10" South latitude. The total area is 132,760 km², with a population of 1.85 Million inhabitants at a male to female ratio of 50:50. Banyumas Regency consists of 27 sub districts, and has 39 community health centres and a total of 331 villages. Purwokerto, capital town of Banyumas regency showed high proportion of high socio-economic with 4 hospitals.

Figure 1: Location of Study. Lower right, map of Java with Banyumas regency (in yellow) and also whole map of Indonesia

2.3 Case definition

Dengue cases which included in this study were all dengue cases reported and ruled infected during dengue outbreak 14 February-31 March 2016 from Banyumas Regency Health Office. All cases with proper information on data included in this study.

2.4 Data Collection

This is a retrospective study to analyze the distribution of relative frequencies of clinical and laboratory variables. Patients data were collected from Banyumas Health Office. The official number of dengue cases during outbreak were 536, however only 463 patient were included in this study due to the complete information. The clinical profile such as fever, abdominal pain, bleeding etc were collected. Serological test was carried out using a rapid dengue IgG/IgM (PT Fokus Diagnostik kit) test based on immunochromatography assay.
3.0. RESULTS

The study area, Banyumas Regency, experienced a regular dengue cases every year, with several outbreak happened in 2008, 2010, 2013 and 2016. In 2016, this area undergo the most devastating outbreak with 990 cases during a year. The detail of dengue cases fluctuation from 2002 to 2016 can be seen in Figure 2.

![Figure 2: Fluctuation of dengue cases in Banyumas Regency from 2002-2016.](image)

This area experienced dengue outbreak from 14 Februari-31 March 2016. 536 dengue cases were recorded during the outbreak, with 7 patients were died. Total cases in Banyumas Regency in 2016 were 990 cases, increased significantly compared to 2015 with a total of 264 cases. The spread of dengue cases within this region during outbreak can be seen in Figure 3.

![Figure 3: Distribution of dengue cases in Banyumas Regency during outbreak. The red point indicated dengue cases.](image)
52.5% of patients were male, and most of the patients in productive age (15-44 years old). Detail of characteristic pf patients can be seen in Table 1.

**Table 1:** Socio-demographic characteristics of patients  \( n = 463 \)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>243</td>
<td>52.5</td>
</tr>
<tr>
<td>Female</td>
<td>220</td>
<td>47.5</td>
</tr>
<tr>
<td>Age groups (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>39</td>
<td>8.4</td>
</tr>
<tr>
<td>5-14</td>
<td>125</td>
<td>26.9</td>
</tr>
<tr>
<td>15-44</td>
<td>225</td>
<td>48.6</td>
</tr>
<tr>
<td>45-60</td>
<td>61</td>
<td>13.1</td>
</tr>
<tr>
<td>&gt;60</td>
<td>13</td>
<td>2.8</td>
</tr>
</tbody>
</table>

A total 463 patient were included in this study due to the complete information of their clinical profile. Fever, limp and nausea were the major presenting symptoms of the patients. The other common symptoms were epigastric pain (55.3%) and Myalgia (51.6%). (Figure 4).

**Figure 4:** Clinical symptoms of hospitalized patient with dengue infections during 2016 outbreak.

Clinical profile on hospitalized patients including thrombocytopenia (platelet count <75,000/cmm), and 59.6% of patients were without thrombocytopenia (Table 2)
Table 2: Platelet counts on patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without thrombocytopenia</td>
<td>59.6</td>
</tr>
<tr>
<td>With thrombocytopenia &lt;20,000</td>
<td>4.8</td>
</tr>
<tr>
<td>With thrombocytopenia 20,000-&lt;50,000</td>
<td>19</td>
</tr>
<tr>
<td>With thrombocytopenia 50,000-75,000</td>
<td>16.6</td>
</tr>
</tbody>
</table>

Based on clinical profile and medical record from hospitals, we classified the dengue cases into three categories. DHF was the major cases among the patients with 84.55 %, then DF (13.25%) and the lowest proportion was DSS (2.20%) (Table 3)

Table 3: Diagnosis on patients during dengue outbreak

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue Fever</td>
<td>13.25%</td>
</tr>
<tr>
<td>Dengue Haemmorhagic fever</td>
<td>84.55%</td>
</tr>
<tr>
<td>Dengue Shock Syndrome</td>
<td>2.20%</td>
</tr>
</tbody>
</table>

Serological test were performed to all samples, and most of them categorized as secondary infection (48.1%). (Table 4).

Table 4: Serology results

<table>
<thead>
<tr>
<th>Serology results</th>
<th>Total</th>
<th>Percentage</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG positive and Ig M negative</td>
<td>68</td>
<td>14.7</td>
<td>Secondary infection</td>
</tr>
<tr>
<td>IgG negative and IgM positive</td>
<td>88</td>
<td>19</td>
<td>Primary infection</td>
</tr>
<tr>
<td>IgG positive and IgM positive</td>
<td>155</td>
<td>33.4</td>
<td>Secondary infection</td>
</tr>
<tr>
<td>IgG negative and IgM negative</td>
<td>152</td>
<td>32.8</td>
<td>No recent infection</td>
</tr>
<tr>
<td>Total samples</td>
<td>463</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.0. DISCUSSION

463 clinical profile from hospitalized dengue patients during outbreak in 2016 in Banyumas, Central Java, Indonesia were collected in this study. 52.5% of patients were male. The result of this study is in accordance with other studies of male-female differences in the number of reported dengue fever cases in six Asian countries (The Lao People’s Democratic Republic, the Philippines, Singapore, Sri Lanka, Malaysia, Cambodia) which found a consistent pattern of male predominance among persons 15 years or older [21]. Based on the age grouping analysis (Table), adult patients in the 14-44 age range are the majority of dengue patients during outbreak (48.6%).

These results are in agreement with the general age shift pattern of dengue patients which is observed in Indonesia and other DENV endemic countries in South-East Asia with adults becoming the predominant age group [22-29]. Historically DENV infection is predominantly detected in children, however since the beginning of 1980s, several studies observed more dengue cases in older age groups [30-32]. In Indonesia, an increase in the number of adult dengue patients was observed for the first time in surveillance data from 1975 to 1984 [8]. Higher activity and mobility in adults than children or older age groups, could possibly explain this pattern change [33,34]. Human movement is also believed to play an important role in the spread of DENV [35,36], since adults tend to be more active in work, travel, and social activities, thus their risk is higher than for children. Less reported dengue cases in children who spent most their time at home may indicating that it could be a change of location where DENV is acquired, for instance in work places or public areas [32]. In addition, demographic changes such as birth and death rates may contribute to the shifting age pattern of dengue cases [22].

The major presenting symptoms of the patients were fever, limp and nausea. These symptoms quite misleading since they could indicating other diseases such as Leptospirosis, Chikungunya etc [37]. Indeed, hemalogical and serological test are important to help the clinician for dengue diagnosis. Surprisingly, 59.6% of patients were without thrombocytopenia. But several study also stated that platelet counts do not correlate well with clinical bleeding [38]. 84.55% DHF was the major cases among the patients during outbreak, and 2.20% was DSS. This indicating that most of patients during outbreak experienced a severe clinical manifestation of dengue infection. Several study proposed that there was correlation between secondary infections by different DENV serotypes and development of more severe clinical manifestations was documented in several publications [13,39-43]. Antibody-dependent enhancement (ADE) has been hypothesized as an explanation of the correlation between secondary infection and severe dengue disease [43-45].

Unfortunately, confirmation of the secondary infection by certain serotypes leading to more severe DENV infection cannot be conducted since no previous DENV serotype data are available but this study sets a baseline. There is a matching finding between the age group shift of reported DENV cases from children to adult patients and the fact of higher secondary infection, because secondary infection usually happened in more middle-age people because it acquires time between first infection and next infection. This facts also supported by serological results, which 48.1% of dengue patients were secondary infection. This study highlights the importance of dengue symptoms, outcome to dengue disease management. The change in clinical profile could happened due to the dynamic inter correlation of dengue virus, host, and its vector.
Acknowledgement

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Declaration

Authors declare that we have no conflict of interest

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References


